The Timing of Tracheotomy in Critically Ill Patients Undergoing Mechanical Ventilation: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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The Timing of Tracheotomy in Critically Ill Patients Undergoing Mechanical Ventilation

A Systematic Review and Meta-analysis of Randomized Controlled Trials

Fei Wang, MD, PhD; Youping Wu, MD, PhD; Lulong Bo, MD, PhD; Jingsheng Lou, MD, PhD; Jiali Zhu, MD; Feng Chen, MD, PhD; Jinbao Li, MD, PhD; and Xiaoming Deng, MD, PhD

Background: The objective of this study was to systematically review and quantitatively synthesize all randomized controlled trials (RCTs), comparing important outcomes in ventilated critically ill patients who received an early or late tracheotomy.

Methods: A systematic literature search of PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, the Cochrane Central Register of Controlled Trials, the National Research Register, the National Health Service Trusts Clinical Trials Register, and the Medical Research Council UK database was conducted using specific search terms. Eligible studies were RCTs that compared early tracheotomy (ET) with either late tracheotomy or prolonged translaryngeal intubation in critically ill adult patients.

Results: Seven trials with 1,044 patients were analyzed. ET did not significantly reduce short-term mortality (relative risk [RR], 0.86; 95% CI, 0.65-1.13), long-term mortality (RR, 0.84; 95% CI, 0.68-1.04), or incidence of ventilator-associated pneumonia (RR, 0.94; 95% CI, 0.77-1.15) in critically ill patients. The timing of the tracheotomy was not associated with a markedly reduced duration of mechanical ventilation (MV) (weighted mean difference [WMD], −3.90 days; 95% CI, −9.71-1.91) or sedation (WMD, −7.09 days; 95% CI, −14.64-0.45), shorter stay in ICU (WMD, −6.93 days; 95% CI, −16.50-2.63) or hospital (WMD, 1.45 days; 95% CI, −5.31-8.22), or more complications (RR, 0.94; 95% CI, 0.66-1.34).

Conclusions: The present meta-analysis suggested that the timing of the tracheotomy did not significantly alter important clinical outcomes in critically ill patients. The duration of MV and sedation, as well as the long-term outcomes of ET in mechanically ventilated patients, should be evaluated in rigorously designed and adequately powered RCTs in the future.

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Abbreviations: ET = early tracheotomy; LT = late tracheotomy; MV = mechanical ventilation; PTI = prolonged translaryngeal intubation; RCT = randomized controlled trial; RR = relative risk; VAP = ventilator-associated pneumonia; WMD = weighted mean difference

Tracheotomy is a frequently performed surgical procedure in critically ill patients.1 For patients who require prolonged mechanical ventilation (MV), replacement of translaryngeal intubation with a tracheotomy is often considered.2 Generally accepted benefits of tracheotomy (relative to prolonged translaryngeal intubation [PTI]) include greater airway security, improved patient comfort, better oral hygiene, and easier nursing care.3,5 However, tracheotomy is not risk free. Complications related to tracheotomy include bleeding, wound infection, tracheal stenosis, and occasionally death.6,8 Recent evidence suggests that the percutaneous dilatational technique is increasingly the first choice for ICU tracheotomy, compared with the open surgical technique.9,10 However, the optimal timing (early vs late) of the tracheotomy in critically ill patients requiring prolonged MV remains unclear.11,12

A meta-analysis published by Griffiths et al13 in 2005 indicated that early tracheotomy (ET) shortened the
duration of MV and length of ICU stay in patients who required prolonged MV. Since then, several other randomized controlled trials (RCTs) have been published on the topic. Consequentially, we conducted an updated systematic review and meta-analysis of RCTs on the timing of tracheotomies to investigate the effect of ET vs either PTI or PTI followed by late tracheotomy (LT) on important clinical outcomes in critically ill patients.

**Materials and Methods**

**Search Strategy**

In reporting our results, we followed the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Relevant articles in all languages were identified by searching PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, the Cochrane Central Register of Controlled Trials, the National Research Register, the National Health Service Trusts Clinical Trials Register, and the Medical Research Council UK database (up to July 10, 2011). Electronic searches were performed using Exploded Medical Subject Headings and the appropriate corresponding keywords: “tracheostomy,” “tracheotomy” AND “critical care,” “critical illness,” “intensive care,” “critically ill.” We restricted the findings of the previous searches using a highly sensitive search strategy recommended by the Cochrane Collaboration for identifying RCTs. We also checked the reference lists of RCTs and previous meta-analyses identified by the previous searches to include other potentially eligible trials.

