

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 48757

Title: Gastric Neuroendocrine Neoplasms Type 1: a Systematic Review and Meta-analysis

Reviewer's code: 02954391

Reviewer's country: Japan

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-30 08:53

Reviewer performed review: 2019-05-01 07:02

Review time: 22 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

These main research findings of this paper will be important for the understanding of prognosis and selectin of therapy for GNEN1. Therefore, this paper is quite a fascinating manuscript, and I believe the paper will be of interest to the readership of WJG However,



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the authors should also clarify and correct the points listed below. 1) In this paper, authors did not deal with endoscopic ultrasonography and laparoscopic surgical resection at all, therefore, it is uncomfortable to discuss these modalities. The paragraph documented about endoscopic ultrasonography and laparoscopic surgical resection should be deleted, therefore, the description about these modalities should be deleted in the core tip. 2) Supplementary figures “2A-4A, 2B-4B cannot be found.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 48757

Title: Gastric Neuroendocrine Neoplasms Type 1: a Systematic Review and Meta-analysis

Reviewer's code: 02954022

Reviewer's country: United States

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-30 10:28

Reviewer performed review: 2019-05-05 12:47

Review time: 5 Days and 2 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Overall, this is a need for meta-analysis for GNEN1s due to limited data with lot of heterogeneity. Hence, this manuscript, in my view provide valuable information to clinicians managing such patients. Strengths: 1. There is limited literature on

GNEN1. The authors included only those studies with at least ten patients with GNEN1. They excluded case reports and small case series. 2. Only the latest eligible study from any institute was included Weaknesses: 1. The confidence interval for LN metastases is very broad and ranges from 1.5 to 80. It is difficult to conclude from these results if a cut-off of 10 mm is accurate versus not. 2. This study does not provide an independent risk assessment. I suppose none of the studies included a multivariate analysis to evaluate which among - size vs. depth of invasion had a higher risk. However, this is a limitation of the study. So also, the study doesn't provide information when both size and depth (propria involvement) are present. Considerations: 1. In study methods, they mention that the study hypothesis was formulated prior to data collection. What was the study hypothesis? It is not clear from the text preceding this statement in the methods. 2. Some spelling errors; such as - greater (in methods/ bias assessment) 3. The rate of LN metastases for a cut-off size of 10 mm was 15.3% vs. 0.8% for lesions >10 mm and <10 mm. The authors need to specify the cut-off size accurately. What did they consider 10 mm as? so they need to use ">" symbol for either >10 mm or < 10 mm. 3. Why is there a number 12 next to title heading 'Discussion'

INITIAL REVIEW OF THE MANUSCRIPT

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[Y] No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 48757

Title: Gastric Neuroendocrine Neoplasms Type 1: a Systematic Review and Meta-analysis

Reviewer's code: 00181208

Reviewer's country: Canada

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-05-01 13:18

Reviewer performed review: 2019-05-10 13:15

Review time: 8 Days and 23 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is a systematic review and meta-analysis attempting to elucidate some aspects of the prognosis and therapy of gastric NEN type 1. Specifically, authors explore the size, grade and depth of invasion of the primary neoplasm as prognostic factors for lymph



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node metastases and the type of surgical intervention (endoscopic versus surgical) for local recurrence. As authors mention, the correlation of LN metastatic disease to survival outcomes is uncertain, and thus the characteristics of the primary tumors examined are not prognostic for survival. However, the review and meta-analysis remains useful as an overview of the field. Some additional comments: - It is unclear from the methods if only studies with localized disease (assumingly this would be the aim?) would be included and how staging was done to exclude metastases in the included studies. This should be clarified. - It is also unclear how the type of NEN (type 1 versus other types) has been ascertained. Have the authors attempted to verify the type from any data provided in the original reports or relied exclusively on the evaluations of the original authors? This is quite important given the lack of clarity of diagnostic criteria and becomes more important for reports from centers with less of an expertise on these tumors. - In the search strategy, terms used do not include outcomes such as lymph node metastases or infiltration and various survivals. Have these included in the search. Articles may have been missed if those terms not included for example in combination with “gastric neuroendocrine tumor” or “neoplasm”. -The size cut -off of 1 cm used is clinically relevant but larger sizes could be also of interest as prognostic factors for LN metastatic disease as larger tumors are often present. It would be clinically relevant to identify larger size tumors with still good prognosis. It would be very interesting and would enhance the report if authors performed such analysis. - Similarly distant metastases as an outcome in addition to LN metastases would be a clinically relevant point, possibly even more relevant than LN metastases. Were distant metastases searched for as an outcome? Authors should comment. - In the local recurrence analysis, the number of patients included should be mentioned. - In table 1 the meaning of initials and * should be explained. - In table 2 the scale used according to NOS should be explained. -In the discussion, authors mention a few relevant points regarding the quality of the included



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studies that may constitute limitations of the meta-analysis. Additionally, heterogeneity of the studies makes CIs of ORs of different summary estimates quite broad to a degree that one wonders about clinical usefulness. Authors should further comment.

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BPG Search:

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- ☐ No