

Response to Review Comments

Major

Comment 1: Please, identify this study as a retrospective cohort study and adhere point-by-point to the relevant reporting guideline of the EQUATOR Network.

Reply: The revised manuscript has been corrected following the STROBE guideline for reporting observational studies.

Comment 2: Was the sampling consecutive? How were the patients identified in medical databases? Altogether, how many cases with any malignancy were diagnosed at the clinic (of which 243 were eligible for inclusion) and what were the main reasons for exclusion? What about lack of data on follow-up/attrition?

Reply: The sampling was consecutive. All patients admitted to our hospital from June, 2016 to June, 2019 were searched. A total of 27,055 patients with solid malignant tumor were found. After reviewing the patients' medical records, 260 patients were with multiple primary malignancies (MPM). After further investigation, 17 patients were excluded from our study, including 11 patients with no pathological diagnosis of one tumor, and 6 patients who were lost to follow-up. The data of the 6 patients lost to follow-up were discarded and not included in the analysis of the study.

Comment 3: I recommend including a third group of patients who were diagnosed with one primary tumor. This would allow you to make predictions of the development of multiple primary tumors as well, which would be a clinically meaningful information regarding follow-up. Besides, immortal time bias should be handled somehow.

Reply: A total of 26,795 with one solid malignant tumor were found. The five most common cancers were non-small cell lung cancer (NSCLC) (18.3%), colorectal cancer (12.5%), breast cancer (10.6%), gastric cancer (9.4%) and liver cancer (7.3%). Patients with multiple primary malignancies (MPM) accounted for 0.96% (260/27055) of all patients with solid malignant tumor. The information above has been added in the revised manuscript. Because our retrospective study did not have specific interventions, immortal time bias may be difficult to determine and eliminate.

Comment 4: I am not sure if the conclusion about having no difference in survival between the synchr. and metachr. groups holds in light of the relatively low number of the patients. Do you consider the statistical power of the analysis sufficient?

Reply: In the synchronous and metachronous MPM patients, the median interval time between the first and second cancer diagnoses was 0.2 months and 73.2 months, respectively. In our study, overall survival (OS) was defined as the time from the diagnosis of the second malignancy to death due to any cause, or to the last follow-up. If the OS was calculated from the diagnosis of the first malignancy, due to the obviously different median interval time, there would be statistically different OS between the synchr. and metachr. Groups. Therefore, despite the relatively small sample size, we believe that the conclusion in our study is reasonable and meaningful.

Minor

Comment: Typos should be amended.

Reply: The revised manuscript has been polished by a professional English language editing

company. And the English editing certificate has been provided

Response to Editorial Office's Comments

Comment 1: Summary of the Peer-Review Report: This study is good. The authors should include a third group of patients who were diagnosed with one primary tumor. The questions raised by the reviewers should be answered.

Reply: The third group of patients with one primary tumor has been added in the revised manuscript. All the questions raised by the reviewer have been answered.

Comment 2: The Biostatistics Review Certificate was not provided.

Reply: The Biostatistics Review Certificate has been provided as 66792-Biostatistics Review Certificate file.

Comment 3: Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Reply: The revised manuscript has been edited by MedE Editing Group: <http://meditorexper.com>. And the English editing certificate has been provided as 66792-Non-Native Speakers of English Editing Certificate file.

Comment 4: The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Reply: The original pictures using PowerPoint have been provided as 66792-Figures.ppt.

Comment 5: PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout

Reply: The references have been revised as suggested.

Comment 6: The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text.

Reply: The "Article Highlights" section has been added at the end of the main text.

Comment 7: STEPS FOR SUBMITTING REVISED MANUSCRIPT.

Reply: The revised manuscript has been revised and submitted as suggested.