

Original Article

Tracheostomy in critically ill Chinese patients: propensity score matching analysis to determine indication and timing

Minjie Ju^{1*}, Hongyu He^{1*}, Yijun Zheng^{1*}, Guowei Tu¹, Lizheng Xuan¹, Jiefei Ma¹, Jianfeng Luo², Duming Zhu¹, Zhe Luo¹, Jing Cang¹

¹Department of Anesthesiology and Intensive Care Unit, Zhongshan Hospital, Fudan University, 136 Yi Xue Yuan Road, Shanghai 200032, P. R. China; ²Department of Health Statistics and Social Medicine, School of Public Health, Fudan University, 138 Yi Xue Yuan Road, Shanghai 200032, P. R. China. *Equal contributors.

Received December 14, 2016; Accepted March 16, 2017; Epub May 15, 2017; Published May 30, 2017

Abstract: Correlation between tracheostomy and intensive care unit (ICU) patient mortality is ambiguous. This retrospective study determined the impact of tracheostomy on outcomes in Chinese ICU patients (n = 377) assigned to intubation (Group I; n = 289) or tracheostomy (Group II; n = 88) groups. Survival analysis was performed using Cox regression, and propensity score matching (PSM) and stratified analyses identified confounding factors. Group II patients had higher Acute Physiologic and Chronic Health Evaluation (APACHE) II scores and comprised more medical and emergency patients. Tracheostomy improved ICU survival ($P < 0.001$), especially in patients with higher APACHE II scores (≥ 17) and prolonged mechanical ventilation (MV) time (≥ 4 days). Tracheostomy survival benefit was verified in the PSM cohort. Tracheostomy patients had prolonged MV time, prolonged ICU and hospital length of stay (LOS_{ICU}/LOS_{HOS}), and greater medical expenses. In the prolonged MV subgroup, tracheostomy reduced daily hospital and ICU-to-hospital ratio expenses. Although early tracheostomy had no survival benefit, it liberated patients from MV earlier and reduced LOS_{ICU}/LOS_{HOS} . Tracheostomy should be individualized. In patients with higher APACHE II score and ventilation ≥ 4 days, tracheostomy benefits survival and should be carried out early, but not within the first 4 MV days.

Keywords: Tracheostomy, outcome, propensity score matching analysis, indication, timing

Introduction

Advances in treating critical illness have resulted in more patients requiring prolonged airway intubation and respiratory support. Consequently, tracheostomy has become a common procedure within the intensive care unit (ICU) for patients requiring long-term mechanical ventilation (MV) [1]. Tracheostomy offers the potential benefits of improved patient comfort, the ability to communicate, the opportunity for oral feeding, and easier and safer nursing care. Additionally, there is less of a need for sedation, and lower airway resistance may facilitate the weaning process and shorten ICU and hospital stay [2, 3]. Furthermore, by preventing microaspiration of secretions, tracheostomy may reduce ventilator-associated pneumonia [4, 5]. However, these benefits have not been confirmed in other studies [6, 7].

Despite increased application of the percutaneous approach [8-10], procedural complications such as stomal infection, pneumothorax, hemorrhage, and tracheal stenosis, continue to influence patient outcome [9]. Moreover, whether tracheostomy improves patient outcome or only transfers mortality from the ICU to the ward remains controversial [11]. Data from several studies suggest that tracheostomy may improve outcomes in patients requiring prolonged MV [12, 13], although others have failed to identify any improved outcomes associated with tracheostomy [14-20].

The absence of generally accepted guidelines [21] may explain these discrepancies. For instance, timing is a key criterion for performing a tracheostomy [22, 23]. However, the survival benefit of early tracheostomy (ET) compared to late tracheostomy (LT) has not been confirmed

until now [19, 24-28]. In addition, there is no uniformity in the literature for the definition of ET [23, 29, 30]. Moreover, different physiological and pathological statuses, such as age and primary disease [4, 20], may also contribute to the decision making or clinical outcome of tracheostomy [5]. On the other hand, the tracheostomy patient cohort is among the most resource-intensive to provide care for [31]. This increased resource expenditure may also relate to clinical practice, especially in developing countries such as China that have limited health care resources and intensivists [32].

It is therefore essential to clarify the relationship between tracheostomy and clinical outcome in critically ill patients in China. However, the lack of obvious signs or an acceptable gold standard for detection of patients requiring tracheostomy [5] has led to selection bias in previous randomized clinical trials. Hence, we carried out this study in a tertiary ICU based on retrospectively collected ICU data, using propensity score matching (PSM) to balance the selection bias between subgroups. The main goal was to explore the relationship between tracheostomy and 28-day ICU survival. Secondary end-points included the duration of MV and length of hospital/ICU stay (LOS_{HOS}/LOS_{ICU}), and medical costs.

Materials and methods

Patient data

From May 1 2011 to December 30 2012, we enrolled 377 consecutive patients who received MV over 12 hours [33]. All patients gave informed consent. This study was approved by the Ethics Committee of Zhongshan Hospital (No. B2016-025). Patients were followed-up until they were successfully weaned from MV, were discharged from the hospital, or had died. All available clinical, physiological, and outcome data were collected for evaluation (see [Additional File 1](#)).

Decision making for tracheostomy

MV indication was selected from a predefined list of categories (see [Additional File 2](#)). The decision to perform tracheostomy and when to perform the procedure was at the discretion of the attending intensivist and was typically adapted to each patient with respect to

patient preference, expected recovery course, risk of continued translaryngeal intubation, and surgical risks of the procedure. Medical indications for tracheostomy included failure of extubation, upper airway obstruction (UAO), airway protection and access for secretion removal, and avoidance of serious oropharyngeal and laryngeal injury from prolonged translaryngeal intubation. Since data were extracted retrospectively from the general ICU database, the decision to perform tracheostomy was not influenced by the study. All tracheostomies were performed at the bedside by experienced intensivists employing a percutaneous dilational technique.

Study design and statistics

Data were analyzed using SPSS 15.0 software (SPSS, Chicago, IL, US). Normal data distribution was assessed by the Kolmogorov-Smirnov test. Continuous variables were expressed as the mean \pm standard deviation (SD) or the median and full range, if normally distributed. Categorical variables were expressed as a numeral and percentage. Comparisons of continuous variables were performed using the Mann-Whitney U test and Wilcoxon test, whereas the chi-square test or Fisher's exact test was applied for categorical variables. Survival curves were estimated using the Kaplan-Meier method and compared using the Log-rank test. The Cox regression model was performed for univariate and multivariate analyses. Because of an imbalance in baseline characteristics, we carried out PSM (see [Additional File 3](#)). *P* values < 0.05 (2-tailed) were considered statistically significant.

