Dear reviewer

Re:manuscript ID: 57127 and title：The value of miR-1271 and Glypican-3 in evaluating the prognosis of patients with hepatocellular carcinoma after transcatheter arterial chemoembolization

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "The value of miR-1271 and Glypican-3 in evaluating the prognosis of patients with hepatocellular carcinoma after transcatheter arterial chemoembolization.ID：57127 ". Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches.We have studied comments carefully and have made correction which we hope meet with approval. The revised part is marked in the paper. The main corrections in the paper and the responses to the reviewer' s are as follows:

Response to the reviewer's comments：

Reviewer #1:

1. Response to comment:(In MATERIALS AND METHODS, the author mentioned that 'Separation and collection of serum: 5ml of venous blood was collected from patients with hepatocellular carcinoma on an empty stomach 1-5 days before TACE and 1 year after operation' It seems to have been measured twice (before TACE and 1 year after TACE). In Patient Characteristics section "After transcatheter arterial chemoembolization, miR-1271 in relapsed patients was lower than in remission patients, and GPC3 levels were higher than in remission patients, the difference was statistically significant (P <0.05). Table 4 for details.", The authors have not mentioned whether the GPC3 and miR-1271 levels are the values measured before TACE or 1 year after TACE. But, it is necessary to explain when was it measured. In addition, Table 3 shows that the remission group (112 patients) have GPC of 6.79±5.32 and the recurrent group (50 patients) have 8.74±2.40 in Group 3. However, if the average of the two groups is calculated, it is not consistent with any of the pre-treatment GPC level of 8.87±3.73 or the post-treatment GPC level of 2.46±1.69 in Group )

Response：a, The level of miR-1271 in recurrent patients was lower than that in remission patients, while the level of GPC3 in relapse patients was higher than that in remission patients. The levels of GPC3 and miR-1271 were measured at the third month of follow-up after TACE.It has been supplemented in the article.b,The GPC was 6.79 ±5.32 in the remission group(112 patients) and 8.74 ±2.40 in the relapse group (50 patients). The known GPC value refers to the GPC level at the third month of follow-up after TACE.

2. Response to comment:(The measurement of the GPC3 and miR-1271 levels 1 year after TACE had been performed may be too late to explain the post-TACE prognosis. In addition, it is possible that it was determined to be TACE refractoriness due to the

lack of the treatment efficacy after 2-3 TACE procedures for 6 months, which might have led to the change or merging into different treatment methods. Therefore, it seems to be desirable for the authors to explain the specific reasons for the measurement of the GPC3 and miR-1271 level 1 year after TACE in the 'MATERIALS AND METHODS' section.)

Response：We have measured GPC3 and miR-1271 levels at this point in our 3-month follow-up after TACE because some patients have already relapsed. It has been perfected in this article.

3. Response to comment:(Haven't the investigators compared the changes in GPC3 and miR-1271 before and 1-3 months after TACE between the remission group and the recurrent group?)

Response：We studied the levels of GPC3 and miR-1271 at 3 months of follow-up after transarterial interventional therapy. It has been supplemented in detail in the article.

4.Response to comment:(The author should explain how patients were enrolled for 'Healthy group' in this study.)

Response：The patients included in the healthy group were the patients who underwent physical examination in our department in the same period, and had no history of liver disease.

5.Response to comment:(In Patient Characteristics section, 42 patients with HCC were child A, 88 patients were child B, and 32 patients were child C by the Child-Pugh scoring system. It seems a significant number of patients with poor liver function were included, but the proportion of cirrhosis patients was 30/1622 (18.5%) patients. Generally, patients with chronic hepatitis without cirrhosis is good liver function (Child A). What do the authors think is the reason for a large number of patients with Child B and C without liver cirrhosis? In addition, although there are some papers that report treatment effects in some of Child C, it is considered a contraindication to TACE, and this study accounts for a relatively large proportion of 32/162 (19.8%). What do the authors think is the reason?)

Response：Yes, there seems to be a large number of patients with poor liver function, but the proportion of patients with liver cirrhosis is 30/1622 (18.5%). Patients with chronic hepatitis without liver cirrhosis generally have good liver function (Child A grade). This is the result in our statistics of patients, and we will continue to analyze the specific reasons. Although some literatures have reported the therapeutic effects of some ChildC patients, it is considered to be a contraindication for TACE. This study accounts for a large proportion of 32/162 (19.8%), which is the strong desire of individual patients in our study.

6.Response to comment:(The first paragraph of the ‘DISCUSSION’ section should be the summary of findings)

Response：Changes have been made in the article as suggested.

Reviewer #2:

1.Response to comment:(‘①’is missing in the ‘Glipican-3 measurements’)

Response：With regard to Glipican-3 measurement, we use ELISA kit (intron) to test according to the manufacturer's instructions.

2.Response to comment:(The investigators described preoperative staging on ‘Table 3’ and ‘RESUTLS’. But there were not any explanations about what staging was used. There are many staging systems (e.g. AJCC/TNM 7th or 8th or other HCC stage) for HCC. The authors would rather mention the staging system used in ‘Table 3’ and ‘RESUTLS’)

Response：Yes, we should add to describe the grading method of HCC, we use TNM 7th stagingsystems to stage the HCC. A supplementary description has been given in this article.

3.Response to comment:(In the US and Europe, the BCLC staging system is widely used. How about mentioning HCC classification by BCLC staging system in ‘Patient Characteristics’ section?)

Response：we use TNM 7th stagingsystems to stage the HCC.

4.Response to comment:(In the ‘RESULTS’ section, there is only a single subsection ‘Patient Characteristics’. It would be easier to understand if you add subsections that represent important results and explain them.)

Response：Yes, we will pay attention to this kind of problem in the future article writing, and this article does not focus on the description of "patient characteristics".

5.Response to comment:(It would be good to describe the limitations of this study.)

Response：Well, the main limitation of this paper is that there is no correlation, this study needs a larger scale of research to verify, as well as the next step of correlation research.

6.Response to comment:(The terms TACE, transcatheter arterial chemoembolization, and transcatheter arterial embolization chemotherapy are used inconsistently. It would be better to proceed with the abbreviation after describing both full term and the abbreviation at first, if possible.)

Response：OK, corresponding changes have been made in the article.

7.Response to comment:(It is desirable to make ‘Table 4’ easier to view and more consistent (e.g. delete or add horizontal lines that divide the table).)

Response：OK, corresponding changes have been made in the article.

8. Response to comment:(In Abstract and Discussion section, two typographic errors 'hace' were found.)
Response：OK, corresponding changes have been made in the article.
9. Response to comment:(The title shown in table 1 "Efficacy of different types of hepatocellular carcinoma embolization chemotherapy" should be corrected.)
Response：OK, corresponding changes have been made in the article.

Special thanks to you for your good comments.