

ORIGINAL ARTICLE

Clinicopathological analysis and prognosis of extrahepatic bile duct cancer with a microscopic positive ductal margin

In Woong Han^{1*}, Jin-Young Jang^{2*}, Kyoung Bun Lee³, Mee Joo Kang², Wooil Kwon², Jae Woo Park², Ye Rim Chang² & Sun-Whe Kim²

¹Department of Surgery, Dongguk University College of Medicine, Goyang, ²Department of Surgery & Cancer Research Institute, and ³Department of Pathology, Seoul National University College of Medicine, Seoul, South Korea

Abstract

Background: The fate of a microscopic positive ductal margin (MPDM) of extrahepatic bile duct (EHBD) cancer is unclear. The purpose of this study was to analyse the clinicopathological features of EHBD cancer with MPDM and to identify the prognostic factors associated with survival.

Methods: Between 1995 and 2007, a retrospective analysis of 464 patients who had undergone surgical resection for EHBD cancer was conducted. Clinicopathological factors likely to influence survival were assessed using univariate and multivariate analysis.

Results: One hundred twenty-four patients had MPDM which included invasive carcinoma (IC) ($n=85$) and carcinoma *in situ* (CIS)/ high-grade dysplasia (HGD) ($n=39$). The median survival (MS) of R0, R1 as CIS/ HGD, and R1 as IC were 41 months, 29 months, and 18 months, respectively. Adverse prognostic factors were 'IC' on the resection margin [HR = 1.66, 95% confidence intervals (CIs) 1.06–2.59, $P=0.026$], and no use of adjuvant chemoradiotherapy (HR = 1.57, 95% CIs 1.04–2.39, $P=0.033$). Adjuvant chemoradiotherapy was beneficial in patients with MPDM as IC (5-year survival rate 19.7 compared with 2.8%, $P=0.011$).

Conclusions: The presence of MPDM is an important prognostic factor in EHBD cancer. When a ductal resection margin is positive, discrimination between 'IC' and 'CIS/ HGD' is important.

Received 31 July 2013; accepted 1 October 2013

Correspondence

Sun-Whe Kim, Department of Surgery, Seoul National University College of Medicine, 28 Yongon-dong, Chongno-gu, Seoul 110-744, South Korea. Tel.: 82 2 2072 2315. Fax: 82 2745 2282. E-mail: sunkim@snu.ac.kr

Introduction

A surgical resection has been the mainstay of curative treatment for extrahepatic bile duct (EHBD) cancer. Overall, 5-year survival rates (5YSR) of 20–35% have been reported after resection of EHBD cancer.^{1–3} In addition, most patients who undergo a resection die of local tumour recurrence.^{4,5} This is because a complete surgical resection with tumour-free histological margins is difficult to obtain.

Anatomically, EHBD cancers are classified as perihilar and distal bile duct cancers.⁴ However, tumours are rarely confined to

the short segment as bile duct cancer tends to longitudinally spread along the bile duct wall.^{6,7} Recent advances in imaging modalities and surgical strategies have improved the outcome of the surgical treatment for EHBD cancer. A surgical resection for EHBD cancer is determined by the location and extent of the tumour.^{3,6–13}

Although a pre-operative diagnosis for the extension of EHBD cancer has improved in recent years, it is difficult to decide the surgical resection margin pre-operatively.^{13,14} In some patients, a margin positive resection was inevitable considering the operative risk. A positive resection margin has been considered an adverse prognostic factor;^{6,15–24} however, the reported incidence of a positive surgical resection margin in patients who have undergone a resection with curative intent has varied from 9% to as high as 74%.^{20,24,25} This could be explained by a variation

*I.W. Han and J.Y. Jang equally contributed to this article.

This manuscript was presented at the 10th World IHPBA Congress, Paris, 1–5 July 2012.

between institutions or investigators on the principle of the operation or the definition of a positive resection margin. However, there are few reports on the long-term outcome and factor analysis associated with survival in patients with a positive resection margin.

The purpose of this retrospective study was to analyse the clinicopathological features of EHBD cancer with a microscopic positive ductal margin (MPDM) after a surgical resection, and to explore the prognostic factors in patients with EHBD cancer with MPDM. The clarification of whether residual carcinoma *in situ* (CIS)/high-grade dysplasia (HGD) at ductal resection margins differs prognostically from residual invasive ductal disease in patients with EHBD cancer was also assessed.