Two authors independently included RCTs in the analysis if they compared ET with either PTI or PTI followed by LT in critically ill adult patients. ET was defined as a tracheotomy performed up to 7 days after initiation of translaryngeal intubation and MV. LT was any time thereafter. Agreement regarding trial inclusion was assessed using the Cohen k statistic.

**Data Extraction**

Two authors independently extracted the following data: study design (ie, date, location, and sample size), patient characteristics, study methodology (ie, inclusion/exclusion criteria, weaning protocol, tracheotomy technique, method of randomization, and analysis method), intervention (ie, definitions of ET and LT), and main outcomes. If data needed clarification or were not presented in the publication, we contacted the original authors. Extracted data were entered into Microsoft Office Excel 2007 (Redmond, Washington) and were checked by the third author. Any disagreement was resolved by discussion.

Analyses were on an intention-to-treat basis. Differences were expressed as relative risks (RRs) with 95% CIs for dichotomous outcomes, and weighted mean differences (WMDs) with 95% CIs for continuous outcomes. A fixed-effect model was used, and a random-effects model was used in the case of significant heterogeneity (P value of $\chi^2$ test < .10 and I² > 50%). Potential sources of heterogeneity were identified by sensitivity analyses conducted by omitting one study in each turn and investigating the influence of a single study on the overall pooled estimate. Publication bias was assessed by visually inspecting a funnel plot. A P value < .05 was considered statistically significant. All statistical analyses were performed using Review Manager, version 5.0 (RevMan; The Cochrane Collaboration; Oxford, England).

**Results**

**Study Identification**

The comprehensive search yielded a total of 1,212 relevant publications, and the abstracts were obtained for all citations (Fig 1). Seven RCTs with a total of 1212 Citations retrieved by search strategy

- 314 Excluded for duplication
- 898 Potentially relevant studies
- 876 Excluded by screening of titles or abstracts
- 22 Full-text articles reviewed
- 15 Excluded after full article review
  - 10 Outcomes of interest not studied
  - 2 quasi-randomized controlled trials
  - 2 Ineligible tracheotomy timing period
  - 1 Skewed allocation assignment

7 Randomized controlled trials included in the meta-analysis

**Figure 1.** Flowchart of study selection.
<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Intensive Care Setting</th>
<th>Timing of Tracheotomy</th>
<th>Mean Age, y</th>
<th>Disease Severity</th>
<th>Weaning Control</th>
<th>Tracheotomy Information</th>
<th>VAP Definition</th>
<th>Intention-to-Treat Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saffi et al 2002</td>
<td>Burn ICU</td>
<td>Next available operative day</td>
<td>Early: 14 d after burn injury</td>
<td>Late: 44.5 ± 19.7</td>
<td>Late: 51.3 ± 19.2</td>
<td>Not reported</td>
<td>Yes</td>
<td>Performed in the operating room, mostly using surgical technique</td>
</tr>
<tr>
<td>Bouderka et al 2004</td>
<td>Units for head injury patients</td>
<td>5-6 d after admission</td>
<td>Early: 41.1 ± 17.5</td>
<td>Late: 40 ± 19</td>
<td>SAPS score: Early: 5.4 ± 1.5</td>
<td>No</td>
<td>Not reported</td>
<td>CDC criteria</td>
</tr>
<tr>
<td>Rumbak et al 2004</td>
<td>3 Medical ICUs</td>
<td>0-2 d after initiation of MV</td>
<td>Early: 14-16 d after initiation of MV</td>
<td>Late: 63 ± 10.4</td>
<td>Late: 63 ± 9.3</td>
<td>APACHE II score: Early: 27.4 ± 4.2</td>
<td>Yes</td>
<td>Percutaneous dilational tracheotomy procedure</td>
</tr>
<tr>
<td>Barquist et al 2006</td>
<td>Trauma center</td>
<td>Before 8 d of admission</td>
<td>Early: 53.7 ± 21.5</td>
<td>Late: 49.9 ± 18.3</td>
<td>APACHE II score: Early: 12.1 ± 3.2</td>
<td>Yes</td>
<td>Performed both at the bedside and in the operating room</td>
<td>CDC criteria</td>
</tr>
<tr>
<td>Blot et al 2008</td>
<td>25 Medical-surgical ICUs</td>
<td>Before 4 d of initiation of MV</td>
<td>Early: After 14 d of initiation of MV</td>
<td>Late: 55 (19-88)</td>
<td>Late: 58 (20-88)</td>
<td>SAPS II score: Early: 50 (17-103)</td>
<td>Yes</td>
<td>Most often performed at the bedside using a surgical technique</td>
</tr>
<tr>
<td>Terragni et al 2010</td>
<td>12 ICUs</td>
<td>6-8 d after endotracheal intubation</td>
<td>Early: 61.8 ± 17.4</td>
<td>Late: 61.3 ± 16.8</td>
<td>SAPS II score: Early: 51.1 ± 8.7</td>
<td>Yes</td>
<td>Performed at the bedside using percutaneous techniques</td>
<td>Using the simplified CPIS, CPIS &gt; 6 was considered to indicate the presence of VAP</td>
</tr>
<tr>
<td>Trouillet et al 2011</td>
<td>Postcardiac surgery ICU</td>
<td>Before 5 d after surgery</td>
<td>Early: 64.1 ± 13.3</td>
<td>Late: 66.0 ± 12.4</td>
<td>SAPS II score: Early: 47.2 ± 12.4</td>
<td>Yes</td>
<td>Performed at the bedside using percutaneous techniques</td>
<td>Clinical features with positive BAL cultures</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD unless indicated otherwise. APACHE = Acute Physiology and Chronic Health Evaluation; CDC = Centers for Disease Control and Prevention; CPIS = Clinical Pulmonary Infection Score; MV = mechanical ventilation; SAPS = Simplified Acute Physiologic Score; VAP = ventilator-associated pneumonia.

