

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 86320

Title: Predictive value of frailty assessment tools in patients undergoing surgery for gastrointestinal cancer: An observational cohort study

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 07779840

Position: Peer Reviewer

Academic degree: N/A

Professional title: N/A

Reviewer's Country/Territory: Indonesia

Author's Country/Territory: China

Manuscript submission date: 2023-06-12

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-08-15 22:30

Reviewer performed review: 2023-08-20 03:47

Review time: 4 Days and 5 Hours

Scientific quality	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Very good <input type="radio"/> Grade C: Good <input type="radio"/> Grade D: Fair <input type="radio"/> Grade E: Do not publish
Novelty of this manuscript	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Good <input type="radio"/> Grade C: Fair <input type="radio"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="radio"/> Grade A: Excellent <input checked="" type="radio"/> Grade B: Good <input type="radio"/> Grade C: Fair <input type="radio"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Thank you for giving me an opportunity to review this study. I provide the following considerations: 1. Introduction: Overall, the text sets the stage for the importance of frailty assessment in patients with gastrointestinal cancer and identifies the existing assessment tools while emphasizing the need for more comprehensive studies to determine the most effective tool for predicting patient outcomes. It provides a clear research objective and context, making it a strong introduction to a study on this subject. But the text should explain why it is important to predict adverse postoperative outcomes and why assessing frailty is relevant to this prediction. 2. Methods: The research design utilizes appropriate methods to explore potential associations and factors that influence outcomes. 3. Clinical Implications: The text touches on the significance of assessing patients with CGA and providing psychological health interventions. Expanding on the practical implications of the study's findings for clinical practice and patient care would make the conclusion more impactful. Overall, the article can be accepted.

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02541712

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor, Chief Physician

Reviewer's Country/Territory: Slovakia

Author's Country/Territory: China

Manuscript submission date: 2023-06-12

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-08-09 06:34

Reviewer performed review: 2023-08-20 08:28

Review time: 11 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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Language quality	<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
Conclusion	<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
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I read with interest the submitted manuscript entitled "Predictive value of frailty assessment tools in patients undergoing surgery for gastrointestinal cancer: An observational cohort study". I think the study is well presented, introduction, patients and methods, results and discussion are valid. Author found, that in a multivariate logistic regression frailty was not associated with complications of GI surgery, but predicted higher cost. I think, that the study is valid, but from the data some more conclusion could be drawn. I have a few comments: 1. Karnofsky score is also viewed as a frailty assessment tool in a general cense, authors should also explore its value 2. A common problem of frailty defitinion in not as much in the scale, but in the cut-off value, and this was nicely demonstrated by the second outcome - the cost, where higher cost was defined as above 75th percentile. When adopting a frailty scale designed on a different population, than in the present study, authors should come-up with their own cut-off of frailty, valid on their population of interest. So, why not exploring the predictive value of 75th or 80 percentile of any frailty scale they have chosen. Is has been done by precious authors in other clinical contexts (Lai et al in the Liver frailty index).



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This way, a fixed proportion of patients would be defined as frail (20 or 25%) and the predictive value of this definition of frailty could come-up in a different perspective.

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Title: Predictive value of frailty assessment tools in patients undergoing surgery for gastrointestinal cancer: An observational cohort study

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03821481

Position: Peer Reviewer

Academic degree: MD, MSc

Professional title: Attending Doctor, Instructor, Surgeon

Reviewer's Country/Territory: Portugal

Author's Country/Territory: China

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Congratulations on your manuscript. Increasing frailty prevalence in surgical patients is a global trend. These patients should be identified in order to prevent and mitigate potential complications and adjust expectations for treatment. Although this subject is not a novelty, there is still a paucity of papers on this matter regarding digestive oncological surgery. This manuscript is a well-written and well-designed prospective study that unfortunately fails to support its initial hypothesis. However, it provides high-quality data (three geriatric scales) on the adult Chinese population who underwent GI oncological surgery. Why do you think that, in your study, frailty was not statistically associated with higher complications? Was your sample underpowered? Did you calculate the sample size before inclusion? Also, how do you explain such a difference in frailty prevalence (CGA, Fried phenotype, and FRAIL scale: 65.9%, 47.6%, and 34.9%, respectively)? You also excluded "patients who were unable to cooperate with and complete data collection". Does this mean that patients who were not able to complete the FRAIL scale were all excluded? This might be an important bias, as a patient who cannot communicate can be the most frail. If you considered major



