Unintended Consequences of An Analog Fix in A Digital Era: Transport Ventilators Associated with Significantly Longer Duration of Intubation for Critically Ill COVID-19 Patients

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Abstract

Background:

The first wave of the COVID-19 pandemic heavily impacted New York City, and stretched healthcare resources to the limits. The sudden spike in acutely ill patients with respiratory failure required the mobilization of the national stockpile of ventilators and a multitude of providers without expert ventilator training to meet the needs of patients. These ventilators do not display easily interpretable parameters of the ventilator-patient interaction, which could have a negative impact on patient care.

Methods:

A retrospective review of all adult patients admitted for at least 24 hours and requiring mechanical ventilation at a heavily impacted urban hospital in New York City during the first wave of the COVID-19 pandemic was undertaken. The type of ventilator (standard vs transport – or limited in display) was evaluated with respect to mortality, hospital length of stay, and factors associated with prolonged intensive care management of acute respiratory distress syndrome (sedation, analgesia, paralytics). Regression analysis was performed to evaluate for confounding factors.

Results:

From March 2, 2020 through May 9, 2020, 313 patients were included. Overall mortality was 84%. When compared to standard ventilators, patients placed on transport ventilators had significantly longer length of stay (17 days vs 9 days, $p = 0.001$), more days intubated (11 days vs 5 days, $p = 0.007$), longer duration of prone-positioning (5 days vs 3 days, $p = 0.05$), a greater need for sedation / analgesia ($p < 0.001$), and greater need for vasopressor support ($p = 0.002$). No difference in mortality ($p = 0.41$), barotrauma ($p = 0.29$), successful extubation ($p = 0.77$) or tracheostomy ($p = 0.36$) was observed.

Conclusions:

The lack of proper ventilation equipment is associated with prolonged hospitalization and critical illness. Given the economic and human burden that results from prolonged acute-care, it would benefit both patients and the healthcare system to recognize the infrastructure requirements required to respond to health crises of the future.

Background:

When COVD-19 was declared a pandemic by the WHO in early 2020 [1], the United States was only beginning to focus on the problem. By the time Elmhurst Hospital Center (EHC) in New York City was nicknamed the “epicenter of the epicenter,” the pandemic had already fully saturated both the hospital systems and locally available backup resources [2]. As the 2019-nCoV surge was largely driven by respiratory failure, the availability of ventilators became a crucial bottleneck to providing optimal patient care [3]. Eventually, the national stockpile of ventilators [4] had to be mobilized to the areas most heavily impacted by the virus. However, from this response arose several issues in the learning curve associated with these newly distributed emergency ventilators [5].

Several unanticipated challenges have arisen with respect to the ventilatory management of severely ill COVID-19 patients with rapidly progressive hypoxemic respiratory failure. Among those challenges were the steep combined learning curves of expert ventilatory management combined with the use of various ventilator types [5]. In addition the paucity of formal training in graduate medical education programs with respect to mechanical ventilation management has been highlighted by these challenges [6].While certain easily targetable objectives like low-tidal-volume ventilation [7] and prone positioning [8] are well known and widely accepted to improve outcomes in Acute Respiratory Distress Syndrome (ARDS) management, multiple other parameters such as plateau pressure and driving pressure, as well as individualized ventilatory strategies have also shown benefit [9]. However, optimizing such techniques and strategies is an acquired skill that takes time to develop, let alone master. Even still, it has been shown that, while most first-year fellows in Pulmonary and Critical Care are not vent-savvy when starting fellowship, this skill is adequately acquired with training and practice when provided with standardized equipment [10]. Furthermore, recent analysis of disaster-readiness has shown that skilled intensivists and respiratory therapists continue to be a bottleneck in providing care during a surge situation such as the first wave of the COVID-19 pandemic [11].

Recognizing ARDS and familiarization with treatment modalities is known to be associated with lung-protective ventilatory use [12], in a tertiary / university care setting and shown to have improved outcomes [13]. However, both these points infer experience with high-acuity patients and quick access to a ventilator's displayed graphics and information. Ventilatory challenges were compounded during the height of the first wave of the pandemic by virtue of the fact that the national stockpile ventilators (Transport Ventilators) are limited in their user-display interface.

