Online Data Supplement

Comparing Prone Positioning Use in COVID-19 Versus Historic Acute Respiratory Distress Syndrome

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Table E1: Study Data Definitions and Missingness

Covariate	Study Definition	Missing n (%)
Age, years	At time of hospital admission	0 (0)
Gender	As documented in EHR	0 (0)
Race/ Ethnicity	Self-reported and documented in EHR. 1 patient documented as "Unknown" in database classified as "Other" for this analysis.	0 (0)
BMI (kg/m^2)	Calculated from first height and weight documented after initiation of MV. If no data after MV, the closest documented height/weight to time of MV initiation used.	1 (0.2)
Charlson Comorbidity Score	Weighted Charlson Score (1). Derived from ICD-10 codes documented in the medical history, and/or encounter ICD-10 code list. Used r-package 'comorbidity' below to calculate this index (2).	0 (0)
Treating ICU	The ICU in which a patient resides 48-hours after eligibility	0 (0)
Early Hospital Transfer	Transferred between Johns Hopkins Medicine hospitals during eligibility period (i.e., meeting oxygenation criteria + 48 hours)	0 (0)
Time to O_2 Criteria (hours)	Time from admission date/time stamp to meeting oxygenation criteria in hours.	0 (0)
Non-respiratory SOFA Score	Derived using the highest SOFA score (worst physiologic value) for each individual element using a hierarchical approach of selecting worst value in the 12-hour period before and after eligibility and if no data available worst value in the 24-hours before or after eligibility. Using this approach 35 liver sub-scores were missing and imputed as normal 0 (mean in population of 0.21).[a]	0 (0)
Vasopressor Infusion‡	Use of Norepinephrine, Epinephrine, Phenylephrine, Vasopressin or Dopamine by continuous infusion as documented in MAR anytime at or 48 hours after meeting eligibility.	0 (0)
NMB Infusion‡	Use of continuous infusion of vecuronium or cisatracurium anytime at or 48 hours after meeting eligibility.	0 (0)
CRRT Before or During Eligibility	Defined as the start of CRRT determined by MAR documentation of dialysate either before meeting eligibility or up to 48 hours after eligibility.	0 (0)
Eligible ABGs in 1st 24 Hours	Number of ABGs in 24 hours of meeting eligibility with $PaO_2/F_IO_2 \leq 150$ mmHg on MV with F_IO_2 and PEEP ≥ 5 cmH2O (includes qualifying P/F ratio)	0 (0)
PaO_2/F_IO_2 (mm Hg)	First eligible PaO_2/F_IO_2 ratio (defines eligibility start time)	0 (0)
Severe ARDS	$PaO_2/F_IO_2 \leq 100$	0 (0)
F_IO_2 (mm Hg)	FiO_2 delivered via MV documented at or prior to first eligible blood gas.	0 (0)
$PaCO_2$ (mm Hg)	From ABG that determined eligibility criteria	0 (0)
PEEP (cm H_2O)	PEEP in cmH20 as determined by last documented PEEP at the time of the first eligible blood gas. Marked as missing in patient was on APRV without other PEEP documented prior to eligibility.	8 (1.6)
TV (ml/kg of IBW) [b]	Tidal volume/IBW documented closest to time of first eligible blood gas, and no longer than 24 hours before or	3 (0.6)

	after eligibility. Collected set tidal volume on volume control or volume targeted ventilation and exhaled tidal volumes on pressure control, APRV or spontaneous modes of MV	
Plateau Pressure (cmH_2O)	Plateau pressure as recorded in nursing or respiratory flowsheet. Selected the value recorded closest in time to oxygenation criteria (within the 48 hours prior to or after). Prioritized values prior to meeting oxygenation criteria and if data were missing used values in the 48 hours oxygenation criteria. NOTE: Prioritized data collected on assist control modes of ventilation. For patients on APRV who had no other plateau pressures recorded in timeframe specified above, used pressure high (Phigh) while on APRV.	6 (1.2)
Vent mode at Eligibility	Documented MV mode at time of oxygenation criteria met. Vent mode classified as below: Volume Control – VC-CMVs, VC-SIMV Pressure Control – PC-CMVs Pressure Regulated Volume Control – PC-CMVa Spontaneous Mode – PS, CPAP, VS APRV – Bi-level/Bi-Vent	0 (0)
Admission Duration	Assessed from time of admission to time of discharge	0 (0)
MV Duration	Assessed from study eligibility to ventilator liberation (those that remained free from MV for $\geq$ considered liberated.	0 (0)
In-hospital Mortality	Vital status at hospital discharge.	0 (0)
VFDs at Day 28	Calculated as 28-ventilator duration at day 28 and given a value of 0 if a patient died before day 28. 5 patients were transferred while on MV to a non-Johns Hopkins Medicine hospital before day 28 and VFDs were considered missing.	5 (1.0)
Discharged home	Those with discharge disposition to home (rather than rehab, hospice, another hospital.)	0 (0)

