

Thank you for giving us the opportunity to revise the paper and the reviewer comments in order to improve it. All corrections were tracked in yellow in the revised version.

Point by point reply

Reviewer

“About incidence of CCA, actually there are not globally homogenous rare. Countries in Southeast Asia eg. Thailand, Laos had extremely high incidence of CCA. Authors should recognise and add this information in the article.”

Authors

Thank you for this observation. The information was included in the revised version (see Introduction: lines 6-9).

Reviewer

“Author mentioned CCA classification were suboptimal and heterogenous genetic aberation, for more consistence of the context, genetic subtype of CCA (doi:10.1158/2159-8290.CD-17-0368) and large vs small duct type of CCA (doi:10.1002/jhbp.154) shuld be briefly included.”

Authors

We thank the reviewer for this comment to improve our manuscript. These informations were included in the revised manuscript (see introduction, page 3, lines 14-23).

Reviewer

“In last section, authors concluded that CCA remain rare, no recognized risks and poor prognosis. This is not exactly correct because in Asia CCA is high incidence, liver fluke infection were known strong risk factor and some type of CCA (papillary CA, intraductal tumor) had good prognosis.”

Authors

The sentence was rephrased according to the reviewer suggestion (see introduction, page 4, lines 5-7 from the end of the paragraph).

Reviewer

“Current phamacological treatment: Author briefly explained two famous landmark trial for systemic treatment in CCA, ABC-02 2010 and BILCAP trial 2017. For better understanding for readers, Authors should discussed in seprated setting, Palliative or adjuvant systemic therapy and included more available completed trials.”

Authors

We thank the reviewer for this comment to improve our manuscript. Palliative and adjuvant therapy were separated in two different sub paragraphs. Reference to other completed trials was included (see paragraph “palliative treatment”, page 5, lines 8-14 and paragraph “adjuvant treatments”, page 5, lines 7-12)

Reviewer

Surgical or Ablative treatment: I not sure why authors put statement "or ablative" since ablation therapy is not a standard treatment for CCA and authors mention only sugical treatment in later part.

Authors

We agree with the reviewer and we remove the term "ablative" throughout the manuscript.

Reviewer

Surgical perspective in perihilar CCA, most of patients present with jaundice and impaired liver function. Role of pre-operative biliary drainage and pre-operative preparation are important and widely discussed, authors should discuss this point.

Authors

We thank the reviewer for this comment to improve our manuscript. We added a new subparagraph named " Preoperative considerations" on this issue (see page 9 and 10).

Reviewer

Figure 1 was not convey the message, table may be better understanding.

Authors

Figure 1 was changed with a table to improve clarity. A new figure 1 was included depicting the classification of CCA according its location within the biliary tree.

Reviewer

I don't see reference to table 1 in the main text.

Authors

The reference was included in the text (see page 15, line9).