While all ventilators used during the surge at EHC, were able to function in both volume-control and pressure-control modes, with titration of parameters such as flow, trigger, and cycle; a significant inter-ventilator difference exists in the display of operator feedback (i.e., loops, alarms, trends, etc.).

For patients in the vast majority of critical care settings, ventilators readily display loops and waveforms on a digital screen that assist the operator in optimizing settings to the patient's individualized needs. In contrast, ventilators meant for patient transport are very limited in capacity and display of this information, especially to the unaccustomed user. Therefore, during a pandemic, in which a multitude of ventilator types, including those with limited display information circulate, it creates an environment in which equipment is being used outside of its design spectrum. This environment gives rise to concern regarding how such unintended use and interpretation could adversely affect patient outcomes.

We report our experience at a heavily impacted safety-net hospital in New York City during the first wave of the pandemic, as a single-center retrospective evaluation of patient outcomes with respect to the different types of ventilators used to treat COVID-19 patients requiring mechanical ventilation.

Methods:

A retrospective review of patients admitted to Elmhurst Hospital Center in New York City during the height of the first wave of the COVID-19 pandemic was undertaken. Patients ages 18 years and older, admitted for at least 24 hours, intubated, and with ventilator data were considered for review, while those admitted for less than 24 hours or with incomplete ventilator data were excluded.

Descriptive analysis of the study population was performed from demographic and clinical information collected retrospectively from hand-review of the electronic medical record. Institutional approval for data evaluation was granted by the local Institutional Review Board.

Ventilator Data:

Each patient's ventilator type was classified into traditional ICU ventilators or transport ventilators (Care-Fusion LTV 1200 - supplied from the national ventilator stockpile). As previously mentioned, the transport ventilators were those limited in their display to a single "manometric" light column, which would dynamically express the selected parameter being measured.

Time from admission to intubation and days intubated were quantified. Data for vent mode and settings, PEEP values, and peak / plateau pressures was not reliably available, and therefore was not incorporated into analysis.

Sedation, Analgesic, and paralytic quantification:

For each medication being used for sedation or analgesia during the patient's course of mechanical ventilation, the number of days of medication used was quantified. Total days of all sedative medications (propofol, midazolam, ketamine), analgesic medications (fentanyl, hydromorphone), and paralytic medication (cisatracurium, vecuronium) was summed for each patient, thereby creating a sedation-days, analgesic-days, and paralytic days quantification for each patient during their course of mechanical ventilation. In addition, the variable of sedative-days was divided by the number of days the patient underwent mechanical ventilation, thereby calculating sedative-vent-days, designed to express the density of sedative/analgesic treatment required by the patient while undergoing mechanical ventilation.

Endpoints:

The following endpoints were compared between patients with traditional versus travel ventilators: duration of mechanical ventilation, duration of hospital stay, incidence of barotrauma, sedation-days, analgesic days, combined sedation/analgesic-days, paralytic days, use of prone positioning while intubated, discharge disposition, and mortality.

Regression analysis was performed with respect to clinical and demographic factors in order to elucidate significant factors related to mortality, and among therapeutic interventions (pharmacologic and prone-positioning) to evaluate for potential inter-variable relationships and confounders.

Results:

During the period of March 2, 2020 and May 9, 2020, a total of 313 patients were evaluated, and 291 had sufficient data for analysis. Demographics and clinical characteristics are displayed in Table 1. Males made up 80% of the population, and the median age was 61 years. Diabetes and Hypertension were the pertinent past medical history evaluated, and were present in 42% of the overall patient population for each variable respectively.

Table 1
Population Characteristics:

Population Characteristics (n = 291)							
		Mean	**Median**	**IQR**	**Survived**	**Expired**	**P-value**
Age (years)		60.84	61	52–70	60 (48–66)	62 (52–71)	0.09
BMI		29.7	28.5	25.9–32.2	28.2 (26–32)	28.5 (25.8–32.3)	0.86
			Frequency	**Percent**	**Survived**	**Expired**	**P-value**
Sex		Female	57	19.60%	10 (17.5%)	47 (82.5%)	0.75
		Male	234	80.40%	37 (15.8%)	197 (84.2%)	
	Risk Factor	**Frequency**		**Percent**	**Survived**	**Expired**	**P-value**
Known Prior Health Risk Factors	HTN (287)	120/287		42%	19 (43%)	101 (84%)	0.84
	DM (260)	110/260		42%	12 (28.5%)	98 (44%)	0.049

The evaluation of ventilator type on therapeutic interventions, length of stay, and mortality is displayed in Table 2. The median length of stay for the population was 10 days (IQR 5–23 days), and median time to intubation was 2 days (IQR 0–6 days). Pneumothorax occurred in 17.5% of the population, while any barotrauma (pneumothorax and/or pneumomediastinum) was appreciated in 25% of patients. The overall mortality was 84% for the study population (Table 2).

