

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36888

Title: Chronic kidney disease severely deteriorates the outcome of GI bleeding: A meta-analysis

Reviewer's code: 00039316

Reviewer's country: Greece

Science editor: Ze-Mao Gong

Date sent for review: 2017-10-31

Date reviewed: 2017-11-05

Review time: 5 Days

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 checked="" 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 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 type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" 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

In the manuscript entitled "Chronic kidney disease severely deteriorates the outcome of GI bleeding: A meta-analysis" authors showed the higher mortality and re bleeding rates as well as higher transfusion requirements and longer in hospital stay of CKD/ESRD patients by meta-analyzing relatively old data. The strength of the manuscript is its rigorous methodology, while old time data and few included studies comprise the limitations. Major comments 1. Further highlight the significance of meta-analyzing old data in the era of different treatment of GI bleeds. Please evaluate the possibility to conduct subgroup analysis to evaluate the effect of the date of data acquisition on all study outcomes. Metaregression analysis can be an alternative. 2. In the presence of significant heterogeneity regarding mortality, please perform sensitivity analysis to identify study(ies) responsible for the heterogeneity and examine if the exclusion of



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these studies affects your result. Metaregression analysis can be an alternative too. Minor comments 1. Abstract. Delete the detailed description of the PICO 2. Introduction. Delete the first 10 sentences of paragraph 2, as the provide redundant info 3. Methods Quality of studies and risk of bias. No need to explain why you did not perform Egger's test and at the end of the same paragraph please delete "Articles earned a potential of 2 points for comparability" since the info is confusing and "We compared the groups based on age and treatment with ulcerogenic drugs (nonsteroidal anti-inflammatory drugs and aspirin)" since you did not make these comparisons in your results. 4. Results Mortality. Please clarify if the mortality OR was higher in the CKD/ESRD group compared to controls or that the OR was different among CKD and ESRD subgroups (not evident, since the CIs overlap) 5. Discussion, There is also redundant info in this section: you may delete almost the whole 3rd paragraph. Please consider to change the statement in this paragraph that "patients ... require almost 2 times more red blood cell units for transfusion" with "patients ... require almost 2 more red blood cell units for transfusion"

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36888

Title: Chronic kidney disease severely deteriorates the outcome of GI bleeding: A meta-analysis

Reviewer's code: 00045989

Reviewer's country: United States

Science editor: Ze-Mao Gong

Date sent for review: 2017-10-31

Date reviewed: 2017-11-07

Review time: 7 Days

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 type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input checked="" 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

The authors undertake a meta-analysis of 6 articles reporting 406,035 patients, 51,315 of whom had impaired renal function. The meta-analysis reinforces multiple previous series that have documented a higher mortality in patients with CKD and ESRD as well as a higher rebleeding rate in those with CKD. ESRD, in turn, was noted to increase transfusion requirements, rebleed rate, and length of hospitalization time compared to controls. There are several limitations of this meta-analysis, some mentioned in the Discussion section. These include: 1. Study heterogeneity in which 383,340 of the 406,035 patients come from a single study and all but 1153 control patients come from this study. Likewise a single study reported outcomes in ESRD patients in 14,483 patients, whereas the other 5 studies reported only 218 additional patients or failed to distinguish CKD from ESRD. The Forest plot square size fails to define the magnitude of these statistics.



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This requires elaboration in the Discussion section. 2. The study suffers from failure to distinguish upper from lower GI bleeding or to define the cause of bleeding in most of the papers reviewed. 3. Although the authors note platelet dysfunction in CKD, the meta-analysis suffers from failure to distinguish between mild, moderate, and severe CKD. Is a patient with a GFR of 50g at the same risk of mortality and rebleeding as one with a GFR of 20? At what GFR does platelet dysfunction become clinically significant?

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36888

Title: Chronic kidney disease severely deteriorates the outcome of GI bleeding: A meta-analysis

Reviewer's code: 03476438

Reviewer's country: Belgium

Science editor: Ze-Mao Gong

Date sent for review: 2017-10-31

Date reviewed: 2017-11-13

Review time: 13 Days

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
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COMMENTS TO AUTHORS

This present manuscript deals with a well-specified clinical question, analyzing the role of chronic kidney disease (CKD) and end-terminal renal disease (ESRD) in gastrointestinal bleeding. The design of the meta-analysis is very well conducted including studies comparing patients presenting with GI bleeding and normal renal function or CKD/ESRD. The search strategy, data extraction, quality assessment, publication bias analysis and statistics seems clear and adequate, with a random effects model approach due to presumed heterogeneity of definitions and techniques. The main problem of the paper relies on the novelty of the topic and the heterogeneity of the included studies. The authors are analyzing four outcomes, such as mortality, required units for transfusion, rebleeding rate and length of hospitalization. It's already known that mortality is increased in GI among CKD patients as stated by the authors, the

required units for transfusion including 4 studies (1983-1996-2010-2010 !) even if statistically significant, may be not clinically relevant or at least very difficult to interpret due to the included studies and different clinical criteria for transfusion. Indeed, the authors are analyzing studies in a very wide time interval that may completely influence the results. Probably, a meta-analysis is not actually the best way to determine the association between GI bleeding and CKD/ESRD. Thus, the justification of the meta-analysis seems poor. Minor concerns: - The authors reported the outcomes related to upper/lower GI-bleeding. What's about small bowel bleeding /OGIB?. There is no comment in this sense. - ESRD should be defined in the main text. - There is so much information regarding the quality of studies and risk of bias. I agree that the methods section is a key point in a systematic review but it seems too long with many sentences probably unnecessary "According to the Cochrane Handbook[16] "tests for funnel plot asymmetry should be used only when there are at least 10 studies included in the meta-analysis, because when there are fewer studies the power of the tests is too low to distinguish chance from real asymmetry" (with the reference to the Cochrane Handbook should be ok). - The authors should discuss more how the comorbidities of these patients presenting with CKD may play a role in the outcomes/GI bleeding influencing the results.