# **ORIGINAL ARTICLE**



# The Timing of Tracheostomy and Outcomes After Aneurysmal Subarachnoid Hemorrhage: A Nationwide Inpatient Sample Analysis

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# Abstract

**Background:** The goal of this study was to investigate the association of tracheostomy timing with outcomes after aneurysmal subarachnoid hemorrhage (SAH) in a national population.

**Methods:** Poor-grade aneurysmal SAH patients were extracted from the Nationwide Inpatient Sample (2002–2011). Multivariable linear regression was used to analyze predictors of tracheostomy timing and multivariable logistic regression was used to evaluate the association of timing of intervention with mortality, complications, and discharge to institutional care. Covariates included patient demographics, comorbidities, severity of subarachnoid hemorrhage (measured using the NIS-SAH severity scale), hospital characteristics, and other complications and length of stay.

**Results:** The median time to tracheostomy among 1380 poor-grade SAH admissions was 11 (interquartile range: 7–15) days after intubation. The mean number of days from intubation to tracheostomy in SAH patients at the hospital (p < 0.001) was the strongest predictor of tracheostomy timing for a patient, while comorbidities and SAH severity were not significant predictors. Mortality, neurologic complications, and discharge disposition did not differ significantly by tracheostomy time. However, later tracheostomy (when evaluated continuously) was associated with greater odds of pulmonary complications (p = 0.004), venous thromboembolism (p = 0.04), and pneumonia (p = 0.02), as well as a longer hospitalization (p < 0.001). Subgroup analysis only found these associations between tracheostomy timing and medical complications in patients with moderately poor grade (NIS-SAH severity scale 7–9), while there were no significant differences by timing of intervention in very poor-grade patients (NIS-SAH severity scale > 9).

**Conclusions:** In this analysis of a large, national data set, variation in hospital practices was the strongest predictor of tracheostomy timing for an individual. In patients with moderately poor grade, later tracheostomy was independently associated with pulmonary complications, venous thromboembolism, pneumonia, and a longer hospitalization, but not with mortality, neurological complications, or discharge disposition. However, tracheostomy timing was not significantly associated with outcomes in very poor-grade patients.

Keywords: Cerebral aneurysm, Nationwide Inpatient Sample, Subarachnoid hemorrhage, Timing, Tracheostomy

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### Introduction

The optimal timing of tracheostomy among mechanically ventilated patients remains debated, with different randomized, controlled trials and meta-analyses arriving at divergent conclusions [1-8]. Advocates of early tracheostomy cite potential advantages to this approach: greater comfort than endotracheal intubation (facilitating decreased sedation, thereby improving neurologic assessment and mobilization), reduction in airway dead space (hastening weaning of mechanical ventilation) and optimizing oral hygiene and airway suctioning [9]. On the other hand, physicians poorly prognosticate who will successfully wean from ventilation [1], and early tracheostomy may lead to overutilization. This is suboptimal as the procedure has an associated (albeit low) rate of complications, and limits verbal response. Additionally, elevation of intracranial pressure and decrease in cerebral perfusion pressure during percutaneous tracheostomy may theoretically lead to secondary brain injury [10–12].

Endotracheal intubation may be necessary in neurocritical care patients for airway protection due to altered sensorium, to maximize control of intracranial pressure, or to optimize ventilation in cardiopulmonary failure [9, 13, 14]. However, there is a dearth of data on tracheostomy timing in neurocritical care patients [14–28]. The SETPOINT trial compared early (1–3 days) and late (7–14 days) tracheostomy among 60 stroke patients and found that there was reduced sedation and intensive care unit (ICU) mortality with early intervention; however, only 14 patients had aneurysmal subarachnoid hemorrhage (SAH) [29].

Aneurysmal SAH provides unique considerations regarding airway management. Initial neurologic status is critical, as patients expected to have an expeditious recovery and those with an extremely poor prognosis should not undergo tracheostomy. Once tracheostomy is indicated, several factors impact timing, including the tempo and severity of delayed cerebral ischemia, cerebral edema, and neurological recovery in addition to the number of ventilator days [30]. Gessler et al. published the first study to evaluate tracheostomy timing among 146 patients with poor-grade SAH at a single institution. Tracheostomy within 7 days was associated with decreased odds of pneumonia and shorter mechanical ventilation, but not with differential neurological function or mortality [30]. However, given the small sample size, it is unclear whether negative associations were due to lack of effect or limited statistical power, and additional data in SAH are needed [30-32]. The goal of the present analysis is to use a large national patient population to examine (1) the predictors of tracheostomy timing and (2) the relationship between the timing of tracheostomy and outcomes (including complications) after aneurysmal SAH.