Table 2
Therapeutics, Incidence of Barotrauma, and Outcomes with respect to ventilator type.

Outcomes with Respect to Endpoints				
Vent Type (n, %)	**Overall**	**Standard (n = 218)**	**Transport (n = 73)**	**P-value**
Mortality	244 (84%)	185 (85%)	59 (81%)	0.42
Incidence of Barotrauma	74 (25%)	52 (24%)	22 (30%)	0.29
Incidence of Pneumothorax	51 (17.5%)	34 (16%)	17 (23%)	0.31
Successfully Extubated	18 (6.9%)	14 (6.4%)	4 (5.5%)	0.77
Tracheostomy	28 (9.6%)	19 (8.7%)	9 (12%)	0.36
Time Interval (median, IQR)	**Overall**	**Standard (n = 218)**	**Transport (n = 73)**	**P-value**
Length of Stay (days)	10 (5–23)	9 (5–20)	17 (9.5–30.5)	< 0.001
Days to Intubation	2 (0–6)	2 (0–5)	4 (1–8)	0.007
Days Intubated	6 (3–15)	5 (2–13)	11 (4–19)	0.004
Days to Tracheostomy (n = 28)	27.5 (23–31)	29 (24–33)	25 (21–26)	0.03
Therapeutic Interventions with Respect to Ventilator Type				
Vent Type	**Overall**	**Standard (n = 218)**	**Transport (n = 73)**	**P-value**
Pressor Days	5 (2–12)	4.5 (2–10)	7 (3–17)	0.002
Sedation Days	14 (6–36)	12 (5–29)	27 (10–45)	< 0.001
Sedation-Vent Days (mean, st. dev)	2.5 (1.68	2.4 (1.46)	2.7 (2.2)	0.25
Neuromuscular Blockade Use	128 (44%)	91 (42%)	37 (51%)	0.18
Neuromuscular Blockade Days (mean, st. dev)	0.45 (0.45)	0.42 (0.31)	0.49 (0.70)	0.48
Prone Positioning	85 (29%)	30 (41%)	55 (25%)	0.01
Days Proned	3 (2–7)	3 (2–6)	5 (3–7)	0.05

Ventilator Type:

Traditional ventilators were used in 218 patients (75%), while transport ventilators were used in 73 patients (25%). Transport ventilators were associated with a longer length of stay (17 days vs 9 days; p,0.001), longer number of days intubated (11 days vs 5 days; p = 0.007); greater number of both pressor-days (7 days vs 4.5 days; $p = 0.002$) and sedative-days (27 days vs 12 days; $p < 0.001$), and longer duration of prone-positioning when implemented (5 days vs 3 days; $p = 0.05$). Transport ventilators were not associated with a difference in mortality (85% and 84% respectively; $p = 0.41$), incidence of barotrauma (24% vs 30%; $p = 0.29$), successful extubation (6.4% vs 6.9%; $p = 0.77$) or need for tracheostomy (8.7% vs 9.6%; $p = 0.36$) (Table 2).

Regression Analysis:

Regression analysis was performed to evaluate for inter-group confounding factors and is displayed in Table 3. With respect to demographics and the incidence of barotrauma, only a history of diabetes was found to be weakly associated with a decreased odds of death (OR 0.49, 95% CI 0.24–1.02, $p = 0.057$), while ventilator type, age, sex history of HTN, and incidence of barotrauma were not significantly associated with risk of death. With respect to therapeutic interventions, sedation days were inversely associated with risk of death (OR 0.93, 95% CI 0.88–0.98, $p = 0.012$), consistent with the fact that those surviving to discharge had a more prolonged course and therefore a higher number of sedation days. The number of days for which a paralytic was used was weakly associated with an increased odds of death (OR 1.5, 95% CI 1.0-2.26, $p = 0.052$), which is consistent with patients requiring paralytics as having more difficult-to-treat ARDS.

