Dear Editor and Reviewers,

Thanks very much for taking your time to review this manuscript. I really appreciate all your comments and suggestions! Please find my itemized responses below and my revisions/corrections in the re-submitted files.

Appended to this letter is our point-by-point response to the comments raised by the reviewers. The comments are reproduced and our responses are given directly afterward in a different color (red).

We would like also to thank you for allowing us to resubmit a revised copy of the manuscript. We hope that the revised manuscript is accepted for publication in the World Journal of Clinical Cases.

Yours sincerely,

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Please resolve all issues in the manuscript based on the peer review report and make a point-by-point response to each of the issues raised in the peer review report. Note, authors must resolve all issues in the manuscript that are raised in the peer-review report(s) and provide point-by-point responses to each of the issues raised in the peer-review report(s); these are listed below for your convenience:

Reviewer #1:
Scientific Quality: Grade C (Good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors: This is a good case report for Esophageal myoepithelial carcinoma. I have some comments as following.

1. This paper make comprehensive description about the labrary examination, treatment and prognosis of four esophageal myoepithelial

carcinoma, maybe some prospects for esophageal myoepithelial carcinoma diagnosis and treatment could be proposed.

Response: Thank you very much for your positive comments of our study. In this study, we described the clinical, pathological, immunohistochemical, and imaging findings of four patients with esophageal MC and report their outcomes. The purpose of this study was to describe the imaging and clinicopathological features of esophageal MC to improve the understanding of this disease. Esophageal MC is more likely to originate from the middle esophagus in elderly populations with male dominance. A fungating type observed on CT scanning may help narrow down the differential diagnosis. Cystic change or necrosis may occur in larger lesions. A characteristic anastomotic recurrence was observed on CT as a cystic-solid mass.

2. The author mentioned that CT is an important tool to evaluate recurrence. Please discuss the importance of endoscopy screening and surveillance for esophageal myoepithelial carcinoma, as the great progression of endoscopy technical.

Response: Thank you very much for your valuable comments. As constantly improved and developed technology, endoscopic imaging techniques have been used to achieve early diagnosis and treatment of early esophageal cancer[1]. Early detection and treatment of ESCC can improve prognosis. Endoscopic imaging techniques may also be used in the detection and treatment of early esophageal myoepithelial carcinoma in the future. We included relevant discussions in the revised manuscript (Line 304, page 12).

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3. The author mentioned that all patients had a high Ki-67 level, and patient 3 developed postoperative lung metastasis, please illuminate if there is Ki-67 expression or other difference between patient 3 and the others.

Response: Thank you very much for your valuable comments. Ki-67 >10% has diagnostic value in differentiating benign myoepithelioma from MC. Moreover, Ki-67 > 50% suggested that MC is more likely to recur or metastasize, indicating a poor prognosis[1-3]. In this study, all patients had a high Ki-67 Level. Patient 3 developed lung metastasis and anastomotic metastasis 4 months after surgery. Patient 4 attended review appointments regularly and remained in a good general condition. However, two patients (patients 1 and 2) were lost to follow-up in this study. We reviewed the clinical, pathological, and imaging data of four patients in detail, and found no obvious difference between patient 3 and the others. Due to the small number of cases and the high rate of loss to follow-up, the information available to us is limited. We believe that as more cases are reported, more characteristics of myoepithelial carcinoma will be identified.

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4. " SOX-10 can provide a basis for diagnosing salivary gland tumors based on tissue origin because it can specifically identify acinar and myoepithelial cells in salivary gland tissue. Most tumors (3/4) in our study were observed to be positive for SOX-10." please clarify what is the diagnosis basis for the rest 1/4. And is there any difference in morphology or phenotype between SOX-10 positive and negative?

Response: Thank you very much for your valuable comments. Histologically, myoepithelial carcinoma is defined as a neoplasm composed almost exclusively of myoepithelial cells and characterized by an infiltrative growth pattern[1]. Studies have revealed that S-100, vimentin, and CK are more definitive markers of myoepithelial cells and help differentiate MC from other malignant tumors[2]. Studies have reported variable staining patterns in these tumors, and it is suggested to use a panel of myoepithelial markers, including S100, p63, GFAP, calponin, myosin, and SMA as well as at least two-three different keratin stains to confirm the diagnosis of MECA[3]. Patient 4 was positive for p63, CK5/6, CK8/18, AE1/AE3,p40, and calponin. And HE staining showed mainly epithelioid cells with hyperchromatic and pleomorphic nuclei and infiltrative growth toward the periphery. So, based on the above criterias, patient 4 was also diagnosed with myoepithelial carcinoma.

