**Peer Review File**

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**Reviewer comments**

**Comment 1**. The English language of the paper is very poor. Extensive language editing is necessary for this study. For example, title should be the prognostic factors of Primary Colorectal Sarcoma, line 28 should be which is associated with.

Reply 1: Thank you for your comment. We apologize for the poor standard of English language and grammar. We have tried our best to reedit the manuscript and polish the English language according to your suggestions. The English language was also polished by native speaking editors at AME Publishing Company.

Changes in the text:

Page 1

Line 2-4, the title has been replaced by "The Prognostic Factors of Primary Colorectal Sarcoma and the Clinical Outcomes of Negative Lymph Node Dissection"

Line 6, running title has been changed to "Prognostic Factors of Primary Colorectal Sarcoma"

Page 2

Line 29-30 has been changed to "Primary colorectal sarcoma is an extremely rare malignancy that is associated with poor patient outcomes."

Line 37-38, we added "and hazard ratio (HR) and 95% confidence interval (CI) of covariates were also estimated"

Line 39, "by" has been replaced by "using"

Line 43-44 has been changed to "The 5-year rate of CSS was 76.73% and 27.8% for the surgery group and the non-surgery group, respectively"

Line 59 has changed to "13 or more have"

Page 3

Line 66 has changed to "More than 50 histological subtypes of STS exist"

Line 69, "have demonstrated"

Line 71, "for managing"

Line 78, "it has higher mortality"

Line 79-80 has changed to ". Interestingly, as gastrointestinal stromal tumors (GISTs) originate in Cajal cells, they are not considered to be colorectal sarcomas"

Line 85 has changed to "age, tumor location, histologic subtype, grade"

Page 4

Line 93-94 has changed to "Furthermore, research into colorectal sarcoma is limited due to the rarity of this malignancy, as only a small number of"

Line 112, "The exclusion criteria"

Line 116, we added "Clinical and demographic variables"

Page 5

Line 128-130 has been changed to "CSS was analyzed using the Kaplan–Meier method and log-rank tests were used for comparisons between two groups"

Line 133 has been changed to "identify the independent prognostic factors and"

Line 134-136 has been changed to "The effect of independent factors on survival were further analyzed. Then, data were analyzed using X-tile software"

Line 143 "After the exclusion of"

Page 6

Line 145, "Of these patients"

Line 146-147, "in the surgery group"

Line 149-150 has changed to "The 5-year CSS rates were 76.73% and 27.8% for the surgery group and the non-surgery group, respectively"

Line 151-152 has changed to "Over half the patients (76.3%) in the surgery group"

Line 162, 165 P value was checked and revised.

Line 166-168, we added "). There was no statistical difference in CSS rates for patient weather to receive radiotherapy (Figure 3A) or chemotherapy (Figure 3B)."

Line 172 was changed to "Figure 4A-C"

Page 7

Line 175 was changed to "Figure 4D"

Line 177-178 was changed to "Its features and heterogeneity have yet to be fully described"

Line 182 was changed to "liposarcoma has been shown to be"

Line 183 was changed to "The SEER database dose not have data on"

Line 196-197 was changed to “One study that analyzed a primary colorectal sarcoma dataset from the National Cancer Database (NCDB) that was”

Page 8

Line 204-205 was changed to “few examples of these histological types were included”

Line 210, “high proportion (more than 60%) of patients receiving”

Line 211, “we speculate that patient survival may be affected by NLN dissection.”

Line 214-216 was replaced by “independent prognostic factors for CSS in nonmetastatic patients. Colonic sarcoma patients had worse survival outcomes than patients with rectal sarcoma. Colon and rectal cancer are well known to be related but distinct”

Page 9

Line 238-239 was changed to “but there is still variational tendency in our study. Few studies have investigated chemoradiotherapy for STS”

Line 242-245 was changed to “Previously, we reported that anlotinib also demonstrated antitumor activity in STS, with a progression-free rate at12 weeks of 75%, median progression-free survival (PFS) and overall survival of 11 months and 15 months for leiomyosarcoma, respectively”

All changes were showed by using a yellow color of text.

**Comment 2**. Line 36-50, in general, hazard ratios for these identified factors should be provided.

Reply 2: Thank you for your suggestion. Hazard ratios (HR) and 95% confidence interval (CI) are necessary for prognostic factors, and we have added both to the manuscript.

