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Research paper

Prevalence and recovery of dysphonia in COVID-19 patients requiring intensive care treatment

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ABSTRACT

Background: Dysphonia and laryngeal pathology are considerable issues in patients hospitalised with COVID-19 with prevalence rates cited between 29% and 79%. Most studies currently are limited to reporting single-institution data with many retrospective.

Objectives: The aims of this study were to prospectively explore the following: (i) prevalence; (ii) treatment; and (iii) recovery pattern and outcomes for dysphonia, in patients with COVID-19 requiring intensive care unit (ICU) treatment.

Methods: Patients admitted to 26 ICUs over 12 months, diagnosed with COVID-19, treated for survival, and seen by speech–language pathology for clinical voice assessment were considered. Demographic, medical, speech–language pathology treatment, and voice outcome data (grade, roughness, breathiness, asthenia, strain [GRBAS]) were collected on initial consultation and continuously monitored throughout the hospital admission.

Findings: Two-hundred and thirty five participants (63% male, median age = 58 yrs) were recruited. Median mechanical ventilation duration and ICU and hospital lengths of stay (LOSs) were 16, 20, and 42 days, respectively. Dysphonia prevalence was 72% (170/235), with 22% (38/170) exhibiting profound impairment (GRBAS score = 3). Of those with dysphonia, rehabilitation was provided in 32% (54/170) cases, with dysphonia recovery by hospital discharge observed in 66% (112/170, median duration = 35 days [interquartile range = 21–61 days]). Twenty-five percent (n = 42) of patients underwent nasendoscopy: oedema (40%, 17/42), granuloma (31%, 13/42), and vocal fold palsy/paresis (26%, 11/42). Presence of dysphonia was inversely associated with the number of intubations ($p = 0.002$), intubation duration ($p = 0.037$), ICU LOS ($p = 0.003$), and hospital LOS ($p = 0.009$). Conversely, duration of dysphonia was positively associated with the number of intubations ($p = 0.012$), durations of intubation ($p = 0.000$), tracheostomy ($p = 0.004$), mechanical ventilation ($p = 0.000$), ICU LOS ($p = 0.000$), and hospital LOS ($p = 0.000$). More severe dysphonia was associated with younger age ($p = 0.045$). Proning was not associated with presence ($p = 0.075$), severity ($p = 0.164$), or duration ($p = 0.738$) of dysphonia.

Conclusions: Dysphonia and laryngeal pathology are common in critically ill patients with COVID-19 and are associated with younger age and protracted recovery in those with longer critical care interventions.

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Lay summary

Voice impairment is common in COVID-19 patients who require intensive care treatment. Those who are younger and require greater periods of mechanical ventilation, take longer to recover their vocal function.

1. Introduction

Laryngeal pathology and dysphonia are well recognised to be common sequelae in patients requiring intensive care unit (ICU) treatment and is most often seen in those requiring endotracheal intubation.[1] Postextubation dysphonia, specifically, is understood to be a manifestation of vocal fold immobility during the intubation period, with presence and duration of intubation and endotracheal-tube-cuff pressure recognised as primary risk factors for impairment.[2]

Disorders of voice are being increasingly identified in patients with COVID-19, with early international evidence citing dysphonia rates between 29% and 79%.[3–10] In studies that specifically examined laryngeal function in the hospitalised patients with COVID-19, rates of dysphonia and laryngeal pathology are observed to be higher in those who require intubation or tracheostomy or had a history of respiratory disease.[7,8] Furthermore, dysphonia and laryngeal pathology are more frequent in patients intubated and diagnosied with COVID-19 than in those intubated for diagnoses other than COVID-19.[4] At the time of initial speech–language pathology (SLP) assessment, severe voice impairment is not uncommon,[7] with the dominant feature being asthenia at the core of perceptual clinical presentation.[5] Patterns of voice recovery appear to be variable, with persistent dysphonia experienced in up to 56% patients at discharge from the acute care facility.[6,7,10]

In addition to disorders of voice, laryngeal sequelae in COVID-19 is of increasing concern with frequent presentations of vocal cord palsy/paresis, vocal cord atrophy, laryngeal oedema, and granulation, apparently.[4,6,9] Documented associations between the presence and severity of COVID-19 voice impairment, laryngeal pathology, and medical outcomes data have been variable to date. Two studies showed an association between dysphonia severity and increased hospital but not ICU length of stay (LOS),[7,8] whereas another study described higher rates of laryngeal pathology in those with shorter hospital LOS, intubation, and tracheostomy.[9] A further study[5] demonstrated a complete absence of correlation between rates of laryngeal pathology diagnosis and the duration of intubation or tracheostomy. Moreover, despite initial theories that prone ventilation positioning in the intubated patient would increase the presence and severity of laryngeal impairments, this has not been proven.[7,10] Consequently, these data suggest that the risk of developing vocal and laryngeal impairment in COVID-19 is different to other critical care populations studied to date.

