OBSERVATIONAL STUDY

OPEN

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

Chad H. Hochberg, MD, MHS[1]
Kevin J. Psoter, PhD[2]
Sarina K. Sahetya, MD, MHS[1]
Eric P. Nolley, MD[1]
Shakir Hossen, MBBS, MSPH[1,3]
William Checkley, MD, PhD[1,3]
Meeta P. Kerlin, MD, MSCE[4]
Michelle N. Eakin, PhD[1]
David N. Hager, MD, PhD[1]

IMPORTANCE: Use of prone positioning in patients with acute respiratory distress syndrome (ARDS) from COVID-19 may be greater than in patients treated for ARDS before the pandemic. However, the magnitude of this increase, sources of practice variation, and the extent to which use adheres to guidelines is unknown.

OBJECTIVES: To compare prone positioning practices in patients with COVID-19 ARDS versus ARDS treated before the pandemic.

DESIGN, SETTING, AND PARTICIPANTS: We conducted a multicenter retrospective cohort study of mechanically ventilated patients with early moderate-to-severe ARDS from COVID-19 (2020–2021) or ARDS from non-COVID-19 pneumonia (2018–2019) across 19 ICUs at five hospitals in Maryland.

MAIN OUTCOMES AND MEASURES: The primary outcome was initiation of prolonged prone positioning (≥ 16 hr) within 48 hours of meeting oxygenation criteria. Comparisons were made between cohorts and within subgroups including academic versus community hospitals, and medical versus nonmedical ICUs. Other outcomes of interest included time to proning initiation, duration of prone sessions and temporal trends in proning frequency.

RESULTS: Proning was initiated within 48 hours in 227 of 389 patients (58.4%) with COVID-19 and 11 of 123 patients (8.9%) with historic ARDS (49.4% absolute increase [95% CI for % increase, 41.7–57.1%]). Comparing COVID-19 to historic ARDS, increases in proning were similar in academic and community settings but were larger in medical versus nonmedical ICUs. Proning was initiated earlier in COVID-19 versus historic ARDS (median hours (hr) from oxygenation criteria, 12.9 vs 30.6; $p = 0.002$) and proning sessions were longer (median hr, 43.0 vs 28.0; $p = 0.01$). Proning frequency increased rapidly at the beginning of the pandemic and was sustained.

CONCLUSIONS AND RELEVANCE: We observed greater overall use of prone positioning, along with shorter time to initiation and longer proning sessions in ARDS from COVID-19 versus historic ARDS. This rapid practice change can serve as a model for implementing evidence-based practices in critical care.

KEY WORDS: adult; COVID-19; implementation science; intensive care units; prone position; respiratory distress syndrome

Early prone positioning has been shown to reduce mortality in patients with moderate-to-severe acute respiratory distress syndrome (ARDS) in a randomized controlled trial (1) and meta-analyses (2, 3), and is recommended in patients with ARDS by multiple guidelines (4, 5). However, prior to the COVID-19 pandemic, large multinational studies showed that proning was only used in 6–14% of patients with ARDS overall and in 16–33% of those with severe ARDS (6–9). Reasons for low adoption have included under-recognition of ARDS by clinicians (10, 11), a view of proning as rescue

DOI: 10.1097/CCE.0000000000000695

therapy (7, 12), clinician preference for other adjunctive interventions (12), and a presumption that proning is labor intensive (12, 13).

During the COVID-19 pandemic, some studies suggested that 25–62% of patients with COVID-19-associated ARDS were managed with prone positioning (14–19). However, whether this greater use of proning was concordant with evidence-based recommendations (i.e., proning sessions of at least 12–16 consecutive hours (hr) in early moderate-to-severe ARDS) (1, 4) is unknown. Furthermore, use has varied with a range of 5–80% of patients proned in different settings (20). Understanding how proning practices have changed in patients with COVID-19 ARDS compared with historical ARDS could help to identify ongoing sources of practice variability and guide interventions to further expand and sustain use of this life-saving therapy (21, 22).

We compared proning practice patterns in patients with COVID-19 ARDS to patients with ARDS from pneumonia treated prior to the pandemic. We determined the frequency of guideline-concordant proning in both cohorts, in subgroups where use of proning may be variable, and examined temporal changes in proning frequency. Furthermore, we evaluated differences in proning practices such as time to proning initiation and proning duration. We hypothesized that prone positioning was used earlier and more frequently in ARDS due to COVID-19 than in ARDS before the pandemic.

METHODS

Study Design and Population

In a multicenter retrospective observational study, we compared the use prone positioning in adult patients receiving mechanical ventilation (MV) for moderate-to-severe ARDS from COVID-19 (March 2020–March 2021) to a historical control group of patients with ARDS from non-COVID-19 pneumonia (January 2018–December 2019). Patients were included if they were: 1) admitted to one of five regional hospitals (two academic and three community) in the Johns Hopkins Health System (JHHS), 2) were greater than 18 years old, 3) met Berlin criteria for ARDS (23) in the setting of a primary admitting diagnosis of pneumonia based on *International Classification of Diseases*, 10th Revision (ICD-10) coding, or were being treated for COVID-19 ARDS, 4) met criteria for proning (Pao_2/Fio_2 < 150 mm Hg, Fio_2 > 0.6, and positive end-expiratory pressure [PEEP] > 5 cm H_2O), and 5) were within 72 hours of starting MV (**Appendix A**, http://links.lww.com/CCX/A990). Exclusion criteria were: 1) cardiac arrest prior to or concurrent with starting MV, 2) chronic MV, 3) tracheostomy as the first documented airway, 4) less than 48 hours of MV from time of eligibility (i.e., deceased, discharged or liberated from MV within 48 hr), 5) presence of a condition in which proning is relatively contraindicated (i.e., elevated intracranial pressure, spinal injury, open abdomen, fresh sternotomy), and 6) initiation of MV outside JHHS unless transfer to JHHS was directly from an outside hospital emergency department. In patients meeting oxygenation criteria, a structured manual chart review was conducted to independently verify that ARDS criteria were met by review of clinical and imaging data and that no exclusion criteria were present.

