## Cover letter

Dear Editors:

Thank you very much for arranging a timely review for our manuscript (Manuscript NO.: 38726). We have carefully evaluated your and the reviewers' comments and thoughtful suggestions. All of the comments have been carefully addressed and a point-to-point revision was made accordingly. I have highlighted the corrections in the revised manuscript for your review. In the revised version, our manuscript has been carefully edited for typographical and grammatical errors. Please find below the details of our revisions. Like other studies of constipation, we hope our revised manuscript also will be beneficial for further study of slow transit constipation in the aged population.

Again, we want to thank you for your effort and help with our manuscript. Should you have any questions, please feel free to contact me at yy_150@126.com.

Very Respectfully,

Dong Wei
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## Point-by-point rely to reviewers' comments

**Reviewer's code:** 03000421

**Reviewer's country:** France

**COMMENTS TO AUTHORS**

This interessant study cannot be published as proposed because clinical and physiological information on constipation are missing. Clinically, does the patients take drugs that can induce constipation like opioids? In addition, what the terminal intestine free of pathologies Physiologically, total and segmental colonic transit time before surgery are not indicated. It is important

to assess the site of delay (transit constipation or outflow constipation) to estimate the surgical procedure.

Re: We would like to express our sincere thanks to you for carefully and patiently reviewing our manuscript. Thanks for your comments.

In our study, the inclusion and exclusion criteria for surgical were very strict. The first inclusion criteria was the Rome III diagnosis criteria for constipation. Rigorous psychological assessment is needed before surgery in order to eliminate the patients with psychological symptoms or with history of mental illness. Most importantly, we excluded patients with life-threatening diseases, such as cancer. These patients excluded may take drugs that can induce constipation like opioids, and they were not included in our study. No one of our patients received antipsychotic drugs which could influence chronic constipation.

We're sorry to say that in our study, there was no excised bowel, so there was no pathological examination after operation. The advantage of this study is the innovation in operative procedures (no bowel removal). The procedure of SCBCAC can be manipulated simply and has characteristic features of less invasion and good effect. It also should intuitively require shorter operation time and less risk of contamination during surgery so that the aged population could be well-tolerated and compatible with this procedure.

The preoperative examination included colonic transit test, defecography, colonoscopy, electromyography, anorectal manometry, and routine preoperative examination for colonic resection. We selected the patients strictly before operation and a careful physiologic assessment is necessary. We combined the results of colonic transit test, defecography, electromyography and anorectal manometry to distinguish between slow transit constipation and outlet obstructive constipation. Also, we excluded patients with obvious signs of outlet obstruction, such as frequent defecation, difficult defecation without dry feces, and anorectal dysfunction. None of our

patients in this study suffered from outlet obstructive constipation which could influence the estimation of the surgical procedure.

Thank you again for your elaborate comment and guidance. In the revised manuscript, we have corrected them according to your suggestion.

**Reviewer's code:** 02549032

**Reviewer's country:** Greece

**COMMENTS TO AUTHORS**

This is an interesting one center retrospective cohort study on two laparoscopic surgical procedures for the treatment of slow transit constipation in aged population. The authors compared subtotal colonic bypass with antiperistaltic cecoproctostomy (SCBAC) to SCBCAC plus colostomy and concluded that SCBCAC plus colostomy is better procedure. The article is interesting for publication.

Re: We would like to express our sincere thanks to you for carefully and patiently reviewing our manuscript. Thanks for your comments.

Some minor issues are:

1. In the colostomy group the end-side anastomosis is end cecum to lateral rectum? This is not clear in the methods section.

   Re: Thanks for pointing out it. In the paragraph of "Surgical procedure", we have revised it as "The head of a 29- to 33-mm circular stapler was placed in the bottom of the cecum. The shaft of the stapler was placed in the rectum via the anal canal to complete end-side anastomosis (end rectum to lateral cecum). The ileocecal junction did not need rotation."

