



Postoperative Complications in Carcinoma Gall Bladder: A Tertiary Care Hospital Experience

¹Qaiser Naveed Haral, ¹Ammad Ud Din Nasir, ¹Ahmed Hassan Malik, ¹Muhammad Qasim Butt, ¹Rashid Zahid Ali, ¹Arwah Mansoor, ²Hassan Mumtaz

¹Department of General Surgery, NUMS, Rawalpindi.

²Department of Clinical Investigation, Maroof International Hospital, Islamabad.

ABSTRACT

Introduction: Gallbladder cancer is more common than any other part of the biliary system. Accounting between 2% and 3% of all cholecystectomies.

Aims & Objectives: To analyze different postoperative complications in various stages of operated gall bladder carcinoma.

Place and duration of study: Army Liver Transplant Unit (A.L.T.U.) Pak Emirates Military Hospital Rawalpindi (P.E.M.H.), from November 2020 to April 2022.

Material & Methods: This cross-sectional descriptive study looked at all patients diagnosed with gallbladder cancer before surgery or who were subsequently found to have benign gallbladder cancer presenting with intra-luminal lesions and localized or diffuse wall thickening amenable to surgical treatment. A sequential sampling method was used to select the patients. A proforma was developed to streamline the data collection process. The patient's gallbladder cancer was staged using the A.J.C.C.'s Eighth Edition staging system, and the degree of complications was classified using the Clavien-Dindo system. Data was entered and analysed using SPSS version 23.

Results: A total of 27 patients were included in the study, with male to female ratio of 1:3; and a mean age of 50.1 ± 4.7 years (range 25-70 years). Six patients were in Stage-1 of whom only 1 (3.7%) developed grade – I complication; 9 patients were in Stage-2, out of which 2 (7.4%) developed grade – II complications; 6 patients were in Stage-3, out of which 2 (7.4%) patients developed grade – III and 1 (4.7%) patient developed grade-II postoperative complications. Six (22.2%) were in Stage-4 and underwent curative resection, where no patient developed postoperative complications.

Conclusion: Surgery remains a solitary curative option for gall bladder carcinoma, and when patients are selected carefully, postoperative complications after radical surgery are not very high. Moreover, as the stage of the disease increases, so does the complication grade.

Keywords: Gall bladder carcinoma, Surgical Resection, T.N.M. staging.

INTRODUCTION

Gallbladder cancer is more common than any other part of the biliary system. Gallbladder cancer accounts for between 2% and 3% of all cholecystectomies. Its incidence has grown in the last two decades¹. The increased incidence of the disease is thought to be attributed to two factors: the general practice of reporting histological findings for all gallbladders removed and the rising popularity of laparoscopic cholecystectomies². People with non-accidental gallbladder cancer are rarely diagnosed with the disease immediately. Surprisingly, even when the severity of the disease is considered, the outcomes are worse than when diseases are discovered by accident. The incidence of gallbladder cancer varies greatly by location³. Approximately 22 out of every 100,000 women in northern India are affected. The incidence rate is 11 per 100,000 Indians and Pakistanis in North

America⁴. There are few reported cases in Europe (between 0 and 4 per 100,000)⁵. The prognosis for gallbladder carcinoma is poor, with a less than 5% 5-year survival rate. With early detection and surgery based on the disease's stage, 75% of patients diagnosed with cancer can survive for five years⁶. Criteria for stage-adjusted therapy have been published in some countries, but there is a significant deal of diversity in the literature, the standards, and the degree to which people adhere to the guidelines. Patients with pT1 cancer and clean margins after cholecystectomy may not need further treatment. Patients with pT2 or pT3 incidental cancer should have a drastic re-operation to increase their chances of survival. Major surgery, including the removal of the liver and lymph nodes, is an appropriate treatment for cancer⁷ for the treatment of gallbladder cancer; the S3 Guidelines suggest either a wedge resection of the gallbladder bed or resection of liver segments 4b and 5¹⁰. Both of these

