

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 71395

Title: Characterization of E-cadherin expression in normal mucosa, dysplasia and adenocarcinoma of gastric cardia and its influence on prognosis

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00722963

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Serbia

Author's Country/Territory: China

Manuscript submission date: 2021-09-06

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-06 13:42

Reviewer performed review: 2021-09-22 05:40

Review time: 15 Days and 15 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 Grade E: Do not publish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 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
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SPECIFIC COMMENTS TO AUTHORS

Title of the manuscript does reflect the main subject and field of interest of the manuscript. It is short, concise and clear. Abstract – abstract summarize and reflect the work described in the manuscript, and points out to the most important results found in this study. Key words - 7 key words are stated, each adequately reflecting the main focus of the manuscript. Background – introduction give sufficient and clear information on what is known and what is yet to be studied, introducing a reader into the research matter. It adequately describe the background, present status and significance of the study. Methods – this section of the manuscript is written very clearly and precisely. Inclusion and exclusion criteria's are very well defined. Methodology is explained in sufficient details to be clear and reproducible. Only remark is to this section: reference 12 is published in 1994. I believe that a more up to date literature should be used. "Histopathological diagnosis Histopathological diagnoses for normal mucosa, dysplasia and adenocarcinoma of the gastric cardia were made according to established criteria [12]. Methods used are standard for clinical practice, and for scientific paper it might be a little more complex. This shortcoming of the research author are compensating by large year span of the provided data, and large number of subjects. Results – Results presented are in accordance with aims and applied methodology, presented in clear and understandable manner. Although significance of E-cadherin expression in gastric cancer has been a topic of other studies, more important findings of this study is the expression in normal, healthy mucosa and in precancerous lesions. These results are of use to both clinicians and researchers. Discussion. The manuscript interpret the findings adequately and appropriately,



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highlighting the key points concisely, clearly and logically. The discussion is accurate and does reflect on scientific facts and related topics, as well as to clinical practice. Illustrations and tables - the figures, diagrams and tables are of good quality, clear and sufficient, appropriately illustrative of the paper contents. Figures do not require additional labeling with arrows, asterisks etc.. Biostatistics. Applied statistical methods are well selected and adequate for this purpose. Units. The manuscript meet the requirements of use of SI units. References. The manuscript cite appropriately selected references,. Most of them are up to date, except for previous comment on reference 12. 14 (from 25 listed references) are from the last 5 years, others are published 5-10 years ago, and ref.12 in 1994. The author does not self-cite, omit, incorrectly cite and/or over-cite references. Quality of manuscript organization and presentation. very good, overall. The style, language and grammar are accurate and appropriate. Research methods and reporting. The author prepared the manuscript according to the appropriate research methods and reporting. Ethics statements. Authors did not provide any document regarding the consent of patients or ethics committee aproval, thez have on their behalf, wrote this: Dear editor and reviewers, Informed consent statement: Patients were not required to give informed consent to the study because the analysis used an an anonymous data that were obtained after each patient agreed to treatment by written consent. Since this is a usual practice in clinics (having patients written consent for treatment, which include using the material for training new doctors and scientific purposes), and that this study comprised data from many years ago, I think that the manuscript does meet the requirements of ethics.

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Title: Characterization of E-cadherin expression in normal mucosa, dysplasia and adenocarcinoma of gastric cardia and its influence on prognosis

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03552126

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Hungary

Author's Country/Territory: China

Manuscript submission date: 2021-09-06

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-08 10:02

Reviewer performed review: 2021-10-14 18:21

Review time: 6 Days and 8 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="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

Dear Authors, I have found your article good and worth publishing. I have some questions, but otherwise I am quite convinced by the manuscript. Data about E-Cadherin expression is not missing, but it is rare. There are a couple of articles describing similar findings as recent manuscript, thought this manuscript has really a huge number of patients involved. The largest by now. Material section needs some clarification, with the detailed description of IHC-process, with all materials' cat.no. Were there any paired samples involved into the study: I mean normal, dysplastic and cancer tissues from the same patient? Or if you had bigger slides where dysplastic and/or normal mucosa was present together with cancerous tissue? Did you see decrease in E-cadherin staining even in this context? Or you did not have samples like this? For me the results describe E-cadherin as a differentiation related marker. Was there significant difference in E-cadherin expression when different grades of tumors were compared? Any graph on that? Well, I saw graphs on this, but this was less mentioned in manuscript. Could you please mention and comment it in your manuscript? I think, we could handle E-cadherin as a kind of differentiation marker. You mentioned that male patients showed weaker expression of E-Cadherin. Was it because males have higher grades and stages of tumor? Some further minor points: "The staged of patients with GCA were based on the 8th edition" rather staging. "group with negative lymph node metastasis" rather patients without LN metastasis. This sentence appears on multiple sentences. "As we know, the present study is the first report about the E-cadherin protein expression in the lesions progressed from normal gastric cardia mucosa to dysplasia and GCA, and the largest sample study of the expression of E-cadherin protein and its influence on

survival with GCA." I would put references here. "there was few reports" plural " It is showed that, in our study, " rather our study showed that.... "negative expression" rather decreased or lacking expression. Again on multiple sentences. "Another interesting finding in the present study was that positive expression of E-cadherin protein in GCA patients at an early stage was higher than in those at an advanced stage (92.3% vs. 83.6%, $P = 0.001$), which indicates that E-cadherin protein may be a potential biomarker for early warning for GCA." how? E-cadherin expression should be preserved in normal mucosa...I do not get the point here. "Lastly, we found that in the GCA patients without lymph node metastasis, positive expression of E-cadherin protein indicated better survival than negative expression." I think it might be again the question of grade! Any data, analysis on this? "The difference in E-cadherin expression can further stratify the prognosis of patients with negative lymph node metastasis, indicating that E-cadherin protein expression may be a promising prognostic biomarker for non-surgical GCA patients." How do you imagine this... I have a concern about the decrease in E-cadherin expression. The decrease is quite small: G1 92% vs, G3 84%. Was it decrease in focal expression, or was it expression or lack of expression, so something which could be dichotomized?

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? YES 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? YES 3 Key words. Do the key words reflect the focus of the manuscript? YES 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? YES 5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? IT NEEDS FURTHER CLARIFICATION, COMPLETION 6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? YES 7 Discussion. Does the manuscript interpret the



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findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? ZES, SOME MINOR CLARIFICATION WOULD BE BENEFICIAL 8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? YES Do figures require labeling with arrows, asterisks etc., better legends? NOT 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? PRIBABLY YES 10 Units. Does the manuscript meet the requirements of use of SI units? YES 11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? YES 12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? YES 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? YES 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? MOST PROBABLY YES, AS IT IS A



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