   Because the head of the stapler was placed in the bottom of the cecum,

not the proximal end of ascending colon transected at a site 2-3 cm distal to the ileocecal junction, we considered that the end-side anastomosis is end rectum to lateral cecum in the bypass plus colostomy group.

2. What about data on colonoscopic surveillance in these groups?

   Re: All the patients were examined with colonoscopy in order to exclude patients with organic colon disease. Through colonoscopy we found that some of the patients had melanosis coli caused by long-term treatment with oral laxative agents. However, we are sorry to say that in this study we could not analyze the data on colonoscopy because of the sample size. A further study with larger sample size will be needed.

3. Many parts of the discussion are the same as in the results. There is plagiarism in this way.

   Re: Thanks for pointing out the mistake. In the revised manuscript, we have deleted some paragraphs of the discussion which are the same as in the results. And we have removed all the numbers from discussion and expend the paragraphs in the discussion.

4. It would be more interesting to compare these results to older studies with subtotal colectomy with ileorectal anastomosis with the strategy of colonic bypass.

   Re: Thank you for giving us this idea. This research will be very meaningful and we will further develop our study to compare the current research results to older studies with subtotal colectomy with ileorectal anastomosis with the strategy of colonic bypass.

5. Obviously permanent colostomy for benign disease did not influence quality

of life in aged population. However, this could not be accepted for younger patient population. A comment of this is important.

Re: Thanks for your constructive suggestion. In the revised manuscript, we have added following sentences in the discussion according to your suggestion: "Of course, there is no denying that colostomy may bring a little inconvenience to the patients' daily life compared with healthy people, but unlike other permanent colostomy, the colostomy in SCBCAC doesn't need to excrete large amount of dung every day. In our study, the healing of the abdominal wall stoma was favorable. A small amount of intestinal fluid or mucus was drained every 1-3 days, but the drainage amount gradually decreased over time. No ulcers or hemorrhages were seen in the skin around the stoma because no feces were discharged from it. The daily life of patients was not negatively affected. Obviously，colostomy for benign disease did not influence quality of life in aged population. However, this could not be accepted for younger patient population. "

**Reviewer's code:** 01206525

**Reviewer's country:** Romania

## COMMENTS TO AUTHORS

In this research paper Yang Y et al., present a new surgical approach for slow transit constipation, consisting of subtotal colonic by-pass plus colostomy with antiperistaltic cecoproctostomy. They validate the superiority of this technique by retrospectively comparing the results with one of the commonly used surgical method - subtotal colonic by-pass with antiperistaltic cecoproctostomy (no colostomy). The approach is interesting and the paper is mostly well written, but the structure is not optimal and the way the results are presented should be improved.

Re: We would like to express our sincere thanks to you for carefully and patiently reviewing our manuscript. Thanks for your comments.

**Major remarks**:

1) Statistical analysis paragraph 1 – this is a key paragraph of the study, try to make it clear how you compare the groups. There are two sentences in this paragraph which are almost identical and create confusion.

   Re: We apologize for our limited facility with English. In the revised manuscript, the first sentence "We compared the preoperative and postoperative parameters of the two groups at 3, 6, 12 and 24 months after surgery, including the WCS, ABS, GIQLI and NRS" has been revised as "We compared the postoperative parameters at 3, 6, 12 and 24 months after surgery of the two groups, including the WCS, ABS, GIQLI and NRS with preoperative parameters."

2) By far the weakest point of this paper are the way the results are presented, which are very hard to understand, I have several requirements:
   - Page 12 – basic information and table 1 and 2, all the basic information and operative data should be included in only 1 Table, to be easy to follow and understand and when coming to preoperative data regarding WCS, NRS, ABS and GIQLI please calculate a p value to convince the reader that the two groups were matched.

     Re: Thanks for your useful suggestions. We have added preoperative data such as WCS, GIQLI, ABS and NRS into Table 1 and all the basic information, preoperative data and operative data are included in Table 1. We have compared the preoperative parameters regarding WCS, GIQLI, ABS and NRS between the two groups and they are not significantly different between the two groups.