## Methods

#### Data Source

Data were extracted from the Nationwide Inpatient Sample (NIS, Healthcare Cost and Utilization Project [HCUP], Agency for Healthcare Research and Quality) for the years 2002–2011. The NIS is a 20% sample of nonfederal hospitals and is the largest all-payer administrative database in the USA and has been previously used to analyze outcomes after aneurysmal SAH [33–39]. Our institutional review board has exempted studies utilizing the NIS from individual review.

The NIS uses survey methodology to provide a nationally representative patient population. There was a redesign of the NIS in 2012: Prior to 2012, the database was a nationally representative sample of hospitals in the HCUP (with all discharges included from selected hospitals), while after 2012, the NIS was a sample of discharges from all hospitals in the HCUP. With the redesign came the introduction of new survey weights (that account for survey design and hospital clustering) in 2012, which prohibit accurate variance calculations using combined populations before and after the redesign. Additionally, the redesign limits the ability to assess hospital-level practice patterns, as only some discharges from a given hospital are included. Thus, the final year included was 2011 [40].

#### Inclusion and Exclusion Criteria

Patients who met the following criteria were included: (1) an International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis of subarachnoid hemorrhage (430) or intracerebral hemorrhage (431, 432.9); (2) underwent microsurgical clipping (ICD-9-CM procedure code: 39.51) or coil embolization (39.72, 39.75, 39.76, 39.79) of an intracranial aneurysm; (3) were aged at least 18 years; (4) a non-elective admission; (5) were designated poor grade, as defined as a Nationwide Inpatient Sample-Subarachnoid Hemorrhage severity scale score greater than 7; and (6) underwent tracheostomy (311, 312.1, 312.9) were included. Admissions with a diagnosis of a cerebrovascular malformation (747.81) and cerebral arteritis (437.4) or a procedure code of treatment of an arteriovenous malformation surgically (39.53) or by radiosurgery (923.x) were excluded. Among poor-grade patients, 99.6% had a procedure code indicating endotracheal intubation (96.04) or mechanical ventilation (96.7x), and the remaining patients (n=28) were excluded.

The NIS-SAH severity scale (NIS-SAH SS) [37], a validated severity adjustment score, was calculated for each patient using the published methodology and utilized to designate poor-grade classification. The score is a weighted calculation based on the ICD-9 diagnosis codes for coma, hydrocephalus, hemiparesis/plegia, aphasia, and cranial nerve deficits, as well as ICD-9 procedure codes for cerebrospinal fluid diversion (ventriculostomy and ventricular shunt placement) and mechanical ventilation to and estimates the severity of subarachnoid hemorrhage for a given patient. The weights are calculated from the effect measures from the multivariable logistic regression model upon which the scale is based. External validation studies have shown a strong concordance with Hunt and Hess grade (including an area under the curve of 0.75), and reported a mean NIS-SAH SS score of 4 for patients with Hunt and Hess grade 3, 7.5 for Hunt and Hess grade 4, and 9 for Hunt and Hess Grade 5 [37].

#### The Timing of Tracheostomy

The timing of tracheostomy after endotracheal intubation was determined using procedure day codes by accounting for the difference in days between tracheostomy and intubation. Those who underwent a very late tracheostomy (greater than 28 days after intubation, n=35) were excluded, consistent with prior observational studies [30], given such prolonged endotracheal intubation is rare. In the primary analysis, the timing of tracheostomy was evaluated continuously to maximize available information. Thereafter, to increase the clinical applicability of the results, complications that significantly differed by tracheostomy timing in the primary analysis were also analyzed dichotomously at 7 and 10 days after hospital admission.

