Critical Care

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Timing of invasive mechanical ventilation in patients with sepsis: the impact of excluding non-intubated patients

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Dear Editor,

Early initiation of invasive mechanical ventilation (IMV) may represent a potentially beneficial approach for sepsis patients [1]. A recent study by Kim et al. [2], published in *Critical Care*, provides evidence supporting this approach, reporting that earlier IMV initiation (on the first day of ICU admission) may be associated with lower mortality.

However, in their study, 2,363 patients who never required IMV during their ICU stay were excluded from the analysis. While this approach focuses on patients who received IMV, it may inadvertently select a population with more severe illness for comparison, potentially introducing bias into the results. In clinical practice, a subset of sepsis patients may benefit from a wait-and-see strategy, where intubation is avoided through the use of non-invasive ventilation or other supportive measures, potentially reducing the risks associated with IMV. Excluding these patients from the analysis may have influenced the reported outcomes and the perceived benefits of early IMV.

To better illustrate this issue, we conducted an analysis of sepsis patients using the Medical Information Mart for Intensive Care (MIMIC)-IV database [3] (refer to Additional file 1: Supplemental methods). Among 24,518 ICU patients with sepsis, 12,654 received IMV on the first day of ICU admission (early IMV group). Of the remaining 11,864 patients (non-early IMV group), 1,217 eventually required IMV later during their ICU stay (delayed IMV group), while the rest did not receive IMV during their ICU stay (Additional file 1: Fig. S1).

First, we compared the early IMV group and the non-early IMV group. Propensity score matching (PSM) improved the balance of baseline characteristics between the two groups, achieving an absolute standardized mean difference (SMD) < 0.10 (Additional file 1: Table S1). After matching, the 90-day mortality rate was 23.3% (1,413/6,067) in the early IMV group and 28.5% (1,731/6,067) in the non-early IMV group. The Kaplan–Meier curve for 90-day mortality in the matched cohort is shown in Fig. 1A. Early IMV was associated with lower 90-day mortality in both univariable analysis (hazard ratio [HR], 0.79; 95% confidence interval (CI), 0.74–0.85; $P < 0.001$) and multivariable analysis (HR, 0.77; 95% CI, 0.72–0.83; $P < 0.001$).

Next, we compared the early IMV group and the delayed IMV group. Similarly, PSM improved the balance of baseline characteristics between the two groups (absolute SMD < 0.10; Additional file 1: Table S2). After matching, the 90-day mortality rate was 27.1% (302/1,116) in the early IMV group and 45.3% (505/1,116) in the delayed IMV group. The Kaplan–Meier curve for 90-day mortality in the matched cohort is shown in Fig. 1B. Early IMV was associated with significantly lower 90-day mortality in both univariable analysis (HR, 0.53; 95% CI, 0.46–0.61;

