Time-dependent bias when analysing COVID-19-associated pulmonary aspergillosis - Authors’ reply

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Time-dependent bias when analysing COVID-19-associated pulmonary aspergillosis

Authors’ reply

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We thank Justin de Brabander and colleagues for their interest in our findings on COVID-19-associated pulmonary aspergillosis (CAPA) reported from the MYCOVID cohort. They raised a very interesting question on the factor time and competing risks in studying the relation between CAPA and mortality as exemplified by their own cohort.

Initially, we observed a statistically significant association between CAPA occurrence and mortality using a Cox model. Then, we decided to refine the Cox model analysis for mortality estimation with a landmark analysis, considering the mean day of proven or probable CAPA development (11 days in our cohort). But, as suggested by de Brabander and colleagues, we performed a complementary analysis, considering the time-dependent bias due to CAPA occurrence on the estimation of mortality. Austin and colleagues previously defined a competing risk as an event whose occurrence precludes the occurrence of the primary event of interest. Here, the competing states were “time to death” or “discharge”, both during intensive care unit (ICU) stay. No follow-up data were collected after ICU discharge as mentioned in the manuscript. Using this model, the cause-specific hazard ratio (CS-HR) at discharge due to CAPA was 0.57 (95% CI 0.38–0.84) and the CS-HR of death due to CAPA was 2.08 (1.47–2.93), compared to 1.45 (1.03–2.03) found with the initial log-rank analysis.

Overall, we provide evidence that the magnitude effect of CAPA on mortality when considering the immortal bias and a cause-specific model increased the strength of the association between development of CAPA and mortality in the MYCOVID cohort.


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