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Benefits of early tracheotomy: a meta-analysis based on six observational studies

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The study was performed at the Emergency Department of Qilu Hospital, Shandong University, China.

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Background: Whether early tracheotomy can improve the clinical outcomes of critically ill patients remains controversial. The current study aimed to discuss the potential benefits of early tracheotomy compared to late tracheotomy with meta-analysis of observational researches. **Methods:** An electronic search (up to February 28, 2013) was conducted by a uniform requirement and then clinical data satisfying the predefined inclusion criteria were extracted. **Results**: Data from a total of 2037 subjects were included from six observational retrospective studies. Meta-analysis suggested that early-tracheotomy was associated with significant reductions in mortality (odds ratio [OR], 0.77; 95% confidence interval [CI], 0.62-0.96), duration of mechanical ventilation(MV) (mean difference: -10.04; 95% CI [-15.15, -4.92]), length of intensive care unit (ICU) stay (mean difference: -8.80; 95% CI [-9.71, -7.89]) and length of hospital stay (mean difference: -12.18; 95% CI [-18.25, -6.11]). However, as compared with late-tracheotomy, early-tracheotomy did not reduce the incidence of ventilation associated pneumonia. **Conclusions**: Our meta-analysis of retrospective observational studies suggests that early tracheotomy performed between days 3 and 7 after intubation had some advantages including decreased mortality, reduced length of ICU stay, length of hospital stay and MV duration in ICU patients.

Key words: tracheotomy, intensive care unit, critically ill patients, mechanical ventilation, meta-analysis

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Introduction

Tracheotomy was originally an usual procedure that was performed in only 6% of critically ill patients for the purpose of prolonged mechanical ventilation (MV) or airway surport.[1,2] The development of the percutaneous dilatation technique allowed physicians to perform tracheotomies at the bedside, rather than in an operating room, which dramatically increased the number performed.[3,4] There are several advantages associated with tracheotomy, such as efficient suction of secretion and easier nursing care, greater comfort and less sedation administration, smaller dead space and lower airway resistance, et al.[5,6,7] Complications relative to tracheotomy included stomal infection and hemorrhage, tracheal stenosis, and occasionally death due to innominate artery rupture.[7,8]

However, whether early tracheotomy is more advantageous than late tracheotomy or prolonged intubation remains controversial. In 1989, The National Association of Medical Directors of Respiratory Care has published a recommendation based solely on expert opinion that tracheotomy should be performed in patients who still required artificial ventilation 21 days after admission.[9] However, tracheotomy timing often depended on the physician's individual views, clinical conditions and the opinions of the patient's relatives. In a retrospective study conducted by Freeman that included 2473 patients, tracheotomy was performed after an average of 9 days of ventilatory support.[2] Meta-analyses published in recent years were mainly based on randomized control trials that did not find any major benefits of early tracheotomy, especially for mortality outcomes.[10-12]

Although some observational studies published in the past several decades have been designed as prospective cohort or retrospective case-control studies, these have not been included in larger analyses. Here, we aimed to systematically review available observational studies and perform a meta-analysis to investigate the relationships between tracheotomy timing and clinical outcomes of critically ill patients.

Methods

Search Source and Strategy

We performed an electronic search (up to February 28, 2013) using the following key words: [tracheotomy] AND [intensive care unit OR critically ill patients] with no restriction on subheadings. Relevant studies were identified by searching the following data sources: MEDLINE (Ovid), EMBASE, J-STAGE, the Cochrane Library (Cochrane Central Register of Controlled Trials), Global Health, International Pharmaceutical Abstracts, ISI Web of Science, the China National Knowledge Internet, and the grey literature (SIGLE) databases. The reference lists of all retrieved studies were checked for other potentially relevant citations.

