Peer Review File

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Reviewer A

Retrospective study of combined pelvic exenteration in the treatment of primary
4 and recurrent pelvic malignant tumors
Comments for the authors:
The authors describe a retrospective analysis of patients undergoing pelvic exenteration surgery for pelvic malignancies at a single site in China. This is an important descriptive study of surgical oncological outcomes.
There are several instances where expansion of details would better inform the surgical and oncological community about the study. The recommendations should also correspond with an updated abstract where necessary.
Thank you very much for your suggestions, for your suggestions, I will be below to reply one by one, the content of the reply is shown in red font.

Introduction
Comment1: As the authors mention, there are limited publications from China but there are several international collaborative studies as well as publications from single sites world-wide. As such, a recommendation to change the wording in the abstract is made, lines 40-41.
Reply1: I've changed it in the text to be more appropriate.
Change in the text: We have modified our text as advised.(see page2, line 42-43)

Comment2: Pelvic exenteration (PE) surgery is not only performed with palliative intent as suggested in the abstract on line 36. It is unclear if the patients included in the present study population were treated with palliative or curative intent and the manuscript should be updated accordingly.
Reply2: Thank you very much for your advice. Patients were included in this study with the aim of achieving R0 resection and improving patient survival time.
Change in the text: We have modified our text as advised.(see page2, line36-38)

Comment3: Line 75 –The incidence of ‘what’ has reduced? This sentence appears to be missing information.
Reply3: Thank you very much for your advice, which refers to the reduced incidence of locally advanced pelvic malignancies, as more widespread routine medical check-ups can screen for early malignancies
Change in the text: We have modified our text as advised.(see page3, line79-80)

Methods

Comment4: Line 95 – Is this Hospital a tertiary institution with a specialised pelvic exenteration unit with multidisciplinary team assessment of patient treatment pathways and specialised surgical expertise involved in the PE procedure?

Reply4: Yes, this hospital has a specialised pelvic surgery treatment unit. Importantly, every patient undergoes a multidisciplinary expert consultation before undergoing treatment, a team that includes imaging specialists, radiotherapists, oncologists, surgeons, gynaecologists and nutritionists. These expert groups assess whether the patient is ready for R0 resection.

Change in the text: We have modified our text as advised.(see page4, line102-104)

Comment5: Line 99 – a statement that patient demographics were collected should be included and a brief description of what this includes could also be informative.

Reply5: Thank you very much for your comment! we have revised the description of this paragraph based on your suggestion to make it more concise and general. Change to (The medical histories and pathology reports were reviewed for basic information, clinical data and tumor characteristics)

Change in the text: We have modified our text as advised.(see page4, line107-108)

Comment6: Line 103 – Can the authors please provide more details regarding what preoperative imaging was undertaken. PET? MRI? PET? What were the indications for 'more extensive rectal and cervical cancer invasion in the pelvis'. Inclusion of clinical staging details for both rectal and cervical cancer patients is necessary. While patients with metastatic disease were excluded, can the authors comment on the incidence of S1-S2 disease involvement?

Reply6: Thank you very much for your comment! Preoperative abdominal CT and pelvic MRI as well as rectal ultrasound endoscopy should be routinely performed, and whole-body enhanced CT is used for 3D reconstruction of critical vessels to assist in preoperative surgical planning and to rule out distant metastases.PET-CT can assist in the diagnosis of patients with distant metastases and in the determination of whether the suspected invasion is malignant.

Regarding the staging of patients with rectal cancer and patients with cervical cancer, all patients were locally advanced patients, and all patients with rectal cancer were clinically staged as Stage III, and all patients with cervical cancer were clinically staged as Stage IV. Lymph nodes have been analysed individually, and so there is no relevant discussion in the text.

Because of the time span of the study, patients with S1-S2 invasions were considered unsuitable for PE at the time of admission, and information on such patients was not included in the study at the initial stage, so there is no specific data in this area, and it is more difficult to collect it again. Complication rates may be significantly higher in patients after high sacrectomy, particularly increasing the risk of neurological deficits, and the risk-benefit ratio of high sacrectomy needs to be considered. Bhangu et al.(1) showed that patients with S1 and S2

resections had the highest complication rate (60% versus 27% and 29%) compared to S3 or S4 and S5 resections.