The institutional review boards (IRBs) at the JHHS hospitals acknowledged this protocol as secondary research exempt from further human subjects review (IRB00280745).

Outcomes

The primary outcome was initiation of prone positioning for at least 16 consecutive hours within 48 hours of meeting eligibility criteria. This primary outcome was chosen to reflect the protocol of a well-recognized randomized controlled trial of prone positioning (1). Secondary outcomes were initiation of prolonged proning (≥ 16 consecutive hr) within earlier timeframes (6, 12, and 24 hr after meeting eligibility), as well as ever receiving proning during the first episode of MV. Among those proned, other outcomes of interest were time to proning initiation as a continuous variable, and duration and number of proning sessions during MV.

Data Collection and Definitions

Data were extracted from the Johns Hopkins Precision Medicine Analytics Platform, which contains comprehensive electronic health record (EHR) data for patients treated across the JHHS (24). Patient characteristics included demographics (age, self-reported race, and gender), clinical parameters (height, weight, vital signs, and laboratories for Sequential Organ Failure Assessment [SOFA] scoring), and the Charlson

comorbidity score derived from ICD-10 codes (25, 26). MV parameters and select treatments (i.e., vasopressors, neuromuscular blockade, and continuous renal replacement therapy) were extracted from clinical flow sheets and medication administration records. A baseline nonrespiratory SOFA score was calculated using the highest (worst) subscores measured within 12 hours of meeting eligibility, with the measurement window expanded to within 24 hours of eligibility if data were missing in the 12-hour window (27). The CNS SOFA subscore was defined using either Richmond Agitation-Sedation Scale scores or Glasgow Coma Scores using previously validated methods (28). The treating ICU was defined as the ICU where the patient was located 48 hours after meeting oxygenation criteria. Within the two academic hospitals, ICUs were further categorized as medical (MICU) if they primarily care for general nonsurgical or nonsubspecialty ICU populations and non-MICU if they included surgical, mixed, or specialty care (e.g., coronary care units, neurologic ICUs). Patient outcomes (vital status at discharge, discharge disposition) were extracted from the EHR data. Ventilator-free days (VFDs) at day 28 were calculated with death (censored at day 28) considered as zero VFDs (29). The initiation, timing, and duration of proning were determined from EHR documentation of patient position and were validated against a structured manual chart review of all included patients (**Appendix B**, http://links.lww.com/CCX/A990). The liver SOFA subscore, defined by total bilirubin, was missing in 35 patients and imputed as zero (normal). Missing data were otherwise minimal (< 1.6% for any variable), no further missing data were imputed, and complete-case data were used in adjusted analyses. For detailed data definitions and frequency of missingness, see **Table E1** (http://links.lww.com/CCX/A990).

Statistical Analysis

Comparisons of demographics and baseline clinical characteristics were performed using Mann-Whitney *U* tests or chi-square and Fisher exact tests for continuous and categorical variables, as appropriate.

For the primary outcome, the absolute percent difference in the frequency of proning within 48 hours between the COVID-19 and historic cohorts was calculated and a 95% CI for this difference was constructed using standard errors from negative binomial regressions accounting for clustering of patients within the same ICUs. We then repeated these calculations for secondary outcomes and prespecified subgroups. Subgroups included ARDS severity (moderate or severe), hospital type (academic or community), ICU type (MICU or non-MICU), body mass index (BMI) (< 30 [kg/m^2], 30–49, 50+), and vasopressor use (yes or no). Differences within subgroups were assessed by including an interaction term for subgroup and period (COVID or historic) in the negative binomial models.

Time from eligibility to initiation of first proning as a continuous variable and duration and number of proning sessions were compared using Mann-Whitney *U* tests. Kaplan-Meier curves were constructed to visualize the cumulative probability of and time to proning within the first 48 hours of study eligibility. To determine whether results were influenced by our definition of proning (≥ 16 consecutive hr), we performed two sensitivity analyses in which we defined proning as remaining in the prone position for greater than 12 or 10 consecutive hours, respectively.

We compared the relative rates of proning in COVID-19 versus historic ARDS using unadjusted and multivariable log-linear Poisson regression based on generalized estimating equations (GEEs) with robust SE estimation and an exchangeable correlation structure to account for clustering within ICUs. Adjusted models included the following covariates identified a priori: age, sex, race, BMI, weighted Charlson comorbidity score, nonrespiratory SOFA score, ARDS severity, plateau pressure, PEEP, F_{IO_2}, number of qualifying arterial blood gases (ABGs) in the first 24 hours of eligibility, academic hospital status, and vasopressor or neuromuscular blockade use. Interpretation of model coefficients takes the form of rate ratios (RRs) with 95% CIs.

Temporal trends in proning were evaluated by plotting the frequency of proning over time. Changes in proning frequency over time prior to the pandemic, at the beginning of the pandemic and during the COVID-19 study period were analyzed using an interrupted time series approach with GEE-based Poisson regression (30). For these analyses, patients were grouped in 3-month intervals by hospital admission date. Results of these models are presented as RRs with corresponding 95% CIs. A p value of less than 0.05 was considered statistically significant. All analyses were performed using the R statistical environment (Version 3.6.3; R Foundation for Statistical

Computing, Vienna, Austria) and Stata Version 17.0 (StataCorp LLC, College Station, TX).

RESULTS

Participant Characteristics

Across 19 ICUs, 389 patients with COVID-19 ARDS and 123 patients with historic ARDS were included (**Fig. 1**). Baseline characteristics and clinical outcomes are presented in **Table 1**. Patients with COVID-19 were more likely to be male, non-White and had higher BMIs and lower Charlson comorbidity and nonrespiratory SOFA scores. COVID-19 patients had a longer duration of time from admission to meeting eligibility and more qualifying ABGs in the 24 hours after eligibility but otherwise had similar ARDS severity compared with historic ARDS. COVID-19 patients were more likely to receive vasopressors and neuromuscular blockade and were treated with higher initial PEEP and lower tidal volumes per predicted body weight. The COVID-19 cohort had longer hospital stay, MV duration, and fewer VFDs at day 28 compared with the historic cohort but had similar inhospital mortality.