Selection Criteria

Studies were included in the present meta-analysis if they met all the following criteria: (i) they assessed critically ill patients who were admitted to intensive care units (ICUs); (ii) they compared early tracheotomy (< 7 days) with late tracheotomy (≥7 days); (iii) they were written in English; and (iv) they included prospective or retrospective observational study design. We selected 7 days as a cutoff point because the median time from onset of MV to tracheotomy in most of observational studies was between 3 and 7 days. .Most of randomized control trials also selected <7 days as the cutoff point.[13]

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Quality Assessment and Data Extraction

The two authors (L.S. and P.H.) independently and blindly selected trials according to the inclusion criteria. The quality assessment was omitted. Next,, we extracted information from published reports using a standardized protocol and reporting form: study design, first author' family name, year of publication, number of enrolled patients, targeted population, original country, tracheotomy timing, and available endpoints. If there were several mortality endpoints, we selected those with longer follow-up results. For example, among ICU mortality, hospital mortality, 90-day mortality, 1-year mortality, we chose 1-year mortality as the final endpoint event. Duration of MV was measured as the time from translaryngeal intubation to weaning day/night or death, length of ICU stay was measured as time from admission/transfer to ICU to discharge from ICU or death, and hospital stay length was measured as the time from admission to hospital to discharge from hospital or death. Ventilation associated pneumonia (VAP) was defined using respective diagnosis criteria. Disagreement was resolved by discussion and arbitration by a third author (Yu-Guo Chen) if necessary.

Statistical Analysis

RevMan 5.0.25 software, developed by the Cochrane Collaboration (http://www.cc-ims.net/revman), was used for the meta-analysis. Heterogeneity between selected articles was tested with use of the inconsistency index (I^2) and chi-square tests. Statistically significant heterogeneity was considered present when a chi-square $P < 0.10$ and $I^2 > 50\%$. We applied the fixed-effects model when there was no statistically significant difference between the results and the random-effects model was applied when there was a significant difference.

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Publication bias was evaluated with using funnel plots and the fail-safe number (N_{fs}). Any calculated N_{fs} value smaller than the number of observed studies indicated a publication bias that might influence the meta-analysis results. We calculated the $N_{fs0.05}$ according to the following formula: $N_{fs0.05} = (\sum Z/1.64)^2 - k$, where k is the number of reports of studies included in the meta-analysis.

Results

A total of 11 observational studies about tracheotomy timing were identified through the electronic database search and four of them[14-17] were excluded because the data were not available. A study conducted by Scales and colleagues was also excluded because they selected 10 days as the cutoff.[18] Ultimately, six retrospective observational studies including 2037 subjects were pulled together, and the data extracted.[19-24] The detailed characteristics of subjects, and therapy information of the eligible studies are listed in Table 1.

We did not observe heterogeneity with regard to mortality or VAP outcomes (P=0.76, I^2=0%; P=0.40, I^2=0%), so a fixed-effects models were used to analyze these variables. However, heterogeneity was found in terms of MV duration, lengths of ICU and length of hospital stays, so random-effects models were employed for their analysis (P<0.00001, I^2=100%; P<0.00001, I^2=92%; P<0.00001, I^2=99%).

Clinical Endpoint Events

The risk of mortality, length of ICU stay, length of hospital stay and MV duration differed between the early tracheotomy groups and late tracheotomy group (Figures 1-4). Mortality events were reviewed for five trials.[19,20,22-24] The risk of mortality in the early tracheotomy group was significantly lower than that in late tracheotomy (26.1% vs. 29.8%, respectively; relative risk [RR] 0.77, 95% confidence interval [CI] (0.62-0.96); p=0.02; Figure 1). MV duration in four trials[20,21,23,24] was shorter in the early tracheotomy group than in the late tracheotomy group (mean difference: -10.04 days, 95% CI (-15.15, -4.92), p=0.0001; Figure 2). The length of ICU stay was included in five trials[19-21,23,24] and was shorter in the early tracheotomy group compared to the late group (mean difference: -8.8 days, 95% CI (-9.71, -7.89), p<0.00001; Figure 3). The length of hospital stay was described in five trials[19-21,23,24] and again it was shorter in the early tracheotomy group (mean difference: -12.18 days, 95% CI (-18.25, -6.11), p<0.00001; Figure 4). There was no significant difference in VAP prevalence between early and late tracheotomy groups in three trials (11.6% vs. 11.0%, respectively; Odds Ratio [OR] 0.71, 95% confidence interval [CI] (0.48-1.04); p=0.08; Figure 5).[21,23,24]

Publication Bias

We constructed a funnel plot to identify possible publication bias of the five trials in terms of mortality events (Figure 6). The funnel plot showed no publication bias for studies included in the meta-analysis in terms of mortality. We also calculated the $N_{fs0.05}$ for each endpoint event and found the $N_{fs0.05}$ values for length of ICU stay, length of hospital stay, MV duration,VAP and mortality were greater than the number of studies included in the meta-analysis.

