

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 77892

Title: A new scoring system to evaluate adjuvant chemotherapy for patients with T2N0M0 gastric cancer after D2 gastrectomy

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05754965

Position: Peer Reviewer

Academic degree: PhD

Professional title: Postdoc

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2022-06-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-11 16:14

Reviewer performed review: 2022-07-14 19:58

Review time: 3 Days and 3 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input 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 Grade E: Do not publish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 checked="" 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="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

This is a significant clinical study in gastric cancer (GC). GC is now a severe healthy problem in China and east Asia. Adjuvant chemotherapy is effective in treat GC at early stage. However, there is no evidence to support the use of adjuvant chemotherapy in T2N0M0 gastric cancer. This study provides new insight into the evaluation of GC patients to decide whether they are suitable for undertake adjuvant chemotherapy. To me, this study is of clinical importance. I have only one minor comment: Can you improve your model by using signature of key genes associated with your risk factors? Combination with gene signature may optimize the prognostic value of your model. At least you can discuss this possibility and feasibility.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03998130

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Senior Lecturer, Surgeon, Surgical Oncologist, Teacher

Reviewer's Country/Territory: Romania

Author's Country/Territory: China

Manuscript submission date: 2022-06-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-12 13:16

Reviewer performed review: 2022-07-15 12:33

Review time: 2 Days and 23 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 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
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SPECIFIC COMMENTS TO AUTHORS

The paper addresses a topic of real interest for clinical practice and would greatly interest the journal readers. The benefit of adjuvant chemotherapy after curative-intent surgery for T2N0M0 gastric adenocarcinoma is controversial. Thus, identifying patients benefitting from adjuvant therapy is of utmost importance. Few comments should be raised: In the multivariate analyses, why were factors included with p values less than 0.250? Few data from Material and Methods appear to fit the Results part. Please consider changing cardiac cancer to cardia cancer. In Table 1, please consider providing data as number (%) and p values for the univariate analyses. There are no data about postoperative complications (particularly the severe ones) that could potentially affect the access to adjuvant therapy and might explain the poor prognosis in the group with postoperative observation. There appears to be redundant data in the text, Table 3 and Figure 3. Please consider eliminating redundant data. In the multivariate analyses, only vascular invasion was found as an independent risk factor for overall survival. Why did the authors introduce BMI and tumor site in the score and not the differentiation grade? To me, there are significant concerns regarding how the score was made. Thus, the results and conclusions of the study could be severely altered.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05556133

Position: Peer Reviewer

Academic degree: MD

Professional title: Consultant Physician-Scientist

Reviewer's Country/Territory: Turkey

Author's Country/Territory: China

Manuscript submission date: 2022-06-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-15 09:06

Reviewer performed review: 2022-07-19 08:51

Review time: 3 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input 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 checked="" 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="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

It is controversial whether adjuvant chemotherapy is necessary for stage T2N0M0 gastric cancer, but there are some risk factors for recurrence for T2N0M0 gastric cancer, such as lymphatic and/or blood vessel invasion, tumor diameter, perineural invasion, proximal tumor location, and poor differentiation. This study aimed to assess the risk score of patients with pathologic T2N0M0 gastric cancer after D2 gastrectomy. The study is very well designed and the results are very interesting. The authors should add data about postoperative complications. And a minor editing is required.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06129259

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: China

Manuscript submission date: 2022-06-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-06-14 06:58

Reviewer performed review: 2022-07-19 08:52

Review time: 35 Days and 1 Hour

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
Language quality	<input type="radio"/> Grade A: Priority publishing <input checked="" type="radio"/> Grade B: Minor language polishing <input type="radio"/> Grade C: A great deal of language polishing <input type="radio"/> Grade D: Rejection
Conclusion	<input type="radio"/> Accept (High priority) <input type="radio"/> Accept (General priority) <input checked="" type="radio"/> Minor revision <input type="radio"/> Major revision <input type="radio"/> Rejection
Re-review	<input checked="" type="radio"/> Yes <input type="radio"/> No



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

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
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SPECIFIC COMMENTS TO AUTHORS

This is an interesting study of the adjuvant chemotherapy for T2N0M0 gastric cancer.