To achieve a better understanding of voice and laryngeal impairment in patients with COVID-19 and to assist in gaining consensus to guide proactive treatment, more evidence is required across larger cohorts and multiple facilities. Consequently, we aimed to prospectively explore the following: (i) the prevalence; (ii) treatment; and (iii) recovery pattern and outcomes for voice, in critically ill patients with COVID-19 across multiple ICUs.

2. Methods

This study was conducted and has been reported in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement.[11]

2.1. Design

The study incorporated a multisite prospective observational cohort study.

2.2. Participants and setting

The current study described in this manuscript was a substudy of a larger parent project examining swallowing outcomes following COVID-19. This substudy was conducted over a 12-month period (1st March 2021–1st March 2022). All adult patients aged between 18 and 100 years, diagnosed with COVID-19, requiring ICU admission as part of their management, treated with the intent for survival, and referred to SLP during the acute hospital admission in line with site-specific referral practices across 26 participating New South Wales public hospitals (metropolitan and rural) were considered for inclusion.

2.3. Demographic data

Medical records for all participants were reviewed, and demographic data consisting of age, sex, hospital LOS (recorded in days), and past medical history were extracted. Medical data relevant to ICU admission were also extracted, which included ICU LOS (days), Acute Physiology and Chronic Health Evaluation II (APACHE-II) score,[12] duration of endotracheal intubation (days), duration of tracheostomy (days), duration of mechanical ventilation (days), number of intubations, medical complications, and discharge destination. All demographic outcomes relating to duration were calculated in days from the date of ICU admission.

2.4. Voice

Vocal function was perceptually assessed by the local site speech–language pathologist prospectively at the time of in-person initial clinical examination with presence and severity of voice impairment (dysphonia) defined by the grade roughness breathiness asthenia strain (GRBAS) scale.[13] The GRBAS is a four-point numerical scale across five components where G (grade) represents overall hoarseness, R (roughness) describes how rough the voice is, B (breathiness) describes the amount of air loss during vocalisation, A (asthenia) describes how “weak” the voice sounds, and S (strain) describes how much extraneous “effort” is applied during vocalisation. The scale ranges between 0 = normal, 1 = slight, 2 = moderate, and 3 = severe.

All voice examinations were conducted in accordance with the clinical guidelines of Speech Pathology Australia[14] and were in line with individual patient needs. All assessments involved detailed medical and voice case history, cranial nerve assessment, and audio perceptual rating of vocal quality. Grading of voice impairment using the GRBAS scale is part of standard SLP training and routine clinical practice.

Vocal function was managed as per usual clinical care throughout the patient's hospital admission, with dysphonia management considered complete once the patient had achieved premorbid voice quality as defined by patient self-report or when their vocal function had stabilised such that the treating speech–language pathologist had determined that further improvement was unlikely. Resolution of dysphonia was defined by a GRBAS rating of 0.

Furthermore, several other specific voice endpoints were recorded, capturing information relevant to whether dysphonia resolved, duration to achieving dysphonia resolution, dysphonia rehabilitation, and endoscopic assessment outcomes (if conducted in accordance with routine clinical care). All voice data relating to

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duration were calculated in days from the date of ICU admission. For those patients who underwent instrumental voice examination via endoscopy, additional outcome measures were used to describe voice and laryngeal impairment.

Outcome measures reported for endoscopy included the presence and type of functional and anatomical laryngeal pathology.

2.5. Data collection

Each individual site collected local participant data and subsequently input this data into a purpose-built password-protected *Research Electronic Data Capture* (REDCap) database[15] via a secure survey link. Bias surrounding data points was minimised through the provision and use of a data dictionary defining each data point. In addition to this, training was provided to all investigators before study commencement on participant recruitment, data collection, and data entry to ensure consistency across investigators. Data was deidentified at the point of data entry. The REDCap database[15] was designed such that each data field (except APACHE-II score)[12] was mandatory to facilitate ensuring data completeness. APACHE-II score was not a mandatory data field as not all participating sites collected this information, and it is beyond the scope of expertise of the SLP investigator to calculate this.