operations necessitate removing a segment of the gallbladder's bed. Gallbladder cancer patients at stages T2 and T3 commonly receive hepatoduodenal ligament lymphadenectomy after undergoing this treatment⁸. According to the criteria provided by the National Comprehensive Cancer Network, this specific method should be used for carcinomas at stages T1b and above⁹. This study aims to examine data from patients with gallbladder cancer at various stages of the disease and following surgery at our institution.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted from November 2020 to April 2022, at the Department of General Surgery, Army Liver Transplant Unit (A.L.T.U.) Pak Emirates Military Hospital Rawalpindi. The Hospital's Board of Directors gave the Ethics Review clearance vide reference number A/28/Ec/450/2022. Patients diagnosed with gallbladder carcinoma either before surgery or after surgery for a benign condition were included in the study." Patients whose diagnoses included metastatic disease were not included in the research.

The study included 27 participants. Sequential sampling was used to select them. Surgeons, gastroenterologists, diagnostic and interventional radiologists, oncologists, and anesthesiologists worked together to treat each patient.

Patient demographic information, surgical details, and post-op complications were recorded on a proforma. Gallbladder cancer in patients were staged using the A.J.C.C. 8th Edition⁷. Clinical outcomes and case-based compensation following surgery strongly correlated with the C.D.C. grading system. As a result, it is a reliable method for contrasting different surgical procedures¹⁰.

Statistical Analysis

The data was analyzed using S.P.S.S. 23. Descriptive statistics calculate values like the mean and standard deviation, while qualitative analysis uses metrics like frequency and percentages.

RESULTS

There was a total of 27 patients who were diagnosed with gallbladder cancer, and the ratio of males to females was 1:3. Table-1 illustrates a variety of characteristics of the group under consideration.

Six of 27 patients were found to be in T1 disease on histopathology report after routine cholecystectomy. Among these six patients, three were in the T1a

category (tumor had invaded lamina propria) for which no further treatment was required, and 3 were in the T1b category (tumor had invaded muscular layer). Out of the patients with T1b disease, three patients had clear cystic duct margin on histopathology report for which radical cholecystectomy plus portal lymph node dissection was done, and one had cystic duct margin involvement on histopathology report for which radical cholecystectomy plus bile duct excision and portal lymphadenectomy was done.

Parameters	N (%)
Gender	
Male	9 (33.33%)
Female	18 (66.66%)
Age (years)	
Mean	50.1 ± 4.7years
Range (min-max)	25-70 years

Table-1: Characteristics of Study Population (n=27)

Nine patients were found with T2 disease (Tumor enters peri-muscular connective tissue without extension into the serosa).

Six individuals had T3 disease (tumor punctures serosa or directly affects the liver or adjacent organs). Five underwent radical cholecystectomy. Two patients' cystic duct margins required bile duct resection. Right hemi hepatectomy was done for hepatic duct involvement.

Six individuals with T4 illness exhibited peritoneal metastases on diagnostic laparoscopy and one during laparotomy. Table-2 shows A.J.C.C. 8th edition stage-wise patient distribution.

Out of these 27 patients studied, 6 patients developed postoperative complications. According to Clavien Dindo's classification of different stages of the carcinoma gall bladder, postoperative complications were studied (Table-3). Among stage I patients, one developed grade-complication (superficial surgical wound infection). Among stage II patients, two patients developed grade – II complications. One developed basal atelectasis, and the other had a minor bile leak. Among stage 3 patients, two developed grade-III complications and one developed grade-II complications. One patient had a biloma, which needed image-guided drainage. And one patient developed a postoperative

hemorrhage, which required laparotomy. Grade – II complication patient had developed pneumonia.

AJCC 8 th Edition	Total	% age
Stage I	6	(22.2%)
T1a, N0, M0	3	(11.1%)
T1b, N0, M0	3	(11.1%)
Stage II	9	(33.3%)
T2a, N0, M0	2	(7.4%)
T2b, N0, M0	7	(25.9%)
Stage III	6	(22.2%)
T3, N0, M0	6	(22.2%)
Stage IV(A&B) (T4N0 M0) (AnyT, N2, M0) (AnyT, AnyN, M1)	6	(22.2%)

Table-2: Stage-wise distribution of patients according to A.J.C.C. 8th edition.