Change in the text: We have modified our text as advised.(see page5, line133-139)

References

(1) BhanguA, BrownG, AkmalM, et al. Outcome of abdominosacral resection for locally advanced primary and recurrent rectal cancer[J]. Br J Surg, 2012, 99(10):1453-1461. DOI: 10.1002/bjs.8881.

Comment7: Details regarding chemotherapy, chemoradiotherapy or radiotherapy could also be included.

Reply7: Thank you very much for your comment! For patients with primary tumours assessed to tolerate treatment, preoperative neoadjuvant chemoradiation can lead to local tumour regression and improve the R0 resection rate. For patients with recurrent tumours who have not previously received chemoradiation, chemoradiation may be considered prior to surgery. For patients with recurrent tumours who have previously received radiotherapy, another preoperative treatment should be carefully considered and the dose, division and extent of radiotherapy need to be individually tailored. The details are shown in Table1.

Change in the text: We have modified our text as advised.(see page5, line139-145)

Comment8: Lines 121-131 – did patients undergo specific lateral pelvic lymph node dissection? Can this be discussed?

Reply8: For PE surgery, there is a complete procedure for lymph node dissection. Lymph node dissection begins at the aortic bifurcation and encompasses the lymph nodes of the main-iliac vascular bifurcation, the common iliac vessels, and the external iliac vessels up to the root of the internal iliac vessels, and lymph nodes in the region of the internal iliac vessels may be subsequently removed as a whole, along with the vessels and tumour specimen. Ligating and dissecting the internal iliac arteries and veins at the beginning effectively reduces the risk of pelvic haemorrhage during or after surgery.

Change in the text: We have modified our text as advised.(see page6, line166-172)

Comment9: The high R0 rate is commendable in this study; the definitions of clear surgical margins vary across units, therefore, inclusion of definitions for R0, R1 and R2 would be informative.

Reply9: Thank you very much for your comment! Evaluation criteria of surgical radicality: according to the postoperative pathological findings, the degree of radicality of pelvic tumour surgery was classified into 3 grades: R0 (pathological findings of negative margins), R1 (complete resection of the lesion by the naked eye, with tumour cell residues at the margins of the microscope) and R2 (tumour residues by the naked eye).

Change in the text: We have modified our text as advised.(see page5, line146-150)

Comment10: Line 139 – Were there any MRI's, colonoscopy/sigmoidoscopy, biopsies or blood tests (CEA, CA125) undertaken at follow-up visits? What is standard of care for both groups of patients at this institution?

Reply10: Patients in both groups were followed up on an outpatient basis, every 3 months for the first three years postoperatively, every 6 months for 4-5 years postoperatively, and annually after 5 years. Routine follow-up of patients in both groups included whole-body CT and tumour markers (including CEA, CA125, CA199). Rectal cancer patients underwent colonoscopy in the 1st, 3rd, and 5th postoperative years. Patients with cervical cancer had one additional SCCA test for tumour markers at each follow-up. MRI and PET-CT were not included as routine follow-up items, and additional tests were performed when CT examination suggested the presence of suspected recurrent foci.

Change in the text: We have modified our text as advised.(see page6, line177-187)

Results

Comment11: A patient selection flow chart would be a valuable inclusion. The STROBE checklist provided incorrectly describes the study as a case control study. While descriptive differences are made between the two patient groups, neither one is a control for the other and a better descriptor is a cohort study.

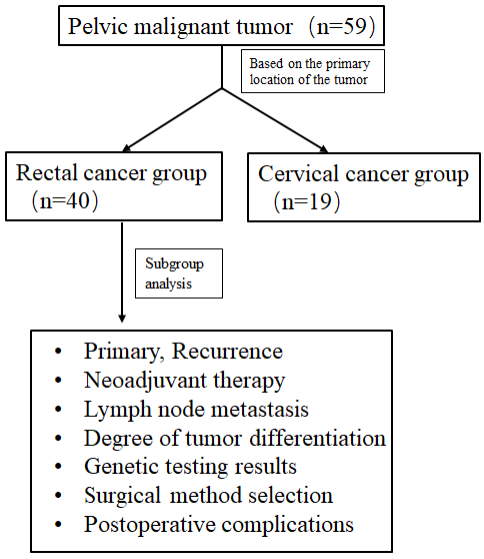

Figure 1 Patient selection flow chart

Reply11: Thank you very much for your comment! I completely agree with your suggestion, Based on your suggestion, I will construct a patient selection flowchart. Our team has carefully reviewed the manuscript and confirmed that it is a cohort study, not a case-control study. We have made the necessary modifications and thank you very much for your reminder.

