

Incidental gallbladder carcinoma during or after cholecystectomy

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Abstract

Aim: We aimed to present the patients who were diagnosed with benign gallbladder diseases preoperatively and performed laparoscopic or open cholecystectomy however detected gallbladder cancer during or after cholecystectomy.

Material and Methods: We performed 1074 cholecystectomies for benign pathologies between January 2012 and December 2017. Incidentally diagnosed gallbladder cancers were retrospectively analyzed in term of demographic features, clinical presentations, pathological stages, treatment methods and outcomes.

Results: Among the 1074 patients participating in this study, 727 (67.6%) were females and 347 (32.4%) were males with a median age 54.6 years (range: 18-92 years). Nine hundred and thirty-four (87%) of these 1074 patients were diagnosed with chronic cholecystitis and in 140 (13%) patients acute cholecystitis was detected. In 11 (8 females, median age: 67.4) patients, gallbladder cancer (four pT2, five pT3 and two pT4) was detected during or after cholecystectomy. Four (36.4%) patients diagnosed with acute cholecystitis and one (9%) with gallbladder perforation. Patients with acute cholecystitis symptoms (0.6% vs. 3.6%, $p = 0.001$) and aged ($80 \pm$) patients (0.7% vs 5.3%, $p < 0.001$) had a higher risk for incidental gallbladder carcinoma following cholecystectomy.

Conclusion: Suspicion of gallbladder cancer especially in elderly patients and patients with acute cholecystitis symptoms had more risk for incidental gallbladder cancers at cholecystectomy.

Keywords: Incidental; Gallbladder Cancer; Cholecystectomy; Prognosis.

INTRODUCTION

Gallbladder cancer (GBC) is an uncommon malignancy that consist of especially in the elderly populations. It is an aggressive tumor with poor prognosis but, incidental GBC (IGBC) diagnosed at an early stage after or during cholecystectomy has better prognosis. In GBC, five years survival rate is about 5% (1). Various studies have reported that IGBC is found in 0.35–2% of all cholecystectomy specimens and is associated with a better prognosis due to early detection (2,3). But in most cases IGBC may be defined as a malignancy detected only on histopathological examination without prior pre-operative or intra-operative suspicion of malignancy (4).

In this single-center study, we analyzed our experience about the patients with GBC diagnosed incidentally during or after cholecystectomy.

MATERIAL and METHODS

This study includes 11 patients with IGBC who detected

during or after cholecystectomy at Inonu University, Department of General Surgery between January 2012- and December 2017. The patients with a suspicion or diagnosed with GBC preoperatively were excluded from this study. We retrospectively evaluated the demographic data, preoperative radiological imagings, operation indications, initial and re-operation types, re-operation times, histopathological examination results, stages of cancers and surveys of these patients. The cancer invasion depths were classified according to the American Joint Commission on Cancer (AJCC) atlas 7th edition criteria (5).

Statistical Analysis

Descriptive statistic (mean or median) were used when appropriate. Chi square test was preferred for comparison of categorical data. $P < 0.05$ was accepted as significant.

RESULTS

Between January 2012- December 2017, 1074

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cholecystectomy (982 laparoscopic and 92 open) were performed at our clinic due to benign gallbladder diseases. In the present study, IGBC was found in 11 of 1074 patients (1%) undergoing or after cholecystectomy for a benign indication without any suspicion of malignancy prior to surgery. Eight (72.7%) patients were female and 3 (27.3%) were male with a median age 67.4 years (range: 44-86 years). Four (36.4%) patients underwent surgery due to acute cholecystitis, one (9%) patient due to gallbladder perforation urgently and six (54.6%) patients due to cholelithiasis electively. Ultrasound scan of the abdomen was done for all patients and was the only imaging modality. In the urgent surgery group, the mean gallbladder wall thickness was 4.5 mm (range: 4.2-4.9 mm) and the elective group, it was normal. In 5 (45.4%) patients, (acute cholecystitis or gallbladder perforation) an open cholecystectomy was performed. The other 6 (54.6%) patients with cholelithiasis underwent laparoscopic cholecystectomy (LC), but in these 2 of 6 patients conversion to open surgery was done because of anatomical difficulty and IGBC suspicion. In 7 patients, frozen section was done intraoperatively because of IGBC suspicion. After histopathologic examination, in these patients GBC was detected and radical resections (segment IVb and V) with lymph node dissection were done in the same session. In 3 patients, radical resections and lymph node dissection were done the mean time 31st day (range: 29-33 days) after the initial surgery. These 3 patients were in laparoscopic cholecystectomy group,

port site excision were added to radical resection and lymph node dissection. Two patients (one in laparoscopic group: pT2 and one in conversion group: pT3) died in 1st month postoperatively due to cardio-vascular problems unrelated to the cancer. The patients' median survival was 11.3 months (range: 1-37 months). The survival outcomes summarized in Figure 1. Demographic data, clinical and radiological indication, radiological imaging results, initial and re-operation types, histopathological examination results and surveys of patients were summarized at Table 1.

