

Article information: <https://dx.doi.org/10.21037/cco-22-115>

Reviewer comments

Intrahepatic cholangiocarcinoma (ICC) is an aggressive primary hepatic malignancy, which has increased in incidence over the past decades. While surgical resection is the standard of care for patients with early-staged disease, many patients present with locally advanced and unresectable tumors. In the manuscript “Management of Locally Advanced Intrahepatic Cholangiocarcinoma: A Narrative Review”, authors made an up-to-date summary of the current literature regarding contemporary management of locally advanced ICC including systemic and liver-directed therapies.

Couple questions are required to be answered before it will be accepted.

- (1) In the sentence “This is a narrative review providing an an up-to-date summary” of abstract, an extra “an” should be deleted.

Reply 1: this change has been made

Changes in the text: page 2, line 47

- (2) What were the roles of hepatolithiasis in the ICC? Please state in the background.

Reply 2: additional information has been added to the background about risk factors for CCA. Hepatolithiasis, like other conditions, cause chronic biliary inflammation and stasis which is thought to be a risk factor for ICC.

Changes in the text: page 4, lines 115-120

CCA occurs in the setting of chronic biliary inflammation and stasis and the causes of which differ in Eastern and Western countries. In Western countries, CCA is commonly associated with primary sclerosing cholangitis, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, cirrhosis, alcohol use, and smoking. In Eastern countries, risk factors for CCA commonly include chronic bile duct calculi (hepatolithiasis), liver fluke infection, and viral hepatitis

- (3) In the introduction, it was proposed to add related reference (DOI: 10.21037/hbsn.2016.12.12) about the management of ICC.

Reply 3: we have added this reference

Changes in text: page 3, line 85

- (4) Please make a brief introduction about liver-directed therapies.

Reply 4: Thank you for this comment. We have a brief introduction to liver-directed therapies under the bold heading “Transarterial Therapies” on page 10, line 328-336. We have included a sentence which indicates what therapies are included under liver directed therapy.

Changes in text: page 10, lines 335-336. Liver directed therapies include transarterial chemoembolization, bland embolization, Yttrium-90 (Y-90), and hepatic artery infusion.

- (5) What were your good suggestions for the optimal patient selection for ICC.

Reply 5: Regarding “optimal patient selection” for surgery, this information is covered in detail

under the “**Defining Locally Advanced Disease**” section. Patient selection for systemic and local directed therapies are similarly covered in their respective sections.

Changes in text: Covered in detail throughout the manuscript text.

(6) How about the prognostic biomarkers for ICC? Please state in the conclusion.

Reply 6: We have included a statement on prognostic biomarkers in the conclusion

Changes in text: page 17, lines 578-580.