Stages	Grade-I	Grade-II	Grade-III	Grade-IV	Grade-V	Total (%)
Stage-1	1	0	0	0	0	1 (3.7%)
Stage-2	0	2	0	0	0	2 (7.4%)
Stage-3	0	1	2	0	0	3 (11.1%)
Stage-4	0	0	0	0	0	0 (0%)
Total	1	3	2	0	0	6 (22.2%)

Table-3: Postoperative Complications according to Clavien Dindo Classification in different stages of Carcinoma (n=6).

*Where the grade is according to ClavienDindo classification and stage according to A.J.C.C. 8th edition.

DISCUSSION

Only surgical resection, which removes the affected portion of the gall bladder, can cure gall bladder cancer¹. Because it is a disease that is so aggressive and potentially fatal, making an early diagnosis is of the utmost significance. Numerous studies have shown that the T.N.M. staging system may give information on survival benefits after surgical procedures¹¹.

In our research, patients were staged using the T.N.M. classification of gallbladder carcinoma according to the Eighth Edition of the A.J.C.C. guidelines. Table 4 presents the T.N.M. classification according to the A.J.C.C.'s eighth edition.

Simple cholecystectomy is sufficient for T1a tumors, but T1b requires more aggressive

treatment¹². Extended cholecystectomy with regional lymph node dissection and en bloc hepatectomy is recommended for T2 patients¹³. In T3 disease, R0 resection (negative margins and lymph node dissection one level beyond microscopically involved lymph nodes) is associated with improved survival¹⁴. Our study followed suit. R0 resection for T4 disease is not possible, and 5-year survival is low, so extended radical surgeries were not attempted. Such patients receive adjuvant chemoradiotherapy. In our study, ClavienDindo classification was used to classify postoperative complications.

Primary Tumor	
Tx	Cannot be evaluated
T0	No indication of a primary tumor
This	Carcinoma in situ
T1a	Tumor enters lamina propria
T1b	Tumor enters the muscular layer
T2	Tumor enters peri-muscular connective tissue without extension into the serosa.
T3	Tumor pierces the serosa (visceral peritoneum) and directly enters the liver or a nearby structure.
T4	A tumor involves the main portal vein or hepatic artery or enters 2 or more organs.
Regional Lymph Nodes	
Nx	Cannot be evaluated
N0	No regional lymph node involved
N1	Metastases to 1-3 regional lymph nodes
N2	Metastases to ≥ 4 regional lymph nodes
Distant Metastasis	
M0	No distant metastasis
M1	Distant metastasis

Table-4: A.J.C.C. 8th edition T.N.M. staging system for gallbladder cancer⁷.

Complications after surgery include hemorrhage, surgical site infection, pneumonia, and bile leakage. A study on 106 patients operated for gallbladder carcinoma demonstrated surgical site infection in 20.8% of patients, pneumonia in 7.5% and bile leakage in 6.6% of patients¹⁵. One patient in our study developed a surgical site infection; one developed basal atelectasis, and one developed pneumonia. Bile leaks also occurred in two patients. No in-hospital mortality occurred in our study. Our results are comparable to those found in literature¹⁶.

Hospital mortality of up to 7.5% after surgery for gallbladder carcinoma has been reported in a study, with failure to rescue from complications as an important cause of mortality¹⁷. Rapid diagnosis and prompt management of postoperative complications after intricate surgeries for carcinoma gallbladder is paramount to ensure a speedy recovery and discharge from the hospital¹⁸.

Compared to any other surgery, surgery on the liver is complex, with risks such as prolonged duration of surgery, intra-operative hemorrhage, massive fluid shifts, and hypotension, along with postoperative complications such as coagulopathy or bleeding, pulmonary complications, bile leaks, liver or renal failure¹⁹. All of these present challenges to the operating team. Enhanced recovery after surgery (ERAS) program has been found to be safe and effective in reducing postoperative complications in patients undergoing hepatobiliary surgery²⁰. It has been found to enhance patient recovery and reduce hospital stays without increasing treatment costs or complications²¹.

