The outcome of early versus late tracheostomy in neurosurgery patients: A preliminary study of open RCT

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Abstract

Background: Tracheostomy is a commonly performed procedure and necessary in patients predicted to use long-term mechanical ventilation. Many neurosurgery patients need prolonged mechanical ventilation but there is controversial evidence to guide clinicians regarding the optimal time of the procedure.

Objective: The primary objective was to compare length of ICU stay, mechanical ventilation support duration, ventilator-associated pneumonia, and mortality rate between early tracheotomy (within 7 days after intubation) and late tracheostomy (more than 7 days after intubation). Whereas, secondary objective was to identify tracheostomy related complications

Patients and Methods: A randomized controlled trial conducted between June 2014 and September 2015 in Maharaj Nakhon Chiang Mai hospital. After informed consent, fifty-six eligible neurosurgery patients, whom intubated more than 72 hours and assessed for tracheostomy by clinical physicians were randomized into early and late tracheotomy group, 28 patients in each group. Primary outcomes, length of ICU stay, mechanical ventilation support duration, ventilator-associated pneumonia and mortality rate, and related complications were measured. The analysis was by intention-to-treat.

Results: In the early group, 28 patients, tracheostomy was performed after seven days in 6 patients (21.4%). Average age and tracheostomy day after intubation were 54.9 ± 20.9 years and 5.9 ± 2.0 days respectively. In the late tracheostomy group, 28 patients, average age and tracheostomy day after intubation were 63.2 ± 12.9 years and 14 ± 3.9 days respectively. Baseline characteristic was not significantly different between the groups. The average length of ICU stay in early and late tracheostomy groups were 14 and 21 days. The hazard ratio was 0.455 (p-value = 0.007), which showed that ICU discharge rate in early group was significantly 2.2 times earlier than in late tracheostomy group. Accordingly, mechanical ventilation support duration in early and late tracheostomy groups were 9 and 18 days. The hazard ratio was 0.22 (p-value < 0.001), which showed that the mechanical ventilator wean-off rate in early group was significantly 4.55 times faster than in late tracheostomy group. Ventilator-associated pneumonia were identified in 15 patients, 6 (21.4%) and 9 (32.1%) patients in early and late group (p-value = 0.55). The mortality rate in early and late group were 10.7% and 17.8%, respectively (p-value = 0.71). There was no tracheostomy complication that occurred during the study.

Conclusion: In neurosurgery patients, early tracheostomy decreases length of ICU stay and mechanical ventilator support duration significantly but no statistical difference in ventilator-associated pneumonia and mortality rate.

Keywords: early tracheostomy, late tracheostomy, neurosurgery patient, ventilator-associated pneumonia

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บทคัดย่อ

การศึกษาเปรียบเทียบผลลัพธ์ของช่วงระยะเวลาการผ่าตัดเจาะคอในผู้ป่วยประสาทศัลยศาสตร์

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ภูมิหลัง: การผ่าตัดเจาะคอเป็นหัตถการที่จำเป็นในผู้ป่วยที่มีแนวโน้มใส่ท่อหายใจในระยะยาว โดยเฉพาะผู้ป่วยศัลยกรรมประสาทที่มีอาการหนัก มักจะต้องใช้เครื่องช่วยหายใจในระยะยาว แต่ยังมีข้อถกเถียงเรื่องระยะเวลาของการทำผ่าตัดเจาะคอในผู้ป่วยเหล่านี้

วัตถุประสงค์: เพื่อเปรียบเทียบระยะเวลาที่รักษาในไอซียู ระยะเวลาในการใช้เครื่องช่วยหายใจ ปอดอักเสบที่สัมพันธ์กับการใช้เครื่องช่วยหายใจและอัตราตาย และภาวะแทรกซ้อนอื่น ระหว่างผู้ป่วยที่ได้รับ early tracheostomy (ภายใน 7 วันหลังใส่ท่อช่วยหายใจ) และ late tracheostomy (ภายหลัง 7 วันหลังใส่ท่อช่วยหายใจ)

