Dear Reviewers of the World Journal of Gastrointestinal Surgery

On behalf of myself and my co-author, I want to thank you for the opportunity to revise and resubmit manuscript number 26174, entitled "Update on Medical and Surgical Options for Patients with Acute Severe Ulcerative Colitis." Below, we have provided a point-by-point response to each reviewer's comments and concerns, and in every instance possible, we have sought to revise our manuscript. Any changes to our manuscript have been denoted with yellow highlighting to assist the reviewer process.

We are grateful for this opportunity to have our work reviewed a second time, and if there are any additional changes required beyond those below, we would be happy to provide them.

Best regards,

Rachel A. Weinheimer, MD

Reviewer #1:

I would suggest adding to the two items: Solina G. et al."Current management of intestinal bowel disease: the role of surgery" Updates surg., 2016
Seah D. De Cruz P."Review article: the practical menagement of acute severe ulcerative colitis" Aliment. Pharmacol. ther., 2016 43 (4): 482-513.

Response: The reviewer introduces two helpful manuscripts that pertain to this paper. Both of them were helpful in providing background on the topic of ASUC, and Seah et al was used as an additional reference. The addition has been incorporated in the revised manuscript on page 5, "Abdominal imaging should be obtained to evaluate for colonic dilation (greater than 5.5 cm) on plain x-ray or

computed tomography scan, and the patient should be monitored for fever, leukocytosis and other signs of systemic sepsis that accompany toxic megacolon."

Reviewer #2: *It is obvious from the article that authors are having very clear fundamentals over this topic, along with that the simple though effective and clearly understood language doesn't allow anything to be misunderstood. Reviewing any subject in comprehensive manner is difficult task for authors, as they have to compile and present all the aspects of that particular subject in brief though without missing anything important, which is taken care of very well in this review. There are some things which would be like cherry on the cake in this review, for which following suggestions should be taken positively and I would like to review the revised manuscript very soon.*

1. Writing needs proper use of spaces and comas, as many words are not separated with space in article. Reformatting by authors themselves will leave no scope of improvement further, so avoiding printing mistakes in final version.

Response: The paper has been reformatted.

2. Title is effective and to the point, but if authors feel that their review provides any new information or it is just the compilation of available information that should be mentioned, i.e. "Update on Medical and Surgical Options for Patients with Acute Severe Ulcerative Colitis: What is new?" Though the final decision for changing or keeping the same title, is upon authors' discretion.

Response: We consider this an update on current management of UC and have made the recommended change to the title. Thank you.

3. Mention the incidence of rectal sparing disease and management aspects which are different in its management.

Response: We agree with the above recommendation and have made the following addition to the revised manuscript on page 10: "In rare cases (5%), patients present with rectal sparing disease, and TAC with end ileostomy remains the first step to patient recovery. Only in these specific cases has ileorectal anastomosis as an alternative to pouch formation been described for reconstruction of the gastrointestinal tract."

4. Give some details on the diagnostic aspects of acute severe ulcerative colitis, like which investigations are must, which one must be avoided, pros and cons of different diagnostic modalities.

Response: The wording of page 5 has been modified so that the "must" investigations are highlighted. Additionally, diagnostic modalities, including imaging, cultures, and endoscopy have been included: "[Patients] must have regular monitoring of vital signs and urine output as well as a comprehensive laboratory workup. Initial tests on admission should include a comprehensive metabolic panel, pre-albumin, albumin, complete blood count, and inflammatory markers (erythrocyte sedimentation rate and C-reactive protein).[4] A tuberculin skin test should also be performed on that admission in preparation for possible treatment with biologic agents. Abdominal imaging should be obtained to evaluate for colonic dilation (greater than 5.5 cm) on plain x-ray or computed tomography scan, and the patient should be monitored for fever, leukocytosis and other signs of systemic sepsis that accompany toxic megacolon.[5] Stool cultures and a clostridium difficile assay must be obtained to exclude infectious pseudomembranous colitis, and the frequency and consistency of bowel movements should be recorded."

5. Specify if all parameters of Truelove and Witt's criteria need to be present to label it as severe acute attack or no?

Response: As denoted in the revised manuscript on page 4, criteria include at least 6 bloody bowel movements per day with one sign of systemic toxicity: "Historically, severe UC has been defined as the passage of at least six daily bloody stools, along with any of the following signs of systemic disease: erythrocyte sedimentation rate > 30 mm/h, temperature > 37.8 °C, pulse rate > 90/min and hemoglobin < 10.5 g/dL (Truelove and Witts criteria)."

6. What are the criteria for toxic megacolon, clinical / radiological and biochemical? Unit for ESR is not mentioned.

Response: The criteria for toxic megacolon have been added to page 5 of the manuscript: "Abdominal imaging should be obtained to evaluate for colonic dilation (greater than 5.5 cm) on plain x-ray or computed tomography scan, and the patient should be monitored for fever, leukocytosis and other signs of systemic sepsis that accompany toxic megacolon." Units for ESR have also been added. Thank you for pointing out these oversights.

7. Thiopurine methyl transferase levels are suggested in investigation; mention whether it is to be done in acute setting or after some interval.

Response: The timing of thiopurine methyl transferase testing is an important topic, and after thoughtful review, we concluded that this test does not in fact have to be done in the acute setting as it is part of the workup for outpatient medical maintenance therapy. For that reason, it was eliminated from the

manuscript as we are focusing only on acute severe UC. Thank you for pointing out this detail.

8. Mention the day of evaluation with Oxford criteria.

Response: Days of evaluation include days 1,3, and 4-7 as noted in the preceding sentence prior to the mention of Oxford criteria: "Kedia et al proposed an algorithm for reassessing patient steroid response at days 1,3, and 4-7 in which incomplete responders and non-responders either advance to rescue therapy or proceed to colectomy.[3] In this algorithm, the Oxford criteria (>8 stools/day or >3 stools/day with a CRP >45 mg/L) are used to determine the need for escalation of therapy."

9. Mention dose and schedule of infliximab, side effects and implications of usage, other newer biologics.

Response: The dosages of both infliximab and cyclosporine have been added to the manuscript (page 6). Additionally the primary concern with the use of biologics, susceptibility to infection, has been noted in the revised paper as well (page 7).

10. Mention pros and cons of distal mucus fistula versus rectal stump closure, and feasibility of each approach, relation with indication for emergency surgery.

Response: Rectal stump vs. mucous fistula closure has been addressed on page 9: "The stapled or hand-sewn rectosigmoid stump can be sutured as a mucous fistula to the distal aspect of the abdominal wall incision, may be closed and sutured to the subcutaneous tissue, or may be left unattached in the pelvis. The primary reason for creation of a mucous fistula or placement of the long rectal

stump in the subcutaneous tissue is to avoid rectal stump breakdown and leakage with subsequent pelvic sepsis, especially in cases of severe inflammation and thickening of tissue.[37] The drawback to a mucous fistula lies in patient dissatisfaction that may occur with persistent discharge during the long-term recovery period. [13, 38] The manner in which the rectosigmoid is closed depends mainly upon patient anatomy and surgeon preference, but transanal rectal decompression is commonly performed following all techniques. [39]

11. If possible give algorithm chart of management, or put some diagram or table.

Response: An algorithm for management of acute severe UC has been added to the revised version of the paper.