

IMPACT OF PREOPERATIVE PARAMETERS ON OUTCOMES FOLLOWING LIVER RESECTION FOR BILIARY CANCERS

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ABSTRACT

Biliary cancers such as gallbladder carcinoma and cholangiocarcinoma are aggressive hepatobiliary malignancies with poor prognosis because many patients present at an advanced stage. Liver resection remains the only potentially curative treatment, but perioperative outcomes depend on preoperative patient factors, tumor extent, operative complexity, and available biomarker information. In this retrospective, observational study, the effect of preoperative clinical, biochemical, imaging and biomarker variables of liver resection performed for biliary cancers was evaluated from April 2017 to September 2025 at Army Liver Transplant Unit, Pak Emirates Military Hospital, Rawalpindi, Pakistan. All 90 patients who underwent liver resection for the treatment of biliary cancers with curative intent were included. These were the parameters evaluated preoperatively: clinical presentation, bilirubin level, alkaline phosphatase, CA 19-9, imaging and ERCP/PTBD status. Operative details, postoperative complications, length of stay in the ICU, requirement for transfusion of blood, histopathology and survival outcome were assessed. The collected data were analysed with SPSS version 25.0. Ninety patients (66.7% males, 33.3% females) were included in the cohort and had a mean age of 59 years. Common presentation was jaundice and weight loss, and the mean level of CA 19-9 was 400 U/mL, supporting the use of this as a useful preoperative biomarker when used with clinical and radiological data. Surgery involved hepatectomy on the right side in 27 patients (30.0%), left side hepatectomy in 21 (23.3%), extended right hepatectomy in 16 (17.8%), extended left hepatectomy in 16 (17.8%) and central hepatectomy in 10 (11.1%). Blood transfusion was needed in 18 (20.0%) patients and the mean length of the ICU stay was 5.4 days, while 6 patients (6.7%) had a bile leak. Liver resection is an important modality for treatment in biliary cancers, and can provide acceptable perioperative results in a dedicated hepatobiliary centre. The integration of clinical assessment, imaging, biochemical markers and CA 19-9 will have a beneficial impact on patient selection, peri-operative optimization and surgical planning.

KEYWORDS: Biliary cancers, Liver resection, CA 19-9, Biomarker, Cholangiocarcinoma, Gallbladder carcinoma, Surgical outcomes, Preoperative parameters.

INTRODUCTION

Biliary cancers are clinically relevant due to their often aggressive nature, relative rarity, and complicated hepatobiliary anatomy, including intrahepatic, perihilar and distal cholangiocarcinoma, as well as gallbladder carcinoma. Their incidence varies geographically and is influenced by risk factors such as gallstone disease, chronic biliary inflammation, primary sclerosing cholangitis, liver fluke infestation and environmental exposures [1-3].

Imaging, endoscopic evaluation and multidisciplinary oncologic pathways have made a significant contribution to the diagnostic process, but an anatomic complexity and advanced disease are still present in many patients. The currently accepted guidelines for assessment are a high-quality cross-sectional image for evaluation, cholangiographic assessment if needed, pathological assessment if possible, and multidisciplinary staging to determine resectability [1,4,5].

The preoperative evaluation takes a central role therefore in decision making. The values of serum bilirubin are indicative of the severity of biliary obstruction, alkaline phosphatase of cholestasis burden, and CA 19-9 gives supportive prognostic and disease-burden information but should be interpreted with caution in the presence of jaundice, cholangitis or recent biliary drainage [6,7]. Imaging establishes local tumour extent, vascular proximity, future liver remnant, lymph node involvement and feasibility of margin-negative resection [5,8].

In selected patients, extended resections can lead to better oncological clearance, but carry a higher perioperative risk, especially if major hepatectomy, biliary reconstruction, vascular proximity or inadequate future liver remnant is anticipated [9-11]. In contrast, with limited resections, there is no guarantee that the treatment is adequate for all tumors, but there is the possibility

of a decreased short-term morbidity. Thus, balancing between tumor clearance and patient fitness, hepatic reserve and expected postoperative risk is imperative to surgical planning [1,8,9].

This study aimed to evaluate the impact of various pre-operative parameters on the outcome of liver resection surgery for biliary cancer at Pak Emirates Military Hospital Rawalpindi.

MATERIALS AND METHODS

Study design and Setting

This is a retrospective, observational study done at Pak Emirates Military Hospital, Rawalpindi, Pakistan during the period of April, 2017 to September 2025.

