Response to Reviewers

Thank you for your valuable comments, which were extremely helpful in improving the quality of our manuscript.

Reviewer #1:

Specific Comments to Authors: This is a retrospective study and it reports that the Narrow pelvic inlet and obesity are independent risk factors for anastomotic leakage after ISR. Anastomotic leakage after ISR may be predicted from a narrow pelvic inlet plane area (≤10,074 mm2). I enjoyed reading the paper and the paper was interesting. I feel that it needs some more details about the techniques/procedure performed. I have a few comments.

1) When was the first postoperative endoscopy or gastrografin enema performed?

Response: We closed the diverting stoma 3-6 months after surgery. Before the closure, we performed colonoscopy, contrast enema radiography, and/or computed tomography (CT). If there was any trouble that suggested a leakage, CT was performed each time. Troubles usually occurred within a month.

This point has been added to the Methods section of the revised manuscript.

2) What was anal bougie?

Response: It was a transanal drain. This information has been added to the revised manuscript.

3) What was the treatment for the patients with grade A and C leakage?

Response: Three cases of grade A leakage were treated conservatively by antibiotics. Two patients with grade C leakage needed re-operation. One patient underwent permanent colostomy, and the other underwent nephrostomy for vesicorectal fistula.

This point has been added to the Methods section of the revised manuscript.

Reviewer #2:

In the present manuscript the author investigate risk factors for anastomotic leakage after intersphincteric resection based on clinicopathological variables and in particular n the role of pelvimetry. The idea of the trial is good, however there are some points that need to be clarified Major points

1. You stated that anastomotic leak was defined as the presence of an anastomotic fistula during the first postoperative endoscopy or gastrographin enema . You mean that no patient in your series experienced fever, leukocytosis or CRP and pro-calcitonin serum levels increase which lead to further diagnostic laboratory or strumental finding ? No CT scan was performed ? (please specify) Moreover in the material and methods section there is no mention of how and when these controls were scheduled ? Do you routinely check all the anastomosis with endoscopy or with rigid rectoscope or only in the presence of clinical suspect of anastomotic leak ? At which day ?

Response: Anastomotic leakage was defined as a defect of the intestinal wall integrity at the coloanal anastomotic site leading to a communication between the intra- and extraluminal components occurring. [1]

All blood test data of Table 1 is preoperative data. All patients experienced fever, leukocytosis, increased CRP, and elevated serum levels of procalcitonin. We use the clinical path after surgery, and blood tests were conducted on the 1st, 3rd, 7th, and 14th day after surgery. Patients with clinically suspicious symptoms, such as a high fever, abdominal tenderness with muscular guarding, abdominal findings on rectal examination, or purulent discharge from the pelvic cavity drain, underwent evaluation of the anastomotic site using contrast enema radiography, CT, or colonoscopy (World journal of surgery 2017; 41(8): 2168-77). Troubles usually occurred within a month. We closed the diverting stoma 3-6 months after surgery. Before the closure, colonoscopy, contrast enema radiography, and/or CT was always performed.

These points have been added to the Methods section of the revised manuscript.

2. In your series approximately 15% of the patients underwent preoperative neoadjuvant treatment (CT+RT). Nevetheless you report almost 50 % of patients who are potentially candidate for neoadjuvant. In table 1, the distance of the tumor form the anal verge how is expressed in millimeters or centimeters (please specify). And adds all the other values in the table since is confounding. In your series, operative time is extremely high, considering that the majority of patients have been operated using a laparotomic approach and considering that splenic flexure mobilization was rarely performed. Could you please comment on this?

Response: At our hospital, preoperative chemoradiotherapy was initially performed for lower rectal cancer with tumors deeper than cT3 or more than N1. One severe anastomotic leakage occurred in the early phase of this study period. Therefore, we did not perform preoperative CT+RT in the middle phase of this study. However, the problem of circumferential resection margin (+) occurred. So, we started to perform CT+RT again in the late phase of this study. Consequently, although 50% of our study patients were potential candidate for neoadjuvant, only 15% of the patients underwent neoadjuvant therapy.

In table 1, the distance of the tumor form the anal verge how is expressed in millimeters or centimeters (please specify). And adds all the other values in the table since is confounding.

Response: In Table 1, the distance was millimeters. Table 1 has been modified.

In your series, operative time is extremely high, considering that the majority of patients have been operated using a laparotomic approach and considering that splenic flexure mobilization was rarely performed. Could you please comment on this?

Response: There are two reasons. (1) We performed laparotomy with a small incision below the umbilicus in order to improve the cosmetic status by minimally invasive surgery. Therefore, it may have resulted in long operative time. (2) Even when the inferior mesenteric artery root was preserved, the lymph node around inferior mesenteric artery root was separately resected in

order to improve the curability. This may also have added to the longer operative time. These points have been added in the Methods section of the revised manuscript.

With respect to the splenic flexure mobilization issue, when an intersphincteric resection is planned, flexure is routinely performed by the majority of authors in the literature, to avoid tension at the anastomotic site? Could you comment on this? You stated that inferior mesenteric artery was ligated in only 5 patients ? is this true ? What about oncologic adequacy ?

Response: Splenic flexure mobilization was performed in 9 (7.7%) of the 117 patients in order to avoid tension at the anastomotic site. Kye et al. reported that the splenic flexure mobilization made it possible to obtain an extra colonic length of about 27.8 cm in rectal cancer surgery (Int J Med Sci 11:857-862, 2014). In their analysis, splenic flexure mobilization occupied 9.8% of total operation time, and could be safely performed without complications.

