Awake Prone Positioning in Patients with Hypoxemic Respiratory Failure Due to COVID-19: The PROFLO Multicenter Randomized Clinical Trial

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Abstract

**Background:** The effect of awake prone positioning on intubation rates is not established. The aim of this trial was to investigate if a protocol for awake prone positioning reduces the rate of endotracheal intubation compared with standard care among patients with moderate to severe hypoxemic respiratory failure due to COVID-19.

**Methods:** We conducted a multicenter randomized controlled trial. Adult patients with confirmed COVID-19, high-flow nasal oxygen or noninvasive ventilation for respiratory support and a \( \text{PaO}_2/\text{FiO}_2 \) ratio \( \leq 20 \) kPa were randomly assigned to a protocol targeting 16 hours prone positioning per day or standard care. The primary endpoint was intubation within 30 days. Secondary endpoints included duration of awake prone positioning, 30-day mortality, ventilator free days, hospital and intensive care unit length of stay, use of noninvasive ventilation, organ support and adverse events. The trial was terminated early due to futility.

**Results:** Of 141 patients assessed for eligibility, 75 were randomized of whom 39 were allocated to the control group and 36 to the prone group. Within 30 days after enrollment, 13 patients (33%) were intubated in the control group versus 12 patients (33%) in the prone group (HR 1.01 (95% CI 0.46-2.21), \( P=0.99 \)). Median prone duration was 3.4 hours [IQR 1.8-8.4] in the control group compared with 9.0 hours per day [IQR 4.4-10.6] in the prone group (\( P=0.014 \)). Nine patients (23%) in the control group had pressure sores compared with two patients (6%) in the prone group (difference -18% (95% CI -2% to -33%); \( P=0.032 \)). There were no other differences in secondary outcomes between groups.

**Conclusions:** A protocol for awake prone positioning increased duration of prone positioning, but did not reduce the rate of intubation in patients with hypoxemic respiratory failure due to COVID-19 compared to standard care.

**Trial registration:** ISRCTN54918435. Registered 15 June 2020 (https://doi.org/10.1186/ISRCTN54917435)

Introduction

Prone positioning reduces mortality in intubated and mechanically ventilated patients with moderate to severe acute respiratory distress syndrome (ARDS)[1, 2]. Awake prone positioning (APP) in non-intubated, spontaneously breathing patients with hypoxemic respiratory failure has gained wide-spread use in health care systems overwhelmed by patients with Coronavirus disease 2019 (COVID-19)[3–5] although previously rarely reported[6–9].

Prone positioning improves respiratory mechanics and gas exchange owing to several mechanisms in non-intubated spontaneously breathing and intubated mechanically ventilated patients. It increases lung volume[10, 11], improves ventilation-perfusion ratio[12–14], and distributes pleural pressure more evenly[15]. Several studies report transient improvement in oxygenation during APP in a majority of
patients with hypoxemic respiratory failure due to COVID-19 pneumonia\cite{3, 16–23}. However, translating physiological improvement into clinically relevant outcomes has not been supported by ARDS-studies\cite{24} and there remains a gap in the current knowledge for the use of APP\cite{25–28}. To date, the effect of APP on intubation rates in patients with hypoxemic respiratory failure has not been studied in a randomized clinical trial.

The primary aim of this trial was to determine if a protocol for APP and standard care reduces the rate of endotracheal intubation compared to standard care alone among COVID-19 patients with hypoxemic respiratory failure supported with high-flow nasal oxygen (HFNO) or noninvasive ventilation (NIV). The secondary aims were to compare differences in duration of APP, mortality, oxygenation, organ support, clinical progression and rate of adverse events between groups.

**Materials And Methods**

**Trial design and study setting**

We conducted a prospective multicenter, open-label, parallel arm, randomized clinical superiority trial in accordance with the 1964 Helsinki Declaration, Good Clinical Practice and the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The trial was conducted at two tertiary teaching hospitals and one county hospital in Sweden between October 7, 2020 and February 7, 2021; 30-day follow-up was complete March 9, 2021. The trial protocol was prospectively registered at the ISRCTN registry (ISRCTN54918435) June 15 2020 (http://isrctn.com/). Ethical approval (2020–02743), was provided by the Swedish Ethical Review Authority June 10 2020. Written informed consent was obtained from all subjects. The trial was overseen by a trial steering committee and an independent data and safety monitoring board.

**Patients**

Adults (≥ 18 years old) with COVID-19 verified by positive SARS-CoV-2 reverse transcription polymerase chain reaction tests on naso- or oropharyngeal swabs and hypoxemic respiratory failure requiring HFNO or NIV with a PaO$_2$/FiO$_2$-ratio ≤ 20 kPa or corresponding values of SpO$_2$ and FiO$_2$ (eTable 1, Additional File 1) for more than one hour, were eligible for inclusion.

Exclusion criteria were the following: oxygen supplementation with a device other than HFNO or NIV; inability to assume prone or semi-prone position; immediate need for endotracheal intubation; severe hemodynamic instability; previous intubation for COVID-19 pneumonia; pregnancy; terminal illness with less than one year life expectancy; do-not-intubate order; inability to understand oral or written study information.

