

# Clinical Predictors of Postintubation Bilateral Vocal Fold Immobility

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## Abstract

**Introduction** Iatrogenic bilateral vocal fold immobility (BVFI) often arises from posterior glottic stenosis (PGS) after endotracheal intubation, whereby posterior commissure mucosal disruption leads to fibrosis and ankylosis of the cricoarytenoid joints. Sequelae can be devastating, resulting in dyspnea, stridor, and death due to asphyxiation.

**Objectives** We sought to review features associated with PGS to better understand how to prevent this condition. A secondary aim is to analyze factors correlating to tracheostomy dependence.

**Methods** Charts from January 2010 to November 2020 were retrospectively reviewed, and adult patients with the diagnosis of BVFI after intubation were included. Data on comorbidities, duration of intubation, laryngoscopy, and decannulation status was analyzed.

**Results** Out of the 68 patients included in the present study, 60.3% were male, and the mean duration of intubation  $14.3 \pm 8.5$  days. A total of 94% of the patients were intubated for at least 7 days, diabetic, and/or obese. Although association with prolonged intubation  $>7$  days was not significant ( $p = 0.064$ ), complete BVFI on fiberoptic exam ( $n = 47$ ) was significantly associated with tracheostomy dependence both in the entire cohort ( $p = 0.036$ ) and in the 56 patients with tracheostomy ( $p = 0.0086$ ). Patients without cardiovascular disease (CVD) were less likely to be tracheostomy dependent compared with those with CVD (odds ratio [OR]: 0.23 [0.053–0.79];  $p = 0.028$ ).

**Conclusions** We identified duration of intubation, DM, and obesity as potential risk factors for PGS. Complete immobility and CVD were significantly associated with tracheostomy dependence. Our findings may have important implications for earlier tracheostomy in high-risk intubated patients, as well as for closer monitoring of disease progression and earlier intervention in those predisposed to tracheostomy dependence.

## Keywords

- ▶ vocal cord paralysis
- ▶ tracheostomy
- ▶ device removal
- ▶ laryngostenosis
- ▶ glottis

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## Introduction

Iatrogenic bilateral vocal fold immobility (BVFI) can be caused by prolonged or traumatic intubation. Sequelae can be devastating, resulting in dyspnea, stridor, and death due to asphyxiation. While the most common iatrogenic cause of BVFI is neural injury after surgery, such as thyroidectomy, BVFI can result from structural injury. Intubation may lead to the development of BVFI from posterior glottic stenosis (PGS) in adults, secondary to the vulnerability of the posterior glottic mucosa.<sup>1,2</sup> Weymuller et al. quantified the degree of endotracheal tube (ETT) pressure in canine larynges, demonstrating pressures that are significantly greater than capillary perfusion pressure. These pressures were highest at the posterolateral aspect of the glottis, where injury occurred in the specimens.<sup>3</sup>

The initial site of development of PGS is at the posterior commissure, a thin mucosal layer overlying the laryngeal cartilage. Significant pressure from the ETT is placed in this region, which leads to inflammation, mucosal disruption, ulceration, and the development of granulation and fibrosis at the posterior glottis. Progression of disease is demonstrated by ankylosis of the cricoarytenoid joint and medial fixation of the arytenoid vocal processes, resulting in a significantly narrowed airway with limited vocal fold abduction.<sup>1,4-6</sup> Bogdasarian et al. established the most commonly used PGS classification (I-IV) based on the progressive fibrosis of the cricoid and arytenoid cartilages.<sup>1</sup> Advanced stage is more often associated with respiratory symptoms, while voice and swallowing are typically less affected.

Identifying individuals at risk for the development of postintubation PGS may help us better understand how to prevent this condition and/or intervene earlier to manage these patients. Specifically, the association of body mass index (BMI) and diabetes mellitus (DM) with postintubation PGS has not been extensively described, despite the implications on ETT size and wound healing for both of these conditions.

