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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 112841

Title: Impact of statin therapy on postoperative outcomes following colorectal cancer surgery: A systematic review

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05384903

Position: Peer Reviewer

Academic degree and professional title: Associate Professor, MD

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2025-08-07

Reviewer chosen by: Jia-Lin Zhang

Reviewer accepted review: 2025-08-12 01:02

Reviewer performed review: 2025-08-13 06:38

Review time: 1 Day and 5 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? Yes Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes
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Is the content of the Introduction adequate? **No**

Is the content of the Materials and Methods complete?
Yes

Is the description of the experiments clear and complete? **Yes**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Yes**

Are the experimental data of the Results true and reliable? **Yes**

Are the quality and resolution of the images up to standard? **No**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **No**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **No**

Do authors omit important references? **No**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?
Yes

Are additional experiments needed for the study? **No**

Does the research scope comply with ethics? **Yes**

Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade C (Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade C (Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Major revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

Title: Impact of Statin Therapy on Postoperative Outcomes Following Colorectal Cancer Surgery: A Narrative Synthesis

Summary:

This study provides a comprehensive narrative synthesis on the role of statin therapy in postoperative outcomes for colorectal cancer (CRC) surgery. The manuscript discusses several observational studies examining the effects of statins on postoperative complications such as anastomotic leak, surgical site infections, and 30- and 90-day



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mortality rates. While the review provides valuable insights, there are several areas that require further clarification and improvement to strengthen the manuscript.

General Comments:

1. Overall Structure and Clarity:

The manuscript is well-structured, but certain sections could be more concise, especially in the methodology section. The discussion of study inclusion criteria and study designs could be streamlined to focus more on the key elements.

There are some formatting issues, particularly with inconsistent spacing and paragraph breaks. Please review the document carefully and ensure consistent formatting throughout to improve readability.

2. Literature Review Depth and Breadth:

While the review covers relevant studies on the impact of statins in CRC surgery, the inclusion of newer studies or related reviews would strengthen the discussion. More recent literature should be referenced to provide a timely and up-to-date perspective.

The manuscript mentions conflicting results in studies regarding the effects of statins on anastomotic leak and postoperative mortality. The authors should explore the reasons behind these discrepancies, particularly in terms of differences in study design, statin types, dosage, and therapy duration. Addressing these factors in the discussion would provide more clarity.

Specific Comments:

1. Literature Support for Postoperative Complications:

The manuscript mentions that approximately one-third of patients undergoing CRC surgery experience postoperative complications (such as anastomotic leak, small bowel obstruction, surgical site infections, etc.). It would be helpful if the authors provide references to support this claim, which would enhance the clinical significance of the study.

2. Clarification of Tumor Recurrence Rate:

The manuscript states that surgical resection itself may lead to tumor recurrence, with a recurrence rate of 25-45% at 5 years post-surgery. This statement is somewhat unclear. The authors should provide more detailed clarification on the source of this recurrence rate and how it is calculated to avoid any ambiguity.

3. Clarification of Statin Types Used in Studies:

Several studies are cited showing that statin use reduces the incidence of anastomotic leak, sepsis, and short-term mortality in CRC patients. However, the types of statins used in these studies are not specified. The authors should clarify which statins (e.g., atorvastatin, simvastatin) were used in the studies mentioned and discuss how different statins might influence the results.

4. Clarification of Liushen Li et al. Meta-analysis:

The manuscript cites a meta-analysis by Liushen Li et al. indicating that statins reduce cancer-specific mortality in CRC patients. However, the cited meta-analysis does not specifically focus on rectal cancer, which could be misleading. The authors should clarify this point and provide more context about the relevance of this meta-analysis to the current review.

5. Study Quality Assessment:

The authors mention using the Newcastle-Ottawa Scale (NOS) to assess the quality of the included studies, but there is limited discussion on how the quality of individual studies might impact the overall conclusions. The authors should provide a more detailed evaluation of the quality scores and how they influence the findings.

6. Figures and Tables:

Tables 1 and 2 summarize the results from the various studies, but the interpretation of some of these data could be clearer. The authors should expand on the explanation of these tables, highlighting key findings and discussing the discrepancies between studies.



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Minor Comments:

1. Formatting Issues:

Please review the manuscript for spacing and consistency. Some sections have inconsistent spacing, which can distract the reader. For instance, ensure there is a space between sentences where needed.

2. Language Expression:

Some sentences could be simplified for clarity. For example, the sentence “Additionally, surgical resection itself may also precipitate tumor recurrence, with an estimated recurrence rate of 25-45% at 5 years post surgery” could be rephrased to make the meaning clearer. The authors should aim to express complex ideas in a more straightforward manner.

3. Explanation of Figures and Tables:

The figures and tables are useful but would benefit from more detailed explanations in the manuscript text. The authors should clarify how to interpret the data presented and address the differences in results across the studies.

Conclusion:

This manuscript provides a valuable synthesis of the current literature on the potential benefits of statin therapy in CRC surgery. However, there are several areas for improvement, including clearer explanations of the data, more comprehensive literature support, and enhanced discussion of study heterogeneity. I recommend that the authors address the points raised above to enhance the manuscript's clarity, consistency, and overall quality. With these revisions, the manuscript will be a valuable contribution to the field.