วิธีการ: เป็นการศึกษาแบบสุ่มและมีตัวควบคุมในผู้ป่วยศัลยกรรมประสาทของโรงพยาบาลมหาราชนครเชียงใหม่ระหว่างเดือนมิถุนายน 2014 ถึงกันยายน 2015 หลังจากให้ข้อมูลและความยินยอมจากญาติ ผู้ป่วยศัลยกรรมประสาท 56 ราย ที่ใส่ท่อช่วยหายใจระยะเวลามากกว่า 72 ชั่วโมงได้รับการประเมินถึงความจำเป็นของการเจาะคอ และแบ่งผู้ป่วยออกเป็น 2 กลุ่ม กลุ่มละ 28 รายเท่ากัน โดยมี primary outcome คือระยะเวลาที่รักษาในไอซียู ระยะเวลาในการใช้เครื่องช่วยหายใจ ปอดอักเสบที่สัมพันธ์กับการใช้เครื่องช่วยหายใจและอัตราตาย และภาวะแทรกซ้อนอื่น

ผลการศึกษา: ผู้ป่วยกลุ่ม early tracheostomy ทั้ง 28 ราย อายุเฉลี่ย 54.9 ± 20.9 ปี มีระยะเวลาในการเจาะคอเฉลี่ย 5.9 ± 2.0 วัน ได้รับการเจาะคอหลังจากใส่ท่อช่วยหายใจภายหลังวันที่ 7เนื่องจากปัญหาห้องผ่าตัดทั้งหมด 6 ราย (21%) ส่วนกลุ่ม late tracheostomy ทั้งหมด 28 ราย มีอายุเฉลี่ย 63.2 ± 12.9 ปี และมีระยะเวลาในการเจาะคอเฉลี่ย 14±3.9 วัน ระยะเวลาเฉลี่ยในการอยู่ไอซียูของกลุ่ม early และ late tracheostomy เป็นระยะเวลา 14 และ 21วันตามลำดับ มี hazard ratio เท่ากับ 0.455 (p-value = 0.007) ซึ่งอัตราการออกจากไอซียูในกลุ่ม early tracheostomy มากกว่ากลุ่ม late tracheostomy เป็น 2.2 เท่า อย่างชัดเจน ระยะเวลาการใช้เครื่องช่วยหายใจเฉลี่ย ในกลุ่ม early และ late tracheostomy เป็น 9 และ 18 วันตามลำดับ โดยมี hazard ratio เท่ากับ 0.22 (p-value < 0.001) โดยมีอัตราการอย่าเครื่องช่วยหายใจในกลุ่ม early และ late tracheostomy เป็น 4.55 เท่า พบปอดอักเสบที่สัมพันธ์กับการใช้เครื่องช่วยหายใจทั้งหมด15 ราย กลุ่ม early 6 ราย (21.4%) และ 9 ราย (32.1%)ในกลุ่ม late tracheostomy (p-value 0.55) โดยมีอัตราตายในกลุ่ม early และ late tracheostomy เป็น 10.7% และ 17.8% ตามลำดับ (p-value= 0.71) และไม่พบมีภาวะแทรกซ้อนอื่นจากการเจาะคอ

สรุป: ในผู้ป่วยศัลยกรรมประสาทการทำ early tracheostomy สามารถลดระยะเวลาการอยู่ไอซียูและระยะเวลาในการใช้เครื่องช่วยหายใจได้อย่างมีนัยสำคัญ แต่ไม่ลดการเกิดปอดอักเสบที่สัมพันธ์กับการใช้เครื่องช่วยหายใจและอัตราตาย

Introduction

Tracheostomy is a commonly performed procedure and necessary in patients predicted to use long-term mechanical ventilation. The advantages of a tracheostomy over endotracheal intubation include decreasing the air dead space thus decrease respiratory effort, decrease prolong endotracheal intubation associated complication such as tracheal stenosis, easier care

by health care providers and facilitation for active ambulation. Many neurosurgery patients need prolonged mechanical ventilation; however, the optimal timing of tracheostomy remains controversial and needs more scientific evidences.

