

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**ESPS manuscript NO:** 31760

**Title:** The incidence of venous thromboembolism and the role of D-dimer as predictive marker in patients with advanced gastric cancer receiving chemotherapy

**Reviewer's code:** 00058401

**Reviewer's country:** Brazil

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-12-06 21:38

**Date reviewed:** 2016-12-14 22:01

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

Congratulations for the manuscript ..We criticized no comment about the arterial thrombosis in the course of chemotherapy.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**ESPS manuscript NO:** 31760

**Title:** The incidence of venous thromboembolism and the role of D-dimer as predictive marker in patients with advanced gastric cancer receiving chemotherapy

**Reviewer's code:** 00048205

**Reviewer's country:** Japan

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-12-06 21:38

**Date reviewed:** 2016-12-20 17:37

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

Dear authors Thank you very much for submitting this interesting draft. In this prospective study using a total of 241 patients, authors demonstrated a relatively high incidence and a risk of venous thromboembolism (VTE) in patients with advanced gastric cancer (AGC) receiving chemotherapy and proposed that pretreatment D-dimer level might be a biomarker for risk stratification of VTE. This study provided clinically useful information of the usefulness of D-dimer in predicting the occurrence of VTE during a median follow-up duration of 10.8 months after the chemotherapy. However, there remain some issue, as follows. Major: 1) Previous studies suggested that smoking and alcohol abuse might be associated with risk of cardio-vascular disorder, so please demonstrate whether these factors can be related to the VTE risk. 2) This cohort was focused on patients suffering from advanced GCs, which can cause upper-GI bleeding, followed by dehydration or severe anemia required for blood transfusion treatment. These phenomena may result in the occurrence of VTE. So, please demonstrate whether symptom of GI-bleeding and blood transfusion treatment can related to the VTE risk. Minor: 1) There seemed to be mistype in the text, such as VETE in the introduction

section. 2) Please change the number of a vertical axis of Figure 1 and Figure 2, from 0~1.0 to 0~100 in one-to-one correspondence to the unit (%). 3) Considering about the relationship between D-dimer and VTE, the pretreatment D-dimer can be originated from microvascular disorder in the existing gastric tumor. If so, high level of the pretreatment D-dimer may indicate the existence of micro-thrombosis prior to chemotherapy, not the predictor of post-chemotherapy VTE. It will be better for authors to discuss this point. Additionally, from the point of view of the above, I wonder if there may be the relationship between the value of serum CRP and the VTE occurrence after the chemotherapy. Please discuss this point, too.

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**Name of journal:** World Journal of Gastrointestinal Oncology

**ESPS manuscript NO:** 31760

**Title:** The incidence of venous thromboembolism and the role of D-dimer as predictive marker in patients with advanced gastric cancer receiving chemotherapy

**Reviewer's code:** 02941416

**Reviewer's country:** South Korea

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-12-06 21:38

**Date reviewed:** 2016-12-25 12:13

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

The authors prospectively examined the incidence rates and risk factors of VTE in AGC subjects who underwent chemotherapy. Unfortunately, the analysis failed to discover any definite predictive factors for VTE. I have some questions and comments. 1. D-dimer levels are associated with liver disease, malignancies and inflammation. Were other inflammatory markers beside WBC count (such as CRP, ESR) checked for inflammation? Did any of the subjects with abnormal D-dimer levels have infections such as UTI or pneumonia which may have confounded the results? The authors should consider checking this. 2. Was there a reason that the authors chose time-to VTE instead of VTE incidence in the statistical analysis? Though they may not be statistically different, the authors should state why they chose such a method of investigating VTE, when the presence of VTE may have been more simple and sufficient. 3. What were the outcomes of VTE treatment. Though the authors state that there were no significant differences brought on OS by VTE, the readers may be interested in the clinical outcomes of VTE (i.e. Were they successfully treated? The symptoms subsided or not? Differences in quality of life?, etc.) This may suggest ways to successfully treat



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VTE in AGC patients. 4. Though the authors stated that they did not serially follow D-dimer levels, D-dimer has been primarily used to rule out VTE. As such, I believe that the authors may have checked D-dimer levels when VTE was suspected. Did these levels indeed show an increase compared to the baseline levels? Also, were there differences in the D-dimer levels of subjects with symptomatic or asymptomatic VTE after VTE was detected? Based on this, would a serial follow-up have detected VTE before symptomatic VTE occurred?

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**ESPS manuscript NO:** 31760

**Title:** The incidence of venous thromboembolism and the role of D-dimer as predictive marker in patients with advanced gastric cancer receiving chemotherapy

**Reviewer's code:** 03017544

**Reviewer's country:** Italy

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-12-06 21:38

**Date reviewed:** 2016-12-27 22:29

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

Comments for WJG manuscript n° 31760, 2016-12-05 20:14:56 The manuscript entitled "The incidence of venous thromboembolism and the role of D-dimer as predictive marker in patients with advanced gastric cancer receiving chemotherapy: A prospective study" by Kwonoh Park, Baek-Yeol Ryoo, Min-Hee Ryu, Sook Ryun Park, Myoung Joo Kang, Jeong Hye Kim, Seungbong Han and Yoon-Koo Kang is showing that the incidence of VTE is relatively high in patients with AGC receiving chemotherapy, and pre-treatment D-dimer level might be a biomarker for risk stratification of VTE. Despite their results might be interesting the are some points which need clarification. Minor points In abstract section: 1. Are required key-words, no key-definitions In the text and tables: 1. Is not clear pre-treatment therapy, surgical treatment and and post-operative mobilization. Clarify it 2. It would be appropriate to add a table with the clinic-pathological features of patients selected for this study. Alternatively improves Table 1 (ex: tumour site, Lauren Classification). 3. The current study showed the incidence of VTE and role of pre-treatment D-dimer as risk factors in a homogeneous group of AGC patients receiving palliative chemotherapy. In this study, you reported



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that VTE was not a statistically significant factor for survival, but in Table 1 you reported 21 P/D patients with VTE versus 6 W/D or M/D patients with VTE, and also you reported 18 VTE cases in patients with number of metastatic sites  $\geq 2$  versus 9 VTE cases in patients with number of metastatic sites 0-1. Clarify it. 4. Improve Table 4 with second line chemotherapy. 5. These data are preliminary, they need to be confirmed to further awaited studies. Discuss it in Conclusions

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Oncology

**ESPS manuscript NO:** 31760

**Title:** The incidence of venous thromboembolism and the role of D-dimer as predictive marker in patients with advanced gastric cancer receiving chemotherapy

**Reviewer's code:** 02537353

**Reviewer's country:** Italy

**Science editor:** Ya-Juan Ma

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

## COMMENTS TO AUTHORS

The authors investigated the incidence and risk factors of venous thromboembolism (VTE) in patients with advanced gastric cancer (AGC) receiving chemotherapy. They concluded that the incidence of VTE is relatively high in patients with AGC receiving chemotherapy, and pretreatment D-dimer level might be a biomarker for risk stratification of VTE. The study show different negative points: 1) The absence of an serial measurements of D-dimer 2) The not calculation of the proper number of patients, to detect statistically significant differences in other characteristics such as risk factors or survival 3) The manuscript need to reviewed by native speaker because there are numerous english mistakes