Author’s response to reviews

Title: DISSECTION OF THE INFERIOR MESENTERIC VEIN VERSUS OF THE INFERIOR MESENTERIC ARTERY FOR THE GENITOURINARY FUNCTION AFTER LAPAROSCOPIC APPROACH OF RECTAL CANCER SURGERY: A RANDOMIZED CONTROLLED TRIAL.

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Gregorio Di Franco, M.D. (Reviewer 1):

The authors accurately describe the criteria used for the definition of post-operative genitourinary complications and the methods used for their evaluation. The definition of the minimum number of patients to be enrolled is defined with a statistical criterion. The statistical methods used for the comparison are also well described.

However, the authors considered only the use of the laparoscopic approach. This could be specified in the title and should be better highlighted in the introduction section.

We have specified in the title that is only in laparoscopic approach (Title, line 2-3, pag 1). Also it was already specified in inclusion criteria (METHODS/DESIGN, Inclusion criteria, line 3, page 5).

Due to the lack of experience in robotic surgery and our long experience in laparoscopic surgery, the design of our study has been made only in laparoscopic approach, to avoid the learning curve bias. However, the objective of the study is the dissection route of the vessels not the surgical approach.

We have added a comment in the introduction (BACKGROUND, line 14-16, page 3) and in the discussion sections (DISCUSSION, line 6-10 , page 10).

G. P. Sao Juliao (Reviewer 2):

Thank you for the opportunity of reviewing this interesting study protocol. This is the description of a randomized trial of patients with rectal cancer that will be submitted to total mesorectal excision by two different approaches to the inferior mesenteric vessels. The aim of this study is to prove that there is a difference in the rate of sexual disfunction related to each surgical technique.

I have a few comments for the authors:

1) I would like to recommend the authors to instead of including patients with rectal cancer up to 15 cm, to include patients with rectal cancer that will be submitted to total mesorectal excision. Some patients with higher tumors may ultimately have a partial mesorectal excision performed and this may impact on the results.

We agree with the comment. We have changed the inclusion criteria to patients with adenocarcinoma ≤ 10 cm from the anal verge, measured by rigid rectoscopy, candidates to TME (METHODS/DESIGN, Inclusion criteria, line 1-2, page 5); we have added the need of a partial TME as a exclusion criteria (METHODS/DESIGN, Exclusion criteria, line 1-2, page 5). Also we have highlighted that in the discussion ( DISCUSSION, line 1,page 10)
2) It would be interesting to know the number of surgeons enrolled in the protocol that will perform the operations. Did they have training on both techniques?
The surgery is performed only by 5 surgeons, who are part of the colorectal unit. All of them experts in laparoscopic surgery and they have training on both techniques (intervention and control arm). (METHODS/DESIGN, Surgical technique, line 4-5, page 7).

3) I would recommend to record the surgeon's impression on autonomic nerve preservation during the procedure. Some patients may need the nerve resection for oncological purposes. This information may be relevant in the final analyses.

In our study we record the surgeon’s impression on autonomic nerve preservation during the procedure, maybe we have not been able to reflect that in our manuscript. But also we record the surgery, because an external surgeon can agree or disagree about the preservation of the nerves. We have stated that more clearly and we will have into account in our study the need of nerve resection for oncological purposes (METHODS/DESIGN, Secondary variables, line 13-15, page 8)

4) I am not comfortable with the criteria for withdrawal - when the dissection cannot be performed or the surgical anatomy cannot be identified is because this is a very difficult case. This can drastically impact on your results as they are at increased risk for nerve injury irrespective of the technique used. Let's say that the only ones that will be removed are those randomized to the intervention group, the control group will have more difficult cases included in the analyzes and consequently worst results.

We agree. We will consider as criteria for withdrawal only the patients who do not attend the subsequent follow-up (METHODS/DESIGN, Criteria for withdrawal, line 1, page 5)

5) It would be interesting to know the expected range of time to recruit all patients.
In our hospital rectal surgery for cancer is expected between 60-70/year, with inclusion criteria, we think that about 45-50 could be included. That means, that probably in two years, the recruitment should be finished. (STATISTICAL ANALYSIS, Sample size, line 5-7, page 9)

6) Finally, including patients submitted to different operations is an important bias. Quality of life and sexual dysfunction rates are not similar among patients submitted to LAR and Miles. One can argue that even different approaches to the same operation may have different outcomes (laparoscopic, robotic, taTME). I would like to recommend the authors to do not include patients submitted to Miles and only those submitted to LAR. This would avoid major bias.

We agree with the comment, it will permit to have more homogeneous sample. We have added abdominoperineal resection (APR) to the exclusion criteria (METHODS/DESIGN, Exclusion criteria, line 1-2, page 5). We have deleted it from METHODS/DESIGN, Surgical technique, page 7. We have added a comment about that in the Discussion (DISCUSSION, line 11-13, page 10.)