Discussion

This was the first meta-analysis that pulled data from observational studies to assess the impact of tracheotomy timing on clinical outcomes of critically ill patients. The great discovery of this updating review was that patients that underwent early tracheotomy had a 12% lower

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mortality rate compared to those who underwent late tracheotomy. Conversely, previously published reviews[10-12] did not find any survival benefit with respect to early tracheotomy. Earlier reviews were all based on randomized controlled trials. Other retrospective analyses drew the same conclusions. In the study conducted by Freeman that included 43,916 critically ill patients, patients undergoing tracheotomy had a lower a mortality rate than nontracheotomy patients.[2] Scales and colleagues compared early (≤ 10days) and late (> 10days) tracheotomies in another retrospective study involving 10927 patients and found significant reductions for unadjusted 90-days, 1-year mortality and study mortality in early tracheotomy groups.[18] One might ask why well-designed, prospectively trials were unable to identify an effect on survival outcome. Firstly, it was difficult to distinguish the population of interest who really required prolonged intubation or MV and inclusion criteria were quite variable. In randomized controlled trial (RCT) research, it is possible that some low-risk patients who did not really need a tracheotomy eventually underwent the procedure, and the potential benefit of early tracheotomy may have been diluted.[25] Secondly, in the observational studies, judgment of tracheotomy performance depended on clinical team' discussions and individual opinions. Conversely, the selection of tracheotomy in retrospective studies reflected the real clinical status and perhaps critically ill patients in observational studies really needed the procedure when it was performed. Third, RCTs generally had small samples due to difficulties associated with implementing this type of study, whereas observational studies had larger samples and in the present analysis, a total of 2037 subjects were enrolled.

The present meta-analysis also found other advantages such as decreased MV duration,

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ICU length of stay and hospital length of stay, which was in accordance with conclusions from other meta-analysis based on RCTs.[10-12] Freeman et al. determined that tracheotomy timing correlated significantly with MV duration, ICU length of stay and hospital length of stay in a study where tracheotomy timing was considered as a consecutive parameter.[2] Therefore, the advantages of resources and time savings should be interpreted as a consensus. We found that early tracheotomy can shortened MV by about 10 days, which greatly reduces the need for nursing care and medical expenditures. The average cost of ICU patients requiring MV was $ 3968 per day according to research conducted by Dasta et al.[26] Therefore, the overall cost-saving of early tracheotomy compared with late tracheotomy could reach $ 40000 based on our finding of 10 days reduction of MV time. Reduction of ICU length of stay and hospital length of stay would also mean saving of ICU cost burden and medical resources.

With regard to VAP, neither our research based on observational studies nor meta-analyses based on RCTs found evidence that early tracheotomy can influence the rate of VAP. Other studies also failed to demonstrate timing of tracheotomy in relation to VAP.[27,28] However, we did observe a trend toward reduced VAP when tracheotomy was performed between days 3 and 7 (Odds Ratio [OR] 0.71, p=0.08). Whether even earlier tracheotomy (before day 3) would have additional benefits remained unclear.. In a study conducted by Rodriguez et al., patients who underwent tracheotomy within the first 48 hours had significantly decreased likelihoods of developing VAP.[29] It was difficult to interpret the controversial results of numerous studies because of varying definition of VAP. Several factors may explain the possible mechanisms of negative result. Performing a tracheotomy destroys the natural structure of the airway, which

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affects its ability to protect the respiratory system. For example, the cough reflex is greatly attenuated because the glottis is inactive.[30] In ICUs circumstance, frequent invasive handling or air contaminated with pathogenic microorganisms may counteract the benefits of tracheotomy such as pulmonary toilet or convenient nursing care.