Change in the text: We have modified our text as advised.(see page21, line578)

Comment12：Line 157 and Table 1 – please include details regarding the preoperative treatment received – radiotherapy dose, types of chemotherapy. Was any adjuvant chemotherapy administered? Given that the patient population did not include metastatic disease, can the authors comment on the rationale behind almost 30% of patients receiving chemotherapy alone?

Reply12: Thank you very much for your comment! Our team has also considered this issue before, as we retrospectively collected patient data from the past 7 years. Over time, the radiotherapy and chemotherapy regimen also changed, and patients with different constitutions received different chemotherapy cycles and regimens, as well as different doses of radiotherapy. Each patient has heterogeneity, and the radiotherapy and chemotherapy regimen for cervical cancer is different from that for rectal cancer. It is too cumbersome to list the specific regimen for each patient alone. Therefore, following your suggestion, we have summarized and listed the specific treatment situation, which has been revised in the text. 30% of patients receive chemotherapy alone, as some were hospitalized 5-6 years ago when neoadjuvant therapy was not yet widely accepted nationwide and could only receive adjuvant chemotherapy regimens. Additionally, some patients are intolerant to neoadjuvant chemotherapy and can only switch to regular chemotherapy regimens.

Change in the text: We have modified our text as advised.(see page7, line209-212)

Comment13:Clinical staging of patients in both patient groups, including nodal metastases should be included in Table 1. This is important to describe the patient population to understand those who were considered suitable for exenteration and may be related to the high R0 rate.

Reply13: Thank you very much for your comment! based on your suggestion, we have included the clinical staging of patients in Table 1, as most of the 59 patients were locally advanced or recurrent pelvic malignant tumors, with the majority of T staging in T4 and lymph node conditions in N+. I have taken into account the clinical staging and will not list it separately.

Change in the text: We have modified our text as advised.(see page17, line546)

Comment14:5 year survival rates in a 7 year study… is that feasible? What is the follow up time – is it skewed?

Reply14: Firstly, thank you very much for your comment. Because five-year survival is widely recognised as an important metric for assessing the effectiveness of cancer treatments, it provides a standardised point in time to compare the effectiveness of different studies and treatments. Five-year survival is also often considered a key clinical milestone. This study focuses on five-year survival of patients, and another reason for not using seven-year survival is for the feasibility of the study and completeness of the data.

Change in the text: No changes in the text

Discussion

This appears to be a skew of data presented tending towards predominant description of rectal cancer patients. Without adequate representation of the cervical cancer group and discussion of the data, this group adds little to the paper.

Comment15: The 5-year survival rate of cervical cancer is reported to be 25.3%. While the acknowledgement is made by the authors that this is low, can they address this in relation to published literature? The papers currently cited relate to rectal cancer. What is the breakdown on 5-year survival rates of primary vs recurrent cervical cancer in the current study?

Reply15: Thank you very much for your valuable feedback. In the early stages of writing the paper, we also attempted to conduct subgroup analysis on cervical cancer, similar to rectal cancer. However, unfortunately, the number of patients who underwent PE for cervical cancer was relatively small, only 19 cases, and a portion of patients came from the gynecology and oncology department. The heterogeneity between each patient was too large, and the number of cases was small. Therefore, we conducted comparative statistical analysis between the two groups, and the evidence was not accurate enough, So this study only reported an analysis of the prognosis of rectal cancer and cervical cancer, and conducted a comprehensive subgroup analysis on 40 rectal cancer patients. We did not include this comparison in the text due to its unclear significance.

