Dear Editor,

Many thanks for giving us the opportunity to publish in the World Journal of Gastrointestinal Endoscopy. I have attached the revised manuscript in Word format as requested, and I have addressed all of the reviewers comments as detailed below:

Comments from reviewer ***02941224***

This is a great and useful review about the role of self-expanding stent in tne management of variceal hemorrhage. However, some minor comments are noted.

1. Page4, line 25, close parenthesis was missed. CORRECTED
2. Page7, line 16, "v" should be writttten as "vs" CORRECTED
3. Page9, line 9, "associated" was misspelled. CORRECTED

Comments from reviewer ***02581987***

I thank the authors giving me the opportunity to review this interesting review on a recent topic. I propose the authors to add illustrations, endoscopi images, fluoroscopic images...
Minor points: typing errors

Comments from reviewer ***03364778***

General comments:
This is a well written, concise review article discussing case series and the one clinical trial documenting the efficacy of self-expanding metal stents (SEMS) in the control of variceal hemorrhage. The paper is informative and clear, and is of benefit to readers.

I would suggest several revisions – most minor, some more involved – before publication, as outlined below.

Title

- "Role" should be "role" or the whole title should be in title capitalization. CORRECTED

Abstract

- Term 'BT' not defined before first use CORRECTED
- 'algorythm' should be 'algorithm' CORRECTED

Introduction

- 'Acute Variceal Bleeding' should be 'Acute variceal bleeding' on first line CORRECTED
- first line: what does "unselected" mean? Do you mean all cirrhotic patients? CORRECTED to 'in patients with cirrhosis'
- second paragraph, second line "form or" should be "form of" CORRECTED
- The term 'MELD' is not defined before use CORRECTED
- third paragraph – 'MELD' should be 'MELD score' CORRECTED

Current options for failure of standard therapy

- Second paragraph – the line about early TIPS leading to reduction of failure is awkward, as it is a double negative, and should be rephrased. Also is that in comparison to no TIPS at all, or TIPS after 72 hours? REPHARASED TO "The importance of early haemostasis was demonstrated in a randomised controlled trial of early TIPS insertion (within 72 hours) versus standard therapy, including rescue TIPS. It demonstrated a reduction in uncontrolled bleeding or re-bleeding in the early TIPS group (3% vs 45%), a reduction in average intensive care unit stay (3.6 v 8.6 days) and a significant reduction in 1 year mortality (14% v. 39%, p=0.001)"

- Last sentence of second paragraph (Similar results have been shown using early TIPS in high-risk patients selected by either HVPG(18)) does not make sense. Either HVPG or what? CORRECTED by removing either.

- Third paragraph – doesn't the study (ref 19) show significantly better 30-day mortality (8.6%) than what you'd expect (30-50%)? The way ref 19 is cited makes it sound like the article didn't show a benefit for early TIPS, but it seems to. Perhaps the first line of the paragraph should be changed to, "Attempts to replicate these results have demonstrated increased rates of bleeding control, but possible also increased rates of complications." REPHRASED to Attempts to replicate these results outside of clinical trials have been encouraging, but show that patient selection is vital and TIPS can be associated with significant complications'

批注 [BH1]: Actually we would expect a mortality rate closer to 15%-20% from variceal bleeding. 30-50% is a historical figure and survival rates have increased significantly.

SEMS for Variceal Hemorrhage

- Term 'SEMS' not previously defined in text prior to first use in section title CORRECTED

- would like a bit more description of how would fit into an algorithm and how the position is confirmed – eg., after placement is it routine to get a radiograph just to show it's in an adequate position? is placement of the SEMS always performed after failed endoscopic intervention? does it have the identical indications that BT has? CORRECTED – paragraph expanded to include the use of CXR to check positioning.

批注 [BH2]: This is a topic of much debate, and we have discussed whether to include an algorithm, however we do not feel there is enough evidence to suggest where SEMS are most effective yet.

批注 [BH3]: This has not yet really been defined – as we discuss in the conclusions. Some units insert the stents routinely for all high risk bleeding (child pugh b/c, active bleeding at endoscopy), and some reserve it for multiple treatment treatment failures, especially in patients not suitable for TIPS.