This study has several limitations. The definition of mortality differed among studies, varying from ICU to 1-year mortality. The detailed VAP diagnostic criteria were not mentioned in all of the studies analyzed, and it was unclear whether VAP was diagnosed before or after tracheotomy.[21,23,24] With regard to MV duration, the lack of a uniform weaning protocol also confused the interpretation of the data. Finally, because the database was not suitable, posthospitalization events and resource expenditures could not be specifically examined.

Although the conclusions drawn from observational studies were less convincing comparing RCTs in evidence-based medicine, the benefits of early tracheotomy were obvious and critical care physicians should carefully consider them when encountering the optimal timing of tracheotomy. Based on our findings, we recommended that tracheotomy be performed between days 3 and 7 once the decision had been made.

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References

1. Durbin CG Jr. Tracheostomy: why, when, and how. Respir Care 2010;55(8):1056-1068.

2. Freeman BD, Borecki IB, Coopersmith CM, Buchman TG. Relationship between tracheostomy timing and duration of mechanical ventilation in critically ill patients. Crit Care Med 2005;33(11):2513-2520.

3. De Leyn P, Bedert L, Delcroix M, Depuydt P, Lauwers G, Sokolov Y, et al. Tracheotomy: clinical review and guidelines. Eur J Cardiothorac Surg 2007;32(3):412-421.

4. Cox CE, Carson SS, Holmes GM, Howard A, Carey TS. Increase in tracheostomy for prolonged mechanical ventilation in North Carolina, 1993-2002. Crit Care Med 2004;32(11):2219-2226.

5. Nieszkowska A, Combes A, Luyt CE, Ksibi H, Trouillet JL, Gibert C, Chastre J. Impact of tracheotomy on sedative administration, sedation level, and comfort of mechanically ventilated intensive care unit patients. Crit Care Med 2005;33(11):2527-2533.

6. Diehl JL, El AS, Touchard D, Lemaire F, Brochard L. Changes in the work of breathing induced by tracheotomy in ventilator-dependent patients. Am J Respir Crit Care Med 1999;159(2):383-388.

7. King C, Moores LK. Controversies in mechanical ventilation: when should a tracheotomy be placed. Clin Chest Med 2008;29(2):253-263, vi.

8. Shah RK, Lander L, Berry JG, Nussenbaum B, Merati A, Roberson DW. Tracheotomy outcomes and complications: a national perspective. Laryngoscope 2012;122(1):25-29.

RESPIRATORY CARE Paper in Press. Published on May 07, 2013 as DOI: 10.4187/respcare.02413

9. Plummer AL, Gracey DR. Consensus conference on artificial airways in patients receiving mechanicalventilation. Chest 1989;96(1):178-180.

10. Griffiths J, Barber VS, Morgan L, Young JD. Systematic review and meta-analysis of studies of the timing of tracheostomy inadult patients undergoing artificial ventilation. BMJ 2005;330(7502):1243.

11. Dunham CM, Ransom KJ. Assessment of early tracheostomy in trauma patients: a systematic review and meta-analysis. Am Surg 2006;72(3):276-281.

12. Wang F, Wu Y, Bo L, Lou J, Zhu J, Chen F, et al. The timing of tracheotomy in critically ill patients undergoing mechanical ventilation: a systematic review and meta-analysis of randomized controlled trials. Chest 2011;140(6):1456-1465.

13. Terragni PP, Antonelli M, Fumagalli R, Faggiano C, Berardino M, Pallavicini FB, et al. Early vs late tracheotomy for prevention of pneumonia in mechanically ventilated adult ICU patients: a randomized controlled trial. JAMA 2010;303(15):1483-1489.

14. Hsu CL, Chen KY, Chang CH, Jerng JS, Yu CJ, Yang PC. Timing of tracheostomy as a determinant of weaning success in critically ill patients: a retrospective study. Crit Care 2005;9(1):R46-52.