Patient selection

90 patients with biliary cancers with curative liver resection were included in the study. Diagnosis was made on the basis of the preoperative imaging such as contrast enhanced computed tomography or magnetic resonance imaging or histopathological confirmation where available, as per the guidelines for diagnostic and staging process for biliary tract cancers [1,4,5,8].

Inclusion criteria

- Patients 18 yrs. and older.
- Patients with proven or suspected histological diagnosis of biliary malignancy.
- Patients who had liver resection as a cure.
- Available pre-operative, operative, post-operative & histopathological records of patients.

Exclusion criteria

- Patients who have disease that cannot be removed by surgery.
- Patients who had palliative bypass, biopsy only or non-resectional procedures.
Benign hepatobiliary disease patients underwent surgery.
People who have incomplete medical records.

Data collection

Data were retrieved retrospectively from hospital electronic medical records, hospital admission notes, operating room notes, anesthesia notes, laboratory notes, radiological notes, intensive care unit notes, discharge notes and histopathology reports. Patient identifiers were deleted prior to analysis and confidentiality was protected throughout the study.

Variables recorded

Demographic data, clinical presentation, preoperative bilirubin, alkaline phosphatase, CA 19-9, ERCP/PTBD status, type of liver resection, blood transfusion requirement after surgery, and survival data were recorded. Other variables recorded included imaging findings, type of liver resection, requirement for blood transfusion after surgery, survival data, ERCP/PTBD status, and histopathological differentiation, among other variables.

The surgical procedures and recovery from surgery.

All surgeries were performed by experienced hepatobiliary surgeons. Liver resection type was determined based on the location, extent of disease, expected future liver remnant, vascular or biliary involvement, and the patients' operative fitness [6,9,10]. The monitoring after surgery was done in the ICU regularly. Clinical and laboratory follow-up and imaging was done to assess for recovery and recurrence. The definition of bile leak and post-hepatectomy liver failure were based on the international hepatobiliary surgery consensus, and postoperative complications were based on the Clavien-Dindo classification as available [12-14].

Statistical analysis

The data were analyzed using SPSS version 25.0. Continuous variables were presented as the mean \pm standard deviation, or median and interquartile range where they were skewed. Categorical variables were presented as frequencies and percentages. Independent t-test was used for comparison of continuous variables, while chi-square or Fisher's exact test was used for categorical variables. Where survival outcomes were available, they were analyzed using Kaplan-Meier survival analysis and log-rank testing. A p-value < 0.05 was defined as statistically significant.

Ethical considerations

This study was approved by Pak Emirates Military Hospital, Rawalpindi [RTMC# HPB-2023-124-26]. The study was carried out in the light of the Declaration of Helsinki. As the study was retrospective, informed consent was not required by the institutional review board. All data provided were anonymous and confidentiality was respected.

RESULTS

A total of 90 patients who underwent liver resection for biliary cancers at Pak Emirates Military Hospital, Rawalpindi, were included in this analysis. The mean age was 59 years. The cohort included 60 males (66.7%) and 30 females (33.3%). Most patients presented with jaundice and weight loss. Mean preoperative CA 19-9 was 400 U/mL.

Table 1. Demographic and preoperative characteristics (n = 90)

S. No.	Variable	Value
1	Total patients	90
2	Age, mean	59 years

3	Male gender	60 (66.7%)
4	Female gender	30 (33.3%)
5	Common presentation	Jaundice, weight loss
6	CA 19-9, mean	400 U/mL
7	ERCP/PTBD	Performed for bilirubin >200 µmol/L

The most common procedure was right hepatectomy in 27 patients (30.0%), followed by left hepatectomy in 21 (23.3%), extended right hepatectomy in 16 (17.8%), extended left hepatectomy in 16 (17.8%), and central hepatectomy in 10 (11.1%). Blood transfusion was required in 18 patients (20.0%). Mean ICU stay was 5.4 days. Bile leakage was in 6 patients (6.7%) and was managed conservatively.

Table 2. Surgical procedures and postoperative outcomes (n = 90)

S. No.	Parameter	Value
1	Right Hepatectomy	27 (30.0%)
2	Left Hepatectomy	21 (23.3%)
3	Extended Right Hepatectomy	16 (17.8%)
4	Extended Left Hepatectomy	16 (17.8%)
5	Central Hepatectomy	10 (11.1%)
6	Blood transfusion required	18 (20.0%)
7	Mean ICU stay	5.4 days
8	Bile leakage	6 (6.7%)

Moderately differentiated adenocarcinoma remained the predominant pattern with 40 patients (44.4%), followed by well-differentiated tumors in 24 (26.7%), poorly differentiated tumors in 19 (21.1%), intraductal papillary neoplasm in 4 (4.4%), and mucinous cystic neoplasm in 3 (3.3%).

