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Ventilatory Mechanics in Early vs Late Intubation in a Cohort of Coronavirus Disease 2019 Patients With ARDS

A Single Center's Experience

To the Editor:

Coronavirus disease 2019 (COVID-19) is associated with a range of presentations, from milder symptoms to severe hypoxic respiratory failure, often meeting criteria for ARDS. Patients admitted to an ICU are likely to require mechanical ventilation (up to 85% in US cohorts), which is associated with increased morbidity and mortality.[1,2]

The near universal approach to early mechanical ventilation at the onset of the COVID-19 pandemic was driven by early data from China describing rapid deterioration with severe hypoxia, fears of patient self-induced lung injury and infection control measures because of concern about aerosolization in non-intubated patients. There remains a paucity of literature describing respiratory mechanics, ventilatory parameters, and outcomes in relation to early and late intubation in COVID-19 patients.

We report the ventilatory parameters and lung mechanics of consecutive early and late intubated and ventilated patients with COVID-19 ARDS by descriptive analysis at a single urban academic center in Philadelphia, Pennsylvania.

Methods

This retrospective study includes adult inpatients requiring invasive mechanical ventilation secondary to COVID-19 at Temple University Hospital between February and May 2020. Positive infection status was confirmed by polymerase chain reaction nasopharyngeal swab. The study was derived from the institutional review board (IRB)-approved Temple University Registry for COVID-19 (TUIRB Protocol Number: 26854). Subsequently, a separate IRB approval was granted for chart review to extract ventilator settings (TUIRB protocol number: 27051).

Data were collected from the electronic medical record and managed using REDCap electronic data capture tools from the Temple University Hospital COVID-19 Registry.[3]

All patients met Berlin criteria for ARDS. Patients required invasive mechanical ventilation for acute hypoxic respiratory failure based on the Pao_2/Fio_2 ratio, or by clinical decision. Lung protective ventilation strategies and adjunct therapies were employed per general guidelines and physician discretion. Daily recorded ventilator parameters were analyzed. Individual patient lung compliance, driving pressures, and ventilatory ratios (VR) were calculated.[4]

Descriptive statistics, either in mean with SD or median with interquartile range (IQR) and percentages, were used to present clinical data. Significance testing between groups was done with Student *t* test or Wilcoxon rank sum with continuous data or χ^2 with categorical data.

Results

Seventy-five patients with nasopharyngeal swab-confirmed COVID-19 required invasive mechanical ventilation at Temple University Hospital during the study period. Average age was 65 years, and median BMI was 31.8. Fifty-eight percent of the patients were male, and 63% were African American.

Median time to intubation was 1.27 days from presentation. Patients were separated into an early intubation (≤1.27 days) or late intubation (>1.27 days) group for analysis.

Patients in the late intubation group had a lower Fio_2 requirement on admission (55% vs 69%; $P = .109$), but a worse Pao_2/Fio_2 ratio (median, 160 vs 205; $P = .46$), higher PEEP (11.29 vs 9.30; $P = .027$), plateau (26.41 vs 22.50; $P = .027$), and peak pressures (32.21 vs 28.62; $P = .044$) at time of intubation in comparison with the early intubation group.

Lower static compliance (34.88 vs 40.68; $P = .311$) and higher VR (1.90 vs 1.57; $P = .078$) was noted in the late intubation group on day 0, although these values were not statistically significant. Static compliance increased by day 6 of intubation in the late group, whereas it decreased in those intubated early (39.80 vs 31.66; $P = .129$). The late intubation group did have a significantly longer length of stay in the ICU (median, 12.31

TABLE 1] Patient Characteristics, Respiratory Support and Parameters, Ventilatory Parameters, and Outcomes in Early vs Late Intubation for Coronavirus Disease 2019 ARDS

