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ORIGINAL ARTICLE

Comparison of the prognostic accuracy of the sixth and seventh editions of the TNM classification for intrahepatic cholangiocarcinoma

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Abstract

Background: The seventh TNM edition introduced a new, specific staging structure for intrahepatic cholangiocarcinoma (IHC).

Objective: To compare the accuracy of the sixth and the new seventh edition to predict survival after hepatectomy for IHC.

Methods: In all, 434 consecutive patients who underwent hepatectomy at 16 tertiary-care centres (1990–2008) were identified. End points were overall (OS) and recurrence-free survival (RFS) for both T cohorts and stage strata.

Results: After a median follow-up of 32.4 months, 3- and 5-year OS and RFS estimates were 47.1% and 32.9%, and 26.5% and 19.1%, respectively. Overall, both the editions were statistically significant discriminators of OS and RFS ($P < 0.05$). However, the survival curves of the new T2a and T2b cohorts appear superimposed. Conversely, the old T2 and T3 cohorts accurately stratify patients into distinct prognostic groups ($P < 0.01$). The seventh edition does not show monotonicity of gradients (the T4 category demonstrates significantly better OS and RFS compared with T2 patients). The seventh edition stage I and II are significantly different whereas the old stage I and II were not.

Conclusions: The new seventh edition of the *AJCC/UICC Staging System* proved to be adequate although further studies are need to confirm its superiority compared with the previous edition.

Keywords

intrahepatic cholangiocarcinoma, hepatic resection, prognosis, staging, TNM classification

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Introduction

Intrahepatic cholangiocarcinoma (IHC) is the second commonest primary malignant neoplasm of the liver, originating from the epithelium of the second-order or more proximal bile ducts. Although rising incidence rates, paralleled by mortality rates, have been documented in most areas worldwide,[1,2] IHC remains a rare disease when compared with hepatocellular carcinoma (HCC). Data from the 17th nationwide follow-up survey of primary liver cancer in Japan indicate that IHC accounts for only 4.1% of the newly diagnosed liver tumours.[3] In non-endemic geographical regions, such as the United States, this proportion is estimated to be slightly higher (approximately 10%).[1] The rarity of the disease and the frequency with which patients present at a late, unresectable stage (80–85%),[4] had hampered an in-depth understanding of the prognostic factors associated with poor survival after resection. In western countries, the severity or stage of an individual's cancer has traditionally been evaluated on the basis of the TNM staging system which classifies cancers by the size and extent of the primary tumour (T), involvement of regional lymph nodes (N) and the presence or absence of distant metastases (M). In 1988, in the 3rd edition of the TNM staging manual, the American Joint Committee on Cancer (AJCC) and the International Union for Cancer Control (UICC) devised a separate staging system for primary liver cancers, which applied to both HCC and IHC. However, this original staging algorithm as well as all subsequent revisions was based only on data obtained from patients resected for HCC. Nonetheless, HCC and IHC differ significantly in pathogenesis, tumour behaviour and prognosis after surgical resection. Therefore, after two decades, the development of a separate staging with specific relevance to IHC was critical as information derived from staging not only provides data regarding prognosis, but also dictates patient stratification in clinical research. Based on the analysis of data obtained form The Surveillance, Epidemiology, and End Results (SEER) database on 598 unselected patients who had undergone surgery for IHC, Nathan *et al.*[5] proposed a new staging schema which was adopted in the seventh edition of the *TNM Staging Manual*.[6] However, this novel staging system, which is independent of the staging systems for HCC and extahepatic bile duct malignancy, has not been externally validated nor compared with the sixth edition classification schema.[7] The purpose of the present study was to compare the prognostic accuracy of the sixth and the new seventh edition of the AJCC/UICC staging systems to predict survival after liver resection for IHC in a large series of patients treated at tertiary hepatobiliary centres.

Methods

In all, 434 consecutive patients treated with curative intent liver resection for IHC between March 1990 and December 2008 at 16 tertiary hepatobiliary centres were identified from each institution's prospectively collected database. Pathological data of all patients were reviewed to confirm the diagnosis of IHC which was based on the histopathological examination of haematoxylin and eosin (H&E) and cytokeratin-stained sections. Patients with mixed IHC/HCC and hilar (Klatskin) adenocarcinomas were considered ineligible for entering this study. Before surgery, all

Table 1 sixth and seventh edition of the AJCC/UICC TNM classification algorithm for intrahepatic cholangiocarcinoma (IHC)

sixth edition		seventh edition	
T1	Solitary tumour without vascular invasion	T1	Solitary tumour without vascular invasion
T2	Solitary tumour with vascular invasion or multiple tumours, none more than 5 cm	T2a	Solitary tumour with vascular invasion
T3	Multiple tumours more than 5 cm or tumour involving a major branch of the portal or hepatic veins	T2b	Multiple tumours, with or without vascular invasion
T4	Tumour(s) with direct invasion of adjacent organs other than the gallbladder or with perforation of visceral peritoneum	T3	Tumour(s) perforating the visceral peritoneum or involving the local extra hepatic structures by direct invasion
		T4	Tumour with periductal invasion
N0 no regional lymph node metastases		N0 no regional lymph node metastases	
N1 regional lymph node metastases		N1 regional lymph node metastases	
M0 no regional lymph node metastases		M0 no regional lymph node metastases	
M1 regional lymph node metastases		M1 regional lymph node metastases	
Stage		*Stage*	
I	T1 N0 M0	I	T1 N0 M0
II	T2 N0 M0	II	T2 N0 M0
IIIa	T3 N0 M0	III	T3 N0 M0
IIIb	T4 N0 M0	IVa	T4 N0 M0, Any T N1 Mo
IIIc	Any T N1 M0	IVb	Any T, Any N, M1
IV	Any T, Any N, M1		