

ORIGINAL ARTICLE

Rates and patterns of recurrence after curative intent resection for gallbladder cancer: a multi-institution analysis from the US Extra-hepatic Biliary Malignancy Consortium

Georgios Antonios Margonis¹, Faiz Gani¹, Stefan Buettner¹, Neda Amini¹, Kazunari Sasaki¹, Nikolaos Andreatos¹, Cecilia G. Ethun², George Poultsides³, Thuy Tran³, Kamran Idrees⁴, Chelsea A. Isom⁴, Ryan C. Fields⁵, Bradley Krasnick⁵, Sharon M. Weber⁶, Ahmed Salem⁶, Robert C.G. Martin⁷, Charles Scoggins⁷, Perry Shen⁸, Harveshp D. Mogal⁸, Carl Schmidt⁹, Eliza Beal⁹, Ioannis Hatzaras¹⁰, Rivfka Shenoy¹⁰, Shishir K. Maithe² & Timothy M. Pawlik^{1,9}

¹Department of Surgery, Johns Hopkins Hospital, Baltimore, MD, USA, ²Department of Surgery, Emory University School of Medicine, Atlanta, GA, USA, ³Department of Surgery, Stanford University Medical Center, Stanford, CA, USA, ⁴Department of Surgery, Vanderbilt University Medical Center, Nashville, TN, USA, ⁵Department of Surgery, Washington University School of Medicine, St Louis, MO, USA, ⁶Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA, ⁷Department of Surgery, University of Louisville, Louisville, KY, USA, ⁸Department of Surgery, Wake Forest University, Winston-Salem, NC, USA, ⁹Department of Surgery, Ohio State University, Columbus, OH, USA, and ¹⁰Department of Surgery, New York University, New York, NY, USA

Abstract

Background: Gallbladder cancer is a relatively rare malignancy. The current study aimed to define the incidence and patterns of recurrence following gallbladder cancer resection.

Methods: Using a multi-institutional cohort we identified 217 patient undergoing curative intent surgery for gallbladder cancer. Patterns of recurrence were classified as locoregional and distant recurrence.

Results: At last follow-up, 76 patients (35.0%) had experienced a recurrence (locoregional only, n = 12, 15.8%; distant only, n = 50, 65.8%; locoregional and distant, n = 14, 18.4%). Median time to recurrence was 9.5 months (IQR 4.7–17.6) and was not associated with recurrence site (all p > 0.05). On multi-variable analysis, T3 disease (HR = 8.44, p = 0.014), lymphovascular invasion (HR = 4.24, p < 0.001) and residual disease (HR = 2.04, p = 0.042) were associated with an increased risk of recurrence. Patients who recurred demonstrated a worse 1-, 3- and 5-year OS (1-year OS: 91.3% vs. 68.6%, p = 0.001, 3-year OS: 79.3% vs. 28.7%, p < 0.001, and 5-year OS: 75.9% vs. 16.0%, p < 0.001). After adjusting for other risk factors, recurrence was independently associated with a decreased OS (HR = 3.71, p = 0.006). Of note, receipt of adjuvant therapy was associated with improved OS (HR = 0.56, p = 0.027) among those patients who developed a tumor recurrence.

Discussion: Over one-third of patients experienced a recurrence after gallbladder cancer surgery. While chemotherapy did not decrease the rate of recurrence, patients who experienced recurrence after administration of adjuvant treatment fared better than patients who did not receive adjuvant therapy.

Received 11 April 2016; accepted 30 May 2016

Correspondence

Timothy M. Pawlik, Department of Surgery, The Urban Meyer III and Shelley Meyer Chair for Cancer Research, Wexner Medical Center at the Ohio State University, 395 W. 12th Avenue, Suite 670, Columbus, OH 43210, USA. Tel: +1 (614) 293 8701. Fax: +1 (614) 293 4063. E-mail: tim.pawlik@osumc.edu

This study was presented as an oral presentation at the 12th International Hepato-Pancreato-Biliary Association (IHPBA) World Congress, April 20–23, 2016, Sao Paulo, Brazil.

