

# Importance of timing and training to implement awake prone positioning in patients with COVID-19: a single-center prospective observational study

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**Background:** Awake prone positioning (APP) is broadly implemented in patients with severe acute respiratory syndrome coronavirus 2 related disease [coronavirus disease 2019 (COVID-19)] admitted to hospital with severe respiratory distress syndrome. This prospective observational study aimed to explore the factors influencing the implementation of APP in patients with acute respiratory failure due to COVID-19.

**Methods:** Patients with COVID-19, all hospitalized with positive X-ray findings and oxygen supplementation requirement, in the Respiratory Step-Down Unit of the Peking University Third Hospital between January 6<sup>th</sup>, 2023, and January 20<sup>th</sup>, 2023, were included in this study. Data regarding basic information, activities of daily living (ADLs) scores, oxygen therapy, vital signs, and duration of APP were collected to investigate the factors influencing prone positioning.

**Results:** Among the 134 patients included, 55.2% showed an improvement in oxygen saturation 1 hour after APP. Logistic regression revealed that the pre-APP heart rate (HR) [odds ratio (OR) =1.032; P=0.046] and peripheral oxygen saturation (SpO<sub>2</sub>) (OR =0.720; P<0.001) were the associated factors of the improvement in SpO<sub>2</sub> after treatment. Multiple linear regression revealed that the ADL scores and pre-APP respiratory rate (RR) were the associated factors of the duration of prone positioning (P<0.01). The APP technical steering group effectively improved duration of APP.

**Conclusions:** Patients with low  $\text{SpO}_2$  and increased HR before treatment showed greater improvement in oxygen saturation. Patients with lower tolerance to ADL but lower RRs were those to demonstrate a longer duration of prone positioning. This is pointing towards establishing the most favorable time window for APP during the course of COVID-19: after the ADLs have already decreased, but before significant tachypnea has appeared.

**Keywords:** Coronavirus disease 2019 (COVID-19); awake prone positioning (APP); influencing factors; peripheral oxygen saturation (SpO<sub>2</sub>)

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# Introduction

The pandemic of coronavirus disease 2019 (COVID-19) has led to significant morbidity and mortality (1), and has pushed the medical system to change itself in order to face the new context (2,3). At the end of 2022, a large number of people in Beijing was affected by COVID-19. Elderly patients had a higher probability of having a severe disease, requiring treatment. The treatment protocol for COVID-19 infection implemented at the Peking University Third Hospital included the awake prone positioning (APP) ventilation technique. APP is to rotate an awake and not intubated patient from supine to ventral position to allow for greater expansion of lung tissue in the dorsal area (4). The protocol recommends it for critical cases, at a high-risk of developing severe complications and rapid progression and it recommends for 12 hours per day (5). The prone positioning technique has been mainly applied to patients with severe respiratory distress syndrome and is used less commonly in other clinical settings. APP is safe and feasible in non-intubated patients with acute hypoxic respiratory failure caused by COVID-19, and can significantly reduce the intubation rate but more studies are needed to better

#### Highlight box

#### Key findings

 This study examined the clinical effects and influencing factors of the awake prone positioning (APP) ventilation technique in patients with coronavirus disease 2019 (COVID-19)-associated pneumonia.

#### What is known and what is new?

- The APP ventilation technique effectively improved the peripheral oxygen saturation in patients with COVID-19-associated pneumonia.
- Decreased activities of daily living were associated with better-, higher respiratory rates with lower compliance with APP. The findings seem to delineate the optimal timing for APP, when used for slowing COVID-19 progression: it is after the ability of daily living has decreased, but before significant tachypnea appears.

#### What is the implication, and what should change now?

 Further investigation of the mechanisms underlying the effect of APP on clinical outcomes is needed to improve patient compliance with treatment and prone positioning. understand its role (6). In addition, its effect on peripheral oxygen saturation (SpO<sub>2</sub>) and outcomes in patients with COVID-19, the effect of the duration of APP on SpO<sub>2</sub> and outcomes in patients with COVID-19, and the means to effectively extending the treatment time of APP must be clarified. This study aimed to examine the role of APP and the main factors affecting its implementation. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1441/rc).