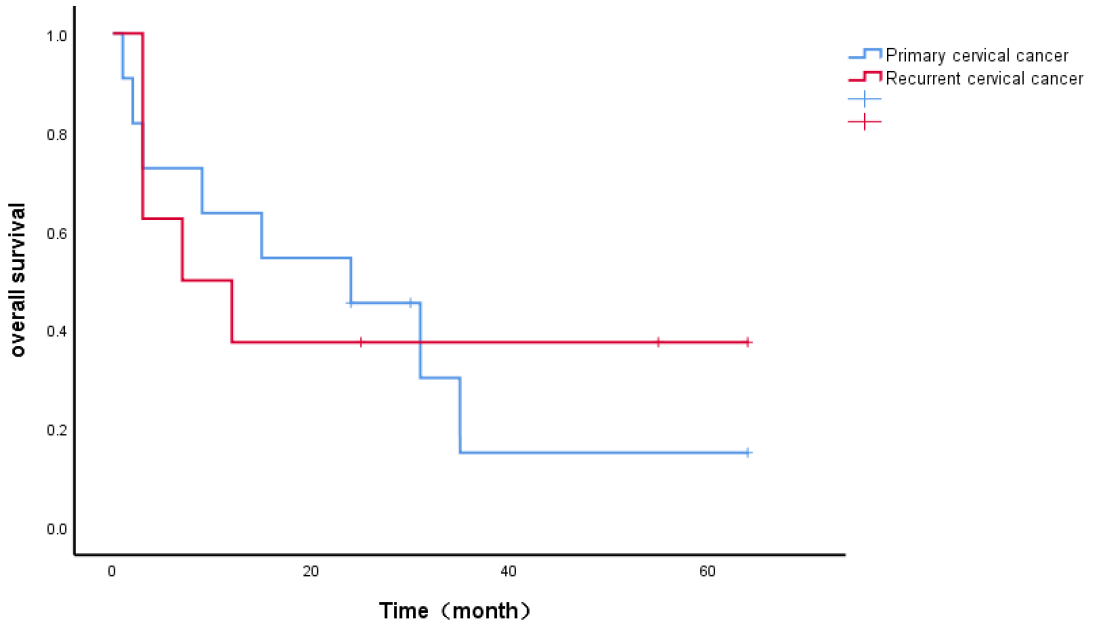

Figure Survival curves of patients in the Primary cervical cancer and Recurrent cervical cancer

Change in the text: No changes in the text

Comment16: 262 – 266 – A recent publication (Ngyuen et al 2023) indicated that patients with

ileal conduit had a high rate or urological postoperative complications, much higher than those with a double-barrelled uro-colostomy. What were the stoma types created within both patient groups?

Reply16: For patients with rectal cancer invading only the male reproductive system, we tend to protect the bladder when R0 can be guaranteed, and there are study(1) that confirm that the difference in overall survival between patients with rectal cancer plus prostatectomy and those with the addition of cystectomy was not statistically significant.

Ileal neobladder surgery is frequently used in our department to reconstruct the urinary system. This technique has a lower infection rate compared to the colon-in-lieu bladder procedure, and there was no statistically significant difference between the two in terms of complications (2). Also thank you very much for the recommended references, this is very good research! In his study(3), DBUC had a lower incidence of postoperative urological complications than the IC group, but there was no statistical difference between the two groups.The DBUC technique has the advantage of having only one stoma, but we did not use the DBUC technique due to the fact that postoperative urine and faeces are discharged together, which may make nursing care more difficult and reduce the quality of life of the patient.

Change in the text: We have modified our text as advised.(see page10, line325-339)

References

(1) PlattE, DovellG, SmolarekS. Systematic review of outcomes following pelvic exenteration for the treatment of primary and recurrent locally advanced rectal cancer[J]. Tech Coloproctol, 2018, 22(11):835-845.

(2) HagemansJ, VoogtE, RothbarthJ, et al. Outcomes of urinary diversion after surgery for locally advanced or locally recurrent rectal cancer with complete cystectomy; ileal and colon conduit[J]. Eur J Surg Oncol, 2020, 46(6):1160-1166.

(3) Nguyen TM, Traeger L, Vather R, et al.Double barrelled uro-colostomy versus Ileal conduit for urinary diversion following pelvic exenteration: a single centre experience. ANZ J Surg. 2023;93(10):2450-2456

Comment17: Line 282 – 295 This paragraph discusses the benefits of neoadjuvant therapy or the lack there of. Was there any downstaging of tumours (particularly rectal cancer patients) before and after neoadjuvant therapy? The benefit of neoadjuvant treatment may be buried in the staging data that is not presented in the paper and may contribute to 100% R0 resection margins.

Reply17: Thank you very much for reviewing my article and asking questions, unfortunately some of the postoperative pathological findings in early cases were not assessed for tumour regression grading. It is now difficult to re-search for a gross specimen from that time for assessment. Tumour regression grading based on MRI findings is usually too subjective.