SOX10 expression pattern of salivary gland tumors mirrors those of normal tissues, showing acinus and intercalated duct differentiation in a biphasic manner. Myoepithelial cells are known to show various morphologies, chondromyxoid, spindle, epithelioid and plasmacytoid, and SOX10 is positive in all of these cells[4]. Higher Proportion of TP53 Mutations and Lower Proportion of PIK3K Pathway Alterations in SOX-10-Positive Patients. And, SOX-10 positivity was associated with a higher proportion of pT1 tumors (n = 24, 52%), compared to SOX-10-negative cases[5].

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1 Kong M, Drill EN, Morris L, West L, Klimstra D, Gonen M, Ghossein R,

Katabi N. Prognostic factors in myoepithelial carcinoma of salivary glands: a clinicopathologic study of 48 cases. Am J Surg Pathol 2015; 39: 931-938 [PMID: 25970687 DOI: 10.1097/PAS.0000000000000452]

2 Tseng CE, Hsieh YH, Wei CK, Huang HY, Chi CL. Myoepithelial carcinoma of the stomach: a diagnostic pitfall. World J Gastroenterol 2015; 21: 4391-4396 [PMID: 25892892 DOI: 10.3748/wjg.v21.i14.4391]

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5. As in line 218, author hypothesized that TAP levels may be increased in esophageal MC, which should be futher exlored and disscussed as the actual result showed only 50% of patients were TAP posotive.

Response: Thank you very much for your valuable comments. I'm sorry that we didn't express it clearly in the original text. In fact, only two of the four patients were tested for TAP, and both were positive. Two other patients were tested for other tumor markers (AFP, CEA, CA125, CA19-9, CA72-4)，and both were negative. We have made some modifications in the revised draft (Line48, page 3) (Line170, page 7).

6. None of the other laboratory values"was used in line 99, line 102 and line 108. Please clarify what does "the other laboratory values" mean?

Response: Thank you very much for your valuable comments. I'm sorry that we didn't express it clearly in the original text. Other laboratory indicators refer to RBC, ESR, WBC, hemoglobin. We have made some modifications in the revised draft (Line172, page 7).

Reviewer #2:

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

Specific Comments to Authors: This study is to describe the imaging and clinicopathological features of esophageal myoepithelial carcinoma. Esophageal MC has not been previously reported. This study shows the characteristics of esophageal myoepithelial carcinoma, but there is little clinically useful information worthy of publication.

Response: Thank you very much for your valuable comments. In this study, we described the clinical, pathological, immunohistochemical, and imaging findings of four patients with esophageal MC and report their outcomes. The purpose of this study was to describe the imaging and clinicopathological features of esophageal MC to improve the understanding of this disease. Esophageal MC is more likely to originate from the middle esophagus in elderly populations with male dominance. A fungating type observed on CT scanning may help narrow down the differential diagnosis. Cystic change or necrosis may occur in larger lesions. A characteristic anastomotic recurrence was observed on CT as a cystic-solid mass. Due to the small number of cases and the high rate of loss to follow-up, the information available to us is limited. We believe that as more cases are reported, more characteristics of myoepithelial carcinoma will be identified.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The author firstly reported 4 myoepithelial carcinoma in esophagus. But, is this a new histological type of esophageal cancer or an esophageal carcinoma showing marked myoepithelial differentiation?

Response: Thank you very much for your positive comments on our study. In this study, we described the clinical, pathological, immunohistochemical, and imaging findings of four patients with esophageal MC and report their outcomes. Myoepithelial carcinoma is an aggressive tumor that occurs mainly in the salivary gland and was first reported by Stromeyer et al in 1975 [1]. MC has a multinodular architecture, and is composed of epithelioid, clear, spindle, and/or plasmacytoid cells, frequently arranged in cords or trabeculae in a myxoid or hyalinized stroma[2]. MC can also originate in the chest, lungs, skin, and stomach[3-5]. Therefore, we consider MC is a new histological type of esophageal cancer.

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3 **Yokose C**, Asai J, Kan S, Nomiyama T, Takenaka H, Konishi E, Goto K, Ansai S, Katoh N. Myoepithelial carcinoma on the right shoulder: Case report with published work review. *J Dermatol* 2016; **43**: 1083-1087 [PMID: 26989835 DOI: 10.1111/1346-8138.13358.]

4 **Choi JW**, Na SY. Image Gallery: Myoepithelial carcinoma involving the skin. *Br J*

Dermatol 2017; **176**: e12 [PMID: 28244091 DOI: 10.1111/bjd.15286]

5 **Tseng CE**, Hsieh YH, Wei CK, Huang HY, Chi CL. Myoepithelial carcinoma of the stomach: a diagnostic pitfall. *World J Gastroenterol* 2015; **21**: 4391-4396 [PMID: 25892892 DOI: 10.3748/wjg.v21.i14.4391]

Reviewer #4:
Scientific Quality: Grade C (Good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Major revision
Specific Comments to Authors: Lu et al. presented the first report of the imaging and clinicopathological features of esophageal MC in four patients and reviewed the relevant literature. They compared tumor characteristics, CT findings, blood, and histological findings with esophageal squamous cell carcinoma and myoepithelial carcinoma at other sites. They described esophageal MC had not been previously reported.

