

Can ventilatory strategies in COVID-19 have an impact on outcomes?

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Abstract: The rapidly evolving understanding of Coronavirus Disease 2019 (COVID-19) respiratory failure pathogenesis, limited disease-specific evidence and demand-resource imbalances have posed significant challenges for intensive care clinicians. In this single-centre retrospective cohort study we describe the outcomes of COVID-19 patients admitted to Guy's and St. Thomas' NHS Foundation Trust (GSTT) critical care service. Patients were managed according to a local respiratory failure management pathway that was predicated on timely invasive ventilation when indicated and tailored ventilatory strategies according to pulmonary mechanics. Between 2nd March and 25th May 2020 GSTT critical care service admitted 316 patients with confirmed COVID-19. Of the 201 patients admitted directly through the Emergency Department with a completed critical care outcome, 71.1% survived to critical care discharge. These favourable outcomes may serve to inform the wider debate on the optimal ventilatory management in COVID-19.

To the Editor:

Acute hypoxemic respiratory failure (AHRF) is the commonest organ dysfunction that results in critical care admission with Coronavirus Disease 2019 (COVID-19). Clinically, it is debatable whether the pathophysiology of AHRF in COVID-19 resembles Acute Respiratory Distress Syndrome (ARDS), as this is influenced by the timing of presentation and may be affected by the treatments received.[1] The uncertainties generated by this new disease have engendered a debate on the optimal strategy for respiratory support and highlighted the need for data to help design clinical trials. However, in the context of a pandemic, institutions needed to develop pragmatic clinical pathways to meet the excess critical care demand and consider how best to use the available local resources - such as ventilators, staffing and oxygen supplies.

The objective of this study was to evaluate the impact of a locally derived respiratory failure management pathway on the outcomes of critically ill COVID-19 patients admitted to a high volume severe respiratory failure centre in the United Kingdom (UK).

Methods

This was a retrospective single-centre cohort study of all RT-PCR confirmed COVID-19 patients admitted to the critical care service at Guy's and St. Thomas' NHS Foundation Trust (GSTT) from 2nd March to 25th May 2020. GSTT, located in central London, is one of six nationally-commissioned severe respiratory failure and extracorporeal membrane oxygenation (ECMO) centres. In response to the pandemic, the service increased its critical care capacity in a phased manner up to 187 beds capable of invasive ventilation and developed a respiratory failure management pathway for COVID-19 (Figure 1), based on published literature as of 20th March 2020 and discussions with international experts.

Briefly, after an initial triage assessment performed on oxygen alone and an assessment of the work of breathing, patients were considered for a time-limited trial of awake proning or non-invasive respiratory support, or otherwise for endotracheal intubation. The overarching objective was the avoidance of delayed invasive mechanical ventilation in patients with increased work of breathing or severe hypoxemia. Subsequent ventilation and positive end expiratory pressure (PEEP) selection were based on categories of static compliance and driving pressure. Preference was given to prone position rather than higher PEEP. This is consistent with emerging phenotypes identified using international observational data.[1] The definition of *a priori* parameters based on a pathophysiological construct, together with a substantial increase in our resources, allowed us to provide the required respiratory support for an individual patient, according to an egalitarian, rather than utilitarian perspective.

The primary outcome was critical care mortality in patients admitted directly to GSTT. Given the wide range of mortality reported in the literature, it is useful to consider our single-centre outcomes in the context of the UK data reported by Intensive Care National Audit and Research Centre (ICNARC).

Results

During the study period, our critical care service admitted 316 confirmed COVID-19 patients, including 52 mobile ECMO retrievals and 51 non-ECMO critical care transfers from other institutions (Figure 2).