- later you described a number of cases where the gastric balloon ruptured. why would that happen? how could that be avoided? CORRECTED – addressed in the 'limitations' section

Current evidence for SEMS

- the subtitle of this section should be in title capitalization like the other subtitles CORRECTED
- second paragraph, 7th line, "fluroscopy" should be "fluoroscopy" CORRECTED
- second paragraph – line "Of the 20 patients 12 went on.." the procedures should not be in title capitalization (eg, Azygoportal, Transplant, etc.) CORRECTED
- in patients who go on to have definitive therapy such as TIPS, does the stent remain in place until the TIPS is performed? Are the stents removed in the same setting, or a few days after the TIPS? REVISED AND EXPLAINED

- third paragraph: what are “standard techniques”? Does that include TIPS? CORRECTED to read ‘standard endoscopic techniques’
- fourth paragraph: remove “Our” and use a more anonymous term CORRECTED
- fifth paragraph: use BT instead of balloon tamponade CORRECTED
- fifth paragraph: the description of the case series is somewhat confusing; are you saying that the stent could not be deployed in the 10th patient because the gastric balloon failed to inflate? In that case, it would be the final case, not the first case. Then, separate out the additional case where the gastric balloon ruptured so a different stent had to be used. In the patient where the balloon did not inflate, why wasn’t a new stent attempted? CORRECTED AND REVISED
- fifth paragraph: the mortality rate is very high. Overall, the mortality rates seem very difficult to compare due to patient group differences between studies. COMMENTS
- sixth paragraph: why is the case series of 9 patients, but then you describe only 7 cirrhotic patients? CORRECTED (two patients included for two separate bleeding episodes)
- sixth paragraph, 3rd line: “ling” should be “line” CORRECTED
- sixth paragraph: how was the stent not deployed correctly? was that detected on radiograph later? or could it have migrated? SEE COMMENTS
- seventh paragraph: what are “cheery red spots”? CORRECTED TO ‘cherry’
- seventh paragraph: Last two sentences, I would lead with “For the two failures, in one the gastric balloon ruptured…” The way it’s written now, the “In one…” seems to refer to one of the successful cases. CORRECTED
- eighth paragraph: this is the most important study that has been referenced, and deserves more detailed description. What exactly were the inclusion and exclusion criteria? What was the treatment algorithm? It seems all patients underwent endoscopy prior to SEMS deployment. Was SEMS placed endoscopically? What was the average MELD score? Did the patients later undergo a definitive procedure? How long were the stents and balloons left in? Also, you could redo their stats putting the SEMS patient who actually got a BT into the BT group – it might make their data statistically significant. The study looks underpowered. You could perform a power analysis for this study: http://biomath.info/power/chsq.htm CORRCTED AND ADDRESSED

批注 [BH4]: This information is not available.

批注 [BH5]: We would agree and have address this in the conclusions suggesting that it is in patients who go on to have a definitive procedure where the mortality rate is improved.

批注 [BH6]: The paper does not address this questions and we do not know why the stent failed.

批注 [BH7]: This was not reported

批注 [BH8]: The protocol states that they would not be undergoing a definitive procedure, however the abstract reports the median time to TIPS for each group.

批注 [BH9]: This was not reported

Table

- This is an important table, comparing the papers that you have included. I suggest adding information about the patient cohort to help compared between the studies. for example, average MELD score is an obvious factor that should be included; also, whether 2nd line definitive therapy was performed should also be included INCLUDED and UPDATED
- Is there a metaanalysis/large case series for BT? perhaps that could be included too for comparison to these SEMS series…SERIES ADDED

Limitations of SEMS

- first paragraph: I would flip the two sentences. CORRECTED

There have been reports of minor oesophageal ulceration several case series describing SEMS placement. However, this resolves spontaneously on removal of the stent and neither mortality nor oesophageal perforation have been observed.

- second paragraph: more discussion is warranted to describe which patients shouldn't undergo TIPS. Patients with MELD score > 20 would not be offered TIPS electively, but are offered emergent TIPS with the understanding that there is a high associated mortality. Are you implying in this paragraph that patients with high MELD scores should get SEMS not TIPS? The risk of encephalopathy is highest in patients who have preexisting encephalopathy. So are patients with preexisting encephalopathy the ones who should have SEMS not TIPS? Or are the patients with right heart failure the targets? I think further elaboration on which patients shouldn't undergo TIPS will help elucidate the group of patients that should instead get SEMS.
- third paragraph: agree the mortality rates are difficult to interpret, and that one important factor is whether definite therapy was later performed. also, preexisting patient factors (MELD score, comorbidities, etc.) are also likely very important
THANK YOU FOR COMMENT WE AGREE
- third paragraph: please place the number reference next to the Escorsell et al reference in the second line – also "suggestes" should be "suggests" – though I disagree with your interpretation since the results weren't significant… was the complication rate statistically significantly different? also "assocated" should be "associated" CORRECTED/REVISED
- last line: please delete "in patients with a high risk of re-bleeding" as you have not defined an algorithm yet CORRECTED
- I might suggest that you offer a treatment algorithm in the form of a figure, delineating the optimal target patients.
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Comments from reviewer ***02861208***

This is an interesting review regarding the use of self expanding metal stents for variceal bleeding. The authors make a concise review of the available data, and add the important references in the field, and also the most recent data addressed in the BAVENO meeting; the overall readability and presentation of the manuscript is good.