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PEER-REVIEW REPORT

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Title: Value of miR-1271 and Glypican-3 in evaluating the prognosis of patients with hepatocellular carcinoma after transcatheter arterial chemoembolization

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
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SPECIFIC COMMENTS TO AUTHORS

<Summary> The manuscript by Zheng et al. reported that after TACE, the serum GPC3 level significantly was lower and the circulating miR-1271 was higher than before TACE; and the circulating miR-1271 of relapsed patients was lower than that of remission patients and the GPC3 level was higher than that of remission patients. Based on the results of this study, the authors suggest that monitoring the levels of serum GPC3 and circulating miR-1271 has important clinical reference value for evaluating the prognosis of patients with HCC and could be used to evaluate the prognosis of patients with HCC and help in tumor recurrence, survival status, and guide the next step of treatment. <Evaluation> The efficacy and long-term prognosis of the patients treated with TACE are highly heterogeneous. Therefore, identification of reliable biomarkers that can be used to predict prognosis of HCC patients would contribute to a more effective clinical management of HCC treatment with TACE. The present study is the first to demonstrate an association between the level of GPC3 and miR-1271 and HCC prognosis after TACE treatment. However, there still remain several points to be revised including some major revisions. -Major points 1. 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

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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 2. So it is necessary to confirm the GPC and miR-1271 levels were correct. An explanation for this discrepancy should be needed. 2. 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. 3. 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? 4. The author should explain how patients were enrolled for 'Healthy group' in this study. 5. 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? 6. The first paragraph of the 'DISCUSSION' section should be the summary of findings. -Minor points 1. '①' is missing in the 'Glipican-3 measurements'. 2. The investigators described preoperative staging on 'Table 3' and 'RESUTLS'. But there were not any explanations

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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' 3. 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? 4. 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. 5. It would be good to describe the limitations of this study. 6. 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. 7. It is desirable to make 'Table 4' easier to view and more consistent (e.g. delete or add horizontal lines that divide the table). 8. In Abstract and Discussion section, two typographic errors 'hace' were found. 9. The title shown in table 1 "Efficacy of different types of hepatocellular carcinoma embolization chemotherapy" should be corrected.