Variable	No. Missing	Time to Intubation			χ^2 or *t* Test *P* Value
		Total (N = 75)	Early (<1.27) (n = 37)	Late (≥1.27) (n = 38)	
Age, No.	0	75	37	38	.575
Mean (SD)		64.97 (14.27)	65.92 (14.79)	64.05 (13.87)	
BMI, No.	2	73	35	38	.002
Median (IQR)		31.80 (25.83-39.48)	28.63 (22.61-35.35)	34.16 (29.52-41.02)	
Sex, No. (%)	0				.921
Female		32 (42.67)	16 (50.00)	16 (50.00)	
Male		43 (57.33)	21 (48.84)	22 (51.16)	
Race, No. (%)	0				.291
African American		47 (62.67)	22 (46.81)	25 (53.19)	
Caucasian		8 (10.67)	3 (37.50)	5 (62.50)	
Hispanic		17 (22.67)	9 (52.94)	8 (47.06)	
Other		3 (4.00)	3 (100.00)	0 (0.00)	
Time to intubation, No.	0	75	37	38	<.0001
Mean (SD)		2.86 (4.47)	0.15 (0.30)	5.51 (5.03)	
Initial F_{IO_2} at time of admission, No.	21	54	25	29	.109
Mean (SD)		0.62 (0.32)	0.69 (0.31)	0.55 (0.33)	
Pa_{O_2}/F_{IO_2} at intubation, No.	4	71	34	37	.460
Median (IQR)		162.00 (106.00-316.00)	205.50 (106.00-378.00)	160.00 (99.00-268.00)	
Positive end expiratory pressure, No.	0	75	37	38	.027
Mean (SD)		10.31 (3.93)	9.30 (3.75)	11.29 (3.89)	
Plateau pressure, No.	16	59	30	29	.027
Mean (SD)		24.42 (6.74)	22.50 (4.76)	26.41 (7.91)	
Peak pressure, No.	0	75	37	38	.044
Mean (SD)	16	30.44 (7.73)	28.62 (6.75)	32.21 (8.29)	
Driving pressure, No.	16	59	30	29	.154
Mean (SD)		14.36 (6.12)	13.23 (4.77)	15.53 (7.16)	
Static compliance day 0, No.	16	59	30	29	.311
Mean (SD)		37.83 (21.95)	40.68 (27.23)	34.88 (14.59)	
Static compliance day 6, No.	41	34	14	20	.129
Mean (SD)		36.45 (16.87)	31.66 (10.16)	39.80 (19.87)	
Ventilatory ratio at intubation, No.	6	69	32	37	.078
Mean (SD)		1.75 (0.78)	1.57 (0.63)	1.90 (0.86)	
Duration of ventilation, No.	33	42	22	20	.102
Mean (SD)		7.98 (8.77)	5.86 (8.40)	10.30 (8.78)	

(Continued)

TABLE 1] *(Continued)*

Variable	No. Missing	Time to Intubation			χ^2 or *t* Test *P* Value
		Total (N = 75)	Early (<1.27) (n = 37)	Late (≥1.27) (n = 38)	
ICU length of stay, days, No.	0	75	37	38	.001
Median (IQR)		9.25 (5.42-16.25)	7.38 (3.88-10.21)	12.31 (7.75-19.96)	
Length of stay, days, No.	0	75	37	38	.037
Median (IQR)		13.00 (4.00-19.00)	10.00 (1.00-15.00)	15.50 (8.00-22.00)	
Living status, No. (%)	0				.563
Deceased		37 (49.33)	17 (45.95)	20 (54.05)	
Living		38 (50.67)	20 (52.63)	18 (47.37)	

vs 7.38 days; $P = .001$) and duration of mechanical ventilation (10.30 vs 5.86; $P = .102$) (Table 1).

As of data censoring on June 20, 2020, 49% of all mechanically ventilated patients had died. The median age for nonsurvivors was higher than those for survivors (70 vs 59; $P = .0006$). Average time to intubation was 3.88 days in nonsurvivors and 1.87 in survivors ($P = .053$). Nonsurvivors had higher initial F_{IO_2} requirement (70% vs 50%; $P = .139$), lower Pa_{O_2}/F_{IO_2} ratio (median, 146 vs 261; $P = .010$), lower static compliance (32.14 vs 34.62; $P = .962$), and higher ventilatory ratios (1.85 vs 1.64; $P = .276$).

Discussion

Our study found late intubation (>1.27 days; median, day 4) was associated with longer ICU length of stay and longer duration of mechanical ventilation than early intubation (≤1.27 days; median, day 0). We found that nonsurvivors had a longer time to intubation than survivors in our cohort.

Patients intubated later had higher driving pressures, lower static compliance, and higher ventilatory ratios. By day 6, static compliance improved in the late intubation group, whereas it declined in the early intubation group. This may be partially explained by disease improvement over time. Additionally, not all patients were included in the static compliance measures by day 6, because several patients had been extubated or expired. Low static compliance was seen in both groups of patients, albeit at varying times during the mechanical ventilation course. We did not find distinct ARDS phenotypes as previously suggested,[5] in line with results from other cohort studies, suggesting that most patients have low compliance.[6-9]

This study has numerous limitations, including its retrospective nature. Only patients who were polymerase chain reaction positive were included. The decision to intubate was based on clinician preference; thus, time to intubation varied. The late intubation group had a significantly longer need for mechanical ventilation and time in the ICU. Although respiratory mechanics seemingly improved in this group, our study does not account for other causes and co-morbidities that may have contributed to prolonged mechanical ventilation. Furthermore, causes of mortality were not fully analyzed. Larger cohort studies are needed to detect a difference in mortality between early and late intubation.

In our cohort, all ventilated COVID-19 patients had low compliance and increased ventilatory ratios. Patients intubated later during their hospitalization appear to have worse compliance or VR with potentially higher mortality. Whether this is progression of disease or the presence of patient self-induced lung injury remains unclear. Further studies will need to be performed to determine whether onset of symptoms, time to hospitalization, timing of intubation, and pharmacotherapies are variables that can alter a patient's clinical course.

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Additional information: The e-Appendix can be found in the Supplemental Materials section of the online article.

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