Many previous studies show the benefits of early tracheostomy. Rizk et al., a retrospective cohort study, collected 3,104 severe head injury patients revealed less hospitalization and resulted in better overall clinical outcome in the patients performed tracheostomy in day 1-7 after admission[1]. One retrospective review found that the length of ICU stay and hospitalization had decreased significantly in early tracheostomy patients (within 7 days after intubation)[2]. Another retrospective study in spinal cord injury patients suggested that early tracheostomy (within 10 days) can reduce length of ICU stay, and mechanical ventilator support duration[3]. One meta-analysis study in critical care patients found that early tracheostomy can reduce mechanical ventilator support duration and length of critical care unit stay but no significant difference in pneumonia and mortality rate[4].

However, many studies report different results. Two randomized control trials reported that pneumonia and mortality rate were not statistically different between early and late tracheostomy group[5,6]. The multicenter randomized controlled trial in critical surgical patients, in the same way, reported that there was no difference in pneumonia and mortality rate, ICU and mechanical ventilator support duration[7]. Another randomized controlled trial in cardiovascular and general critical patients also reported that early tracheostomy (within 4 days after intubation) did not reduce mortality rate compared to other groups[8].

The benefits of early tracheostomy are still controversial, especially in neurosurgery patients. Many studies reported the advantages of early tracheostomy. One randomized controlled trial in severe head injury group found that early tracheostomy (before 5 days) had reductions in ventilator duration and length of ICU stay but not in pneumonia and mortality rate[9]. However, some retrospective studies reported different results of early tracheostomy advantages over late tracheostomy groups[10-12]. Previous reports emphasize the necessity of more randomized controlled trials in neurosurgery patients in the benefit of early tracheostomy.

According to the guideline in management of severe head injury, 4th edition (2016), early tracheostomy is recommended to reduced mechanical ventilator days. However, it does not alter mortality of the rate of nosocomial pneumonia (level IIA recommendation)[13]. Nevertheless, the standard guideline for tracheostomy in neurosurgery patients in Thailand does not sufficiently describe. The primary objective was to compare length of ICU stay, mechanical ventilation support duration, ventilator-associated pneumonia, and mortality rate between early tracheotomy (within 7 days after intubation) and late tracheostomy (more than 7 days after intubation). Whereas, secondary objective was to identify tracheostomy related complications

Patients and Methods

Research type:

Open randomized controlled trial

Ethical approval registry number: SUR-2556-02054 from the institution

Population:

All neurosurgery patients admitted in the neuro-

surgery department, consist of general ward, neurosurgery ICU/Sub-ICU and Trauma unit, of Maharaj Nakhon Chiang Mai Hospital, whom intubated and eligible for tracheostomy assessed by clinical physician, from June 2014 to September 2015, with following criteria

Inclusion criteria:

- Age more than 18 years old.
- Glasgow coma score ≤ 8
- Assessed for intubation at least 72 hours due to neurosurgical or respiratory problems and expected to use long-term mechanical ventilation.

Exclusion criteria:

- Life-saving emergency tracheostomy
- Brain death patient
- Tracheostomy contraindication i.e. coagulopathy, high-risk comorbidity
- Patients with a history of tracheostomy
- Not informed consent

Methodology:

All neurosurgery patients who met the criteria, informed consent by patients or authorized people, eligible for tracheostomy assessed by clinical physician, will be allocated by "box of four" randomization into 2 groups, early tracheostomy (within 7 days after intubation) and late tracheostomy (more than 7 days after intubation) group (Diagram 1). Demographic data (age, sex, comorbidity, admission and discharge date),