Comparison of Proning Frequency and Practice

Among patients with COVID-19, 58.4% were proned within 48 hours of meeting eligibility compared with 8.9% of the historic cohort (absolute difference, 49.4%; 95% CI, 41.7–57.1) (**Table 2**). Proning initiation within earlier time frames (24, 12, 6 hr) was also greater in the COVID-19 versus historic ARDS patients.

Among subgroups, absolute increases in proning within 48 hours were similar in moderate and severe ARDS, between academic and community hospitals (Table 2 and **Fig. 2**) and across BMI categories. There was a greater absolute increase in proning in those not receiving versus receiving vasopressor infusions

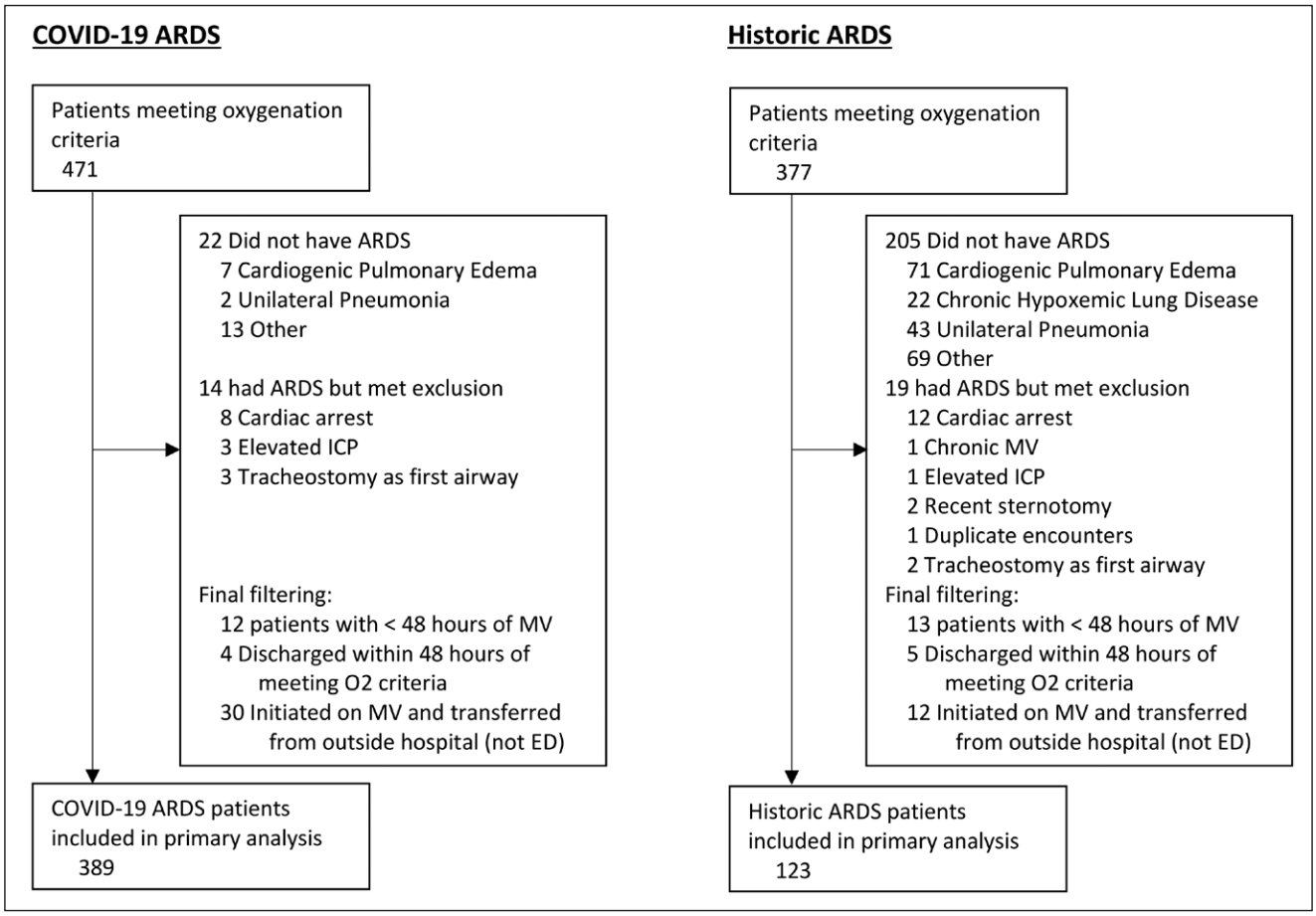

Figure 1. Study population. We identified 471 COVID-19 and 377 historic acute respiratory distress syndrome (ARDS) patients who met initial oxygenation and ventilation criteria. After manual chart review, we excluded those without ARDS as defined by Berlin criteria and those with ARDS but other exclusion factors. The final study population consisted of 389 COVID-19 and 123 historic ARDS patients. ED = emergency department, ICP = intracranial pressure, MV = mechanical ventilation.