Results

Basic clinical data

Of a total of 377 patient cases, 289 were ventilated using an endotracheal tube (Group I) and 88 were tracheotomized (Group II). The mean age was 63 years and 260 patients were male (**Table 1**). The majority of patients ($n = 345$, 91.5%) in the ICU were admitted postoperatively or underwent surgery during their ICU stay. The emergency admission rate was 56.2% ($n = 212$). The median LOS_{HOS} was 22 days and the median LOS_{ICU} was 86 hours. The crude and 28-day ICU mortality rates were 23.9% (90/377) and 20.7% (78/377), respectively. The

Propensity score matching analysis to determine tracheostomy indication and timing

Table 1. Patient baseline characteristics

	Total patients	Total cohort		P	PSM cohort		P	
		Intubation (Group I) (289)	Traceotomy (Group II) (88)		Intubation (Group I') (100)	Traceotomy (Group II') (84)		
Age (year, mean)		63	62	70	< 0.001 [‡]	67	70	0.194 [‡]
Gender (n)	Male	260	190	70	0.014 [†]	76	68	0.417 [†]
	Female	117	99	18		24	16	
Medical insurance (n)	No	202	162	40	0.081 [†]	47	38	0.811 [†]
	Yes	175	127	48		53	46	
APACHE II score (mean)		17	16	22	< 0.001 [‡]	20	22	0.062 [‡]
Surgery (n)	No	32	20	12	0.048 [†]	14	12	0.956 [†]
	Yes	345	269	76		86	72	
ICU readmission (n)	No	338	272	66	< 0.001 [*]	87	64	0.177 [*]
	Second	32	16	16		12	14	
	Third	4	1	3		1	3	
	Fourth	2	0	2		0	2	
	Fifth	1	0	1		0	1	
Emergency (n)	No	165	140	25	0.001 [†]	30	24	0.832 [†]
	Yes	212	149	63		70	60	
Blood transfusion (n)	No	236	197	39	< 0.001 [†]	45	36	0.771 [†]
	Yes	141	92	49		55	48	
Primary diseases (n)	Thoracic	63	48	15	0.004 [†]	18	14	0.488 [†]
	General surgery	84	69	15		26	15	
	Neurosurgery	127	105	22		18	21	
	Cardiovascular surgery	25	19	6		7	5	
	Orthopedics	40	28	12		17	11	
	Others	38	20	18		14	18	
Time for MV (mean, hours)			58.5	303.3	< 0.001 [‡]	69.6	307.06	< 0.001 [‡]
Time for MV (mean, hours) early vs. late traceotomy)				210.9 419.3	0.001		214.8 384.1	0.015
LOS _{hos} (median, day)		22	27	120	0.001 [‡]	22	123	0.001 [‡]
LOS _{icu} (median, hour)		86	106	530	< 0.001 [‡]	150	552	< 0.001 [‡]
Hospital expenses (mean, CNY)		129,111.3	76,142.9	303,064.4	< 0.001 [‡]	94,952.3	309,178.3	< 0.001 [‡]
ICU expenses (mean, CNY)		42,776.9	24,895.6	101,094.4	< 0.001 [‡]	35,010.2	104,806.3	< 0.001 [‡]
Daily hospital cost (mean, CNY)		4,791.6	4,832.5	4,657.3	0.879 [‡]	5,911.8	4,752.1	0.337 [‡]
ICU cost per hour (mean, CNY)		269.8	275.5	251.2	0.348 [‡]	321.5	246.5	0.010 [‡]
ICU to hospital expenses (mean, %)		.36	.33	.44	0.001 [‡]	.44	.46	0.638 [‡]

*Fisher's Exact Test; †chi-square test; ‡Mann-Whitney U test. APACHE II, Acute Physiologic and Chronic Health Evaluation II; MV, Mechanical ventilation, ICU, Intensive care unit; LOS_{hos}, Length of stay in the hospital; LOS_{icu}, Length of stay in the ICU.

Propensity score matching analysis to determine tracheostomy indication and timing

Table 2. Clinical characteristics of prolonged and short-term MV patients

		Prolonged MV patients		P	Short-term MV patients		P
		Intubation (57)	Tracheotomy (76)		Intubation (232)	Tracheotomy (12)	
Age (year, mean)		63	70	0.019 [‡]	61	67	0.121 [‡]
Gender (n)	Male	48	61	0.558 [†]	142	9	0.383 [†]
	Female	9	15		90	3	
Medical insurance (n)	No	31	32	0.160 [†]	131	8	0.486 [†]
	Yes	26	44		101	4	
APACHE II score (mean)		21	22	0.155 [‡]	14	19	0.003 [‡]
Surgery (n)	No	8	12	0.779 [†]	12	0	†
	Yes	49	64		220	12	
ICU readmission (n)	No	50	56	0.287 [*]	222	10	0.143 [*]
	Second	6	14		10	2	
	Third	1	3		0	0	
	Fourth	0	2		0	0	
	Fifth	0	1		0	0	
Emergency (n)	No	22	23	0.315 [†]	118	2	0.021 [†]
	Yes	35	53		114	10	
Blood transfusion (n)	No	31	33	0.210 [†]	166	6	0.190 [*]
	Yes	26	43		66	6	
Primary diseases (n)	Thoracic	16	14	0.394 [*]	32	1	0.097 [*]
	General surgery	15	13		54	2	
	Neurosurgery	9	17		96	5	
	Cardiovascular surgery	4	6		15	0	
	Orthopedics	4	11		24	1	
	Others	9	15		11	3	
Time for MV (mean, hours)		182	344	< 0.001 [‡]	28	47	< 0.001 [‡]
LOS _{HOS} (median, day)		25	129	0.001 [‡]	28	66	0.025 [‡]
LOS _{ICU} (median, hour)		254	594	0.004 [‡]	69	122	< 0.001 [‡]
Hospital expenses (mean, CNY)		144,439.5	202,491.7	0.268 [‡]	99,544.6	163,181.7	0.092 [‡]
ICU expenses (mean, CNY)		47,698.4	51,266.102	0.739 [‡]	39,151.1	36,139.441	0.960 [‡]
Daily hospital cost (mean, CNY)		6,058.69	4,249.38	0.048 [‡]	4,531.20	7,240.50	0.602 [‡]
ICU cost per hour (mean, CNY)		259.78	225.11	0.119 [‡]	279.28	416.62	0.333 [‡]
ICU to hospital expenses (mean, %)		0.58	0.47	0.028 [‡]	0.27	0.30	0.234 [‡]

^{*}Fisher's Exact Test; [†]chi-square test; [‡]Mann-Whitney U test. APACHE II, Acute Physiologic and Chronic Health Evaluation II; MV, Mechanical ventilation, ICU, Intensive care unit; LOS_{HOS}, Length of stay in the hospital; LOS_{ICU}, Length of stay in the ICU.

mean admission APACHE II score was 17. An APACHE II score ≥ 17 was designated as the high score subgroup and an APACHE II score ≤ 16 as the low score subgroup.

