

Reviewer 1

Conclusion: Accept (General priority)

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

the topic is interesting, but there are some points to discuss: 1- are these biomarkers specific for esophageal squamous cell carcinoma, what about their price 2- the number of cases is relatively small. 3- some corrections in the language and grammar are in the uploaded file.

Reply: Thanks for your comments. These biomarkers are associated with the malignant phenotype of esophageal squamous cell carcinoma, which has been confirmed in previous studies. In addition, single miRNA test kit is relatively inexpensive. We have added the small sample size as one of deficiencies in the manuscript.

Reviewer 2

Conclusion: Minor revision

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Lan XY et al.: Correlation of plasma miR-21 and miR-93 with radiotherapy and chemotherapy efficacy and prognosis in patients with esophageal squamous cell carcinoma. (MS No. 50513) The authors explored the usefulness of the values of plasma miR-21 and miR-93 with radiotherapy and chemotherapy efficacy and prognosis in patients with esophageal squamous cell carcinoma (ESCC). They found that high expressions of miR-21 and miR-93 suffered increased risks of ineffective radiotherapy and chemotherapy as well as increased risks of death in 3 years. The manuscript is generally well written and the results seem to be clinically interesting; however, there are some points of concern that preclude the manuscript from being accepted in the journal. Specific comments: 1.

The authors described that the current study was approved by the Ethics Committee. The approval number should be included. 2. In addition to miR-21 and miR-93, multivariate analysis demonstrated that other factors such as T stage and M stage were independent risk factors and prognostic factors, suggesting that pathological and/or radiographic assessment might be enough to predict risks and prognosis. The reviewer would like to know what the superiority of miR-21 and miR-93 evaluation for ESCC patients is, compared to TNM information. The authors should discuss about these issues. 3. The authors should also suggest the speculation about the mechanism why high miR-21 and miR-93 expression induces resistance to radiotherapy and chemotherapy, although these microRNAs are known to involve in malignant phenotypes. 4. The ESCC patients with low plasma miR-21 and miR-93 values showed better 3-year OS compared to those with high microRNAs. The authors should show Kaplan-Meier curves according to the microRNA values.

Reply: Thanks for your evaluation. We have added the advantages of plasma miRNA detection in the manuscript, and we have discussed the fact that high expressions of miR-21 and miR-93 lead to radiotherapy and chemotherapy resistance, but we still don't know the mechanism, so it requires additional validation in vitro. We used miR-21 (≤ 5.60 vs > 5.60) and miR-93 (≤ 3.87 vs > 3.87) to distinguish between high and low expression, so as to observe the correlation of high and low expressions of miR-21 and miR-93 with prognosis of patients.