Table 3
Regression Analysis evaluating factors associated with mortality.

Odds of Death				
	Odds Ratio	P-Value	95% Confidence Interval	
Regular Vent	0.68	0.301	0.32	1.42
Male Sex	1.59	0.257	0.71	3.52
Age	1.02	0.104	1.00	1.05
Barotrauma	0.73	0.413	0.35	1.54
DM	0.49	0.057	0.24	1.02
HTN	1.38	0.379	0.68	2.80
	Odds Ratio	P-Value	95% Confidence Interval	
Sedation Days	0.93	0.012	0.88	0.98
Pressor Days	1.01	0.915	0.91	1.10
Days Intubated	0.96	0.374	0.87	1.05
Days Proned	1.12	0.246	0.92	1.36
Paralytic Days	1.50	0.052	1.00	2.26

Discussion:

The long-term morbidity associated with critical illness has been directly associated with the duration of organ support [14, 15], and the 1-year mortality in the general ICU patient population has also been noted to be 21–28% [16, 17]. However, discrepancies against such findings exist, including one large retrospective analysis, suggesting prolonged ICU admission beyond 10 days was not necessarily associated with an increase in mortality [17]. These results from pre-pandemic ICU care parallel our results in which the length of stay was significantly longer in the transport ventilator group, while mortality was not significantly different between groups. The importance of this distinction, however, is that, while overall in-hospital mortality was not significantly different in our study, the consequences of prolonged admission requiring longer intubation and burden of sedative drugs has significant post-acute care consequences for the patient, and the healthcare system as a whole.

There are two factors that resonate in the COVID-19 population: consequences related to prolonged mechanical ventilation, and consequences related to prolonged ICU stay, frequently referred to as Post-Intensive-Care Syndrome (PICS) [18]. These effects have been observed both separately and together in large scale analysis [19].

Intubation Duration and Overall Morbidity / Mortality:

While it may be interpreted that delayed intubation could lead to a more protracted critical illness course, this appears unlikely. This is supported by our regression analysis in that the odds of death were not increased with respect to time to intubation (Table 3). While data is limited, timing of intubation (delayed vs early) has not been conclusively shown to be associated with a difference in mortality in COVID-19 patients with ARDS [20]. This supports our observation that the difference in time to intubation in our population was not only consistent with other studies, but was not likely a significant confounder in mortality analysis.

While the above addresses the acute-care aspects of prolonged intubation in the index hospitalization, it does not account for the longer-term consequences of prolonged intubation. These can be classified into those for which the patient suffers, such as, increased risk of ventilator associated pneumonia, increased risk of delirium, and substantial neuromuscular weakness with associated long-term morbidity. Prolonged intubation has been associated with significant morbidity, with the decreased capacity to regain functional status within 3 years [21]. However, significant mortality exists for older patients, and those with a greater comorbid burden [21, 22]. In addition, there has been an observed increased incidence of post-intubation tracheal stenosis in COVID-19 patients, with a suspected pathophysiologic relationship secondary to prolonged mechanical ventilation, hypoxia, and inflammation [23]. We did observe an increase in days of intubation, thus increasing the probability of complications due to prolonged intubation. Although we did not appreciate an increased incidence of tracheal stenosis in the travel ventilator group, we must recognize that many of these patients were lost to follow up in the ongoing adaptation of providing prolonged critical care across a multitude of hospital systems.

Ventilator associated Pneumothorax

Pneumothorax in patients with severe ARDS was previously thought to be associated with poor prognosis [24]. In contrast, our findings support recent literature which suggests that pneumothoraxes in COVID-19 pneumonia may not be an independent marker of poor prognosis [25]. Such findings concur with literature describing pneumatoceles and cysts even in patients not requiring invasive positive pressure ventilation [26, 27]. While the exact etiology of pneumothorax in COVID-19 patients remains unknown, our findings suggest that incidence may be most closely related to parenchymal degeneration and air leaks from prolonged inflammation and unlikely to be increased by prolonged exposure to travel vents. In our study the incidence of barotrauma was not significantly impacted by ventilator type. Therefore, we suggest that survival after a pneumothorax or isolated pneumomediastinum may not be as consequential as once presumed.

