Author's response to reviews

Title: High APACHE 2 score and long length of bowel resection impair the outcomes in patients with necrotic bowel induced hepatic portal venous gas

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Version: 2 Date: 16 January 2011

Author's response to reviews: see over
Dear editor in chief,

We appreciate for the chance to revise the manuscript. In our study, we focused on patients with the necrotic bowel contributing to hepatic portal venous gas- the worst outcome among different etiologies and analyzed the surgical outcomes. We had replied the questions of two reviewers below. The modification of manuscript was shown in red-color words. In addition, we had applied the IRB in National Taiwan University Hospital (reference number: 201101031RC ). We are looking forward to being accepted in *BMC Gastroenterology* because our report investigates the rare but important clinical disease.

Thanks very much.
Sincerely yours,

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Below is the letters of response to reviewers:

Referee 1:

Dear Authors;
I read with great interest your article. You have posed that APACHE scoreII and the resected segment of the bowel are predicting factors for the outcome of the HPVG. I appreciate that great efforts have been put in the article, however the paper need further revision to improve the quality and put more insights and knowledge in the subject.
Please address these comments carefully;

INTRODUCTION:
1. You have mentioned the largest reported series up to date is 7 patient. that is not true, several papers in the literature are reporting more than this number. I'm attaching one reference, please check: Paran H, Epstein T, Gutman M, Shapiro Feinberg M, Zissin R. Mesenteric and portal vein gas: computerized tomography findings and clinical significance. Dig Surg. 2003;20(2):127-132.
   Ans: Thanks for your correction. There were several reports studying the benign and lethal outcomes in patients with mesenteric and portal vein gas. In our study, we focused on the worst results – necrotic bowel inducing portal vein gas. Based on
published papers, the largest series include 1. Arch Surg 1997, 132:1071–5 (cited in our study) and 2. Dig Surg. 2003;20(2):127-132. (provided by the reviewer; 12 cases including 7 patients with underlying disease of ischemia of the small or large bowel). We will add the latter reference in the manuscript and change the sentence “Until now, the largest series contained only 7 patients [9]” (page 3, line 8) to “Until now, the largest series that investigated the necrotic bowel inducing hepatic portal venous gas contained only 7 patients [9, 10]”. The previous reference numbers after 9 are also changed (plus one).

2. The pathophysiology of HPVG can be explained by
a. mucosal damage and lumenal gas escape to the portal system via portal microvenules.
b. Septic embolization or abscess that rupture through the small portal venules.

Other less important factors are increased lumenal pressure such as during colonoscopy or large bowel enema which are associated with HPVG.

Ans: Thanks for your suggestion. Because there is still no conclusive mechanism of this phenomenon, various proposed theories exist. We appreciated your excellent theoretical explanation, which made our theory part more comprehensive. We will modify the sentences (Discussion-first sentence) by your suggestions.

PATIENTS AND METHODS:
1. Diagnosis is depending on the clinical presentation of septic shock and peritoneal signs and also on the CT demonstrating poor enhancement:
Although this statement is generally true, however sepsis and peritoneal signs are not specific for bowel ischemia and other abdominal catastrophes can present similarly. Therefore taking this as a proof of diagnosis is not completely true.
Again CT scan specificity for bowel ischemia is not 100% as we all know it is radiologist dependent as in all other cross sectional studies. The final diagnosis is made in theatre. Therefore the 6 patients who have been diagnosed on clinical and perhaps radiological bases should be excluded from this study.

Ans: We totally agreed with your opinion. Angiography may be the most “golden” criteria of ischemic bowel if there was no surgical intervention. In our study, there were six patients receiving medical management without the pathologic validation.

The modification of the manuscript includes:
a. delete the “28” in Abstract – Method- first sentence
b. The first and second sentences in Abstract – Results were replaced by “There were 22 consecutive patients receiving definite bowel resection. 13 cases (59.1%) died after surgical intervention.”
c. The first sentence in Main text-Patients and Methods “Between January 2000 and December 2007, 28 consecutive patients that presented on computed tomography (CT) scans with HPVG caused by small- or large-bowel ischemia, were retrospectively reviewed” is modified to “Between January 2000 and December 2007, 22 consecutive patients that presented on computed tomography (CT) scans with HPVG caused by small- or large-bowel ischemia and received definite bowel resection, were retrospectively reviewed”.

d. The last sentence in Main text-Patients and Methods “In patients undergoing surgery (n=22), pathological findings proved the diagnosis finally.” is changed to “All patients in our study had the pathological diagnosis of necrotic bowels.”

e. The first and second sentences in Main text-Result were deleted and were replaced by “We did analysis of mortality to the 22 patients who underwent bowel resection.”

2. Why end stoma has been performed for every patients. Double barrel stoma can be very helpful to assess the proximal and distal bowel in borderline cases.
Ans: It is a good idea to do double barrel stoma in selected cases. However, the patients were critically ill and had unstable vital signs. In our experiences, most cases could not tolerate second-look operation. Therefore, the surgeons preferred time-saving method with end stoma, which, consequently, may result in more bowel resection.

3. Second look laparoscopy rather than laparotomy may be indicated in some cases.
Ans: Thanks for your brilliant suggestion. In selected cases of acute abdominal disease with relatively stable vital sign (PPU, ileus), we do apply laparoscopic method. Most patients received inotropic agents for shock management during second-look operation. It is still beyond our capability of doing such exploration in these difficult cases. In the future, we will consider laparoscopic second-look operation in stable patients.

THE RESULTS:
1. No data are mentioned on the type of procedure? small bowel resection, right hemicolecetomy, total colectomy, etc.
ANS: Thanks for your comment. There were 14 small bowel resection, 4 small bowel resection plus right hemicolecetomy, 3 small bowel resection plus total colectomy, and 1 subtotal colectomy in our study (add this sentence in Result-2nd paragraph-5th line).
In addition, we add the method of operation in Table 2.

