

## Original Article

## An Approach to Soft Tissue Mass In The Gall Bladder

Hasina Alam<sup>1\*</sup>, Tanvir Ahmed<sup>1</sup>, Hashim Rabbi<sup>2</sup>, Md. Mamunur Rashid<sup>2</sup>, Mohammad Ali<sup>3</sup>**Abstract:**

**Background:** Soft tissue mass in gall bladder (GB) is a radiologic finding commonly encountered in surgical practice. It needs proper evaluation as there is a fair chance that it can be a malignant lesion. Gall bladder cancer (GBC) is considered an incurable disease with an extremely poor prognosis. However, there is good chance of survival if it can be diagnosed in earlier stages (stage Ib, II, selective III).

**Methods:** All consecutive cases of soft tissue mass lesions of GB found in ultrasonogram of abdomen and admitted in Hepato-Biliary-Pancreatic Surgery (HBPS) unit of BIRDEM hospital, from January 2009- September 2016, were included in this study. Detailed history and thorough clinical examination was done in all cases. Pre-operative evaluations were done by ultrasound, Tumor marker (CA19.9) & CT scan. CT scan was a crucial investigation for all the patients, as depending on the findings, decision was made whether a patient is eligible for a possible curative surgery or not. On-table frozen section biopsy or imprint cytology was done for tissue diagnosis. Radical resection was done for the histology/ cytology proved malignancy of gallbladder (stage Ib, II, selective III). Post-cholecystectomy patients also underwent full thickness excision of the umbilical port. In benign cases only cholecystectomy was done. Advanced GBC cases underwent FNAC for tissue diagnosis followed by palliative chemotherapy. Some needed endoscopic or surgical palliation in the form of percutaneous external biliary drainage, endobiliary prosthesis, triple bypass, hepaticojejunostomy, left duct anastomosis, gastrojejunostomy, ileotransverse anastomosis, external biliary drainage etc before chemotherapy. All the GBC patients were regularly followed according to a schedule.

**Results:** We are reporting 334 cases of soft tissue mass lesions of GB. Female 191 (57.2%) and male 143 (42.81%), M : F = 1 : 1.3, between the ages of 32 and 88 years. Of these, 81 patients (24.2%) turned out to be benign; another 81 patients (24.2%) were in early stage (Ib, II selective III). The rest of 172 patients (51.5%) showed signs of advanced malignancy in USG & CT scan. Post-operative complications occurred in 27 cases (8.1%). During follow-up, 34 patients (42%) have crossed their 5 years of disease free survival after curative surgery. Rest of the patients (44 cases), after curative surgery, are still under follow-up. The 172 patients in Stage III & IV disease who underwent some sort of palliative procedure, had a mean survival of 7.2 months.

**Conclusion:** Soft tissue mass in gall bladder picked up by imaging has a very high chance to be malignant. Among these malignant patients, a good number has a chance of curative resection if evaluated and managed properly.

**Key words:** Soft tissue mass in gall bladder; gall bladder cancer; radical resection.

**Introduction**

Soft tissue mass in gall bladder (GB) is a sonographic finding commonly encountered in medical practice. It needs proper valuation as there is a fair chance that it can be a malignant lesion. Sonologic findings such as thick walled GB, single large gall bladder polyp, porcelain gall bladder, and polypoid mass in the lumen of GB are more common in early

gallbladder cancer (GBC) compared with benign gallbladder disease. GBC is considered an incurable disease with an extremely poor prognosis. However, there is good chance of survival if it can be diagnosed in earlier stages (stage Ib, II, selective III). Early GBC can be offered a curative radical cholecystectomy.

**Methods**

All consecutive cases of soft tissue mass lesions of GB found in ultrasonogram of abdomen and admitted in Hepato-Biliary-Pancreatic Surgery (HBPS) unit of BIRDEM hospital, from January 2009- September 2016, were included in this study. Detailed history of all the patients were taken, particularly about dyspepsia, fever, right hypochondriac pain, nausea/vomiting, weight loss and jaundice. Thorough clinical examination was done with particular attention to anaemia, jaundice and any palpable mass in right hypochondriac region. All patients' complete blood count, liver function test, CA 19.9 and CEA were done. In addition to the ultrasonogram of abdomen, a CT scan of whole abdomen was done for staging purpose. Depending on CT findings, decision was made whether a patient is eligible for a possible curative surgery or not. Pre-operative FNAC was not advised in patients with no sign of advanced malignancy in CT scan.

