

ORIGINAL ARTICLE

# Risk factors for a high Comprehensive Complication Index score after major hepatectomy for biliary cancer: a study of 229 patients at a single institution

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## Abstract

**Background:** The Comprehensive Complication Index (CCI) is a new tool to evaluate the postoperative condition by calculating the sum of all complications weighted by their severity. The aim of this study was to identify independent risk factors for a high CCI score ( $\geq 40$ ) in 229 patients after major hepatectomies with biliary reconstruction for biliary cancers.

**Methods:** The CCI was calculated online via [www.assessurgery.com](http://www.assessurgery.com). Independent risk factors were identified by multivariable analysis.

**Results:** 57 (25%) patients were classified as having CCI  $\geq 40$ . On multivariable analysis, volume of intraoperative blood loss ( $\geq 2.5$  L) ( $p = 0.004$ ) and combined pancreatoduodenectomy (PD) ( $p = 0.006$ ) were independent risk factors for CCI  $\geq 40$ . A high level of maximum serum total bilirubin was identified as independent risk factors for a high volume of intraoperative blood loss. Liver failure ( $p = 0.046$ ) was more frequent in patients with combined PD than in those without.

**Discussion:** Patients who undergo preoperative external biliary drainage for severe jaundice might have impaired production of coagulation factors. When blood loss during liver transection becomes difficult to control, surgeons should consider various strategies, such as second-stage biliary or pancreatic reconstruction. In patients planned to undergo major hepatectomy with combined PD, preoperative portal vein embolization is mandatory to prevent postoperative liver failure.

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## Introduction

For patients with biliary cancers, including perihilar cholangiocarcinoma or gallbladder carcinoma, surgical resection offers the only possibility of cure.<sup>1</sup> However, hepatectomy for these diseases is more difficult than for hepatocellular carcinoma or metastatic disease to the liver. The increased complexity comes from the need for biliary tract reconstruction and, on occasion, the need to resect and reconstruct the portal vein or hepatic artery, or add pancreatoduodenectomy (PD).<sup>1–3</sup> Therefore, it is possible that risk factors for postoperative complications in patients who undergo such complex procedures are different from

those who undergo simple hepatectomy. Few reports have examined independent risk factors for morbidity or mortality in patients who have undergone hepatectomy for cholangiocarcinoma (Table 1).<sup>1,4–9</sup>

In recent years, the Clavien–Dindo classification (CDC) grade has become the standard for reporting postoperative complications. This classification grades complications according to the most severe complication or events judged to be relevant.<sup>10</sup> By this system, complications of lesser magnitude, as well as the total number of complications, are not accounted for. To address this issue, in 2013, Slankamenac *et al.* presented a new tool for

**Table 1** Independent risk factors for morbidity or mortality of patients who underwent resection for perihilar cholangiocarcinoma or tumor in previous reports

Risk factor for endpoints	Endpoint	
	Morbidity	Mortality
	No. Reference	
Variable		
Preoperative cholangitis	4	1,5,9
Intraoperative blood loss or blood transfusion <sup>8</sup> (>900 ml)		<sup>1</sup> (≥2500 ml), <sup>6</sup> (blood transfusion)
Low liver function or %FLR <sup>a</sup>		1,9
Preoperative bilirubin (>3 mg/dL)		7

<sup>a</sup> Plasma disappearance rate of indocyanine green (ICGK) < 0.14(1), FLR < 30%.<sup>9</sup>

scoring, the so-called “Comprehensive Complication Index (CCI)”<sup>11,12</sup>. The CCI is calculated as the sum of all complications weighted by severity (available at [www.assessurgery.com](http://www.assessurgery.com)).<sup>10,13</sup> The formula for the CCI yields a continuous scale to rank the severity of any combination of complications from 0 (no complications) to 100 (death) in a single patient. For example, a patient with a CCI of 8.7 would have a single CDC grade I complication, one with a CCI of 20.6 would have a grade II complication, one with a CCI of 26.2 would have a grade IIIa complication, one with a CCI of 33.7 would have a grade IIIb complication, one with a CCI of 44.2 would have a grade IVa complication, and one with a CCI of 46.2 would have a grade IVb complication. In addition, the formula for the CCI can calculate the summative severity of several complications in a single patient. For example, the CCI index for the sum of one CDC grade I and two CDC grade II complications in a single patient is 30.8. There have been no reports that have identified risk factors for a severe postoperative CCI score (CCI > 40) in a large cohort of patients undergoing hepatectomy for malignant biliary disease.