ERAS program involves various pre-operative, intra-operative and postoperative elements²². Pre-operative elements include minimal fasting, no mechanical bowel preparation, pre-operative carbohydrate load and venous thromboembolism prophylaxis. Intra-operative elements include antimicrobial prophylaxis, skin preparation, use of balanced crystalloids, normothermia and glycemic control. Postoperative elements include multimodal analgesia, early mobilization and early oral intake²³. ERAS program should be implemented in true letter and spirit in our setup to reduce postoperative complications, as it has been proven its utility in multiple studies²³.

Grades	Definition
Grade I	Any nonconformity from usual postoperative recovery without requiring pharmacological, surgical, endoscopic or radiological interventions. Anti-emetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy may be utilized. Wound infections opened at the bedside are also included.
Grade II	Pharmacological treatment with drugs other than those mentioned for grade I complications.
Grade III	Requiring surgical, endoscopic or radiological intervention
- IIIa	Intervention not under general anesthesia

- IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication requiring I.C./ICU-management
- IVa	single organ dysfunction (including dialysis)
- IVb	Multi-organ dysfunction
Grade V	Death of a patient

Table-5: ClavienDindo Classification for Postoperative Complications¹³.

CONCLUSION

Surgery remains a solitary curative option for carcinoma gallbladder, and when patients are selected carefully, postoperative complications after radical surgery are not very high. Moreover, as the stage of the disease increases, so does the complication grade.

REFERENCES

- Gourgiotis S, Kocher HM, Solaini L, Yarollahi A, Tsiambas E, Salemis NS. Gallbladder cancer. *Am J Surg.* 2008 Aug;196(2):252–64.
- Toyonaga T, Chijiwa K, Nakano K, Noshiro H, Yamaguchi K, Sada M, et al. Completion of Radical Surgery after Cholecystectomy for Accidentally Undiagnosed Gallbladder Carcinoma. *World J Surg.* 2003 Mar 4;27(3):266–71.
- Schmidt MA, Marciano-Bonilla L, Roberts LR. Gallbladder cancer: epidemiology and genetic risk associations. *Chin Clin Oncol.* 2019 Aug;8(4):31. doi: 10.21037/cco.2019.08.13. P.M.I.D.: 31484487.
- Pawlik TM, Gleisner AL, Vigano L, Kooby DA, Bauer TW, Frilling A, et al. Incidence of Finding Residual Disease for Incidental Gallbladder Carcinoma: Implications for Re-resection. *J Gastrointest Surg.* 2007 Nov 1;11(11):1478–87.
- Key statistics for Gallbladder Cancer [Internet]. [www.cancer.org](https://www.cancer.org/cancer/gallbladder-cancer/about/key-statistics.html). Available from: <https://www.cancer.org/cancer/gallbladder-cancer/about/key-statistics.html>
- Goetze TO. Gallbladder carcinoma: Prognostic factors and therapeutic options. *World J Gastroenterol.* 2015 Nov 21;21(43):12211-7. doi: 10.3748/wjg.v21.i43.12211. P.M.I.D.: 26604631; P.M.C.I.D.: PMC4649107.
- Adjusted A.J.C.C. 6th ed T,N,M, and Stage-SEER Documentation [Internet]. SEER. [cited 2023 Jan 16]. Available from: <https://seer.cancer.gov/seerstat/var-iables/seer/ajcc-stage/6th>
- Goetze TO, Paolucci V. Influence of high- and low-volume liver surgery in gallbladder carcinoma. *World J Gastroenterol WJG.* 2014 Dec 28;20(48):18445–51.