#### Covariates

Patient age, sex, year of admission, expected primary payer, and hospital characteristics are directly encoded in the NIS and were extracted. The total number of comorbidities using the Elixhauser index was computed for each patient. However, neurological deficits, paralysis, and electrolyte complications were not included in the comorbidity score given the potential for misclassification with the admission diagnosis and its associated complications, and given that severity of subarachnoid hemorrhage was captured by the NIS-SAH SS.

The treatment modality used for aneurysm obliteration (microsurgical clipping compared with endovascular coiling) was included as a covariate due to differences in institutional practice and aneurysm location. Additionally, decompressive craniectomy (01.25), cerebral edema (348.5), and cerebral herniation (348.4) were evaluated to account for documented elevated intracranial pressure. The number of days between hospital admission and endotracheal intubation as well as procedural aneurysm repair was calculated using procedure day codes, and evaluated as continuous variables. Given that all discharges from selected hospitals are included in the NIS (from years before 2012), differences in hospital practice patterns can be evaluated. Therefore, the mean number of days between admission and tracheostomy in the aneurysmal SAH population was calculated at each hospital and evaluated as a covariate.

Finally, the probability of in-hospital mortality after aneurysmal SAH varies based on baseline patient characteristics and the severity of SAH. Additionally, the likelihood of mortality may also impact the timing of tracheostomy, as those expected to survive the hospitalization may be more likely to undergo early intervention. To model the probability of in-hospital death, a logistic regression construct evaluating the predicted probability of in-hospital death was created analyzing all patients with aneurysmal SAH (both good and poor grade). Covariates in this model were patient age, sex, year of admission, comorbidities, NIS-SAH SS, treatment modality used for aneurysm repair, intracerebral hemorrhage, craniectomy, herniation, and hospital characteristics. Subsequently, this predicted probability of death was used as a covariate in regression models evaluating complications.

#### **Outcomes and Complications**

Outcomes analyzed were in-hospital mortality, complications, length of hospital stay, and discharge disposition. Complications evaluated were those reported in prior publications to be potentially associated with the timing of tracheostomy [30], namely neurologic complications (including seizures: 345.xx, stroke: 433.x and 434.x, transient cerebral ischemia: 435.x, and post-procedural neurologic complications: 997.01, 997.09); pulmonary (pneumothorax 512.89, acute respiratory distress syndrome 518.82, post-procedural pulmonary complications 997.3x); tracheostomy (subglottic/laryngeal stenosis: 478.74, tracheostomy complications: 519.0x, subglottic web: 748.2); venous thromboembolic (453.x, 415.x); infectious (urinary tract infections: 595.0, 996.64, pneumonia: 481-486, 507.0, 997.31, sepsis: 38.x, 995.9x, meningitis: 320.x, surgical site infections: 998.59, and other infections: 041.x, 324.1, 790.7, 999.31, and); and decubitus ulcers (707.0x). Discharge to institutional care was a designation of a nursing facility, extended care facility, or hospice, but did not include acute rehabilitation, and was only evaluated among patients discharged alive (to differentiate discharge disposition from mortality).

#### **Missing Data**

Data that are missing in the NIS are primarily absent because that variable is not reported from a specific state from that year. Data on the timing of tracheostomy were missing for 25.4% of patients (n=481), as data on time to procedure are not reported from Hawaii, Ohio, Oklahoma, Utah, Wisconsin or West Virginia, or reported only during part of the data collection period, by Illinois, Kansas, or Washington. Moreover, while data on complications were available from all states, data are not provided on discharge to institutional care from California, Maryland, or Maine. Patients from these states constituted 25.7% (n=367) of the patients with known time to tracheostomy. These admissions were excluded from the analyses of discharge disposition, as this outcome is not expected to vary by state.

#### **Statistical Analyses**

Statistical analyses were performed using STATA 13 (College Station, TX) accounting for the survey design as well as clustering of the NIS, with the hospital ID as the sampling unit, the discharge weight as the sampling weight, and the NIS stratum as the strata. Descriptive statistics were noted, and baseline characteristics were evaluated for association with timing of tracheostomy using univariable linear regression. Thereafter, a multivariable linear regression model was constructed to evaluate predictors of tracheostomy timing, which was based on a univariable screen, with entry criteria into the multivariable model of p < 0.10. Subsequently, multivariable logistic regression models were constructed to examine the association of tracheostomy timing with each outcome and complication evaluated. In the models evaluating outcomes, all analyzed characteristics were included as covariates in the model given their association with outcomes after SAH. Concordance (C) statistics assessed the discrimination of regression constructs. A p value of less than 0.05 was considered significant.