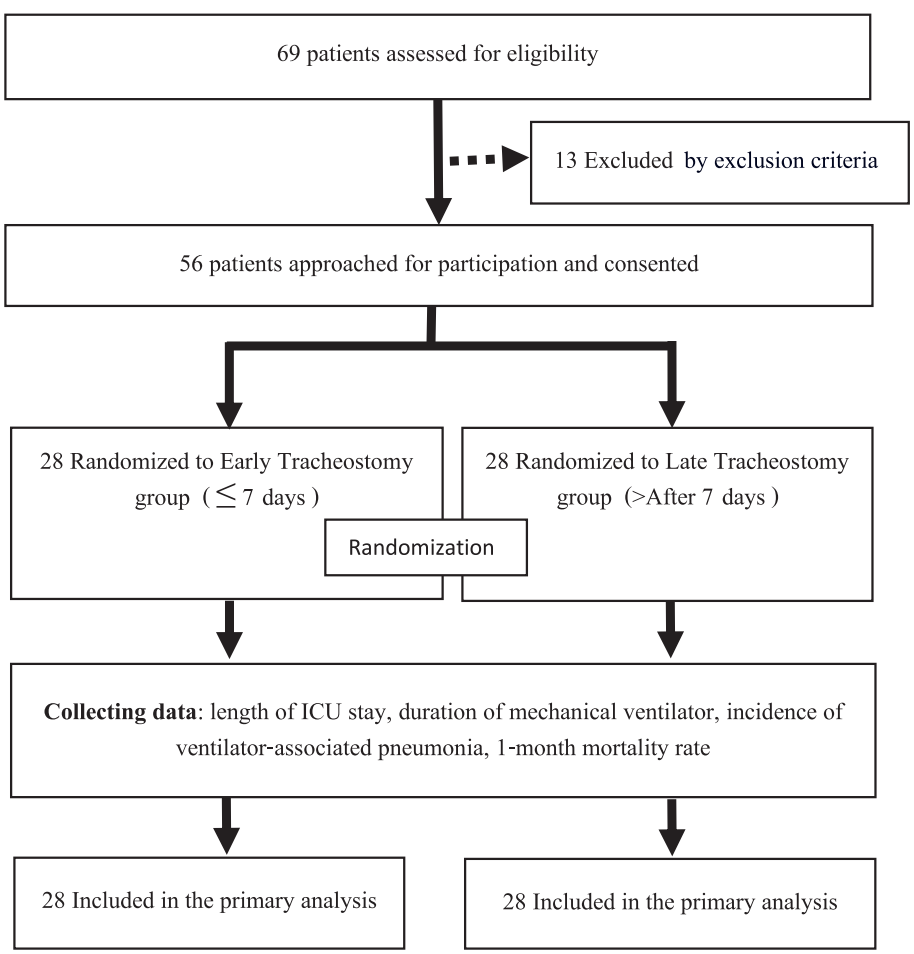

Diagram 1 Study diagram of randomized controlled trial

baseline characteristics (initial and discharge Glasgow coma score, diagnosis, operation), primary outcomes (length of ICU stay, mechanical ventilation support duration, ventilator-associated pneumonia and mortality rate) and tracheostomy related complications, were collected by neurosurgery residents (corresponding author) with supervision of senior neurosurgery staff in our institution. The analysis was by intention-to-treat method. The diagnosis of ventilator-associated pneumonia was investigated using CDC criteria[14]. A tracheostomy was performed by general surgery and neurosurgery residents using "Standard open technique". However, tracheostomy might not necessary in high-risk mortality patients or the patients expected to be easily liberated from mechanical ventilation and have a good neurological recovery in observation period. Statistical analysis: We used the student t-test to compare basic data of each group. Chi-square test was used for categorical variables. Student t-test for continuous data with normal distribution was also an analytic tool. Mann-Whitney U test was used for continuous data. Outcomes were analyzed by Fisher's exact test and Cox proportional hazard model. SPSS version. was used for statistical analysis. A *p*-value less than 0.05 was considered statistically significant.