9. Pluchino LA, D'Amico TA. National Comprehensive Cancer Network Guidelines: Who Makes Them? What Are They? Why Are They Important? *Ann Thorac Surg.* 2020 Dec;110(6):1789-1795. doi: 10.1016/j.athoracsur.2020.03.022. Epub 2020 Apr 13. P.M.I.D.: 32298647.
10. Téoule P, Bartel F, Birgin E, Rückert F, Wilhelm TJ. The Clavien-Dindo Classification in Pancreatic Surgery: A Clinical and Economic Validation. *J Invest Surg.* 2019 Jun;32(4):314-320. doi 10.1080/08941939.2017.1420837. Epub 2018 Jan 16. P.M.I.D.: 29336625.
11. Benson AB, Abrams TA, Ben-Josef E, Bloomston PM, Botha JF, Clary BM, et al. N.C.C.N. clinical practice guidelines in oncology: hepatobiliary cancers. *J NatlComprCancNetw.* 2009 Apr 1;7(4):350-91.
12. Liao X, Zhang D. The 8th Edition American Joint Committee on Cancer Staging for Hepato-pancreato-biliary Cancer: A Review and Update. *Arch Pathol Lab Med.* 2021 May 1;145(5):543-53.
13. Dindo D, Demartines N, Clavien P-A. Classification of Surgical Complications: A New Proposal With Evaluation in a Cohort of 6336 Patients and Results of a Survey. *Ann Surg.* 2004 Aug;240(2):205-13.
14. Yuza K, Sakata J, Hirose Y, Miura K, Ando T, Katada T, et al. Outcome of radical surgery for gallbladder carcinoma according to T.N.M. stage: implications for adjuvant therapeutic strategies. *Langenbecks Arch Surg.* 2021 May;406(3):801-11.
15. Mekeel KL, Hemming AW. Surgical Management of Gallbladder Carcinoma: A Review. *J Gastrointest Surg.* 2007 Aug 22;11(9):1188-93.
16. Park TJ, Ahn KS, Kim YH, Kim T-S, Hong JH, Kang KJ. The optimal surgical resection approach for T2 gallbladder carcinoma: evaluating the role of surgical extent according to the tumour location. *Ann Surg Treat Res.* 2018 Feb 28;94(3):135-41.
17. Hong EK, Kim KK, Lee JN, Lee WK, Chung M, Kim YS, et al. Surgical outcome and prognostic factors in patients with gallbladder carcinoma. *Korean J Hepato-Biliary-Pancreat Surg.* 2014 Nov 30;18(4):129-37.
18. Wu XS, Zhu YD, Jin YP, Li ML, Gong W, Liu YB. [Diagnosis and treatment for unexpected gallbladder carcinoma(a retrospective study of 45 cases)]. *ZhonghuaWaiKeZaZhi.* 2019 Apr 1;57(4):265-70.
19. Filmann N, Walter D, Schadde E, Bruns C, Keck T, Lang H, et al. Mortality after liver surgery in Germany. *Br J Surg.* 2019 Oct;106(11):1523-9.
20. Agarwal V, Divatia JV. Enhanced recovery after surgery in liver resection: current concepts and controversies. *Korean J Anesthesiol.* 2019 Apr;72(2):119-29.
21. Utsumi M, Aoki H, Nishimura S, Une Y, Kashima H, Kimura Y, et al. Safety of Surgical Treatment for Elderly Patients with Gallbladder Carcinoma. *Acta Med Okayama.* 2019;73(3):6.
22. Wu X, Li B.L., Sun J, Zheng CJ, He XD, Liu W, et al. [Application of enhanced recovery after surgery in the perioperative management of patients with gallbladder carcinoma]. *ZhonghuaWaiKeZaZhi.* 2022 Apr 1;60(4):373-8.
23. Melloul E, Hübner M, Scott M, Snowden C, Prentis J, Dejong CHC, et al. Guidelines for Perioperative Care for Liver Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations. *World J Surg.* 2016 Oct 1;40(10):2425-40.

The Authors:

Dr. Qaiser Naveed Haral
Postgraduate Resident
Department of General Surgery
NUMS

Dr. Ammad Uddin Nasir,
Classified Gen Surgeon,
Department of General Surgery,
NUMS.

Dr. Ahmed Hassan Malik,
Postgraduate Resident,
Department of General Surgery,
NUMS.

Dr. Muhammad Qasim Butt,
Classified Gen Surgeon,
Department of General Surgery,
NUMS.

Dr. Rashid Zahid Ali,
Postgraduate Resident,
Department of General Surgery,
NUMS.

Dr. Arwah Mansoor,
Postgraduate Resident,
Department of General Surgery,
NUMS.

Dr. Hassan Mumtaz,
Senior Clinical Research Associate,
Department of Clinical Investigation,
Maroof International Hospital.

Corresponding Author:

Dr. Hassan Mumtaz,
Senior Clinical Research Associate,
Department of Clinical Investigation,
Maroof International Hospital.
Email: hassanmumtaz.dr@gmail.com