   - Paragraph – surgical data and postoperative results – please add the p-values in text.

     Re: Thanks for pointing out it. In the revised manuscript, we have added the P values you mentioned: "However, the operative time was significantly longer in the bypass plus colostomy group than in the bypass group ($P < 0.001$). The blood loss was negligible in both groups (14.43 ± 3.11 in the bypass plus colostomy group and 11.13 ± 2.93 in the bypass group). However,

the blood loss was significantly less in the bypass group than in the bypass plus colostomy group ($P$ = 0.007). No significant differences were observed in first flatus time or length of hospital stay between the two groups ($P$ = 0.317 and $P$ = 0.644, respectively). We compared each complication of Clavien-Dindo > 1 and did not note differences between the groups ($P$ = 0.007) (shown in Table 1)."

- Paragraph - Functional recovery, needs to be rewritten, please present the data clearer, when do you compare between the same patient group over time and when do you compare between the two groups. I suggest having two subchapters – a. Functional recovery compared at different time points inside the same group and b. Functional recovery compared between groups;

Re: Thank you for reminding us these mistakes. In the revised manuscript, we have corrected them according to your suggestion.

***"Functional recovery***

***a. Functional recovery compared at different time points inside the same group***

WCS and GIQLI significantly improved (P < 0.001) at 3, 6, 12, and 24 months after surgery in both groups. In the bypass plus colostomy group, NRS significantly improved at 12 and 24 months after surgery (P < 0.001); ABS significantly improved (P < 0.001) at 3, 6, 12, and 24 months after surgery. In the bypass group, NRS did not improve at 3, 6, 12, and 24 months after surgery; ABS significantly improved (P = 0.003) at 3 and 6 months but did not improve at 12 and 24 months after surgery (P = 0.207 and P = 0.670, respectively) (shown in Table 2).

***b. Functional recovery compared between groups***

At 3, 6, 12, and 24 months after surgery, WCS, GIQLI, NRA, and ABS were compared between the two groups. WCS and NRS remained unimproved at 3 and 6 months after surgery, and ABS remained unchanged at 3 months after surgery. Additional above-noted parameters were significantly better in the bypass plus colostomy group than in the bypass group at each time point. These improvements continued over the time course, as shown in Figures 1-3 and Table 3.

At 1 year after surgery, barium enema examinations were performed in all patients of both groups. The barium emptying times were 22.71 ± 4.41 hours and 113.60 ± 110.53 hours in the bypass plus colostomy group and the bypass group, respectively. The former group was significantly better than the latter group ($P$ = 0.007). In the bypass group, a barium emptying time ≥ 72 hours was seen in 8 (53.33%) patients. In contrast, the longest barium emptying time was 30 hours in

the bypass plus colostomy group and did not exceed 72 hours ($P$ = 0.002)."

- Paragraph functional recovery – at one point you change the way you report the data, instead of mean and SD you start using percentages why? The NRS scale is from 1-10, you can still calculate the mean and SD for each group.

  Re: This is our mistake. This part is the same as in the results, and in the revised manuscript, we have deleted this paragraph.

- For the last paragraph of the results you can use Fisher test to compare the probability of having an emptying time < 72h.

  Re: Thanks for your constructive suggestions. Following your suggestions, Fisher test is used to compare the probability of having an emptying time < 72h in the revised manuscript: "In the bypass group, a barium emptying time ≥ 72 hours was seen in 8 (53.33%) patients. In contrast, the longest barium emptying time was 30 hours in the bypass plus colostomy group and did not exceed 72 hours ($P$ = 0.002)."

- The figures are far from optimal: please prepare only 1 figure with 5 panels for each of the parameters you study – WCI, WCS, ABS, NRS and GIQLI – 5 different graphs. Please add the p values inside the graphs and I do not understand why in figure 3 you have two different scores?