Comparison between Group I and II patients

Comparisons between Group I and II demonstrated that the ratios of emergency admissions (51.6% vs. 71.6%), medical patients (6.9% vs. 13.6%), APACHE II scores (16 vs. 22), mean age (62 vs. 70 years), male/female ratio (190/99 vs. 70/18), blood transfusion ratio (92/289 vs. 49/88), and distribution of primary disease were significantly different, respectively (**Table 1**). In addition, Group II patients had a greater likelihood of ICU readmission compared with Group I patients (22/88 vs. 17/289, respec-

tively; $P < 0.001$). In Group II compared with Group I, LOS_{HOS} (median, 120 vs. 27 days, respectively; $P = 0.001$), LOS_{ICU} (median, 530 vs. 106 hours, respectively; $P < 0.001$) and total MV duration (mean, 303.3 vs. 58.5 hours, respectively; $P < 0.001$) were significantly longer. Furthermore, hospital and ICU expenses were significantly higher in Group II compared with Group I patients (Chinese Yuan Renminbi (CNY) 303,064.4 vs. 76,142.9, $P < 0.001$; CNY 101,094.4 vs. 24,895.6, $P < 0.001$, respectively), and the ICU/hospital cost ratio rose significantly from 33% in Group I patients to 44% in Group II patients ($P < 0.001$). However, the daily hospital cost and ICU cost per hour were not significantly different between Group I and II patients (CNY 4,832.5 vs. 4,657.3, $P = 0.879$; CNY 251.2 vs. 275.5, $P = 0.348$; respectively).

Propensity score matching analysis to determine tracheostomy indication and timing

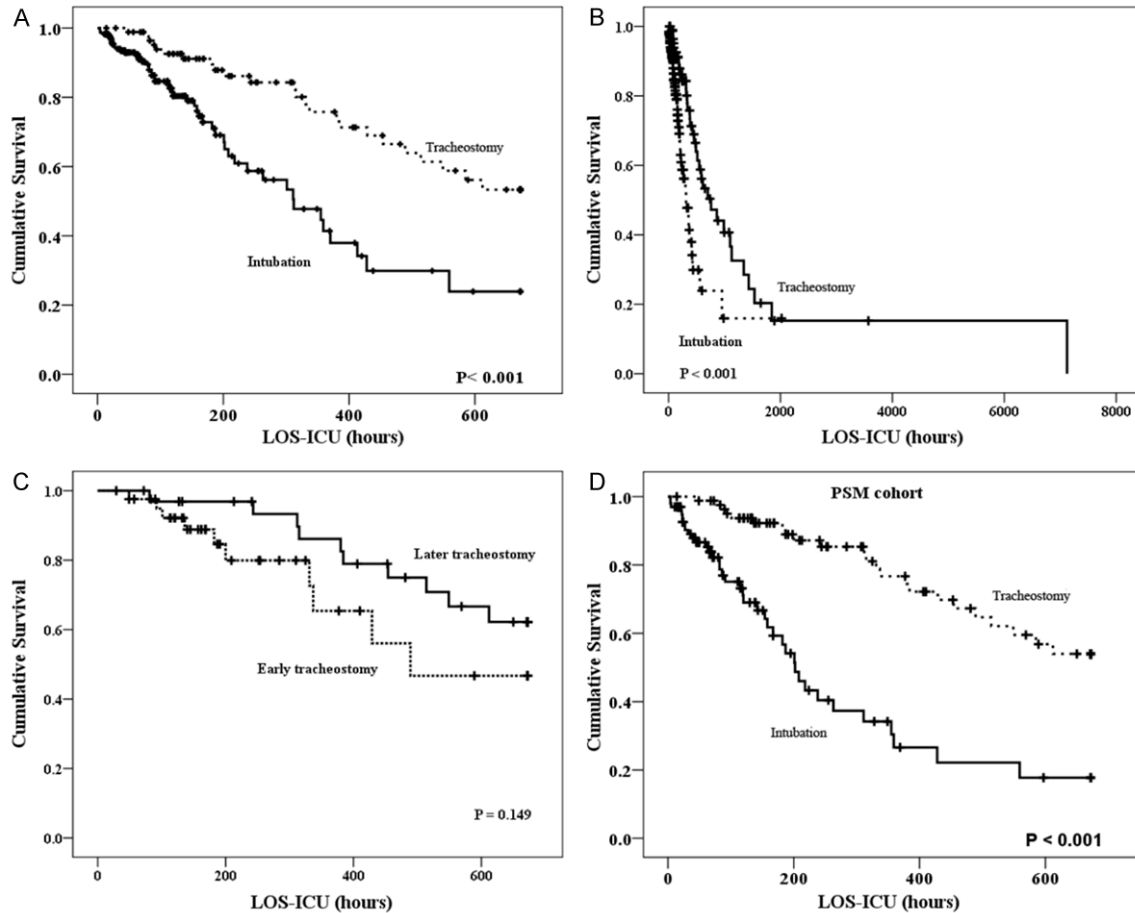


Figure 1. Compared to intubation, tracheostomy resulted in a better 28-day ICU survival (HR 0.356, 95% CI 0.213-0.597, $P < 0.001$) (A) and crude ICU survival (HR 0.409, 95% CI 0.255-0.656, $P < 0.001$) (B) following univariate survival analyses. Compared to LT, ET did not influence 28-day ICU survival (HR 0.513, 95% CI 0.207-1.269, $P = 0.149$) (C). In the PSM cohort, tracheostomy was related to increased 28-day ICU survival (D).

Comparisons according to MV time

For Group II patients, mean MV time before tracheostomy was 20.01 ± 51.65 hours, which positively correlated to total MV time (Spearman $r = 0.514$, $P < 0.001$). Consequently, ET ($n = 41$, tracheostomy within 4 days after endotracheal intubation [24]) was associated with shorter total MV time compared with LT ($n = 47$, tracheostomy > 4 days after endotracheal intubation) (mean, 210.9 vs. 419.3 hours, respectively; $P = 0.001$). The MV time before tracheostomy was also associated with LOS_{HOS} (Spearman $r = 0.428$, $P < 0.001$) and LOS_{ICU} (Spearman $r = 0.514$, $P < 0.001$).

Furthermore, the whole cohort was divided into short-term (< 4 days) and prolonged MV (≥ 4 days) subgroups. In the prolonged MV sub-

group, the major baseline characteristics were evenly distributed between patients with endotracheal intubation and patients with tracheostomy (**Table 2**). In the prolonged MV subgroup, patients with tracheostomy had a longer MV time, LOS_{HOS} , and LOS_{ICU} than patients with endotracheal intubation (**Table 2**). Although there were no significant differences in hospital and ICU expenses between groups, patients with tracheostomy were associated with lower daily hospital costs compared with patients with endotracheal intubation (CNY 4,249.38 vs. 6,058.69, respectively; $P = 0.048$), ICU cost per hour (CNY 225.11 vs. 259.78, respectively; $P = 0.119$), and ICU-to-hospital expenses (0.47 vs. 0.58, respectively; $P = 0.028$). In the short-term MV subgroup, patients with tracheostomy had higher admission APACHE II scores and emergency admission rates when compared

Propensity score matching analysis to determine tracheostomy indication and timing