Changes in the text:

Line 37-38, we have added “and hazard ratio (HR) and 95% confidence interval (CI) of covariates were estimated” to the Methods in the Abstract.

Line 48-49, we have added “(HR 1.964; 95% CI, 1.005–3.839; $P = 0.048$)”

Line 50, “(HR 2.903; 95% CI, 1.348–6.250; $P = 0.006$)”

Line 51, “(HR 3.431; 95% CI, 1.725–6.823; $P < 0.001$)”

Line 52-53, “(HR 0.946; 95% CI, 0.911–0.983; $P = 0.004$)”

**Comment 3**. line 52 “limited evidence to support the benefits of radiotherapy” this sentence is problematic because findings show no effect, not limiting effect, of radiotherapy and chemotherapy.

Reply 3: Thank you for your valuable comment. We apologize for the confusing description in the original manuscript. Our data show that radiotherapy and chemotherapy have no effect on CSS from the statistical analysis. We have added the survival curves for cancer-specific survival in nonmetastatic patients with primary colorectal sarcoma as stratified by radiotherapy, chemotherapy in the revision manuscript (Figure 3). In addition, we added some discussion about it in the manuscript. The details of radiotherapy and chemotherapy, including dosage, time, and pre- or postoperative, could not be acquired from SEER database which is insufficient to interpret whether radiotherapy and chemotherapy is for or against for the patients. We have also clarified the details in the conclusion in the Abstract and Conclusions.
Changes in the text:
Line 56-58 was changed to "Primary colorectal sarcoma patients can benefit significantly from primary tumor surgery, and age, tumor site, grade and NLN dissection are independent prognostic factors of nonmetastatic patients."
Line 256-258 was changed to "Primary colorectal sarcoma patients can benefit significantly from primary tumor surgery, and age, tumor site, grade and NLN dissection are independent prognostic factors of nonmetastatic patients."
Line 260-261, we added "Radiotherapy and chemotherapy have no effect on survival of nonmetastatic patients while the data is limited."

**Comment 4**. Line 39, median and range of follow up time should also be reported here.
Reply 4: Thank you for your comment. We agree, follow-up time is a vital statistical variable for survival. We have now added the median and range of follow-up.
Changes in the text:
Line 42-43, we have added "The median follow-up time was 34 months with an interquartile range (IQR) of 9-79 months"

**Comment 5**. Abstract and line 87-88, the study focused on the identification of prognostic factors, not the effect of prognostic factors, because prognostic factors are unknown before the analysis. Please check this all throughout the paper.
Reply 5: Thank you for pointing this out. Indeed, we aimed to identify the candidate prognostic factors of colorectal sarcoma that affected clinical outcomes. Firstly, we included some common variables from the SEER database to perform in univariate and multivariate Cox regression analysis, and age, tumor grade, site and NLN dissection were identified as having statistical significance. Then, we evaluated the effect of treatments such as radiotherapy, chemotherapy and NLN count on survival. We have added the survival curves as stratified by radiotherapy and chemotherapy in the revision manuscript

(Figure 3). Moreover, we have added some description and analysis about our identification of prognostic factors to the manuscript
Changes in the text:
Line 30-32 has been changed to “The aim of this study was to identify the prognostic factors of primary colorectal sarcoma and evaluate the clinical outcomes associated with these prognostic factors”
Line 36-37 has been changed to “The prognostic factors were identified”
Line 96-98 has been changed to “identify the prognostic factors of primary colorectal sarcoma and evaluate the clinical outcomes associated with these prognostic factors”
Line 413-414 has been changed to “Identification of prognostic factors of 251 nonmetastatic patients with primary colorectal sarcoma from surgery group”