## Methods

#### Patients

Patients with COVID-19 pneumonia who were hospitalized in the respiratory step-down unit of the Peking University Third Hospital between January 6<sup>th</sup>, 2023, and January 20<sup>th</sup>, 2023, were selected as study participants. The inclusion criteria were as follows: (I) patients aged  $\geq 18$  years who met the diagnostic criteria for COVID-19 infection according to the Diagnostic Protocol for COVID-19 Infection (9<sup>th</sup> edition) (5); (II) patients with chest imaging findings suggestive of combined pulmonary infection; (III) patients with acute hypoxemic respiratory failure, defined as the need for supplemental oxygen to maintain an oxygen saturation of 89% or higher; and (IV) patients who were conscious and able to cooperate with prone positioning. The exclusion criteria were as follows: (I) patients in critical condition requiring mechanical ventilation; (II) patients unable to tolerate the change in position; and (III) patients who refused prone positioning.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Ethical Review Board of Peking University Third Hospital (No. 2023-088-01) and informed consent was taken from all the patients.

#### Study methods

# Establishment of an APP technical steering group and nursing staff training

The hospital established an APP technical steering group responsible for training and assessing the technical skills of the staff nurses. In addition, the technical steering group assisted and guided the respiratory step-down unit in performing prone positioning. The study group comprised one respiratory therapist and six intensive care unit (ICU) specialist nurses. All nursing staff in the respiratory step-down unit successfully completed the training and assessment of the APP technique and received training for the data collection method used in this study. The APP order was included in the patients' medical records. As the optimal duration of prone positioning was unknown, nurses encouraged patients to use prone positioning as often and as consistently as possible.

# Data collection

Data regarding basic information, demographic characteristics, medical history, activities of daily living (ADLs), mode of oxygen therapy, oxygen concentration, SpO<sub>2</sub>, heart rate (HR), and respiratory rate (RR) of the patients before APP and the SpO<sub>2</sub>, HR, and RR of patients 1 hour after the end of prone positioning were collected on the first day of APP. If the patients used the prone position for several sessions per day, the parameters of the first session were recorded. The basic information, demographic characteristics, and medical histories of the patients were obtained from their medical records.

ADL was assessed using the internationally recognized Barthel Index scale, which assesses the ability of the patient to perform ADLs using 10 dimensions, including eating, bathing, grooming, dressing, and bladder and bowel control. The total score ranges from 0 to 100, with a higher score indicating a better ability to perform ADL (7).

Since the duration spent in the prone position was determined by the patients, bedside nurses estimated and recorded the time each patient spent in the prone position. The duration of prone positioning, defined as the total cumulative duration of prone positioning for patients per day, was recorded each day until the end of the study period. In addition, two technical steering group members regularly visited the patients in each unit to inspect the implementation of prone positioning, solve clinical problems promptly, and communicate with the patients to understand their concerns during prone positioning.

## Statistical methods

Data entry was completed using Microsoft Excel while data analysis was completed using SPSS 24.0 statistical software (IBM Corp., Armonk, NY, USA). Measures with normal or approximately normal distributions are expressed as the mean  $\pm$  standard deviation (SD). Categorical data are expressed as frequencies and percentages. The clinical data of the patients among the different groups were compared using the *t*-test, chi-squared test, analysis of variance (ANOVA), and nonparametric test. Pearson correlation analysis was used to analyze the correlations between the variables, and multiple linear regression analysis was performed to determine the factors contributing to the duration of prone position. Logistic regression analysis was used to determine the associated factors of the initial improvement in SpO<sub>2</sub> after prone positioning.