A total of 213 COVID-19 patients were admitted directly to our critical care service through our Emergency Department, and 201 patients had a completed critical care discharge outcome. The median [IQR] age of patients was 58 [49,66] years, 66.7% were men, 52.2% were from Black, Asian and Minority Ethnic (BAME) groups, and the median [IQR] Acute

Physiology And Chronic Health Evaluation (APACHE) II score was 14 [11,18]. 166 (82.6%) patients required invasive ventilation and 61 (30.3%) non-invasive respiratory support. Of the 61 patients who received non-invasive support, 41 (67.2%) received it only following extubation. Of the 48 patients coded as receiving 'High flow nasal oxygen', 28 (58.3%) received it primarily for humidification purposes with flow rates ≤ 15 litres-per-minute. Only one patient originally admitted to GSTT required ECMO initiation for AHRF due to a concurrent massive pulmonary embolism. Our critical care mortality was 28.9%.

Discussion

This is one of the largest single-centre studies describing outcomes of critically ill COVID-19 patients managed according to a local respiratory failure management pathway. The survival to critical care discharge of 71.1% provides reassurance that a strategy predicated on timely invasive ventilation and personalised ventilatory strategies can confer favourable outcomes. This strategy and outcomes are similar to the one adopted and described by Ziehr et al, where in a smaller cohort of 66 patients, the authors report a mortality of 16.7%. [2] When comparing to the contemporaneous ICNARC report of 9,026 COVID-19 patients admitted to critical care in the UK, our cohort had comparable baseline characteristics (age, sex, BMI and APACHE II scores) but with higher rates of advanced respiratory support (82.6% versus 72.5%), lower use of basic respiratory support (30.3% versus 63.3%) and a lower mortality (28.9% versus 44.3%). [3]

COVID-19 is an inflammatory vasculopathy that is initially associated with minimal parenchymal edema and atelectasis but significant pulmonary shunt, dead space and hypoxemia. [1] As lung edema increases, use of non-invasive positive pressure ventilation may improve oxygenation. However, unless the work of breathing and lung shear stress are reduced, there is concerns that prolonged non-invasive support can mask ongoing patient

self-inflicted lung injury (P-SILI) resulting in progressive inflammation and potentially refractory hypoxemia.[4] This possibility was recognized and reported by intensive care experts in Wuhan, China.[5] Whilst difficult to estimate the impact of the individual components of our management pathway, we postulate that avoiding delayed invasive mechanical ventilation and adapting mechanical ventilation to pulmonary mechanics can affect outcome in COVID-19. This may explain the significant mortality difference observed between our cohort and national data, and is congruent with the established evidence base suggesting high failure rates and excess mortality observed in patients receiving non-invasive ventilation in moderate-to-severe de novo AHRF.[6-9]

This study has a number of limitations. With a single-centre retrospective study it is difficult to adjust for unmeasured confounders, including thresholds for critical care admission and adjunctive management strategies beyond ventilation. When comparing local data to the national ICNARC data, the authors accept that confounding by indication influences any inference.

Despite these limitations, the strategy and outcomes reported may serve to inform the wider debate on the optimal ventilatory management of COVID-19. Further prospective clinical trials comparing time-limited non-invasive respiratory support with standard care may help guide such debate.[10]

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Figure 1. Guy's and St. Thomas' NHS Foundation Trust suggested management of respiratory failure in Coronavirus Disease 2019 (COVID-19). RR - Respiratory rate, NRBM - Non-Rebreather Mask, CRT - Critical Care Response Team, MERIT - Mobile Emergency Response Intubation Team, HCID - High Consequence Infectious Disease, HDU - High Dependency Unit, ED - Emergency Department, MV - Minute ventilation, PEEP - Positive End Expiratory Pressure, Vt - Tidal Volume, PBW - Predicted Body Weight, RM - Recruitment Manoeuvre and ECMO - Extracorporeal Membrane Oxygenation.

