

## ORIGINAL ARTICLE

# Outcomes of hepatectomy for hepatocellular carcinoma with bile duct tumour thrombus

Tiffany C. L. Wong, Tan To Cheung, Kenneth S. H. Chok, Albert C. Y. Chan, Wing Chiu Dai, See Ching Chan, Ronnie T. P. Poon, Sheung Tat Fan & Chung Mau Lo

Department of Surgery, The University of Hong Kong, Hong Kong, China

## Abstract

**Background:** Hepatocellular carcinoma (HCC) with bile duct tumour thrombus (BDTT) is rare. The aim of the present study was to determine the prognosis of HCC with BDTT after a hepatectomy.

**Methods:** A retrospective analysis was performed on all HCC patients with BDTT having a hepatectomy from 1989 to 2012. The outcomes in these patients were compared with those in the control patients matched on a 1:6 ratio.

**Results:** Thirty-seven HCC patients with BDTT having a hepatectomy (the BDTT group) were compared with 222 control patients. Patients in the BDTT group had poorer liver function (43.2% had Child–Pugh B disease). More patients in this group had a major hepatectomy (91.9% versus 27.5%,  $P = 0.001$ ), portal vein resection (10.8% versus 1.4%,  $P = 0.006$ ), en-bloc resection with adjacent structures (16.2% versus 5.4%,  $P = 0.041$ ), hepaticojejunostomy (75.7% versus 1.6%,  $P < 0.001$ ) and complications (51.4% versus 31.1%,  $P = 0.016$ ). The two groups had similar hospital mortality (2.7% versus 5.0%,  $P = 0.856$ ), 5-year overall survival (38.5% versus 34.6%,  $P = 0.59$ ) and 5-year disease-free survival (21.1% versus 20.8%,  $P = 0.81$ ). Multivariate analysis showed that lymphovascular permeation, tumour size and post-operative complication were significant predictors for worse survival whereas BDTT was not.

**Discussion:** A major hepatectomy, extrahepatic biliary resection and hepaticojejunostomy should be the standard for HCC with BDTT, and long-term survival is possible after radical surgery.

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## Correspondence

Sheung Tat Fan, Department of Surgery, The University of Hong Kong, 102 Pok Fu Lam Road, Hong Kong, China. Tel: +852 2255 4703. Fax: +852 2855 1897. E-mail: stfan@hku.hk

## Introduction

Hepatocellular carcinoma (HCC) is the fifth most common cancer in men and the ninth in women and is the second most common cause of cancer death worldwide.<sup>1</sup> Jaundice is a poor prognostic sign and occurs in 5–44% of HCC patients.<sup>2</sup> It is often caused by tumour infiltration or liver failure owing to underlying decompensated cirrhosis. Obstructive jaundice is a rare phenomenon and the first case of obstructive jaundice in HCC was reported in 1947 by Mallory *et al.* where the tumour invaded the gall bladder and caused extrinsic compression of the bile duct.<sup>3</sup> Besides direct tumour invasion, obstructive jaundice could also be

caused by bile duct tumour thrombus (BDTT), haemobilia and extrinsic compression of the bile duct by metastatic lymphadenopathy at the porta hepatis.<sup>2</sup> Among them, BDTT in HCC is a special clinical entity as the pathological characteristics of these tumours and their impact on disease prognosis remain unclear.

Obstructive jaundice together with the very often concomitant haemobilia and cholangitis caused by BDTT has made the assessment and evaluation of hepatectomy difficult. Treatment such as resection, transarterial chemoembolization or systemic treatment for HCC is usually not possible as a result of poor liver function. The prognosis of HCC with BDTT is also not well understood.<sup>4,5</sup> There is controversy whether HCC with BDTT has the same outcomes after hepatectomy as HCC without BDTT.<sup>5–12</sup> Besides prognosis, evidence is lacking on the preferred method for biliary drainage, extent of hepatectomy and the need

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for extrahepatic bile duct resection and hepaticojejunostomy (HJ) in these patients.<sup>6–8,13–20</sup> The aim of this study was to review the pathological characteristics of HCC with BDTT and the outcomes of these tumours after a hepatectomy.

## Patients and methods

From January 1989 to December 2012, 1459 patients underwent a hepatectomy for HCC at the Department of Surgery, Queen Mary Hospital, The University of Hong Kong, Hong Kong. Base-line demographic data of patients including age, gender, liver function, medical comorbidity and hepatitis status, as well as clinicopathological data including tumour size, number, site, radiological features of tumour, operative details and histology of resected tumours, were prospectively collected and entered into a computerized database. Thirty-seven patients with pathologically confirmed HCC with BDTT were identified and their outcomes were compared with those of the 222 (1:6) control patients (i.e. HCC without BDTT) during the same study period. The matching criteria were TNM stage (UICC 6<sup>th</sup> edition) and lymphovascular permeation status.