Treatment typically involves procedures to open the airway with the goal of avoiding a tracheostomy or decannulation if a tracheostomy is present. This often comes at a cost to the patient, sacrificing voice quality and increasing aspiration as the airway is opened surgically. Several studies have identified certain factors in patients with laryngotracheal stenosis that are associated with prolonged tracheostomy placement.<sup>7-9</sup> To date, only one study has evaluated risk factors solely in patients with a diagnosis of postintubation PGS.<sup>5</sup> The pathophysiology of this condition is unique, and factors associated with both the development and consequences of PGS after intubation may differ from other etiologies.

In the present article, we review the risk factors associated with PGS development to better understand how to prevent and manage this condition. A secondary aim is to highlight the variables associated with successful decannulation or maintenance of an adequate airway without the need for tracheostomy. We hypothesize that obesity, DM, smoking history, cardiovascular conditions, and prolonged intubation > 7 days are potential risk factors for the inci-

dence of PGS and worsening degree of immobility. We suspect that these same risk factors may have implications on the need for prolonged tracheostomy, in addition to complete immobility with compromised abduction.

## Materials and Methods

### Patient Identification

A review of institutional records at our tertiary care institution was conducted to identify patients with BVFI seen as outpatients by the senior author (Rosow D. W.) at the Department of Otolaryngology of our tertiary care institution between October 2011 and November 2020 using ICD-10 code J38.02. The study was approved by the institutional review board at our tertiary care institution (IRB # 20210028). Patients > 18 years old were included in the study if they had a diagnosis of bilateral vocal fold paralysis or of paresis after intubation. Patients were excluded if the etiology of BVFI was unrelated to intubation. Individuals < 18 years old, pregnant women, radiated patients, and prisoners were excluded.

### Data Collection

Relevant patient details were collected from the electronic medical record system. We reviewed demographic data including age, gender, race, ethnicity, body mass index (BMI), tobacco and alcohol use, and comorbidities including hypertension (HTN), cardiovascular disease (CVD), diabetes mellitus (DM), gastroesophageal reflux disease, and obstructive lung disease. Tobacco and alcohol use were defined as never, former, or current user.

Additional information regarding the hospital stay of the patients was gathered from chart review. We extracted data regarding duration of intubation and ETT size when information was available. Given that the majority of the hospitalizations of the patients was at outside institutions, verbal consent was obtained from the patient prior to request of outside medical records.

Symptomatology was assessed both at initial presentation and at the most recent follow-up. Voice changes were documented as positive if the patient reported subjective changes other than mild hoarseness. Fiberoptic laryngoscopy exam videos were reviewed by the senior author to assess the degree of immobility. "Complete" indicated that the patient had total BVFI; "partial" included either those with unilateral immobility and contralateral hypomobility or those with bilateral hypomobility.

The patients were categorized according to existing tracheostomy status, whereby those with no existing tracheostomy included both those who were decannulated after tracheostomy placement or if tracheostomy was avoided altogether. In addition, decannulation status in patients who had a history of tracheostomy was evaluated separately.

### Statistical Analysis

All statistical analyses were performed by using RStudio statistical software version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria). Associations between categorical

variables were analyzed using the chi-squared or the Fisher exact test, as appropriate. Simple logistic regression was performed to explore the relationship between each potential predictor with binomial outcomes, in order to determine which factors may be predictive for complete BVFI, decannulation, and existing tracheostomy as described above. Multivariable analyses were subsequently performed using binomial logistic regression to predict outcomes by adjusting covariates. The variables included in the model were gender, age, race, ethnicity, smoking and alcohol history, CVD, diabetes, BMI, and duration of intubation. The reduced models were selected using backward stepwise selection with the lowest Akaike Information Criteria (AIC) as criteria for best fit model. Statistical significance was defined as  $p$ -value  $< 0.05$ , and Bonferonni correction for multivariate analyses yielded  $p$ -value  $< 0.017$ . Power analyses were also performed for each of the outcomes and are reviewed in ► **Supplemental Table S1** (online only).