Change in the text: No changes in the text

Comment18: Line 305 – 315 - The current literature debates the treatment of rectal cancer patients presenting with metastatic lymph nodes at diagnosis with differences in standard of care in western and eastern worlds (Kusters et al., Clin Colon Rectal Surg 2017;30:346–356, Kroon et al., European Journal of Surgical Oncology 48 (2022) 1475e1482). Can the authors define the standard of care for these patients in the current study with reference to lateral lymph node dissection and neoadjuvant chemoradiotherapy? While the best approach is debated, it is important to include these details and discuss.

Reply18: Thank you very much for your comment, the references you gave me were very interesting!

The surgical indications, areas of dissection and principles of management of lateral lymph node dissection for rectal cancer have been highly controversial in Eastern and Western countries(1-2). Western countries prefer total mesorectal excision (TME) for rectal cancer after neoadjuvant therapy. Eastern countries prefer prophylactic lateral lymph node dissection (3). According to the results of a meta-study (4), lateral lymph node dissection after neoadjuvant therapy does not increase long-term patient survival and only reduces local recurrence compared with TME surgery after neoadjuvant therapy. However, a single-centre study (5) from a Chinese authority reported significant differences in both overall and disease-free survival in patients with positive lateral lymph nodes in studies spanning a decade. For patients undergoing PE, if preoperative imaging suggests the presence of suspected malignant lymph nodes, MRI and PET-CT should be performed to determine this and to avoid unnecessary extended dissection. If lymph node positivity cannot be determined preoperatively, prophylactic dissection is considered necessary by us because it is related to the long-term survival of the patient.

Change in the text: We have modified our text as advised.(see page12, line393-407)

References

(1) Weiser MR. AJCC 8th Edition: Colorectal Cancer. Ann Surg Oncol. 2018;25(6):1454-1455.

(2) Hashiguchi Y, Muro K, Saito Y, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2019 for the treatment of colorectal cancer. Int J Clin Oncol. 2020;25(1):1-42.

(3) Kusters M, Uehara K, Velde CJHV, et al. Is There Any Reason to Still Consider Lateral Lymph Node Dissection in Rectal Cancer? Rationale and Technique. Clin Colon Rectal Surg. 2017;30(5):346-356.

(4) Kroon HM, Hoogervorst LA, Hanna-Rivero N, et al. Systematic review and meta-analysis of long-term oncological outcomes of lateral lymph node dissection for metastatic nodes

after neoadjuvant chemoradiotherapy in rectal cancer. Eur J Surg Oncol. 2022;48(7):1475-1482.
(5) Tang JQ, Li HY, Liu T, et al. Zhonghua Wei Chang Wai Ke Za Zhi. 2021;24(10):889-896.

Tables

Comment19: It is more common to present the data as 'Yes' or 'No' rather than 'Not' or 'Have'

Reply19: Thank you very much for your comment! I have modified the table content in the article

Change in the text: We have modified our text as advised.(see page17, line546)

Comment20: Where 'n' is presented in tables, please also include percentages.

Reply20: Thank you very much for your comment! I have modified the table content in the article

Change in the text: We have modified our text as advised.(see page17, line546)

Comment21: Table 1 – the order of data could be better presented if the table was split into two or if the order of information was changed. Suggest amending to demographics, followed by clinical data (ie all data relating to surgery).

Reply21: Thank you very much for your comment! I have divided Table 1 into two tables, with demographic data and surgical related information presented separately, as follows: Table 1.Comparison of demographic data of patients with PE; Table 2.Comparison of operation-related data of patients with PE

Change in the text: We have modified our text as advised.(see page18, line551)

Comment22: Table 2 - It would be useful to include 30-day readmissions given the high rate of post-operative complication rates.

Reply22: Thank you very much for your comment! I have modified the table content in the article. By reviewing specific patient case data, 6 patients in the rectal cancer group were readmitted 30 days after discharge, while 4 patients in the cervical cancer group.

Change in the text: We have modified our text as advised.(see page18, line559)

Comment23: An indication of median follow-up time and local or distant recurrence rates together with disease free survival would be informative.

Reply23: Our team fully agrees with your suggestion, as we initially envisioned. However, there is a situation that we would like to explain to you. Among the 59 cases of pelvic malignant tumors, each patient has a complex situation, including primary tumor patients and some recurrent tumor patients. If postoperative DFS is considered, it will be difficult to evaluate the postoperative DFS of recurrent patients. Some patients may die from reasons other than tumors,

For example, (kidney failure, sepsis, intestinal fistula, etc.), rather than tumor progression, the patient's postoperative follow-up methods mainly rely on outpatient and telephone follow-up. Some postoperative imaging data are lost and cannot be consulted in a timely manner, which brings us a lot of trouble in statistical data. In the end, our team considered OS as the outcome indicator.