2.6. Data analysis

At completion of data collection, data were exported from the REDCap[15] database via a secure encrypted link. Data were then downloaded into Excel and the Statistical Package for Social Sciences (SPSS Version 27.0) for analysis.

Descriptive statistics were employed for data analysis. A conservative approach of non-normal data distribution was assumed with data reported as medians and interquartile ranges (IQRs) (median [IQR]). Categorical data are presented as a proportion of the sample (n [%]). Correlation statistics between variables were determined a priori and were conducted using nonparametric (Mann–Whitney U) assessments between continuous and dichotomous variables, Pearson's correlation between two continuous variables and Fishers Exact Test between dichotomous variables, with statistical significance set at $p < 0.05$.

Ethical approval was sought and obtained from Concord Repatriation General Hospital Human Research & Ethics Committee (2020/ETH01301). Written consent for the purposes of recording outcomes was sought and obtained before data collection in all cases except for those who satisfied the waiver of consent in accordance with the conditions of ethical approval.

3. Results

3.1. Demographic and critical care outcomes

Across 26 New South Wales public hospitals, 235 patients (149 male; 86 female), with a median age of 58 years (range = 21–97 years, IQR = 48–70 years), were recruited to participate. Most participants (n = 196; 83%) required intubation and mechanical ventilation as part of their ICU treatment, with a median intubation duration of 14 days (IQR = 9–22 days). Tracheostomy insertion occurred in 33% (n = 78) patients with a median duration of 31 days (IQR = 21–49 days). APACHE-II score was available for 91 participants with a median score of 15 (IQR = 12–17). ICU and hospital LOSs varied with median periods recorded at 20 days (IQR = 10–42 days) and 42 days (IQR = 23–71 days), respectively.

Most patients had multiple pre-existing comorbidities documented at the time of hospital admission. Hypertension (n = 110, 47%) and diabetes (n = 106, 45%) were the most frequently observed comorbidities.

Hospital-acquired comorbidities were observed at a high frequency across the cohort with the most common being ICU-acquired weakness (54%), delirium (49%), cardiac event (17%), pressure injury (14%), and failed extubation (12%). A mortality rate of 11% was recorded.

Just over half of the cohort was discharged home from acute care (55%), with almost a quarter of them requiring inpatient rehabilitation (24%) and a smaller proportion transferred to another acute care facility (9%).

3.2. Voice outcomes

Prevalence of dysphonia on initial SLP assessment was 72% (n = 170) across the total cohort (N = 235) with a higher rate (n = 152, 89%) in those who were intubated (n = 197). This initial SLP assessment occurred at a median of 17 days (IQR = 10–36 days) after admission to the ICU.

Of those who were dysphonic (n = 170), 22% (n = 38) exhibited severe dysphonia (GRBAS score = 3), 44% (n = 74) demonstrated moderate dysphonia (GRBAS score = 2), and 34% (n = 57) had mild dysphonia (GRBAS score = 1) on initial examination. Dominant features of dysphonia were asthenia/weakness (81%), breathiness (79%), and roughness (78%), with a lesser proportion demonstrating strain (47%). Fig. 1 illustrates the distribution of severity across each of these parameters.

Voice rehabilitation was reported in 32% (n = 54) patients with a range of therapeutic treatments provided, most frequently vocal hygiene (n = 49, 91%) followed by laryngeal deconstriction (n = 9, 17%). Fig. 2 summarises dysphonia rehabilitation delivered across the cohort.

Resolution of dysphonia was achieved by hospital discharge in 66% (n = 112) of participants, with a median duration to recovery of 35 days (IQR = 21–61 days). This left 25% of the total cohort (58/235) and 34% of the dysphonic cohort (58/170) with persistent dysphonia at hospital discharge. Given that this study was conducted in the acute hospital environment only, it was not possible to collect follow-up data for those who exhibited unresolved dysphonia at the point of hospital discharge.

In those diagnosed with dysphonia on initial speech pathology assessment, 25% (n = 42) underwent nasendoscopy to further evaluate laryngeal anatomy and function with all but one (n = 41, 98%), diagnosed with laryngeal pathology. The one participant who was not diagnosed with laryngeal pathology had undergone nasendoscopy for the purposes of tracheostomy weaning only. The most frequently identified laryngeal pathology was oedema (n = 17, 40%), followed by granuloma (n = 13, 31%), vocal fold palsy/paresis (n = 11, 26%), muscle tension dysphonia (n = 4, 10%), and erythema (n = 4, 10%). All patients who were diagnosed with laryngeal pathology had undergone intubation.

