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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 46427

Title: Current surgical treatment of esophagogastric junction adenocarcinoma

Reviewer's code: 03766580

Reviewer's country: Greece

Science editor: Ying Dou

Reviewer accepted review: 2019-03-28 05:46

Reviewer performed review: 2019-04-24 16:52

Review time: 27 Days and 11 Hours

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[ ] Grade E: Do not publish		[ ] Rejection	[Y] Advanced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

SPECIFIC COMMENTS TO AUTHORS

The present review article summarizes in an excellent way the surgical approach of this group of tumors

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 46427

Title: Current surgical treatment of esophagogastric junction adenocarcinoma

Reviewer's code: 02554808

Reviewer's country: Romania

Science editor: Ying Dou

Reviewer accepted review: 2019-04-14 19:52

Reviewer performed review: 2019-04-30 08:26

Review time: 15 Days and 12 Hours

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[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High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

SPECIFIC COMMENTS TO AUTHORS

The abstract contains informations about tumors of the GEJ which is too general and too vague. There is lack of methodology for the construction of the review. There is no data on the method used to collect the papers analyzed for the review and also no explanation why these specific papers were chosen and not others. The paper iself is a

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compilation of data taken from the literature but lacking the must needed critical appraisal. Instead of running through definition and classification of GEJ cancers, incidence of lymoph node metastasis, types of surgery and endoscopic submucosal dissection providind incomplete data, without a correct comparision and with no clear reccomendations and conclusions, the authors should better choose one of these issues and adress it correctly, in a scientific manner, to provide a critical view on the status of knowledge on this field and try to offer some scientifically valid reccomendations. Otherwise, the paper is just a sum of scarce data on various topics mixed together and with almost null scientific and practical value. Below is a list of some of the isses that should be reanalized in this paper: The results showed that the incidence of metastasis or recurrence was 4%,7%, and 11% in the upper, middle, and lower mediastinal LNs respectively. It also revealed the length of esophageal invasion correlated with the number and location of mediastinal LN metastases. The incidence of metastasis was much higher when the length of esophageal invasion was >3 cm for the upper or middle mediastinal nodes and >2 cm for the lower mediastinal nodes[14]. In practice, this result means that if esophageal invasion of >3cm is noted, the upper and middle mediastinal LNs should be harvested 11% lower mediastinal lymh node metastases for pT2-4 Siewert Type II is a figure that is difficult to accept. The authors should be more cautious and discuss there hard-to-be-true values. The incidence of metastasis was much higher when the length of esophageal invasion was >3 cm for the upper or middle mediastinal nodes and >2 cm for the lower mediastinal nodes[14] Is is also difficult to explain a significant difference in lymph node metastases on a difference of 1 cm esophageal invasion. It does not correlate with the later statements of the authors that the proximal resection margin o the sophagus may be as low as 2-3 cm. These results may indicate that harvest of the peri gastric nodes of the lower half of the stomach is not beneficial if the distance from the EGJ to the anal edge of the tumoris

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greater than 5cm. - this is a false statement Esophagectomy with proximal gastrectomy might be enough in type II cancer, however it is better that the lower mediastinal compartment be routinely sampled during the operation – what type of esophagectomy, Ivor-Lewis or McKeown? Why mediastinal lymphadenectomy if the authors state that there is still an uncertain incidence of metastasis to the lower mediastinal compartment? It seems that even the authors do not have a clear idea of the operation recommended for the Siewert II type cancers and therefore they are not able to send a message to the reader. The length of esophageal invasion is a reference point in a surgical strategyof whether a transthoracic or a transabdominal approach is used? Does it mean that is the esophagus is invaded 3.1 cm a different operation is performed compared with a 1.9 cm invasion? What happens with a patient with 2.6 cm invasion of the esophagus? The data in the literature does not fully support such strategy and the authors should be more careful when advocating it. Although the incidence of Nos 10 LN metastasis ranged from 10-20%, there was no survival benefit associated with adding splenectomy to carry out a D2 lymphadenectomy[25, 26]. Itis recommended that splenectomy is done only to get an R0 resection[27, 28] – The authors do not mention about the possibility to retrieve the No 10 lymph nodes with preservation of the spleen. LNs metastasis isis also an indicator of prognosis. The highest risk factor is the number of metastatic LN≥7[15, 31] A multicenter retrospective study fromthe USA indicated that the number of LNs harvested was an independent predictor for survival after surgery. They concluded that a minimum of 23 regional LNs harvested can offer a survival benefit[35] The authors do not mention the ration metastased/total LN as prognostic factor. The researchers indicated that more than 15 LNs were recommended for patients undergoing curative resection.[36]. However,a Dutch study found thatthere is no benefit from an extended lymphadenectomy for type II disease[37] The authors imply that removing more than 15 LN represents extended surgery which is actually not. Removing at least 15 LN is a