15. Combes A, Luyt CE, Nieszkowska A, Trouillet JL, Gibert C, Chastre J. Is tracheostomy associated with better outcomes for patients requiring long-term mechanical ventilation. Crit Care Med 2007;35(3):802-807.

16. Clec'h C, Alberti C, Vincent F, Garrouste-Orgeas M, de Lassence A, Toledano D, et al. Tracheostomy does not improve the outcome of patients requiring prolonged mechanical

ventilation: a propensity analysis. Crit Care Med 2007;35(1):132-138.

17. Arabi YM, Alhashemi JA, Tamim HM, Esteban A, Haddad SH, Dawood A, et al. The impact of time to tracheostomy on mechanical ventilation duration, length of stay, and mortality in intensive care unit patients. J Crit Care 2009;24(3):435-440.

18. Scales DC, Thiruchelvam D, Kiss A, Redelmeier DA. The effect of tracheostomy timing during critical illness on long-term survival. Crit Care Med 2008;36(9):2547-2557.

19. Armstrong PA, McCarthy MC, Peoples JB. Reduced use of resources by early tracheostomy in ventilator-dependent patients with blunt trauma. Surgery 1998;124(4):763-766; discussion 766-767.

20. Arabi Y, Haddad S, Shirawi N, Al SA. Early tracheostomy in intensive care trauma patients improves resource utilization: a cohort study and literature review. Crit Care 2004;8(5):R347-352.

21. Moller MG, Slaikeu JD, Bonelli P, Davis AT, Hoogeboom JE, Bonnell BW. Early tracheostomy versus late tracheostomy in the surgical intensive care unit. Am J Surg 2005;189(3):293-296.

22. Flaatten H, Gjerde S, Heimdal JH, Aardal S. The effect of tracheostomy on outcome in intensive care unit patients. Acta Anaesthesiol Scand 2006;50(1):92-98.

23. Zagli G, Linden M, Spina R, Bonizzoli M, Cianchi G, Anichini V, et al. Early tracheostomy in intensive care unit: a retrospective study of 506 cases of video-guided Ciaglia Blue Rhino tracheostomies. J Trauma 2010;68(2):367-372.

24. Tong CC, Kleinberger AJ, Paolino J, Altman KW. Tracheotomy timing and outcomes in

the critically ill. Otolaryngol Head Neck Surg 2012;147(1):44-51.

25. Veelo DP, Gajic O, Schultz MJ. Benefits of early tracheotomy: underpowered or overestimated. Intensive Care Med 2008;34(12):2309; author reply 2310-2311.

26. Dasta JF, McLaughlin TP, Mody SH, Piech CT. Daily cost of an intensive care unit day: the contribution of mechanical ventilation. Crit Care Med 2005;33(6):1266-1271.

27. Carrilho CM, Grion CM, Bonametti AM, Medeiros EA, Matsuo T. Multivariate analysis of the factors associated with the risk of pneumonia in intensive care units. Braz J Infect Dis 2007;11(3):339-344.

28. Apostolopoulou E, Bakakos P, Katostaras T, Gregorakos L. Incidence and risk factors for ventilator-associated pneumonia in 4 multidisciplinary intensive care units in Athens, Greece. Respir Care 2003;48(7):681-688.

29. Rodriguez JL, Steinberg SM, Luchetti FA, Gibbons KJ, Taheri PA, Flint LM. Early tracheostomy for primary airway management in the surgical critical care setting. Surgery 1990;108(4):655-659.

30. Boitano LJ. Management of airway clearance in neuromuscular disease. Respir Care 2006;51(8):913-922; discussion 922-924.

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Figure Legends

Figure 1. Meta-analysis of five observational studies estimating the impact of early tracheotomy on mortality event compared late tracheotomy. CI, confidence interval; RCT, randomized controlled trial; M-H, Mantel-Haenszel.

Figure 2. Meta-analysis of four observational studies estimating the impact of early tracheotomy on duration of mechanical ventilation compared to late tracheotomy. CI, confidence interval; RCT, randomized controlled trial; IV: inverse variance.