Table 3. Survival analyses

	Total Cohort				PSM Cohort			
	95.0% CI for HR				95.0% CI for HR			
	P*	HR	Lower	Upper	P*	HR	Lower	Upper
Univariate Survival Analysis								
MV Mechanical Ventilation (Tracheotomy/Intubation)	<0.001	0.356	0.213	0.597	<0.001	0.248	0.145	0.424
Multivariate Survival Analysis								
MV (Tracheotomy/Intubation)	<0.001	0.188	0.107	0.330	<0.001	0.178	0.101	0.315
Times of intubation (n)	0.819	1.048	0.702	1.565	0.987	0.997	0.655	1.517
MV time before tracheotomy (hours)	0.468	0.998	0.993	1.003	0.421	0.998	0.996	1.007
Emergency (No/Yes)	0.518	0.851	0.521	1.389	0.654	0.870	0.475	1.596
Insurance (No/Yes)	0.226	1.367	0.824	2.268	0.313	1.352	0.753	2.427
Blood Transfusion (No/Yes)	0.442	0.818	0.490	1.365	0.228	0.709	0.406	1.239
Admission APACHE II score	<0.001	1.100	1.065	1.136	<0.001	1.081	1.038	1.125
Age (years)	0.119	1.013	0.997	1.031	0.835	1.057	0.629	1.776
Gender (Male/Female)	0.678	1.137	0.620	2.087	0.133	1.094	0.973	1.230
Type of admission (Surgical/Medical)	0.033	1.886	1.054	3.376	<0.001	2.023	1.106	3.700
Primary Diseases (Thoracic/General surgery/Neurosurgery/Cardiovascular Surgery/Orthopedics/Others)	0.096	1.096	0.984	1.211	0.987	0.997	0.655	1.517

*Cox proportional hazards regression model. HR, Hazard ratio; MV, mechanical ventilation, APACHE II, Acute Physiologic and Chronic Health Evaluation II.

with patients with endotracheal intubation (19 vs. 14, $P = 0.003$; 114/232 vs. 10/12, $P = 0.021$, respectively). Furthermore, in the short-term MV subgroup, patients with tracheostomy had longer MV time, LOS_{HOS}, and LOS_{ICU} than patients with endotracheal intubation (Table 2). However, in the short-term MV subgroup, patients with tracheostomy were not related to lower daily hospital cost or ICU-to-hospital expenses.

Survival analyses

Following univariate survival analyses, 28-day ICU survival was significantly better in Group II compared with Group I patients (Hazard ratio [HR] 0.356, 95% CI 0.213-0.597, respectively; $P < 0.001$) (Figure 1A). In addition, tracheostomy ameliorated crude ICU survival (HR 0.409, 95% CI 0.255-0.656, $P < 0.001$) (Figure 1B). Conversely, ET/LT did not influence 28-day ICU survival (HR 0.513, 95% CI 0.207-1.269, $P = 0.149$) (Figure 1C).

Further multivariate survival analysis indicated that lower admission APACHE II score (HR 1.100, 95% CI 1.065-1.136, $P < 0.001$), tracheotomized patients (HR 0.188, 95% CI 0.107-0.330, $P < 0.001$), and surgical patients (HR 1.886, 95% CI 1.054-3.376, $P = 0.033$), were related to significantly superior 28-day ICU survival (Table 3).

PSM analysis

Following PSM analysis, the main clinical characteristics were comparable between groups (Table 1). However, MV time of the tracheotomized patients (Group II') was longer than that of the intubated patients (Group I') (307.06 vs. 69.6 hours, respectively; $P < 0.001$). In addition, MV time of ET was shorter than that of LT (214.8 vs. 384.1, respectively; $P = 0.015$), and LOS_{HOS} and LOS_{ICU} were longer in Group II' than in Group I' (123 vs. 22 days, $P = 0.001$; 552 vs. 150 hours, $P < 0.001$; respectively). Furthermore, both hospital and ICU expenses of Group II' were greater than those of Group I' (CNY 309,178.3 vs. 94,952.3; CNY 104,806.3 vs. 35,010.2; $P < 0.001$; respectively). Contrarily, the per hour ICU cost of Group II' was lower than that of Group I' (CNY 246.5 vs. 321.5, respectively; $P = 0.010$), and the daily hospital cost or ICU-to-hospital expenses ratio was not significantly different between groups (Table 1). In the PSM cohort, tracheostomy was related to increased 28-day ICU survival in univariate (Figure 1D) and multivariate analyses (Table 3).

Stratified analyses

In both the medical ($P = 0.006$, Figure 2A) and surgical subgroups ($P = 0.002$, Figure 2B), tra-

Propensity score matching analysis to determine tracheostomy indication and timing

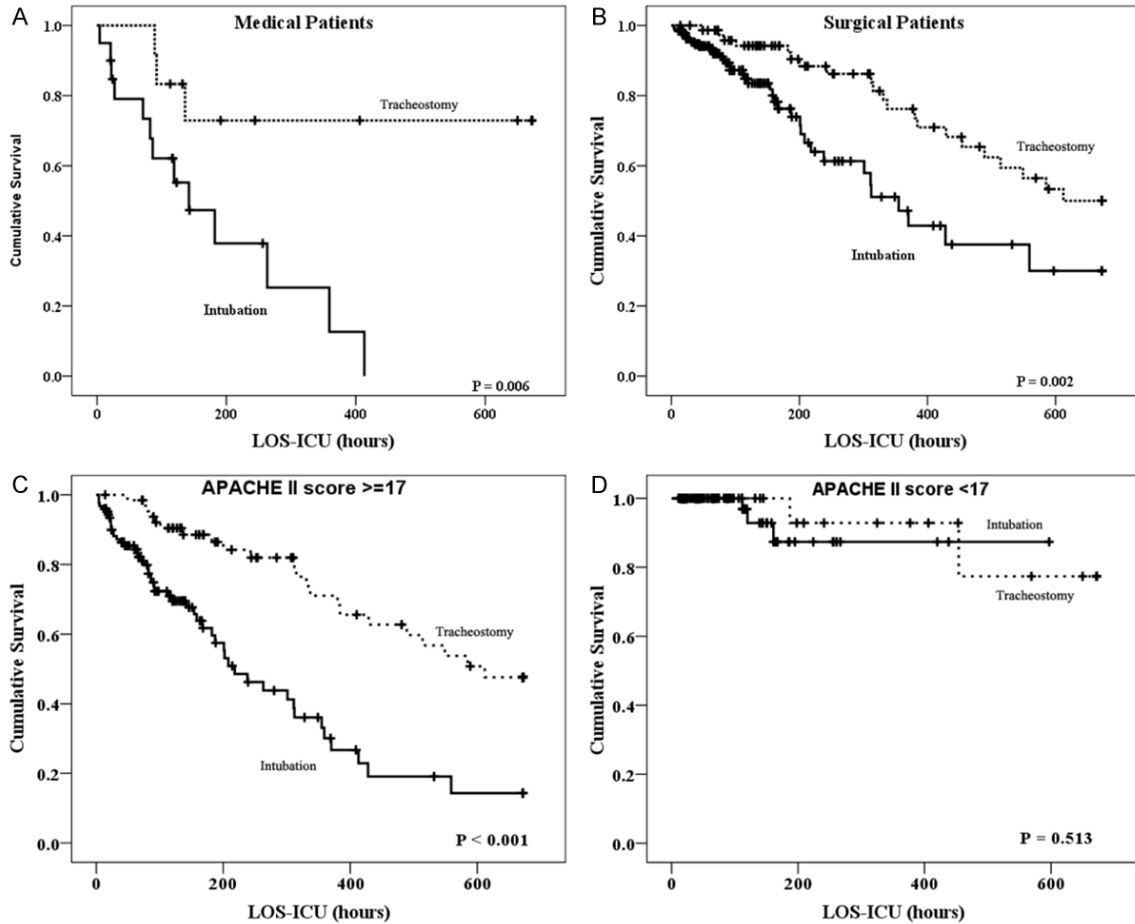


Figure 2. In both the medical ($P = 0.006$) (A) and surgical ($P = 0.002$) (B) subgroups, tracheostomy was related to enhanced 28-day ICU survival. Tracheostomy was associated with improved 28-day ICU survival in the admission APACHE II score ≥ 17 subgroup ($P < 0.001$) (C) compared with the APACHE II score < 17 subgroup ($P = 0.513$) (D).