Results

Fifty-six neurosurgery patients were informed consent, collected data and randomized into early and late tracheostomy group (28 patients in each group). Demographic data and baseline characteristics were compared between groups (Table 1). There was no statistical difference between groups concerning demographic data and baseline characteristics.

In the early tracheostomy group, 28 out of 56 patients, tracheostomy was performed after 7 days in 6 patients (21.4%) despite meeting study criteria at randomization because of unavailable operating room. The duration of tracheostomy in these 6 patients was 8 to 10 days after endotracheal intubation. So, this group was adjusted to be "intentional early tracheostomy" group. Average age and tracheostomy days after intubation were 54.9 ± 20.9 years and 5.9 ± 2.0 days, respectively. In late tracheostomy group, 28 patients, average age and tracheostomy day after intubation were 63.2 ± 12.9 years and 14 ± 3.9 days, respectively. Average length of ICU stay in early and late tracheostomy group were 14 and 21 days, respectively. Hazard ratio was 0.455 (*p*-value 0.007), showed that ICU discharge rate in early group was 2.20 times earlier than in late tracheostomy group, significantly (Figure 1).

Mechanical ventilation support duration in early and late tracheostomy group were averagely 9 and 18 days. Hazard ratio was 0.22 (*p*-value < 0.001), showed that the mechanical ventilator wean-off rate in early group was 4.55 times faster than in late tracheostomy group, significantly (Figure 2). Six patients in early group and 5 patients in late group were re-intubated. Thus, they needed mechanical ventilation support and were readmitted to ICU. Moreover, ventilator-associated pneumonia was identified in 15 patients, 6 (21.4%) and 9 (32.1%) patients in early and late group (*p*-value = 0.55) (Table 2). In both groups, the most common sputum culture was Klebsiella pneumoniae. In early group, one patient diagnosed with ventilator-associated pneumonia was dead and 3 patients were dead in late group. Three patients were dead in early group and 5 patients were dead in late

Table 1 Demographic data and baseline characteristics of the study population, p-value less than 0.05 was considered statistically significant.

Baseline characteristics	Early Tracheostomy (n=28)	Late tracheostomy (n=28)	*p*-value
Age (year), (mean ± SD)	54.9±20.9	63.2 ± 12.9	0.08
Sex (male) (%)	24 (85.7%)	18 (64.3%)	0.12
Initial Glasgow Coma Scale Score (median)	6	7	0.21
Re-intubation (n, %)	6 (21.4)	5 (17.9)	1.00
Tracheostomy days after intubation (mean ± SD)	5.9 ± 2.0	14.0 ± 3.9	NS#
Diagnosis (n,%)			
Traumatic brain injury	18 (64.3)	12 (42.9)	
Epidural hemorrhage	3	2	
Subdural hemorrhage	9	7	
Subarachnoid hemorrhage	0	2	
ICH and contusion	4	1	
Diffuse axonal injury	1	0	
Primary Tumor	2 (7.1)	5 (17.8)	0.17
GBM	1	2	
Primary CNS lymphoma	0	2	
Pituitary adenoma	0	1	
PNET	1	0	
Vascular disease	10 (35.7)	12 (42.8)	
Spontaneous ICH	7	6	
Aneurysm	2	6	
Cavernoma	1	0	
Operation (n,%)			
Craniotomy/Craniectomy	13 (46.4)	17 (60.7)	
Aneurysm clipping/coiling	2 (7.1)	4 (14.2)	
Ventriculostomy/shunting	11 (39.2)	17 (60.7)	0.33
None	6 (21.4)	2 (7.1)	
Others (i.e. biopsy, cranioplasty)	0 (0.0)	2 (7.1)	
Comorbidity (n,%)			
DM	0 (0.0)	4 (14.3)	
Hypertension	6 (21.4)	7 (28.6)	
Dyslipidemia	3 (10.7)	2 (7.1)	NS#
Cerebrovascular disease	0 (0.0)	2 (7.1)	
Cardiovascular disease	1 (3.6)	2 (7.1)	

NS# was statistically insignificant.