Definition of abbreviations: ABG=Arterial Blood Gas; APRV=Airway Pressure Release Ventilation; CRRT=Continuous Renal Replacement Therapy; IBW=Ideal body weight; MV=Mechanical Ventilation; NMB=Neuromuscular Blocker; PRVC=Pressure Regulated Volume Control; SOFA=Sequential Organ Failure Assessment; TV=Tidal Volume; VFD=Ventilator-free Days

[a]Notes on SOFA sub-scores: CNS score used methods from Vasilevskis et al.,(3). to use RASS in addition to GCS to define subscore. CV subscore used norepinephrine equivalents as outlined by Lambden et al.,(4). We considered Milrinone as equivalent to dobutamine for purposes of calculating CV sub score. Renal SOFA score modified to only include lab values for serum Creatinine (urine output not included).

[b]IBW calculated in men as 50 + (0.91 × [height in centimeters − 152.4]) and in women as 45.5 + (0.91 × [height in centimeters − 152.4]).

Table E2: Unadjusted and Adjusted Comparisons of Proning in COVID-19 vs. Historic ARDS

	COVID-19 vs Historic Rate Ratio[a]	
	Unadjusted, RR (95% CI)	**Adjusted[b], RR (95% CI)**
Primary Outcome		
Proning within 48 Hours	6.71 (3.83-11.74)	5.14 (3.34-7.90)
Secondary Outcomes		
Ever Proned	4.87 (2.99-7.96)	4.09 (2.76-6.05)
Proned within 24 Hours	7.59 (3.89-14.80)	5.63 (3.48-9.12)
Proned within 12 Hours	13.81 (4.00-47.76)	9.36 (3.57-24.52)

Definition of abbreviations: CI=Confidence Interval, PEEP=Positive end expiratory pressure, NMB=Neuromuscular blockade, MICU=medical ICU, SOFA=Sequential Organ Failure Assessment

[a]Rate ratio from generalized estimating equation Poisson models with robust variance estimation and exchangeable correlation to account for clustering by ICU.

[b]Models adjusted for age greater than 80, gender, non-white race, BMI category, weighted Charlson score, ARDS severity category (moderate vs. severe), number of eligible arterial blood gases in 24-hours following eligibility, non-respiratory SOFA score, PEEP, F_IO_2, plateau pressure, Vasopressor Use, NMB use, and academic vs. community hospital. Complete case analysis (n=497) used for adjusted analyses.

Table E3: Interrupted Time Series Analysis of Proning Rates

	COVID-19 Rate of Change IRR [95% CI] Per Quarter[a]	Pre-COVID Rate of Change IRR [95% CI] Per Quarter[a]	Pre-to-Post p value for interaction
Proned Within:			
Anytime[b]	1.05 [1.00-1.10]	1.02 [0.84-1.23]	0.78
48 Hours	1.02 [0.97-1.06]	1.04 [0.83-1.30]	0.86
24 Hours	1.06 [1.01-1.11]	1.09 [0.86-1.37]	0.81
12 Hours	1.09 [0.96-1.24]	0.65 [0.54-0.79]	<0.001
6 Hours[c]	1.13 [1.01-1.26]	--	--

Definition of abbreviations: CI=Confidence Interval; IRR=Incidence Rate Ratios.
Regression model used generalized estimating equations with Poisson regression with robust variance estimation to model risk ratio accounting for clustering by ICU. Model: Proning outcome = $B_0 + B_1$[COVID] + B_2[Study Month] + B_3[COVID Month]. Pre-to-post p-value is p value for B_3.

[a]Time is defined as quarters (i.e., 3-month periods) starting in January 2018.

[b]Proned anytime during the first episode of mechanical ventilation for ARDS.

[c]Zero patients proned within 6 hours in pre-COVID period.