#### Results

#### **Demographics of Study Population**

This study included 1380 poor-grade patients with SAH. The median time to tracheostomy following intubation was 11 (interquartile range: 7–15) days; the 10th percentile was 4 and the 90th percentile was 19 days. The demographics of the study population are shown in Table 1. The majority of patients underwent intubation on the day of admission (63.6%, n=878) or the day after admission (13.8%, n=190), while the remainder (22.6%, n=312) required intubation thereafter.

#### **Predictors of Tracheostomy Timing**

To evaluate the predictors of tracheostomy timing, after univariable screen (Table 1), a multivariable linear regression model was constructed (Table 2). The only significant variables in univariable screen were mean hospital time to tracheostomy and time from admission to intubation, which had individual  $R^2$  values of 0.32 and 0.08, respectively. Both variables remained independently significant in the multivariable model, with mean hospital tracheostomy time positively and the time to intubation negatively associated with tracheostomy time for an individual patient; the  $R^2$  value of the overall model was 0.35. The timing of tracheostomy was not associated with other demographics or treatment variables, including patient age, number of comorbidities, or treatment modality used for aneurysm repair.

#### **Outcomes and Complications**

Multivariable logistic regression models evaluated the association of tracheostomy timing (as a continuous variable) with outcomes and complications (Table 3) among poor-grade patients who underwent tracheostomy. The first model included all patient demographics, SAH characteristics, year of admission, as well as hospital characteristics (including mean hospital tracheostomy time), listed in Table 1 as covariates. A second model was constructed which, in addition to the covariates from the first model, also included mortality, other significant complications, and length of hospital stay as covariates.

Mortality, neurologic complications, and discharge disposition were not significantly associated with tracheostomy time. However, later tracheostomy was associated in both models with increased odds of pulmonary complications, venous thromboembolism, and pneumonia. Furthermore, multivariable linear regression construct after including patient and hospital characteristics, mortality, and complications as covariates showed that later tracheostomy was associated with a longer hospital stay (assessed continuously, regression coefficient: 0.80 days, 95% CI: 0.55–1.05 days, p < 0.001,  $R^2$ : 0.22, and after logarithmic conversion due to non-normal distribution, regression coefficient: 0.024, 95% CI: 0.019–0.029, p < 0.001,  $R^2$ : 0.29).

Subsequent subgroup analyses stratified patients based on severity of SAH, as assessed by the NIS-SAH SS (Table 3). Among patients with a NIS-SAH SS score of 7–9 (indicating a moderately poor grade), later tracheostomy was associated with increased odds of pulmonary complications, venous thromboembolism, and pneumonia. However, no significant association between complications and the timing of intervention was seen among