## Results

### Demographics

Demographic data for the 68 patients are shown in ► **Table 1**. The mean age was  $53.9 \pm 15.3$  years old, with an average follow-up period of 1.80 years. The majority of the patients was male (60.3%), and 40% met criteria for obesity, that is BMI  $\geq 30$ . More than half of the patients had been smokers at some point ( $n = 36$ ), whereas only 18 patients had a positive alcohol history. A total of 43 patients had HTN or CVD, and 23 had DM. The median duration of intubation was 14 days, with a mean of  $14.3 \pm 8.5$  days. Out of the 52 patients with documented length of intubation, 49 (94%) were intubated for at least 7 days, diabetic, or obese (BMI  $\geq 30$ ), or a combination of these factors. Of the remaining 3 patients, 2 were overweight (BMI  $\geq 25$ ) and had documented traumatic intubations.

At the initial clinic visit, 29 patients without tracheostomy had audible stridor, and 37 reported voice changes. Fifty-six patients had tracheostomy either while in the hospital for prolonged intubation or subsequent to intubation secondary to airway concern. The surgical approaches for BVFI were primarily endoscopic ( $n = 38$ ). Findings before and after endoscopic intervention are depicted in ► **Figure 1**.

### Degree of Immobility

The degree of immobility was assessed for each patient on fiberoptic laryngoscopy. Forty-eight patients (70.6%) had complete BVFI. No significant association between degree of immobility and factors including gender, age, race, ethnicity, BMI, HTN/CVD, DM, smoking history, and duration of intubation was identified on bivariate analysis. On multivariate analysis, the effect of duration of intubation did not quite achieve significance (odds ratio [OR]: 0.27; 95% confidence interval [CI]: 0.067–1.06;  $p = 0.064$ ) (► **Table 2**).

### Existing Tracheostomy

No existing tracheostomy was noted in 56 patients (82.3%), whereas 12 (17.6%) remained with tracheostomy at follow-

**Table 1** Patient demographics and other characteristics

Characteristics	n (%) (n = 68)
<b>Age</b>	
< 60	48 (70.6%)
$\geq 60$	20 (29.4%)
<b>Gender</b>	
Male	41 (60.3%)
Female	27 (39.7%)
<b>Race</b>	
White	51 (75.0%)
Black	17 (25.0%)
<b>Ethnicity</b>	
Hispanic	19 (27.9%)
Non-hispanic	49 (72.1%)
<b>Smoking History</b>	
Yes	36 (52.9%)
No	32 (47.1%)
<b>Alcohol Use</b>	
Yes	18 (26.5%)
No	50 (73.6%)
<b>Comorbidities:</b>	
<i>Cardiovascular Disease</i>	
Yes	43 (63.2%)
No	25 (36.8%)
<i>Diabetes</i>	
Yes	23 (33.8%)
No	45 (66.2%)
<i>Asthma/COPD</i>	
Yes	11 (16.2%)
No	57 (83.8%)
<i>Overweight<sup>a</sup></i>	
Yes	49 (72.1%)
No	19 (27.9%)
<i>Obese<sup>b</sup></i>	
Yes	28 (41.2%)
No	40 (58.8%)
<b>Intubation Duration</b>	
> 7 days	38 (55.9%)
$\leq 7$ days	14 (20.6%)
Unknown	16 (23.5%)
<b>Bilateral Immobility</b>	
Complete	48 (70.6%)
Partial	20 (29.4%)
<b>Symptoms:</b>	
<i>Voice Changes</i>	

**Table 1** (Continued)

Characteristics	n (%) (n = 68)
Yes	37 (54.4%)
No	31 (45.5%)
<b>Dysphagia</b>	
Yes	10 (14.7%)
No	58 (85.3%)
<b>Stridor</b>	
Yes	29 (42.6%)
No	39 (57.4%)
<b>Ever Underwent Tracheostomy</b>	
Yes	56 (82.4%)
No	12 (17.6%)
<b>Decannulated</b>	
Yes	28 (41.2%)
No	28 (41.2%)
No tracheostomy	12 (17.6%)

<sup>a</sup>Overweight includes patients with BMI  $\geq 25$ .

<sup>b</sup>Obese includes patients with BMI  $\geq 30$ .