  Re: Thanks for your constructive suggestions. Following your suggestions, we have used 1 figure with 4 panels for WCS, GIQLI, ABS and NRS. But WIS wasn't included in the figure because there was lack of data before operation. The Wexner incontinence scale (WIS): on a scale of 0-20, in which 0 represents the best and 20 represents complete incontinence. And we thought that patients with slow transit constipation of shouldn't be tested with scale of incontinence before operation.

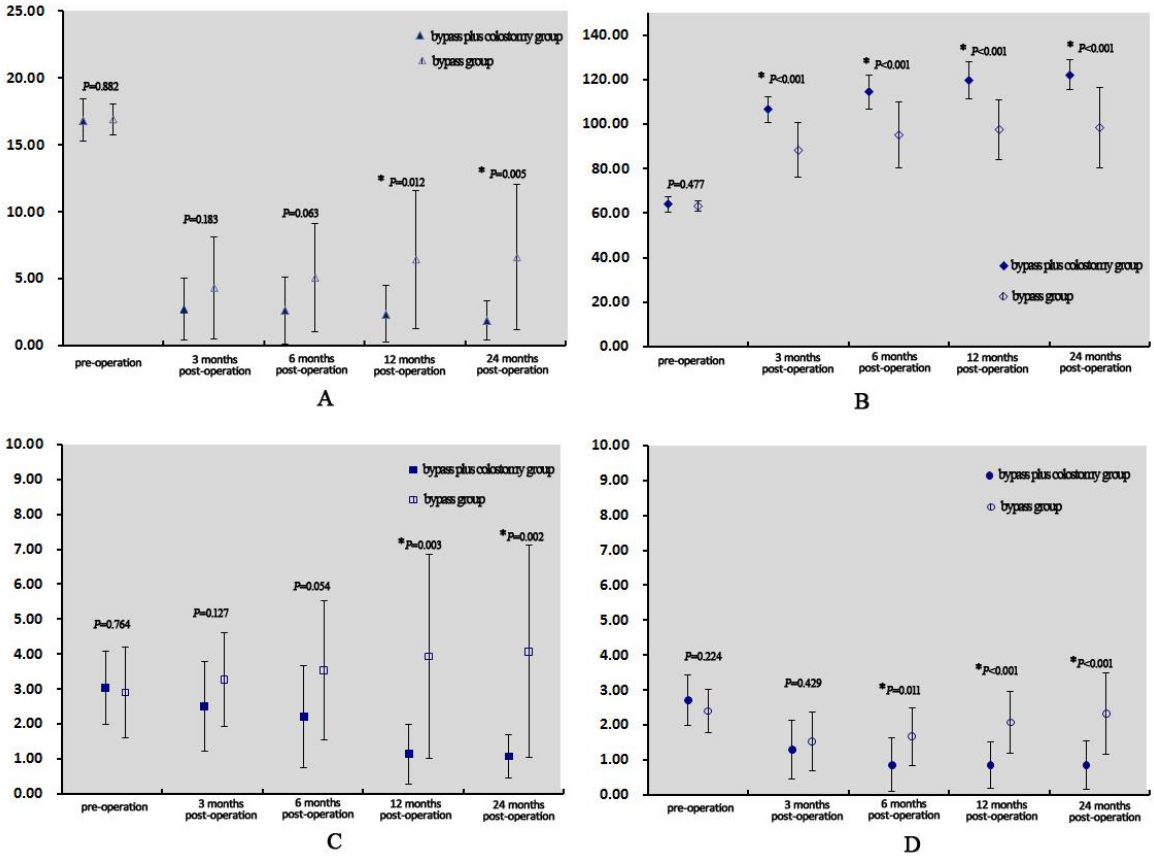


**Figure 1**. X-axis: preoperative and postoperative time points.
**A:** Y-axis: WCS scores; ▲: mean of WCS in the bypass plus colostomy group; △: mean of WCS in the bypass group; |: 95% confidence interval of WCS.
**B:** Y-axis: GIQLI scores; ◆: mean of GIQLI in the bypass plus colostomy group; ◇: mean of GIQLI in the bypass group; |: 95% confidence interval of GIQLI.
**C:** Y-axis: NRS scores; ■: mean of NRS in the bypass plus colostomy group; □: mean of NRS in the bypass group; |: 95% confidence interval of NRS.
**D:** Y-axis: ABS scores; ●: mean of ABS in the bypass plus colostomy group; ○: mean of ABS in the bypass group; |: 95% confidence interval of ABS.