High ligation of the inferior mesenteric artery requires large open wound and splenic flexure mobilization in order to anastomose the descending colon and rectum. Splenic flexure mobilization can cause damage to the spleen. Spleen injury adversely affects surgical mortality and the prognosis. Therefore, we ligated the root of the inferior mesenteric artery for limited cases (4.3%). Even when the inferior mesenteric artery root was preserved, the lymph node around inferior mesenteric artery root was separately resected in order to improve the curability.

There is a meta-analysis of randomized controlled trials comparing high and low ligation of the inferior mesenteric artery in rectal cancer surgery. The conclusion stated that there was no difference between high and low ligation of the inferior mesenteric artery in terms of oncological outcomes or postoperative morbidity and mortality (Hajibandeh et al. Dis Colon Rectum. 2020;63(7):988-999.).

Minor Points There are some grammatical errors that need to be corrected I.e table 1 : protain (protein) page 7 : introduction chapter : …. where access and visualization of the narrow pelvis difficult (the verb is lacking) and others.. I recommend a linguistic polishing

Response: Thank you very much for your valuable comment. We have polished the language accordingly.

Reviewer #3:

The author raised an important question in the field, however, he did not explain few major issues: What is the explanation that pelvic inlet surface area (and not the outlet area) impacts that much an anastomosis that is done manually trans-analy (through the pelvic outlet)? It is important to notice that is not only statistics that matters, but rather its explanation.

Response: As you pointed out, coloanal anastomosis was hand-sewn with the approach from the anus. This procedure is performed in front of the operator with the aid of Lone Star Retractor (Cooper-Surgical Thumbull, CT). Experienced operators can overcome narrow pelvic outlet. However, almost all surgical procedures are performed with the approach from the abdominal cavity. Narrow pelvic inlet could hinder the procedures with the approach from the abdominal cavity. Especially, it is difficult to dissect along the correct layer. Difficult

procedure could induce damage to the blood vessels, intestinal tract, external sphincter, levator ani, pelvic nerves, and surrounding organs, resulting in anastomotic leakage.

This point has been added to the Discussion section of the revised manuscript.

Moreover, he recommended robotic surgery for better results, while he did not explain the original relation of the pelvic inlet to the transanally manually done anastomosis, which will not be done by the robot in all cases. The author considered open and laparoscopic set of patients together, which should not be the case, since the latter gives better vision in tight area as the pelvis.

Response: Yamaguchi et al. reported that robotic-assisted laparoscopic surgery may be a useful modality for locally advanced low rectal cancer (Surgical Endoscopy. 2018; 32:4498–4505). Robotic-assisted laparoscopic surgery may be applied in the future, even when the inlet plane area is small; accordingly, we have stated that. The Discussion was modified in the revised manuscript.

In our study, the number of laparoscopic cases was small, and anastomotic leakage did not occur in laparoscopic cases. Therefore, the laparoscopic effect was not determined. Anastomotic leakage in laparoscopic surgery is also an issue for the future. This point has been added to the limitations in the Discussion section.

Step 6: Editorial Office's comments

(1) Science Editor: 1 Scientific quality: The manuscript describes a retrospective cohort study of the narrow pelvic inlet plane area and obesity as risk factors for anastomotic leakage after intersphincteric resection. The topic is within the scope of the WJGS. (1) Classification: Grade C, Grade C, and Grade D; (2) Summary of the Peer-Review Report: The authors investigated the risk factors for anastomotic leakage after intersphincteric resection based on clinicopathological variables and in particular on the role of pelvimetry, which is interesting. However, some more details about the techniques/procedure performed should be added. The questions raised by the reviewers should be answered; and (3) Format: There are 2 tables and 2 figures. A total of 20 references are cited, including 2 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade B, Grade B, and Grade B. A language editing certificate issued by editage was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the signed Copyright License Agreement, the STROBE Statement, and the Institutional Review Board Approval Form. Written informed consent was waived. ***The Conflict-of-Interest Disclosure Form is not qualified.*** *No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The topic has not previously been published in the WJGS. 5 Issues raised: (1)* ***The "Author Contributions" section is missing.*** *Please provide the author contributions; (2) The authors did not provide original pictures.* ***Please provide the original figure documents.*** *Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (3)* ***PMID and DOI numbers are missing in the reference list.*** *Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout; and (4)* ***The "Article Highlights" section is missing.*** *Please add the "Article Highlights" section at the end of the main text. 6 Re-Review: Required. 7 Recommendation: Conditional acceptance.*

(2) Editorial Office Director: I have checked the comments written by the science editor. The authors need to complete the Conflict-of-Interest Disclosure Form. The authors have written the "author contribution" section. ***The author should number the references in Arabic numerals according to the citation order in the text. The reference numbers will be superscripted in square brackets at the end of the sentence with the citation content or after the cited author's name, with no spaces.***
(3) Company Editor-in-Chief: I have reviewed the Peer-Review Report, the full text of the manuscript and the relevant ethics documents, all of which have met the basic publishing requirements, and the manuscript is conditionally accepted with major revisions. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report and the Criteria for Manuscript Revision by Authors.

Response: The following items have been modified in the revised manuscript: (i) Conflict-of-Interest Disclosure Form and (ii) In-text citations.

The following items have been added in the revised manuscript: (i) Author contributions section, (ii) Original figure documents, (iii) PMID and DOI numbers in the reference list, (iv) Article highlights section.