evaluating medical content is unclear, and the increasing number of research manuscripts in the top search results are less relevant and more difficult for patients to interpret. Healthcare organizations that create websites for patient education purposes also risk losing their viewership if they unknowingly miss a specific algorithm criterion, emphasizing the importance of familiarization with these algorithms and continual analysis of their website's search metrics.

In summary, we show that the currently available Internet resources on IPF are of higher content and quality compared with 2015, but there are now less patient-relevant resources appearing in the top search results. Healthcare organizations not only must produce high-quality online content for patients but also should remain informed on changing search engine algorithms so their resources reach the patients they intend to educate.

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Patient-directed Prone Positioning in Awake Patients with COVID-19 Requiring Hospitalization (PAPR)

To the Editor:

Before coronavirus disease (COVID-19), reports of prone positioning in nonintubated patients with acute respiratory distress syndrome suggested it may improve oxygenation and avert intubation (1–4). This potential value was magnified by the COVID-19 pandemic, prompting clinicians to implement prone positioning protocols to manage the surge of patients presenting with acute hypoxic respiratory failure (5–7). We aimed to assess the feasibility and efficacy of a patient-directed prone positioning protocol compared with usual care in nonintubated, spontaneously breathing patients hospitalized with COVID-19.

Author Contributions: S.A.J., D.J.H., M.J.F., J.Y., N.A., J.P.B., J.H.C., and M.J.L. participated in the study design, research, and manuscript preparation. S.A.J. is the guarantor of this manuscript and takes responsibility for the integrity of the work from inception to completion.

Clinical Trial Registration: *ClinicalTrials.gov* (NCT04368000).

Methods

Patients. We conducted a nonblinded pragmatic randomized controlled trial in symptomatic patients hospitalized with suspected or laboratory-confirmed COVID-19. Patients were enrolled within 48 hours of admission from April 29 to August 6, 2020. Eligibility for enrollment required symptoms of COVID-19 combined with either a high clinical suspicion and a pending COVID-19 assay or a positive COVID-19 assay within 10 days. We excluded patients if they were

Table 1. Baseline demographics and clinical status at admission

Baseline Characteristics	Usual Care (*n* = 15)	Prone Positioning (*n* = 15)	Combined (*N* = 30)
Demographics			
Age, median (IQR), yr	62 (49–75)	52 (40–65)	56.5 (45–70)
Sex, M, *n* (%)	8 (53.3)	8 (53.3)	16 (53.3)
BMI, median (IQR), kg/m^2	29.3 (24.4–32.9)	32.9 (27.5–39.4)	30.3 (27.4–37.4)
Charlson Comorbidity Index, median (IQR)	3 (1–5)	1 (0–2)	2 (1–4)
Race/ethnicity, *n* (%)			
White	6 (40.0)	6 (40.0)	12 (40.0)
Latinx	2 (13.3)	5 (33.3)	7 (11.2)
African American	2 (13.3)	1 (6.7)	3 (10.0)
Pacific Islander	3 (20.0)	1 (6.7)	4 (13.3)
Asian	—	1 (6.7)	1 (3.3)
American Indian or Alaskan native	2 (13.3)	—	2 (6.7)
Other	—	1 (6.7)	1 (3.3)
Clinical status			
Positive COVID-19 PCR assay, *n* (%)	14 (93.3)	15 (100)	29 (96.7)
Admission O_2 saturation, median (IQR), %	94 (87–96)	94 (93–95)	94 (90–96)
Admission F_{IO_2}, median (IQR)	21 (21–29)	21 (21–29)	21 (21–29)
Admission oxygen delivery method, *n* (%)			
Room air	9 (60.0)	10 (66.7)	19 (63.3)
Nasal cannula	6 (40.0)	5 (33.3)	11 (36.7)

Definition of abbreviations: BMI = body mass index; COVID-19 = coronavirus disease; F_{IO_2} = fraction of inspired oxygen; IQR = interquartile range; PCR = polymerase chain reaction.

unable to change position without assistance, pregnant, incarcerated, admitted to an intensive care unit (ICU) or transfer was imminent, mechanically ventilated, or receiving hospice.