- Figure legends contain also mistakes – figure 3 you write – 95% CI for GIQLI. Change this and also include P values in the legends.
  Re: Thank you for reminding us these mistakes. In the revised manuscript, we have corrected them according to your suggestion.

- Table 3 needs some formatting is very hard to read.
  Re: Thanks for pointing out it. In the revised manuscript, we have modified the format of Table 3.

3) Discussion – the role of the discussion is not to repeat the results, but to comment the results. Remove all the numbers from discussions and add

comments and also expend the paragraph on limitations. I am curious which are the limitations of the surgical approaches, what would you expect to encounter in a larger patient group? What complications? Etc.

Re: Thanks for pointing out the mistake, we have removed all the numbers from discussion and expend the paragraphs as your suggestions in the revised manuscript.

4) Also a very curious point is that despite colostomy the GIQLI improves in the SCBCAC group. This observation should be extensively commented.

Re: Thanks for pointing out it. Of course, there is no denying that colostomy may bring a little inconvenience to the patients' daily life compared with healthy people, but unlike other permanent colostomy, the colostomy in SCBCAC doesn't need to excrete large amount of dung every day. In our study, the healing of the abdominal wall stoma was favorable. A small amount of intestinal fluid or mucus was drained every 1-3 days, but the drainage amount gradually decreased over time. No ulcers or hemorrhages were seen in the skin around the stoma because no feces were discharged from it. The daily life of patients was not negatively affected. So, we think that colostomy doesn't affect the GIQLI too much. This has been added in the revised manuscript.

**Minor remarks**:

1) The abstract is match too long – the authors should consider shortening it, especially the result part, which is over a page long (page 4).

Re: Thanks for your constructive comments. We have shortened the abstract in the revised manuscript,

***"RESULTS***

All patients successfully underwent laparoscopic surgery without open surgery conversion or surgery-related death. The operative time and blood loss were significantly less in the bypass group than in the bypass plus colostomy group ($P = 0.007$). No significant differences were observed in first flatus time, length of hospital stay or complications with CD > 1 between the two groups. No patients had fecal incontinence after surgery. At 3, 6, and 12 months after surgery, the number of BMs was significantly less in the bypass plus colostomy group than in the bypass group. The parameters at 3, 6, 12, and 24 months after surgery in both groups significantly improved compared with the preoperative conditions ($P< 0.05$) except NRS at 3, 6 months after surgery in

both groups, ABS at 12, 24 months after surgery and NRS at 12, 24 months after surgery in the bypass group. WCS, GIQLI, NRS and ABS significantly improved in the bypass plus colostomy group compared with the bypass group at 3, 6, 12, and 24 months after surgery ($P < 0.05$) except WCS, NRS at 3, 6 months after surgery and ABS at 3 months after surgery. At 1 year after surgery, a barium enema examination showed that the emptying time was significantly better in the bypass plus colostomy group than in the bypass group ($P = 0.007$)."

2) In the introduction – page 6, two citations are missing: the sentence from line 3 to 5 – "In terms of treatments …" this should be supported by a citation and lines 12-15 – sentence "The other surgical approach …" please add citation.