Variable	Total population ( <i>n</i> = 1380)	Regression coefficient (Days)	95% CI	<i>p</i> value
Age years (mean_SD)	584(132)	0.00	-0.03 to 0.03	0.93
Sex	56(15.2)		0.05 10 0.05	0.20
Male	31.2	Ref.	_	-
Female	68.8	0.19	- 0.51 to 0.90	0.59
Year of admission				
2002–2004	19.6	Ref.	_	_
2005–2007	29.4	-0.23	- 1.52 to 1.06	0.73
2008–2011	50.9	-0.13	- 1.28 to 1.01	0.82
Insurance status				
Private	40.7	Ref.	-	-
Medicare	32.5	-0.43	- 1.08 to 0.23	0.20
Medicaid	20.9	0.06	- 0.78 to 0.89	0.90
Self-pay or other	5.9	-0.54	- 1.95 to 0.87	0.46
Number of comorbidities (mean, SD)	1.9 (1.3)	0.03	- 0.22 to 0.27	0.84
NIS SAH severity scale				
7–9	67.3	Ref.	-	-
>9	32.8	-0.14	- 0.81 to 0.54	0.69
Aneurysm repair				
Endovascular coiling	49.2	Ref.	-	-
Microsurgical clipping	50.8	0.49	- 0.23 to 1.20	0.18
Intracerebral hemorrhage	13.0	0.95	- 0.08 to 1.97	0.07
Cerebral edema	12.4	0.48	- 0.69 to 1.65	0.42
Craniectomy	2.8	0.98	- 0.85 to 2.81	0.29
Cerebral herniation	6.4	-0.13	- 1.34 to 1.08	0.83
Time to aneurysm repair, days (mean, SD)	2.5 (6.5)	-0.03	- 0.15 to 0.08	0.56
Predicted probability of death (mean, SD)	0.26 (0.13)	0.60	- 2.08 to 3.28	0.66
Mean hospital time to tracheostomy, days (mean, SD)	11.7 (3.8)	0.87	0.82 to 0.92	< 0.001
Time from admission to intubation, days (mean, SD)	2.1 (5.5)	-0.30	- 0.39 to - 2.1	< 0.001
Hospital bed size				
Small/medium	17.2	Ref.	-	-
Large	82.8	0.50	- 0.88 to 1.87	0.48
Teaching hospital				
Non-teaching	12.8	Ref.	-	-
Teaching	87.2	-0.60	- 1.71 to 0.51	0.29
Hospital region				
Northeast	28.3	Ref.	_	-
Midwest	12.1	-0.08	- 1.67 to 1.51	0.93
South	39.4	-0.86	- 2.03 to 0.30	0.15
West	20.1	- 0.46	- 1.98 to 1.05	0.55

Table 1 Demographics of the study population and univariable associations with the timing of tracheostomy

All data are presented as percentages, with the exception of those designated as mean/standard deviation

Statistically significant differences in univariable linear regression are bolded

CI confidence interval, IQR interquartile range, Ref reference; SD standard deviation

patients with an NIH-SAH SS greater than 9 (indicating a very poor grade).

#### **Dichotomous Analysis**

While treating the timing of tracheostomy as a continuous variable maximizes available information, tracheostomy time is often evaluated clinically at distinct time points. Therefore, multivariable logistic regression analyses were performed where tracheostomy time was divided dichotomously at 7 and 10 days after intubation, analyzing complications that differed significantly in the continuous analysis (Table 4). The proportion of patients

Variable	Regression coefficient (Days)	95% Cl	<i>p</i> value
Time from admission to intubation	-0.16	- 0.26 to - 0.06	0.002
Mean hospital time to tracheostomy	0.81	0.76 to 0.87	< 0.001
Intracerebral hemorrhage	0.48	-0.37 to 1.34	0.27
R <sup>2</sup> : 0.35			

Table 2 Multivariable linear regression model evaluating the predictors of the timing of tracheostomy

Statistically significant differences in multivariable linear regression are bolded

who underwent tracheostomy within 7 days was 25.6% (n = 353), and within 10 days was 46.0% (n = 635).

#### Discussion

In this NIS analysis, 1380 patients with poor-grade aneurysmal SAH who underwent tracheostomy were extracted. The median time from admission to tracheostomy was 11 days, and the primary predictor of tracheostomy timing was institutional practice. After adjustment for severity of SAH, other demographic, and clinical factors, earlier tracheostomy was not independently associated with mortality, neurologic complications, or discharge disposition. However, delayed tracheostomy was associated with increased odds of pulmonary complications, venous thromboembolism, and pneumoniaprimarily in patients with moderately poor grade. These data suggest that earlier tracheostomy may offer some advantages in the medical management of aneurysmal SAH but is unlikely to improve neurological outcomes or mortality.

#### **Predictors of Tracheostomy Timing**

Few studies have evaluated the predictors of tracheostomy timing among neurocritical care patients. In this study, intervention timing was not associated with premorbid or SAH clinical variables; instead 32% of the variance was attributable to mean institutional tracheostomy time (within the SAH population), which was the greatest predictor of an individual patient's timing. The only other significant predictor was intubation timing. Patients who required intubation later in the hospitalization were more likely to undergo tracheostomy sooner after intubation, which may indicate patients with deterioration due to delayed cerebral ischemia. Given the lack of consensus on the timing of tracheostomy, such variability in institutional practice patterns is not surprising, and underscores the need for additional data on outcomes.