# **Results**

#### General characteristics of the participants

Totally 677 patients were admitted to the Respiratory Step-Down Unit of the Peking University Third Hospital between January 6<sup>th</sup>, 2023, and January 20<sup>th</sup>, 2023, 423 of them met the indication for APP. Based on the initial inclusion and exclusion criteria, 150 patients with COVID-19 pneumonia were included. Among these 150 patients, 15 patients were excluded due to incomplete records of vital signs, and a patient was excluded due to unclear records of prone positioning time. Thus, the final analysis included 134 patients, comprising 89 men and 45 women aged 33-97 (76.88±12.04) years; 52 patients (38.8%) had combined cardiovascular system diseases, whereas 13 patients (9.7%) had respiratory diseases. The mean duration of treatment in the prone position was 272.89±185.44 min while the mean duration of hospitalization was 14.54±6.80 days. Among them, 112 patients received regular nasal cannula oxygen, eight patients received oxygen storage masks, eight patients received high-flow nasal cannula, and six patients received bilevel positive airway pressure (BiPAP) ventilation. Among the 134 patients included in the study, 126 patients (94.0%) were cured and discharged.

Among the included patients, eight patients refused to be intubated for further treatment and died, including six men and two women. The mean age of the deceased patients was 74.88±4.02 years; their mean duration of treatment in the prone position was 194.50±154.40 min, and the mean duration of hospitalization was 14.00±6.59 days. Moreover, two patients received nasal cannula oxygen, four patients received oxygen storage masks, and two patients received BiPAP ventilation.

# Analysis of the factors influencing the improvement of $SpO_2$ in patients after prone positioning

#### Changes in SpO<sub>2</sub> during and after APP

One hour after the end of the first prone positioning session, the SpO<sub>2</sub> increased from  $95.72\%\pm0.30\%$  to  $97.99\%\pm0.22\%$  in 74 (55.2%) of the 134 patients. In contrast, no change was observed in 34 patients (25.4%), and SpO<sub>2</sub> decreased from  $97.81\%\pm0.42\%$  to  $95.85\%\pm0.72\%$  in 26 (19.4%) patients.

# Univariate analysis of the factors influencing improvement in SpO<sub>2</sub>

According to the changes in SpO<sub>2</sub> after prone positioning, the 134 patients included in the study were divided into SpO<sub>2</sub> improvement (increase in SpO<sub>2</sub>) and nonimprovement (no change or decrease in SpO<sub>2</sub>) groups. The results of the univariate analysis revealed statistically significant differences between the two groups (P<0.05) in terms of sex, presence of comorbid respiratory diseases, HR, and SpO<sub>2</sub> before prone positioning (*Table 1*).

# Logistic regression analysis of the factors influencing SpO<sub>2</sub> improvement after prone positioning

The variables that were statistically different in the univariate comparison between the groups with and without improved oxygen saturation were used as independent variables. Logistic regression analysis was performed with improvement in SpO<sub>2</sub> as the dependent variable. The following values were assigned for each variable: gender, 1= men and 2= women; and combined respiratory disease, 0= no and 1= yes. The original values were used for HR and SpO<sub>2</sub> before prone positioning. The results revealed that pretreatment HR [odds ratio (OR) =1.032; P=0.046] and SpO<sub>2</sub> (OR =0.720; P<0.001) were the factors influencing the improvement in SpO<sub>2</sub> in patients after prone positioning (*Table 2*).

## Analysis of the factors influencing the duration of APP

**Univariate analysis of the duration of prone positioning** The *t*-test revealed no statistically significant difference in the duration of prone positioning between the different subgroups according to gender, presence of combined cardiovascular system or respiratory diseases, oxygen therapy method, and patients' outcome (Table S1).

Pearson correlation analysis revealed that ADL score (r=-0.209; P=0.016), SpO<sub>2</sub> (r=0.207; P=0.017), HR

(r=-0.232; P=0.007), and RR (r=-0.340; P<0.001) before prone positioning were correlated with the duration of prone positioning.