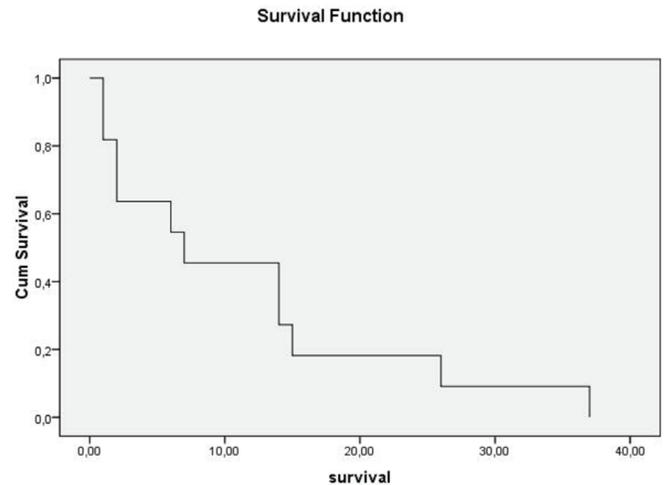


Figure 1. The survival outcomes

Table 1. Demographic data, clinical and radiological indication, radiological imaging results, initial and re-operation types, histopathological examination results and survival of patients

No	Age Gender	Clinical & radiological indication	GB wall thickness (USG) (mm)	Initial operations	Frozen	Re-operations & time (days)	Pathology	Stage	Survival (months)
1	44/ F	Acute cholecystitis	4.2	OC, RR, LND	Yes	No	Adenocancer	PT3N1	15/ D
2	86/ F	GB perforation	4.8	OC, RR, LND	Yes	No	Adenocancer	PT4N1	6/ D
3	80/ F	Cholelithiasis	Normal	LC	No	No	Adenocancer	PT2N1	1/ D
4	58/ F	Cholelithiasis	Normal	LC	No	RR, LND, PSE/ 33	Adenocancer	PT3N1	7/ D
5	71/ F	Cholelithiasis	Normal	LC	No	RR, LND, PSE/ 32	Adenocancer	PT2N0	37/ D
6	64/ F	Cholelithiasis	Normal	CC, RR, LND	Yes	No	Adenocancer	PT4N1	14/ D
7	64/ M	Acute cholecystitis	4.6	OC, RR, LND	Yes	No	Adenocancer	PT3N1	26/ D
8	80/ F	Cholelithiasis	Normal	CC, RR, LND	Yes	No	Adenocancer	PT3N0	1/ D
9	83/ M	Acute cholecystitis	4.9	OC, RR, LND	Yes	No	Adenocancer	PT3N1	2/ D
10	46/ F	Acute cholecystitis	4.2	OC, RR, LND	Yes	No	Adenocancer	PT2N1	2/ D
11	66/ M	Cholelithiasis	Normal	LC	No	RR, LND, PSE/ 29	Adenocancer	PT2N1	14/ D

F: Female, M: Male, GB: Gall bladder, OC: Open cholecystectomy, LC: Laparoscopic cholecystectomy, CC: Conversion cholecystectomy, RR: Radical resection, LND: LN dissection, PSE: Port site excision, D: Died

DISCUSSION

GBC is the most common biliary tract malignancy and the fifth most common gastrointestinal cancer (6). IGBC is rare clinical entity that is detected with a suspicion during or with histopathologic examination after cholecystectomy. In this study IGBC was detected at a rate of 1% and it was compatible with the English language literature. However, according to some reports from Turkey that published in the literature, the IGBC rates were lower than ours. Duzkoylu et al. (7) reported the IGBC rate in 8698 cholecystectomies as 0.17%, Genc et al. (8) in 5164 cases as 0.09% and while Akyurek et al. (9) detected the rate as 0.72% in 548 cases. These high rates are probably due to the fact that our clinic is a reference center.

