Format for ANSWERING REVIEWERS

June 01, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 18309-edited.doc).

Title: Minimally Invasive Surgery for Paediatric Inflammatory Bowel Disease. Personal experience and Literature review

Author: Alessio Pini Prato, Maria Grazia Faticato, Arrigo Barabino, Serena Arrigo, Paolo Gandullia, Cinzia Mazzola, Nicola Disma, Giovanni Montobbio, Girolamo Mattioli

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 18309

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer. All changes have been highlighted in the updated version of the paper according to Editor's indications.

Reviewer #1
Review of ESPS manuscript NO: 18309 Journal: World Journal of Gastroenterology Title: Minimally invasive surgery for children with inflammatory bowel diseases: personal experience and literature review Comment: The authors introduced the indication of surgery in paediatric inflammatory bowel disease (PIBD) and the overall result of laparoscopic surgery of PIBD from the data of publications and personal experience in Giannina Gaslini Children Hospital from 2006 to 2014. They provide nice review of diagnostic (before 2000) and therapeutic laparoscopy (after 2000). However, there are some minor points to be cleared. In Table 1 and 2, the authors need to separate title and result description — If possible, please insert result description into the main body of the manuscript. If needed, please add more descriptions of pros and cons of minimal surgery in paediatric patients compared with those of the adult.

Author – We do agree with reviewer considerations. We separated title and description in Table 1 and 2. Furthermore results were reported in the main body of the manuscript for both Tables trying to avoid repetition. Finally we included a brief statement regarding the impact of minimally invasive surgery in adults and children (second statement of Conclusions section): "…**Overall technical details and indications do not significantly differ between adults and children. Minimally invasive surgery can be adopted either in the elective or emergency setting thanks to incidence of complications that does not significantly differ from that of conventional open surgery but shorter hospitalization and fewer long term sequelae[49]….**"

Reviewer #2

The paper “Minimally Invasive Surgery for Paediatric Inflammatory Bowel Disease. Personal experience and Literature review” by Pini Prato A. et al. is a comprehensive review of minimally invasive approaches for the treatment of IBD in children with interesting part concerning authors’ own experience in that issue. The article has a high priority for publications. However, several amendments could be considered. The weakness of the paper is its length. The main aim of the study could have been achieved on less pages, e.g. by omitting some obvious data about IBD and focusing on the role of minimally invasive surgery in PIBD in section "Background". In the part “Personal series” I strongly suggest to present data in more readily accessible way e.g table. The term “NSAID” for aminosalicylates is inappropriate and is associated with non-selective inhibitors of the enzyme cyclooxygenase.

Author – I do agree that the paper is long but I feel that an *invited review* should try to address all issues of a specific topic regardless of its length. Nonetheless, I tried to shrink the size of the manuscript by shortening results section. Most of the results have been moved in Table 2 to make this section more readily accessible as suggested by this same reviewer. The section regarding personal series now reads like this: “**Between January 2006 and December 2014 (9 years) a total of 104 laparoscopic procedures (98 primary laparoscopy, 6 reoperations for complication) were performed in 61 patients with PIBD. Diagnoses included 39 UC, 20 CD and 2 IBD-U.**

Indications to surgery for patients with UC were mostly represented by haemorrhagic colitis, followed by failure of medical treatment and intestinal obstruction/stricture.

Forty-five patients underwent laparoscopic subtotal colectomy (LSTC) and 38 laparoscopic J-Pouch Ileo-Rectal restorative Anastomoses (JPIRA) (Figure 1 to 3 illustrate our JPIRA technique according to what previously published[38]). In 41 patients LSTC was associated to a protective temporary ileostomy. Four patients underwent LSTC along with JPIRA in a single stage procedure. Definitive ileostomy closure was accomplished in 38 patients.

Fifteen laparoscopic segmental resection have been performed in patients with CD. Two patients required conversion to laparotomy due to the extremely difficult mobilization and manipulation of the inflamed and fragile small bowel. Twelve of these procedures were either ileo-colic resections or right hemicolectomies, all with extracorporeal anastomoses except one that was performed totally intracorporeal. Three were segmental small bowel resections with extracorporeal anastomoses. See Table 2 for details.

A total of 18 complications requiring some sort of surgical intervention were experienced by 13 patients (21% of patients being 8 UC, 4 CD and 1 IBD-U). Patients with UC experienced 4 bowel obstruction (all dealt with laparoscopically), 2 anastomotic leaks, 1 endoperitoneal bleeding, 1 anastomotic stricture, 1 ileostomy prolapse, 1 J-pouch prolapse (treated by laparoscopic pouch-pexy). Complications occurred after a median of 2 years postoperatively (range 1 day – 4 years). Patients with CD (20% of patients, 30% of overall procedures) experienced 2 anastomotic leaks, 1 bowel obstruction due to anastomotic stricture, 1 anastomotic leak, 1 pelvic abscess, and 1 ileostomy prolapse. Complications occurred after a median of 52 days postoperatively (range 3-240 days). One patient with IBD-U experienced enterocutaneous fistula at the stoma site...”.

