Association of Severe Tongue Edema With Prone Positioning in Patients Intubated for COVID-19

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Objectives/Hypothesis: Prone positioning is frequently used in patients intubated for COVID-19-related lung injury to improve oxygenation. At our institution, we observed severe tongue edema develop in some of these patients. Hence, we sought to determine the incidence of tongue edema in this cohort and whether prone positioning was a risk factor associated with this complication.

Study Design: Retrospective cohort study.

Methods: A single-system retrospective cohort study of patients intubated for respiratory failure secondary to COVID-19 who subsequently developed clinically notable tongue edema from March 13 to July 5, 2020.

Results: 260 patients were intubated for COVID-19-related respiratory failure during the study period. 158 patients (60.8%) underwent at least one episode of proning. Twelve patients in total (4.6%) developed clinically significant tongue edema. Eleven of the twelve patients (91.7%) who developed tongue edema underwent proning prior to the development of edema. Prone positioning was associated with an increased incidence of tongue edema (odds ratio [OR] 7.56, 95% confidence interval [CI] 0.96–59.46, $P = .027$). In all proned patients who developed edema, this complication was noted during proning or shortly after supination (range, 0–4 days). Tongue edema was primarily managed with conservative measures; one patient required tracheostomy for definitive management.

Conclusions: Tongue edema appears to develop in a subset of patients with COVID-19 who are intubated. It appears to be associated with prone positioning but is likely multifactorial in nature. Further investigation into its incidence and pathophysiology is warranted.

Key Words: COVID-19, intubation, proning, prone positioning, tongue edema.

Level of Evidence: 4

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INTRODUCTION

The SARS-CoV-2 virus, which is responsible for the disease known as COVID-19, has caused a global pandemic, with over 195 million cases and 4.1 million deaths to date.[1] The spectrum of symptoms at presentation can range from completely asymptomatic to acute respiratory failure requiring endotracheal intubation and mechanical ventilation. A case series of 5,700 patients diagnosed with COVID-19 in the New York City area indicated that the rate of intubation for patients diagnosed with COVID-19 is as high as 12.2%.[2] Many intubation-related complications arise in this patient population, which often require otolaryngology consultation and management in the acute setting. At our institution, we observed an increased number of consultations for the evaluation and treatment of severe tongue edema and tongue injuries in patients who were intubated for COVID pneumonia. There has been only one case report of tongue edema in a patient intubated for COVID pneumonia, which was attributed solely to prolonged prone positioning and was managed conservatively with steroids, a bite block, and lingual compression.[3]

Hence, we sought to study the cohort of patients intubated for COVID-19-related respiratory failure at our institutions to determine the incidence of tongue edema. In our study, we also examined clinical factors and outcomes associated with this potential complication.

MATERIALS AND METHODS

This was a single-system multicenter retrospective cohort study of patients intubated for respiratory failure secondary to COVID-19. This study was approved by the MedStar Health Research Institute (MHRI) Institutional Review Board. A database search of all patients intubated for COVID-19 pneumonia between the dates of March 13 and July 5, 2020 at MedStar Washington Hospital Center and MedStar Georgetown University Hospital was conducted by the Department of Biostatistics and Bioinformatics. The primary study endpoint was the

development of severe tongue edema. A careful review of the electronic medical record (EMR) was used to identify patients that were rendered a diagnosis of significant tongue edema based on the medical documentation. Clinical descriptions were variable but often included floor of mouth/tongue edema that led to tongue protrusion beyond the teeth or even beyond the confines of the oral vestibule. Patients were excluded from analysis if they were younger than 18 years old, if there was an incomplete data set, or if they were initially intubated for reasons other than COVID-related respiratory failure.

Data collected included patient demographics, duration of intubation, proning status, tracheostomy status, mortality rate, and whether the otolaryngology service was consulted. Special attention was paid to timing of proning in relation to intubation, duration of proning, and number of proning episodes. At our institution, indications for prone positioning in intubated COVID + patients included severe ARDS, which was defined as a PaO2: FiO2 ratio <150 on FiO2 0.6 and TV 6 cc/kg of ideal body weight.

Continuous variables were summarized as means and categorical variables were aggregated as frequencies. Odds ratio (OR) was calculated to assess for an association between prone positioning and the development of tongue edema. Paired two-tailed t-tests were used to compare mean duration of intubation in patients with and without tongue edema as well as mean duration of proning in patients with and without tongue edema. GraphPad QuickCalcs (GraphPad Software Inc.) was used for statistical analysis.

RESULTS

260 patients were intubated for COVID-19-related respiratory failure during the study period. The mean age of the patients studied was 62 years old (range, 25–99 years old). Men comprised 56.2% of the cohort. 158 patients (60.8%) underwent at least one episode of proning. 12 patients (4.6%) developed clinically significant tongue edema. Tongue edema was identified a mean of 14 days after intubation (range, 5–32 days). The duration of intubation for patients that developed tongue edema was significantly longer than those who did not (mean [SD] 24.9 [6.96] days vs. 11.8 [9.93] days, $P < .0001$).

Of the 12 patients who developed tongue edema, 11 had undergone at least one episode of proning prior to the development of edema (91.7%). The mean duration of time from intubation to the first episode of proning was 1.3 days, but many patients underwent multiple episodes of proning. Prone positioning was associated with an increased incidence of tongue edema (odds ratio [OR] 7.56, 95% confidence interval [CI] 0.96–59.46, $P = .027$). All proned patients who developed edema did so during an episode of proning or shortly after supination (Fig. 1). The mean number of proning episodes was greater in proned patients who developed tongue edema (1.73 episodes) than in proned patients who did not develop tongue edema (1 episode) ($P = .0039$). In addition, the mean number of days spent in the prone position was greater in patients who developed tongue edema (7.36 days) than in patients who did not develop edema (4.71 days) ($P = .0397$).