Response: Thank you very much for your positive comments on our study. In this study, we described the clinical, pathological, immunohistochemical, and imaging findings of four patients with esophageal MC and report their outcomes. Esophageal MC is more likely to originate from the middle esophagus in elderly populations with male dominance. A fungating type observed on CT scanning may help narrow down the differential diagnosis. Cystic change or necrosis may occur in larger lesions. A characteristic anastomotic recurrence was observed on CT as a cystic-solid mass.

This study is thought-provoking, but I think it has major problems. This article dose not discuss why four cases of esophageal MC, which had never been reported before, were found at one facility. For example, esophageal squamous cell carcinoma is common in China, but is it related to it?

Response: Thank you very much for your valuable comments. Esophageal cancer is the fourth most common cause of cancer death in China[1]. Our organization is located in a province with a population of over 100 million. And, our annual outpatient volume is 7.76 million (2018). In the case collection phase of this study, a total of 5 patients were collected, but one of

them was excluded due to lack of clinical and imaging data. MC can be confused with many other tumors when arising outside the salivary glands because it presents with a broad spectrum of cytomorphological and immunohistochemical (IHC) features[2]. The combination of histopathology and immunohistochemistry has diagnostic significance for myoepithelial carcinoma[3]. However, there are no studies on esophageal myoepithelial carcinoma. We also found no association between esophageal myoepithelial carcinoma and esophageal squamous cell carcinoma in the four patients in this study. Although esophageal myoepithelial carcinoma is only found in our center at present, we believe that with the development and advancement of immunohistochemical technology and the improvement of people's understanding of MC, more and more esophageal myoepithelial carcinoma will be reported.

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Minor Although esophageal MC is depicted as a fungating type on CT, please explain the fungating type in an easy-to-understand manner.

Response: Thank you very much for your valuable comments. Fungating type is one of the morphological subtypes of esophageal cancer. Esophageal cancers are classified as medullary type, fungating type, ulcerative type, and scirrhous type according to gross morphology[1]. Fungating type mainly presents as a protruding intraluminal mass[2]. We also present a case of esophageal myoepithelial carcinoma which was classified as fungating type.

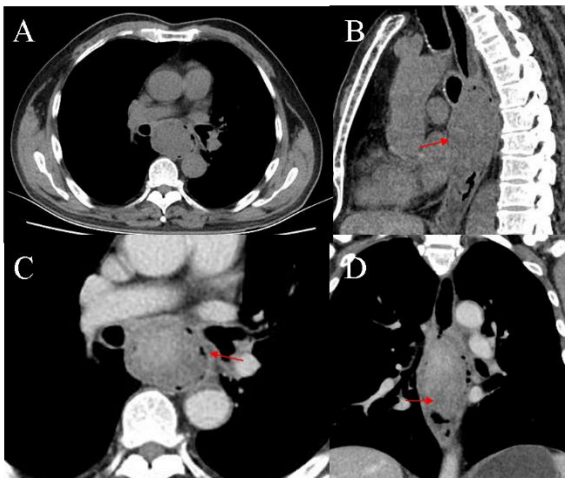

Figure 2. Chest CT images of patient 2. A, B: CT scan showed an intraluminal mass (fungating-type) of the middle esophagus with ulcers (red arrow) and cystic changes, or necrosis. **C, D:** After contrast injection, the mass showed heterogeneously, marked enhancement.

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The tumor size in our patients ranged from 2.9 cm to 4.5 cm (mean, 3.5 cm), larger than tumors observed in gastric cancer patients. Why do you compare it with stomach cancer?

Response: Thank you very much for your valuable comments. I'm sorry that we didn't express it clearly in the original text. Esophageal myoepithelial carcinoma has not been reported. To our knowledge, there is only one case of upper gastrointestinal myoepithelial carcinoma[1]. We attempted to compare the size of esophageal myoepithelial carcinoma in this study with that of gastric myoepithelial carcinoma[1]. We have made some modifications in the revised draft (Line264, page 11).

REFERENCES

1 Tseng CE, Hsieh YH, Wei CK, Huang HY, Chi CL. Myoepithelial carcinoma of the stomach: a diagnostic pitfall. World J Gastroenterol 2015; 21: 4391-4396 [PMID: 25892892 DOI: 10.3748/wjg.v21.i14.4391]

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper.

We appreciate for Editors/Reviewers' warm work earnestly and hope that the

correction will meet with approval.

Once again, thank you very much for your comments and suggestions.