



ORIGINAL ARTICLE

Clinical factors associated with the survival of patients with intrahepatic cholangiocarcinoma



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KEYWORDS

Cholangiocarcinoma;
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Summary *Background and aim:* Intrahepatic cholangiocellular carcinoma (ICC) is an uncommon but lethal cancer. The aim of this study is to assess the factors affecting the survival of ICC patients and to evaluate the benefit of these factors when various therapeutic modalities are used.

Methods: Between October 2007 and June 2012, 66 ICC cases among 2255 liver cancer patients were identified by pathology and divided into two groups: Group I (surgery group; $n = 17$) and Group II (nonsurgery group; $n = 49$). Group II was further divided into Group IIa (those receiving palliative treatment; $n = 19$) and Group IIb (no treatment received; $n = 30$). Factors affecting patient survival over the study period were assessed (3- and 6-month results were reported) and therapeutic benefits identified within each of the groups were evaluated.

Results: Of the 66 patients identified (male/female = 36/30), 10.6% (7/66) were in the early stages of illness. Overall, the mean patient survival duration was 3.50 ± 0.92 months (1.69–5.31 months). The mean survival duration of Group I patients was 10.50 ± 2.84 months (4.94–16.06 months). The mean survival duration of Group II patients was 3.50 ± 0.65 months (2.24–4.76 months) with Group IIa patients surviving on average 9.50 ± 3.27 months (3.10–15.90 months) and Group IIb patients surviving on average 1.50 ± 0.12 months (1.26–1.74 months). Better survival outcomes were observed in the groups receiving treatment, Group I and Group IIa, than in Group IIb, which did not receive treatment [9.50 ± 1.73 months (6.12–12.89 months) vs. 1.50 ± 0.12 months (1.26–1.74 months), $p < 0.001$]. Lower albumin, higher

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bilirubin, higher CA19-9, advanced tumor stage, and no treatment were identified as important predictors of patient mortality at the 3- and 6-month time-points. These factors remained relevant throughout the entire study period ($p = 0.002, 0.029, 0.027, 0.028, < 0.001$, respectively).

Conclusion: This study identified surgery as the treatment that provided the best survival prognosis for patients with ICC. Treatment involving either chemotherapy or radiotherapy could also prolong ICC patient survival. Better liver preservation, lower CA19-9, and less aggressive tumor conditions were identified as factors which play crucial roles in enhancing patient survival.

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Introduction

Cholangiocarcinoma is a relatively uncommon but lethal cancer of the biliary epithelium; it accounts for 10–25% of all hepatobiliary malignancies [1,2]. Various risk factors for cholangiocarcinoma and a number of different diagnostic/therapeutic modalities have been examined in clinical scenarios in order to understand the factors affecting survival of patients with this disease. To date a satisfactory solution to this global problem has not been found. Attempts to identify the factors affecting patient survival have been impeded by: (1) a lack of disease-specific symptoms in early stages; (2) surgical resection not being an appropriate treatment option; and (3) high rates of tumor recurrence following surgical resection [3–9].

According to anatomic locations, cholangiocarcinoma is classified into three subtypes, including: (1) intrahepatic cholangiocarcinoma (ICC); (2) perihilar cholangiocarcinoma (PCC); and (3) distal cholangiocarcinoma (DCC) [8]. Results from a large, single-centered study found that ICC accounted for less than 10% of cases of cholangiocarcinoma; PCC for 50%; and DCC for approximately 40% [10]. In contrast to PCC and DCC, the incidence of ICC saw a steady increase of 22% between 1979 and 2004 due to advances in diagnostic techniques in Western countries [6,11,12]. This increase in incidence was accompanied by a 39% increase in mortality [12]. ICC has overtaken hepatocellular carcinoma (HCC) as the leading cause of death in the UK since the mid-1990s [13]. Previous studies describe the distinction between ICC and extrahepatic cholangiocarcinoma [14], but potential risk factors remain unknown [2]. Therefore, establishing the prognostic factors and locations of tumor involvement such as peripheral or main bile ducts or extrahepatic metastasis may decide the patient's prognosis prior to implementation of intervention options.

To attain the greatest benefit in clinical scenarios, two points were assessed in this study. First the predictive factors affecting survival over the study period (including 3- and 6-month results) were investigated. These factors were then used to further elucidate the benefits of various modalities, which included curative, palliative, and no treatment, in ICC patients. We expect this study to provide valuable information which can be used in clinical settings.

Patients and methods

Patients

Between October 2007 and June 2012, 2255 patients with liver cancer were identified at China Medical University Hospital, Taichung, Taiwan. Well-characterized clinical data were recorded for all patients: e.g., liver function, renal function, hematological examination, and tumor markers. Tumor staging was based on abdominal computerized tomography and confirmed histopathology by pathologists. After exclusion criteria were applied, 66 ICC patients with positive pathology were enrolled in this study; their clinical results were recorded until July 2014. The exclusion criteria included patients with hepatocellular carcinoma (HCC), combined HCC with cholangiocarcinoma, secondary tumors, and cholangiocarcinoma subtypes PCC and ICC.

Definition

ICC is a cholangiocarcinoma subtype affecting the intrahepatic biliary tract and classification of tumor involvement is made according to the American Joint Committee on Cancer (AJCC) TNM (tumor, node, and metastases) Staging System [15]. According to initial therapy, therapeutic modalities were classified into three groups which were Group I, Group IIa and Group IIb. Group I (surgery group) included patients with potentially resectable tumors according to standard operative approach [16]; Group II (nonsurgery group) included patients with unresectable tumors. Group II was further divided into two sub-groups: Group IIa (palliative treatment) which included patients treated by chemotherapy (e.g., cisplatin, gemcitabine, fluorouracil, leucovorin) or radiotherapy, and Group IIb (no treatment) which included patients receiving either palliative biliary drainage or no treatment.

Serological virus markers and liver biochemical assays

Commercial enzyme immunoassay rated HBV (hepatitis B virus) markers (HBsAg, anti-HBs, HBeAg, anti-HBe) (AxSYM, Abbott, North Chicago, IL, USA) and anti-HCV (hepatitis C

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