*Median (range).
1,044 patients met the inclusion criteria. 4,14,15,20-23 The Cohen κ statistic for agreement on study inclusion was 0.92.

Among the seven trials, three were conducted in North America, 4,14,20 three in Europe, 15,22,23 and one in North Africa. 21 Three trials were multicenter studies. 4,15,22 All trials were published in English. The mean age of the patients ranged from 40 to 66 years. The selected trials examined various populations in critical care units, including medical, 4 medical-surgical, 15,22 trauma, 14 head injury, 21 burn, 20 and postcardiac surgery patients. 23 The definitions of VAP differed across the trials, among which three 4,14,20 used Centers for Disease Control and Prevention criteria, 24 three required microbiologic confirmation, 4,15,23 and the remaining one used the simplified Clinical Pulmonary Infection Score. 22 Tracheotomy techniques were reported in six trials, 4,14,15,20,22,23 including surgical procedure, percutaneous dilational procedure, or both, and were performed at the bedside, operating room, or both. Six of the included seven trials reported the weaning protocols. 4,14,15,20,22,23 Details of the included trials are summarized in Table 1.

Among all the selected trials, randomized sequence and allocation sequence concealment were conducted adequately. Because of the nature of the intervention of the tracheotomy, physicians could not be blinded to the randomization arm, and the objective outcomes (eg, mortality) were not likely to be influenced by lack of blinding. Blinded fashion was clearly stated in the adjudication of VAP in two trials. 15,22 The numbers and reasons for withdrawal/dropout were reported in all trials. Two trials 14,20 were defined as having other sources of bias because one was stopped early after the first interim analysis 14 and the other had a baseline imbalance after adequate randomization. 20 An overview of the risk of bias is shown in Table 2.

**Primary Outcomes**

Data on primary outcomes were available from all seven trials (N = 1,044) (Table 3). ET did not significantly reduce short-term mortality (RR, 0.86; 95% CI, 0.65-1.13; P = .28; P for heterogeneity = .09; I² = 45%) (Fig 2) or incidence of VAP (RR, 0.94; 95% CI, 0.77-1.15; P = .54; P for heterogeneity = .0009; I² = 74%) (Fig 3).