# Multiple linear regression analysis of the duration of prone positioning

Multiple linear regression analysis was performed with the duration of prone positioning time as the dependent variable. The statistically significant variable (P<0.05) in the correlation analysis was selected as the independent variable. The results showed that ADL score and RR before prone positioning associated the duration of prone positioning (*Table 3*).

## Gradual increase in the duration of APP

In total, 134 patients participated in prone positioning, the number of participants gradually decreased as patients conditions changed (cured, death, or suspended the APP). The longest duration of participation was 12 days, and the average daily duration of APP implementation increased from  $272.66 \pm 185.39$  min on day 1 to  $505.00 \pm 55.05$  min on day 12 (*Figure 1*).

# Barriers to compliance with the implementation of prone positioning

Two out of the 134 included patients developed complications during prone positioning: one developed facial edema (APP treatment 5.5 hours) while the other developed scrotal edema (APP treatment 4 hours). Consequently, they suspended the APP. The technical steering group conducted on-site observations, interviewed 45 patients on the implementation of prone positioning, and summarized the factors that impeded compliance with the implementation of APP. In 14 cases (31.1%), that factors were related to patients themselves, in 4 cases (8.9%), they were related to medical personnel, and in 2 cases (4.4%) to equipment. The patient factors mainly included the following: objective factors, such as decreased oxygen saturation, increased HR, and violent cough after APP; subjective factors, such as complaints of breath-holding, precordial discomfort, dizziness, discomfort (neck, head, and face), weakness, inability to cooperate with turning, shoulder pain, lumbago, muscle pain, and fear that the compression of the heart during APP would affect the infusion of fluids. Medical staff factors mainly included the following: incomplete preparation before APP, such as not asking the patient to defecate and not preparing soft pillows; irregular operation by the medical staff, such as APP not

Table 1 Univariate analysis of the associated factors with improvement in SpO<sub>2</sub> (n=134)

Items	Improvement group (n=74)	Non-improvement group (n=60)	Statistical value	P value
Age (years)	77.62±10.88	75.97±13.37	0.790 <sup>†</sup>	0.431
Sex			4.632 <sup>‡</sup>	0.031
Male	55 (74.3)	34 (56.7)		
Female	19 (25.7)	26 (43.3)		
Payment scheme			4.963 <sup>‡</sup>	0.175
Medical insurance	68 (91.8)	59 (98.3)		
Other	6 (8.2)	1 (1.7)		
Marital status			2.271 <sup>‡</sup>	0.518
Married	65 (87.8)	54 (90.0)		
Widowed/single/divorced	9 (12.2)	6 (10.0)		
Occupational status			1.517 <sup>‡</sup>	0.911
Retired	50 (67.6)	37 (61.7)		
Employed	24 (32.4)	23 (38.3)		
Cardiovascular disease			$0.938^{\ddagger}$	0.333
Yes	26 (35.1)	26 (43.3)		
No	48 (64.9)	34 (56.7)		
Respiratory disease			5.030 <sup>‡</sup>	0.025
Yes	11 (14.9)	2 (3.3)		
No	63 (85.1)	58 (96.7)		
ADL score	61.01±25.31	55.00±27.46	$1.317^{\dagger}$	0.190
APP duration (min)	255.93±176.90	293.80±194.92	$-1.177^{\dagger}$	0.241
Oxygen therapy method			-0.211 <sup>§</sup>	0.833
Normal nasal cannula	60 (81.1)	52 (86.6)		
Face mask	6 (8.1)	2 (3.3)		
High flow nasal cannula	6 (8.1)	2 (3.3)		
<b>BiPAP</b> ventilation	2 (2.7)	4 (6.7)		
FiO <sub>2</sub> (%)	35.86±11.08	34.10±10.12	0.953 <sup>†</sup>	0.342
SpO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	288.16±75.23	304.44±65.94	$-1.316^{\dagger}$	0.190
Pre-APP HR	80.36±13.58	74.52±12.48	$2.569^{\dagger}$	0.011
Pre-APP RR	19.91±3.56	19.72±5.47	0.241 <sup>†</sup>	0.810
Pre-APP SpO <sub>2</sub> (%)	95.72±2.58	97.68±2.33	$-4.582^{\dagger}$	<0.01
Patient outcome			0.182 <sup>‡</sup>	0.670
Death	5 (6.8)	3 (5.0)		
Discharged	69 (93.2)	57 (95.0)		