2. No thing mentioned about vascular involvement; some of the patients need revascularization if the SMA critical narrowing is confirmed as the cause of ischemia. The issue is very important for patients who need extensive resection as revascularization my keep the patient with more than 110 cms of small bowel that safe
him nutritional support.

ANS: In patients with ischemic bowel disease, angiography has an important role in early diagnosis and provides evidences for physicians to do revascularization including surgery or thrombolytic medication. During exploratory laparotomy, we routinely palpated the SMA. Thrombectomy will be considered if residual thrombus was suspected. On the other hand, revascularization should be done in patients with SMA proximal stenosis, which is diagnosed by angiography or intra-operative vascular sonography. In our report, all patients had massive necrotic bowel, not impending ischemic bowel so only resection was done to rescue the patients.

3. Nothing mentioned about the extreme cases that surgeon do nothing but to close the abdomen. How many of these have been encountered?
Ans: We had one case who had non-therapeutic laparatomy with totally icchemic bowle of all small instestine and proximal colon. The patient died within 48 hours after being sent out of OR. Initially, we did not include the case because the patient received conservative management only and no record of the lengths of bowel infarction.

4. How many patients have small bowel remanant less than 110 cms after resection? and how may subjected to nutritional support as intestinal failure cases.
ANS: There were 7 cases whose remnant small bowel is less than 110 centimeters. Among them, only one patient survived to be discharged and depended on home TPN.

DISCUSSION:
1. The author should also consider benign causes of HPVG and should clarify that it is not ominous sign in all patients as the course in benign cases is complete recovery.
ANS: It’s a good suggestion to emphasize the “benign” HPVG in our study. We add the sentence “However, HPVG may just be a radiological finding when the underlying disease is benign. The patients recover uneventfully.” in Discussion-3th paragraph-last line.

2. Other tests as arterial blood gas and lactate level should be mentined as supportive especially in unconscious patients [intubated ITU ]patients for example.
Ans: We added the sentence “Other laboratory tests such as arterial blood gas and lactate level should be checked especially in unconscious patients to detect the severe sepsis earlier” in Discussion-5th paragraph-6th lines.

Level of interest: An article of limited interest
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: I declare that I have no competing interests
Referee 2:

We have been asked to review the article titled ‘high APACHE 2 score and long length of bowel resection impair the outcomes in patients with necrotic bowel induced hepatic portal venous gas?’.

The authors studied the risk factors of mortality in patients with hepatic portal venous gas secondary to intestinal necrosis. This is a retrospective study.

28 consecutive patients had been identified in 7 years. It is an important series of patients according to the others reported series.

We identified some points that should be taken in account in order to ameliorate the manuscript:

Major compulsory revisions:

6 patients were excluded of the series. These 6 patients were treated medically. No medical data justify this attitude among these patients. Were they excluded because of a major mesenteric infarction? Otherwise in the first paragraph of results section, the authors claim that 6 patients receiving medical treatment all expired within three days, indicating the necessity of surgical treatment?. No data in this paper allows such a conclusion. These 6 patients could modify the statistics in intention to treat.

ANS: Thanks for your correction. We deleted the six patients from our study as the suggestions of both reviewers. In our study, we emphasized the surgical outcomes in patients with necrotic bowel inducing HPVG.

The modification of the manuscript includes:

a. delete the “28” in Abstract – Method- first sentence
b. The first and second sentences in Abstract – Results were replaced by “There were 22 consecutive patients receiving definite bowel resection. 13 cases (59.1%) died after surgical intervention.”
c. The first sentence in Main text-Patients and Methods “Between January 2000 and December 2007, 28 consecutive patients that presented on computed tomography (CT) scans with HPVG caused by small- or large-bowel ischemia, were retrospectively reviewed” is modified to “Between January 2000 and December 2007, 22 consecutive patients that presented on computed tomography (CT) scans with HPVG caused by small- or large-bowel ischemia and received definite bowel resection, were retrospectively reviewed”.
d. The last sentence in Main text-Patients and Methods “In patients undergoing surgery (n=22), pathological findings proved the diagnosis finally.” is changed to “All patients in our study had the pathological diagnosis of necrotic bowels.”
Table 2 is unclear. Some patients appear several times. It seems that patients with both small and large bowels involved appear in other sections either in small bowel involved or large bowel involved. It would be better if the total of patients of column 1 matches to the overall number of patients.

Ans: We had modified the Table 2 according to the ideas of both reviewers.

In the last paragraph of introduction the authors claim that the largest series contained only 7 patients [9]. Some of the references report more than 7 patients: ref 19 (11 patients), ref 14 (15 patients, 12 bowel obstructions).

Ans: We apologize for the unclear description in our report. There were several reports studying the benign and lethal outcomes in patients with mesenteric and portal vein gas. In our study, we focused on the worst results – necrotic bowel inducing portal vein gas. Based on published papers, the largest series of necrotic bowel inducing HPVG include 1. Arch Surg 1997, 132:1071–5 (cited in our study) and 2. Dig Surg. 2003;20(2):127-132. (provided by the reviewer 1; 12 cases including 7 patients with underlying disease of ischemia of the small or large bowel). We will add the latter reference in the manuscript and change the sentence “Until now, the largest series contained only 7 patients [9]” (page 3, line 8) to “Until now, the single report that investigated the necrotic bowel inducing hepatic portal venous gas contained less than ten patients [9, 10]”. The previous reference numbers after 9 are also changed (plus one).

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests: I declare that I have no competing interests