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## PEER-REVIEW REPORT

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

**Manuscript NO:** 32089

**Title:** Characterisation and risk assessment of venous thromboembolism in gastrointestinal cancers

**Reviewer's code:** 00003940

**Reviewer's country:** Australia

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-12-28

**Date reviewed:** 2016-12-30

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" 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 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"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

This is an interesting manuscript but there is a major concern when the diagnosis of VTE is dependent on scrutinising the electronic records. This is partly resolved when the CT scan report is scrutinised and finds asymptomatic cases but the fact that there were cases that were only identified by CT scan makes me concerned that the diagnosis of VTE is imprecise which results in a poor relationship between VTE and survival. My understanding of the event of VTE in these cases indicates a process where plasminogen activators are released into the circulation and is a sinister event. This paper tends to dispute this preconceived idea. I would like to see that discussed.



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## PEER-REVIEW REPORT

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

**Manuscript NO:** 32089

**Title:** Characterisation and risk assessment of venous thromboembolism in gastrointestinal cancers

**Reviewer's code:** 00613748

**Reviewer's country:** Canada

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-12-28

**Date reviewed:** 2017-01-11

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" 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"/> 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"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

Re Manuscript number 32089 Metcalf and coworkers present the results of a very interesting manuscript assessing the performance of the Khorana VTE risk score on a cohort of patients with gastrointestinal tumors. This study highlighted the limitations of said score. Overall the paper is well written and the analysis and discussion are sound and balanced. I do not have any major issues. I think the authors could better highlight the following points: a. This study illustrates the fact that moving from a general to a particular application of a predictive score may be tricky. The original Khorana score was developed in a large cohort of cancer patients, and was not intended to be used in a particular site-restricted cancer population. This data suggests that whereas in CANCER patients in general, the score might perform reasonably well, when applied to a specific site this might not be the case and thus, validation studies in SITE SPECIFIC cancer groups is needed. b. The fact that authors found a higher frequency of incidentally found pulmonary emboli en patients with colorectal cancer is, from my perspective, very



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important. It raises the possibility that a significant survival bias has affected this and other studies, including Khorana's. This should be addressed more emphatically. More importantly, few if any studies have used an analytical strategy accounting for competing risks and this data strongly suggests that such approach is needed in these studies. This could be expanded in the discussion (paragraph 5). c. Please better describe in the methodology the nested case-control study described in results. The information is there but rather scatter between the methods and the results sections of the manuscript. d. I agree with the authors' assessment of the limitations of the Khorana score regarding the rather short follow up time which would preclude the assessment of longer term risks. This limitation stems from the fact that Khorana's finding was unexpected and done in a cohort that was intended to have a different purpose. e. A final issue that needs to be clarified is that in this cohort, the authors included upper limb and splanchnic thromboses. Such events were not included in the original score, as far as I know. I strongly suggest running a sensitivity analysis by excluding such events. Whereas splanchnic thromboses were relatively rare, upper thrombosis are very frequently associated to the presence of indwelling catheters, rather than to the tumor biology or other factors. If the findings of such analysis are consistent (which I think they will) this would further support the author's findings .