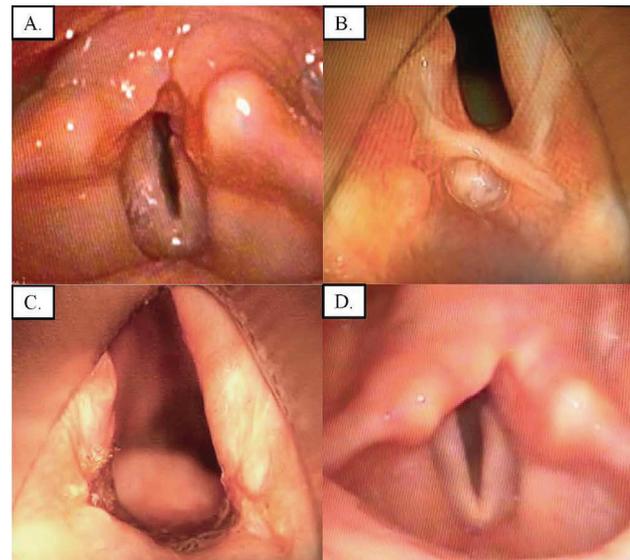
up. Patients with complete BVFI on fiberoptic exam were significantly less likely to have no tracheostomy compared to those with partial BVFI (OR: 0.25; 95%CI: 0.064–0.80;  $p = 0.028$ ). Multivariate analysis demonstrated a significant effect of HTN/CVD on the presence of a tracheostomy. Specifically, the odds of having an existing tracheostomy in patients without HTN/CVD was 0.23 times that of those with HTN/HLD (OR: 0.23; 95%CI: 0.053–0.79;  $p = 0.028$ ). The degree of immobility was also significantly correlated, as patients with complete BVFI were more likely to have an existing tracheostomy compared with partial BVFI (OR: 4.15; 95%CI: 1.18–17.70;  $p = 0.036$ ) (► **Table 3**).

### Status

Half of the patients who had a tracheostomy placed either as inpatients or after hospitalization due to airway concerns were subsequently decannulated. We found a significant association between complete immobility and failure to be decannulated (OR: 0.19; 95%CI: 0.047–0.66;  $p = 0.012$ ). On multivariable analysis including all variables and after adjustment, there was a very significant relationship between the degree of immobility and decannulation status, as patients with complete BVFI were more likely to fail decannulation (OR: 6.23; 95%CI: 1.73–27.86;  $p = 0.0086$ ) (► **Table 4**).

### Discussion

Optimal timing for a tracheostomy in intubated patients is hotly debated. In a large multicenter randomized control trial, Young et al. found no difference in 30-day or 2-year mortality between early ( $\leq 4$  days) and late ( $> 10$  days)



**Fig. 1** (A) Videostroboscopy demonstrating posterior commissure ulceration and bilateral vocal fold paralysis in the median position with severely narrowed airway. (B) Thick posterior glottic scar band with fibrosis and cricoarytenoid joint ankylosis on direct laryngoscopy. (C) Appearance of the posterior glottis after laser and balloon dilation of scar band. (D) Normal appearing posterior glottic mucosa and improved airway patency 6 months postoperatively.

tracheostomy. However, this study primarily focused on mortality, and none of the measured secondary outcomes concerned laryngeal injury.<sup>10</sup> Meanwhile, it is well-known that prolonged intubation has important implications for the development of laryngeal injury, which can occur in up to 20% of individuals.<sup>11</sup> The correlation between BVFI and prolonged intubation has been shown previously.<sup>5,12,13</sup> A landmark study published in 1984 demonstrated a 100% increase in the development of PGS for patients intubated for between 11 and 24 days compared with those intubated for between 5 and 10 days.<sup>13</sup> Similarly, the mean duration of intubation in our cohort was 14.3 days, with 73% intubated for  $> 7$  days.

Several studies have highlighted a relationship between large ETT size and the development of SGS.<sup>9,14</sup> The implications of larger ETT in PGS has been described in only one study, by Hillel et al., who noted that all male cases of PGS were intubated with a size 8.0 ETT.<sup>5</sup> Male patients may be more prone to the development of PGS secondary to larger ETT size. In our study, the majority of patients were male (60.3%). Given the retrospective design,  $< 1/4$  of our patients had data regarding ETT size, so we were unable to describe the effect of this variable.