Table E4. Sensitivity Analysis: Use of Prone Positioning in COVID-19 and Historic Cohorts, Using Prolonged Proning (≥ 12 hour) Definition

Outcome	COVID-19 N=389	Historic N=123	Absolute Difference %
Primary	**No. (%)**	**No. (%)**	**% [95% CI][ab]**
Proned within 48 Hours	237 (60.9)	12 (9.8)	51.2 [42.2-60.1]
Secondary			
Ever Proned	291 (74.8)	19 (15.5)	59.4 [49.2-69.6]
Proned within 24 Hours	203 (52.2)	9 (7.32)	44.9 [36.0-53.7]
Proned within 12 Hours	143 (36.8)	3 (2.4)	34.3 [25.3-43.3]
Proned within 6 Hours	91 (23.4)	0 (0)	23.4 [18.5-28.3]

Definition of abbreviations: CI=Confidence Interval

[a]95% CIs calculated accounting for clustering by ICU.

[b]p<0.05 for all COVID vs. Historic comparisons of proning proportions.

Table E5. Sensitivity Analysis: Use of Prone Positioning in COVID-19 and Historic Cohorts, Using Prolonged Proning (≥ 10 hour) Definition

Outcome	COVID-19 N=389	Historic N=123	Absolute Difference %
Primary	**No. (%)**	**No. (%)**	**% [95% CI][ab]**
Proned within 48 Hours	240 (61.7)	13 (10.57)	51.1 [42.2-60.1]
Secondary			
Ever Proned	294 (75.6)	19 (15.5)	60.1 [49.8-70.4]
Proned within 24 Hours	204 (52.4)	9 (7.32)	45.1 [36.3-53.9]
Proned within 12 Hours	144 (37.0)	3 (2.4)	34.6 [25.7-43.5]
Proned within 6 Hours	92 (23.7)	0 (0)	23.7 [18.8-28.5]

Definition of abbreviations: CI=Confidence Interval

[a]95% CIs calculated accounting for clustering by ICU.

[b]p<0.05 for all COVID vs. Historic comparisons of proning proportions.

Appendix A: ICD-10 Codes For Inclusion to Cohort

For both COVID and Historic non-COVID Cohorts: Initial data comprised patients having *International Classification of Diseases, Tenth Edition* procedure codes (ICD-10 PCS) of 5A1945Z (Respiratory Ventilation, 24-96 Consecutive Hours) or 5A1955Z (Respiratory Ventilation, Greater than 96 Consecutive Hours).

For the historic non-COVID Cohort: Patients further filtered to those with a discharge diagnosis of pneumonia coded as present on admission (present on admission [POA] flag = yes).

Pneumonia ICD-10 codes for inclusion:
Pneumonia (main category)
J10 – J18
J09.X1 Influenza due to identified novel influenza A virus with pneumonia

For the COVID Cohort: The COVID-19 cohort included patients identified as having COVID-19 by positive polymerase chain reaction (PCR) testing for SARS-CoV-2, and/or ICD-10 diagnosis of COVID-19 and/or those flagged as a "patient under investigation" for suspected COVID-19.

Appendix B: Identifying and Validating Prone Positioning Start and Duration

Steps for Defining Start and Duration of Prone Positioning:

A. Data Processing

1A) Extracted patient position data from the EHR comprehensive flowsheets that contain data entered by nursing and respiratory therapy staff.

2A) Defined position as supine or prone with language processing (not case sensitive) of recorded values based on the following definitions:
- Proned if values contain → "prone"
- Supine if values contain → "supin" [Not supine to account for use of "supinated"], or "Semi-fowlers" position

NOTE: "Lying down", "Lying left/right side" or "HOB 30 Degrees" were also recorded values and were not always accompanied by an indicator of supine/prone (i.e., "Lying down/Supine"). If a value was accompanied by a supine or proning indicator, then it was classified as supine/prone. If not accompanied by classifier, then it was labeled as "ambiguous", meaning that position could not be determined, and was not used to define transition states [see below].

The total number of position documentations, and ambiguous position documentations during supine and prone periods are shown in Table B1 below. To give readers a sense of the data structure, example data is included in Figure B1.

3A) Sorted and grouped the data by patient and arranged the position data by time within patients. Then defined transition states (i.e., supine → prone or prone → supine) and filtered data to include only position transitions. Calculated proning duration as time from transition from supine to prone either to next prone to supine transition or to the last observation if the last observation was proned without intervening supination.

4A) Filtered data to supine/proning data ONLY during time periods where the patients were receiving mechanical ventilation.

