

Dear Editors and Reviewers:

We appreciate your letter and reviewer comments on our manuscript entitled " Advanced hepatocellular carcinoma in adolescent, young adults and older adults ". All of these comments are very valuable and helpful for revising and improving our paper, as well as the important guiding significance to us researches. We have studied comments carefully and have made correction which we hope meet with approval. The main corrections in the paper and the responds to the reviewer's comments are as following:

Q1: Title: Advanced hepatocellular carcinoma in adolescent, young adults and older adults This is an interesting article. The title has not imparted sufficient information on the subject of the manuscript, please rephrase it. The key words reflect the focus of the manuscript. Some concerns are listed as follow.

Answer: We have rephrased the title into "Comparison of survival between adolescent and young adults (AYA) and the older patients with hepatocellular carcinoma".

Q2: Abstract---Methods--- ##of "datas" data.

Answer: We have made corresponding changes in the text.

Q3: Abstract--Results----- ## Of "The Cox proportional hazards regression model showd advanced age (HR=1.405, 95%CI: 1.218-1.621, P<0.001) was risk factor for OS of HCC. In the subgroup analysis, the Cox proportional hazards regression model showd in AJCC I/ II, "

Answer: We have modified errors of words: change "showd" into "showed".

Q4: Introduction: ## Of 'Research by Lewis R. Roberts et al. shows that the age at which HCC was likely to occur was different in different regions of the world¹⁴. The authors are not those in the references. ## Of "Lewis R. Roberts et al. shows that the age at which HCC was likely to occur was different in different regions of the world¹⁴. ". The reference did not match.

References 13 and 14 are the same, please check them.

Answer: We have perfected references 13 and 14. Now the references and conclusions match.

Q5: Results: ## Of "sex(P=0.934) 、 race(P=0.985) 、 marital status(P=1.000) 、 AJCC stage(P=0.974) 、 grade(P=0.887) 、 surgery(P=1.000) 、 radiation(P=1.000) 、 chemotherapy(P=0.937)". ## Fig. 1 Forest map of multivariate analysis of OS in patients with HCC. All variables are statistically significant. Advanced age、 blacks、 advanced AJCC stage、 advanced grade are risk factors for OS of HCC; Female、 other races、 married status、 surgery、 radiation、 chemotherapy are protective factors for OS of HCC.

Answer: We have corrected the punctuation errors.

Q6: Discussion: ## Please clarify>>>>>In this article: "AYA cancer survivors had inferior 5-year OS compared with the general population, while the long-term survival was increasing¹⁷. " In reference 17: "AYA cancer survivors have inferior long-term survival compared with the general population. "

Answer: Our expression needs to be clearer and has been changed to: "AYA cancer survivors

still had inferior 5-year OS compared with the general population, while the long-term survival of AYA cancer survivors has improved[17]. However, the improvement of survival rate and mortality of AYA cancer patients were not as good as those of younger or older patients”

Q7: ## In the Discussion: “After comparing the baseline data, we found that AYA hepatocellular carcinoma patients had worse SEER stage, more advanced AJCC stage and more likely to receive surgery. This was consistent with previous research: Cancer in AYA patients were often in advanced stages, and the cancer showed more aggressiveness²³. This may be related to the poor prognosis of AYA cancer patients.” More address and references are needed to make it sound and robust.

Answer: We have added the clinical and biological differences between acute lymphoblastic leukemia and Burkitt’s lymphoma in different age groups to prove our point as new reference 24 and 25.

Q8: ## In the Discussion: “Insufficient exercise, mental illness, bad living habits, and comorbidities were not conducive to the OS of AYA cancer patients, resulting in poor prognosis.” are there any evidence relating to the conclusion?

Answer: This sentence has been changed into “Insufficient exercise, mental illness, bad living habits, and comorbidities may be not conducive to the OS of AYA cancer patients” , which is the central sentence of this paragraph. All the contents of this paragraph come to the conclusion of this sentence.

We have done our best to improve the manuscript and have made some changes in the manuscript. These changes do not affect the integral 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.

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