

Dear Editor,

Thank you very much for your decision letter and advice on our manuscript (Manuscript NO.: 87683) entitled “Development and Validation of a Machine Learning-Based Early Prediction Model for Massive Intraoperative Bleeding in Patients with Primary Hepatic Malignancies”. We also thank the reviewers for the constructive comments and suggestions. We have revised the manuscript accordingly, and all amendments are highlighted with yellow color in the revised manuscript. In addition, our point-by-point responses to the comments are listed below this letter.

This revised manuscript has been edited and proofread by Medjaden Inc.

We hope that our revised manuscript is now acceptable for publication in your journal and look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Li Peng

First of all, we would like to express our sincere gratitude to the reviewers for their constructive and positive comments.

Replies to Reviewer 1

Specific Comments:

1. Primary liver cancer including HCC and intrahepatic cholangiocarcinoma, the risk of operative bleeding was different. Why not to focus on HCC if possible?

Response: Thank you for your thoughtful question. It is true that primary liver

cancer encompasses different subtypes, such as hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma, and the risk of operative bleeding varies among these subtypes. We agree that focusing on a specific subtype, such as HCC, could provide more targeted insights into the factors influencing intraoperative bleeding in that particular group of patients. However, it is important to consider that studying all primary hepatic malignancies collectively allows for a broader understanding of the overall risk factors and predictive factors associated with intraoperative bleeding in primary liver cancer patients as a whole. This inclusive approach provides a comprehensive perspective on the condition and allows for comparisons between different subtypes.

2. All the patients treated by laparoscopic liver resection based on the including criteria 2? or part of patients by traditional liver resection?

Response: Thank you for asking us to clarify this issue. This information has been added in the text. The study enrolled patients diagnosed with primary hepatic malignancies who underwent laparoscopic liver resection surgery in the Hepatobiliary Surgery Department of the Fourth Hospital of Hebei Medical University between 2010 and 2020.

3. Please descript more about volume of the operative bleeding.

Response: Intraoperative blood loss was categorized into two groups: >1000ml and ≤1000ml. Blood loss exceeding 1000ml was defined as massive bleeding. Among the 406 patients, 65 (16.0%) suffered massive intraoperative bleeding(≥1000ml), while the median bleeding volume among patients was measured at 1267.4ml. Detailed data tables can be found in the supplementary file, providing further insights into the distribution of blood loss in the study population.

Replies to Reviewer 2

Specific Comments:

The study is retrospective in nature, needs to be prospective one Retrospective study are too weak to validate a prediction model for significant intraoperative blood loss in patients with primary hepatic malignancies. Reference for "This retrospective study aimed to develop and validate a prediction model for significant intraoperative blood loss in patients with primary hepatic malignancies. " You are exaggerating use of statistics used.

Response: Thank you for pointing out the issue with the study design. We apologize for any confusion caused. You are correct that retrospective studies have limitations in validating prediction models compared to prospective studies. Retrospective studies rely on analyzing past data and are subject to biases and limitations in data collection. We have revised the following text: "A prediction model for significant intraoperative blood loss in patients with primary hepatic malignancies was constructed in this retrospective analysis."

Comments of Editorial Board

Specific Comments:

1. In the conclusion of the abstract, you should mention the four clinical factors.

Response: Thank you for asking us to clarify this issue. This information has been added in the text. We have revised the conclusion of the abstract, the four clinical factors are mentioned and highlighted with yellow color in the revised manuscript.