



Editorial

The risk factors and prognostic factors of intrahepatic cholangiocarcinoma



Intrahepatic cholangiocarcinoma (ICC) originates from the small intrahepatic ductules or the large intrahepatic ducts proximal to the bifurcation of the right and left hepatic ducts. ICC is the second most common primary malignancy of the liver after hepatocellular carcinoma (HCC).^{1,2}

Given the rising incidence of ICC, further studies clarifying its risk factors are warranted. Well-established risk factors for ICC are similar to those known for cholangiocarcinoma, including hepatobiliary flukes, primary sclerosing cholangitis, biliary tract cysts, and hepatolithiasis—all of them sharing the common features of chronic inflammation and biliary stasis, which are associated with malignant biliary transformation.³ Moreover, recognized risk factors for ICC are also similar to those known for HCC, such as chronic hepatitis B and C, cirrhosis, obesity, nonalcoholic fatty liver disease, diabetes, and alcohol consumption.^{4,5} Chronic liver diseases with the aforementioned conditions might be related to ICC in a similar manner to HCC, particularly because there is evidence that both types of primary liver cancers arise from common progenitor cells that might give rise to tumors with hepatocellular or cholangiocellular phenotypes.⁶

At the time of diagnosis, patients with ICC are frequently found to have disease beyond the limits of surgical therapy owing to the presence of multiple intrahepatic metastases, peritoneal carcinomatosis, or extrahepatic metastases. Surgery with curative resection (R0) of ICC is the most effective treatment, emphasizing the importance of resectability as a major prognostic factor.⁷ Unfortunately, the resectability rate remains low and varies in the literature from 19% to 74%.⁸ Even subsequent to curative-intent surgery, the clinical outcomes of patients undergoing liver resection are disappointing, with a 5-year survival rate of 20–45%.^{9,10}

The seventh edition of the American Joint Committee on Cancer staging system for ICC included the parameters of the tumors' number, vascular invasion, direct invasion of extrahepatic structures, periductal invasion, lymph node metastasis, and distant metastasis for staging.¹¹ A meta-analysis study involving seven large studies revealed that male sex, older age, larger tumor size, presence of multiple tumors, lymph node metastasis, vascular invasion, and poor tumor differentiation instead of a positive surgical margin were poor prognostic

factors following surgical resection of ICC.¹² However, Chang et al's¹⁰ study showed that positive resection margin in addition to regional lymph node metastasis, periductal infiltration, and poor differentiation were poor prognostic factors in patients with ICC after curative surgery. Doussot et al¹³ developed validated preoperative and postoperative models to stratify high risk patients of recurrence, which may benefit from perioperative therapy instead of surgery alone. In their study, tumor size and multifocality based on image study were independent preoperative prognostic factors for disease-free survival, and tumor size, multifocality, vascular invasion, and lymph node metastases based on pathology were postoperative risk factors for disease-free survival.¹³

In conclusion, ICCs are aggressive malignancies with a fair prognosis in general. However, future studies are warranted to explore other potential risk factors leading to the prevention of ICC, to develop early detection methods for early curative surgery, and to identify potential prognostic factors related to improved therapy and outcome.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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