Change in the text: No changes in the text

Reviewer B

Thank you for your manuscript. It needs some major revisions that I added to the text. Please see the PDF.

Comment1:"Line36-39"---- Consider revising this statement.

Reply1: Thank you very much for your suggestions, I have made the changes in the text.

Change in the text: We have modified our text as advised.(see page2, line36-38)

Comment2: "Line74-75"----has reduced the incidence of patients with what?

Reply2: Thank you very much for your suggestions, Population-based medical screening has reduced the incidence of locally advanced pelvic tumours, Because tumours can be detected at an earlier stage by routine physical examination.I have made the changes in the text.

Change in the text: We have modified our text as advised.(see page3, line79-80)

Comment3: "Line78-79"----how you define bulky? Better to mention multiorgan and structures involvement.

Reply3: Thank you very much for your suggestions, I have made the changes in the text.

Change in the text: We have modified our text as advised.(see page3, line84-85)

Comment4: "Line81-82"---- what you mean by relative invasiveness?

Reply4:Thank you very much for your comment! The meaning is that the trauma caused by the surgery is significant. I apologize for not expressing my original intention clearly. After discussing with our team, we have revised the statement and have made the necessary changes in the text. Change to (its widespread adoption has been slow due to **the severe trauma caused by surgery , implementation difficulty , and risk of the procedure**)

Change in the text: We have modified our text as advised.(see page3, line87-88)

Comment5: "Line103"---- What imaging was used, CT scan, MRI or US?

Reply5: Thank you very much for your suggestions, I have made the changes in the text.

Preoperative abdominal Computed Tomography (CT) and pelvic Magnetic Resonance Imaging (MRI) as well as rectal ultrasound endoscopy should be routinely performed, and whole-body enhanced CT is used for 3D reconstruction of critical vessels to assist in preoperative surgical planning and to rule out distant metastases. Positron Emission Tomography / Computedtomography (PET-CT) can assist in the diagnosis of patients with distant metastases and in the determination of whether the suspected invasion is malignant.

Change in the text: We have modified our text as advised.(see page5, line133-139)

Comment6: “Line122”---- Does it means pelvic side wall lymph nodes? Were they removed selectively or as part of the tumor? what was the criteria for it?
Reply: This refers to the pelvic lymph nodes, not just the lateral pelvic lymph nodes. For PE surgery, we have a standard lymph node dissection procedure, the exact steps of which have been added in the text.
Change in the text: We have modified our text as advised.(see page6, line168-174)

Comment7: “Line131”---- what does that mean, sacrocolpopexy? Does it means sacral resection with proctectomy?
Reply7: Yes, that's what I was trying to say, it was a grammatical error on my part, thank you very much for the suggestion, I've already made the change in the text
Change in the text: We have modified our text as advised.(see page6, line164)

Comment8: “Line139”---- No tumour markers or pelvic MRI and colonoscopy in case of rectal malignancy?
Reply8: Thank you very much for your comment, here is my incomplete description, the main follow up is CT, I have already described the follow up details of both diseases in detail in the article.
Change in the text: We have modified our text as advised.(see page6, line177-187)

Comment9: “Line164-165”---- Is the sigmoidostomy permanent? Is the transverse colostomy temporary? In 22 patients with anus preservation, did they have defunctioning ileostomy?
Reply9: Thank you for your valuable suggestion. After careful discussion, our team has revised the description of digestive tract reconstruction according to the editor's suggestions. Change to (38 patients underwent non anal sphincter preserving surgery, of which 34 underwent sigmoidostomy, 3 underwent transverse colostomy, and 1 underwent ileostomy, all of which were permanent stomas; 22 patients underwent anal sphincter preservation surgery, of which 12 underwent functional ileostomy and 10 underwent rectosigmoid anastomosis)
Change in the text: We have modified our text as advised.(see page7, line219-223)