**Secondary Outcomes**

Two trials (n = 443) 22,23 reported data on long-term mortality. No significant difference was detected (RR, 0.84; 95% CI, 0.68-1.04; P = .10; P for heterogeneity = .52; I² = 0%) (Fig 4). Information on duration of MV and sedation was available for four trials (n = 442) 4,20,21,23 and two trials (n = 336) 4,23 respectively. ET did not significantly shorten the duration of MV (WMD, −3.90 days; 95% CI, −9.71-1.91; P = .19; P for heterogeneity <.0001; I² = 86%) (Fig 5), or sedation (WMD, −7.09 days; 95% CI, −14.64-0.45; P for heterogeneity <.00001; I² = 98%) (Fig 6). Data on length of ICU (n = 396) 23 and hospital (n = 260) 20,23 stay were available for two trials, respectively. ET was not associated with a shorter length of ICU (WMD, −6.93 days; 95% CI, −16.50-2.63; P = .16; P for heterogeneity = .001; I² = 91%) (Fig 7) or hospital (WMD, 1.45 days; 95% CI, −5.31-8.22; P = .67; P for heterogeneity = .97; I² = 0%) (Fig 8) stay. Five trials 15,21,23 (n = 744) reported data on complications. No significant difference was detected (RR, 0.94; 95% CI, 0.66-1.34; P = .74; P for heterogeneity = .66; I² = 0%) (Fig 9).

**Sensitivity Analyses and Publication Bias**

Tests for heterogeneity identified the trial by Rumbak et al8 as having outlying results. Exclusion of this trial resolved the heterogeneity, but did not change the results (short-term mortality: RR, 0.94; 95% CI, 0.77-1.15; P = .54; incidence of VAP: RR, 1.01; 95% CI, 0.89-1.14; P = .93; duration of MV: WMD, −1.84 days; 95% CI, −4.86-1.19; P = .23). For the meta-analysis of ET on short-term mortality, there was no evidence of significant publication bias by inspection of the funnel plot (Fig 10).

**Discussion**

Our meta-analysis suggested that ET did not significantly reduce short- or long-term mortality or incidence of VAP in critically ill patients. In addition, the

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**Table 2—Assessing Risk of Bias**

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Sequence Generation</th>
<th>Allocation Concealment</th>
<th>Blinding</th>
<th>Incomplete Outcome Data Addressed</th>
<th>Selective Outcome Reporting</th>
<th>Free of Other Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saffie et al0/2002</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Boudierka et al0/2004</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Rumbak et al0/2004</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Barquist et al0/2006</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Blot et al0/2008</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Terragni et al0/2010</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Trouillet et al0/2011</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Table 3—Summary of Results of Included Trials

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Patients, No.</th>
<th>Short-term Mortality, No. (%)</th>
<th>Pneumonia, No. (%)</th>
<th>Long-term Mortality, No.</th>
<th>Duration of MV, Mean ± SD</th>
<th>Duration of Sedation, Mean ± SD</th>
<th>Length of ICU Stay, Mean ± SD</th>
<th>Length of Hospital Stay, Mean ± SD</th>
<th>Complications, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ET</td>
<td>LT</td>
<td>ET</td>
<td>LT</td>
<td>ET</td>
<td>LT</td>
<td>ET</td>
<td>LT</td>
<td>ET</td>
</tr>
<tr>
<td>Saffle et al 2002</td>
<td>21</td>
<td>23</td>
<td>4 (19.0)</td>
<td>6 (26.1)</td>
<td>21 (100)</td>
<td>22 (95.7)</td>
<td>35.5 ± 20.62</td>
<td>31.4 ± 24.94</td>
<td>...</td>
</tr>
<tr>
<td>Bouderka et al 2004</td>
<td>31</td>
<td>31</td>
<td>12 (38.7)</td>
<td>7 (22.6)</td>
<td>18 (58.1)</td>
<td>19 (61.3)</td>
<td>...</td>
<td>...</td>
<td>14.5 ± 7.3</td>
</tr>
<tr>
<td>Rumbak et al 2004</td>
<td>60</td>
<td>60</td>
<td>19 (31.7)</td>
<td>37 (61.7)</td>
<td>3 (5.0)</td>
<td>15 (25.0)</td>
<td>...</td>
<td>...</td>
<td>7.6 ± 4.0</td>
</tr>
<tr>
<td>Barquist et al 2006</td>
<td>29</td>
<td>31</td>
<td>2 (6.9)</td>
<td>5 (16.1)</td>
<td>28 (96.6)</td>
<td>28 (90.3)</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Blot et al 2008</td>
<td>61</td>
<td>62</td>
<td>21 (34.4)</td>
<td>20 (32.3)</td>
<td>30 (49.2)</td>
<td>31 (50.0)</td>
<td>...</td>
<td>...</td>
<td>14(2-60)*</td>
</tr>
<tr>
<td>Terragni et al 2010</td>
<td>209</td>
<td>210</td>
<td>55 (26.3)</td>
<td>66 (31.4)</td>
<td>30 (14.4)</td>
<td>44 (21.0)</td>
<td>72/144</td>
<td>85/148</td>
<td>...</td>
</tr>
<tr>
<td>Trouillet et al 2011</td>
<td>109</td>
<td>107</td>
<td>33 (30.3)</td>
<td>32 (29.9)</td>
<td>50 (45.9)</td>
<td>47 (43.9)</td>
<td>12/76</td>
<td>17/75</td>
<td>17.9 ± 14.9</td>
</tr>
</tbody>
</table>