Patients and methods

Patients and surgical procedures

With the approval from the institutional review board, all patients with EHBD cancer who underwent a resection at Seoul National University Hospital (SNUH) were entered into a prospectively maintained database between 1995 and 2007.

Pre-operatively, the predominant location of the tumour and the extent of the tumour along the biliary tract were evaluated using imaging studies, including an enhanced computed tomography (CT) scan, ultrasonography, magnetic resonance imaging (MRI), cholangiography and sometimes choledochoscopy. Surgical procedures were decided by each attending surgeon with consideration of the balance between the tumour extent and the safety of each procedure. Distant metastasis, extensive lymph node metastasis such as para-aortic lymph node involvement, bilateral extensive intrahepatic duct infiltration, involvement of major vessels except focal portal vein invasion and other systemic poor operative risk factors were contraindications of a curative resection.

After a laparotomy and the exclusion of distant metastasis, all of the following surgical procedures including a regional lymphadenectomy at the right side of the celiac artery, and all tissues in the hepatoduodenal ligament except the portal vein and the hepatic artery, were removed (skeletonization of the hepatoduodenal ligament).⁶ The type of resection was determined by the location and extent of the tumour. In patients with localized bile duct cancer in the hepatoduodenal ligament, an EHBD resection (BDR) was adopted, especially in patients in a poor general health condition or with high-risk factors. As the tumour was mainly located in the perihilar bile duct or involved in the liver parenchyma, unilateral hepatic artery, or portal vein, an extended hemihepatectomy including caudate lobectomy combined with bile duct resection (HBR) was performed.⁶ When the tumour was chiefly located in the distal bile duct, a pancreatoduodenectomy (PD) was usually performed. Since 1991, pylorus preservation has been attempted in all patients undergoing PD, except when duodenal ischaemia, duodenal ulcer or duodenal tumor infiltration was present. A hepatopancreatoduodenectomy (HPD) was indicated in patients with diffuse bile duct cancer.⁶

Diagnosis and definition of surgical margins

A R0 resection was defined as no residual ductal disease. Intra-operative evaluation of the proximal (hepatic)-side and/or distal (duodenal)-side ductal margins was performed using frozen sections among all patients. Operative specimens were submitted for permanent histopathology. On the basis of the type of resection procedure performed, the appropriate proximal and distal bile duct margins were identified, and a cross-section of each was submitted for histology. When the distal-side ductal margin was positive, additional resection of the intra-pancreatic bile duct or PD was performed, as far as possible in principle. When the proximal-side ductal margin was positive, additional resection of the hepatic duct or an additional hepatectomy was performed where possible. Positive surgical margins were classified into two categories: 'invasive carcinoma (IC)' and 'CIS/HGD'. In the present study, HGD was included in the category of CIS owing to the extreme difficulty of distinguishing between the two epithelial lesions.²⁰ Radial margins were defined as surgical margins other than the ductal margins of the resected specimen, but there were no isolated positive radial margins without MPDM. Microscopic positive ductal margins were confirmed by permanent pathological examination of a resected margin.

Comparison of clinicopathological variables in patients with MPDM and patients follow-up

Resected specimens were submitted to the Department of Pathology in SNUH for histological evaluation, in which experienced hepatobiliary pathologists examined all the specimens without knowledge of any previous diagnoses and clinical details. Clinicopathological variables including age, gender, location of a positive margin, histological grade and type of patient with MPDM were evaluated. Histological findings were described in accordance with the 7th edition TNM staging of the American Joint Committee on Cancer (AJCC).²⁶

Patients were followed regularly in outpatient clinics every 3–6 months, and the information during follow-up for all patients was obtained. The sites of initial disease recurrence were determined from cross-sectional imaging studies, such as computed tomography or magnetic resonance imaging. They were classified as local disease recurrence (resection margin, bilioenteric anastomosis, or porta hepatis), regional disease recurrence (retroperitoneal lymph nodes) and distant disease recurrence (intrahepatic, peritoneum, or extra-abdominal sites). The overall survival was analysed from the date of surgical resection to the date of death from all causes. The causes of death were determined from the medical records. The follow-up period was defined as the intervals between the date of surgical resection and that of the last follow-up.

Adjuvant treatment

Other than for poor performance status or refusal to the chemotherapy or chemoradiation, adjuvant treatment was performed after the patients were informed of the prognosis and of the effects of each treatment modality. Decisions were made after thorough discussions with patients, physicians and each attending surgeon.

Download English Version:

<https://daneshyari.com/en/article/3269091>

Download Persian Version:

<https://daneshyari.com/article/3269091>

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