Sometimes, gallbladder cancer may not be recognized even during surgery. Gulwani et al. (10) reported in their study in which 26.4% IGBC were diagnosed on histopathology. In the other study, Zhang et al. (11) reported that IGBC was detected as rate of 40% on postoperative histopathology after cholecystectomy. Intraoperative frozen section is very important for detection of IGBC. It should be performed when surgeons suspect GBC intraoperatively (12). In the present study in 7 (63.6%) patients, IGBC was detected during surgery and in the other 4 (36.4%) patients, it was diagnosed on histopathological examinations after cholecystectomy. In accordance with the literature, we also think that frozen section must be done if surgeon suspects GBC.

GBC is more common in women and its frequency increases with age. The etiologic factors for GBC are gallbladder stones, chronic inflammation, porcelain gallbladder, polyps, exposure to carcinogenic substances, gallbladder adenomatous and abnormal pancreaticobiliary channel (13). In our study, 72.7% of the patients were female and the median age of all patients were 67.4 years (range: 44-86 years). All patients had gallbladder stone. On the other hand, this study showed that GBC risk increases especially in patients older than eighty years and the patients with acute cholecystitis. Moreover, the risk of GBC increases to 8.3% in elderly patients with acute cholecystitis. The relationship between the risk of GBC and age was shown in Figure 2.

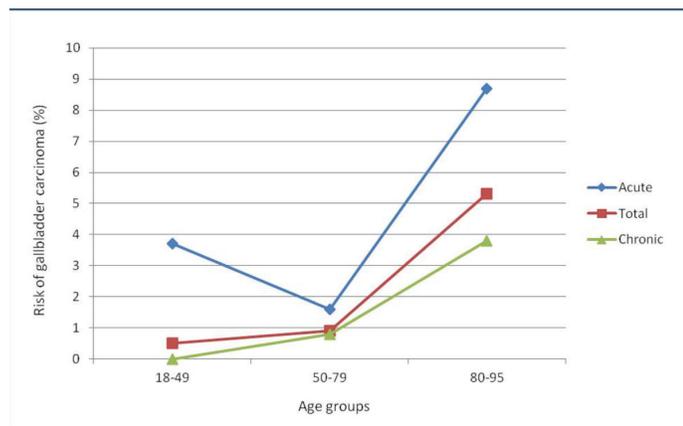


Figure 2. The relationship between the risk of GBC and age

Although the technical advances in USG and computed tomography (CT) have contributed to earlier diagnosis of GBC preoperatively, IGBC is still reported in literature (14). In the present study, USG was performed in all patients preoperatively, however GBC was not defined in any patient. Because of without doubtful findings on USG for GBC, CT was not used in any patient preoperatively. Cholelithiasis was detected in 5 patients and acute cholecystitis in 6 patients (one of them had gallbladder perforation) by USG. Results of our study showed us that prior to cholecystectomy, IGBC should be suspected especially in elderly and with increased gallbladder wall thickness patients with acute cholecystitis. So in these patients, CT can be performed preoperatively for diagnosis of GBC and frozen section can be added to the surgical procedure.

The management of GBC including IGBC depends on the T stage (depth of invasion) (15). For patients with stage Tis and T1a GBC without positive cystic duct margin, a simple cholecystectomy is sufficient. For stages T1b and beyond, radical resection (segment IVb and V resection with lymph node dissection) is the standard procedure of choice. If the primary procedure is LC, then all the port sites should be excised during radical resection (16). In the present study, all of the patients had beyond the pT1 tumors (four pT2, five pT3 and two pT4) so, except one patient, who died in postoperative first month, we performed segment IVb and V resection with lymph node dissection in initial or second operation. The incidence of port site recurrences in IGBC after LC was 0–40% in various reported series (17-19). So we performed port site excision with radical resection and lymph node dissection in 3 patients after LC. In these patients, port site metastasis were not detected with an average of 19.3 months survival.

CONCLUSION

In conclusion; GBC is a rare but an aggressive tumor. The prognosis and management of GBC is directly related to the depth of tumor. For patients with stage Tis and T1a GBC without positive cystic duct margin, a simple cholecystectomy is sufficient. For stages T1b and beyond, re-exploration and radical re-resection is the standard procedure of choice. If the primary procedure is LC, then all the port sites should be excised during re-resection. IGBC can be detected during or after cholecystectomy. Despite advances in radiological imaging, it may be misconceptions in the diagnosis. To doubt of GBC intraoperatively is very important for incidentally diagnosis. The elderly patients and the patients with acute cholecystitis have greater risk for GBC. In particular, in patients older than 80 years old with acute cholecystitis the risk of GBC increases even more. So, in elderly patients with acute cholecystitis the frozen section should be performed.

Competing interests: The authors declare that they have no competing interest.

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