Table 3. Histopathological findings (n = 90)

S. No.	Histopathology type	Value
1	Moderately differentiated adenocarcinoma	40 (44.4%)
2	Well differentiated tumor	24 (26.7%)
3	Poorly differentiated tumor	19 (21.1%)
4	Intraductal papillary neoplasm	4 (4.4%)
5	Mucinous cystic neoplasm	3 (3.3%)

Age distribution was comparable between male and female patients, with similar median age values in both groups. Male patients showed a relatively wider distribution, but no major difference in age pattern was identified between genders. Postoperative outcomes varied by type of liver resection. Complex and intermediate procedures showed a higher frequency of postoperative complications, ICU stay, and blood transfusion requirement compared with less extensive procedures. However, Kaplan-Meier survival analysis showed no statistically significant survival difference between simple, intermediate, and complex resection groups using the log-rank test ($p = 0.37$). Correlation analysis demonstrated a moderate positive correlation between age and postoperative recovery time ($r = 0.29$), indicating relatively longer recovery in older patients. Other correlations were weak.

DISCUSSION

The results overall agree with the hypothesis that liver resection for biliary cancer is feasible with acceptable peri-operative morbidity in a specialized center in which careful selection is key.

The study further underscores the importance of multidisciplinary care. There is an emphasis on coordination of input from hepatobiliary surgeons, radiologists, gastroenterologists, oncologists, pathologists, anesthetists and critical care teams in the diagnosis, staging, decisions regarding biliary drainage, surgical planning, post-surgical management with the use of adjuvant therapy, and follow-up surveillance [1,15-18]. This model can be used in a hepatobiliary specialist center to decrease unnecessary morbidity, by identifying appropriate surgical candidates and preparing patients for major resection.

Postoperative bile leak is a complication which is of particular relevance following hepatobiliary resection. This international consensus definition of bile leakage severity will enable more uniform reporting of postoperative bile leakage, and this parallel consensus definition for post-hepatectomy liver failure will allow a structured approach in the classification of hepatic insufficiency following resection [12,13]. These definitions would be useful in the current set of data to provide more uniformity with hepatobiliary literature internationally.

This age-dependent relationship between postoperative recovery time and age suggests the importance of careful perioperative planning in older patients. Surgery should not be denied to patients because of their chronological age, but in the older patients,

there may be greater need for evaluation of frailty, cardiopulmonary reserve, nutritional status, renal function, and tolerance of the major surgical procedure. Overall, the Clavien-Dindo classification system is still applicable for the standardisation of the severity of postoperative complications, to facilitate the comparison of studies and to enhance the reporting of results in future analyses [14].

The difference in survival rates by surgical categories was not statistically significant in the present analysis where extensive resections had increased peri-operative morbidity. This finding should be interpreted cautiously. Many factors play a role in survival following biliary cancer surgery: tumour biology, nodal status, margin status, vascular invasion, postoperative recovery, recurrence pattern and access to adjuvant or systemic therapy [1,3,17].

On histopathological examination, moderately differentiated adenocarcinoma was observed to be predominant, followed by well-differentiated and poorly-differentiated adenocarcinoma. This pattern has contributed to the histological heterogeneity of the biliary cancers. The role of conventional morphology is complemented by that of anatomical subtype, growth pattern, molecular alterations and margin status that are increasingly recognized in modern practice to contribute to prognosis and to assist in treatment selection [5,8,19].

The surgical procedure also varies depending on the type of tumor. The surgical resection needed for gall bladder carcinoma is determined by the T stage, liver bed involvement, nodal disease, and the potential for complete resection. Based on international data and consensus recommendations, individualized surgery, lymphadenectomy (where appropriate) and multidisciplinary planning are more beneficial than a standard surgical approach to all patients with gallbladder cancer [20–22]. Multimodality reviews in recent years also point to the fact that surgery will play a major role with resectable disease, while systemic therapy, adjuvant therapy and careful follow-up play an increasing role in the care of resectable disease [23,24].

One of the major problems associated with large liver resection is the ability to ensure that post-hepatectomy liver failure will not occur because of the remaining liver volume and function. Increased liver remnant following portal vein embolization and other maneuvers can help to minimize postoperative liver failure in high-risk resections, particularly perihilar cholangiocarcinoma [11]. Preoperative assessment should not only include the determination of resectability or unresectability, but also detection of patients who require biliary drainage, nutritional optimization, volumetric assessment or staged preparation prior to surgery [6,8,11].