The manuscript is well written. The reviewer has some minor comments to the authors:

1. A minor editing of the manuscript is required. 2. Some redundant data in the text,

Tables and Figures should be eliminated

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05445850

Position: Editorial Board

Academic degree: MD

Professional title: Director, Professor

Reviewer's Country/Territory: Taiwan

Author's Country/Territory: China

Manuscript submission date: 2022-06-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-10 23:44

Reviewer performed review: 2022-07-19 10:27

Review time: 8 Days and 10 Hours

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 type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" 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
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SPECIFIC COMMENTS TO AUTHORS

Xu et al. aim to develop a new scoring system to evaluate benefits of adjuvant chemotherapy for T2N0M0 gastric cancer after radical surgery. I have the following comments:

1. The number of lymph node retrieved is important to clarify the curative resection in patients with T2N0M0.
2. Other prognostic factors such as tumor size, lymphatic invasion or perineural invasion should be included for survival analysis.
3. In the introduction, the author should describe in detail the controversial results of beneficial effects of adjuvant chemotherapy for T2N0M0 gastric cancer. The effects of adjuvant chemotherapy in stage I gastric cancer including T1N0M0, T2N0M0 and T1N1M0 should not interpret the same as T2N0M0.
4. The demographic difference in the Table 1 between adjuvant and observation groups should be shown.
5. How do you choose adjuvant regimen for patients?
6. The follow-up time should be at least for 3 years for patients with early-stage disease.
7. How do you explain the huge benefit for high-risk patients with adjuvant chemotherapy compared with those without?
8. Please show the recurrence pattern in each group.
9. The patient number who underwent chemotherapy is too small (n=63) to make solid conclusion.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05755508

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Academic Fellow, Research Associate, Surgeon

Reviewer's Country/Territory: Greece

Author's Country/Territory: China

Manuscript submission date: 2022-06-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-16 07:38

Reviewer performed review: 2022-07-26 09:49

Review time: 10 Days and 2 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 type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" 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 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

The purpose of this article is to introduce a new scoring system that evaluates the need for adjuvant chemotherapy for T2N0M0 gastric cancer after radical surgery. This retrospective study has interesting aspect. There are some critical problems and limitation for publication as pointed below: - Please explain why you chose the specific exclusion criteria, especially loss of follow up and neoadjuvant chemotherapy. Since cox regression analysis takes into account the loss of follow up why you excluded those patients? - The table with the univariable cox regression analysis is missing. Please consider to add this table. - How did you choose which variables to use in the multivariable analysis? Were the results of the univariable analysis considered? - Why other risk factors, such as poorly differentiated or higher-grade cancer, perineural invasion and age <50 years old were excluded from multivariable analysis and the creation of prognostic score? - Why was the type of chemotherapy regimen administered excluded from the multivariable analysis? - It is unclear why, while in the multivariable analysis the p for two variable is not 0.01 and thus have no independent effect, they are ultimately used for the prognostic score. Probably if the statistical analysis is carried out again, taking the above into account, then we will have more strongly founded results. - Please specify how common is gastric cancer - Please fully explain the abbreviations used to report the regimens patients received

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Manuscript NO: 77892

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03998130

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Senior Lecturer, Surgeon, Surgical Oncologist, Teacher

Reviewer's Country/Territory: Romania

Author's Country/Territory: China

Manuscript submission date: 2022-06-09

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2022-08-23 17:45

Reviewer performed review: 2022-08-24 09:45

Review time: 15 Hours

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
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
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This fascinating study shows that gambogic acid inhibits gastric cell proliferation through necroptosis. Previous studies show the effect of gambogic acid in different types of cancer, including gastric cancer, with various anti-cancer mechanisms. The methodology in the study is appropriately used, the results entirely sustain the conclusions, and the results are meaningfully discussed in the context of pre-existing literature. Only a few minor comments: The last paragraph from the Introduction showing the results of the present study briefly maybe should be moved to Discussion. The Abstract should be provided in the format required by the journal for an original article. In line 231, replace indictor with indicator.