TABLE 1.
Characteristics of Mechanically Ventilated Acute Respiratory Distress Syndrome Patients by Cohort

Patient Characteristics	COVID-19 (*n* = 389)	Historic ARDS (*n* = 123)
Demographics		
Age (yr)	64 (54–72)	62 (51–70)
Female	154 (40)	62 (50)
Race/ethnicity		
White	110 (28)	69 (56)
Black	157 (40)	38 (31)
Asian	26 (7)	9 (7)
Hispanic	77 (20)	3 (2)
American Indian	1 (0)	0 (0)
Other	18 (5)	4 (3)
Clinical/treatment characteristics		
Body mass index (kg/m^2)	32 (27–38)	28 (24–35)
Charlson comorbidity score	1 (0–2)	2 (1–4)
Treated at academic hospital	278 (71)	82 (67)
Treated in medical ICU[a]	226 (81)	60 (73)
Early hospital transfer[b]	52 (13)	0 (0)
Time to O_2 criteria (hr)	58 (21–119)	32 (7–73)
Nonrespiratory Sequential Organ Failure Assessment score[c]	8 (7–9)	9 (7–10)
Vasopressor infusion, 1st 48 hr[d]	339 (87)	94 (76)
Neuromuscular blocker infusion, 1st 48 hr[d]	169 (43)	31 (25)
Continuous renal replacement therapy before or during eligibility	32 (8)	13 (11)
Respiratory variables at eligibility		
Eligible arterial blood gases in 1st 24 hr	4 (2–6)	2 (1–5)
Pao_2/Fio_2 (mm Hg)	99 (77–122)	93 (70–124)
Severe ARDS ($Pao_2/Fio_2 < 100$ mm Hg)	196 (51)	68 (55)
Fio_2 (mm Hg)	1.0 (0.8–1.0)	1.0 (0.7–1.0)
$Paco_2$ (mm Hg)	45 (39–51)	45 (40–54)
Positive end-expiratory pressure (cm H_2O)	10 (10–14)	10 (5–12)
Tidal volume (mL/kg of ideal body weight)	6.1 (5.9–6.7)	6.3 (6.0–7.2)
Plateau pressure (cm H_2O)[e]	25 (22–28)	26 (22–29)
Patient outcomes		
Hospital length of stay (d)	25 (16–39)	16 (10–27)
Duration of mechanical ventilation (d)	13 (8–24)	7 (4–13)
Inhospital mortality	149 (38)	53 (43)
Ventilator-free days at day 28[f]	0 (0–17)	8 (0–22)
Received extracorporeal membrane oxygenation	13 (3)	2 (2)
Discharged home	105 (27)	26 (21)

ARDS = acute respiratory distress syndrome.

[a]Assessed in subgroup treated an academic center (*n* = 278 for COVID-19; *n* = 82 for historic ARDS).

[b]Early hospital transfers defined as transfer between Johns Hopkins Medicine hospitals during 1st 48 hr of eligibility.

[c]Calculated as sum of highest subscores in the 24-hr period before or after eligibility.

[d]Infusion during proning eligibility period.

[e]Plateau pressure extracted as the recorded value closest to eligibility.

[f]Ventilator-free days defined as number of days free of mechanical ventilation at day 28, with those that died before day 28 given 0 d.

Data are presented as median (interquartile range) or *n* (%).

TABLE 2.
Use of Prone Positioning in COVID-19 and Historic Cohorts, Overall and in Subgroups

Outcome	COVID-19, *n* = 389	Historic, *n* = 123	Absolute Difference
Primary	*n* (%)	*n* (%)	% (95% CI)[a,b]
Proned within 48 hr	227 (58.4)	11 (8.9)	49.4 (41.7–57.1)
Secondary			
Ever proned	284 (73.0)	18 (14.6)	58.4 (48.7–68.0)
Proned within 24 hr	190 (48.8)	8 (6.5)	42.3 (33.9–50.8)
Proned within 12 hr	134 (34.5)	3 (2.4)	32.0 (23.6–40.5)
Proned within 6 hr	86 (22.1)	0 (0)	22.1 (17.2–27.0)
Subgroup			
Proned within 48 hr	*n*/*N* (%)	*n*/*N* (%)	% (95% CI)[c]
Acute respiratory distress syndrome severity			
Moderate, P/F 100–150	100/193 (51.8)	4/55 (7.3)	44.5 (35.1–54.0)
Severe, P/F < 100	127/196 (64.8)	7/68 (10.3)	54.5 (43.7–65.3)
Hospital setting			
Academic	170/278 (61.2)	9/82 (11.0)	50.2 (41.2–59.1)
Community	57/111 (51.4)	2/41 (4.9)	46.4 (34.6–58.3)
ICU type[d]			
Non-MICU	20/52 (38.5)	0/22 (0)	38.5 (30.5–46.4)[e]
MICU	150/226 (66.4)	9/60 (15.0)	51.4 (45.1–57.6)[e]
Body mass index (kg/m^2)			
< 30	80/166 (48.2)	8/72 (11.1)	37.1 (24.5–49.6)
≥ 30 and < 50	139/206 (67.5)	2/43 (4.7)	62.8 (51.2–74.5)
≥ 50	8/16 (50.0)	1/8 (12.5)	37.5 (7.2–67.9)
Hemodynamics			
No vasopressors	28/50 (56.0)	0/29 (0)	56.0 (40.6–71.4)[e]
On vasopressors	199/339 (58.7)	11/94 (11.7)	47.0 (38.7–55.3)[e]

MICU = medical ICUs, P/F = Pao_2/Fio_2.

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

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

[c]Statistical difference in rates between subgroups assessed in clustered negative binomial regression with an interaction term between COVID status and subgroup.

[d]Evaluated in subgroup of patients treated in academic hospitals.

[e]Interaction term *p* significant at the $p < 0.05$ level.

during the first 48 hours of eligibility ($p < 0.001$). In academic hospitals, the absolute increase in proning was greater in MICUs versus non-MICUs ($p < 0.001$).

After adjusting for prespecified covariates, the relative rate of proning within 48 hours was increased in the COVID-19 versus the historic cohort (adjusted RR, 5.14; 95% CI, 3.34–7.90) and was not substantially different from the unadjusted estimate (**Table E2**, http://links.lww.com/CCX/A990). Relative increases were also seen for initiation of prone positioning within 24 hours and within 12 hours. Zero patients in the historical cohort were proned within 6 hours.