Introduction

Gallbladder cancer (GBC) is a relatively rare malignancy estimated to affect approximately 10,500 patients in the United States in 2016.¹ Many patients who present with GBC are diagnosed incidentally following a laparoscopic cholecystectomy.^{2,3} In fact, many cases of GBC are unapparent on gross evaluation and may initially go undiagnosed until the cholecystectomy specimens are closely examined on pathology.⁴ Another subset of patients will have non-incidental GBC and will frequently be asymptomatic, resulting in delayed diagnosis that, in turn, is associated with advanced disease.^{5,6} As a result, only around 10% of patients diagnosed with non-incidental GBC are eligible for potentially curative surgery.⁷ While the prognosis of patients with GBC ranges widely and depends on disease stage, prognosis can be dismal even after surgical resection.⁸ The poor prognosis associated with GBC is largely due to postoperative recurrence that can be as high as 30–65% in certain patients.^{9,10}

To date, only a few studies have investigated factors associated with postoperative recurrence of GB cancer.^{11,12} For example, lymph node metastasis, positive resection margin, moderate or poor tumor differentiation and a tumor located on the “hepatic side” have been associated with a shorter time to recurrence.^{11,12} Most previous studies, however, examined GBC along with other bile duct malignancies, such as cholangiocarcinoma under the ‘umbrella’ of biliary tract cancers.⁹ GBC differs, however, from other biliary tract cancers in terms of pathogenesis, surgical management and long-term outcomes.¹³ As such, the validity and applicability of these data to patients with GBC is somewhat questionable. In addition, the low incidence of GBC in most Western countries and a lack of centralized care has precluded large institutional studies. Most reports derive from Asian countries while contemporary data from the United States are lacking.^{12,14,15} In fact, one of the largest studies from a North American center comprised fewer than 100 patients with GBC.⁹ Furthermore, detailed data on recurrence are currently lacking. Given this, the objective of the current study was to define the overall incidence of recurrence following curative intent resection of GBC, as well as to characterize patterns of recurrence. Additionally, we sought to identify clinicopathologic factors associated with recurrence-free survival utilizing a large cohort of patients derived from multiple institutions in the United States.

Methods

Data sources and patient population

Patients undergoing surgical resection for GBC between January 01, 2000 and December 31, 2014 were identified at one of ten academic institutions participating in the Extra-hepatic Biliary Malignancies Consortium (Johns Hopkins University, Baltimore, Maryland; Emory University, Atlanta, Georgia; Stanford University, Stanford, California; University of Wisconsin, Milwaukee, Wisconsin; Ohio State University, Columbus, Ohio;

Washington University, St. Louis, Missouri; Vanderbilt University, Nashville, Tennessee; New York University, New York, New York; University of Louisville, Louisville, Kentucky; Wake Forest University, Winston-Salem, North Carolina). Only patients undergoing a curative intent resection were included in the study population; patients presenting with metastatic disease, grossly positive surgical margins at resection (R2 disease), advanced N2 nodal disease, or AJCC 7th edition stage T4 tumors were excluded (Fig. 1).

Sociodemographic data including patient age, sex and race, as well as clinicopathologic information including American Society of Anesthesiologist (ASA) physical classification score, preoperative peak serum bilirubin, serum CA-19-9, tumor size, AJCC T-Stage, histologic grade, presence of lymph node metastasis, final resection margin, and the presence of vascular/perineural invasion were recorded. For patients with multiple lesions, tumor size was defined using the diameter of the largest tumor as per the 7th Edition of the AJCC Staging System.¹⁶ Similarly, histologic grade was classified according to the highest observed tumor grade and categorized as either well, moderate, or poorly differentiated. Surgical margin status and the presence of lymph node metastasis were determined using the final histopathology report. Additionally, operative details including the type and extent of surgery, as well as information pertaining to the administration of neoadjuvant and adjuvant chemotherapy and/or radiation therapy were recorded.

Recurrence of disease, recurrence-free and overall survival

The primary outcomes of interest were disease recurrence and recurrence-free survival. Tumor recurrence was defined as radiological evidence of disease or the presence of biopsy-proven disease following surgical resection. According to the site of tumor recurrence, recurrence was classified as either local (hepatic resection margin, bilioenteric anastomosis, porta hepatis, retroperitoneal lymph nodes) or distant (intrahepatic, peritoneum, or other extra-abdominal sites). Recurrence-free survival (RFS) was calculated from the date of surgery to the date of recurrence or last follow-up. Similarly, overall survival (OS) was calculated from the date of surgery to the date of death or last follow-up, as appropriate. For each patient, death was confirmed using hospital charts, as well as through the social security death index.

Statistical analysis

Continuous variables were reported as medians with interquartile range (IQR) or as means with standard deviation (SD) as appropriate and compared using Student's t-test or the Kruskal–Wallis test. Categorical data were reported as whole numbers and proportions and then compared using Pearson's chi-squared test. RFS and OS were estimated using the Kaplan–Meier method. Differences in RFS and OS were compared between patient groups using the log-rank test. Univariable and

Download English Version:

<https://daneshyari.com/en/article/5656332>

Download Persian Version:

<https://daneshyari.com/article/5656332>

[Daneshyari.com](https://daneshyari.com)