

Peer Review File

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Reviewer A

The authors show that extraskeletal Ewing's sarcoma evidence and prognostic factors. However, I have some concerns.

Comment 1: Please describe the novelty of the current study.

Reply 1: We are very sorry for my unclear expression causing your misunderstanding. The skeleton is the most common site for EWS, and EES only accounts for about 20% of all ESFTs. Due to the rarity of EES, there is still a lack of high-quality research of EES and its clinical characteristics, therapeutic strategies, and prognostic factors vary among studies. Here, we report and compare the clinical characteristics and outcomes of a series of EES patients at our institution. The aim was to identify significant risk factors for EES prognosis. On the other hand, Preoperative diagnosis and thorough imaging of the characteristics of EES are important, especially for endoceliac tumours which are hard to identify by physical examination and are always misdiagnosed preoperatively. We describe the imaging characteristics of endoceliac EES by reviewing the data from computed tomography (CT). These findings are important for accurate diagnosis and treatment of EES. We also add some details in the paper.

Changes in the text: Page 3, line 41-42.

Comment 2: The patient number is small, so the author's claim has not been proved.

Reply 2: We understand the reviewer's concern. Although the patient number is small, the statistical methods of this study are meticulously designed. Via the univariate and multivariate analysis, we suggest that patients with larger tumour size and regional lymph node metastasis are independent predictors of overall survival for EES patients underwent surgery. To achieve an exact statistical analysis, the rule of thumb is 10 events per variable in the Cox regression. On the other hand, the endoceliac EES is rarer than EES and we only have limited imaging data for these patients. We use descriptive statistical methods to conclude imaging characteristics of the endoceliac EES and its objective is to understand this rare tumour from the perspective of imaging. The findings of this study contribute to the understanding of both the clinicopathological and imaging characteristics of this rare disease.

Comment 3: The discussion and conclusion are ordinary.

Reply 3: We understand the reviewer's concern. In the section of discussion, our study introduces this unusual tumour comprehensively from various sides, including clinical characteristics, prognosis and imaging features. In fact, the conclusion of this study

has potential value in formulating the standard diagnostic and therapeutic strategies for the EES, especially for the endoceliac EES.

Comment 4: Please cite the chemotherapy protocol reference.

Reply 4: We thank the reviewer's suggestion. We cite the chemotherapy protocol reference in the corresponding site.

Changes in the text: Page 4, line 75-78.

Comment 5: Please give space in Line 30: "data(n=8)".

Reply 5: We are sorry for the mistake. We give the space for "data(n=8)".

Changes in the text: Page 3, line 9.

Comment 6: Please describe the background in the "Background of abstract".

Reply 6: We are very sorry for my unclear expression. We have described the background in the "Background of abstract".

Changes in the text: Page 3, line 4-7

Reviewer B

Comment: There is no word endoceliac, or at least not one in common medical terminology or one that can be found by Google. The fact that the diagnosis was missed by imaging is not uncommon. Only a few tumors have distinct radiographic characteristics. That said, I suspect that the majority of patients in this series with intra-abdominal tumors did not have Ewing sarcoma. EES is not vastly more common in males. The most common tumor with an EWS rearrangement in the abdomen is desmoplastic small round cell tumor, and it is much more common in males. It is not even considered in the discussion.

Reply: The reviewer's concern on the diagnostic accuracy is justifiable as he/she pointed out the "radiographic characteristics" is insufficient. However the diagnosis was not made by CT but by pathological features; Clearly the reviewer has extensive experience in differentiating pathological features of mesenchymal origin tumors and intra-abdominal tumors. Even comparing to EES, the DSRCT is a rare type of tumor. Based on our institution experiences, although DSRCT also may have similar CD99 and NKX2.2 expression, its other uncommon IHC signatures would be likely to be given Ewing-like sarcoma primary diagnosis instead of EES (apparently these cases were not considered in this series). Because of these, it might be more prudent to suspect the rare DSRCT diagnosis by the gender distribution. Currently only sequencing method plus pathological features may give precise diagnosis in these complex Ewing-like tumors. Due to the retrospective nature and our primary object, such a high-cost diagnostic method cannot be fulfilled.

Reviewer C

Comment: This retrospective study documented the detail of the Extraskkeletal Ewing's sarcoma well, and the results look reasonable. However, I'm afraid this research cannot categorize a 'translational' research (just clinical retrospective study). I recommend to transfer another journal.

Reply: We thank the reviewer's kind reminder. As we carefully examined the history in each issue, we have discovered the journal accepted many clinical investigations without lab research. The journal, on the other hand, has been categorized in "Radiology, Nuclear Medicine and Imaging" subject area according to which we believe our manuscript may meet the journal's publishing standard. Thus, we believe the EIC may had more say on this question. Still, we are glad to hear from the reviewer's generous comments.

Reviewer D

Comment 1: Extraskkeletal Ewing sarcoma (EES) is divided into two types such as surface origin type and endoceliac origin type. The surface origin type of EES can be treated with the same strategy as the extremity origin type; therefore, targeted patients should be those in the endoceliac origin type.

Reply 1: We understand the reviewer's concern. We have indicated that the surface origin type of EES include the extremity origin type (Page 5, line 92-93). We discuss the clinical characteristics and prognosis of both surface and endoceliac origin types. However, we conclude the CT imaging features only in the endoceliac type.

Comment 2: The process of obtaining the histological diagnosis is unclear. Please specify the number of cases in which an incisional biopsy or a preoperative needle biopsy was performed.

Reply 2: We are very sorry for my unclear expression causing your misunderstanding. We specify the number of cases in which the needle biopsy was performed.

Changes in the text: Page 4, line 81-84.

Comment 3: There are no specific findings on CT images, and CT is useful only to show the tumor size and lymph node metastasis. The description of the CT findings should therefore be shorter.

Reply 3: We understand the reviewer's concern. The aim of the description of CT findings in the article is to make a portrayal for the basic imaging features of endoceliac EES, which is a little-known malignant tumour. Although we have discovered larger tumour size and lymphadenopathy as the risk factors for poor prognosis of EES, making description of CT features of endoceliac EES is to make a more accurate diagnosis instead of being related to the previous conclusion simply.

Comment 4: Chemotherapy plays a very important role in the treatment of ESS. In

particular, adjuvant chemotherapy is essential. The author stated in line 104 that 17 patients underwent resection only. Please specify how many of the 17 patients had postoperative adjuvant chemotherapy.

Reply 4: We are very sorry for my unclear expression causing your misunderstanding. Actually, all of 17 patients underwent resection have received postoperative chemotherapy and we add corresponding contents in the paper.

Changes in the text: Page 4, line 83.

Comment 5: Risk factors for poor prognosis are mentioned in this manuscript, but there are no suggestions for improving the prognosis of EES.

Reply 5: We understand the reviewer's concern. In fact, we have mentioned corresponding contents in the section of discussion. We suggest that regional lymph nodes metastasis and undergoing surgery are risk factors for poor prognosis of EES. We indicate that sentinel lymph node biopsies and routine regional lymph node dissection, which may be closely related to better prognosis, have potential application prospects for the treatment of EES (Page 8, line 225-227). On the other hand, we recommend that aggressive multimodality treatment including surgery should be performed in EES (Page 7, line 217-218).

Comment 6: The author stated in line 296 that undergoing surgery was a risk factor for poor prognosis; however, this sentence seems unclear.

Reply 6: We are very sorry for my unclear expression. We simply mean to say that non-surgical treatment is the risk factor for poor prognosis of EES and we have replaced undergoing surgery with non-surgical treatment.

Changes in the text: Page 3, line16

Page 9, line264