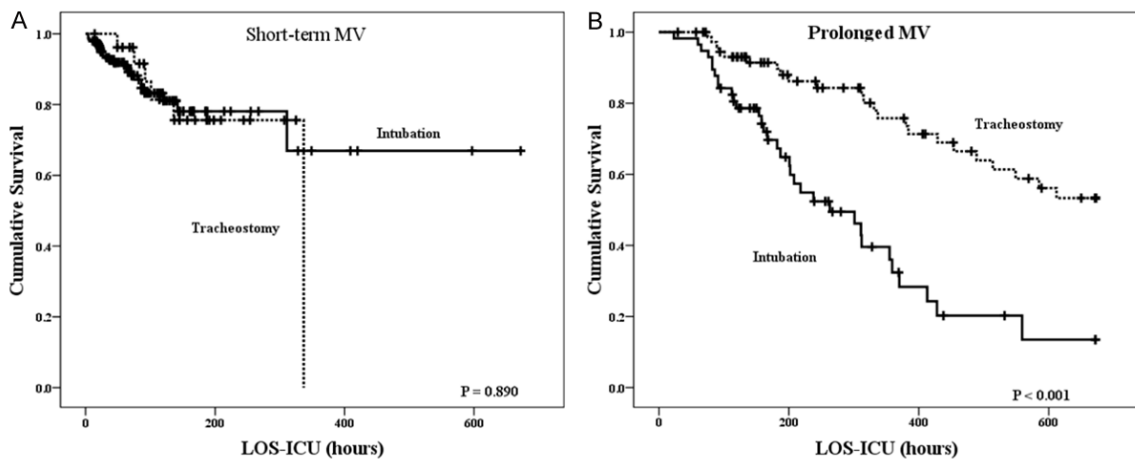


Figure 3. Tracheostomy had no effect on 28-day ICU survival in patients with short-term MV ($P = 0.890$) (A), whereas tracheostomy significantly improved 28-day ICU survival ($P < 0.001$) in patients with prolonged MV (B).

cheostomy was related to a better 28-day ICU survival. On the other hand, in the high ($P <$

0.001, **Figure 2C**) rather than the low ($P = 0.513$, **Figure 2D**) APACHE II score subgroup,

Propensity score matching analysis to determine tracheostomy indication and timing

tracheostomy was associated with improved 28-day ICU survival.

In patients with short-term MV, tracheostomy had no relationship to 28-day ICU survival ($P = 0.890$, **Figure 3A**) and in patients with prolonged MV, tracheostomy resulted in significantly increased 28-day ICU survival ($P < 0.001$, **Figure 3B**).

Following stratified analyses in the PSM cohort, tracheostomy remained associated with improved 28-day ICU survival in medical patients ($P = 0.001$) (see [Additional File 4, Figure S1A](#)), surgical patients ($P < 0.001$) (see [Additional File 4, Figure S1B](#)), patients with an admission APACHE II score ≥ 17 ($P < 0.001$) (see [Additional File 4, Figure S1C](#)) and in the prolonged MV subgroup (see [Additional File 4, Figure S2A](#)).

Discussion

In this retrospective study, we found that tracheostomy was associated with better 28-day ICU survival in both the whole and PSM cohorts (HR 0.188 and 0.178, respectively; $P < 0.001$), and especially in more critically ill patients (APACHE II score ≥ 17) and in medical or surgical patients who had undergone prolonged MV (≥ 4 days). However, tracheostomy could result in prolonged MV time, LOS_{HOS} , and LOS_{ICU} . These results are consistent with previous data [12, 13, 33, 34] that indicate tracheostomy is related to lower ICU and hospital mortality, in addition to longer MV time, LOS_{HOS} , and LOS_{ICU} .

The impact of tracheostomy on survival is controversial [15, 35]. Such uncertainty may result from the following reasons. First, the indication for tracheostomy is ambiguous. For instance, one of the major indications is “expected prolonged MV” which remains a variant among documents and guidelines [5]. In the current study, we found that in patients ventilated for ≥ 4 days, tracheostomy benefitted survival when compared with endotracheal intubation (**Figure 3B** and [Figure S2A](#)). On the contrary, tracheostomy did not benefit survival in patients ventilated for < 4 days (**Figure 3A** and [Figure S2B](#)). These finding, together with those of other researchers [23], indicate that ventilation over 4 days is paramount for “prolonged MV”, and that tracheostomy should be considered by the intensivist after this point.

However, it remains to be determined whether this 4 day timeframe is optimal for tracheosto-

my. Although tracheostomy timing has been shown to be crucial for patient survival [20, 23, 25], there is little consensus [29]. In the current study, ET was not beneficial to survival when compared with LT, which supports previous studies [24, 28]. These results demonstrate that tracheostomy should not be carried out within the first 4 ventilation days.

Additional parameters, such as primary disease and disease severity, should be taken into account prior to tracheostomy. Previous studies have shown that trauma [14, 36], burn [16], and neurosurgical [28] patients had no survival benefits from tracheostomy, while tracheostomy reduced mortality for medical patients [4] and post-cardiac surgery patients [37].

Our stratified analyses showed that tracheostomy increased survival in medical and surgical patients, and in critically ill patients (APACHE II score ≥ 17) (**Figure 2**). Hence, the decision to carry out a tracheostomy should be based on both the primary disease and disease severity. Conversely, in the short-term MV subgroup, mean APACHE II score of the tracheostomy patients was ≥ 17 , higher than that of the intubation patients. However, tracheostomy provided no benefit for patient survival. This result can be explained by the presumption that these patients were so ill that their survival was compromised in the ICU (median LOS_{ICU} : 122 hours), therefore the survival benefit of tracheostomy was attenuated. Hence, we believe that total ventilation time before tracheostomy and disease severity are related, therefore both factors should be considered for tracheostomy.

Because our study was retrospective, primary disease and disease severity were not evenly distributed (**Table 1**). PSM is a method utilized in previous studies to control confounding factors [15]. In the PSM cohort, all patient characteristics were well-balanced (**Table 1**). Tracheostomy remained independently associated with better 28-day ICU survival (**Table 3** and **Figure 1D**). Following stratified analyses of the PSM cohort, both medical and surgical patients, and especially critically ill patients (APACHE II score ≥ 17), survived longer following tracheostomy ([Figure S1](#)). In addition, tracheostomy was associated with improved 28-day ICU survival in the prolonged MV subgroup ([Figure S2A](#)) compared with the short-term MV group ([Figure S2B](#)) in the PSM cohort. These results reflect those of the whole cohort and support that tra-

cheostomy practice should be based on primary disease and disease severity of these prolonged (≥ 4 days) ventilated patients.