3.3. Associations between demographic, critical care, and voice data

Several associations were identified between demographic, critical care, and voice outcomes. Negative linear associations were observed between the presence of dysphonia and number of intubations ($Z = -3.801$, $p = 0.002$), duration of intubation ($Z = -2.091$, $p = 0.037$), ICU LOS ($Z = -3.021$, $p = 0.003$), and hospital LOS ($Z = -2.604$, $p = 0.009$). Conversely, duration of dysphonia was positively associated with several critical care outcomes including number of intubations ($r = 0.235$, $p = 0.012$), intubation duration ($r = 0.450$, $p = 0.000$), tracheostomy duration ($r = 0.425$, $p = 0.004$), mechanical ventilation duration ($r = 0.664$, $p = 0.000$), ICU LOS

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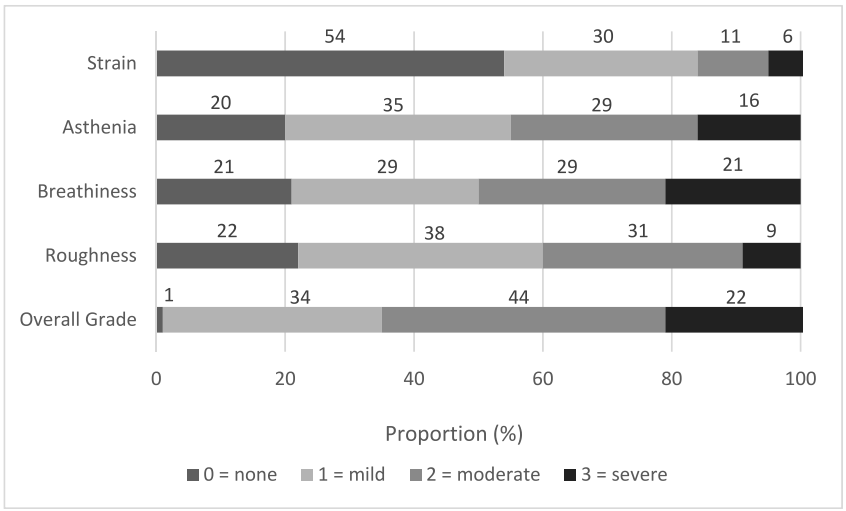

Fig. 1. Distribution of dysphonia severity (grade roughness breathiness asthenia strain [GRBAS]) at speech–language pathology initial assessment (n = 170).

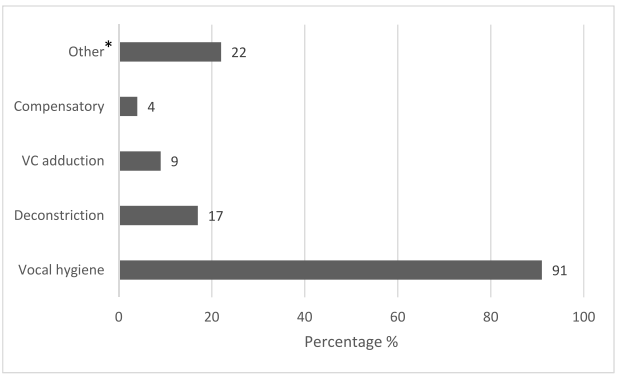

Fig. 2. Methods of voice rehabilitation implemented for dysphonic cohort (n = 170). *Other voice rehabilitation methods included expiratory muscle strength training, cough suppression, and respiratory-control techniques.

(r = 0.738, p = 0.000), as well as hospital LOS (r = 0.805, p = 0.000). These data are summarised in Table 1.

More severe dysphonia was associated with younger age (r = −0.153, p = 0.045) but with no other demographic or critical care outcomes. Finally, the use of prone positioning as a ventilation treatment method was not associated with either the presence (r = 3.165, p = 0.075), severity (Z = −1.390, p = 0.164), or duration (Z = −0.335, p = 0.738) of dysphonia.

4. Discussion

To the authors' knowledge, this is the most expansive geographical and multisite prospective study to report voice outcomes in patients diagnosed with COVID-19 requiring ICU treatment. It confirms that the prevalence of dysphonia in those referred to SLP in this population is high. In addition to this, whilst the *presence* of dysphonia was not associated with mechanical ventilation and medical outcomes, the *duration of dysphonia recovery* was longer in those who required extended ICU interventions as well as ICU and hospital LOS. Perceptual voice impairment levels were also more *severe* in younger patients.