Comment10: “Line172-176”--- What caused a higher complication rate in cervical cancer group compared to rectal group?
Reply10: Thank you very much for your valuable suggestion. Line172-176 is a statement on the results of two groups of complications. We will provide a detailed discussion on the differences in complications between rectal cancer and cervical cancer in the third paragraph, based on the current research results. Explain Some 47.3% of cervical cancer patients at our institution had postoperative complications, with urinary complications being more common, which were reported in the literature to be related to urinary reconstruction; Houvenaeghel et al. also reported a rate of similar complications associated with ureteral skin fistula of 42%. In addition, the incidence of postoperative complications in patients with rectal cancer was lower than that of those with cervical cancer, at 33.9%. perineal infections were predominant, and other complications mainly included gastrointestinal manifestations
Change in the text: We have modified our text as advised.(see page10, line325-339), (see page11, line347-350)

Comment11: “Line178”--- On line 153 its mentioned no perioperative death
Reply11: Thank you very much for your advice, We appreciate your valuable feedback and apologize for the author's carelessness in writing the article. After thorough verification by the team, the results have been slightly revised, Change to (all of whom successfully completed PE surgery without intraoperative deaths, **1 patient died within 30 days after surgery**)
Change in the text: We have modified our text as advised.(see page7, line205)

Comment12: “Line182”--- correct to III
Reply12: Thank you very much for your detailed comment, it was an oversight on my part and I have amended it in the text to be correct.
Change in the text: We have modified our text as advised.(see page8, line242)

Comment13: “Line198-199”---What criteria used for patient either to have or omit neoadjuvant treatment?
Reply13: Thank you very much for your comment! For patients with primary tumours assessed to tolerate treatment, preoperative neoadjuvant chemoradiation can lead to local tumour regression and improve the R0 resection rate. For patients with recurrent tumours who have not previously received chemoradiation, chemoradiation may be considered prior to surgery. For patients with recurrent tumours who have previously received radiotherapy, another preoperative treatment should be carefully considered and the dose, division and extent of radiotherapy need to be individually tailored.
Change in the text: We have modified our text as advised.(see page5, line139-145)

Comment14: “Line206”--- “hypofractionated adenocarcinoma” what does that mean?
Reply14: Thank you very much for your suggestion, here is a terminology error. “hypofractionated adenocarcinoma” means poorly differentiated adenocarcinoma, I have made a change in the corresponding part of the text.
Change in the text: We have modified our text as advised.(see page9, line266)

Comment15: “Line231”--- No subgroup analysis for cervical cancer?
Reply15: Thank you very much for your valuable feedback. In the early stages of writing the paper, we also attempted to conduct subgroup analysis on cervical cancer, similar to rectal cancer. However, unfortunately, the number of patients who underwent PE for cervical cancer was relatively small, only 19 cases, and a portion of patients came from the gynecology and oncology department. The heterogeneity between each patient was too large, and the number of cases was small. Therefore, we conducted comparative statistical analysis between the two groups, and the evidence was not accurate enough, So this study only reported an analysis of the prognosis of rectal cancer and cervical cancer, and conducted a comprehensive subgroup analysis on 40 rectal cancer patients. We did not include this comparison in the text due to its unclear significance