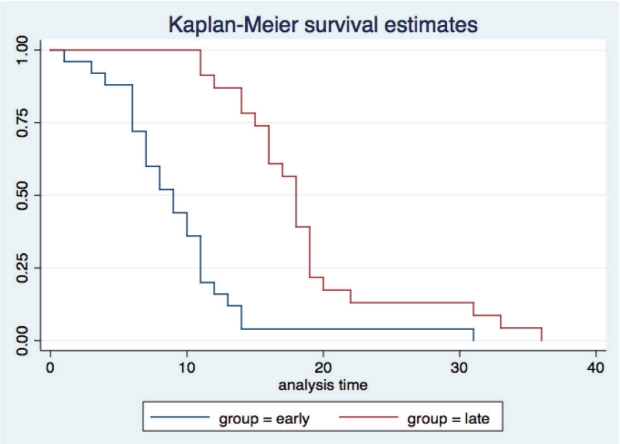

Figure 1 Length of ICU stay compared between early and late tracheostomy group. X is analysis time, Y is the proportion of patients admitted in ICU. The mean of early group was 14 days and late group was 21 days, Hazard ratio = 0.45, *p*-value = 0.007

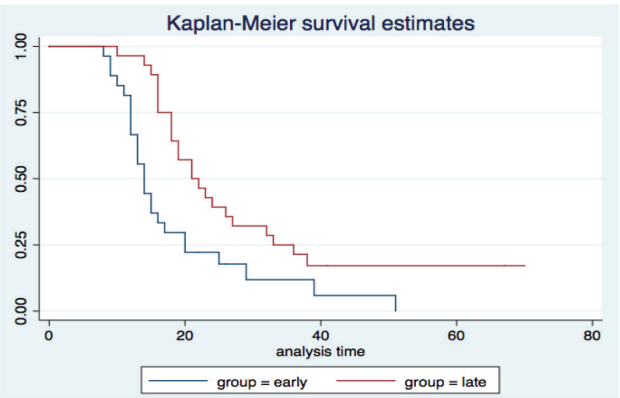

Figure 2 Ventilator days compared between early and late tracheostomy group. X is analysis time, Y is the proportion of patients using ventilator. The mean of early group = 9 days and late group = 18 days, hazard ratio = 0.22, *p*-value < 0.001.

group. Mortality rate in early and late group were 10.7% and 17.8%, respectively (*p*-value = 0.71) (Table 3). Pneumonia with septic shock is the major mortality cause of 1 patient in each group (33% in early group vs. 20% in late group). The mode of 30-day Glasgow outcome scale assessment is 2 in both groups (Table 3). Perfectly, there were no tracheostomy complications that occurred during the study.

Table 2 Ventilator-associated pneumonia in early and late tracheostomy group

Group	Total	Early tracheostomy	Late tracheostomy	*p*-value
Pneumonia n (%)	15 (26.79)	6 (21.43)	9 (32.14)	
No pneumonia n (%)	41 (73.21)	22 (78.57)	19 (67.86)	0.54
Total n (%)	**56 (100)**	**28 (100)**	**28 (100)**	

Table 3 Mortality rate in early and late tracheostomy group. There are no statistic significant.

Group	Total	Early tracheostomy	Late tracheostomy	*p*-value
Death n (%)	8 (14.29%)	3 (10.71%)*	5 (17.86%)**	0.70

*Mortality cause was pneumonia with septic shock in 1 patient. Others cause were primary disease progression.
**Mortality cause was pneumonia with septic shock in 1 patient. Others cause were primary disease progression and hypovolemic shock from GI hemorrhage.