5 patients (41.7%) with tongue edema also developed tongue injuries ranging from ulcerations secondary to the endotracheal tube (ETT) to penetrating injuries
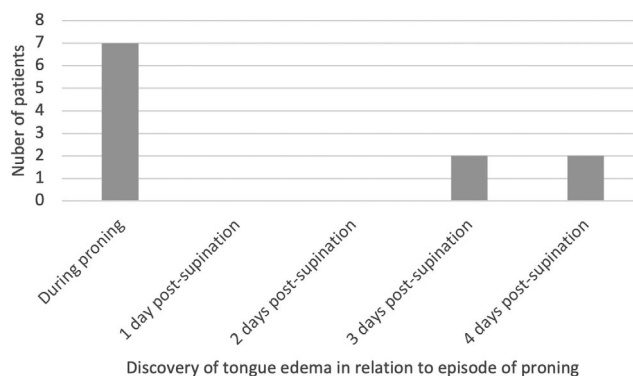

Fig. 1. Timing of development of tongue edema in relation to proning. Eleven out of 12 patients who developed tongue edema had undergone at least one episode of proning. Tongue edema was noted in the majority of patients (seven of 11) during an episode of proning. No patients developed tongue edema prior to proning.

secondary to biting. 10 patients (83%) who developed tongue edema also developed other pressure-related injuries of the head and neck. Only one patient who developed edema was taking an ACE-inhibitor. Otolaryngology was consulted in 11 (91.7%) of patients who developed tongue edema. Tongue edema was primarily managed with conservative measures including bite blocks, occlusive dressings, frequent oral care, application of ointment to the lips and tongue to prevent desiccation of mucosa, and head of bed elevation. Tracheostomy was offered for definitive treatment of tongue edema in one patient after they failed to respond to conservative measures.

DISCUSSION

In our study, we found that approximately one in twenty patients who were intubated for COVID-19 developed clinically significant tongue swelling. Consultation to the otolaryngology service at our institutions was requested in the majority of patients who developed tongue edema. Given the relatively high incidence of this complication and the potential for sequelae such as severe tongue lacerations, autoamputation, or inability to extubate, it behooves otolaryngologists and critical care providers to be aware of the risk factors and outcomes associated with this condition. This study is the first to examine this clinical entity in detail and demonstrated an association between prone positioning and the development of tongue edema in patients intubated for COVID-19. Previously, our group had also found an increased degree of facial pressure injuries occurring from proning in this patient population.[4] Together, these results highlight the importance of standardized screening for tongue edema and other facial pressure injuries in patients who are proned.

It is worth noting that our institutional proning checklist did include precautionary measures intended to prevent the development of facial and tongue edema. These include performing oral care and ensuring that the tongue is inside the mouth or using a bite block prior to

proning, and positioning the head in a way that minimizes pressure to the face and enables visualization of the ETT once the patient is prone. Given that our study was retrospective in nature, however, we were unable to ascertain the degree of adherence to our institutional protocol. Of note, the ICU proning protocol at our institution does not include suggestions on how the ETT should be managed with respect to the tongue or the holster; given that pressure from the ETT may in part be responsible for the development of tongue edema and injuries, it is worth considering the use of offloading techniques, such as frequent repositioning of the ETT.

Although proning may contribute to tongue edema, we acknowledge that its etiology is likely still multifactorial. Other possible contributing factors may include medication effect (i.e., ACE-inhibitors), poorly positioned endotracheal tubes and holsters, generous volume replacement, and perhaps even arterial/venous thrombosis secondary to the hypercoagulable state seen in COVID-19.[5] In our cohort, only one patient who developed tongue edema was taking an ACE-inhibitor, a common cause of upper airway angioedema in the general population. Interestingly, there is a growing body of literature describing a possible link between angioedema and COVID-19.[6,7] The SARS-CoV-2 virus has been shown to bind with high affinity to the ACE-2 receptor, which is expressed by epithelial cells of the tongue.[8] Inhibition and downregulation of available ACE receptors leads to unregulated bradykinin production, which is key to angioedema pathogenesis.[9] It is plausible that the tongue edema observed in this cohort could in part be attributed to the molecular interaction of the SARS-CoV-2 virus with the ACE-2 receptor.

We observed in our study that patients who develop tongue edema while intubated for COVID-related respiratory failure exhibit longer periods of intubation than patients who do not develop tongue edema. The tongue edema may in part be related to longer intubation and pressure from the endotracheal tube because the mean time to identification of tongue edema was 14 days, which is even longer than the mean total intubated time of patients who did not develop tongue edema. Upper airway swelling may preclude a safe extubation even if it is clinically appropriate from a pulmonary standpoint. Tracheostomy may be considered in those who fail to respond to conservative measures, especially if it delays extubation. Several studies have demonstrated that prolonged periods of intubation are associated with higher frequencies of acute laryngeal injuries including ulceration, granuloma formation, vocal cord paralysis, and subglottic stenosis.[10,11] This underscores the need for prompt recognition and treatment of tongue edema in this patient cohort as well as early consideration of tracheostomy.

Our study was limited by its retrospective nature, which impacted the ability to clearly define the severity of tongue edema in this population because it was not documented according to a standardized rating tool. In addition, the time to resolution was often not documented, which precluded analysis of the efficacy of our interventions. It is also worth noting potential selection bias given that more critically ill patients are often the ones that require proning.

CONCLUSION

Severe tongue edema develops in a subset of patients with COVID-related respiratory failure that require intubation. An increased incidence of tongue edema in this cohort appears to be associated with prone positioning, but likely arises from a complex interaction of multiple factors. Hence, appropriate screening will be key to prompt recognition and management of this potential complication in the COVID-era.

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