5A) Defined prolonged proning as ≥ 16 consecutive hours in prone position (i.e., prior to transition to supine, OR discharge without recorded transition to supine)

Table B1: Characteristics of Positioning Documentation During Mechanical Ventilation[ab]

Position Data Metric	**COVID-19 ARDS (N=389)**	**Historic ARDS (N=123)**
Total Count of Position Data, n	69,080	11,769
Ambiguous Position Values, n (% of total positions)	24,256 (35.1)	5,286 (44.9)
Patients with any ambiguous documentation, n (% of patients)	384 (98.7)	123 (100)

Position Values During Supine Periods, n (% of total positions)	51,147 (74.0)	11,205 (95.2)
Ambiguous Position Values During Supine Periods, n (% of supine position values)	23,648 (46.2)	5,263 (47.0)
Position Values During Prone Periods, n (% of total positions)	17,933 (26.0)	564 (4.8)
Ambiguous Position Values During Prone Periods, n (% of prone position values)	608 (3.4)	23/564 (4.1)

[a]Only position data recorded during mechanical ventilation are counted here
[b]Ambiguous position is a recorded value for position from which prone/supine positioning cannot be directly inferred

id	position_time	position_value	prone	supine	ambiguous
1	5/20/20 22:00	Supine	0	1	NA
1	5/21/20 0:00	Lying right side	0	1	TRUE
1	5/21/20 2:00	Lying left side	0	1	TRUE
1	5/21/20 4:00	Supine	0	1	NA
1	5/21/20 6:00	Lying right side	0	1	TRUE
1	5/21/20 8:00	Lying left side	0	1	TRUE
1	5/21/20 10:00	Lying right side	0	1	TRUE
1	5/21/20 12:00	Supine	0	1	NA
1	5/21/20 13:30	Lying left side;Other (Cc	0	1	TRUE
1	5/21/20 17:00	Lying right side;Other (C	0	1	TRUE
1	5/21/20 20:00	Prone	1	0	NA
1	5/21/20 22:15	Prone;Other (Comment	1	0	NA
1	5/22/20 2:00	Prone	1	0	NA
1	5/22/20 5:37	Prone	1	0	NA
1	5/22/20 8:00	Prone	1	0	NA
1	5/22/20 9:30	Prone	1	0	NA
1	5/22/20 13:23	Prone	1	0	NA
1	5/22/20 16:00	Prone	1	0	NA
1	5/22/20 17:25	Prone	1	0	NA

Figure B1: Example Position Data
In this figure, an example table of position data for a patient is shown. Values labeled as, ambiguous=TRUE, are values in which supine/prone cannot be directly determined from the charting. When determining position transitions from prone to supine or supine to prone, these ambiguous positions were excluded.

B. Structured Chart Review for Data Validation

A manual chart review was performed for all patients meeting oxygenation criteria to determine accuracy of prone positioning data. We used the following protocol to abstract the date/time of prolonged (≥ 16 consecutive hours in prone positioning).

1B) Evaluate patient position in flowsheet:

Enter the comprehensive flowsheet in Epic and manually review recorded position in the 48 hours after meeting study eligibility.

If documented as receiving prolonged proning (≥ 16 consecutive hours), record date and time of proning initiation.

2B) Provider Documentation

If no proning found in Step 1B, we used Epic (EMR at Johns Hopkins) word search to Find Provider Documentation of prone positioning. Searched for "prone", "proned", "proning" in that order. Goal was to find provider documentation in notes OR proning that occurred > 48 hours after eligibility. Documented datetime of proning initiation (≥ 16 hours) if clearly indicated that patient received this therapy in provider notes or received but after 48 hours of eligibility.

C. Results of Data Validation

The proning identification algorithm was highly accurate. The following errors in classification were noted and fixed manually:

-2 of 512 (0.4%) patients had their outcome misclassified using the data algorithm (1 classified as receiving proning but never received prolonged proning and 1 classified as never proned but had received prone positioning)

-8 of 324 (2.5%) patients were proned earlier than the data algorithm identified. All errors in start time were within 12 hours from the start time determined by manual chart review. All but 2 errors were within 6 hours of the manual chart review determined proning initiation time.

In all cases with errors leading to misclassification of proning, these errors arose form charting errors. For example, "proned" charted in middle of supine stretch" or "supine" in middle of prone stretch. The mistakes (if could be clearly determined) in the individual position data were fixed in the database, and algorithm re-run after fixes uploaded.

Additional References:

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