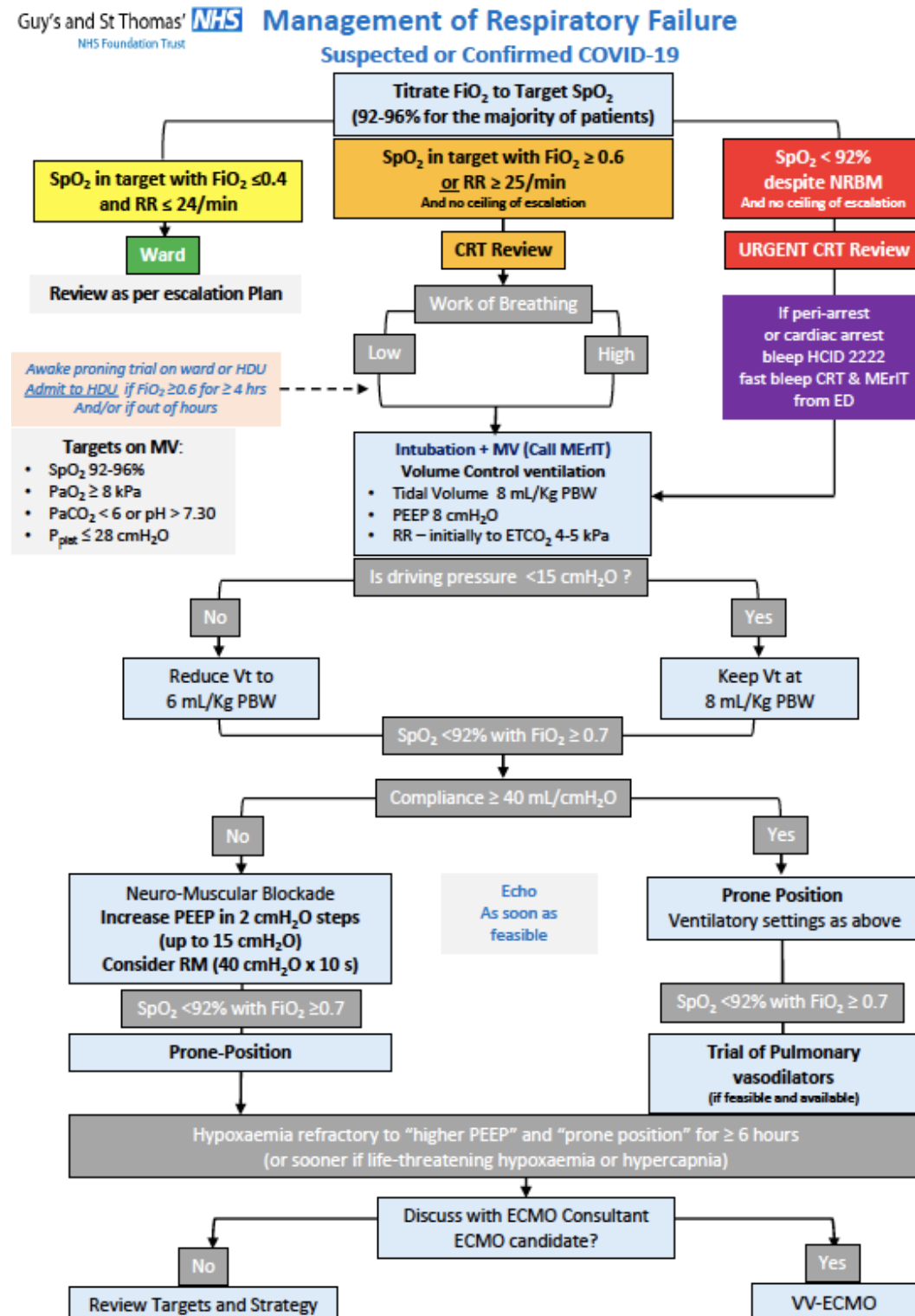


Figure 2. Flowchart of the 316 patients admitted to Guy’s and St. Thomas’ NHS Foundation Trust (GSTT) Critical Care with confirmed Coronavirus Disease 2019 (COVID-19). ECMO - Extracorporeal Membrane Oxygenation, BMI - Body Mass Index, BAME - Black, Asian and Minority Ethnic, APACHE - Acute Physiology And Chronic Health Evaluation, NIV - Non-Invasive Ventilation, and HFNO - High Flow Nasal Oxygen. *Of the 48 patients coded as receiving ‘High flow nasal oxygen’, 28 (58.3%) received it primarily for humidification purposes with flow rates ≤ 15 litres-per-minute.