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Rather per-operative frozen section biopsy or Imprint Cytology was arranged for them. Pre-operative FNAC was done only in patients with evidence of advanced gallbladder cancer in CT scan, where there was no scope for curative surgery. Radical resection was done for the histology/ cytology proved malignancy of gallbladder (stage Ib, II, selective III). Radical resection included loco-regional enblock resection of malignant gall bladder with regional hepatic segments (IVB & V), without violating the cystic plate, skeletonization of hepatoduodenal ligament, clearance of fascia, fat of hepatic hilum with/without excision of bile duct followed by Roux-en-Y Hepatico/ Cholangio-jejunosotomy, where necessary. Post-cholecystectomy patients also underwent full thickness excision of the umbilical port. Patients with benign GB disease underwent cholecystectomy only. Histopathology of the resected specimen was done. The advanced GBC cases were referred to Oncologist for chemotherapy. Some of the advanced GBC cases required endoscopic or surgical palliation in the form of percutaneous external biliary drainage, endobiliary prosthesis, triple bypass, hepatico-jejunosotomy, left duct anastomosis, gastrojejunostomy, ileotransverse anastomosis, external biliary drainage etc before chemotherapy. All the GBC patients were regularly followed according to a schedule - 3 monthly in 1st year, 6 monthly in 2nd year and then yearly upto 5years. In each follow-up visit the followings were done -detail patient's history, thorough physical examination and appropriate investigations (Liver function tests, CA 19.9, ultrasonogram of whole abdomen and other investigations as required).

**Results**

We are reporting 334 cases of soft tissue mass lesions of GB, found in ultrasonogram of abdomen, over a period of 7 years and 9months. Out of 334 patients, 191(57.2%) were female and 143 (42.8%) were male. Male to female ratio was 1: 1.3. Among them youngest patient was 32 years of age and eldest was of 88 years. All of them had an ultrasonogram report of soft tissue mass in GB. Sonographic description of polypoid mass in the lumen of GB, unusually thick walled GB, large gall bladder polyp, dystrophic calcification in gall bladder wall, porcelain gall bladder, were common in early malignancy compared to benign gallbladder disease. Advanced malignancy cases presented sonographically as inhomogeneous mass replacing all or part of the gallbladder with variable extension into the liver & surrounding structures, intra-abdominal lymph node enlargement, metastatic deposits in liver, pancreas etc. CT scan showed various findings (Table I) starting from soft tissue mass inside the gall bladder to mass replacing the gall bladder with variable invasion into the surrounding structures and/or abdominal lymphadenopathy. 162 patients were selected for curative surgery. Three patients presented at the time of admission, with preoperative FNAC report of GBC, advised by the primary treating physician. 28 patients presented after laparoscopic cholecystectomy, with a histopathology report of GBC. For the rest,131 patients, on table per-operative frozen section biopsy was arranged for tissue diagnosis. Of the 162

patients, 81 patients (24.2%) turned out to be benign. The rest 81 patients (24.2%) were in early stage GBC (Ib, II selective III). 172 patients (51.5%) showed signs of advanced malignancy in USG and/or CT scan. Surgical procedures done on the patients are shown in Table II. Histology report of the GBC patients is shown in Table III. Stage Ib patients were not sent for chemotherapy. All the other cases were sent for chemotherapy. Post-operative complications occurred in 27 cases (8.1%) as shown Table IV. During follow-up, 3 patients (2 were in post cholecystectomy status) developed distant metastases within 2 years of curative surgery and 34 patients (42%) have crossed their 5 years of disease free survival after curative surgery. Rest of the patients (44 cases), after curative surgery, are still under follow-up. The 172 patients in Stage III & IV diseases, who underwent some sort of palliative procedure, had a mean survival of 7.2 months.