ET = early tracheotomy; LT = late tracheotomy. See Table 1 legend for expansion of other abbreviations.

*1-60 d duration, median (range), P = .64.

*Mean (interquartile range).
present study showed that ET was not associated with a markedly reduced duration of MV or sedation, shorter stay in ICU or hospital, or more complications.

Differences between the current meta-analysis and a previous one by Griffiths et al.\textsuperscript{13} should be noted. In their meta-analysis,\textsuperscript{13} five trials with a total of 406 patients were included, among which two trials were quasi-randomized, thereby producing a potential for selection bias. Because of the nature of the intervention of tracheotomy, physicians could not be blinded to the randomization arm. Therefore, true randomization adopted in assigning patients becomes a more crucial factor to warrant the internal validity of a trial. In our meta-analysis, the inclusion criteria were strictly restricted to RCTs, and thus seven RCTs with a total of 1,044 patients were finally included.

Our meta-analysis indicated that ET did not significantly shorten the duration of MV or length of ICU stay, which was different from the results of Griffiths et al.\textsuperscript{13} Among the included trials, only two\textsuperscript{4,21} reported a significantly shorter duration of MV in the ET group. However, Bouderka et al.\textsuperscript{21} did not describe their weaning methods, which raises concern about the validity of their finding of shorter MV with ET, because it was certainly possible that physicians were more aggressive in their weaning attempts once tracheotomy was performed.\textsuperscript{5} In the study by Rumbak et al.,\textsuperscript{4} although the weaning protocol was described, the mean duration of MV in the ET group exceeded the mean length of ICU stay, whereas it did not in the LT group, which might be because of earlier transfer out of the ICU, while still on MV. This earlier transition of patients in the ET group to a lower-level care area might cause a potential bias between the two groups. Therefore, based on the relatively high-quality trials included, our meta-analysis calls into question Griffiths et al’s\textsuperscript{13} findings of a shorter duration of MV and length of ICU stay with ET.

The anticipated benefits of tracheotomy included improved patient comfort due to reduced oropharyngeal and laryngeal stimulation, which might in turn shorten duration of sedation.\textsuperscript{25} In a retrospective study, Nieszkowska et al.\textsuperscript{26} first reported that

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>ET Events</th>
<th>Total</th>
<th>LT Events</th>
<th>Total</th>
<th>Risk Ratio M-H</th>
<th>Random, 95% CI</th>
<th>Risk Ratio M-H</th>
<th>Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barquist 2006</td>
<td>2</td>
<td>29</td>
<td>5</td>
<td>31</td>
<td>0.43 [0.09, 2.03]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blot 2008</td>
<td>21</td>
<td>61</td>
<td>20</td>
<td>62</td>
<td>1.07 [0.65, 1.76]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bouderka 2004</td>
<td>12</td>
<td>31</td>
<td>7</td>
<td>31</td>
<td>1.71 [0.78, 3.77]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rumbak 2004</td>
<td>19</td>
<td>60</td>
<td>37</td>
<td>60</td>
<td>0.51 [0.34, 0.78]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saffie 2002</td>
<td>4</td>
<td>21</td>
<td>6</td>
<td>23</td>
<td>0.73 [0.24, 2.23]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Terragni 2010</td>
<td>55</td>
<td>209</td>
<td>66</td>
<td>210</td>
<td>0.84 [0.62, 1.13]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trouillet 2011</td>
<td>33</td>
<td>109</td>
<td>32</td>
<td>107</td>
<td>1.01 [0.67, 1.52]</td>
<td></td>
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</tr>
<tr>
<td>Total (95% CI)</td>
<td>520</td>
<td></td>
<td>524</td>
<td>100.0%</td>
<td>0.86 [0.65, 1.13]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>146</td>
<td></td>
<td>173</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.06; Chi^2 = 10.85, df = 6 (P = 0.09); I^2 = 45%</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 1.09 (P = 0.28)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