Dysphonia as a feature of COVID-19 has been reported as an issue regardless of the need for hospitalisation or ICU treatment. This appears to be due to the proposed cause for dysphonia in COVID-19 being two-fold. First, the nature of this respiratory virus manifests as an inflammatory process of the upper and lower airways, with oedema and erythema recognised as core symptoms.[16] Second, for those who require hospitalisation, ICU admission, and invasive mechanical ventilation, these treatments further exacerbate existing irritation to the upper aerodigestive tract, resulting in localised tissue trauma, primarily at the larynx.[8] This is supported in the current study in that *presence* of dysphonia was not dependent on whether intubation occurred, but the *duration to recovery* of voice was associated with longer durations of intubation and mechanical ventilation.

The prevalence of dysphonia reported in the current study (72%) is higher than the international data documented to date. Rouhani et al.[5] describe a dysphonia rate of 54% in their study; however, evaluation of vocal function occurred 2 months after hospital discharge, potentially allowing for dysphonia resolution in a proportion of their group. Archer et al.[10] cited a 58% prevalence rate, although this included all hospitalised COVID-19 patients, not just those admitted to the ICU. Regan et al.[7] identified 66% of participants as dysphonic in their cohort, with perceptual SLP voice assessment taking place after extubation, representing the closest methodological comparison to the present study. Specifically exploring those who underwent intubation as part of their ICU treatment, Archer et al.[10] detailed that the rate of dysphonia in their intubated subset increased to 86%, which is commensurate with our finding of 89% for our intubated subset. Only two other published studies have discussed dysphonia severity at the time of initial SLP consultation, with a slightly higher rate of dysphonia severity classified as “severe” on the GRBAS scale identified in the present study (22%) than that documented by Regan et al.[7] (14%) and Regan et al.[8] (19%). It is challenging to ascertain the reason for the difference between the studies; however, given the critical care outcomes including duration of intubation, ICU and hospital LOSs appear relatively comparable across each cohort.

The positive associations between medical outcomes and duration of dysphonia identified within our study are not only consistent with other published findings within the COVID-19 population[7] but also synonymous with other critical care patient groups.[1] Surprisingly however, more severe dysphonia was not associated with longer durations of intubation, tracheostomy, or ICU or hospital LOS in our study. This differs from Regan et al.[7] who found a weak positive correlation between GRBAS rating and LOS, with those who had more severe dysphonia, having a longer

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Table 1
Associations between demographic, critical care, and voice outcomes across total cohort (n = 235).

	Median (IQR)	Age	APACHE-II	Number of intubations	Intubation duration	Tracheostomy duration	Mechanical ventilation duration	ICU LOS	Hospital LOS
Presence of dysphonia	–	−1.842	−1.006	−3.801**	−2.091*	−0.571	−0.851	−3.021**	−2.604**
Z (p-value)		(0.065)	(0.315)	(0.002)	(0.037)	(0.568)	(0.395)	(0.003)	(0.009)
Dysphonia Severity	2 (1–2)	−0.153*	−0.154	0.117	−0.037	−0.046	−0.085	−0.018	0.093
r (p-value)		(0.045)	(0.200)	(0.128)	(0.650)	(0.727)	(0.298)	(0.820)	(0.229)
Duration to recovery of dysphonia	35 (21–61)	−0.175	−0.168	0.235*	0.450**	0.425**	0.664**	0.738**	0.805**
r (p-value)		(0.064)	(0.265)	(0.012)	(0.000)	(0.004)	(0.000)	(0.000)	(0.000)

* sig at 0.05; ** sig at 0.
Abbreviations: APACHE: Acute Physiology and Chronic Health Evaluation; ICU: intensive care unit; IQR: interquartile range; LOS: length of stay.

hospital LOS. While Archer et al.[10] reported that dysphonia severity improved between initial assessment and discharge, they did not examine if any associations between dysphonia severity and medical outcomes were present.

While use of prone ventilation has been previously suggested as a possible contributing factor for presence of laryngeal pathology and voice impairment in early stages of the pandemic, it was not found to be associated with voice outcomes in this study. This finding is supported by the work of Archer et al.[10] and Regan et al.[7] who reported a similar lack of association, although the current authors do acknowledge that each study may not have been sufficiently powered to illustrate a statistically significant result. Despite this, we do acknowledge that the impact of prone positioning may still be important at a clinical level.[17,18] Further data collection should be recorded and evaluated to gain further knowledge around this.