**Table I: CT scan findings of patients:**

CT SCAN findings	No. of pts	% of pts
Intraluminal polypoid mass	102	32.9%
Focal or diffuse thickening of gallbladder wall	98	31.6%
Mass replacing the gallbladder with or without extension into adjacent organs	110	35.4%
Contrast enhancement of the soft tissue	90	29.0%
Regional & distant lymph node involvement	103	30.8%
Obvious metastatic deposits in the liver, pancreas, lungs or ovaries	60	19.3%

**Table II : Name of procedure done**

Procedure done	No. of pts	% of pts
1. Open cholecystectomy	81	24.25 %
2. Enmass resection of seg IVB & V & gallbladder with hepatoduodenal lymphadenectomy	53	15.8 %
3. Bisegmentectomy with hepatoduodenal lymphadenectomy & port excision	28	8.38 %
4. Hepaticojejunostomy & Gastrojejunostomy & entero-enterostomy & Biopsy	70	20.9 %
5. Gastrojejunostomy & Biopsy from Gallbladder/ Lymph node/ hepatic metastases	34	10.2 %
6. Endoscopic Internal biliary drainage	19	5.7 %
7. Percutaneous external biliary drainage	21	6.3 %
8. External biliary drainage & gastrojejunostomy & biopsy	15	4.5 %
9. Laparotomy & biopsy	13	3.9 %
Total no of patients (n)	334	100%

**Table III : Histopathological Report: n=253 (172+81)**

Histopathological Report	No. of pts	% of pts
Stage IV: Metastatic adenocarcinoma in liver or mesenteric nodes or para-aortic lymph nodes.	106	42.0%
Stage III: Tumor cells have traversed the whole thickness of gall bladder wall and involved >2cm of liver tissue &/or involved hepatoduodenal lymph node.	82	32.4 %
Stage II : Tumor cells have infiltrated throughout the muscle coat and reached the serosa.	45	17.8%
Stage Ib: Tumor cells have infiltrated the muscle coat but not reached the serosa.	20	7.9 %

**Table IV: Post-operative complications**

Post-operative complications	No. of Pts	% of Pts
Wound infection	10	3%
Pulmonary infection	9	2.7%
Bile leak	3	0.9%
Port site incisional hernia	5	1.5%

**Table V : Prognosis (n=253)**

Stage of GBC	5 year Survival
Early GBC (Ib, II, selective III)	42%
Advanced GBC (III, IV)	0

## Discussion

Gall bladder diseases are mostly benign but GBC although rare, is the most common and aggressive malignancy of the biliary tract<sup>1</sup>. It is the sixth most common gastrointestinal cancer worldwide<sup>2,3</sup> with extremely poor prognosis. However recently, many authors all over the world have shown improved survival in patients undergoing radical surgery for resectable GBC<sup>4-6</sup>. Unfortunately, diagnosis of GBC is traditionally challenging. Most often it is diagnosed late due to its non-specific nature of symptoms and signs common to other benign diseases such as cholelithiasis or chronic cholecystitis<sup>7</sup>. However in recent years, much more GBC cases are identified. GBC presenting as soft tissue mass in gall bladder in sonograph is a recognized presentation. Moreover, with the widespread adoption of laparoscopic cholecystectomy, incidentally discovered GBC is becoming an increasingly common presentation<sup>8</sup>. The incidence of incidental GBC in gall bladder removed laparoscopically is 0.2-3.3%<sup>9,10</sup>. Approximately 3,700 new cases of GBC are documented annually in USA, 50% of which are diagnosed incidentally either intra-operatively (29%) or after laparoscopic cholecystectomy (21%)<sup>11-13</sup>.