Height has also been implicated as an important factor in ETT selection. One study analyzed tracheal luminal diameters on computed tomography (CT) and concluded a significant relationship between the height of the patient and airway diameter only in males. They deduced that, depending on height in male patients, larger ETT may not always be indicated.<sup>15</sup> A case-control study by Katsantonis et al. evaluated risk factors for postintubation PGS and found that shorter height was significantly predictive of PGS. This

**Table 2** Bivariate and multivariate logistic regression analysis for degree of immobility

Bivariate Analysis				
Prognostic Factor	Category (n)	Complete	OR (95%CI)	p-value
Gender	Male (41)	31	Reference (1)	0.26
	Female (27)	17	0.055 (0.019–1.59)	
Age (years old)	< 60 (48)	35	Reference (1)	0.51
	≥ 60 (20)	13	0.69 (0.23–2.18)	
Race	White (51)	36	Reference (1)	1.00
	Black (17)	12	1.0 (0.31–3.59)	
Ethnicity	Hispanic (19)	16	Reference (1)	0.15
	Non-hispanic (49)	32	0.35 (0.075–1.25)	
Smoking history	Yes (36)	26	Reference (1)	0.75
	No (32)	22	0.85 (0.29–2.42)	
Alcohol history	Yes (18)	13	Reference (1)	1.00
	No (50)	35	0.87 (0.233–2.79)	
Obesity	Yes (18)	19	Reference (1)	0.68
	No (40)	29	1.25 (0.43–3.60)	
Diabetes	Yes (23)	17	Reference (1)	0.78
	No (45)	31	0.78 (0.24–2.34)	
Hypertension/Cardiovascular disease	Yes (43)	29	Reference (1)	0.58
	No (25)	19	1.53 (0.51–4.95)	
Duration of intubation <sup>a</sup>	> 7 days (38)	29	Reference (1)	0.075
	≤ 7 days (14)	7	0.31 (0.083–1.12)	
Multivariate Analysis				
Model	Prognostic factor	Category	OR (95% CI)	p-value
1	Duration of intubation	> 7 days	Reference (1)	0.082
		≤ 7 days	0.27 (0.062–1.16)	
2	Duration of intubation	> 7 days	Reference (1)	0.064
		≤ 7 days	0.27 (0.067–1.07)	

Abbreviations: OR (95% CI), estimated odds ratio and corresponding 95% confidence interval.

In bold  $p < 0.05$ .

Multivariable logistic regression **model 1** includes degree of immobility (complete versus partial) plus the following 10 variables: Gender (male versus female), age (< 60 versus ≥ 60 years old), race (white versus black), ethnicity (Hispanic versus non-Hispanic), smoking history (yes versus no), alcohol history (yes versus no), obesity (yes versus no), diabetes (yes versus no), hypertension/cardiovascular disease (yes versus no), and duration of intubation (> 7 versus ≤ 7 days).

Multivariable logistic regression **model 2** includes the particular marker(s) reported plus the following 2 variables: gender, ethnicity, and duration of intubation.

<sup>a</sup>Numbers do not sum to group totals due to information available in retrospective analysis.

may be secondary to ETT that are too large for shorter patients.<sup>16</sup> Larger multicenter studies may be important for implementing updated algorithms for ETT selection.

Prior studies have demonstrated a relationship between comorbid conditions and the development of airway pathology after intubation.<sup>12,17</sup> Diabetic patients are at an eight-fold increased risk of development of laryngeal stenosis. Diabetes leads to a systemic hypoperfusion, which leads to poor wound healing and exacerbates ulceration and scarring seen in PGS.<sup>4,18</sup> Similarly, ischemia in patients with CVD may contribute to PGS via a similar mechanism. Both CVD and DM were noted to be significant risk factors for PGS in the aforementioned study by Hillel et al. In our cohort, over

1/3 of patients were diabetic, and nearly 2/3 had HTN or ischemia, highlighting that these may be risk factors for the development of PGS.