Time from eligibility to initiating proning was shorter in the COVID-19 versus historic group (median hr [interquartile range (IQR)], 12.7 [4.2–36.8] vs 30.6 [17.5–126.4]; $p = 0.002$). In addition, COVID-19 patients had longer proning sessions (median hr [IQR], 43.0 [28.3–60.3] vs 28.0 [21.5–42.0]; $p = 0.01$)

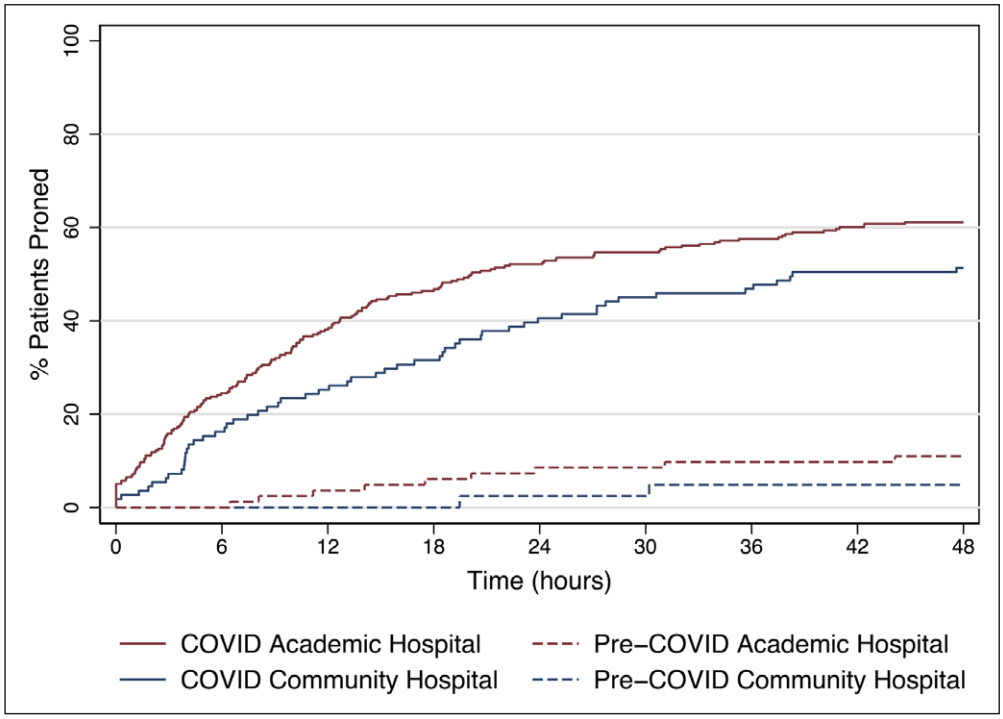

Figure 2. Initiation of prone positioning within 48 hr by hospital type. The cumulative probability of initiating a prone positioning session of greater than 16 hr is shown for the first 48 hr after meeting eligibility and stratified by academic versus community hospital setting. For this analysis, in patients in whom prone positioning was initiated prior to meeting eligibility criteria, the time of proning initiation was considered to be right at the beginning of the eligibility period.

and more proning sessions (median [IQR], 2 [1–3] vs 1 [1–1]; $p = 0.003$) compared with historic ARDS.

Temporal Trends and Sensitivity Analysis

Unadjusted rates of proning binned in 3-month intervals are plotted in **Figure 3** and show an abrupt increase in proning at the beginning of the pandemic followed by sustained rates of use. There were no significant temporal trends in the frequency of proning initiation within 48 hours prior to or during the COVID-19 pandemic (**Table E3**, http://links.lww.com/CCX/A990). During the pandemic, there were small increases in the frequency of secondary proning outcomes over time (p-trend < 0.05 for "ever prone," proned within 24 hr and proned within 6 hr).

In sensitivity analyses comparing definitions of prolonged proning of greater than 12 or greater than 10 versus greater than 16 consecutive hours, an additional 10 and 13 patients met the primary outcome, respectively. This led to minor differences in proning frequencies (**Tables E4** and **E5**, http://links.lww.com/CCX/A990), but the changes between the COVID-19 and historic periods remained similar.

DISCUSSION

In this retrospective cohort study of adults with moderate-to-severe ARDS requiring MV, we identified a 49.4% absolute increase in early prone positioning in patients with COVID-19 ARDS compared with historical controls. Similar increases in prone positioning were observed in academic and community hospitals and in patients with moderate and severe ARDS, while greater increases in use were observed in MICUs compared with non-MICUs. Time to proning initiation was significantly shorter and median duration of proning sessions was significantly longer in the COVID-19 versus historic ARDS cohorts.

The rates of prone positioning found in our study align with previous reports of proning in COVID-19 (15–17, 20) and non-COVID-19 ARDS (6–10). Our study adds to previous findings by showing that the greater use of proning observed in COVID-19 ARDS consisted of evidence-based proning practice and comprised earlier and more prolonged proning. Unlike prior studies showing large variation in proning use among U.S. hospitals (9, 20), we observed consistently higher use across all included hospitals. However, we did find greater increases in proning in MICUs versus non-MICUs, which may reflect specific expertise in caring for patients with ARDS. In regard to other subgroups, the largest absolute percentage increase in proning was in patients with obesity (62.8%), which is notable as obesity has been identified as a barrier to prone positioning (12). Further work to understand sources of proning practice variation within and across health systems is needed to fully understand