Figure 3. Meta-analysis of five observational studies estimating the impact of early tracheotomy on ICU stay length compared to late tracheotomy. CI, confidence interval; RCT, randomized controlled trial; .IV: inverse variance.

Figure 4. Meta-analysis of five observational studies estimating the impact of early tracheotomy on hospital stay length compared to late tracheotomy. CI, confidence interval; RCT, randomized controlled trial; IV: inverse variance.

Figure 5. Meta-analysis of three observational studies estimating the impact of early tracheotomy on VAP compared to late tracheotomy. CI, confidence interval; RCT, randomized controlled trial, VAP, ventilation associated pneumonia; M-H, Mantel-Haenszel.

Figure 6. Funnel plot of of publication bias in terms of mortality.

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Table 1 Chief characteristics of studies included in the Meta-analysis

study	Armstrong et al.[19]	Arabi et al.[20]	Moller et al.[21]	Flaatten et al.[22]	Zagli et al.[23]	Tong et al.[24]
Year of publication	1998	2004	2005	2006	2010	2012
Country	USA	Saudi Arabia	USA	Norway	Italy	USA
Study design	Single-certer retrospective	Single-certer retrospective	Multi-center retrospective	Single-certer retrospective	Single-certer retrospective	Single-certer retrospective
Number of cases	157	136	185	461	506	592
Mean age,years	39	31	52	53	55	68
Men, n(%)	75	91	62	NA	71	52
Timing of tracheotomy						
Early	< 6 days	<7 days	<7 days	< 6 days	⩽3 days	< day 7
Late	⩾7 days	>7 days	>7 days	> 6 days	>3 days	> 7 day
Study population	ventilator-dependent trauma patients	Trauma ICU patients	Surgical ICU patients	ICU patients	Emergency ICU patients requiring MV	nontrauma ICU patients
Available end-points	ICU/hospital LOS, Mortality	DMV, ICU/hospital LOS, Mortality	ICU and hospital LOS, DMV, VAP	DMV, ICU/hospital LOS, Mortality	VAP, DMV, ICU/hospital LOS, Mortality	DMV, ICU/hospital LOS,Mortality,VAP
Type of tracheotomy	open surgery	PDT	PDT or open surgery	PDT or open surgery	PDT	open surgery

EI: endotracheal intubation; MV: mechanical ventilation; LTC: laryngeal and tracheal complication; LOS: length of stay; DMV: Duration of MV; VAP: ventilator- associated pneumonia; NA: not available; PDT: percutaneous dilational tracheotomy; VFD: ventilator-free days; ICU: intensive care unit

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	early-tracheotomy		late-tracheotomy			Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year
Armstrong et al.	7	62	11	95	4.3%	0.97 [0.36, 2.66]	1998
Arabi et al.	5	29	15	107	3.0%	1.28 [0.42, 3.87]	2004
Flaatten et al.	78	230	94	231	34.6%	0.75 [0.51, 1.09]	2006
Zagli et al.	63	256	72	250	30.7%	0.81 [0.54, 1.20]	2010
Tong et al.	31	128	150	464	27.5%	0.67 [0.43, 1.05]	2012
Total (95% CI)		**705**		**1147**	**100.0%**	**0.77 [0.62, 0.96]**	
Total events	184		342				

Heterogeneity: Chi² = 1.46, df = 4 (P = 0.83); I² = 0%
Test for overall effect: Z = 2.31 (P = 0.02)

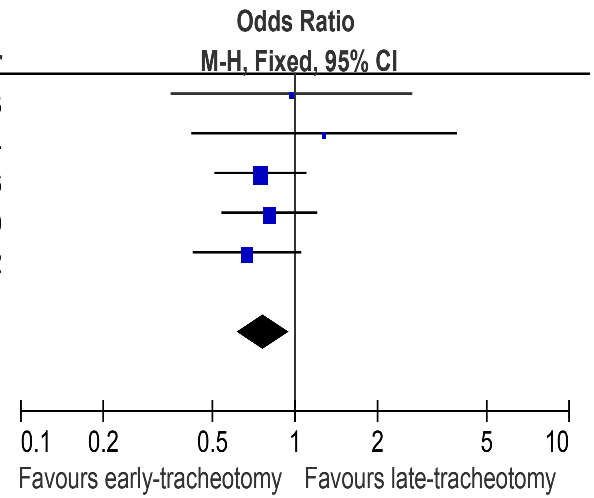

Figure 1.