We are reporting 334 cases of soft tissue mass in gall bladder, of which 253 cases were of GBC over a period of 7years and 9 months. Our male to female ratio was 1:1.3. Youngest GBC patient in our series was 32years of age. However a study

from Delaware reported 109 new cases of GBC diagnosed from 1995-2012 (17years), M: F ratio was 2.7: 1 and average age limit at diagnosis was 68 years. This higher incidence is seen in Asian countries, as population here share a high prevalence of gallstone and/or Salmonella typhi infection, both recognized risk factors<sup>14</sup>. In this region, women are affected 2-6 times more often than men<sup>15</sup>. In our series 225 (89%) cases presented as soft tissue mass in gallbladder and 28(11%) presented after laparoscopic cholecystectomy. In other studies, only 16.5% of patients were identified on initial imaging as gall bladder mass<sup>16</sup>. Incidental GBC cases comprised 47-70% of the total cases, which were discovered at the time of laparoscopic cholecystectomy or post-operatively on pathologic assessment<sup>17,18</sup>. This is because the proportion of laparoscopic cholecystectomy has increased from 2.5%-76.6% for elective cases and from 0.7%-67.5% for urgent cases between the years 1988 and 1997<sup>19</sup> in a center in USA alone. Proportion of laparoscopic cholecystectomy has also increased significantly in our centre in last 15years, but not to such extent. Ultrasonogram was used as the initial investigation for gall bladder diseases, in our series as well as other studies<sup>7</sup> and in determining the next suitable modality for further evaluation<sup>20</sup>. Sonographic findings were similar in our series and others<sup>21,22</sup>. We used CT scan (Table I) for staging as of other studies<sup>21</sup>. Some studies also used endoscopic ultrasound<sup>23</sup>, MRI<sup>22</sup>, PET<sup>7</sup> as a staging investigation.

In our series, 32 % cases underwent radical surgery. Other studies reported 4-16% of GBC, led to radical surgery<sup>24-26</sup>. This difference is possibly because ours<sup>7</sup> is a specialized Hepato-Biliary- Pancreatic surgery centre. Our cases underwent loco-regional enblock resection of malignant gall bladder with regional hepatic segments (IVB & V), without violating the cystic plate, skeletonization of hepatoduodenal ligament, clearance of fascia, fat of hepatic hilum with/without excision of bile duct followed by Roux-en-Y Hepatico/ Cholangio- jejunostomy, where necessary. Post-cholecystectomy patients also underwent full thickness excision of the umbilical port. Optimal surgical management of GBC is controversial. Laparoscopic simple cholecystectomy alone is now widely accepted treatment in Tis and T1a GBC<sup>27-29</sup>. Most centers practice, S4b5 segmentectomy of liver, with lymph node dissection around the hepatoduodenal ligament with or without extrahepatic bile duct resection, for T1b, TII and some TIII GBC<sup>24, 30</sup> with a 5year survival of 88.9%<sup>24</sup>. But few centers avoid lymph node dissection in T1b GBC<sup>24</sup>.

You et al reported lymph node metastasis in 0% of T1a tumors, 3.8% of T1b tumors<sup>31</sup>. In one report, the rate of lymph node metastasis in patients with T2 tumors was as high as 46 %<sup>32</sup>, while in another report it was 9%<sup>33</sup>. The validity of bile duct resection has also been the subject of debate. While some surgeons routinely resect the common bile duct, several reports suggest that the procedure does not increase survival and instead recommend preservation of the common bile duct<sup>34</sup> and some recommend resection of extrahepatic bile duct because lymph node dissection of hepatoduodenal

ligament can be incomplete without biliary resection, and lymph node resection may result in ischemia of bile duct<sup>24,35</sup>.