Discussion

Many neurosurgery patients need prolonged mechanical ventilation if they have recovered from unstable conditions and assessed to require long-term mechanical ventilation. However, there is controversial evidence to guide clinicians regarding the optimal time of the procedure.

Various clinical trials investigated the optimal timing of tracheostomy. Although, several studies showed advantages of early tracheostomy[1-4], the various group of patients is the limitations of the study interpretation. There are some specific groups of neurosurgery patient literatures. One randomized controlled trial in severe head injury group found that early tracheostomy (before 5 days) had reductions in ventilator duration and

length of ICU stay but not in pneumonia and mortality rate[9]. However, this trial compared early tracheostomy group with prolonged endotracheal intubation. Some retrospective studies reported various results of early tracheostomy advantages over late tracheostomy groups[10-12], and no clear consensus regarding the definition of early tracheostomy. In presents study, early tracheostomy was defined within 3-10 day after mechanical ventilation[1-13]. Because of many reasons that made the early tracheostomy group in our study was all cases were operated within 7 days after endotracheal intubation even 6 patients (21.4%) were intended to do an intervention within the 7 days despite meeting study criteria at randomization study but the exact duration was 8-10 days after intubation. But the mean tracheostomy days after intubation was 5.9 ± 2.0 that seems to be within acceptable range of intended duration (within 7 days after intubation)[2,4,10].

In our study, early tracheostomy did not provide beneficial effect in the mortality rate. Consistently, literature review showed the result in the same direction. A recent large multicenter randomized controlled trial in critical care unit demonstrated that the 30-day mortality rate in both group was not statistically different[8]. Besides, one meta-analysis study showed no significant difference in the mortality rate between early and late tracheostomy groups[4]. However, a retrospective study showed a lower mortality rate in early group, insignificantly[2,11,12].

In the present study, there was no benefit in ventilator-associated pneumonia reduction in early tracheostomy group. Moreover, the result showed insignificantly less pneumonia incidence in early tracheostomy group. Several studies demonstrated accordant result. Two large retrospective studies showed no beneficial effect in pneumonia reduction in early tracheostomy group[2,3] as well as two randomized controlled trial reports that studied in critical care unit patients[5,6]. On the contrary, two small retrospective trials, studied in neurosurgery and severe head injury patients, reported different result[10,11]. Unfortunately, no previous randomized controlled trial in neurosurgery patients compared the incidence of ventilator-associated pneumonia between early and late tracheostomy group. However, caution regarding the interpretation of the beneficial outcome of early tracheostomy group is needed in the studies because of the variety of studied groups and different definitions of early tracheostomy among these studies.

Our study demonstrated the beneficial effect of the length of ICU stay and mechanical ventilator support duration. One retrospective study in neurosurgery patients showed that early tracheostomy reduces the total mechanical ventilator duration and ICU length of stay[12]. Furthermore, the meta-analysis showed the result in the same direction[4]. However, some studies demonstrate no benefit in both length of ICU stay and mechanical ventilator support duration in the early tracheostomy group[5,6]. This may be explained, at least, that there was less ventilator-associated pneumonia incidence in early tracheostomy group, although there was not significantly different.

Multiple factors were considered before the decision to perform tracheostomy such as patient characteristics, comorbidities, and disease severity. In the current study, patient characteristics were similar between two groups, thus the clinical results may be reasonable. Several limitations found in this study. Firstly, it is a single center, blinded randomization was unable to assign because we could not blind

the surgeon, technically. Secondly, 1/5 (20%) of early tracheostomy group patients, the procedure was performed after 7 days due to limitation of operation room availability and inappropriate condition of patients at the time of planned surgery, therefore, analysis was by intention-to-treat.

Conclusion

In neurosurgery patients, early tracheostomy significantly decreased the length of ICU stay and duration of mechanical ventilator support but early tracheostomy had no statistical difference in ventilator-associated pneumonia and mortality rate.

Acknowledgement

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