Data are presented as n (%) or mean  $\pm$  SD.<sup>†</sup>, *t* value; <sup>‡</sup>,  $\chi^2$  value; <sup>§</sup>, *Z* value. SpO<sub>2</sub>, peripheral oxygen saturation; ADL, activity of daily living; APP, awake prone positioning; BiPAP, bilevel positive airway pressure; FiO<sub>2</sub>, inspired fraction of oxygen; HR, heart rate; RR, respiratory rate; SD, standard deviation.

Table 2 Logistic regression analysis of the associated factors with SpO2 improvement after prone positioning (n=134)

Variables	B value	Standard error	Wald	P value	OR	95% CI
Constants	29.550	8.454	12.218	<0.001	0.000	-
Pre-APP HR	0.032	0.016	3.999	0.046	1.032	1.001-1.065
Pre-APP SpO <sub>2</sub>	-0.328	0.086	14.546	<0.001	0.720	0.608-0.852

SpO<sub>2</sub>, peripheral oxygen saturation; OR, odds ratio; CI, confidence interval; APP, awake prone positioning; HR, heart rate.

Table 3 Multiple linear regression analysis of the duration of prone positioning (n=134)

Items	Partial regression coefficient	Standard error	Standardized regression coefficient	t value	P value
Constant term	-48.705	605.248	-	-0.080	0.936
ADLs score	-1.601	0.559	-0.228	-2.863	0.005
RR	-10.667	3.683	-0.259	-2.897	0.004

R=0.436, R<sup>2</sup>=0.190, adjusted R<sup>2</sup>=0.165, F=7.557, P<0.001. ADL, activity of daily living; RR, respiratory rate.

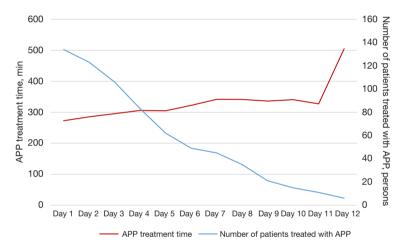


Figure 1 The duration of APP in patients. APP, awake prone positioning.

being standardized and incorrect use of soft pillows; and constraints of medical staff. The equipment factors included hard mattresses, uncomfortably soft pillows, and not using soft pillows.

#### Discussion

### Effect of prone positioning on oxygen saturation

This study showed that  $SpO_2$  effectively increased in 55.2% of the patients with COVID-19 treated with APP; this result is consistent with previous studies. For instance, reviews reported that the implementation of APP improves oxygenation in patients with COVID-19-associated

pneumonia (8-10). Patients with COVID-19 pneumonia have a higher  $\text{SpO}_2/\text{inspired}$  fraction of oxygen (FiO<sub>2</sub>) to RR and oxygenation indices when ventilated in APP with high-flow nasal cannula oxygen therapy (11). The improved ventilation-perfusion ratio in the lungs and enhanced oxygen saturation may be attributed to the shift of the patient from the supine position to APP.

The results of the present study suggest that  $\text{SpO}_2$ before prone positioning may be a factor contributing to the improvement in  $\text{SpO}_2$  after prone positioning. Lower  $\text{SpO}_2$  before treatment resulted in a higher  $\text{SpO}_2$ improvement rate after prone positioning, likely due to the physiological effect of prone positioning. In patients

