**Author's response to reviews**

**Title:**Laparoscopic versus open adhesiolysis for small bowel obstruction - a multicenter, prospective, randomized, controlled trial

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**Author's response to reviews:** see over

**Editorial request:** 1.) Copyediting:
After reading through your manuscript, we feel that the quality of written English needs to be improved before the manuscript can be considered further.

**Answer:** We have edited the manuscript to improve the quality of written English.

**Editorial request:** 2.) Line numbering: Please revise your manuscript to include line and page numbers. Authors are asked to ensure that line numbering is included in the main text file of their manuscript at the time of submission to facilitate peer-review. Once a manuscript has been accepted, line numbering should be removed from the manuscript before publication. For authors submitting their manuscript in Microsoft Word please do not insert page breaks in your manuscript to ensure page numbering is consistent between your text file and the PDF generated from your submission and used in the review process.

**Answer:** We have added line numbering.

**Editorial request:** 3.) Place Acknowledgement section after Authors? Contributions section.

**Answer:** We have done this.

**Referee 1:**
Overall this is an interesting and original randomized investigation on a topic which has not been previously investigated by other RCTs.
The Study protocol, registered on ClinicalTrials.gov, is overall well written and the statistics, particularly the sample size calculation, seems to be correct.
However I would like to raise some issues regarding the inclusion and exclusion criteria, that need to be clarified and should be at least discussed within the discussion (since they can not be changed because the Trial is already registered and already recruiting).
Why the trigger for operation is considered the failure of passage of Water Soluble Contrast inn the colon within 8 hours? In the literature most authors consider 24-36 hours to be the time limit for considering failed the trial of NOM for ASBO with Gastrografin. Please explain the decision to choose the limit of 8 hours to proceed to surgery. Don't you think some of these patients could have resolved SBO in the following hours? Please give a reason for that.

**Answer:** Two large meta-analyses have shown that the sensitivity, specificity, PPV or NPV does not differ between 8 hours and 24 hours (Abbas et al, 2008, Branco et al, 2010). As there appears to be no advantage of waiting more than 8 hours, we chose that for out threshold. We have also added discussion about choosing 8 hour time point. In addition, it is stated in the protocol that a minimum 12 hours' nonoperative management preceeds Gastrografin-study meaning that the minimum time of nonoperative management is 20 hours, usually over 24 hours.

**Referee 1:** - There are probably too many exclusion criteria and this in my opinion can make
the enrolment a bit challenging. Furthermore I do not agree with some of these exclusion criteria. E.g.:
1) Previous (change earlier to previous please) generalized peritonitis should not

be an exclusion criteria; in my experience it can rather be a predictive factor of finding diffuse matted adhesions (although this is not demonstrated and not always true) and can therefore be associated with higher risk of conversion, but it is not an absolute contraindication to approach ASBO laparoscopically.

**Answer:** We agree with the referee that previous generalized peritonitis is not an absolute contraindication. However, it is associated with higher risk of conversion, and we wanted to keep the conversion rate at minimum. Why? Because the higher the conversion rate on the laparoscopic group, the more diluted the results would be. The sample size is relatively small (n = 102), and high conversion rate could easily lead to loss of power in the study.

**Referee 1:** 2) Previous obesity surgery; in obese patients laparoscopy is rather an advantage!!! Furthermore surgical procedures for obesity are usually performed in the supramesocolic region and most often they are not associated with significant adhesions causing ASBO or strangulating bands needing surgery. Why consider previous obesity surgery an exclusion criteria?

**Answer:** The refee is absolutely right: The patients that have undergone obesity surgery should be treated laparoscopically. In our study, 50% of patients undergo open surgery, and thus we feel that it would be unethical to randomize these patients. They should be treated laparoscopically.