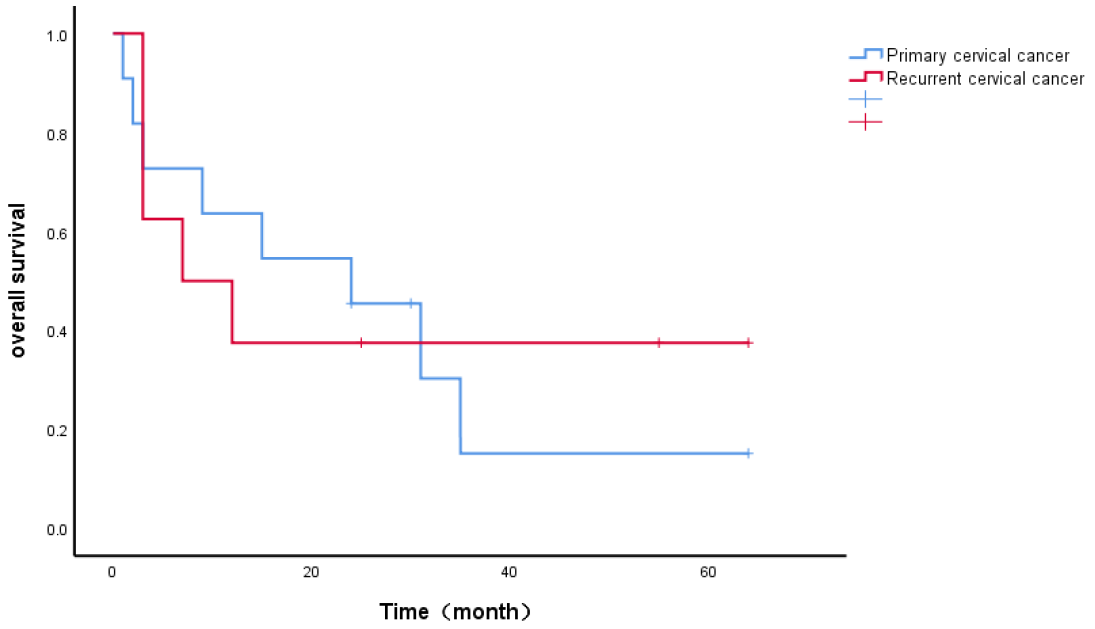

Figure Survival curves of patients in the Primary cervical cancer and Recurrent cervical cancer

Change in the text: We have no change in text.

Comment16: “Line223-235”--- “it is used with curative intent and to achieve R0

Reply16: Thank you very much for your suggestions, I have made changes in the corresponding parts of the text.

Change in the text: We have modified our text as advised.(see page9, line293)

Comment17: “Line252”--- What is the relation between resectability (R) and survival?

Reply17: Thank you very much for your valuable feedback. This relationship is explained in the discussion section. The overall 5-year postoperative survival rate of the 19 cervical cancer patients included in the study was 25.3%, which was low due to the small number of cervical cancer patients and the presence of 2 cases with R1 resection and poor long-term prognosis. the long-term prognosis of patients with rectal cancer was better than that of those in the cervical cancer group, with a 5-year survival rate of 36.7% on the basis of R0 radical resection achieved in all 40 patients. Corresponding RO radical resection was a determining factor in the survival prognosis of patients.

Change in the text: We have modified our text as advised.(see page10, line311-314)

Comment18: “Line261”--- Was there difference in survival for cervical cancer patients who received or not neoadjuvant treatment?

Reply18: Thank you very much for your advice, because our team collected medical records of cervical cancer patients undergoing PE surgery, only 19 cases were collected, and there were 16 patients receiving neoadjuvant therapy and 3 patients not receiving treatment. The comparison between the two groups did not meet the minimum sample size required for statistical analysis, and there was significant heterogeneity between patients, which was not comparable, In the future, we need to conduct a large sample of data for comparative analysis to determine whether neoadjuvant therapy has an impact on patient prognosis.

Change in the text: We have no change in text.

Comment19: “Line 268”--- What was the cause of mortality? Local recurrence? Distant metastasis? where to?
Reply19: We are very grateful for your valuable reminder. Discuss how we can supplement the patient's mortality situation. Discussion of supplementary content: the main cause of postoperative death in rectal cancer patients is distant metastasis (lung, liver, brain), followed by severe complications such as sepsis, intestinal fistula, and abdominal bleeding.
Change in the text: We have modified our text as advised.(see page11, line338-340)

Comment20: “Line 292”--- subplasma layers mean?
Reply20: Thank you very much for your comment, the terminology applied here was not standardised, “subplasma layers” means “subserous layer”. This was my mistake and I have made the changes.
Change in the text: We have modified our text as advised.(see page12, line363)

Comment21: “Line 318”--- Was the perineal wound closed primary or using a myocutaneous flap?
Reply21: Thank you very much for your comment, the management of perineal wounds is individualised and we routinely perform direct suturing and negative pressure drainage. For patients with unsatisfactory intraoperative haemostasis, intraoperative contamination or large perineal wounds, we choose to tamponade the perineum with iodophor gauze. For difficult-to-heal perineal incisions, we choose to perform flap grafting at a later stage.
Change in the text: We have modified our text as advised.(see page13, line409-413)

Comment22: “Line 423”--- Different numbers for patients not receiving neoadjuvant therapy, 15 and 17!
Reply22: We are very grateful for your valuable reminder. We apologize for the author's carelessness in writing the article. The data entered in Table 1 by the author was confusing. After careful verification by the team, the results have been slightly modified and the correct changes have been made. revise the comparative statistical analysis results of two groups
Change in the text: We have modified our text as advised.(see page17, line546)