with acute respiratory distress syndrome, the ventral alveoli are better ventilated in the supine position due to transpulmonary pressure, and the dorsal alveoli become less ventilated due to gravity, resulting in fluid compression and an increase in blood flow to the dorsal lung due to gravity. Consequently, the ventilation-perfusion ratio does not reach the normal range, and the oxygen saturation remains low. With APP, the volume of the dorsal alveoli increases due to transpulmonary pressure (12), and the lung tissue initially compressed by the heart in the supine position loses cardiac compression and is converted to an effective ventilation area (12). In addition, the dorsal lung ventilation area is larger than the abdominal ventilation area due to the lung structure; thus, the effective ventilation area increases as the volume of the dorsal alveoli increases after APP, resulting in significantly better ventilation. In contrast, the ventilationperfusion ratio improves and reaches the normal range due to the gravitational redistribution of blood in the lungs, but not more so in the ventral lung, resulting in a more uniform distribution of blood in the whole lung (13). Consequently, the oxygen saturation level effectively improves.

It is possible that the patients with better  $\text{SpO}_2$  do not reach the state of acute respiratory distress syndrome, and the ventilation-perfusion ratio is already within the normal range; thus, prone positioning does not effectively improve the ventilation-perfusion ratio. In contrast, a decrease in chest wall compliance (14), compression of the thoracic cavity by intra-abdominal organs, oxygen consumption due to turning, and artificial downward adjustment of oxygen saturation after an increase in the inhaled oxygen concentration can cause a decrease in  $\text{SpO}_2$  in patients. However, the underlying physiological effects of these factors require further investigation.

The results of the present study showed that the HR status before APP was an associated factor of the improvement in SpO<sub>2</sub> after prone positioning, with a higher HR before treatment associating in a greater improvement in SpO<sub>2</sub> after prone positioning. This finding is related to the effect of APP on the circulatory system (15). Prone positioning leads to intra-abdominal organ compression, followed by an increase in venous return volume and higher right-sided heart preload; concurrently, the prone position improves the oxygenation and promotes lung recruitment maneuver. This results in a decrease in the pulmonary vascular resistance and proper heart preload, thereby increasing the cardiac output. A higher HR with better cardiac output improves the pulmonary circulation and ventilation-perfusion ratio, thereby improving oxygen

saturation.

However, the results of this study also demonstrated that clinical outcomes were not related to the improvement in oxygen saturation after APP or the duration of prone positioning. In a study that included 501 patients with COVID-19-associated pneumonia, Qian et al. (16) reported no advantage in patient mortality in a comparison of a prone positioning group with a non-prone positioning group. Previous reviews reached no definitive conclusions regarding the effect of APP implementation on the rates of tracheal intubation and mortality in patients with COVID-19-associated pneumonia (3,4). However, a multicenter observational study reported a tracheal intubation rate of 23.6% and 40.4% along with a mortality rate of 19.8% and 37.3% in an APP group (505 patients with COVID-19associated pneumonia) and a supine group (322 patients), respectively; thus, the mortality and intubation rates were significantly higher in the supine group (17). Another observational study of 125 patients found that the early implementation of prone positioning reduced the mortality rate but had no effect on the tracheal intubation rate (18). However, the median duration of prone positioning in these two studies ranged from approximately 8 to 12 hours, whereas the mean duration of prone positioning in our study was only approximately 4.5 hours, which did not meet the requirement of 12 hours stated the treatment protocol for COVID-19 infection. Thus, the impact of the implementation of APP ventilation, the duration of prone positioning, and the underlying mechanism of effect on the clinical outcomes of patients with COVID-19-associated pneumonia require further investigation.

# Factors influencing the duration of prone positioning

Previous studies on prone positioning have focused on patients with acute respiratory distress syndrome admitted to the ICU who are critically ill and have no ability to perform ADLs. Therefore, studies on the correlation between the ability to perform ADLs and prone positioning are rare. In our study, all patients were conscious and able to perform ADLs, and the results showed the ADL score to be an associated factor of the duration of prone positioning, with a negative correlation observed between the two. The main reasons for this relationship are as follows. First, a high ADL score indicates mild pneumonia, which has less of an impact on mobility, and those with milder disease are less likely to adhere to treatment. Second, patients with high ADL scores have a greater ability to self-turn during

APP compared with patients with low ADL scores. Thus, patients with higher ADL scores can turn themselves when experiencing any discomfort, making supervision more difficult for medical staff. Finally, most patients with high ADL scores do not have family members staying with them during hospitalization, and certain medical and life factors may interrupt prone positioning. Hence, patients with high ADL scores had shorter durations of APP than did those with low ADL scores.

