Reviewer's report

Title: A systematic review of the pathophysiology of 5-fluorouracil-induced cardiotoxicity

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Reviewer: Guoqing Qian

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Major Complimentary Revisions:

This systematic review manuscript made a nice summarization of the current studies relating to 5-fluorouracil induced cardiotoxicity and discussed the potential mechanisms underlying each different cardiotoxicity. The paper provided further insight into the mechanisms underlying 5-FU induced cardiotoxicity. However, the manuscript can still be significantly improved. A major concern is that this manuscript did not clearly distinguish between effects and mechanisms. While the results parts literally listed the findings from different studies. The discrepancy between these studies and possible reasons should be provided. The discussion parts somehow repeated the results and more efforts should put into the mechanistic insight into 5-FU induced cardiotoxicity.

Some more specific comments:

1. It is not clear about the objective of this study in the abstract. Introduction mentioned the objective is to evaluate the pathophysiology, however, the methods stated that only papers evaluating the “pathophysiological mechanisms” were included.

2. If there is no capecitabline-related studies that can be found, (At least there are many case reports and a few reviews), then it is not necessary to mention it in the title or abstract. Instead, in the results part the author can briefly mention this.

3. In abstract, the results listed “The studies demonstrated 5-FU induced: Hemorrhagic infarction, … …”, it is not clear whether the author is talking about effects or mechanisms. If the objective is about mechanisms, then the author should include this information here. In addition, no need to capitalize “Hemorrhagic”.

4. In introduction part, there is a lack of the statement of the significance of the study and also a lack of reference support.

5. There is a lack of logic in the subtitles of Results. Some subtitles are based on different effects while others are specialized by animal studies or in vitro studies. The author should be consistent.

6. For each subtitle of results, the author almost always failed to mention any reasons for the discrepancy between studies. For example, Page 9 lines 190-193. And there is a lack of a possible conclusion for each effect.
Minors:
1. Introduction, the incidence of 5-FU induced cardiotoxicity should be specified.
2. Page 3 line 55, “to a lesser extent” instead of “to lesser extent”. Line 56, delete “in” after “varies”.
3. Page 7, line 152, there is no point of mentioning “Levofolene ……..”. Lines 154-156, there is no comparison between these two studies. Also which medium was used for iron? Blood? Tissue?
4. Page 8. Lines 170-171, what is the point of this sentence. The author should mention.
5. Page 9, lines 185-189, the sentences are redundant.
6. Page 10, line 226, “to which extent” instead of “to with extent”.
7. Page 11, lines 238-240, the meaning of the sentence is not clear.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declared that I have no competing interestss.