

Original Article

Impact of Therapeutic Interventions on Survival of Elderly Patients with Gallbladder Carcinoma: A 10-year Single Center Experience[☆]

Ching-Wei Chang^{1, 2, 3, 4}, Chun-Han Cheng^{1, 2, 3}, Tsang-En Wang^{1, 2, 3}, Chih-Jen Chen^{1, 2, 3}, Chia-Yuan Liu^{1, 2, 3, 4}, Chien-Yuan Hung^{1, 2, 3}, Horng-Yuan Wang^{1, 2, 3}, Fang-Ju Sun^{2, 5}, Ming-Jen Chen^{1, 2, 3}*

¹ Division of Gastroenterology, Department of Internal Medicine, MacKay Memorial Hospital, ² MacKay Medicine, Nursing and Management College, Taipei,

³ Department of Medicine, MacKay Medical College, New Taipei, ⁴ Institute of Traditional Medicine, National Yang-Ming University, ⁵ Department of Medical Research, MacKay Memorial Hospital, Taipei, Taiwan

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SUMMARY

Background: Primary gallbladder carcinoma (GBC) is associated with poor prognosis. This study aimed to clarify the age-specific clinical characteristics of primary GBC among elderly patients.

Methods: We retrospectively reviewed the medical records of patients with GBC treated in Mackay Memorial Hospital, Taipei, Taiwan over a period of 10 years, from 2003 to 2012. Patients aged 65 years or older at the time of diagnosis of primary GBC were defined as the elderly group. According to the Kaplan–Meier method, survival curves were compared between patients receiving surgical treatment or not.

Results: In total, 64 patients with primary GBC were reviewed. Forty-eight patients (75%) were included in the elderly group. Mean age of the patients at the time of diagnosis was 77.8 ± 7.1 years. Compared with young group, the serum level of carcinoembryonic antigen was significantly higher ($p = 0.025$) and hemoglobin was significantly lower ($p = 0.025$) in the elderly group. The percentages of elderly patients in the tumor–node–metastasis (TNM) Stages 0–III and IV were 50.0%, and 50.0%, respectively. Twenty-six patients received surgical resection. The cumulative survival curves of the surgical intervention and nonsurgical intervention groups differed significantly for elderly patients in the TNM Stages 0–III ($p = 0.002$) and Stage IV ($p = 0.041$).

Conclusion: Most elderly patients at the time of diagnosis of GBC were in TNM Stage IV. Surgery was the predominant treatment at our hospital. Surgical interventions might be associated with better survival for elderly patients with GBC.

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1. Introduction

Primary gallbladder carcinoma (GBC) is relatively rare, although it is the most common biliary tract cancer^{1,2}. Due to the low incidence and the lack of recognized symptoms, GBC patients often have advanced disease when diagnosed, leading to a poor prognosis and high mortality rate. The risk of developing GBC is known to be age dependent;³ therefore, an increased number of elderly

patients will be diagnosed with GBC in the coming years owing to the general increase in the population longevity. The only effective and potential curative treatment is surgery. However, the majority of instances the lesions are considered unresectable at the time of surgical exploration because of local invasion into critical structures or metastases beyond locoregional confines. In these situations, treatment is palliative in nature. The goals of palliation for advanced GBC are relief of pain, jaundice, and bowel obstruction, and prolongation of life^{1,2}.

The elderly are usually defined as to be aged 65 years and older. Approximately 60% percent of new cases and 70% of mortality from cancer occur in patients older than 65 years^{4–6}. As a result, the care of older patients constitutes an important part of everyday clinical practice. Compared with younger age patients, the elderly group shows significantly higher comorbidity, particularly with

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* Correspondence to: Dr Ming-Jen Chen, Division of Gastroenterology, Department of Internal Medicine, MacKay Memorial Hospital, Number 92, Section 2, Chung-Shan North Road, Taipei 10449, Taiwan.

E-mail address: mingjen.ch@msa.hinet.net (M.-J. Chen).

pulmonary and cardiovascular diseases⁷. Due to the fact that treatment is often withheld from them for fear of potential toxicities or perceived minimal survival benefit, many elderly patients do not receive optimal cancer treatment^{4–6}. Hence, clarifying the optimal treatment strategy for elderly patients with GBC has become an urgent necessity. To our knowledge, there have been few studies evaluating elderly patients with GBC. In this study, our aim was to clarify the age-specific clinical characteristics of GBC, and to evaluate the survival and characteristics of elderly patients with GBC aged over 65 years retrospectively.

2. Materials and methods

From January 2003 to December 2012, a total of 99 patients were diagnosed with GBC at MacKay Memorial Hospital, Taipei, Taiwan. Patients aged 65 years or older at the time of diagnosis of primary GBC were defined as the elderly group.

