

Puzzle and Challenge in Routine Extrahepatic Bile Duct Resection for Advanced Gallbladder Carcinoma

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To the Editor:

Gallbladder carcinoma (GBC) is the most common malignancy of the biliary tract. Curative resection is the only potentially curative treatment for GBC. For advanced GBC, radical resection including gallbladder and liver resection plus regional lymphadenectomy has been widely performed to achieve R0 resection. However, it remains controversial whether routine resection of the extrahepatic bile duct (EHBD) is needed in advanced GBC.¹⁻¹⁰

Shimizu *et al.*¹ analyzed 50 advanced GBC patients with radical resection (including EHBD resection); 30 patients had hepatoduodenal ligament invasion (HDLI), of whom 24 lacked preoperative obstructive jaundice. They found that advanced GBC patients had a higher frequency of HDLI and that invasion was difficult to diagnosis before surgery. Moreover, the 1-, 2-, and 3-year survival rates of the 30 patients with HDLI (50%, 17%, and 6%, respectively) were significantly worse than those of the 20 patients without HDLI (75%, 69%, and 64%, respectively). Consequently, they suggested that EHBD resection and lymphadenectomy should be performed in advanced GBC patients. Similar results were reported by Chikamoto *et al.*² and Kohya and Miyazaki.³ In the study conducted by Chikamoto *et al.*,² 186 paraffin-embedded specimens from 15 GBC patients with stage T2 disease were analyzed. They demonstrated that there were lymphangions in the submucosal layer of the EHBD and that tumor cells could travel through these channels. Therefore, they recommended routine resection of the EHBD as part of radical resection for T2 GBC. Additionally, Kohya and Miyazaki³ reported that T2/T3 GBC patients with EHBD resection had better survival than patients who did not undergo EHBD resection. Thus, they highly recommended the hepatectomy of segments S4b+5 combined with EHBD resection and lymph node dissection for T2/T3 GBC patients.

However, it had been reported that routine EHBD resection

does not prolong survival but rather increases complications. D'Angelica *et al.*⁴ reported routine EHBD resection had no statistically significant impact on disease-specific survival ($p=0.12$). Furthermore, EHBD resection was associated with more perioperative complications (19 of 66 patients with EHBD resection and hepaticojejunostomy had abscesses and/or biliary fistulae). Choi *et al.*⁵ analyzed 71 T2/T3 GBC patients, of whom 31 underwent EHBD resection. There was no difference in the 5-year survival rates between patients without and with EHBD resection (54.2% vs 34.8%, $p=0.112$), but the length of hospital stay, operative time, proportion of patients needing blood transfusions and proportion of patients developing complications were higher in the group undergoing EHBD resection than in the group not undergoing EHBD resection (19 ± 21 days vs 11 ± 5 days, $p=0.034$; 345 ± 136 minutes vs 186 ± 93 minutes, $p<0.001$; 12.7% vs 21.1%, $p=0.022$; 4.2% vs 14.1%, $p=0.007$, respectively). In the study reported by Gani *et al.*,⁶ 449 patients who underwent surgical resection were analyzed. EHBD resection was performed in 109 patients (34.2%). They found the median number of lymph nodes dissected was similar in patients who did and did not undergo EHBD resection (4 vs 3, $p=0.108$). In addition, the median overall survival of patients who underwent EHBD resection was shorter than that of patients who did not undergo EHBD resection (19.2 months vs 32.4 months, $p<0.001$), although EHBD resection did not impact the overall survival rate ($p=0.170$). However, the proportions of patients with lymph node metastasis and advanced American Joint Committee on Cancer T stage were higher in patients who underwent EHBD resection than in those who did not (52.3% vs 32.4%, $p<0.001$; 57.0% vs 40.8%, $p=0.002$). Araida *et al.*⁷ analyzed 838 R0 advanced GBC patients without HDLI or cystic duct invasion. Their results demonstrated that there was no significant differences in the rates of 5-year survival, lymph node metastasis, complications and local recur-

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rence along the hepatoduodenal ligament between patients who did and did not undergo EHBD resection. Moreover, Yokomizo *et al.*⁸ reported that the 5- and 10-year survival rates were lower in patients who underwent EHBD resection than in those who did not (66.7%, 50.0% vs 81.1%, 66.2%, respectively), although there was no significant difference between the two groups ($p=0.134$).

From the above studies, it is unclear whether the routine resection of the EHBD can improve survival in patients with GBC. However, in a study reported recently by our team,⁹ 213 advanced GBC patients were analyzed, and 87 patients underwent EHBD resection. We used a propensity score matching analysis to reduce the selection bias inherent in retrospective observational studies. Our results showed that the median overall survival time of patients who underwent EHBD resection was longer than that of patients who did not undergo EHBD resection (25 months vs 11 months, $p=0.032$). In addition, the median number of lymph nodes dissected in patients who underwent EHBD resection was greater than that in patients who did not undergo EHBD resection (6 vs 4, $p<0.001$). Furthermore, our results demonstrated that EHBD resection was an independent prognostic factor for overall survival in advanced GBC patients. Patients who underwent EHBD resection were more likely to undergo simultaneous lymph node dissection. The percentage of patients who had a least one lymph node sampled was higher in the group that underwent EHBD resection than in the group that did not (94.5% vs 81.5%, $p<0.001$).⁶ Moreover, EHBD resection may improve survival in patients with perineural invasion, even in the absence of biliary infiltration, according to a report by Sakamoto *et al.*¹⁰

At present, most of the existing studies do not support routine EHBD resection. However, routine EHBD resection may increase the number of lymph nodes dissected and allow the complete dissection of potentially invasive tissue. It is useful for TNM staging and determining the next step in treatment for patients with GBC. EHBD resection and biliary reconstruction have no severe complications; therefore, we recommend that experienced surgeons routinely perform EHBD resection in patients with advanced GBC to ensure patient safety. It remains controversial whether routine EHBD resection can improve survival. Further evaluation in randomized clinical trials and multicenter studies is needed. Internationally recognized guidelines are needed for clinical surgery programs.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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