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Reply on "Prognosis according to the timing of recurrence in breast cancer" (Ann Surg Treat Res 2023;104:1-9)

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Dear Dominik Hlauschek and Michael Gnant,

I understand your concerns about 'immortal time bias.'

In this study, the median follow-up time was 60 months, which is believed to be different from the 'immoral time bias' found in epidemiological studies.

In general, early recurrence is associated with a worse prognosis compared to late recurrence, and patients with late recurrence can expect better overall survival (OS). However, it is necessary to determine whether there is a difference in the course of the disease depending on the time of recurrence. This is because, if the course of the disease is worse in early compared to late recurrence, treatment and evaluation methods must differ between such cases. If there is no difference, the same protocol can be considered regardless of the time of recurrence.

To analyze this more accurately, an analysis of the progression-free survival rate is necessary. This requires confirmation of a difference between the disease course after early relapse and the disease course after late relapse.

When planning this study, we wanted to report whether the time from relapse to disease progression or death was the same regardless of early or late relapse. The results of the analysis showed that patients with late recurrence had better disease-free survival than patients with early recurrence.

In the analysis, 'immortal time bias' should have been considered, as you pointed out. However, it was not included because it was determined that further analysis was not necessary after sufficient follow-up time.

Our analysis of OS allows disregard of the 'immortal time bias' and indicates that the results reflect reality. Additionally, for a more accurate understanding, patients who did not relapse were also compared for OS.

The 'immortal time bias' did not show any differences across subtypes. Figs. 2 and 3 demonstrate an absence of the horizontal straight line you pointed out in the neoadjuvant chemotherapy group, triple-negative breast cancer, and HER2 subtype [1]. This is thought to be due to differences in recurrence and progression depending on subtype rather than an immortal time bias.

As shown in the results, the clinicopathologic features of patients with early and late relapses are different. In the luminal type, OS shows a similar pattern after recurrence whether early or late. In the triple-negative breast cancer and human epidermal growth factor receptor 2 subtypes, patients who relapsed after 5 years showed an excellent OS rate close to that of patients without recurrence, unlike patients with early recurrence.

I hope this answers the questions you raised. We are happy to explain our advanced analytics if you desire. If your team can help with further analysis, we will ensure no issues with the data transfer for that patient.

Thank you for your interest and excellent comments on this paper.

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REFERENCE

1. Lee YJ, Jung SP, Bae JW, Yang SM, You JY, Bae SY. Prognosis according to the timing of recurrence in breast cancer. Ann Surg Treat Res 2023;104:1-9.