Intervention. Patients were randomized using a 1:1 allocation to prone positioning or usual care. Those randomized to prone positioning received verbal and written instructions explaining the protocol and a tracking log, and they were offered a massage therapy cushion for comfort. Nursing documentation of patient position was collected as a secondary measure of protocol adherence. During the day, patients were instructed to position themselves in a prone (preferred), left-lateral, or right-lateral (alternati++) position every 4 hours for a duration of 1–2 hours or as long as tolerated. At night, patients were allowed to sleep in any position. Nursing staff did not instruct patients to change positions.

Endpoints. The primary endpoint was the change in partial pressure of oxygen (Pa_{O_2}) to fraction of inspired oxygen (F_{IO_2}) ratio at 72 hours after admission. Secondary endpoints were change in Pa_{O_2}/F_{IO_2} at 48 hours, need for endotracheal intubation, ICU transfer, escalation in oxygen delivery system, length of stay, ventilator-free days, and in-hospital mortality. We performed nonlinear imputation of Pa_{O_2}/F_{IO_2} from oxygen saturation (Sp_{O_2})/F_{IO_2} at the time of admission and 48 and 72 hours after admission (8).

Results

We assessed 238 patients for eligibility; 76 did not meet inclusion criteria, 51 patients declined to participate, 42 patients were already admitted to an ICU or transfer was imminent, and 39 patients were unable to provide consent. Our target enrollment was 60 patients; however, after a prespecified interim safety analysis, enrollment was stopped because of a lack of protocol adherence. A total of 30 patients were randomized, with 15 (50%) to prone positioning and 15 (50%) to usual care. Baseline characteristics were balanced between groups (Table 1).

Interim analysis revealed that protocol adherence was poor (Table 2). None of the patients completed the tracking log despite in-person or telephone reminders. Nursing documentation was available for every patient and was used in place of the tracking log. Only six (40%) patients in the prone positioning arm were observed in the prone position at least once within 72 hours of admission (Table 2). The cumulative time spent prone accounted for only 2.4% of the total time within the first 72 hours of admission (censored for discharge within 72 h), with a mean (95% confidence interval [CI]) duration of 1.6 (0.2–3.1) hours.

Eleven (36.7%) patients required supplemental oxygen upon admission, and the median (interquartile range) Sp_{O_2} was 94%

Table 2. Observation and duration of prone positioning

Measure	Usual Care (*n* = 15)	Prone Positioning (*n* = 15)	*P* Value
Patients observed in prone position during initial 72 h of hospitalization, *n* (%)	0 (0)	6 (40.0)	0.017
Average hours observed in prone position during initial 72 h of hospitalization, mean (95% CI)	0 (0)	1.6 (0.2–3.1)	0.024
Percentage of time observed in prone position during initial 72 h of hospitalization, %	0	2.4	—

Definition of abbreviation: CI = confidence interval.

Table 3. Primary and secondary outcomes

Outcomes	Usual Care ($n = 15$)	Prone Positioning ($n = 15$)	P Value*
Primary outcome			
Change in Pa_{O_2}/FI_{O_2} at 72 h, mean (95% CI)	−18.2 (−63.0 to 26.5)	−80.1 (−138.8 to −21.4)	0.077
Secondary outcomes			
Change in Pa_{O_2}/FI_{O_2} at 48 h, mean (95% CI)	−15.0 (−45.0 to 15.0)	−70.5 (−116.4 to −24.6)	0.036
Length of stay, median (IQR), d	4.6 (3.1 to 5.0)	4.7 (2.8 to 8.2)	0.694
Required escalation of O_2 delivery system, *n* (%)	7 (46.7)	12 (80.0)	0.128
Maximal amount of oxygen support, *n* (%)			0.339
Room air	3 (20.0)	4 (26.7)	—
Nasal cannula	11 (73.3)	7 (46.7)	—
High-flow nasal cannula	0 (0)	2 (13.3)	—
Endotracheal intubation/mechanical ventilation	1 (6.7)	2 (13.3)	—
Transferred to ICU, *n* (%)	2 (13.3)	5 (33.3)	0.390
Required intubation/mechanical ventilation, *n* (%)	1 (6.7)	2 (13.3)	1.000
In-hospital mortality, *n* (%)	0 (0)	2 (13.3)	0.483
Ventilator-free days, mean (95% CI)	27.0 (24.8 to 29.2)	24.3 (18.8 to 29.7)	0.332