Tracheostomy was also associated with prolonged MV time, LOS_{ICU} , and LOS_{HOS} in the whole cohort, the PSM cohort, the prolonged MV subgroup, and the short-term MV subgroup (**Tables 1** and **2**). Therefore, tracheostomy could be used in a number of indications [38]. Fortunately, our results and those of previous studies indicate that ET can liberate patients from MV earlier (**Table 1**) [4, 23, 28] and reduce both LOS_{HOS} and LOS_{ICU} [23]. We therefore propose that when the decision to perform tracheostomy is made, the procedure should be carried out as early as possible after the first 4 MV days.

The majority of previous studies on tracheostomy are from developed western countries where high resource expenditures are sustained [4, 12, 14, 24, 38]. This current study is one of only a few from a developing eastern country. We found that the MV time, LOS_{HOS} , and LOS_{ICU} were lengthened after tracheostomy, together with higher hospital and ICU expenses (**Table 1**). Determining the merits (survival) and demerits (cost) of tracheostomy is intractable to the clinician. We found that for prolonged ventilated patients, there were no significant differences in hospital or ICU expenses between tracheostomy and intubation (**Table 2**). However, compared within tubation, tracheostomy reduced the daily hospital cost, ICU cost per hour, and ultimately the ICU-to-hospital expenses. Hence, we propose that proper selection of the candidate and timing of the procedure are paramount to success.

Although the present study is of clinical value, several limitations exist. First, although PSM was applied, the study was carried out retrospectively. Second, data for this study was obtained from only one centre in East China, therefore cannot reflect the current situation in other areas of China, especially central and western regions. Third, the sample size of this cohort was relatively small therefore patient heterogeneity was a major study limitation. The majority of patients were surgical, including those with sepsis after gastrointestinal perforation and those in deep coma after severe intracranial hemorrhage. Consequently, the inclusion of medical patients was low. Forth, we

included patients in deep coma and those with UAO. These patients represent the “absolute” indication conditions for tracheostomy, therefore were tracheostomized shortly after intubation. In future studies, these patients should not be included in the study population. Consequently, a multicentre prospective study is being carried out to validate the current study.

Conclusions

The present study indicates that for surgical or medical patients with a higher APACHE II score, tracheostomy may provide survival benefits; especially in patients ventilated for more than 4 days. For these patients, the decision to perform a tracheostomy should be made as early as possible and only carried out after the first 4 ventilation days. Furthermore, the procedure should be individualized with respect to patient primary disease and pathology, patient preference, expected recovery course, risk of continued translaryngeal intubation, and surgical risks.

Acknowledgements

This article was supported by grants from the National Natural Science Foundation of China (81201712) and Outstanding Youth Training Program from Zhongshan Hospital, Fudan University (2015 ZSYXQN29).

Disclosure of conflict of interest

None.

Abbreviations

APACHE II, Acute Physiologic and Chronic Health Evaluation II; ET, early tracheostomy; HR, hazard ratio; ICU, intensive care unit; LOS_{ICU} , length of stay in the ICU; LOS_{HOS} , length of stay in the hospital; LT, later tracheostomy; MV, mechanical ventilation; PSM, propensity score matching; SD, standard deviation; UAO, upper airway occlusion.

Address correspondence to: Zhe Luo and Jing Cang, Department of Anesthesiology and Surgical Intensive Care Unit, Zhongshan Hospital, Fudan University, 136 Yi Xue Yuan Road, Shanghai 200032, P. R. China. Tel: +86-21-64041990-3659; Fax: +86-21-64041990-3659; E-mail: ZheL6986@163.com (ZL); CANGjing0706@126.com (JC)

References

- [1] Scales DC, Ferguson ND. Tracheostomy: it's time to move from art to science. *Crit Care Med* 2006; 34: 3039-3040.
- [2] MacIntyre N. Discontinuing mechanical ventilatory support. *Chest* 2007; 132: 1049-1056.
- [3] 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: 2513-2520.
- [4] Rumbak MJ, Newton M, Truncale T, Schwartz SW, Adams JW, Hazard PB. A prospective, randomized, study comparing early percutaneous dilational tracheotomy to prolonged translaryngeal intubation (delayed tracheotomy) in critically ill medical patients. *Crit Care Med* 2004; 32: 1689-1694.
- [5] Groves DS, Durbin CG Jr. Tracheostomy in the critically ill: indications, timing and techniques. *Curr Opin Crit Care* 2007; 13: 90-97.
- [6] Terragni PP, Antonelli M, Fumagalli R, Faggiano C, Berardino M, Pallavicini FB, Miletto A, Mangione S, Sinardi AU, Pastorelli M, Vivaldi N, Pasetto A, Della Rocca G, Urbino R, Filippini C, Pagano E, Evangelista A, Ciccone G, Mascia L, Ranieri VM. Early vs. late tracheotomy for prevention of pneumonia in mechanically ventilated adult ICU patients: a randomized controlled trial. *JAMA* 2010; 303: 1483-1489.
- [7] Costello JP, Emerson DA, Shu MK, Peer SM, Zurakowski D, Reilly BK, Klugman D, Jonas RA, Nath DS. Outcomes of tracheostomy following congenital heart surgery: a contemporary experience. *Congenit Heart Dis* 2015; 10: E25-9.
- [8] Mirski MA, Pandian V, Bhatti N, Haut E, Feller-Kopman D, Morad A, Haider A, Schiavi A, Efron D, Ulatowski J. Safety, efficiency, and cost-effectiveness of a multidisciplinary percutaneous tracheostomy program. *Crit Care Med* 2012; 40: 1827-1834.
- [9] Mallick A, Bodenham AR. Tracheostomy in critically ill patients. *Eur J Anaesthesiol* 2010; 27: 676-682.
- [10] Vargas M, Sutherasan Y, Antonelli M, Brunetti I, Corcione A, Laffey JG, Putensen C, Servillo G, Pelosi P. Tracheostomy procedures in the intensive care unit: an international survey. *Crit Care* 2015; 19: 291.
- [11] Gerber DR, Chaaya A, Schorr CA, Markley D, Abouzgheib W. Can outcomes of intensive care unit patients undergoing tracheostomy be predicted? *Respir Care* 2009; 54: 1653-1657.
- [12] Flaatten H, Gjerde S, Heimdal JH, Aardal S. The effect of tracheostomy on outcome in intensive care unit patients. *Acta Anaesthesiol Scand* 2006; 50: 92-98.
- [13] 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: 802-807.
- [14] Barquist ES, Amortegui J, Hallal A, Giannotti G, Whinney R, Alzamel H, MacLeod J. Tracheostomy in ventilator dependent trauma patients: a prospective, randomized intention-to-treat study. *J Trauma* 2006; 60: 91-97.
- [15] Clec'h C, Alberti C, Vincent F, Garrouste-Orgeas M, de Lassence A, Toledano D, Azoulay E, Adrie C, Jamali S, Zaccaria I, Cohen Y, Timsit JF. Tracheostomy does not improve the outcome of patients requiring prolonged mechanical ventilation: a propensity analysis. *Crit Care Med* 2007; 35: 132-138.
- [16] Saffle JR, Morris SE, Edelman L. Early tracheostomy does not improve outcome in burn patients. *J Burn Care Rehabil* 2002; 23: 431-438.
- [17] Trouillet JL, Luyt CE, Guiguet M, Ouattara A, Vaissier E, Makri R, Nieszkowska A, Leprince P, Pavie A, Chastre J, Combes A. Early percutaneous tracheotomy versus prolonged intubation of mechanically ventilated patients after cardiac surgery: a randomized trial. *Ann Intern Med* 2011; 154: 373-383.
- [18] Boudierka MA, Fakhir B, Bouaggad A, Hmamouchi B, Hamoudi D, Harti A. Early tracheostomy versus prolonged endotracheal intubation in severe head injury. *J Trauma* 2004; 57: 251-254.
- [19] Blot F, Similowski T, Trouillet JL, Chardon P, Korach JM, Costa MA, Journois D, Thiery G, Fartoukh M, Pipien I, Bruder N, Orlikowski D, Tankere F, Durand-Zaleski I, Auboyer C, Nitenberg G, Holzappel L, Tenailon A, Chastre J, Laplanche A. Early tracheotomy versus prolonged endotracheal intubation in unselected severely ill ICU patients. *Intensive Care Med* 2008; 34: 1779-1787.
- [20] Alali AS, Scales DC, Fowler RA, Mainprize TG, Ray JG, Kiss A, de Mestral C, Nathens AB. Tracheostomy timing in traumatic brain injury: a propensity-matched cohort study. *J Trauma Acute Care Surg* 2014; 76: 70-76; discussion 76-78.
- [21] Vargas M, Pelosi P, Servillo G. Percutaneous tracheostomy: it's time for a shared approach! *Crit Care* 2014; 18: 448.
- [22] Scales DC, Kahn JM. Tracheostomy timing, enrollment and power in ICU clinical trials. *Intensive Care Med* 2008; 34: 1743-1745.
- [23] Hosokawa K, Nishimura M, Egi M, Vincent JL. Timing of tracheotomy in ICU patients: a systematic review of randomized controlled trials. *Crit Care* 2015; 19: 424.
- [24] Young D, Harrison DA, Cuthbertson BH, Rowan K; TracMan Collaborators. Effect of early vs. late tracheostomy placement on survival in patients receiving mechanical ventilation: the