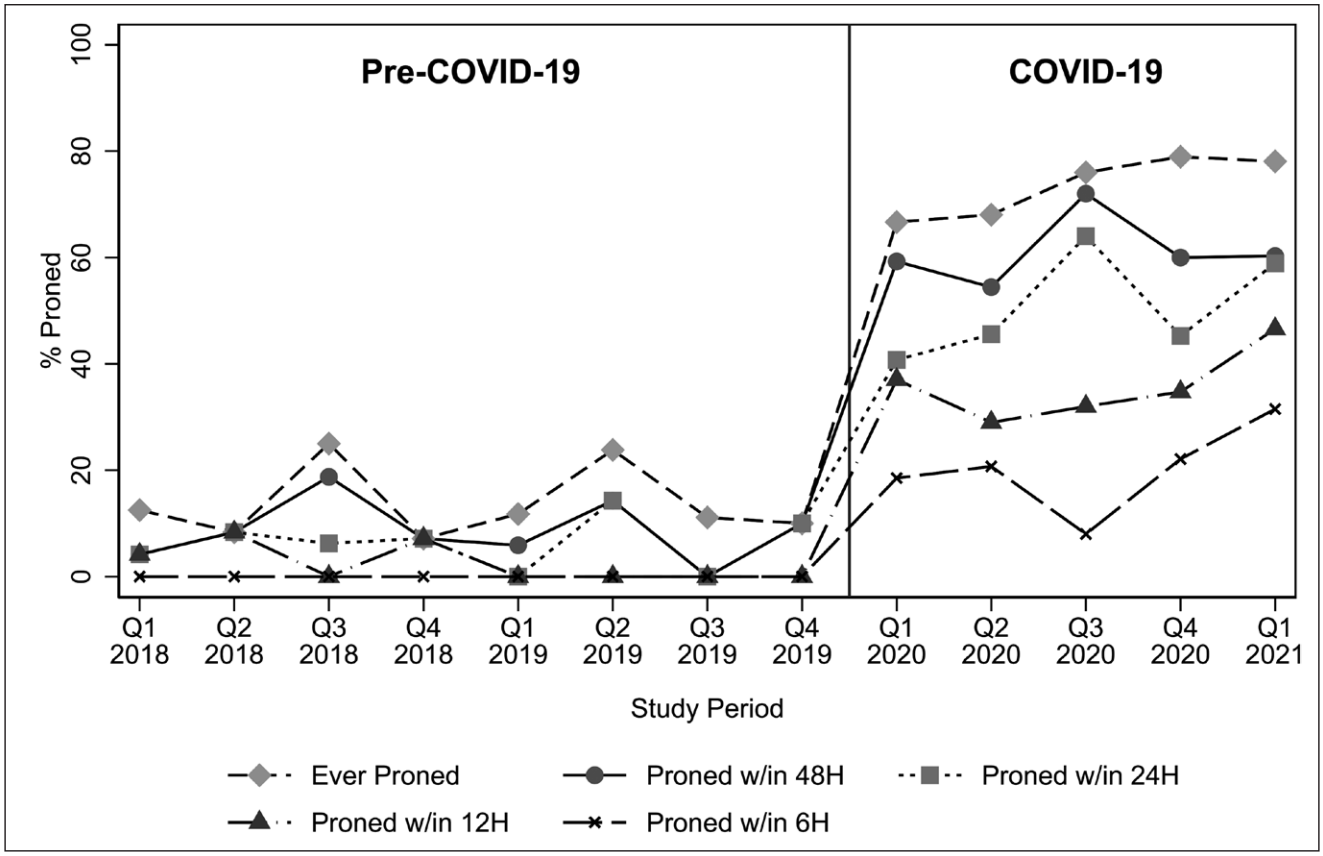

Figure 3. The frequency of prone positioning by study quarter in the COVID-19 and historic study periods. The rates of prone positioning per study quarter (3 mo periods starting on January of 2018) are shown. The demarcation between the historic and COVID-19 periods are noted with a *vertical black line*. The unadjusted frequency of proning initiation within various time frames (assessed from the time of meeting oxygenation criteria) are shown.

the current implementation challenges for prone positioning.

Proning practice has changed rapidly, whereas incorporating evidence-based therapy into practice typically takes more than a decade (9, 21). This rapid implementation may serve as a model for understanding how to further increase and sustain the use of proning and other evidence-based practices in critical care. There are several potential contributors to this rapid practice change. First, early in the pandemic, there were few therapeutic interventions for patients with COVID-19 and many patients exhibited profound hypoxemia. Prone positioning typically improved oxygenation, which may have provided immediate positive feedback to clinicians and influenced them in continuing to use proning in other patients (31). Second, the large influx of patients with severe ARDS highlighted the limited therapeutic options for COVID-19 ARDS specifically, and perhaps ARDS more generally. Although response to this uncertainty was variable throughout the critical care community, this led some to call for a refocusing on best practices (32, 33). Third, COVID-19 ARDS may be more clinically homogeneous than ARDS from other causes (34). This may lead to increased clinician recognition of ARDS, whereas under-recognition of this syndrome has been a barrier to use of best practices (10, 11).

In our health system, several factors may have influenced the use of proning. Patients with COVID-19 were often treated in units dedicated to COVID-19 care. In these units, staff rapidly accumulated experience in treating patients with ARDS, and this may have reinforced adherence to evidence-based practices through developing team expertise and comfort with ARDS therapies. In addition, locally developed guidance for treating critically ill patients with COVID-19 included a recommendation for proning. This guideline and links to proning-specific instructional videos were made available to all hospitals in our system. While some hospitals in the health system did develop proning teams (35), they were only available in two of the five hospitals and were not available consistently

throughout the COVID-19 study period. Given the sustained increases in proning observed, these teams are unlikely to fully explain greater proning use. Although community and academic hospitals in our system do share an EHR (including a proning-specific order), practices in each hospital are otherwise independent and faculty are not shared between the community and academic sites.

There are several implications and future lines of inquiry that stem from this work. For one, the significantly earlier and longer application of prone positioning in this study may be of interest to researchers and clinicians. If the beneficial mechanism of proning is a more homogenous distribution of transpulmonary pressures leading to decreases in lung stress and strain, earlier and longer proning (a larger dose) could further improve outcomes (36). While potential benefits of earlier (1, 2, 31, 37) and longer proning (38) have been suggested, the incremental benefit of earlier initiation and/or sessions greater than 16 hours is unclear (39). Further studies of the tradeoffs between the cumulative impact of adverse effects (e.g., pressure wounds, facial/laryngeal edema, and increased use of sedation), which are likely to increase as proning sessions are extended and incremental physiologic benefits are needed (40, 41). In addition, whether proning should be a top priority very early after MV initiation (with very early proning in competition with further diagnostics/procedures/ventilator optimization/time to resolve) is unclear.