Incidental GBC patients are mainly T1b or T2 disease in our series as in other studies<sup>17</sup>. In our series all (28 cases) underwent radical resection but only 10-25% of incidentally discovered tumors were amenable to radical surgery in other centers<sup>16, 17, 18</sup>. This is probably because patients presented 3-7 days post-cholecystectomy in our series but median time between initial cholecystectomy and second surgery was 85 days in other studies<sup>10</sup>. It is thought that manipulation & traction of unsuspected malignancy, contact of tumour laden instruments to different abdominal organs, port site implantation by instruments or cancerous GB, accidental perforation of cancerous GB, physical effects of closed continuously circulating pneumoperitoneum and damage of cystic plate, gives rise to a high chance of early peritoneal, locoregional & systemic dissemination<sup>36,37,38,39</sup>. Current practice is to perform a second open surgery for excision of segment 4b & 5 and local lymphadenectomy<sup>10</sup> and resection of the common bile duct as necessary, to obtain negative margins<sup>40,41</sup> and excision of extraction port site<sup>42</sup>, which was also done in our study. None of the resection specimen showed residual disease in our series. The proportion of residual disease in resection specimen was 50% -61% in several studies<sup>10, 43</sup>. Port site metastasis was nil in our studies but occurred in 10.3 -30% of patients in other studies<sup>44, 45</sup>. Other reports show port site metastasis to be 53% at extraction and 47% at non-extraction ports<sup>46</sup>. This difference is possibly due to the small number of post-cholecystectomy GBC patients in our series. It has been suggested that port site metastasis is not related to operative technique but related to disease stage as well as biological nature of tumor. Therefore port site excision is not practiced in several centers<sup>40, 41, 46, 47</sup> and not recommended in 2014 consensus statement issued by the American Hepato-Pancreato-Biliary Association<sup>40</sup>. Their median overall 5 year survival in incidental GBC is upto 90%<sup>10</sup>.

In this golden age of laparoscopic surgery, laparoscopic radical resection is still extremely challenging. Therefore, if any suspicion arises preoperatively or peroperatively, current practice is to abandon the laparoscopic procedure<sup>48</sup>. But recently few authorities have shown feasibility of laparoscopic radical resection for early GBC<sup>49, 50, 51</sup>. Adequate lymphadenectomy is invaluable to improve survival after resection<sup>34</sup>. Most authors advocate a nodal retrieval count of six or more<sup>6, 52, 53</sup>. Better magnification in laparoscopy and improved experience in advanced minimal access procedures was shown to achieve 4-14 nodal clearance<sup>54</sup>. Careful and minimal handling of gall bladder during surgery and use of plastic retrieval bag for removal of specimen prevented intra-operative peritoneal dissemination of cancer cells<sup>50, 55</sup>. Overall, 5-year survival after laparoscopic radical resection was found to be 68.75% -100%<sup>50, 54</sup>.

Palliative procedures done in our series are similar to other studies<sup>20</sup>. All patients of stage II and above, were sent for chemotherapy in our study. Gemcitabine/5-fluorouracil-based adjuvant chemotherapy is recommended for stage II and

above GBC<sup>54</sup>. Median survival was significantly longer for radical cholecystectomy with adjuvant therapy (23.3 months)<sup>56</sup>.

Traditionally outcome of GBC was reported as poor, median survival 5-8 months and overall 5year survival rate of 5% to 10%<sup>11, 57</sup>. However, recent studies have shown 5year survival of 24.4%-63% with radical resection strategies<sup>58-60</sup>. Our study shows a 42% five year survival.

### Conclusion:

Soft tissue mass in gall bladder picked up by imaging maybe a malignant or a benign lesion. However, only 24% turn out to be benign and the rest are malignant. Almost 32% of these malignant patients have a chance of curative resection. Pre-operative FNAC is therefore contraindicated in patients with a potentially resectable gallbladder cancer as there is high chance of tumor seeding in biopsy tracts and false negative reports are significantly high in early gallbladder cancer. Frozen section biopsy is the standard method of tissue diagnosis in cases of early GBC. Imprint cytology is an alternative method of tissue sampling, but it is inferior to frozen section biopsy as the depth of invasion by tumor cells can't be assessed. More importantly, laparoscopic cholecystectomy is contraindicated in patients with a potentially resectable GBC. Therefore inadvertent FNAC or cholecystectomy can significantly change their prognosis. Unfortunately, in reality, incidental GBC is discovered in 0.2-3.3% of patients undergoing cholecystectomy for cholelithiasis. If there is no evidence of disseminated disease, after such a non-curative cholecystectomy, a repeat resection is warranted. So soft tissue mass lesions in gall bladder must be evaluated and managed properly.

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