Minimally invasive and open gallbladder cancer resections: 30- vs 90-day mortality

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BACKGROUND: Minimally invasive surgery is increasingly used for gallbladder cancer resection. Postoperative mortality at 30 days is low, but 90-day mortality is underreported.

METHODS: Using National Cancer Database (1998-2012), all resection patients were included. Thirty- and 90-day mortality rates were compared.

RESULTS: A total of 36 067 patients were identified, 19 139 (53%) of whom underwent resection. Median age was 71 years and 70.7% were female. Ninety-day mortality following surgical resection was 2.3-fold higher than 30-mortality (17.1% vs 7.4%). There was a statistically significant increase in 30- and 90-day mortality with poorly differentiated tumors, presence of lymphovascular invasion, tumor stage, incomplete surgical resection and low-volume centers (P<0.001 for all). Even for the 1885 patients who underwent minimally invasive resection between 2010 and 2012, the 90-day mortality was 2.8-fold higher than the 30-day mortality (12.0% vs 4.3%).

CONCLUSIONS: Ninety-day mortality following gallbladder cancer resection is significantly higher than 30-day mortality. Postoperative mortality is associated with tumor grade, lymphovascular invasion, tumor stage, type and completeness of surgical resection as well as type and volume of facility.

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KEY WORDS: **gallbladder cancer; laparoscopic; minimally invasive; survival; radical cholecystectomy; complications**

Introduction

Gallbladder cancer (GBC) is the most frequent malignancy of the biliary tree.[1] The annual incidence of GBC is around 1.13 cases per 100 000 making it the 5th most common cancer of the gastrointestinal tract,[2] especially in high-risk ethnic groups.[3] The overall 5-year survival, even after resection, is reported to be 5%-21%,[4-9] likely due to the aggressive nature of the cancer, delayed presentation, and lack of effective adjuvant therapy.

Complete resection of GBC with negative margins is the only potentially curative treatment for this malignancy. Curative-intent resection recommended for T1b and more invasive tumors[10, 11] includes cholecystectomy with *en-bloc* liver resection and portal lymphadenectomy. If the cystic-duct margin is involved, then excision of the extrahepatic biliary tree is necessary. Postoperative 30-day mortality following resection of GBC has been reported to be between 1.7% and 4.2%.[5, 11] Minimally invasive surgery has long been shown to decrease length of hospital stay, recovery time, and complications following simple cholecystectomy. Laparoscopic and robotic radical cholecystectomy for GBC has been suggested to be safe, with equivalent outcomes to open resection, but generally 90-day morbidity and mortality is not reported.[12-15]

Indeed, 90-day postoperative mortality may be a more accurate marker of true postoperative mortality due to complications, since complication-related deaths are widely recognized to occur after 30 days (very few cancer-related deaths are expected within 90 days). Indeed, 90-day mortality has recently been shown to be almost double that of the 30-day mortality following

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pancreatic resection for malignancy.[16] However, data on 90-day mortality following surgical resection of GBC are limited. We hypothesized that 90-day mortality would be significantly higher than 30-day mortality following resection of GBC, but that this difference may be mitigated by minimally invasive surgery.

Methods

A retrospective review of the National Cancer Database (NCDB) was performed of all patients who were diagnosed with GBC between 1998 and 2012. NCDB is a clinical oncology database jointly sponsored by the American College of Surgeons (ACS) and the American Cancer Society. The database is a compilation of cancer registries of more than 1500 facilities accredited by the ACS Commission on Cancer and captures around 70% of the newly diagnosed cancers across the United States, including their treatments and outcomes.

Data for all patients who underwent surgical resection for a pathologically confirmed malignancy originating from the gallbladder were included. Patient comorbidities were evaluated using the Charlson/Deyo score.[17] The scores were truncated to 0, 1 and 2 where a score of 0 indicated no comorbidities, a score of 1 indicated one comorbid condition present and a score of 2 indicated more than one comorbid condition. Definitions for surgical resections were defined in NCDB and obtained from the Facility Oncology Registry Data Standards (FORDS).[18] Only patients with FORDS codes 30-60 were included, which thereby included only patients who underwent surgical resection of the gallbladder. Patients with pathologically proven malignancy originating from the gallbladder were selected as defined by the International Classification of Diseases of Oncology (ICD-O-3) histology codes.[19] Patients with codes: 8160, 8161, 8162, 8170, 8180, 8430, 8453, 8500, 8503, 8504, 8507 were excluded as these malignant diseases were not believed to have originated from the gallbladder. Pathological stage of the tumor (pTNM) was defined using the 5th, 6th, or 7th edition of the American Joint Commission on Cancer based on the year when the tumor was diagnosed. Patients with a pathological tumor stage of pT0 and pTx were also excluded.

The stage of the tumor was defined using the NCDB analytic stage group which represents the pathological stage group if reported, or the clinical stage group if the pathological stage group is not recorded. Data on the surgical approach were available only for patients diagnosed between 2010 and 2012. Surgical approaches included open, minimally invasive (laparoscopic or robotic), and minimally invasive converted to open. Hospital volume was calculated as the number of cases of GBC performed at the facility during the entire study period. Annual hospital volume was calculated by dividing hospital volume by duration of the study. Hospital volume groups and annual hospital volume groups were divided based on the quartiles. Status of margins was defined as: R0 for complete resection, R1 for incomplete resection with microscopic residual disease, and R2 for incomplete resection with macroscopic residual disease.

Patient demographic data including: age, gender, race, insurance type, income, education and distance from hospital in miles were collected. Type and location of the facility where the surgery was performed were analyzed. Histological grade of the tumor, presence of lymphovascular invasion, pathological TNM stage, and the NCDB stage were obtained. Type of surgical procedures, surgical approach, margins and the performance of lymphadenectomy were reviewed. Thirty- and 90-day mortality was compared by demographic, facility-related, pathologic and surgical variables using Fisher's exact and Chi-square tests.

Continuous variables are presented as median with interquartile range (IQR) and compared using the Wilcoxon two-sample test. Categorical variables are presented as number (percentage) and analyzed using the Fisher's exact test. Statistical significance was accepted at $P<0.05$. When comparing 30- and 90-day mortality, statistical significance was defined as nonoverlapping 95% confidence intervals (CI).

Results

We identified 36 067 patients in the NCDB with the diagnosis of GBC, 19 139 (53%) of whom underwent resection and were included in our study. The median age at diagnosis was 71 years (IQR: 62-79), and the majority were female (70.7%) and white (81.8%). The majority of the patients had insurance, either Medicare or private (59.6% and 29.0%, respectively) (Table 1).

Proportionally, GBC prevalence was greater in the South and Mid Atlantic regions and in the East North Central region (20.0%, 17.5% and 18.7%, respectively). The majority (53.5%) of operations were performed in comprehensive community cancer programs followed by academic and research programs (33.6%). The median number of resections performed by each facility during the study period was 21 cases (IQR: 13-34). Median annual hospital volume was 1.4 cases/hospital per year (IQR: 0.87-2.26) (Table 1). There was a steady increase in the number of newly diagnosed cases of GBC each year between 1998 and 2012 (Fig.).

Tumor characteristics are shown in Table 2. The vast