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prerequisite for correct oncological surgery A LN harvest of at least 23 nodesisenough for maximizing the outcomes after EGJ cancer surgery. The present day bench mark for oncological gastric surgery is to remove 15 LN. The authors extrapolate the conclusion of a single study which is not scientifically correct. To date there is no standardized rule to remove more that 23 LN. Barbour et al. identified that 5 cm of grossly normal in vivo (approximately 3.8cm ex vivo) proximal esophagus was associated with improved survival for patients (≥T2 and≤6 positive lymph nodes) with Siewert types I/II/III[40] – improved versus what? What happens with tumors with more than 6 LN invaded? Esophagogastrectomy with moderate lymphadenectomy is still considered the standard surgical strategy to EGJ cancer – what is moderate lymhdenectomy? This parameter is new to the surgical community. Lymphadenectomy is either 2 field or 3 field and should involve at least the LN from the inferior mediastinum and stations 1,2,3,7,8,9,10p. Is that moderate? The authors should be more exact in the expression of their ideas. For type II cancers, some recommendesophagectomy with proximal gastrectomy, which allows for dissection of both abdominal and mediastinal LNs –what type of esophegctomy, Ivor-Lewis or McKeown? Which is the extent of lymphadenectomy, should the carinal lymph nodes be removed, should the recurrent lymph nodes be evaluated as sentinel nodes? The information provided by the authors is too vague and general. Surgerychoiceaccording to Siewert classification – is just an enumeration of some of the surgical techniques available. There is no critical discussion related to their indications and pitfalls. allowing exposure to the entire mediastinum to harvest even the upper mediastinal LNs. – previously the authors showed data that the upper mediastinal LN are invaded in 4% of cases. There is no discussion as to whether such lymphadenectomy is necessary. Based on these results, the researchers suggested that LTA should be avoided as a surgicaltherapyfor adenocarcinoma of the EGJ or gastric cardia – This statement may be true for the Siewert type II and II cancers. Siewert Type I cancer

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benefits from an Ivor Lewis procedure Transthoracic vs transhiatal esophagectomy – the authors ignore the papers that show a trend for a higher survival in patients operated by a transthoracic technique with adequate lymphadenectomy starting 3 years postoperatively. This is significant in those with less than 8 LN metastasized. The role of neoadjuvant chemoradiotherapy followed by radical surgery is also ignored. Bothminimally invasive surgeriesshowsimilar surgical and oncological outcomes compared with open surgeries – this statements should be more cautious. MIS s generally reserved for less advanced cases and patients with better performance status, hence there is a selection bias. Usually, the minimally invasive Ivor-Lewis technique is the main choice, although the intrathoracic anastomosis is sometimes difficult - the anastomosis is especially difficult, the double stapling techniques has a higher risk of insufficiency, introduction of the circular stapler is cumbersome, newer approaches use a linear stapler for the anastomosis - all these details are forgotten by the authors. Favorable oncological results were also reported in severalstudies.A meta-analysis analyzed 359 early EGJ adenocarcinoma patients whoreceived ESDtreatment. More than 20% of tumors were reported to have deep submucosal invasion – which is the criteria for deep submucosal invasion? Why was ESD performed in these cases? According to the above-mentioned risk factor for LN metastasis, there were 277 patients in the low risk group and 95 in the high risk group - the authors provide no definition of low risk and high risk features. Taken together, ER may be a good therapy for early EGJ cancer – this statement may be confusing for those that do not have a good knowledge on the indications of EMR – which are not stated in this paper. Can all patients with early EGJ cancer treated with ER? Of course not but the authors give this impression.

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Manuscript NO: 46427

Title: Current surgical treatment of esophagogastric junction adenocarcinoma

Reviewer's code: 00182891

Reviewer's country: France

Science editor: Ying Dou

Reviewer accepted review: 2019-04-27 12:39

Reviewer performed review: 2019-05-03 17:12

Review time: 6 Days and 4 Hours

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

SPECIFIC COMMENTS TO AUTHORS

Authors should be commended for their effort to highlight gastroesophageal junction cancer's surgical treatment. This is a well written review that summarizes current state of care regarding that pathology. A few comments: 1) Did the authors mean "is not greater than 5 cm" instead of "is greater than 5 cm" in the "LN metastases in Type II EGJ

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cancer" section? 2) "Is" is wrongly repeated at the beginning of the "Lymphadenectomy with prognosis" section. 3) Authors should not use "meta-analysis" term for reviews of literature.

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