FIGURE 2. Comparison of the short-term mortality between the ET group and the LT group. df = degrees of freedom; ET = early tracheotomy; LT = late tracheotomy; M-H = Mantel-Haenszel.

Figure 3. Comparison of the incidence of ventilator-associated pneumonia between the ET group and the LT group. See Figure 1 legend for expansion of abbreviations.

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tracheotomized mechanically ventilated patients required less IV sedative administration, spent less time heavily sedated, and achieved more autonomy earlier. However, another retrospective study, by Veelo et al,\textsuperscript{27} suggested that no reduction in sedation requirements was observed after tracheotomy. In the present study, pooled analysis did not indicate a statistically significant reduction in the duration of sedation ($P = .07$), although both trials\textsuperscript{4,23} demonstrated a significantly shorter duration of sedation in the ET group. To date, because of the limited number of RCTs investigating the outcome of duration of sedation, it is difficult to draw a firm conclusion about it.

Despite being a commonly performed procedure, tracheotomy is not risk free. In a retrospective study, Goldenberg et al\textsuperscript{28} reported a major complication rate of 4.3%, with 0.7% mortality, related to tracheotomy. In the present study, pooled analysis suggested no significant difference regarding complications between the ET group and the control group (RR, 0.94; 95% CI, 0.66-1.34; $P = .74$). Besides balancing the benefits and risks of tracheotomy, a major concern is the ability to identify early which patients require prolonged MV. This issue was highlighted by Terragni et al\textsuperscript{22} study showing that a significant number of patients (43.3%) in the LT group improved to the extent that tracheotomy was not required. There had been attempts to produce a formula to help identify which burn patients would require long-term ventilation.\textsuperscript{29} However, such a formula applicable to the general population had yet to be produced and validated.\textsuperscript{30}

So far, little is known about the long-term outcomes of ET. Among the included trials, Terragni et al\textsuperscript{22} reported that no difference was detected regarding
the need for a long-term care facility after hospital discharge (P = .92) or 1-year mortality (P = .25). Trouillet et al. reported no significant difference in activities of daily living (P = .52), anxiety (P = .87), depression (P = .45), posttraumatic stress disorder (P = .78), or mortality (P = .49) after a median follow-up of 873 days. Our pooled analysis also suggested no significant difference in long-term mortality (RR, 0.84; 95% CI, 0.68-1.04; P = .10). Therefore, RCTs powered to address the long-term costs related to ET are warranted in future.

The Intensive Care Society of the United Kingdom recently completed a large, multicenter, randomized trial, the TracMan trial (N = 909). The full TracMan results await publication but provisional results have been presented in a conference. Of note, the TracMan results presented were consistent with the findings of our meta-analysis.

There are several limitations to the present study. First, the geographic regions covered included North America (United States), Europe (France and Italy), and North Africa (Morocco). Therefore, our results limited generalizability to other regions (for example, Asia and Latin America). Second, there was considerable heterogeneity among the included trials. The targeted population varied greatly. The adopted definitions of ET and LT differed: ET from day 2 to day 8 after intubation; LT from day 14 to day 28 after intubation. Therefore, because of considerable heterogeneity, as well as the limited number of RCTs regarding some outcomes (eg, duration of MV and sedation, length of stay in ICU, and hospital), caution should be taken when interpreting the results. Finally, although there was no evidence of potential bias by inspection of the funnel plots, it is possible that RCTs not identified for this
review could have had an impact on the pooled effect estimates.

CONCLUSIONS

Our meta-analysis suggested that the timing of tracheotomy did not significantly alter important clinical outcomes in critically ill patients. A sensitive and validated formula to identify early those who need prolonged MV in the global increasing population of intubated critically ill patients is warranted. In addition, the duration of MV and sedation, as well as the long-term costs of ET in mechanically ventilated patients, should be evaluated in rigorously designed and adequately powered RCTs in the future.

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