Propensity score matching analysis to determine tracheostomy indication and timing

- TracMan randomized trial. *JAMA* 2013; 309: 2121-2129.
- [25] Siempos, II, Ntaidou TK, Filippidis FT, Choi AM. Effect of early versus late or no tracheostomy on mortality and pneumonia of critically ill patients receiving mechanical ventilation: a systematic review and meta-analysis. *Lancet Respir Med* 2015; 3: 150-8.
- [26] Arabi YM, Alhashemi JA, Tamim HM, Esteban A, Haddad SH, Dawood A, Shirawi N, Alshimemeri AA. 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: 435-440.
- [27] Clum SR, Rumbak MJ. Mortality and tracheostomy. *Crit Care Med* 2007; 35: 963-964.
- [28] Jeon YT, Hwang JW, Lim YJ, Lee SY, Woo KI, Park HP. Effect of tracheostomy timing on clinical outcome in neurosurgical patients: early versus late tracheostomy. *J Neurosurg Anesthesiol* 2014; 26: 22-26.
- [29] Durbin CG Jr, Perkins MP, Moores LK. Should tracheostomy be performed as early as 72 hours in patients requiring prolonged mechanical ventilation? *Respir Care* 2010; 55: 76-87.
- [30] Thomas M, Marsh A. The ideal timing of tracheostomy remains uncertain. *Crit Care Med* 2013; 41: e30.
- [31] Dewar DM, Kurek CJ, Lambrinos J, Cohen IL, Zhong Y. Patterns in costs and outcomes for patients with prolonged mechanical ventilation undergoing tracheostomy: an analysis of discharges under diagnosis-related group 483 in New York State from 1992 to 1996. *Crit Care Med* 1999; 27: 2640-2647.
- [32] Ju MJ, Tu GW, Han Y, He HY, He YZ, Mao HL, Wu ZG, Yin YQ, Luo JF, Zhu DM, Luo Z, Xue ZG. Effect of admission time on mortality in an intensive care unit in Mainland China: a propensity score matching analysis. *Crit Care* 2013; 17: R230.
- [33] Frutos-Vivar F, Esteban A, Apezteguia C, Anzueto A, Nightingale P, Gonzalez M, Soto L, Rodrigo C, Raad J, David CM, Matamis D, D'Empaire G; International Mechanical Ventilation Study Group. Outcome of mechanically ventilated patients who require a tracheostomy. *Crit Care Med* 2005; 33: 290-298.
- [34] Kollef MH, Ahrens TS, Shannon W. Clinical predictors and outcomes for patients requiring tracheostomy in the intensive care unit. *Crit Care Med* 1999; 27: 1714-1720.
- [35] Martinez GH, Fernandez R, Casado MS, Cuena R, Lopez-Reina P, Zamora S, Luzon E. Tracheostomy tube in place at intensive care unit discharge is associated with increased ward mortality. *Respir Care* 2009; 54: 1644-1652.
- [36] Dunham CM, Cutrona AF, Gruber BS, Calderon JE, Ransom KJ, Flowers LL. Early tracheostomy in severe traumatic brain injury: evidence for decreased mechanical ventilation and increased hospital mortality. *Int J Burns Trauma* 2014; 4: 14-24.
- [37] Ben-Avi R, Ben-Nun A, Levin S, Simansky D, Zeitlin N, Sternik L, Raanani E, Kogan A. Tracheostomy after cardiac surgery: timing of tracheostomy as a risk factor for mortality. *J Cardiothorac Vasc Anesth* 2014; 28: 493-496.
- [38] Sole ML, Talbert S, Penoyer DA, Bennett M, Sokol S, Wilson J. Characteristics, resource utilization, and nursing care of patients who undergo percutaneous tracheostomy. *Clin Nurse Spec* 2014; 28: 288-295.

Additional Files

Additional File 1

Detail of the available clinical, physiological, and outcome data in the current study.

Patient data

We collected the following clinical, physiological, and outcome data for evaluation: age, gender, primary diagnosis, APACHE II score at the time of admission, LOS_{HOS}, LOS_{ICU}, type of admission (surgical or medical, emergency or non-emergency), transfusion or not during ICU stay, and hospital expenses. Total number of ventilator days and the time to tracheostomy (defined as the total number of ventilator days before tracheostomy) were also documented.

Additional File 2

Indications for MV in the current study.

Indications for MV

Patient indications included: a) acute-on-chronic respiratory failure; b) coma; c) neuromuscular disease; and d) acute respiratory failure. Patients in the category of acute respiratory failure were further divided into the following subgroups: 1) acute respiratory distress syndrome; 2) postoperative state; 3) acute pulmonary edema/congestive heart failure; 4) aspiration; 5) pneumonia; 6) sepsis/septic shock; 7) trauma; 8) cardiac arrest; and 9) other.