Definition of abbreviations: CI = confidence interval; FI_{O_2} = fraction of inspired oxygen; ICU = intensive care unit; IQR = interquartile range; Pa_{O_2} = partial pressure of arterial oxygen.
**P* values are not adjusted for multiple comparisons.

(90–96%). Five (16.7%) patients were discharged within 72 hours. The remaining 25 (83.3%) patients were included in the primary analysis (Table 3). No significant difference was observed in the change in PaO_2/FiO_2 at 72 hours between prone positioning and usual care (mean [95% CI], −80.1 [−138.8 to −21.4] vs. −18.2 [−63.0 to 26.5]; $P = 0.077$). The change in PaO_2/FiO_2 at 48 hours was significantly worse in the prone positioning arm compared with the usual care arm (mean [95% CI], −70.5 [−116.4 to −24.6] vs. −15.0 [−45.0 to 15.0]; $P = 0.036$). Twelve (80%) patients in the prone positioning arm required an escalation in oxygen delivery system, five (33.3%) patients were transferred to the ICU, and two (13.3%) required endotracheal intubation/mechanical ventilation. Two deaths occurred, both in the prone positioning arm, and were deemed unrelated to study procedures. No study-related adverse events were observed.

Discussion

In this pragmatic randomized controlled trial, we investigated the feasibility and efficacy of patient-directed prone positioning among nonintubated, spontaneously breathing patients hospitalized with COVID-19. We found that adherence to our prone positioning protocol was very low, suggesting that a patient-directed approach is not feasible. Our protocol appeared safe, although it did not improve oxygenation, an unexpected finding.

Despite receiving verbal and written instructions and either telephone or in-person follow-up, none of the participants tolerated or adhered to the protocol as designed. Most patients verbalized laying prone one or two times daily for 30–90 minutes within the first 72 hours of hospitalization. Nursing documentation confirmed poor protocol adherence, with only 40% of patients assigned to the intervention being observed in the prone position. This observation reinforced our decision to stop enrollment early and conclude our protocol is not feasible. It is possible a nursing-directed protocol may improve adherence, though we opted against this approach to minimize contagion risk.

Given the considerable physiologic evidence for improved oxygenation in the prone position combined with the aforementioned poor protocol adherence, it is difficult to draw inferences from our primary and secondary outcomes. The lack of improvement in Pa_{O_2}/FI_{O_2} observed at 72 and 48 hours may represent the natural disease course of COVID-19, with little to no measurable effect of prone positioning.

Our study has several limitations, including the small sample size, which limits the power to detect outcome differences; missing data from tracking logs; lack of protocol adherence; and use of a surrogate outcome measure (i.e., imputed Pa_{O_2}/FI_{O_2}). Many patients (63.3%) did not require supplemental oxygen upon admission, suggesting that they were less acutely ill compared with other studied cohorts, possibly accounting for their lack of adherence and improvement (2, 6, 9). Regardless, we believe our results are informative to future studies and urge investigators to develop respiratory therapy– (9) or nursing-directed protocols rather than relying on patient-directed protocols.

Conclusions. Our results suggest that patient-directed prone positioning is not feasible in spontaneously breathing, nonintubated patients hospitalized with COVID-19. No improvements in oxygenation were observed at 72 or 48 hours.