Re: Thank you for reminding us these mistakes. In the revised manuscript, we have corrected them according to your suggestion: "In terms of treatments for constipation[2], …/The other surgical approach is subtotal colectomy with cecorectal anastomosis (SCCRA) [9-10], …"

2 **Park MI**, Shin JE, Myung SJ, Huh KC, Choi CH, Jung SA, Choi SC, Sohn CI, Choi MG. Guidelines for the treatment of constipation. Korean J Gastroenterol 2011; 57: 100-114 [PMID: 21350321]

9 **Sarli L,** Costi R, Sarli D, Roncoroni L. Pilot study of subtotal colectomy with antiperistaltic cecoproctostomy for the treatment of chronic slow-transit constipation. Dis Colon Rectum 2001; 44: 1514-1520 [PMID: 11598483 DOI: 10.1007/BF02234608]

10 **Marchesi F,** Sarli L, Percalli L, Sansebastiano GE, Veronesi L, Di Mauro D, Porrini C, Ferro M, Roncoroni L. Subtotal colectomy with antiperistaltic cecorectal anastomosis in the treatment of slow-transit constipation: Long-term impact on quality of life. World J Surg 2007; 31: 1658-1664 [PMID: 17541684 DOI: 10.1007/s00268-007-9111-6]

3) Page 8 – The inclusion criteria included – please avoid repetitive structures and the next sentence – diagnosis was consistent with Rome III diagnosis, chose other words.

Re: We apologize for our limited facility with English. In the revised manuscript, "The inclusion criteria inclusion" has been revised as "Inclusion criteria" and "patient diagnosis was consistent with Rome III diagnostic criteria for constipation" has been revised as "the Rome III diagnosis criteria for constipation".

4) Inclusion criteria number 4 is actually an exclusion criterion.

Re: Thank you for reminding us the mistake. In the revised manuscript, we have corrected them according to your suggestion.

5) Exclusion criteria number 3 is actually very important – data from literature reports that 88% of patients who undergo surgery for constipation suffer from mental illness of rectal/vaginal abuse (it would be ideal also to exclude patients with any of these abuses).

Re: Thanks for your constructive suggestions. Following your suggestions, we have revised exclusion criteria number 3 as: "patients with psychological symptoms or with history of mental illness, such as rectal abuse, vaginal abuse, etc."

6) Page 10, line 5 – a drainage tube was placed – please specify where the drainage tube was placed.

Re: Thanks for pointing out the mistake, we have revised it as "a drainage tube was placed in the Douglas' pouch ".

7) Page 10 – patient and data collection – 0-10 numerical rating scale, what kind of scale, probably you mean pain intensity NRS – please change.

Re: Thanks for pointing out the mistake, we have revised it as "abdominal pain intensity indicated by the numerical rating scale (0–10)

8) We decided to study only Clavien Dindo complications defined as II or above, why? Motivate your choice or also include complications grade I.

Re: Thanks for pointing out it. Grade I in the Clavien-Dindo classification: Any deviation from the normal postoperative course without the need for pharmacologic treatment or surgical, endoscopic, and radiologic interventions. Allowed therapeutic regimens are drugs as antiemetics, antipyretics, analgetics, and diuretics, and electrolytes and physiotherapy. So, in our study, we collect data of complications defined as class II and above.

9) Page 11 – line 8 – The variables were expressed as the mean (exclude the word the).

Re: Thank you for reminding us the mistake. We have corrected it in the revised manuscript as "The variables were expressed as mean ± standard deviation (SD)".

10) You say you used Pearson chi square – where? There are some comparisons where this test would have been necessary but I did not find any results. Moreover, Fischer is much better for small groups of samples – your case.

Re: This is our mistake. We have corrected it in the revised manuscript: "For the comparison of data between the two groups, independent samples t-test and Fisher's exact test were applied ". In our study, we use Fisher's exact test to comparison data such as sex, morbidity and the probability of having an emptying time < 72h.

11) Page 11 – the average ages of patients were – please use singular (the average is only one).

Re: Thank you for reminding us the mistake. We have corrected it in the revised manuscript: "The average age of patients was 74.86 ± 3.42 in the bypass plus colostomy group and 74.73 ± 3.11 in the bypass group ".