The term NSAID have been removed and the text changed accordingly. The statement in Introduction section now reads like this: “**Medical management of PIBD include nutritional therapy, aminosalicylates, steroids, antibiotics, immunomodulators (i.e. thiopurine, methotrexate), and biologic therapy (infliximab, adalimumab).**”

Reviewer #3

This paper evaluated safety and efficacy of minimally invasive surgery for pediatric IBD patients through a literature review and the authors' personal series. This paper is interesting, but there are several points to be addressed. Major 1. The authors should discuss the differences between laparoscopic surgery in children and adult procedures. 2. Is there any situation where open laparotomy is preferable to laparoscopic surgery? For example, in subtotal colectomy for fulminant colitis, open laparotomy seems to be safer than laparoscopic surgery. Minor 1. It is unclear whether descriptions on disease localization in Background are about UC or CD. 2. Aminosalicylates are not NSAIDs. 3. Immunomodulators are usually used for maintaining remission, not for achieving remission. 4. The authors should explain one-, two-, three-stage procedures.

Author – All issues have been addressed as follows:

Major:

1. Although I do agree that the differences between laparoscopic surgery in children and adults could have been discussed in details, given the length of the paper I did only include a brief literature-based statement in the conclusion section that reads like this: **"…Overall technical details and indications do not significantly differ between adults and children. In fact, minimally invasive surgery have been adopted either in the elective or emergency setting thanks to incidence of complications that proved not to significantly differ from that of conventional open surgery but shorter hospitalization and fewer long term sequelae[49]…"**.
2. Although most of pediatric papers in literature do not specifically differentiate results basing on elective or emergency surgery we tried to address this issue basing on adults reports. Therefore, we included a statement in section 3.4.3 Total or Subtotal Colectomy that now reads like this: "**Either in elective or emergency setting, total or subtotal colectomy can be carried out with results that overlap and/or overcome those of conventional open surgery[18]…"** Furthermore, as stated above, a sentence on this regard was included in the conclusion section that now reads like this: **"…Overall technical details and indications do not significantly differ between adults and children. In fact, minimally invasive surgery have been adopted either in the elective or emergency setting thanks to incidence of complications that proved not to significantly differ from that of conventional open surgery but shorter hospitalization and fewer long term sequelae[49]…"**.

Minor

1. I agree with the reviewer that this paragraph needed revision. Disease localization in background has been clarified and the paragraph now reads like this: "**Disease localization and severity in children with UC vary. At onset UC involvement is extensive (pancolitis) in 60-80% of all patients, while rectosigmoid and left-sided disease are less frequent. Disease extent is consistently associated with disease severity and children have more aggressive disease course with at least one acute severe colitis (ASC) before adulthood[6]. In case of CD, isolated involvement of terminal ileum (± limited to the caecum) is seen at presentation in 16% of cases. Isolated colonic disease is reported in 27% and ileocolonic in 53% of cases. Of note, although isolated upper gastrointestinal localization is reported in 4% of patients, 30% have esophagogastroduodenal involvement and 24% jejunal/proximal ileal disease[7]. Perianal disease accounts for 15% of patients. Of note, CD may have insidious onset that leads to delay in diagnosis[6,7].**"
2. I agree that the use of NSAID was incorrect in the paper. The term NSAID have been removed and the sentence in introduction now reads like this: "**Medical management of PIBD include**

nutritional therapy, aminosalicylates, steroids, antibiotics, immunomodulators (i.e. thiopurine, methotrexate), and biologic therapy (infliximab, adalimumab)."

3. Again, the reviewer correctly pointed out a mistake in the paragraph dealing with medical treatment that was changed and now reads like this: "**Medical management of PIBD include nutritional therapy, aminosalicylates, steroids, antibiotics, immunomodulators (i.e. thiopurine, methotrexate), and biologic therapy (infliximab, adalimumab). All drugs can be administered in patients with mild to severe forms of PIBD in order to achieve or to maintain remission."**
4. We agree with the reviewer that a brief description of staged procedures would have made the paper more readily accessible and complete. The section **3.4.6 Single or staged procedures** was therefore changed and now reads like this: "**Total colectomy and J-pouch reconstruction can be accomplished as a single stage (Total colectomy with J-pouch reconstruction and no protective ileostomy), two-stages (Total colectomy with ileostomy followed by J-pouch reconstruction without protective ileostomy) or three-stages procedure (Total colectomy with ileostomy followed by J-pouch reconstruction and protective ileostomy) depending on surgeons' attitude and on patients' general conditions. Protective ileostomy is chosen by most surgeons[8,9,18,38].**"

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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