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	early-tracheotomy			late-tracheotomy				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Arabi et al.	9.6	1.2	29	18.7	1.3	107	25.1%	-9.10 [-9.60, -8.60]	2004
Moller et al.	12.2	0.9	81	21.9	1.3	104	25.1%	-9.70 [-10.02, -9.38]	2005
Zagli et al.	13.3	9.6	256	16.7	8.3	250	24.6%	-3.40 [-4.96, -1.84]	2010
Tong et al.	21.5	1.86	128	39.3	1.3	464	25.1%	-17.80 [-18.14, -17.46]	2012
Total (95% CI)			**494**			**925**	**100.0%**	**-10.04 [-15.15, -4.92]**	

Heterogeneity: $Tau^2 = 27.05$; $Chi^2 = 1521.45$, $df = 3$ ($P < 0.00001$); $I^2 = 100\%$

Test for overall effect: $Z = 3.85$ ($P = 0.0001$)

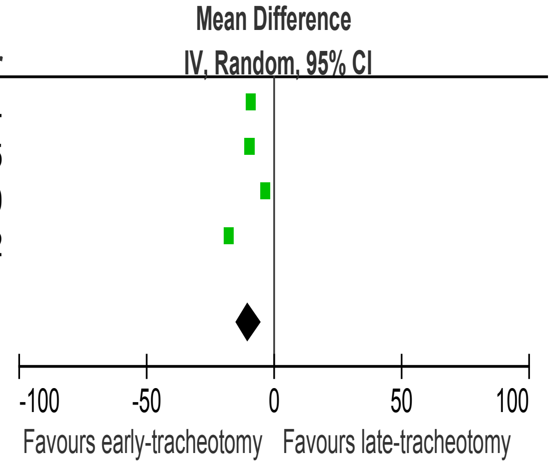

Figure 2.

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	Experimental			Control				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Armstrong et al.	15	12	62	29	26	95	2.1%	-14.00 [-20.02, -7.98]	1998
Arabi et al.	10.9	1.2	29	21	1.3	104	27.4%	-10.10 [-10.60, -9.60]	2004
Moller et al.	16.7	1	81	26	1.3	104	28.8%	-9.30 [-9.63, -8.97]	2005
Zagli et al.	16.9	13.1	256	20.8	9.2	250	12.4%	-3.90 [-5.87, -1.93]	2010
Tong et al.	17.5	1.4	128	26.3	0.7	464	29.3%	-8.80 [-9.05, -8.55]	2012
Total (95% CI)			**556**			**1017**	**100.0%**	**-8.80 [-9.71, -7.89]**	

Heterogeneity: Tau² = 0.72; Chi² = 51.41, df = 4 (P < 0.00001); I² = 92%

Test for overall effect: Z = 19.00 (P < 0.00001)

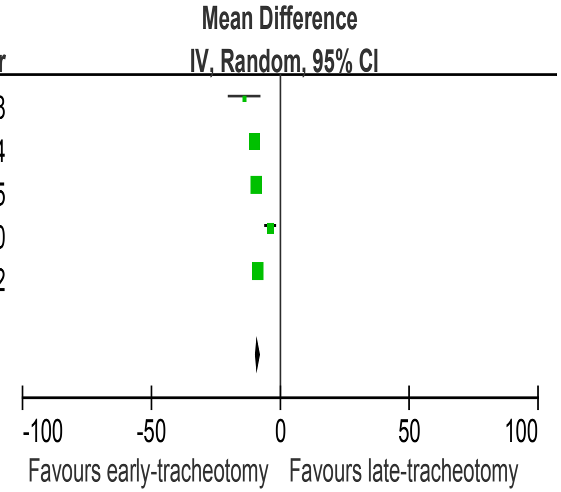

Figure 3.