Additional File 3

A detailed description for PSM construction.

Construction of PSM

A multivariable logistic regression model, including all available factors such as emergency admission, surgical/medical patients and APACHE II scores, was developed for the propensity score. Psmatch2 macro in STATA 11.0 software (StataCorp LP, Texas) was used for PSM. The PSM and analytic methods used in this study incorporated aspects from several sources [1, 2]. The propensity score represented the tracheostomy probability of each patient, based on variables that were known or suspected as confounding factors regarding ICU survival. As a result, 84 tracheotomy and 100 paired intubated patients were selected.

References

- [1] Ju MJ, Tu GW, Han Y, He HY, He YZ, Mao HL, Wu ZG, Yin YQ, Luo JF, Zhu DM, Luo Z, Xue ZG. Effect of admission time on mortality in an intensive care unit in Mainland China: a propensity score matching analysis. *Crit Care* 2013; 17: R230.
- [2] Luellen JK, Shadish WR, Clark MH. Propensity scores: an introduction and experimental test. *Eval Rev* 2005; 29: 530-558.

Additional File 4

Survival analyses of the PSM cohort. Admission subgroup (medical or surgical) and level of admission APACHE II score subgroup are shown in [Figure S1](#). [Figure S2](#) displays the comparison of prolonged and short-term MV subgroups.

Propensity score matching analysis to determine tracheostomy indication and timing

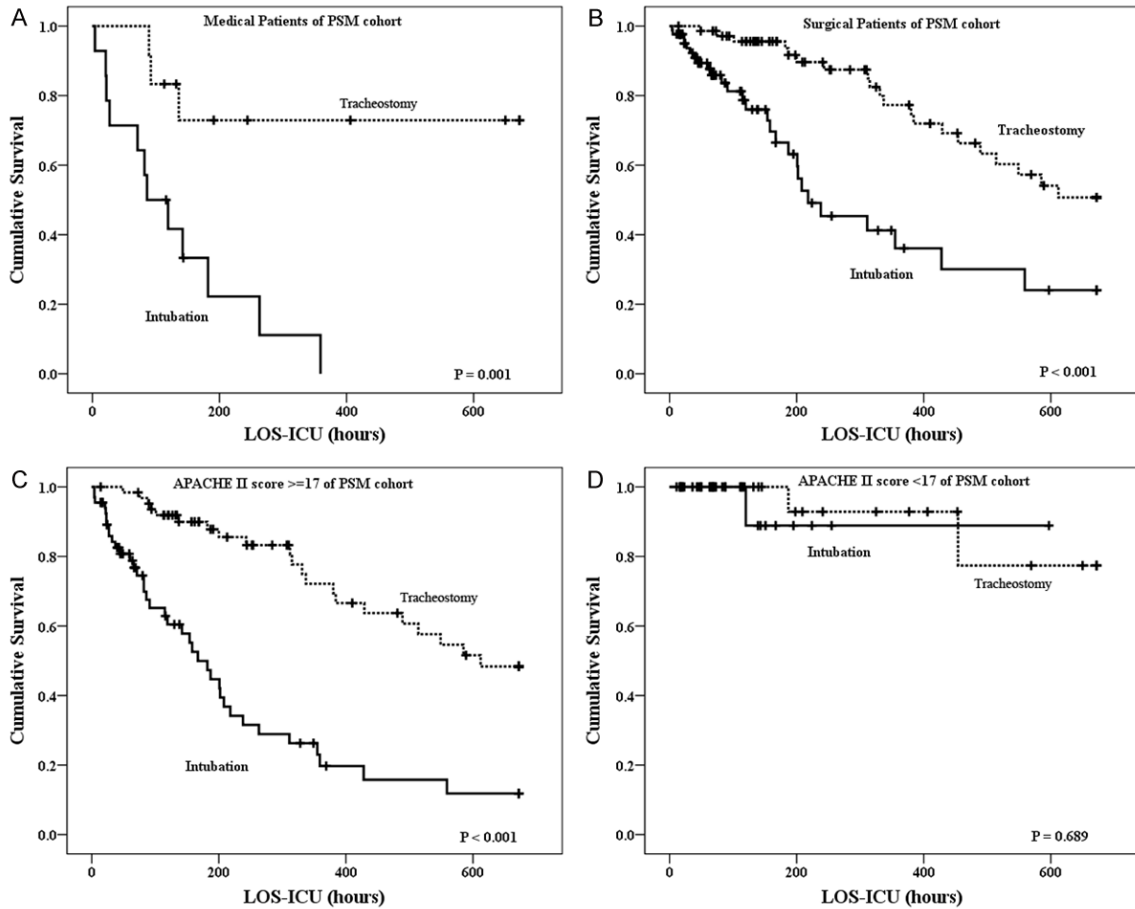


Figure S1. In the PSM cohort, relationship existed between tracheostomy and improved 28-day ICU survival in medical patients ($P = 0.001$) (A), surgical patients ($P < 0.001$) (B), and patients with an admission APACHE II score ≥ 17 ($P < 0.001$) (C). Tracheostomy had no survival benefit for patients with an admission APACHE II score < 17 ($P = 0.689$) (D).

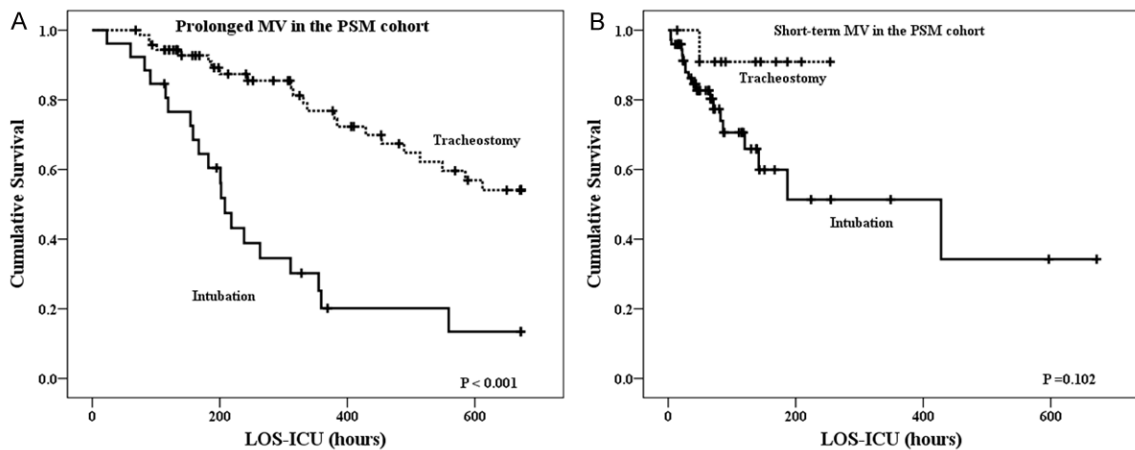


Figure S2. Tracheostomy was associated with improved 28-day ICU survival in the prolonged MV subgroup (A) rather than in the short-term MV subgroup (B) in the PSM cohort.