For each patient, the following data were recorded by retrospective chart review: patient demographics; presence of medical comorbidities; symptoms at presentation; biochemical analysis; serum carbohydrate antigen (CA19-9) and carcinoembryonic antigen (CEA) level; tumor staging; initial therapy; extents of resection; pathology; and survival. The imaging studies included abdominal ultrasonography, computed tomography, magnetic resonance imaging, magnetic resonance cholangiopancreatography, and endoscopic retrograde cholangiopancreatography. The follow-up end point was December 2013. The medical records of 35 patients did not contain sufficient information and those patients were excluded from this report. The series consists of the remaining 64 patients who were treated, and the data concerning these patients were reviewed retrospectively. The treatments were performed according to the current guidelines for treatment of GBC^{1,2,8}. Performance status was not disclosed because many patients lacked this information.

The 7th edition of the American Joint Committee on cancer staging system was used for tumor–node–metastasis (TNM) cancer staging⁹. The types of initial treatment for GBC were categorized into four categories: (1) surgical resection, extended surgery, and palliative surgery; (2) systemic chemotherapy; (3) radiotherapy; and (4) supportive care. Extended surgery was defined as cholecystectomy with one or more of the following procedures: liver resection (partial hepatectomy or resection of gallbladder fossa), lymph node dissection along the hepatoduodenal ligament, resection of extrahepatic bile duct. Palliative surgery included cholecystostomy, tube drainage of the bile duct, or biopsy of the tumor only. Cholecystectomy was defined as cholecystectomy alone or cholecystectomy with drainage of the bile duct. The TNM stage categories were grouped as 0–III and IV for statistical analysis because of the low number of patients within such categories. According to the Kaplan–Meier method, survival curve were compared between patients receiving surgery or not. This study was approved by the Institute Review Board of MacKay Memorial Hospital.

2.1. Statistical analysis

The data are expressed as the mean \pm standard deviation for continuous variables and n (%) for categorical variables. Statistical analyses were carried out using the Student t test for unpaired continuous data, or χ^2 test or Fisher's exact test as appropriate for categorical data. The cumulative survival curves according to the Kaplan–Meier method were compared using the log-rank test. A p value < 0.05 was considered to represent statistical significance. All statistical analyses were performed using the SPSS version 21.0 software package (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Demographic characteristics of the study population

A total of 64 consecutive patients were enrolled in this study. The age distribution of patients with GBC is shown in Figure 1. The most common symptom was epigastric pain (55%), followed by right upper quadrante pain (23%), jaundice (23%), and nausea/vomiting (23%; Table 1). The demographic and characteristics of the patients with GBC are summarized in Table 2. The mean age of the 64 patients with GBC at the time of diagnosis was 70.9 ± 13.4 years (range, 36–92 years; median, 73 years). Most patients with GBC had gallstone (60%) and thickened gallbladder (GB) wall (> 3 mm; 47.4%). Forty-eight patients (75%) were older than 65 years (elderly group). Mean age of the elderly patients at the time of diagnosis was 77.2 ± 7.4 years. The sex ratio (male to female) was 17:31. There were no significant difference between the elderly and young groups in sex, gallstone, thickened GB wall, or GB polyps. However, compared with young patients, there was a trend increase in the proportion of elderly patients in recent years (data not shown).

On biochemical analysis (Table 3), there was significantly lower level of hemoglobin in the elderly group compared with young group ($p = 0.025$). The level of CEA was significant higher in elderly group compared with young group ($p = 0.025$). Most of the histologically proven GBC (94.3%) were adenocarcinomas and the others were undifferentiated carcinoma (data not shown).

3.2. Therapeutic management and outcome of GBC

There was no significant difference between the elderly and young groups in mortality at the end of the follow-up time (Table 2). The overall 5-year survival rate was 9.4% ($n = 6$). Table 4 shows the initial treatment modalities for these elderly patients. The percentages of elderly patients in the TNM Stages I–III and IV were 50.0%, and 50.0%, respectively. A total of 26 patients underwent surgery treatment. TNM Stages IIIa + IIIb ($n = 10$, 38.5%) was the most frequent group. Most of these 26 patients received surgical interventions; the portion of the surgical resection, extended surgery, and palliative surgery was 69.2%, 26.9%, and 3.8%, respectively. Twenty-two patients received nonsurgery treatment; the portion of chemotherapy, radiotherapy, and supportive care was

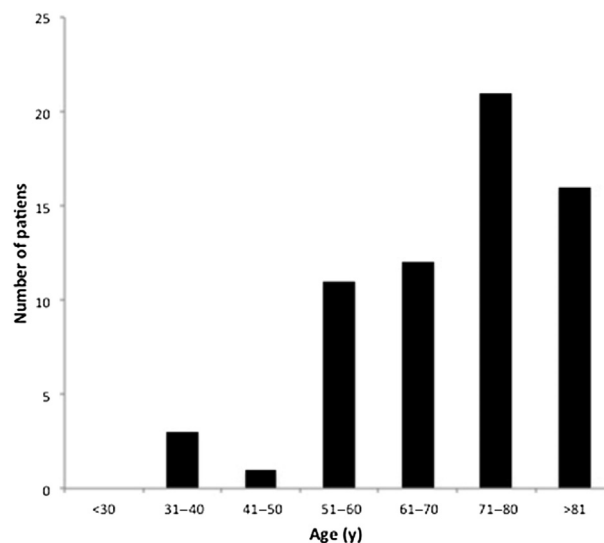


Figure 1. Age distribution of the patients with primary gallbladder carcinoma.

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