	early-tracheotomy			late-tracheotomy				Mean Difference		Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**	**IV, Random, 95% CI**
Armstrong et al.	33	24	62	68	48	95	13.0%	-35.00 [-46.35, -23.65]	1998	
Arabi et al.	101	19	29	105	7	107	18.1%	-4.00 [-11.04, 3.04]	2004	
Moller et al.	23.8	1.2	81	33.4	1.7	104	23.8%	-9.60 [-10.02, -9.18]	2005	
Zagli et al.	41.5	26.6	256	42.6	23.1	250	21.3%	-1.10 [-5.44, 3.24]	2010	
Tong et al.	35.9	2.6	128	54.3	1.6	464	23.8%	-18.40 [-18.87, -17.93]	2012	
Total (95% CI)			**556**			**1020**	**100.0%**	**-12.18 [-18.25, -6.11]**		

Heterogeneity: Tau² = 40.23; Chi² = 797.14, df = 4 (P < 0.00001); I² = 99%

Test for overall effect: Z = 3.93 (P < 0.0001)

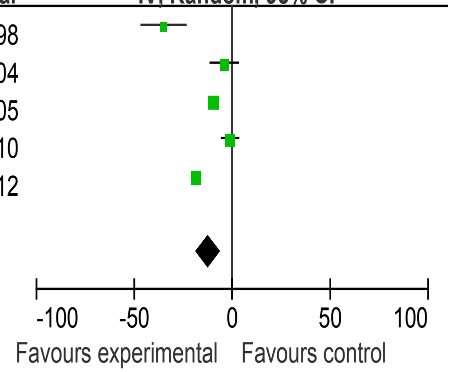

Figure 4.

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	early-tracheotomy		late-tracheotomy			Odds Ratio		Odds Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**	**Year**	**M-H, Fixed, 95% CI**
Moller et al.	22	81	44	104	45.1%	0.51 [0.27, 0.95]	2005	
Zagli et al.	29	256	31	250	44.7%	0.90 [0.53, 1.55]	2010	
Tong et al.	3	128	15	464	10.2%	0.72 [0.20, 2.52]	2012	
Total (95% CI)		**465**		**818**	**100.0%**	**0.71 [0.48, 1.04]**		
Total events	54		90					

Heterogeneity: Chi² = 1.86, df = 2 (P = 0.40); I² = 0%

Test for overall effect: Z = 1.77 (P = 0.08)

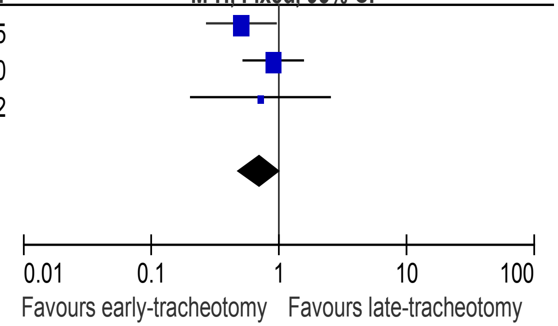

Figure 5.

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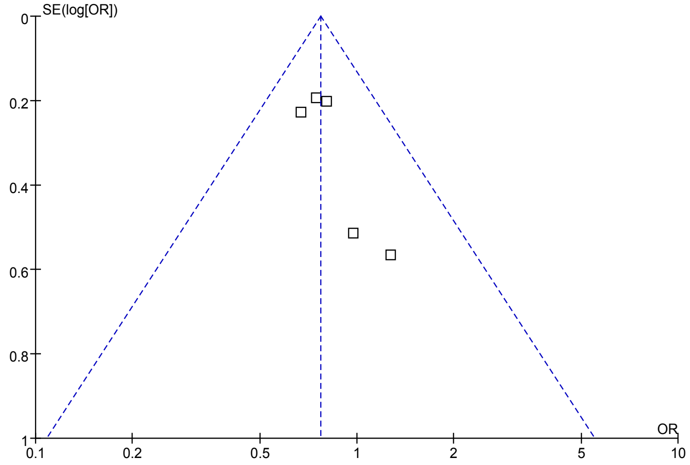

Figure 6.