In contrast to DM and prolonged intubation, the effect of BMI on the development of postintubation BVFI has not been well-described. D'Anza et al. identified a significant inverse correlation between BMI and tracheal size on imaging in patients undergoing tracheostomy.<sup>19</sup> In our clinical experience, we have seen that typically larger patients with higher BMI are intubated with larger ETT, particularly in the emergency, trauma, and critical care settings. As noted above, this has important implications for the development of BVFI, given that large ETT may predispose to the mucosal

**Table 3** Bivariate and multivariate logistic regression analysis for existing tracheostomy

Bivariate Analysis				
Prognostic factor	Category (N)	Yes	OR (95% CI)	p-value
Gender	Male (41)	16	Reference (1)	0.066
	Female (27)	12	1.25 (0.46–3.36)	
Age (years old)	< 60 (48)	22	Reference (1)	0.23
	≥ 60 (20)	6	0.51 (0.16–1.49)	
Race	White (51)	21	Reference (1)	1.00
	Black (17)	7	1.00 (0.32–3.03)	
Ethnicity	Hispanic (19)	11	Reference (1)	0.086
	Non-Hispanic (49)	17	0.39 (0.13–1.13)	
Smoking history	Yes (36)	15	Reference (1)	0.93
	No (32)	13	0.96 (0.36–2.53)	
Alcohol history	Yes (18)	6	Reference (1)	0.48
	No (50)	22	1.50 (0.496–4.91)	
Obesity	Yes (18)	13	Reference (1)	0.46
	No (40)	15	0.69 (0.26–1.85)	
Diabetes	Yes (23)	11	Reference (1)	0.43
	No (45)	17	0.66 (0.24–1.84)	
Hypertension/Cardiovascular disease	Yes (43)	20	Reference (1)	0.24
	No (25)	8	0.54 (0.19–1.49)	
Duration of intubation <sup>a</sup>	> 7 days (38)	16	Reference (1)	0.68
	≤ 7 days (14)	5	0.76 (0.20–2.66)	
Degree of immobility	Partial (20)	4	Reference (1)	<b>0.028</b>
	Complete (48)	24	0.25 (0.064–0.80)	
Multivariate Analysis				
Model	Prognostic factor	Category	OR (95% CI)	p-value
1	Degree of immobility	Partial	Reference (1)	<b>0.025</b>
		Complete	5.52 (1.37–29.04)	
	Hypertension/Cardiovascular disease	Yes	Reference (1)	<b>0.045</b>
		No	0.21 (0.041–0.90)	
	Ethnicity	Hispanic	Reference (1)	0.077
		Non-Hispanic	0.28 (0.61–1.09)	
2	Degree of immobility	Partial	Reference (1)	<b>0.036</b>
		Complete	4.15 (1.18–17.70)	
	Hypertension/Cardiovascular disease	Yes	Reference (1)	<b>0.028</b>
		No	0.23 (0.053–0.79)	
	Ethnicity	Hispanic	Reference (1)	0.065
		Non-Hispanic	0.30 (0.076–1.03)	

Abbreviations: OR (95% CI), estimated odds ratio and corresponding 95% confidence interval.

In bold  $p < 0.05$ .

Multivariable logistic regression **model 1** includes existing tracheostomy (no versus yes) plus the following 11 variables: Gender (male versus female), age (< 60 versus ≥ 60 years old), race (white versus black), ethnicity (Hispanic versus non-Hispanic), smoking history (yes versus no), alcohol history (yes versus no), obesity (yes versus no), diabetes (yes versus no), hypertension/cardiovascular disease (yes versus no), duration of intubation (> 7 versus ≤ 7 days), and degree of immobility (partial versus complete).

Multivariable logistic regression **model 2** includes the following 4 variables: age, hypertension/cardiovascular disease, ethnicity, and degree of immobility.

<sup>a</sup>Numbers do not sum to group totals due to information available in retrospective analysis.