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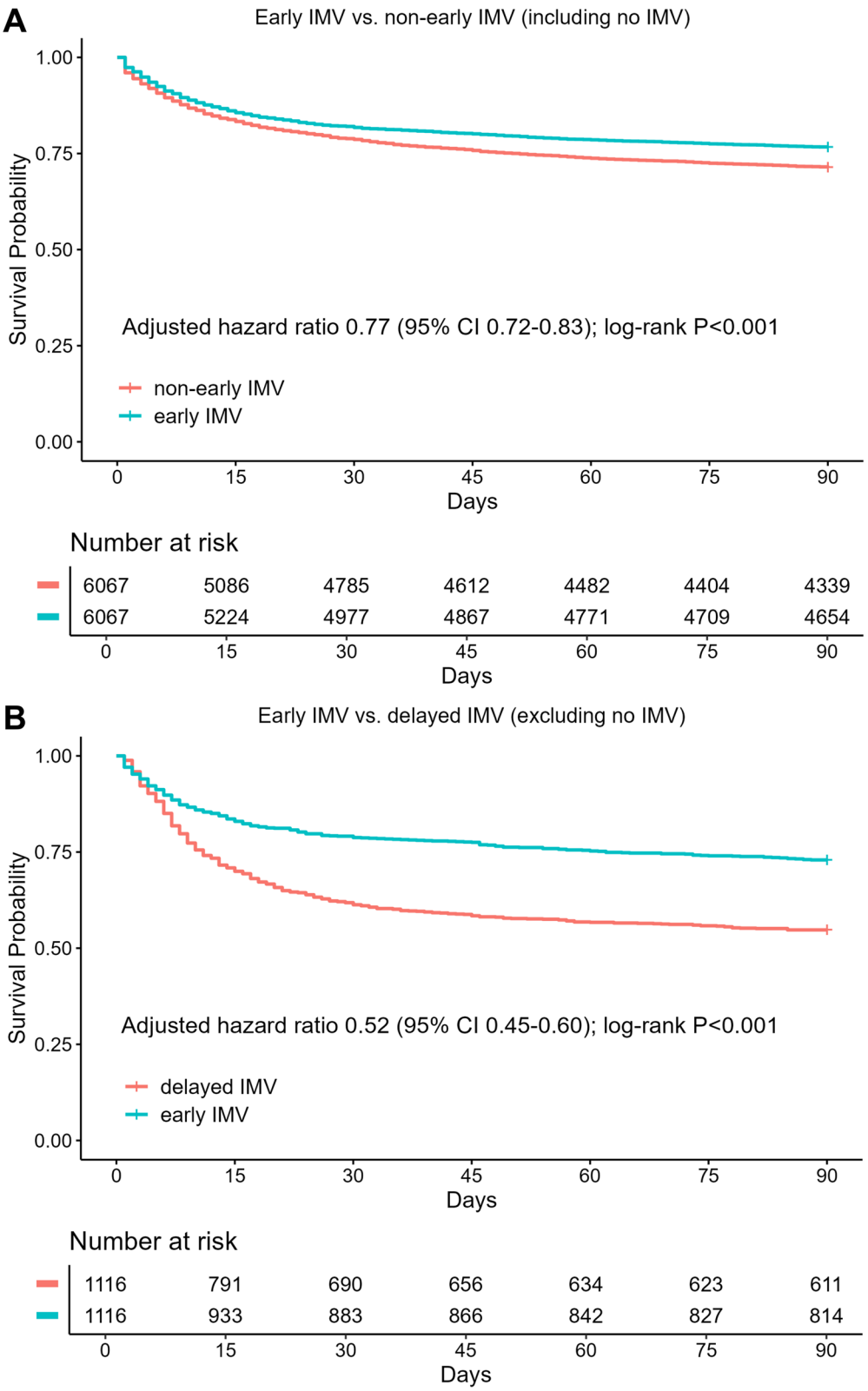

Fig. 1 (See legend on previous page.)

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Fig. 1 Kaplan–Meier curves for 90-day mortality based on the timing of IMV in the matched cohort. **A** Comparison between the early IMV group and the non-early IMV group (including patients who did not receive IMV during their ICU stay). The multivariable Cox proportional hazards model was adjusted for weight, mean arterial pressure, temperature, and GCS, which were identified as statistically significant in the univariable analysis ($P < 0.05$) (Table S1). **B** Comparison between the early IMV group and the delayed IMV group (excluding patients who did not receive IMV during their ICU stay). The multivariable Cox proportional hazards model was adjusted for temperature and GCS, which were identified as statistically significant in the univariable analysis ($P < 0.05$) (Table S2). CI, confidence interval; GCS, Glasgow coma scale; IMV, invasive mechanical ventilation

$P < 0.001$) and multivariable analysis (HR, 0.52; 95% CI, 0.45–0.60; $P < 0.001$).

Our findings demonstrate that early IMV is associated with lower mortality, aligning with the results reported by Kim et al. [2]. However, as shown in Fig. 1, the exclusion of patients who never received IMV during their ICU stay may lead to an overestimation of the mortality benefits associated with early IMV. Thus, we believe that including the 2,363 patients who did not receive IMV during their ICU stay could provide a more comprehensive understanding of the mortality benefits associated with early IMV and potentially refine the findings of Kim et al.'s study [2].

Abbreviations

CI	Confidence interval
HR	Hazard ratio
ICU	Intensive care unit
MIMIC	Medical information mart for intensive care
IMV	Invasive mechanical ventilation
PSM	Propensity score matching
SMD	Standardized mean difference

Supplementary Information

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Additional file1 (DOCX 192 KB)

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Author contributions
YJ extracted the data and performed the statistical analyses. YJ and LL participated in the discussion and wrote the manuscript.

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Availability of data and materials
The datasets presented in the current study are available in the MIMIC-IV database (https://mimic.mit.edu/).

Declarations

Ethics approval and consent to participate
The establishment of this database was approved by the Massachusetts Institute of Technology (Cambridge, MA) and Beth Israel Deaconess Medical Center (Boston, MA) and consent was obtained for the original data collection. Therefore, the ethical approval statement and the need for informed consent were waived for this manuscript.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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