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Ratio of Oxygen Saturation Index to Guide Management of COVID-19 Pneumonia

Coronavirus disease (COVID-19) caused by novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged from China in December 2019, leading to a global pandemic (1). Approximately 17% of patients admitted to hospital require critical care, the majority of whom undergo mechanical ventilation (MV) for pneumonia complicated by hypoxemia (2).

High-flow nasal cannula (HFNC) and continuous positive airway pressure (CPAP) are recognized treatments for hypoxemic respiratory failure caused by community-acquired pneumonia (CAP) (5–7). HFNC and CPAP may represent definitive therapy, avoiding unnecessary MV, or provide bridging respiratory support that offsets the need for immediate MV, preserving finite critical care resources. The ratio of oxygen saturation (ROX) index is used to predict the failure of HFNC in the treatment of CAP (6, 7). There are little published data describing the use of the ROX index to guide use of HFNC to treat COVID-19–associated respiratory failure; we provide further evidence to validate ROX index use in this setting (8, 9). The ROX index was developed as a simple bedside test to predict the failure of HFNC and need for MV, although patients with viral pneumonia were likely underrepresented in derivation and validation studies (6).

We undertook a retrospective observational study of individuals with laboratory-confirmed COVID-19 presenting to a single East London hospital between March 16, 2020, and April 6, 2020. Patients who received HFNC, CPAP, or MV were identified. Electronic notes review captured demographic data and clinical and respiratory parameters.

Of 393 inpatients with laboratory-confirmed COVID-19 during the study period, 255 individuals (255/393; 65.0%) were eligible for HFNC or CPAP as determined by the treating clinicians, consistent with national and local guidelines (10). A total of 108 individuals (108/255, 42.4%) received HFNC or CPAP; 69 individuals received HFNC only (63.8%), 18 received CPAP only (16.7%), and 21 received both devices (19.4%; Table 1). The majority of individuals receiving HFNC and/or CPAP experienced severe outcomes, defined as mortality or MV at 30-day follow-up (77/108; 71.3%). Most individuals who were deemed eligible for CPAP and HFNC at the time of admission were judged by treating clinicians not to require devices (147/255; 57.6%), and the majority of these individuals experienced nonsevere outcomes (138/147; 93.8%).

Table 1. Clinical variables for all patients receiving CPAP and/or HFNC

Patients	Value
Total	108
Age, yr	
Median (IQR)	62 (53–68)
Sex, *n* (%)	
M	82 (76)
Number of comorbidities	
Median (IQR)	1 (0–2)
HFNC only, *n* (%)	69 (64)
CPAP only, *n* (%)	18 (17)
CPAP and HFNC, *n* (%)	21 (19)
P/F ratio at admission (*n* = 73)	
Median (IQR)	112.5 (75.3–266.7)
ROX index at admission (*n* = 90)	
Median (IQR)	9.6 (4.3–17.0)
Do-not-intubate order at admission, *n* (%)	19 (21)
Mechanical ventilation, *n* (%)	49 (54)
Mortality, *n* (%)	33 (37)

Definition of abbreviations: CPAP = continuous positive airway pressure; HFNC = high-flow nasal cannula; IQR = interquartile range; P/F ratio = arterial oxygen pressure/fraction of inspired oxygen ratio; ROX index = ratio of oxygen saturation index.

Author Contributions: D.L.F. and N.R.G. contributed equally to the manuscript in terms of conception of the work, acquisition of data drafting, and approval of the version to be published. D.L.F. provided the majority of analysis and interpretation of the data and led redrafting of the manuscript. J.C., K.H.E.-S., and G.E.S. all contributed to the work in terms of acquisition of the data and revising and approval of the version to be published. A.G.-W. contributed analysis and interpretation of data and revising and approval of the version to be published. C.X.T. contributed in terms of conception of the work and revising and approval of the version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.