**Comment 6**. Introduction. Possible prognostic factors of colorectal sarcoma are poorly reviewed or hypothesized. I understand there are very limited data on this disease, however, the authors may consider them from similar cancers, as informed by soft tissue sarcoma and GISTs. These reviews should be related to the current study findings such as age, tumor site, tumor grade, and NLN dissection. This part should also explain why there is a special focus on MLN.
Reply 6: Thank you for your comment. We apologize for the inadequate review of prognostic factors associated with colorectal sarcoma and similar sarcomas. We have reread the literatures from the past 5 years and added some reviews according to your suggestions. First, we retrieved studies about the possible prognostic factors of soft tissue sarcoma (retroperitoneal liposarcoma) and GISTs, and reviewed them as valuable factors for predicting the patient outcomes in the Introduction. Second, we reviewed the relationship between NLN resection and survival in colorectal cancer to explain why we focused on NLN. The details are as follows:
Changes in the text:
Line 85-92 has been changed to “Studies have shown that age, tumor location, histologic subtype, grade and lymph node status are associated with the presence and persistence of other sarcomas, such as retroperitoneal sarcoma13,14. Similarly, age, tumor location and surgery are also significantly associated with overall survival (OS) and cancer-specific survival (CSS) in patients with GISTs.15 Negative lymph node (NLN) resection is associated with improved survival in colorectal cancer patients of all stages16. Additionally, extended negative lymphadenectomy can improve disease-free survival (DFS), CSS, and OS in node-positive colorectal cancer patients.”

13 Patel H D, Joice G A, Schwen Z R, et al. Retroperitoneal lymph node dissection for testicular seminomas: population-based practice and survival outcomes [J]. World J Urol, 2018, 36(1): 73-8.
14 Nazzani S, Preisser F, Bandini M, et al. Surgically Treated Retroperitoneal Sarcoma: A Population-based Competing Risks Analysis [J]. Eur Urol Oncol, 2018, 1(4): 346-51.

15 Chen Z, Lin R M, Bai Y K, et al. Establishment and Verification of Prognostic Nomograms for Patients with Gastrointestinal Stromal Tumors: A SEER-Based Study [J]. Biomed Res Int, 2019, 2019(8293261.
16 Ogino S, Nosho K, Irahara N, et al. Negative lymph node count is associated with survival of colorectal cancer patients, independent of tumoral molecular alterations and lymphocytic reaction [J]. Am J Gastroenterol, 2010, 105(2): 420-33.

**Comment 7**. Methodology. The authors may consider the reason for analyzing the cut-off value of NLN because MLN is only one of the many prognostic factors. Relying on one factor only to predict the prognosis of colorectal sarcoma is inadequate.
Reply 7: Thank you for pointing this out. In fact, age, tumor site, grade and NLN dissection were independent prognostic factors in multivariate Cox regression analysis, and the results are shown in Table 2. Among these factors (age, tumor site, grade, and NLN), age, tumor site, grade have been explored in previous studies, while NLN dissection has not been evaluated in colorectal sarcoma in researches to date. In this study, we focused on NLN dissection and analyzed the cut-off value of NLN count. The analysis revealed that NLN count is an independent prognostic factor for nonmetastatic patients. We are sorry for not describing it clearly in the Methods section. Thus, we have revised this part of the paper.
Changes in the text:

Line 131 “prognostic” → “risk”

Line 133, we added “identify the independent prognostic factors and”
Line 134-135, we added “The effects of the independent factors on survival were further analyzed.”

**Comment 8**. Methodology. Please provide details of outcome assessment and clinical and demographic variables collected. These are important.
Reply 8: Thank you for your comment. We apologize for not describing the variables and its definition sufficiently. All clinical and demographic variables were transformed from code according to SEER Program Coding and Staging Manual 2018. All continuous data including age and follow-up time were expressed as median and interquartile range, and categorical data including sex, year of diagnosis, race, tumor site, grade, histologic subtype, lymph node status, radiotherapy, chemotherapy, and surgery were classified to make a statistical analysis. We have added the above details in the manuscript according to your suggestions.
Changes in the text:
Line 116, we added “Clinical and demographic variables”
Line 117-123 was changed to “Data collected from eligible patients included the following: age at diagnosis (median and range), sex (female and male), year of diagnosis

(2000-2005, 2006-2010 and 2011-2016), race(white, black, other or unknown) , primary tumor site (colon [code 180, 182-189, 260] and rectum [code 199, 209]), histologic subtype, tumor grade (grade □ - □ or unknown), lymph node status (N0 [code 0] and N1 [code 1]), negative lymph node (NLN) count, radiotherapy, chemotherapy, surgery and follow-up time. CSS was defined according to SEER cause-specific death classification.”