This study also showed that RR of patients before prone positioning was an associated factor of the duration of prone positioning, with a negative correlation observed between the two. This finding may be attributed to patients with higher RRs performing more breath work and thus being more likely to be fatigued. However, most patients with higher RRs exhibited shallow, fast breathing, which is not conducive to gas exchange in the lungs. Therefore, such patients had a shorter duration of APP. Since patients with lower tolerance to ADL but lower RRs were those to demonstrate a longer duration of prone positioning, the most favorable time window for APP during the course of COVID-19 seems to establish as: after the ADLs have already decreased, but before significant tachypnea has appeared.

# Role of medical staff in the improvement of compliance with prone positioning

This study showed that the APP technical steering group provided targeted professional guidance to medical staff and patients during clinical rounds, resulting in a gradual increase in the duration of prone positioning, with only two patients out of 134 experiencing complications. During the pandemic of COVID-19-associated pneumonia, establishment of an APP technical steering group was found to reduce patient complications and improve medical staff satisfaction in the United States (19). A qualitative study showed that factors promoting the implementation of APP, including health education and supervision, selfmotivation and support from healthcare staff and family members, finding a comfortable position and having access to entertainment, and symptom improvement (20). The current wave of this infection has spread rapidly in China, and a respiratory step-down unit was temporarily established in response to the sudden increase in the number of critically ill patients. In addition, nursing staff were temporarily drawn from various departments within the hospital. Although all nurses received training and

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assessments related to prone positioning, their clinical practice skills required improvement. Therefore, the training of medical staff should focus on improving their knowledge and skills to perform APP ventilation techniques properly, effectively implement health education on prone position therapy for awake patients, and improve patient compliance.

The results of this study showed that equipment factors, including the hardness of mattresses and the discomfort of pillows, are barriers to compliance with prone positioning. Previous studies have shown that pressure injury is a complication of prone positioning (21) and is regulated as a care-sensitive indicator (22). Since the patients included in this study were awake, the possibility of pressure injury was lower, as they adjusted their position when they felt the discomfort caused by the pressure. A pilot trial which wanted to identify contextual factors relevant to implement a definitive clinical trial evaluating APP strategy for nonintubated hypoxic patients with COVID-19, showed that none of 40 patients managed the 12 to 16 hours prone target time suggested by clinicians, they estimated spending only between 10 and 120 min a day in prone position because of the discomfort (23). Song et al. showed that split-prone ventilation cushions could effectively extend the duration of prone positioning (24). Further optimization of the prone positioning application equipment must be continued to improve the duration of prone positioning and achieve improved oxygen saturation.

Based on the above results, we designed an APP checklist to help medical staff perform APP and improve the duration of prone positioning (Figure S1).

# Limitations

This study had several limitations. First of all, it is a singlecenter prospective observational study, with a small sample size, which might have affected the results. Moreover, not being a randomized controlled trial, it could not directly determine the effect of APP on patients. Another important limitation is that SpO<sub>2</sub> was not continuously recorded during APP, and for this reason we could not determine the changes in SpO<sub>2</sub> according to patient position.

# Conclusions

The implementation of the APP ventilation technique improved oxygen saturation in most patients with COVID-19-associated infections and involved few complications, even when the clinical implementation time fails to meet the requirements of the treatment specifications. In terms of APP implementation, the period when after the daily living activities have already decreased, but before significant tachypnea has appeared, seems to be the most favorable time window for APP during the course of COVID-19. In the future, nursing staff should further investigate the mechanisms underlying the effects of APP on clinical outcomes to improve patient compliance with treatment and prone positioning.