Low rates of dysphonia rehabilitation were reported in the current study (32%), and it is unclear the role rehabilitation had on vocal recovery. Similarly, Regan et al.[7] described low rates of voice treatment (20%), with constraints on service delivery including poor access to early endoscopy because of the pandemic, cited as a likely influencing factor. Another factor that may have limited the provision of voice therapy is the disparity of perceived vocal impairment between the patient and treating clinician. In a study by Rouhani et al.,[5] clinicians rated 54% of their cohort as dysphonic, where only 13% of the patients themselves considered their voice abnormal. As such, it may be postulated that patients are either not concerned by their voice change or that voice therapy may not be of high priority with other aspects of their care-taking precedence.

Nasendoscopy was conducted in only 25% of those with dysphonia in the current study with all but one participant exhibiting some form of laryngeal pathology. All those who were diagnosed with functional or anatomical laryngeal pathology had undergone intubation as part of their ICU treatment and were at high clinical suspicion of laryngeal pathology based on SLP clinical examination. This confirms that whilst the diagnosis of COVID-19 alone may be enough to increase chance for laryngeal impairment,[19] the addition of ICU therapies heightens the risk. This is supported by Boggiano et al.[4] who reported high rates of laryngeal pathology in their ICU COVID-19 cohort following translaryngeal intubation or tracheostomy, describing that 63% had $\geq$1 clinically significant laryngeal pathology on flexible endoscopic evaluation of swallowing, which was higher than that of the non-COVID group. More information is required detailing the pathophysiology and recovery pattern of laryngeal impairment in COVID-19 to inform optimal timing of assessment and treatment to enhance patient outcomes. This notion is reinforced by Dawson et al.[20] who propose that a proactive standardised scoring and review protocol including functional laryngeal assessment, with application of scales including the Patterson oedema scale,[21] is important to facilitate the early identification and management of contributing risk factors.

4.1. Limitations

Whilst this study is the first Australian and largest geographical prospective multisite project examining dysphonia prevalence and outcomes in the ICU COVID-19 population to date, limitations do exist. Not every patient admitted to the ICU across each site was screened for dysphonia, only those referred to SLP. As such, it can be postulated that the prevalence rates documented in this manuscript are likely an under-representation of the true dysphonia prevalence in ICU COVID-19 patients. Furthermore, instrumental assessment was not routinely administered due to time, service provision, and infection control constraints. Thus, potentially

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further contributing to the under-representation of functional and anatomical laryngeal impairment in this population. Lastly, the tool administered to assess the presence and severity of voice impairment was the GRBAS scale. Whilst it is acknowledged that this tool may not be as rigorous or the most sensitive to detect dysphonia presence or severity, it was chosen for its practical and easy-to-use nature, given voice outcomes were being collected by ICU clinicians, not voice specialists. The decision to use the GRBAS scale was hence a pragmatic one. Furthermore, this tool has been successfully applied in other studies examining voice impairment in patients with COVID-19.[5,7,8,10]

5. Conclusion

Dysphonia is frequently observed in critically ill patients with COVID-19 with invasive mechanical ventilation contributing to the protracted duration of voice recovery. Those who are younger in age appear to experience more severe dysphonia at the time of initial SLP consultation. Laryngeal pathology is not uncommon, although is potentially under-recognised due to low rates of endoscopic examination in the acute environment. More evidence on dysphonia pathophysiology is still required to guide early rehabilitation and ultimately enhance communication function and outcomes.

Data availability statement

All data from individual sites have been retained within a purpose-built password-protected REDCap database, saved on a secure password-protected shared drive housed on the Sydney Local Health District Speech Pathology server. All data may be downloaded via a secure encrypted link to which only the listed authors have access to.

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CRediT authorship contribution statement

NA Clayton: Conceptualisation, Methodology, Formal analysis, Investigation, Writing—original draft, Visualisation; Supervision; Project administration; **A Freeman-Sanderson**: Methodology, Formal analysis, Writing—review and editing, Visualisation; **E Walker**: Conceptualisation, Methodology, Investigation, Writing—review and editing, Visualisation.

Conflict of interest

The authors have no financial or nonfinancial disclosures to declare in the conduct of this study or preparation of this manuscript.

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