The aim of this study was to identify predictive factors for patients who developed a severe postoperative CCI score following major hepatectomy with biliary reconstruction for biliary cancer.

## Patients and methods

### Patients

Between March 1999 and March 2013, 255 patients underwent hepatectomy with biliary reconstruction for biliary cancer (perihilar cholangiocarcinoma or gallbladder carcinoma) with curative intent at the Department of Gastroenterological Surgery II, Hokkaido University Hospital. Twenty-six (10%) patients were excluded from the present study due to a lack of clinical records (n = 10), having a history of surgery including biliary reconstruction (n = 11), or undergoing minor hepatectomy (n = 5). Thus, 229 (90%) patients were included for the further

study. This study was approved by the Institutional Review Board of Hokkaido University Hospital (No. 014-0374).

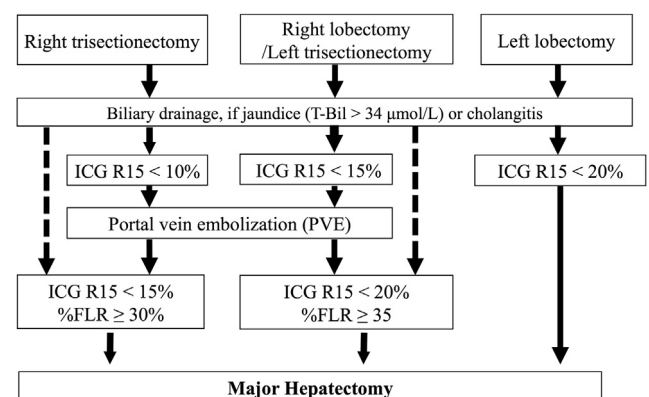
### Preoperative preparation

The patients were treated in accordance with departmental guidelines, which were established in 1999 for patients with hilar cholangiocarcinoma.<sup>14,15</sup> Pre-operative biliary decompression was performed to reduce serum bilirubin concentrations below 34 μmol/L (2 mg/dL) for all patients with jaundice and to control segmental cholangitis. Previously, percutaneous transhepatic biliary drainage (PTBD) was used for drainage. Beginning in 2005, endoscopic nasobiliary drainage (ENBD) of the future remnant liver was adopted for initial drainage.

Preoperative portal vein embolization (PVE) of the liver to be resected was considered when right hepatectomy or right- or left-trisectionectomy was planned.<sup>16</sup> More than 2 weeks after PVE, the patients' liver volumes were semi-automatically measured using contrast-enhanced computed tomography imaging data (volume data or 5-mm-thick axial imaging data).<sup>16</sup> The basic decision criteria for the ratio of the future liver remnant volume/total liver volume (%FLR) limit for each type of hepatectomy are shown in Fig. 1.

### Surgical technique

In patients with gallbladder carcinoma and intrahepatic cholangiocarcinoma, before radical resection, para-aortic lymphadenectomy and pathological examination by frozen sections were performed immediately after laparotomy to decide whether radical resection should be performed.<sup>17–19</sup> For patients with extrahepatic cholangiocarcinoma, para-aortic lymphadenectomy



**Figure 1** Decision criteria for the strategy for preoperative management of major hepatectomy in biliary cancer. Preoperative biliary decompression is performed to reduce the serum bilirubin concentration to below 2 mg/dL. When the value of the indocyanine green retention rate at 15 min (ICG R15) after relief of jaundice meets the requirements, limited PE is performed. At 2 weeks after PVE, patients with ICG R15 and the appropriate ratio of the future liver remnant volume/total liver volume (%FLR) are considered candidates for major hepatectomy with biliary reconstruction

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