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# Footnote

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*Ethical Statement:* The authors are 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Ethical Review Board of Peking University Third Hospital (No. 2023-088-01) and informed consent was taken from all the patients.

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Table S1 Univariate analysis of the duration of prone positioning (n=134)

Items	Patient (%)	APP duration (min/day)	Statistical value	P value
Sex			0.107 <sup>†</sup>	0.915
Male	89 (66.4)	274.11±192.24		
Female	45 (33.6)	270.47±173.27		
Marital status			$0.955^{\dagger}$	0.341
Married	119 (88.8)	267.45±186.88		
Widowed/single/divorced	15 (11.2)	316.00±173.40		
Cardiovascular diseases			$-1.082^{\dagger}$	0.281
Yes	52 (38.8)	251.13±196.39		
No	82 (61.2)	286.68±178.00		
Respiratory diseases			-0.861 <sup>†</sup>	0.391
Yes	13 (9.7)	230.77±176.80		
No	121 (90.3)	277.41±186.48		
Oxygen therapy method			1.519 <sup>‡</sup>	0.200
No	7 (5.2)	139.29±100.52		
Nasal cannula	105 (78.4)	290.22±190.99		
Face mask	8 (6.0)	207.25±179.27		
High flow nasal cannula	8 (6.0)	230.00±148.52		
BiPAP ventilation	6 (4.5)	270.17±163.99		
Patient outcome			$1.235^{\dagger}$	0.219
Death	8 (6.0)	194.50±154.40		
Discharged	126 (94.0)	277.87±186.64		

Data are presented as n (%) or mean  $\pm$  SD.<sup>†</sup>, *t* value; <sup>‡</sup>,  $\chi^2$  value. APP, awake prone positioning; BiPAP, bilevel positive airway pressure; SD, standard deviation.

APP checklist (Medical staff version)				
	Training	□ All team members have completed APP technical training		
	Assessment	Evaluate the patient's disease status: $\Box$ oxygen therapy mode $\Box$ vital signs,		
		HR: RR: BP: SpO <sub>2</sub> : □ self-care ability		
Before	Patient	□ Inform the patient of the purpose, operation methods, advantages and		
implementation	education	disadvantages, precautions of the APP		
Implementation	Preparation	$\hfill\square$ Adjustable multifunctional hospital bed $\hfill\square$ comfortable cushions $\hfill\square$ soft		
		pillows $[3-5] \square$ oxygen therapy device $\square$ ECG monitor $\square$ aspirator $\square$ rescue		
		car $\square$ 2–3 people (if needed)		
		Department Patients should begin APP 1 hour after meals and after defecation		
	Turning	□ Assist patient to be APP, reduce oxygen consumption		
	Oxygen	$\Box$ Continue oxygen therapy and pay attention to SpO <sub>2</sub>		
	Optimizing	□ Guide the patient to adjust, optimize the position in bed, and promote the		
		patient's comfort as much as possible		
Implementation	Monitoring	□ Monitor the vital signs, HR: RR: BP: SpO <sub>2</sub> :		
	Attention	□ The call bell is placed side to the patient		
		□ Assist patients to satisfy their basic needs to avoid interrupting the APP		
		□ Pay attention to the complaints and try the best to solve them		
		Encourage patients to extend the APP as long as possible		
After implementation	Conclusion	□ Summarize and discuss this APP session with the patient, such as tolerance		
		and efficacy		
	Record	□ Record the vital signs after 1 hour of APP		
		Record the adverse events during the APP		
Warning: This is the pr	eliminary recomn	nendations are based on the preliminary results of the first observational studies,		
and that the correct app	plication of APP r	equires further investigations.		

**Figure S1** Checklist of suggestion for successful APP implementation (Medical staff version). APP, awake prone positioning; HR, heart rate; RR, respiratory rate; BP, blood pressure; SpO<sub>2</sub>, peripheral oxygen saturation; ECG, electrocardiogram.