#### Mortality and Neurologic Outcomes

Several prior observational studies evaluating the timing of tracheostomy among neurocritical care patients [17, 29], including SAH [30], did not report differential mortality, neurologic outcomes, including functional status based on interventional timing. However, the SET-POINT trial did report reduced ICU mortality in the early tracheostomy arm [29]. In the present analysis, tracheostomy time was not found to be significantly associated with in-hospital death, neurological complications, or discharge to institutional care. Therefore, tracheostomy timing may not directly impact mortality or neurological status after SAH.

#### **Medical Complications**

Prior evaluation of tracheostomy timing in traumatic brain injury has reported that later tracheostomy was associated with pneumonia, deep venous thrombosis, and longer length of stay [17, 27]. Moreover, Gessler et al. found decreased odds of pneumonia and respiratory adverse events, but no differences in ICU length of stay or other medical complications, with early tracheostomy in poor-grade SAH [30]. In the present analysis, later tracheostomy was associated with some medical complications-pulmonary, venous thromboembolic, and pneumonia-as well as a longer hospitalization. In the first regression model, accounting for patient demographics, SAH severity, and hospital characteristics, later tracheostomy was associated with pulmonary, venous thromboembolic, and infectious complications, as well as decubitus ulcers; however, these associations may be attributable to a longer hospitalization with the accrual of additional complications. Therefore, a second model was constructed which also included mortality, other significant complications, and length of hospital stay as covariates, and tracheostomy timing remained significantly associated with pulmonary complications, venous thromboembolism, and pneumonia. In this subgroup analyses of patients stratified by severity of SAH the association with tracheostomy timing and medical complications were only seen among moderately poor-grade patients, while no significant differences were seen among the very poor-grade subgroup.

Tracheostomy time was first evaluated as a continuous variable due to variability regarding the definition of early intervention. However, to increase the clinical applicability, dichotomous analyses were performed using two

Outcomes	Total %	Odds ratio	95% Cl	p value	C Statistic
Model 1: Patient and hospital characte	ristics as covariates				
Mortality	11.6	0.98	0.94-1.02	0.33	0.70
Discharge to institutional care	48.0	1.00	0.97-1.03	0.97	0.73
Neurologic complications	41.4	1.02	1.00-1.05	0.10	0.64
Tracheostomy complications	2.9	0.98	0.92-1.04	0.47	0.72
Pulmonary complications	18.8	1.04	1.01–1.07	0.002	0.67
Venous thromboembolism	17.8	1.04	1.01–1.07	0.007	0.66
Decubitus ulcers	7.8	1.05	1.01–1.10	0.02	0.64
Any infectious complications	80.7	1.04	1.01–1.07	0.01	0.62
Pneumonia	45.9	1.04	1.01–1.06	0.004	0.61
Model 2: Patient and hospital characte	eristics, death, complica	ations, and LOS as covariat	tes		
Mortality	11.6	1.01	0.97–1.05	0.71	0.73
Discharge to institutional care	48.0	1.00	0.97-1.03	0.97	0.73
Neurologic complications	41.4	1.02	0.99–1.04	0.21	0.65
Tracheostomy complications	2.9	0.96	0.89–1.03	0.25	0.74
Pulmonary complications	18.8	1.04	1.01-1.07	0.004	0.67
Venous thromboembolism	17.8	1.03	1.00–1.06	0.04	0.69
Decubitus ulcers	7.8	1.03	0.98–1.07	0.20	0.70
Any infectious complications	80.7	1.01	0.98-1.04	0.56	0.69
Pneumonia	45.9	1.03	1.00-1.05	0.02	0.63
Model 3: Model 2 if NIS-SAH severity se	cale 7–9 ( <i>n</i> = 928)				
Mortality	10.3	1.02	0.97-1.07	0.53	0.76
Discharge to institutional care	49.2	1.00	0.96-1.03	0.86	0.73
Neurologic complications	42.2	1.01	0.98-1.05	0.45	0.67
Tracheostomy complications	2.9	0.95	0.88-1.02	0.15	0.77
Pulmonary complications	19.2	1.04	1.01–1.08	0.01	0.72
Venous thromboembolism	18.5	1.04	1.00–1.07	0.04	0.68
Decubitus ulcers	7.9	1.03	0.98-1.09	0.26	0.75
Any infectious complications	80.6	1.01	0.97-1.05	0.60	0.69
Pneumonia	48.0	1.04	1.01–1.06	0.01	0.64
Model 4: Model 2 if NIS-SAH severity se	cale > 9 ( <i>n</i> = 452)				
Mortality	14.2	0.99	0.92-1.07	0.79	0.74
Discharge to institutional care	45.3	1.01	0.95-1.06	0.85	0.77
Neurologic complications	39.6	1.03	0.98–1.07	0.20	0.71
Tracheostomy complications	2.9	1.00	0.85-1.17	0.97	0.86
Pulmonary complications	18.1	1.02	0.96-1.07	0.51	0.71
Venous thromboembolism	16.2	1.02	0.96-1.07	0.53	0.77
Decubitus ulcers	7.5	1.03	0.96-1.10	0.37	0.82
Any infectious complications	81.0	1.01	0.94-1.09	0.75	0.74
Pneumonia	41.8	1.02	0.97-1.07	0.47	0.68