Sedation Burden and Post-Intensive Care Syndrome (PICS):

PICS is defined as the constellation of physical, psychological, and cognitive deficits appreciated following a prolonged critical illness [18, 28], and has been accepted as an integral part of understanding critical illness and its consequences [29]. Delirium is associated with Cognitive Deficit [30], and a significant decrease in cognition at 12 months has been noted in patients with a clinical course requiring ICU-level care complicated by delirium [31]. Prolonged sedation and mechanical ventilation increase the incidence of ICU-related delirium. Given the fact that patients on travel ventilators experienced about twice the burden of sedation, intubation duration, pressor requirements and overall hospital length of stay, it is reasonable to assume that this patient population is at a significantly increased risk for long-term consequences of PICS. This ultimately results in an enormous burden of post-acute care and rehabilitation, which carries a significant economic burden on the healthcare system [28].

Economic Consequences:

The cost of caring for critically ill patients varies widely from country to country as well as depending on the complexity of disease. However, respiratory failure requiring mechanical ventilation in the ICU incurs some of the highest cost, with approximations as high as 94% for those suffering from ARDS [32]. The exact costs of caring for a critically ill patient during the peak of the first wave of the pandemic is difficult to calculate given the influx of emergency funding, personnel, and dynamic resource changes. However, nationwide data demonstrated that those requiring ICU stay and mechanical ventilation had some of the highest incurred cost to the healthcare system, especially during the first wave of the pandemic [33, 34]. Even so, the mean length of stay for patients in the United States requiring mechanical ventilation was 16 days in the hospital and 11 days in the ICU respectively, with a mean ICU daily cost of approximately $4000/day [33]. This LOS duration is more consistent with our data for those with standard ICU ventilators compared with the significantly longer LOS for those with travel ventilators. Therefore, given the doubling of the ICU length of stay and ventilator time, without taking into account the ongoing post-acute healthcare needs, it can be inferred that the difference in ventilator type likely resulted in at least doubling of the per-patient care of these patients.

Limitations:

Several limitations are recognized in the current work. First off, data with respect to ventilator settings is not available for the patient population. This is an unintended consequence of an emergent situation during the first wave of the pandemic. While having this information would be ideal, it is also recognized that the present retrospective analysis is from an evaluation of a situation which stretched a healthcare system beyond its capacity.

Secondly, the frequent transfer of patients to other facilities to “offload” the more heavily-impacted facilities resulted in patient data lost as they transition across healthcare systems. Therefore, there is likely an underestimated mortality, and unreliable time-to-event analysis for longer-term variables such as vent-weaning, tracheostomy decannulation, ongoing assessment of functional status and recovery, as well as longer-term mortality that was not feasible.

Finally, the inability to reliably quantify daily and cumulative dosage of sedatives and analgesics for many of the patients means that a more-accurate assessment of vent-desynchrony and acute management changes is not possible. These limitations are in the context of the first-wave of the COVID-19 pandemic, and while they may limit conclusions, they are representative of the information available in such a situation.

Conclusions:

The lack of proper ventilation equipment is associated with worse clinical outcomes, as shown here in the context of the COVID-19 pandemic. Given the economic and human burden that results from prolonged acute-care, it would benefit not only our patients, but our healthcare system as a whole to recognize the infrastructure required to respond to health crises of the future. The experience during this phase of the pandemic leads to the observation that improvement of the existing ventilator stockpile with those able to provide clearer more user-friendly digital displays could likely improve long-term patient outcomes as well as overall healthcare cost.

Abbreviations

WHO
World Health Organization
EHC
Elmhurst Hospital Center
NYC
New York City
ARDS
Acute Respiratory Distress Syndrome
LOS

Length of Stay
ICU
Intensive Care Unit
PEEP
positive end-expiratory pressure
IQR
interquartile range
PICS
post-intensive care syndrome
HTN
Hypertension

Declarations

Ethics Approval: The study protocol was approved by the Institutional Review Board at the Icahn School of Medicine at Mount Sinai and the Research Committees of NYC H&H Elmhurst and Queens Hospitals. IRB 20-00547

Consent for publication: we have received institutional consent for publication of this study.

Availability of Data: All study data can be made available upon reasonable request.

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