



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastrointestinal Oncology*

**Manuscript NO:** 71871

**Title:** Pathological, molecular, and clinical characteristics of cholangiocarcinoma: A comprehensive review

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 03479136

**Position:** Editorial Board

**Academic degree:** FEBS, MD, PhD

**Professional title:** Assistant Professor, Surgeon

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** India

**Manuscript submission date:** 2021-09-25

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-09-25 07:46

**Reviewer performed review:** 2021-09-30 14:30

**Review time:** 5 Days and 6 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No
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### **SPECIFIC COMMENTS TO AUTHORS**

I read with interest this comprehensive review that effectively summarises the current knowledge on clinico-pathological characteristics of cholangiocarcinoma by Dr Vij and colleagues. I would like to anyway point out some concerns: - There are several typos and mistakes, and the English language needs a review - In the text some parts are repetitive and do not help the logical flow of the manuscript (e.g. regarding liver flukes role as risk factor) - In the "EPIDEMIOLOGY AND RISK FACTORS" section the authors state that CCA incidence is rising. This does not appear accurate, since it is true for intrahepatic CCA but not quite for the extrahepatic ones. Moreover, it would be worth mentioning that CCA subtypes appear to show distinct epidemiological trends. - The intraductal papillary mucinous neoplasm are described with different acronyms throughout the text (IPNB, which is preferable, and IPMN-B). This should be uniformed - The Authors should add a section/paragraph on liquid biopsies and their role in the diagnosis/management of CCA (e.g. in the Role of Molecular Pathology in Diagnosis and Management section) - In the Clinical management section would be worth expanding resection criteria and role of lymphadenectomy



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**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** India

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**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-09-26 03:41

**Reviewer performed review:** 2021-10-06 12:29

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<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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### **SPECIFIC COMMENTS TO AUTHORS**

This review focuses on the current knowledge of pathological characteristics, molecular alterations of cholangiocarcinoma and its precursor lesions (including biliary intraepithelial neoplasia, intraductal papillary neoplasms of the bile duct, intraductal tubulopapillary neoplasms and mucinous cystic neoplasm). It gives a comprehensive review of all pathological types of cholangiocarcinoma. There are some minor concerns about this review article. 1. Molecular basis of different risk factors may be different. This could be described in detail. 2. In the section of "Sarcomatoid Cholangiocarcinoma", hpayerchromatic should be corrected as hyperchromatic. 3. In the section of "Sarcomatoid Cholangiocarcinoma", a "survival" is missing after "shorter overall". 4. The sentence "NCAM and EMA are often negative or weakly positive for tumour cell cytoplasm in HCC-like IHCC, but are are strongly positive for stem cell makers, including TROP2, EpCAM and Nestin" in section "IMMUNOHISTOCHEMICAL FEATURES" should be corrected for grammatic error.



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**Position:** Editorial Board

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**Professional title:** Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** India

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**Reviewer performed review:** 2021-10-08 06:17

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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Although there are dozens of published reviews focusing on cholangiocarcinoma, such as recent work by Rodrigues PM, et al. (Pathogenesis of cholangiocarcinoma. Annual review of Pathology-Mechanisms of Disease. 2021;16:433-463. doi: 10.1146/annurev-pathol-030220-020455), the manuscript by Dr Mukul Vij is expected to give many new knowledge to readers. The review is well organized and written, it can be accepted after minor revision. Minor comments: 1. There are several errors in or inconsistencies in writing, for example, "A losses of SMAD4" on page 21, and "EPCAM" and "EpCAM" on page 10. 2. The format of references needs to be re-edited. 3. Some currently published articles regarding the pathology and tumorigenesis of cholangiocarcinoma are suggested to be cited, such as 1. Huang YH, et al. J Hepatol. 2021;74(4):838-849. doi: 10.1016/j.jhep.2020.10.037. and 2. Zhou YJ, et al. Hepatology. 2021;74(2):797-815. doi: 10.1002/hep.31780.