Liver

Extended liver resections for intrahepatic cholangiocarcinoma: Friend or foe?

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Background. *In patients with intrahepatic cholangiocarcinoma (ICC), extended liver resections (ELRs) increase the rate of resectability. The aims of the present study were to evaluate the morbidity and oncologic outcomes of ELR compared with other liver resections (LR) for ICC.*
Methods. *All LR for ICC that were performed in our center between January 1997 and September 2013 and conducted with curative intent were included in this retrospective analysis. ELRs were defined by resections of ≥5 liver segments. The factors that influenced the occurrence of major complications (Clavien ≥ 3) and overall survival (OS) were tested with univariate and multivariate analyses.*
Results. *One hundred seven patients (82 men and 25 women) were resected, and 27 (25.3%) underwent ELRs. Compared with the LRs, the ELRs were performed in larger tumors (*$P = .003$*) and were significantly associated with more complex surgeries such as vascular (*$P < .001$*) or biliary reconstructions (*$P < .001$*). Multivariate analysis revealed that ELR was an independent risk factor for major complications (odds ratio [OR], 6.2; 95% CI, 2.11–19.62;* $P < .001$*). Compared with the other LRs, ELRs had no effects on OS or disease-free survival (*$P = .881$ *and* $P = .228$*, respectively). Perioperative blood transfusion (Hazard ratio (HR), 2.51; 95% CI, 1.49–4.23;* $P < .001$*), the presence of >1 nodule (HR, 3.17; 95% CI, 1.67–5.97;* $P < .001$*), and age ≥65 years (HR, 1.72; 95% CI, 1.03–2.86;* $P = .036$*) were independent prognostic factors for OS.*
Conclusion. *This study suggests that ELRs performed for large ICCs do not affect negatively oncologic outcomes, despite the increased risk of major complications. (Surgery 2015;157:656-65.)*

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Liver resection (LR) is the most suitable curative treatment for intrahepatic cholangiocarcinoma (ICC). ICC has become a public health issue with an incidence that has increased in all Western countries in the last 2 decades.[1-4] Moreover, the prognosis for ICC has not or only slightly improved. Indeed, the median survival ranges between 18 and 39 months.[5,6]

This poor prognosis is first related to the high rate of recurrence, particularly during the first year after LR,[7] and to the low rate of resectability. Indeed, in the majority of cases, ICC arises in patients without identifiable underlying liver disease and is thus frequently diagnosed at a late stage with large tumors.[8-10] Under these conditions, the only available curative resection options are extended LRs (ELR) or orthotopic liver transplantation. Unfortunately, the first studies that reported on the primary results of orthotopic liver transplantation in ICC revealed a 5-year overall survival (OS) rate of only 25%.[11] These poor results are inconceivable in periods of liver graft scarcity.

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In contrast, with the recent progress in operative techniques, perioperative management, and postoperative care, ELR has become increasingly common, and the risks associated with these major procedures have decreased. For example, portal vein occlusion via ligation or embolization allows for the possibility of increasing the remaining liver and thus reducing the risk of liver failure after ELR. In recent years, our experiences have revealed an increase in the indications for ELR in ICC from 17% to 33% of cases (Fig 1). However, this surgical aggressiveness has not yet been evaluated. Although some reports have analyzed the effects of vascular reconstruction on survival and outcome,[12] none have specifically compared ELR and LR in terms of outcomes and survival. The aim of the present study was to analyze the outcomes and survival after LR with curative intent for ICC with a special focus on ELR.

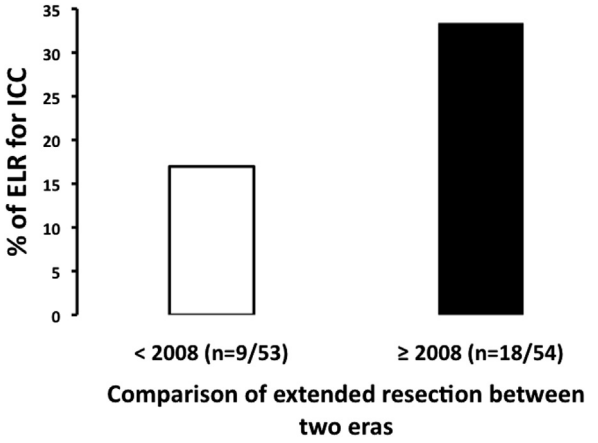

Fig 1. Evolution of the frequency with which extended liver resections (ELR) were performed before and after 2008. *ICC*, Intrahepatic cholangiocarcinoma.

METHODS

Patients. The study population included all with LRs performed with curative intent for mass-forming type ICCs as defined by the liver Cancer Study Group of Japan at a single tertiary referral center between January 1, 1997, and September 1, 2013. Hepatocellular cholangiocarcinoma, gallbladder carcinoma, hilar cholangiocarcinoma, and periductal infiltrating types were excluded from the analyses. The clinical data were collected retrospectively from an LR database and analyzed after institutional review board approval was obtained.

Data were collected regarding demographics (age, sex, and body mass index), surgical variables, duration of hospital stay, morbidity, postoperative chemotherapy, and follow-up, including disease recurrence and death. Pathologic data, such as the tumor size, satellite nodes, lymph node involvement, UICC 7th edition TNM staging, perineural invasion, and microvascular involvement, were collected.

Surgery. Before surgery, each patient was evaluated by thoracoabdominal CT with intravenous contrast. Portal vein embolization was indicated when the LR volume/total liver volume ratio was <35%. ELR was defined by the resection of ≥5 Couinaud liver segments. Right or left hepatectomy extended to segment 1 and right or left trisectionectomy were considered to be ELRs. All LRs were performed with curative intent by senior surgeons. Intraoperative ultrasonography of the liver was performed to ensure the extension and the resectability of the tumor. Vascular or biliary reconstructions (partial or complete) were performed when necessary. Vascular reconstructions were classified into 3 categories: portal vein reconstruction, inferior vena cava reconstruction, and hepatic artery reconstruction. In 1 case, LR was performed ex situ. The absence of bulky lymph nodes in the celiac or para-aortic area, absence of tumor residue in the remnant liver, and absence of peritoneal extension defined curative hepatectomies. The resection margin was classified as microscopically negative (R0) or positive (R1). When macroscopic tumoral tissue was left in situ, the resection was R2.

Postoperative morbidity. Postoperative morbidity was defined by any complication that occurred within 90 days after the LR and was categorized according to the Dindo and Clavien system.[13] Major complications were categorized as grades III–V in the Dindo and Clavien classification. Postoperative liver failure was defined by the "50–50" criteria on postoperative day 5 as described by Balzan et al.[14] Postoperative mortality was defined by the occurrence of death within 90 days postoperatively.

Survival analyses. The end of the follow-up was set to be between December 1, 2013, and January 1, 2014, or the time of death. OS was calculated from the date of the intervention to the time of death (regardless of cause) or to the end of follow-up. Disease-free survival (DFS) was calculated from the date of the intervention to the time of recurrence or the time of death. To identify the prognostic factors for OS, the following data were analyzed: age, gender, American Society of Anesthesiologists score ≥ 2, body mass index ranking in categories (<25, 25–30, and >30 kg/m^2), known cirrhosis, neoadjuvant chemotherapy, portal embolization, ELR, vascular resection, bile duct resection, lymph node