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 112841

Title: Impact of statin therapy on postoperative outcomes following colorectal cancer surgery: A systematic review

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 06165404

Position: Peer Reviewer

Academic degree and professional title: Assistant Professor, MD, PhD

Reviewer’s Country/Territory: Hungary

Author’s Country/Territory: United States

Manuscript submission date: 2025-08-07

Reviewer chosen by: Jia-Lin Zhang

Reviewer accepted review: 2025-08-12 03:38

Reviewer performed review: 2025-08-21 03:01

Review time: 8 Days and 23 Hours

Content to be reviewed	<p>Does the manuscript’s content fall within the scope of the journal? Yes</p> <p>Is there any Key Word that is not included in the manuscript title? No</p> <p>Do authors’ affiliations correspond to the content of the manuscript? Yes</p> <p>Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes</p> <p>Are the Key Words complete? Yes</p>
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Is the content of the Introduction adequate? **Yes**

Is the content of the Materials and Methods complete?

Yes

Is the description of the experiments clear and complete? **Yes**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable**

Are the experimental data of the Results true and reliable? **Yes**

Are the quality and resolution of the images up to standard? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **No**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **Yes**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers? **Yes**

Are additional experiments needed for the study? **No**



	Does the research scope comply with ethics? Yes
Scientific quality	Grade A (Excellent)
Novelty of this manuscript	Grade A (Excellent)
Creativity or innovation of this manuscript	Grade A (Excellent)
Scientific significance of the conclusion in this manuscript	Grade A (Excellent)
Language quality	Grade A (Excellent)
Does this manuscript describe a study of the existing knowledge system?	No
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Accept
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

The manuscript entitled "Impact of Statin Therapy on Postoperative Outcomes Following Colorectal Cancer Surgery: A Narrative Synthesis" presents a well-structured and comprehensive review of the available observational evidence on the relationship between statin use and postoperative outcomes in colorectal cancer (CRC) surgery. The authors clearly describe their search strategy, inclusion criteria, and methodological quality assessment.



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The narrative synthesis is thorough, logically organized, and supported by up-to-date references, including studies up to 2025. The discussion appropriately acknowledges the limitations inherent to the available literature, especially heterogeneity in study designs and outcome definitions, while also highlighting consistent trends – notably the reduction in 30-day mortality among statin users. The review offers meaningful clinical context by considering confounders such as comorbidities, surgical type, and perioperative care variations, which adds depth to the interpretation of results.

The manuscript is written in clear, academic English, and figures/tables (e.g., PRISMA diagram, outcome comparisons) are appropriate and informative.

Significance of results

- The review synthesizes observational data suggesting that perioperative statin use is associated with reduced 30-day mortality in CRC surgical patients, an effect plausibly linked to anti-inflammatory, endothelial-stabilizing, and immunomodulatory mechanisms.
- While evidence on anastomotic leak rates is inconclusive, the balanced discussion - noting conflicting findings and possible confounding factors - is a strength, as it avoids overinterpretation.
- The results have practical significance for perioperative management strategies, particularly in high-risk surgical populations with cardiovascular comorbidities.
- The authors appropriately position their findings as hypothesis-generating, underlining the need for prospective randomized trials. This approach enhances credibility and clinical applicability.
- By integrating surgical risk factors (e.g., rectal vs. colon resections, emergency vs. elective surgery) and systemic-level care variations into the analysis, the paper provides a more nuanced understanding than prior overviews.

The topic is clinically relevant, and the balanced presentation will be useful for both



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clinicians and researchers interested in perioperative pharmacological adjuncts in CRC surgery.

Overall, the work meets the standards for publication in the World Journal of Gastrointestinal Surgery without the need for substantive revision.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 112841

Title: Impact of statin therapy on postoperative outcomes following colorectal cancer surgery: A systematic review

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05384903

Position: Peer Reviewer

Academic degree and professional title: Associate Professor, MD

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2025-08-07

Reviewer chosen by: Qian Zuo

Reviewer accepted review: 2025-09-22 06:01

Reviewer performed review: 2025-09-22 06:15

Review time: 1 Hour

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes
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Is the content of the Introduction adequate? **Yes**

Is the content of the Materials and Methods complete?
Yes

Is the description of the experiments clear and complete? **Yes**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Yes**

Are the experimental data of the Results true and reliable? **Yes**

Are the quality and resolution of the images up to standard? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **No**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **No**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?
Yes

Are additional experiments needed for the study? **No**

Does the research scope comply with ethics? **Yes**

Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	No

SPECIFIC COMMENTS TO AUTHORS

Reviewer's Comments:

I have reviewed the revised manuscript titled "Impact of Statin Therapy on Postoperative Outcomes Following Colorectal Cancer Surgery: A Narrative Synthesis". The authors have thoroughly addressed all previous comments and made necessary improvements to the manuscript.

The study is well-structured, and the findings regarding the potential benefits of statin therapy in reducing 30-day mortality following colorectal cancer surgery are valuable. The manuscript is now clear, well-supported by evidence, and appropriately highlights



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the need for future prospective studies.

I recommend accepting this manuscript for publication in World Journal of Gastrointestinal Surgery.