### Pre-operative assessment

All patients had contrast computed tomography (CT) or magnetic resonance imaging (MRI) to evaluate liver or biliary pathology. Assessment of liver function was based on patients' liver biochemistry, coagulation profile, Child–Pugh classification and the indocyanine green (ICG) clearance test. Before 1997, ICG retention at 15 min (ICG R-15) of  $\leq 14\%$  was considered the safety limit for a major hepatectomy. Since 1997, the safety limit has been extended to ICG R-15 up to 20%.<sup>21,22</sup> A major hepatectomy was defined as resection of three or more Couinaud liver segments.<sup>23</sup> CT volumetry of the liver was performed to evaluate the size of the liver remnant. Portal vein embolization was done to induce hypertrophy of the contralateral lobe if the remnant liver volume was  $\leq 30\%$ .

### Pre-operative biliary drainage

In patients with biochemical and radiological features of biliary obstruction, biliary drainage was indicated and the choice between endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic biliary drainage (PTBD) was based on individual surgeons' preference. ERCP at our centre was performed by the same team of hepatobiliary surgeons. In general, ERCP was the drainage method of choice as it was associated with lower procedure risks and obviated the problems of external drainage. A proper cholangiogram was essential to demonstrate the extent of BDTT, as it would guide our subsequent resection strategy. Extraction of BDTT would be done whenever possible, using a balloon catheter and stone basket to facilitate bile drainage. In the case of obstructive jaundice, drainage of the remnant liver was mandatory. For the tumour involved

lobe, drainage was performed whenever there was biliary sepsis. An antibiotic was prescribed according to bile bacteriology.

Aggressive biliary drainage was an important step to improve patients' liver function and to treat cholangitis. Therefore, more than one attempt of ERCP/PTBD might be necessary and sometimes with a combined approach (both ERCP and PTBD) as well. A total bilirubin level  $\leq 50$   $\mu\text{mol/l}$  or a decrease in total bilirubin level by  $>50\%$  and the absence of sepsis were prerequisites for a major hepatectomy.

### Operative details

In general, our standard procedure was a major hepatectomy with extrahepatic bile duct resection with HJ in HCC with BDTT. Resection of the main portal vein and reconstruction would be performed if the main portal vein was encased. The ultimate goal for surgery was clearance of the tumour (both macroscopic and microscopic) and because of potential seeding of tumour cells along the bile duct into the common bile duct, resecting the extrahepatic bile duct with HJ reconstruction has been our routine in the past 15 years.

Our operative techniques were published in detail previously.<sup>24</sup> Patients were given a light meal on the day before a hepatectomy. Antibiotic and proton pump inhibitor were given at induction of anaesthesia. Surgery was performed usually through a right subcostal incision with midline extension, sometimes converted to a bilateral subcostal incision if necessary. A full laparotomy was done to rule out occult metastasis. Intra-operative ultrasonography was performed routinely to detect an additional nodule, to determine the tumour margin and the transection plane, and to define the tumour's relationship with major vasculatures. A liver transection was performed using an ultrasonic dissector. Branches of the bile duct and vessels were controlled with metal clips or ligatures. The anterior approach was reserved for patients with large tumours. The Pringle manoeuvre was not used routinely unless liver transection was difficult as a result of venous congestion. The hepatic vein was divided extrahepatically with a vascular linear stapler (Ethicon Endo-surgery, Cincinnati, OH, USA). The hepatic duct and common bile duct were isolated and divided, the hepatic duct and distal common bile duct margins were sent for frozen section to rule out tumour involvement. The extrahepatic bile duct was delivered en bloc with a hepatectomy specimen. Bilioenteric reconstruction was fashioned with Roux-en-Y HJ using 6/0 PDS, the posterior layer was sutured in a continuous and the anterior layer was sutured in an interrupted manner. No biliary stent or splintage tube was inserted to the HJ.

Meticulous attention was paid to protect the liver remnant with avoidance of excessive rotation or compression. Haemostasis was secured using diathermy, argon beam coagulator and sutures. Thorough irrigation with normal saline was performed and no drain was deployed unless there was doubt about bile leakage.

### Post-operative care

After surgery, all patients who had a major hepatectomy were cared for in the high-dependency unit. Patients were extubated

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