

Specific Comments to Authors: The review by Díaz del Arco C et al. discussed the updating on liquid biopsy (LB) for Gastric Cancer. Although this is a very interesting report, the content of LB is too much and boring. The significance of LB for gastric cancer need to be more thoroughly focused.

REVIEWER #1

Dear reviewer,

Thank you very much for your helpful suggestions. Following your recommendations, we have included tables, diagrams, and figures to enhance the manuscript while striving to avoid excessive text length.

We have expanded and specified the information on the topics you suggested, which we find highly relevant. Consequently, we have included 1) two tables summarizing the main findings from previous studies on the value of liquid biopsy in early diagnosis, prognosis, and specific treatments of GC (Tables 2 and 3). 2) We have also briefly summarized the main features of ongoing clinical trials. 3-4) We have added a paragraph discussing the value of the multi-omics approach and the role of liquid biopsy within that context, as well as a brief paragraph highlighting the potential advantages of non-blood studies. 5) We have included a dedicated section and a figure on artificial intelligence in liquid biopsy and its potential utilities in pre-analytical, analytical and post-analytical stages, enhancing the practical aspects of our review.

We believe that these suggested changes significantly contribute to defining the future landscape of liquid biopsy and molecular studies in gastric cancer. Therefore, we express our gratitude once again.

Specific Comments to Authors: This manuscript reports on the liquid biopsy technique and its application in gastric cancer. The manuscript provides a comprehensive summary of liquid biopsy technology, discusses the current application of liquid biopsy technology in gastric cancer, and proposes future obstacles to be overcome. This review covers many aspects of the topic. However, some minor revision is needed. 1. It will be more perfect if the author adds some summary tables of its clinical studies/trials and clinical application. 2. Instead of a simple description, authors can add separate paragraphs and tables to elaborate on the value of liquid biopsy techniques in the early diagnosis and treatment (including chemotherapy, targeted therapy, and immunotherapy) in gastric cancer. 3. If possible, the authors should add a comparison of the potential clinical utility of different liquid biopsy techniques in the early diagnosis of gastric cancer based on multi-omics biomarkers. 4. Compared with traditional liquid biopsy techniques, what are the specific advantages of non-blood derived liquid biopsy techniques? 5. If possible, introduce the research progress of liquid biopsy techniques combined with deep machine learning in gastric cancer.

REVIEWER #2

Dear reviewer,

Our objective is to provide a comprehensive overview of both liquid biopsy and gastric cancer, ensuring that there is sufficient information for the average reader to have the necessary tools to understand other studies on liquid biopsy. However, we recognize that the first section of the manuscript was excessively long and dull. Consequently, we have shortened 7 pages of the

text in the first part of the article, and integrated numerous diagrams and figures to facilitate faster and more practical reading without losing significant information.

Specific Comments to Authors: 1. This research focused on Liquid Biopsy for Gastric Cancer - Techniques, Applications, and Future Directions, after check the pubmed, there were so many articles about this topic such as PMID: 36627698, so this manuscript was not very prospective and significant. 2. This manuscript focus on clinical problems of gastric cancer, with strong clinical value and importance, very interesting research, and also met the submission topic of this journal, the results was real and the conclusion was convincing, but some places can be more perfect. 3. No tables and no Figures, I think not suitable for this famous journal, the authors can read this review paper PMID: 36627698. 4. References should be renewable such as PMID: 36627698. 5. Language can be more polish.

REVIEWER #3

Dear reviewer,

Thank you very much for your suggestions, which we believe enhance the quality of our article.

Following your recommendations and to maintain the practical aspect of the review, we have shortened the first section (covering the generalities of liquid biopsy) by 7 pages to focus more on the second part about gastric cancer. In this initial section, we have removed text and created tables, diagrams, and multiple figures that complement the text, enabling a smoother and more practical reading experience without losing significant information. In the gastric cancer section, we have also included explanatory figures as summaries to make the review more engaging.

Secondly, we found the referenced article very interesting. However, compared to the article you mentioned and other similar articles, our review aims to offer a more practical and broad view of both liquid biopsy and gastric cancer for the average reader. Hence, we first provide a global overview of liquid biopsy, describing the potential uses of all analyzable structures, including tumor-educated platelets. Moreover, we delved into non-blood samples, multi-omics, and artificial intelligence, areas often overlooked in articles on liquid biopsy in gastric cancer. We have strived to adopt a more practical approach than the mentioned article, focusing on delineating the advantages and disadvantages of each method and summarizing their potential clinical applications, rather than delving into specific methodology, cutoff points, or specific results of each previous publication. Thus, we have solely concentrated on detailing the specific methodological procedures of technologies approved for CTCs such as CellSearch or Parsortix (included as figures and removed from the main text), which are closer to clinical practice. However, to ensure no loss of information, we have included in two new tables (2 and 3) a summary of the main data from previous studies on liquid biopsy in gastric cancer, based on the article you provided and two additional ones containing further information (Zhang et al., Ma et al., and Ha et al.).

Finally, we have reviewed the English and corrected some typos and writing mistakes.

EDITORIAL OFFICE

Dear members of the editorial office,

Thank you very much for your thorough review.

1) We have incorporated 11 figures and 3 tables into the manuscript.

2) Additionally, we have meticulously revised the English language throughout the document.

Please let us know if there are any further adjustments or clarifications needed.