In this cohort, a higher rate of perioperative morbidity was observed with more extensive resections. This is biologically feasible: the operation of hepatobiliary resection is associated with increased operative time, blood loss, degree of dissection of the hilar region, need for biliary reconstruction and physiological demand after surgery [9,10,19]. The relationship between complex resections and transfusion and longer ICU stay, therefore, seems clinically plausible but should be interpreted with caution and needs to be validated in a larger, multicenter study.

Radiological assessment is still an essential aspect of surgical planning. Contrast-enhanced CT and MRI/MRCP aid in determining tumor location, longitudinal biliary involvement, liver infiltration, nodal involvement, vascular abutment/encasement and metastatic disease. Modern recommendations also focus on the future liver remnant and the potential for achieving an R0 resection, as technically feasible surgery may not be oncologically or physiologically suitable [4,5,8]. This is especially important in perihilar and intrahepatic cholangiocarcinoma, where surgical margins, vascular inflow and outflow and biliary reconstruction significantly impact operative risk.

Demographic profile indicated a male dominance and an average age of 59 years. Most common presenting symptoms were jaundice and weight loss, consistent with the obstructive, and often advanced, presentation of cholangiocarcinoma and gallbladder carcinoma. The high level of CA 19-9 confirmed its value as a marker of disease burden and potential prognosis, however, should not be used singly as elevated levels can be caused by obstructive jaundice, cholangitis, and biliary manipulation [6,7]. CA 19-9 should be regarded here more as an adjunct to imaging, clinical status and histopathologic confirmation, and not as an independent criterion for resectability.

The study is interesting in terms of a biomarker dimension since CA 19-9 is included in the preoperative evaluation. CA 19-9 is not a tumor specific molecular marker, but can be raised in biliary obstruction, cholangitis and following biliary manipulation, is a useful and readily available marker for the assessment of disease burden and for risk stratification in biliary cancers. The CA 19-9 level in the present cohort was around 400 U/mL, confirming its clinical relevance when used together with the level of bilirubin, alkaline phosphatase, imaging data and surgical difficulty. Hence, CA 19-9 is not a stand-alone criterion for resectability, but should be incorporated into a comprehensive pre-operative assessment process.

Biliary cancers are now known to be genetically heterogeneous from a molecular oncology point of view. In some patients, molecular changes like IDH1/2 mutations, FGFR2 fusions, KRAS mutations, TP53 changes, and mismatch repair deficiency could affect their prognosis and treatment with systemic drugs. Due to the variability of patients included in the present study, molecular profiling has not been available for all patients, and the combination of these factors with clinical, imaging, and other tumoral and surgical characteristics could add to the predictive models of future studies. This further underscores the importance of future studies integrating routine surgical risk stratification with molecular/bio-marker based classification of biliary cancer patients who are undergoing liver resection.

The purpose of this study was to analyse the results of liver resection for biliary malignancies in a tertiary hepatobiliary and liver transplant centre. Findings are related to the degree and complexity of resection to the perioperative burden, which included postoperative complications, ICU stay and requirement for blood transfusion. This is in line with the accepted principles that cancers of the biliary tract are technically challenging to operate on, especially if they are located near the major vascular and biliary structures, and should be carefully staged [1-3].

Limitations

- There may be selection biases and lack of documentation associated with the retrospective design.
- This study was conducted at a single center, in a hepatobiliary/liver transplant center, and so the findings may not be representative of other centers.
- The number of patients in the subgroups was limited due to stratification by surgery type, which further limited the power for the subgroup and survival analyses.
- All patients were not subjected to detailed molecular profiling and complete staging stratification and all were not given standardised adjuvant therapy information.

CONCLUSION

Liver resection remains an important treatment modality for biliary cancers despite technical complexity and perioperative risk. Here, the perioperative burden was higher for the patients undergoing complex resections and there was no significant difference in long-term survival between the surgical types. The most common histopathological type was moderately differentiated adenocarcinoma. The key to improving outcomes in patients with biliary cancer is careful preoperative assessment, patient selection, multidisciplinary perioperative care and surgical planning.

Declarations

Ethics approval and consent to participate: Ethical approval for this study was obtained from the Ethical Committee of Pak Emirates Military Hospital, Rawalpindi (Ref: RTMC# HPB-2023-124-26). The study was conducted in accordance with the Declaration of Helsinki. Due to the retrospective nature of the study, the requirement for informed consent was waived. Patient confidentiality was maintained and all data were anonymized before analysis.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request and with institutional permission.

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