 Table 3 Multivariable logistic regression evaluating the association of the timing of tracheostomy (when evaluated as a continuous variable) with complications

All multivariable logistic regression models included all characteristics listed in Table 1 as covariates, including patient age, sex, year of admission, insurance status, comorbidities, severity of subarachnoid hemorrhage (measured with the NIS-SAH severity scale), treatment modality used for aneurysm repair, intracerebral hemorrhage, cerebral edema, craniectomy, herniation, time to aneurysm repair, time to intubation, mean hospital timing of tracheostomy, predicted probability of death, and hospital characteristics

Odds ratios in the continuous analysis represent the increased odds of that outcome occurring with each additional day of the exposure variable (timing of tracheostomy)

Statistically significant differences are bolded

Cl confidence interval, LOS length of stay

Outcome	Early trach (%)	Late trach (%)	Odds ratio	95% CI	<i>p</i> value	С
Model 1: Patient and hospital ch	aracteristics as covariates					
After 7 Days						
Pulmonary complications	15.6	20.0	1.59	1.03–2.45	0.04	0.67
Venous thromboembolism	13.9	19.1	1.47	1.02-2.13	0.04	0.66
Infectious complications	74.5	82.9	1.63	1.16-2.27	0.005	0.62
Pneumonia	42.2	47.2	1.23	0.91-1.65	0.17	0.62
Decubitus ulcers	5.4	8.6	1.92	1.10-3.35	0.02	0.64
After 10 Days						
Pulmonary complications	17.2	20.3	1.43	1.02–2.00	0.04	0.66
Venous thromboembolism	15.1	20.0	1.35	0.99–1.84	0.06	0.66
Infectious complications	77.0	83.8	1.46	1.08–1.97	0.01	0.62
Pneumonia	41.1	50.1	1.41	1.06–1.87	0.02	0.62
Decubitus ulcers	5.7	9.5	2.16	1.41-3.32	< 0.001	0.65
Model 2: Patient and hospital ch	aracteristics, death, comp	lications, and LOS as cova	ariates			
After 7 Days						
Pulmonary complications	15.6	20.0	1.59	1.04–2.45	0.03	0.68
Venous thromboembolism	13.9	19.1	1.32	0.92–1.89	0.13	0.69
Infectious complications	74.5	82.9	1.34	0.93-1.92	0.12	0.69
Pneumonia	42.2	47.2	1.06	0.78–1.44	0.69	0.62
Decubitus ulcers	5.4	8.6	1.59	0.94–2.69	0.09	0.70
After 10 Days						
Pulmonary complications	17.2	20.3	1.41	1.00–1.98	0.047	0.67
Venous thromboembolism	15.1	20.0	1.21	0.88–1.67	0.24	0.69
Infectious complications	77.0	83.8	1.18	0.86-1.64	0.31	0.69
Pneumonia	41.1	50.1	1.32	1.01–1.74	0.04	0.63
Decubitus ulcers	5.7	9.5	1.87	1.16-3.01	0.01	0.71

Table 4 Association of the timing to tracheostomy (evaluated dichotomously) with complications

