

## Peer Review File

Article information: <https://dx.doi.org/10.21037/tcr-23-301>

### Reviewer A

The paper titled “Characteristics and survival analysis of breast cancer survivors with metachronous double primary cancers: a retrospective cohort study” is interesting. The identification of double primary cancers in earlier stages could play a critical role in guidance and lead to better outcomes. A prolonged follow-up examination period for BC survivors is needed to provide better guidance and treatments. However, there are several minor issues that if addressed would significantly improve the manuscript.

The description of figure legend in this study is too simplistic, please describe in detail.

Reply: Thank you for your suggestion. We have described in detail.

Changes in the text:

Figure 1 The process used to screen patients of breast cancer with metachronous double primary cancers.

Figure 3 a. Kaplan-Meier survival curve for OS in the first primary breast cancer patients with other primary cancers; b. Kaplan-Meier survival curve for cancer-specific survival in the first primary breast cancer patients with other primary cancers. OS, overall survival.

The content of this study is too simple and it is recommended to increase the analysis of cancer-specific survival.

Reply: Thank you for your suggestion. We have added the analysis of cancer-specific survival in Fig. 3b.

What type of patients benefit most from the results of this study? What is the author's next research plan? It is recommended to add relevant content to the discussion.

Reply: Thank you for your suggestion. We have added relevant content to the discussion.

Changes in the text:

We find that the survival of breast cancer patients with thyroid cancer is better than that of breast cancer patients, so we need to further study the mechanism of the conclusion to help us plan and carry out adequate and timely surveillance programs and preventive measures in clinical practice.

In the introduction of the manuscript, it is necessary to clearly indicate the knowledge gaps and limitations of prior study and the clinical significance of this study.

Reply: Thank you for your suggestion. We have added the knowledge gaps and limitations of prior study and the clinical significance in the corresponding part of the manuscript.

Changes in the text:

In clinical practice, the occurrence of metachronous double primary cancers is common. However, most of the reports about metachronous double primary cancers are case reports. Other studies covered fewer types of cancers. Investigating the risk factors and prognosis associated with metachronous primary cancer can increase awareness the identification of double primary cancers in earlier stages could play a critical role in guidance and lead to better health outcomes.

The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as “Contralateral axillary lymph node metastasis and molecular changes in second primary breast cancer: a case report, Gland Surg, PMID: 33968707”. It is recommended to quote this article.

Reply: Thank you for your suggestion. We have quoted this article, which makes the argument more complete.

What is the time interval rules and survival outcomes of individuals with metachronous breast cancer and ovarian cancer? It is recommended to add relevant content.

Reply: Thank you for your suggestion. We have added relevant content.

Changes in the text:

The time interval rules and survival outcomes of individuals with metachronous breast cancer and ovarian cancer was  $\geq 6$  months as other cancers.

## **Reviewer B**

This descriptive study investigated the prognosis of breast cancer survivors with metachronous double primary cancers. This is an interesting study and of highly clinical relevance. The strength of this study is the large sample size. However, it has some limitations.

1. Because this is a retrospective study and some of the participants have passed away.

Reply: Yes, some of the participants did have passed away.

2. Figure 3 is redundant and should be deleted.

Reply: Thank you for your suggestion. We have deleted it.

3. Page 8, lines 22 to 25, please indicate the inconsistency and discuss the possible interpretations.

Reply: We indicated the inconsistency and discuss the possible interpretations in the manuscript.

Changes in the text:

One study reported that thyroid cancer did not affect the prognosis of patients with breast cancer. The inconsistent results may be due to the small number of samples and inconsistent inclusion criteria involving patients with stage IV disease.

4. Page 8, lines 27 to 29, this sentence is confusing.

Reply: Thank you for your suggestion. We revised the manuscript about the sentence. We have described it in the manuscript.

Changes in the text:

Mutations of the same gene can result in cancers happened in different places.

5. Page 9, lines 20 to 21, this sentence is confusion. Do you mean similar survival in BC patients with and without thyroid cancer?

Reply: Thank you for your suggestion. We revised the manuscript about the sentence.

Changes in the text:

Lei et al. reported better survival in BC survivors with thyroid cancer in 2019.

6. Page 9, lines 27 to 30, the clinical implications of this study should be discussed.

Reply: Thank you for your suggestion. We have added the clinical implications in the corresponding part of the manuscript.

Changes in the text:

These independent risk factors can help stratify the patients into high or low-risk groups. If we pay more attention to patients with these independent risk factors, we could give patients earlier clinical intervention to prolong their survival.

7. Some details of follow up should be reported, such as the method and frequency of follow up, the time of last follow up, the endpoint and its definition.

Reply: Thank you for your suggestion. We have reported more details of follow up in the manuscript.

Changes in the text: Patients eligible for inclusion were followed up and recorded by telephone interview per six months. Follow-up information included patients' tumor recurrence and metastasis, survival status and other items. The time of last follow up was December 31, 2015. The endpoint was the overall survival (OS), OS was calculated from the date of surgical treatment to the date of death.

8. Table2 is meaningless and should be removed.

Reply: Thank you for your suggestion. We have removed it.

9. Page 7, lines 15 to 17: it seems that the participants were patients with breast cancer as a primary cancer, rather than all double primary cancer patients.

Reply: Thank you for your suggestion.

Changes in the text: Among all patients with metachronous double primary cancer, the proportion of breast cancer as the first primary cancer is the highest, so we analyzed the clinical factors for OS in breast cancer that is as the first primary cancer in Table 4.

10. Language quality needs to be improved.

Reply: Thank you for your suggestion. We have tried our best to improve the quality of the language.

## **Reviewer C**

### **1. Abstract**

Please defined BC and OS in the abstract.

Reply: We have defined BC and OS in the abstract.

### **2. Figure 3**

Please provide a clearer version of figure 3, the current version cannot be seen clearly.

Reply: We have provided a clearer version of figure 3.

### **3. Table 4**

Please explain BMI in the table footnote.

Reply: We have explained BMI in the table footnote.