Given the sustained increases in proning use across the multiple settings in our study, we expect that proning for COVID-19 ARDS has become firmly embedded in ICU practice. Additional studies, including those using qualitative and survey methods, are needed to understand the potentially complex mechanisms behind this rapid practice change. An understanding of these factors would inform the design of proning implementation interventions. Such interventions could target institutions where rates of proning remain low, or aim to sustain higher proning rates for both COVID-19 and non-COVID-19 ARDS in institutions with high frequency of proning. Potential interventions may include decision support to help clinicians recognize early ARDS, protocols and tools to facilitate proning when indicated, and multidisciplinary team training.

There are several limitations to this study. First, our study was conducted in one health system, which may limit generalizability. However, the system is large, demographically diverse, and includes both academic and community hospitals. Second, although access to comprehensive EHR data allowed for detailed data collection, these data are recorded for clinical purposes and may be subject to error in charting and/or extraction. Third, our analysis was limited to ARDS from COVID-19 or non-COVID pneumonia. Proning practice patterns for ARDS of other etiologies (e.g., trauma or nonpulmonary sepsis) may be different. Last, we did not describe proning practice in concurrent non-COVID ARDS patients (i.e., ARDS without COVID treated during COVID era). It is possible that the increases in proning that we did observe primarily represent our health system's approach to COVID-19 ARDS and do not generalize to ARDS from other etiologies. This is an area for further study, as significant implementation work may still be required in non-COVID-19 ARDS.

CONCLUSIONS

This study highlights a rapid increase in the use of prone positioning among patients with COVID-19 ARDS compared with ARDS from pneumonia in the 2 years prior to the pandemic. Further study is needed to understand the context, mechanisms, and sustainers underlying the implementation of this rapid change.

ACKNOWLEDGMENTS

The data used for this publication were from the Johns Hopkins COVID-19 Precision Medicine Analytics Platform Registry (JH-CROWN). This resource is made possible by the contributions of many patients, clinicians, and data scientists. We sincerely thank them for this important resource.

1 *Division of Pulmonary and Critical Care Medicine, Department of Medicine, Johns Hopkins University, Baltimore, MD.*

2 *Department of Pediatrics, Johns Hopkins University, Baltimore, MD.*

3 *Center for Global Non-Communicable Disease Research and Training, Johns Hopkins University, Baltimore, MD.*

4 *Pulmonary, Allergy and Critical Care Division, Palliative and Advanced Illness Research Center, Department of*

Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccxjournal).

Drs. Hochberg, Sahetya, Nolley, Checkley, Eakin, and Hager involved in conceptualization. Drs. Hochberg, Nolley, Hossen, and Checkley involved in data curation. Drs. Hochberg, Psoter, Hossen, Kerlin, Eakin, and Hager involved in analysis and interpretation of data. Drs. Hochberg, Eakin, and Hager involved in writing–original draft. All authors involved in writing–review and editing and final approval of article.

Dr. Hochberg has received funding from the National Institutes of Health/National Heart, Lung, and Blood Institute (NIH/NHLBI) F32HL160039-01 and NIH/NHLBI T32HL007534 for this work. Dr. Sahetya received funding from the NIH/NHLBI K23HL155507 to support this work. The remaining authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: chochbe1@jh.edu

REFERENCES

1. Guérin C, Reignier J, Richard JC, et al; PROSEVA Study Group: Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med* 2013; 368:2159–2168
2. Munshi L, Del Sorbo L, Adhikari NKJ, et al: Prone position for acute respiratory distress syndrome. A systematic review and meta-analysis. *Ann Am Thorac Soc* 2017; 14:S280–S288
3. Sud S, Friedrich JO, Adhikari NKJ, et al: Comparative effectiveness of protective ventilation strategies for moderate and severe acute respiratory distress syndrome. A network meta-analysis. *Am J Respir Crit Care Med* 2021; 203:1366–1377
4. Fan E, Del Sorbo L, Goligher EC, et al; American Thoracic Society, European Society of Intensive Care Medicine, and Society of Critical Care Medicine: An official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical Practice Guideline: Mechanical ventilation in adult patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2017; 195:1253–1263
5. Alhazzani W, Møller MH, Arabi YM, et al: Surviving Sepsis Campaign: Guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Intensive Care Med* 2020; 46:854–887
6. Duan EH, Adhikari NKJ, D'Aragon F, et al; Canadian Critical Care Trials Group: Management of acute respiratory distress syndrome and refractory hypoxemia. A multicenter observational study. *Ann Am Thorac Soc* 2017; 14:1818–1826
7. Guérin C, Beuret P, Constantin JM, et al; Investigators of the APRONET Study Group, the REVA Network, the Réseau recherche de la Société Française d'Anesthésie-Réanimation (SFAR-recherche) and the ESICM Trials Group: A prospective international observational prevalence study on prone positioning of ARDS patients: The APRONET (ARDS Prone Position Network) study. *Intensive Care Med* 2018; 44:22–37
8. Duggal A, Rezoagli E, Pham T, et al; LUNG SAFE Investigators and the ESICM Trials Group: Patterns of use of adjunctive therapies in patients with early moderate to severe ARDS: Insights from the LUNG SAFE study. *Chest* 2020; 157:1497–1505
9. Qadir N, Bartz RR, Cooter ML, et al; Severe ARDS: Generating Evidence (SAGE) Study Investigators; Society of Critical Care Medicine's Discovery Network: Variation in early management practices in moderate-to-severe ARDS in the United States: The severe ARDS: Generating evidence study. *Chest* 2021; 160:1304–1315
10. Bellani G, Laffey JG, Pham T, et al; LUNG SAFE Investigators; ESICM Trials Group: Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA* 2016; 315:788–800
11. Sjoding MW: Translating evidence into practice in acute respiratory distress syndrome: Teamwork, clinical decision support, and behavioral economic interventions. *Curr Opin Crit Care* 2017; 23:406–411
12. Klaiman T, Silvestri JA, Srinivasan T, et al: Improving prone positioning for severe acute respiratory distress syndrome during the COVID-19 pandemic. An implementation-mapping approach. *Ann Am Thorac Soc* 2021; 18:300–307
13. Law AC, Forbath N, O'Donoghue S, et al: Hospital-level availability of prone positioning in Massachusetts ICUs. *Am J Respir Crit Care Med* 2020; 201:1006–1008
14. Dequin PF, Heming N, Meziani F, et al; CAPE COVID Trial Group and the CRICS-TriGGERSep Network: Effect of hydrocortisone on 21-day mortality or respiratory support among critically ill patients with COVID-19: A randomized clinical trial. *JAMA* 2020; 324:1298–1306
15. Botta M, Tsonas AM, Pillay J, et al; PRoVENT-COVID Collaborative Group: Ventilation management and clinical outcomes in invasively ventilated patients with COVID-19 (PRoVENT-COVID): A national, multicentre, observational cohort study. *Lancet Respir Med* 2021; 9:139–148
16. Estenssoro E, Loudet CI, Ríos FG, et al; SATI-COVID-19 Study Group: Clinical characteristics and outcomes of invasively ventilated patients with COVID-19 in Argentina (SATICOVID): A prospective, multicentre cohort study. *Lancet Respir Med* 2021; 9:989–998
17. Sjoding MW, Admon AJ, Saha AK, et al: Comparing clinical features and outcomes in mechanically ventilated patients with COVID-19 and acute respiratory distress syndrome. *Ann Am Thorac Soc* 2021; 18:1876–1885
18. Mathews KS, Soh H, Shaefi S, et al; STOP-COVID Investigators: Prone positioning and survival in mechanically ventilated patients with coronavirus disease 2019–related respiratory failure. *Crit Care Med* 2021; 49:1026–1037
19. Johnson SW, Garcia MA, Sisson EKQ, et al: Hospital variation in management and outcomes of acute respiratory distress syndrome due to COVID-19. *Crit Care Explor* 2022; 10:e0638
20. Gupta S, Hayek SS, Wang W, et al; STOP-COVID Investigators: Factors associated with death in critically ill patients with coronavirus disease 2019 in the US. *JAMA Intern Med* 2020; 180:1436–1447
21. Barr J, Paulson SS, Kamdar B, et al: The coming of age of implementation science and research in critical care medicine. *Crit Care Med* 2021; 49:1254–1275