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complications only (Clavien Dindo higher or equal to 3), do you think it would show a more significant difference between groups? You conclude that "Frailty assessment should be included as part of routine preoperative risk assessment to improve adverse postoperative outcomes" but after reading your paper, this does not appear to be the case. Also, you might want to include "Sandini M, Pinotti E, Persico I, Picone D, Bellelli G, Gianotti L. Systematic review and meta-analysis of frailty as a predictor of morbidity and mortality after major abdominal surgery. *BJS Open*. 2017 Nov 9;1(5):128-137. doi: 10.1002/bjs5.22. PMID: 29951615; PMCID: PMC5989941." in your references. You mention that "The authors have read the ARRIVE guidelines, and the manuscript was prepared and revised according to the ARRIVE guidelines." The ARRIVE guidelines are for Animal Research: Reporting of In Vivo Experiments. You submitted as attachment the STROBE checklist and should change this on your manuscript accordingly, also adding the correct citation to your references.

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Title: Predictive value of frailty assessment tools in patients undergoing surgery for gastrointestinal cancer: An observational cohort study

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

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Reviewer's code: 02533702

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

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Reviewer chosen by: Geng-Long Liu

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Reviewer performed review: 2023-08-26 23:26

Review time: 45 Days and 16 Hours

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

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

three commonly used frailty assessment tools were studied to investigate the current status of preoperative frailty and to analyse their predictive value for prognosis in patients undergoing surgery for gastrointestinal cancer. The considered tools showed a poor agreement between assessing scales, which makes sense with the rationale of this study. However, the outcome measures were total complications and increased hospital costs. The first bias was to consider only postoperative complications that developed during hospitalisation: the effect of frailty can be evident within 30 days from surgery and the considered cut-off is in effect a huge study limitation and the possible explanation of the following result : None of the frailty assessment tools were associated with postoperative complications. The second consideration concerns the results discussion: the employed tools investigate functional and cognitive aspects, and consider malnutrition only by assessing weight loss. In particular CGA typically assesses comorbidities, polypharmacy, functional status, cognition, psychological status and nutritional status, FRIED exhaustion, low physical activity, slowness and weakness and FRAIL Fatigue, Resistance (inability to climb stairs), Ambulation (inability to walk a certain distance), Illnesses. Due to the considered items I do not agree that it is necessary to explore patients' frailty across all ages, as in younger ages the nutritional issues are the main concern. 83 (36.2%) patients had gastric cancer, 81 (35.4%) had colon cancer, and 65 (28.4%) had rectal cancer: these three clinical situations are linked to a slightly different metabolic upset in terms of malnutrition and sarcopenia, so a bias in this analysis can be speculated. This specific aspect is not analyzed in discussing the study data. I agree that such patients are more vulnerable to frailty due to cancer cachexia,

cancer-related fatigue and gastrointestinal symptoms: however to state that these latter contribute to the high prevalence of frailty in this population is too generic, as malnutrition, sarcopenia and cachexia are not synonyms, and the concept of frailty has a wider acception. “Nevertheless, our study had several limitations that need to be noted”. I think that to consider emergency surgery or palliation is a powerful confounding factor in evaluating frailty assessment and must not be considered

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03317309

Position: Peer Reviewer

Academic degree: MD

Professional title: Academic Fellow

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

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

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous
	Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No

SPECIFIC COMMENTS TO AUTHORS

<Major> English should be polished. What is your perspective based on the results in this study in the future? How do you manage the patients with abnormalities of CGA in performing surgery for gastrointestinal cancer? I think the cutoff value of B.I. <100 is too high. Several studies reported use the cutoff of B.I. < 85. In the Introduction section, the authors described that they aimed to assess the most useful tool among three, and to investigate which tool was significantly relevant to prognosis. However, the outcomes of this study was factors associated with complications and increasing hospitality cost. There seems to be a gap between aims and outcomes. How about the relationship between the scores of three tools and prognostic factors such as recurrent-free survival time or overall survival? <Minor> Line number should be restarted from one in every page. In the results section, I recommend that baseline patients characteristics are shown and described firstly.