**Table 4** Bivariate and multivariate logistic regression analysis for decannulation status

Bivariate analysis				
Prognostic factor	Category (n)	Not decannulated	OR (95% CI)	p-value
Gender	Male (41)	16	Reference (1)	0.79
	Female (27)	12	0.87 (0.30–2.49)	
Age (years old)	< 60 (48)	22	Reference (1)	0.24
	≥ 60 (20)	6	0.49 (0.14–1.58)	
Race	White (51)	21	Reference (1)	0.76
	Black (17)	7	0.83 (0.25–2.74)	
Ethnicity	Hispanic (19)	11	Reference (1)	0.082
	Non-Hispanic (49)	17	0.34 (0.091–1.11)	
Smoking history	Yes (36)	15	Reference (1)	1.00
	No (32)	13	1.00 (0.35–2.88)	
Alcohol history	Yes (18)	6	Reference (1)	0.75
	No (50)	22	1.22 (0.35–4.37)	
Obesity	Yes (18)	13	Reference (1)	0.28
	No (40)	15	0.55 (0.18–1.60)	
Diabetes	Yes (23)	11	Reference (1)	0.78
	No (45)	17	0.86 (0.29–2.54)	
Hypertension/Cardiovascular disease	Yes (43)	20	Reference (1)	0.4
	No (25)	8	0.62 (0.20–1.88)	
Duration of intubation <sup>a</sup>	> 7 days (38)	16	Reference (1)	0.71
	≤ 7 days (14)	5	1.33 (0.30–6.22)	
Degree of immobility	Partial (20)	4	Reference (1)	<b>0.012</b>
	Complete (48)	24	5.20 (1.52–21.28)	
Multivariate analysis				
Model	Prognostic factor	Category	OR (95% CI)	p-value
1	Degree of immobility	Partial	Reference (1)	<b>0.016</b>
		Complete	7.17 (1.62–42.32)	
2	Degree of immobility	Partial	Reference (1)	<b>0.0086</b>
		Complete	6.23 (1.73–27.86)	

Abbreviations: OR (95% CI), estimated odds ratio and corresponding 95% confidence interval.

In bold  $p < 0.05$ .

Multivariable logistic regression **model 1** includes decannulation status (yes versus no) plus the following 11 variables: Gender (male versus female), age (< 60 versus ≥ 60 years old), race (white versus black), ethnicity (Hispanic versus non-Hispanic), smoking history (yes versus no), alcohol history (yes versus no), obesity (yes versus no), diabetes (yes versus no), hypertension/cardiovascular disease (yes versus no), duration of intubation (> 7 versus ≤ 7 days), and degree of immobility (partial versus complete).

Multivariable logistic regression **model 2** includes the particular marker(s) reported plus obesity.

<sup>a</sup>Numbers do not sum to group totals due to information available in retrospective analysis.

disruption and subsequent scarring that develops. In our cohort, 94% of the patients were intubated for at least 7 days, diabetic, and/or obese (BMI ≥ 30). This suggests that higher BMI may be an important risk factor for the development of PGS.

Cigarette smoke has been shown to reduce capillary blood flow, to promote reactive oxygen species within microvasculature, to increase mucin secretion, and to induce an inflammatory response in the upper and lower airways.<sup>20</sup> More than 50% of our patient cohort were smokers, indicat-

ing that smoking may exacerbate PGS and have a compounding effect on the fibrosis that ensues. Prior studies have noted a relationship between smoking and tracheostomy dependence in patients with PGS, as well as poorer outcomes after surgical intervention for BVFI.<sup>9,21</sup> We did not elucidate a difference in tracheostomy status based on smoking history. This may be due to the fact that we described smoking as patients who had ever smoked at some point rather than as the current smoking status, since only five patients identified as current smokers. Further evaluation of the impact of

continued smoking on the outcomes of postintubation BVFI would be an interesting topic for future study.

According to the Bogdasarian classification, Class IV PGS presents with complete BVFI, whereas classes I-III may have hypomobility of one or both vocal folds. No prior studies have reviewed risk factors for the development or consequences of complete versus partial immobility. We deduced an association between prolonged intubation and complete immobility, although it was not significant ( $p = 0.064$ ). The failure to achieve significance may be due to the retrospective design with absent data on intubation duration in nearly half of the patients. Large studies may help to deduce the implication of prolonged intubation on the degree of immobility.

