

CORRESPONDENCE



# Early versus late tracheostomy in patients with traumatic brain injury

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Dear Editor,

We read with great interest the research article by Robba et al. [1] that showed that early tracheostomy after traumatic brain injury (TBI) is associated with better neurological outcomes and shorter length of intensive care unit (ICU)/hospital stays compared with late tracheostomy. Although the authors openly discuss the limitations of their findings, some inherent bias in the study design should be discussed and clarified.

Time-related bias, such as immortal time bias, is inherent in observational studies examining the association of exposures (e.g., resuscitation management, tracheostomy) in an intensive care setting, where early death is common [2–4]. In this study, the definition of late tracheostomy as tracheostomy occurring after >7 days after TBI makes these participants “immortal” from the time of cohort entry until tracheostomy occurs (i.e., patients undergoing late tracheostomy cannot die until the time of tracheostomy) [2]. Therefore, inclusion of “immortal time” in the survival analysis may bias the results toward a beneficial effect of late tracheostomy [5]. This is consistent with the reported lower mortality rate at 6 months with late tracheostomy than with early tracheostomy (15.0% vs. 20.6%) (Supplementary Table 3 in [1]).

Patients with late tracheostomy undergo longer mechanical ventilation than those undergoing early tracheostomy. Longer mechanical ventilation increases the risk of ventilator-associated pneumonia (VAP) and is consistent with results of this study (incidence of VAP 39.7% for late tracheostomy versus 27.2% for early tracheostomy;  $p=0.010$ ) [1]. High incidence of VAP can be associated with worse outcome. While immortal time bias tends to favor the late tracheostomy group, the

higher incidence of VAP and more intensive treatment, as stated by the author, can un-favor the late tracheostomy group, which makes the interpretation of this study difficult.

To evaluate time-related bias, we would like to examine Kaplan–Meier survival curves in terms of the influence of the timing of tracheostomy on mortality. Although Robba et al. transferred the start of follow-up (ICU admission) to the end of the immortal time period (the time point of tracheostomy) in both groups [4], this analysis excluded immortal time, which can cause selection bias. If possible, we recommend that the authors perform sensitivity analyses using risk set matching [2] and time-fixed analysis to quantify the immortal time bias [4]. This information will be valuable to the readers of *Intensive Care Medicine*.

#### Compliance with ethical standards

#### Conflicts of interest

There are no potential conflicts of interest relevant to this letter to declare.

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