



### PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 54391

**Title:** Thalidomide for refractory gastrointestinal bleeding from vascular malformations in patients with significant comorbidities

**Reviewer's code:** 01221666

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Associate Professor, Doctor, Surgeon

**Reviewer's Country/Territory:** Taiwan

**Author's Country/Territory:** United States

**Manuscript submission date:** 2020-02-08

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-02-09 02:09

**Reviewer performed review:** 2020-02-09 02:32

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

Figures are missing which impedes further review



### PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 54391

**Title:** Thalidomide for refractory gastrointestinal bleeding from vascular malformations in patients with significant comorbidities

**Reviewer's code:** 05210352

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** South Korea

**Author's Country/Territory:** United States

**Manuscript submission date:** 2020-02-08

**Reviewer chosen by:** Jia-Ping Yan

**Reviewer accepted review:** 2020-04-27 08:11

**Reviewer performed review:** 2020-05-04 00:56

**Review time:** 6 Days and 16 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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## **SPECIFIC COMMENTS TO AUTHORS**

This study is simple, was well conducted. This study was aimed to conduct a study of thalidomide in treating refractory GI bleeding from GIVM in patients with significant comorbidities. Authors are focusing on patients with significant comorbidities and this is interesting concern. However, some aspects may be needed to clarify. # Major comments

1. As author mentioned, in previous many studies, patients with significant comorbidities were excluded. Including patients with comorbidities may be a differentiation from other studies, but it may also be a limitation in evaluating the effectiveness of thalidomide. -> Comorbidities can be an important confounding variable in assessing treatment effectiveness. If we assess treatment effectiveness in patients with significant comorbidity, it would be better to target patients with one specific disease, like previous study (Garrido Serrano et al (2012) 17).
2. Severity or status of comorbidities before and during thalidomide treatment Bleeding tendency is often closely related to the condition of underlying disease, especially liver cirrhosis, ESRD, and hematologic disorder. The changes in the status of underlying disease can also be a confounding variable. -> How was the status or severity of underlying disease before and during treatment? -> At initial inclusion, how was the severity of disease? For example, child class of liver cirrhosis, stage of CKD -> It would be better to mention the details above.
3. Antiplatelet or anticoagulation

- 1) In section of Results, 5 patients remained on antiplatelet or anticoagulation such as aspirin, coumadin, clopidogrel, or cilostazol. All 4 patients who remained on anticoagulation or antiplatelet therapy, including 2 with an LVAD, had a significant decrease in GIB. -> In table 3, only 1 patient (number 3) in 4 patients (number 2,3,5,6) had no recurrence of bleeding after 6 months (primary endpoint). Does the sentence "significant decrease in GIB" mean the secondary outcomes (number of hospitalization, unit RBC transfused, number of



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endoscopic treatments)? 2) Anticoagulation or antiplatelet agents In discussion, only 1 patient with severe GAVE and platelet count < 30,000/mL due to MDS received 99 units of PRBC in the one year before thalidomide treatment, and required no transfusion after treatment. -> Based on the result of only 1 patient, it is difficult to agree that patients with hematologic disorder and thrombocytopenia may not be necessary to aggressively correct thrombocytopenia. -> Further large-scale studies are needed to clarify this issue.

# Minor comments 1. Type of previous endoscopic therapy Various methods are used for endoscopic hemostasis in GI bleeding from GIVM, but APC is effective and widely used in clinical practice. It is helpful to mention which endoscopic method was used prior to thalidomide treatment. 2. Inclusion criteria Documented vascular malformation (either GIAD or GAVE) on upper endoscopy (EGD), colonoscopy, balloon enteroscopy, or capsule endoscopy -> Was all of the tests (EGDS, CFS, Enteroscopy, or capsule endoscopy) done in included patients? Enteroscopy or capsule endoscopy was performed in patients with no bleeding focus found in EGDS and CFS? -> It would be better that other causes of bleeding (peptic ulcer, diverticular bleeding) were excluded (exclusion criteria). -> It is necessary to mention about the location of vascular malformation (stomach or colon or small bowel) of 15 patients (in Results section or Table 2 patient characteristics). 3. Iron supplementation 8 patients continued with iron supplementation after initiation of thalidomide treatment. (2nd paragraph of Results section). -> How was the patients' hemoglobin level before starting thalidomide treatment? Was anemia (especially iron deficiency anemia) assessed or excluded? -> The presence of anemia (especially IDA) before starting thalidomide tx and iron supply during tx are thought to be variables in assessing treatment effectiveness (especially secondary outcomes including "Units RBC transfused") . 4. Coumadin is the brand name of warfarin. It would be better to use a term "warfarin" or Coumadin®. 5. As author mentioned in discussion, the major limitations of this study are the limitations



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inherent with a retrospective study and small sample size. -> I agree that recruiting patients is very difficult in aspects of cost and safety. In this regard, it is thought that this study is meaningful.



### PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 54391

**Title:** Thalidomide for refractory gastrointestinal bleeding from vascular malformations in patients with significant comorbidities

**Reviewer's code:** 02445618

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Canada

**Author's Country/Territory:** United States

**Manuscript submission date:** 2020-02-08

**Reviewer chosen by:** Xiao-Quan Yu

**Reviewer accepted review:** 2020-05-14 13:16

**Reviewer performed review:** 2020-05-14 13:29

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

Well done retrospective cohort study. Minor issue: It is important to obtain more info about the two patients who were lost to follow up. If they were lost to follow up because they died from massive GI bleeding this would change the conclusions of the study. The investigators should try to contact the patients or their relatives, and explain these efforts in the manuscript.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 54391

**Title:** Thalidomide for refractory gastrointestinal bleeding from vascular malformations in patients with significant comorbidities

**Reviewer's code:** 05210352

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** South Korea

**Author's Country/Territory:** United States

**Manuscript submission date:** 2020-02-08

**Reviewer chosen by:** Jia-Ping Yan

**Reviewer accepted review:** 2020-06-19 21:50

**Reviewer performed review:** 2020-06-20 01:14

**Review time:** 3 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS



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This study was well conducted. Some aspects have been clarified after author's revision.