**Referee 1:** 3) Suspicion (PRE-operative suspicion I assume) of other cause of obstruction than adhesions. Once again in such cases a diagnostic laparoscopy is rather indicated and if a different cause is found at laparoscopy, the patient will be dropped out from the study. There is no need to exclude preoperatively such patients, unless you clarify that patients with CT scan finding of SBO caused by a clear intrabdominal cancer or mass, will be excluded. In all other patients the suspicion should not be enough to consider the patients excluded from the possibility to be enrolled. If the cause of obstruction is other than ASBO then the patient will be excluded (drop out) and perhaps the procedure can still be carried out laparscopically without need for conversion

**Answer:** We agree with the referee that an exploratory laparoscopy could be a possibility in some of these patients. However, laparoscopic exploration is quite difficult in the setting of small bowel obstruction as the dilated bowels block the field and might lead to misdiagnosis. Especially if there are also adhesions in addition to other pathology. For these reasons, in our institution, we use laparotomy approach in patients with suspicion of other causes of obstruction than adhesions. Further, we intend to analyze these patients as intention-to-treat basis, which means we cannot exclude patients after the randomization has been carried out. This is important as iatrogenic trauma can occur already at port insertion, before the final reason for bowel obstruction is known.

**Referee 1:** 4) Previous abdominal operation within 30 days should not be contraindication to
laparoscopy in my experience neither to the enrolment in such a Trial, if the first operation was done laparoscopically (if it was done via open laparotomy the risk of fascial breakdown with penumoperitoneum is consistent). I.e. a patient underwent lap appy and presenting with SBO 20 days later suspected for adhesion SBO, should be approached laparoscopically and can be enrolled.

**Answer:** We agree with the referee that this is not a contraindication to laparoscopy. However, occurence of such postoperative SBO that is not resolving by conservative means are rare. Furthermore, these patients differ from the basic population of patients that present with adhesive SBO: e.g. their lenght of stay is longer and they tend to have more complications. In such a small sample size (n = 102), it is possible that one or two patients would end up in one group, and thus create a bias.

**Referee 1:** 5) Previous surgical operation for aorta or iliac vessels surgery; this is also not an absolute contraindication but rather a predictor of failure of laparoscopy

**Answer:** We agree, we excluded these for the same reasons as the ones above.

**Referee 1:** 6) I can not also understand why over 1 week of hospital stay directly prior surgical consultation should be an exclusion criteria for enrolment in the Laparoscopic Trial. In addition I would like to ask to the authors what exactly that sentence does mean? Please clarify

**Answer:** Patients that have already spend a week in hospital (probably because of some other comorbidity such as ischemic heart disease, pneumonia, etc) are prone to have longer hospital stay and complications. In a small sample set, rare occurence of such patient to one arm would create a strong bias on the primary outcome (length of stay).

**Referee 1:** I suggest to the authors to explain and discuss more the reason for choosing the
above exclusion criteria.

**Answer:** We have added discussion about the exclusion criteria.

**Referee 1:** Regarding the criteria for conversion:
- If peritoneal carcinomatosis is found, why not to take advantage of laparoscopy and spare the patient a painful and useless median laparotomy? A biopsy can be done laparoscopically and eventually if needed, a loop ileostomy proximal to the obstruction, can be fashioned without need for conversion.

**Answer:** We agree that in some patients with peritoneal carcinosis can be treated by using laparoscopic approach. However, getting a proper field of vision and exploration in the presence of dilated bowel loops is quite difficult in our opinion. We approach patients with bowel obstruction due to peritoneal carcinosis by laparotomy to obtain good exploration since sometimes a bypass from small bowel to large bowel can be fashioned and spare the patient a stoma. Additionally, bowel lenght is difficult to measure in an abdomen filled with dilated bowel loops.

**Referee 1:** Finally I would consider an additional endpoint to be the conversion rate / success rate of laparoscopic approach, since this is one of the biggest debated issues and of the most often reported data by the relevant literature on this topic.

**Answer:** We thank the referee for pointing this out and we will include this as an endpoint.

**Referee 2:** Reviewer's report:
nice paper, minor revisions
please cite

Di Saverio S, Coccolini F, Galati M, Smerieri N, Biffl WL, Ansaloni L, Tugnoli G, Velmahos GC, Sartelli M, Bendinelli C, Fraga GP, Kelly MD, Moore FA, Mandalà V, Mandalà S, Masetti M, Jovine E, Pinna AD, Peitzman AB, Leppaniemi A, Sugarbaker PH, Goor HV, Moore EE, Jeekel J, Catena F. Bologna guidelines for diagnosis and management of adhesive small bowel obstruction (ASBO): 2013 update of the evidence-based guidelines from the world society of emergency surgery ASBO working group. World J Emerg Surg. 2013 Oct 10;8(1):42.

**Answer:** We have added the reference.