Successful airway outcomes can be defined by decannulation potential or avoidance of a tracheostomy. Compared with BVFI from other entities, patients with postintubation PGS require more commonly surgical interventions to have a favorable outcome.<sup>9</sup> A meta-analysis by Kremer et al. reviewed 19 articles to analyze the impact on the type of surgical approach and noted that patients with prior open surgery had an increased likelihood of additional surgery and that those who underwent stent placement were less likely to be decannulated.<sup>22</sup> The effect of various endoscopic approaches would be an interesting topic for future analysis.

Factors associated with decannulation in patients with laryngotracheal stenosis have been studied. Gelbard et al. found that both patients with iatrogenic etiology, for example, postintubation, and diabetic patients were less likely to be decannulated.<sup>17</sup> Another study by Snow et al. reported that for those with subglottic or tracheal narrowing, airway firm scarring as opposed to granulation had a greater association with tracheostomy dependence.<sup>8</sup> Applying this notion to PGS, significant scarring would be more likely to result in a higher Bogdasarian classification and increased likelihood of complete immobility. As Snow et al. described for SGS and tracheal stenosis, we similarly identified a significant relationship on multivariate analysis between complete BVFI and decreased likelihood of decannulation.

While the association between ischemia and development of PGS has been reported, the relationship between this risk factor and patient outcome is not well-established. We determined a significant correlation between CVD and tracheostomy dependence. This again may be due to the hypoperfusion also seen in diabetic patients, leading to poor wound healing and rebound fibrosis after intervention.<sup>18</sup>

A recent study by Meenan et al. reviewed factors associated with the development of laryngeal lesions precluding decannulation in 371 tracheostomy patients. Similar to our study, the authors did not observe an association between age, gender, race, DM, or duration of intubation and the likelihood of tracheostomy dependence. Interestingly, they did elucidate a significant association between BMI  $\geq 25$  and the development of laryngeal lesions precluding decannulation.<sup>7</sup> Although a substantial proportion of our patients were overweight, we did not identify a relationship between higher BMI and tracheostomy dependence. This may be due to our smaller sample size and may be better studied with a larger population.

Several limitations are inherent of the retrospective study design. Although we attempted to gather data regarding ETT size and duration from outside hospitals, this proved to be extremely difficult, and documentation was notably poor. As a single institution study, our sample size was relatively small, precluding more in-depth analysis of certain factors, such as current smoking history, ETT size, and the effect of specific interventions. Another limitation was the subjectivity of the vocal fold impairment grading, as the fiberoptic laryngoscopy videos were only reviewed by the senior author. In addition, several patients had limited follow-up. This may have increased bias toward poorer outcomes, as those with tracheostomy may be more inclined to follow-up for additional procedures. Data on the number and nature of surgical interventions was not included, which may have been a confounding factor when assessing the propensity toward decannulation and/or avoidance of tracheostomy.

In the era of the coronavirus (COVID-19) pandemic, assessment of factors associated with the development and consequences of PGS may prove to be exceedingly important. Secondary to high patient mortality and virus aerosolization, the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) guidelines initially recommended intubation duration of at least 2 weeks prior to tracheostomy in COVID-19 patients. In one study, the average duration of intubation in 20 COVID-19 patients was 21.8 days; all patients demonstrated laryngeal pathology on fiberoptic exam at the outpatient visit, and 15% had PGS.<sup>23</sup> Our group has started to review factors associated with laryngeal injury and outcomes in patients who have been intubated for COVID-19.

## Conclusions

In the present study, we reviewed variables associated with outcomes in patients with postintubation BVFI. We identified duration of intubation, DM, and obesity as potential risk factors for the development of PGS. Complete immobility may be related to prolonged intubation and was noted to be significantly associated with tracheostomy dependence. Ischemia also appeared to play a significant role, as patients with HTN/CVD were more likely to be tracheostomy dependent. Larger studies with control groups are needed to evaluate the clinical importance of these variables, particularly during a time when the risk of COVID-19 virus aerosolization has dramatically increased the average duration of intubation.

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