All multivariable logistic regression models included all characteristics listed in Table 1 as covariates, including patient age, sex, year of admission, insurance status, comorbidities, severity of subarachnoid hemorrhage (measured with the NIS-SAH severity scale), treatment modality used for aneurysm repair, intracerebral hemorrhage, cerebral edema, craniectomy, herniation, time to aneurysm repair, time to intubation, mean hospital timing of tracheostomy, predicted probability of death, and hospital characteristics

C concordance statistic, Cl confidence interval

Statistically significant p values from multivariable logistic regression are bolded

time points—within 7 and 10 days after intubation—representing approximately the lower quartile and median tracheostomy time within the study population. Tracheostomy after 7 days was associated with increased odds of pulmonary complication, while tracheostomy after 10 days was also associated with greater odds of pneumonia and decubitus ulcers.

#### Limitations and Advantages to Study Design

There are many limitations of this analysis. Clinical data are recorded in the NIS using ICD-9-CM indicators. Therefore, several variables including postoperative neurological examination, sedative and vasopressor use, mechanical ventilation liberation protocol, attempted extubation, tracheostomy technique (percutaneous versus open), the timing of delayed cerebral ischemia, and number of ICU and ventilator days—are not available from the NIS due to a lack of corresponding ICD-9-CM indicators. Moreover, although the NIS-SAH SS has been validated with excellent concordance with Hunt and Hess grade, World Federation of Neurological Surgeons and Fisher grade could not be assessed. As a retrospective, observational analysis, timing to tracheostomy was not randomized and the timing of the complications with regards to tracheostomy was not documented. Therefore, causation and reverse causation regarding the association of tracheostomy timing and medical complications cannot be differentiated. Additionally, this study only evaluated patients who underwent tracheostomy, and did not compare the results of patients who underwent a trial of extubation with those who underwent tracheostomy, as some patients who underwent early tracheostomy may have successfully weaned from the ventilator, obviating the need for a tracheostomy.

Nevertheless, there are several advantages to the use of a nationally representative patient population to evaluate the association of tracheostomy timing and outcomes among subarachnoid hemorrhage patients. Data are recorded on many patient demographics, which were evaluated as potential predictors of tracheostomy timing; additionally, the association of tracheostomy timing with different pertinent medical complications was evaluated. Furthermore, the multiinstitutional patient population increases the generalizability compared with single-institution studies, and allows for comparisons of practice patterns between hospitals.

#### Conclusion

The present analysis suggests that the timing of tracheostomy in poor-grade SAH patients is primarily determined by institutional practice patterns. Additionally, the timing of tracheostomy was not associated with mortality, neurologic complications, or discharge disposition. However, later tracheostomy was associated with increased odds of pulmonary complications, venous thromboembolism, and pneumonia among patients with moderately poor grade, but not among very poor-grade patients. Future studies—including additional prospectively collected data, but ideally a randomized, controlled trial—may further elucidate the relationship between tracheostomy timing with outcomes in neurocritical care patients, including those with aneurysmal SAH.

#### Author contribution

HHD contributed to conception and design, acquisition of data, analysis and interpretation of data, drafting the article, critically revising the article, reviewed submitted version of the manuscript, and statistical analysis. RFR contributed to acquisition of data, analysis and interpretation of data, critically revising the article, reviewed submitted version of the manuscript, and statistical analysis. WBG contributed to analysis and interpretation of data, critically revising the article, reviewed submitted version of the manuscript, and administrative/technical/material support. KUF contributed to analysis and interpretation of data, critically revising the article, reviewed submitted version of the manuscript, and administrative/technical/material support. MAA-S contributed to analysis and interpretation of data, critically revising the article, reviewed submitted version of the manuscript, and administrative/technical/ material support. RD contributed to conception and design, acquisition of data, analysis and interpretation of data, critically revising the article, reviewed submitted version of the manuscript, administrative/technical/material support, and study supervision.

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#### **Compliance with Ethical Standards**

#### **Conflict of interest**

Hormuzdiyar H. Dasenbrock, Robert F. Rudy, Kai U. Frerichs, and Rose Du have nothing to disclose; M. Ali Aziz-Sultan received consulting honoraria from

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