22. Taylor SP, Kowalkowski MA, Beidas RS: Where is the implementation science? An opportunity to apply principles during the COVID-19 pandemic. *Clin Infect Dis* 2020; 71:2993–2995
23. Ranieri VM, Rubenfeld GD, Thompson BT, et al; ARDS Definition Task Force: Acute respiratory distress syndrome: The Berlin definition. *JAMA* 2012; 307:2526–2533
24. Johns Hopkins Medicine: Precision Medicine Portal. 2019. Available at: https://pm.jh.edu/. Accessed September 24, 2020
25. Charlson ME, Pompei P, Ales KL, et al: A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis* 1987; 40:373–383
26. Gasparini A: comorbidity: An R package for computing comorbidity scores. *J Open Source Softw* 2018; 3:648
27. Lambden S, Laterre PF, Levy MM, et al: The SOFA score-development, utility and challenges of accurate assessment in clinical trials. *Crit Care* 2019; 23:374
28. Vasilevskis EE, Pandharipande PP, Graves AJ, et al: Validity of a modified Sequential Organ Failure Assessment score using the Richmond Agitation-Sedation Scale. *Crit Care Med* 2016; 44:138–146
29. Yehya N, Harhay MO, Curley MAQ, et al: Reappraisal of ventilator-free days in critical care research. *Am J Respir Crit Care Med* 2019; 200:828–836
30. Bernal JL, Cummins S, Gasparrini A: Interrupted time series regression for the evaluation of public health interventions: A tutorial. *Int J Epidemiol* 2017; 46:348–355
31. Camporota L, Sanderson B, Chiumello D, et al: Prone position in coronavirus disease 2019 and noncoronavirus disease 2019 acute respiratory distress syndrome: An international multicenter observational comparative study. *Crit Care Med* 2022; 50:633–643
32. Rose MR, Hiltz KA, Stephens RS, et al: Novel viruses, old data, and basic principles: How to save lives and avoid harm amid the unknown. *Lancet Respir Med* 2020; 8:661–663
33. Fan E, Beitler JR, Brochard L, et al: COVID-19-associated acute respiratory distress syndrome: Is a different approach to management warranted? *Lancet Respir Med* 2020; 8:816–821
34. Bos LDJ, Sjoding M, Sinha P, et al; PRoVENT-COVID collaborative group: Longitudinal respiratory subphenotypes in patients with COVID-19-related acute respiratory distress syndrome: Results from three observational cohorts. *Lancet Respir Med* 2021; 9:1377–1386
35. Short B, Parekh M, Ryan P, et al: Rapid implementation of a mobile prone team during the COVID-19 pandemic. *J Crit Care* 2020; 60:230–234
36. Guérin C, Albert RK, Beitler J, et al: Prone position in ARDS patients: Why, when, how and for whom. *Intensive Care Med* 2020; 46:2385–2396
37. Xin Y, Martin K, Morais CCA, et al: Diminishing efficacy of prone positioning with late application in evolving lung injury. *Crit Care Med* 2021; 49:e1015–e1024
38. Jochmans S, Mazerand S, Chelly J, et al: Duration of prone position sessions: A prospective cohort study. *Ann Intensive Care* 2020; 10:66
39. Douglas IS, Rosenthal CA, Swanson DD, et al: Safety and outcomes of prolonged usual care prone position mechanical ventilation to treat acute coronavirus disease 2019 hypoxemic respiratory failure. *Crit Care Med* 2021; 49:490–502
40. Grant GP, Szirth BC, Bennett HL, et al: Effects of prone and reverse trendelenburg positioning on ocular parameters. *Anesthesiology* 2010; 112:57–65
41. Shearer SC, Parsa KM, Newark A, et al: Facial pressure injuries from prone positioning in the COVID-19 era. *Laryngoscope* 2021; 131:E2139–E2142