**Randomization and masking**

Randomization was performed with an allocation ratio of 1:1 and a block size of eight. Randomization allocation was obtained via a centralized web-based system. Due to the nature of the intervention, the
patient, the treating physician, care providers, data collectors and outcome assessors were aware of the allocation.

**Trial protocol**

After enrollment by members of the research team, patients were randomly assigned to one of two groups (eFigure 1, Additional File 1):

1. *Control group.* APP was not encouraged but could be prescribed by the attending clinician at his/her discretion.

2. *Prone group.* A protocol targeting at least 16 h APP per day was initiated. Prone and semi-prone positioning were allowed (eFigure 2, Additional File 1). Flat supine positioning was discouraged and patients were instructed to place themselves in the semi-recumbent or lateral position in between proning sessions. During in-hospital transportation, oxygenation by face mask and positioning appropriate for adequate monitoring and safety was allowed.

Protocol discontinuation criteria were intubation, death or clinical improvement defined as the use of standard nasal cannula or open face mask with an oxygen flow rate of \( \leq 5 \text{ L min}^{-1} \) for 12 hours. Attending clinicians could withdraw the patient from the trial at any time if they considered APP unsafe.

**Standard care**

Standard care was delivered in both groups according to clinical practice in participating hospitals. Intravenous sedation was allowed but not protocolized. Decision to intubate was made at the discretion of the attending clinician but followed local guidelines. Positioning after intubation was not protocolized, but liberal prone positioning was part of the clinical routine for mechanically ventilated patients with COVID-19 fulfilling criteria for moderate to severe ARDS[29] at all three centers.

**Data collection**

Data on age, sex, weight, length, comorbidities, location of enrollment (ward or ICU), \( \text{PaO}_2 \), \( \text{SpO}_2 \), \( \text{FiO}_2 \), respiratory rate and positive end expiratory pressure (PEEP) for patients treated with NIV was recorded at the time of enrollment. APP duration was recorded continuously by health care providers on case report forms or in electronic data monitoring systems as available. Intubation and use of NIV, continuous renal replacement therapy (CRRT), vasopressor/inotropic support and extracorporeal membrane oxygenation (ECMO) was recorded daily. Data quality and compliance to Good Clinical Practice was verified by independent reviewers. Anonymized data was entered in a secure electronic case report form (OpenClinica®, OpenClinica LLC, Waltham, MA, USA).

**Outcome measures**

The primary endpoint was intubation within 30 days after enrollment. Secondary endpoints were duration of APP, use of NIV and time to NIV for patients included with HFNO, use of vasopressors/inotropes, CRRT, ECMO, ventilator-free days, days free of NIV/HFNO for patients not intubated, hospital and ICU length of stay, 30-day mortality, WHO-ordinal scale for clinical improvement[30] at day 7 and 30, and adverse
events. Ventilator-free days were calculated for intubated patients and defined as days free from invasive mechanical ventilation from enrollment until day 30.

**Sample size calculation**

Sample size calculation was based on previous studies[31, 32]. Assuming an intubation rate of 88% in the control group, we estimated a sample size of 224 patients to detect a 20% decrease of intubation in the prone group with 90% power at a type I error rate of 5%. To compensate for patients withdrawing consent, 240 patients were planned for inclusion.

**Statistical methods**

An interim analysis was planned *a priori* when half the patients had been included. The decision to terminate the trial could be based on futility, safety or efficacy (eTable 2, Additional File 1). Due to rapidly declining case numbers, the interim analysis was performed when 75 patients had been included in the study. Based on this analysis, the data and safety monitoring board recommended to stop the trial due to futility.

The analysis was performed on an intention-to-treat basis. Continuous variables were reported as median (interquartile range [IQR]). Categorical variables were expressed as numbers and percentages. The primary endpoint, intubation within 30 days was analyzed using Kaplan-Meier survival analysis and compared between groups with Cox's proportional-hazards model. Mann-Whitney U-test was used to compare non-normally distributed variables. Categorical variables were compared using Chi2-test or Fisher's exact test. We did not correct for multiple statistical testing in the analysis of secondary and exploratory endpoints. Two-sided p-values < 0.05 were considered statistically significant. Statistical analyses were performed using R Statistical Software.

**Results**

**Patient characteristics**

From October 7, 2020 through February 7 2021, 1290 patients with confirmed COVID-19 were admitted to the three participating hospitals. 141 patients were screened, of whom 75 were randomized (Fig. 1). No patients were lost to follow-up or withdrew consent. End of follow-up was March 9, 2021.

Hypertension, diabetes, obesity and lung disease were the most common comorbidities (Table 1).
Table 1
General characteristics of the study cohort at inclusion

| Variable                        | Control group | Prone group |
|---------------------------------|---------------|-------------|
| Count                           | 39            | 36          |
| Male                            | 32 (82%)      | 23 (64%)    |
| Age                             | 65 [55–70]    | 66 [53–74]  |
| BMI                             | 29 [27–33]    | 28 [25–30]  |
| Obesity (BMI $\geq 30$ kg m$^{-2}$) | 12 (32%) | 8 (23%)    |
| Hypertension                    | 21 (55%)      | 17 (47%)    |
| Ischemic cardiac disease        | 5 (13%)       | 6 (17%)     |
| Congestive heart failure        | 6 (15%)       | 2 (6%)      |
| Lung disease                    |               |             |
| - Asthma                        | 5 (13%)       | 1 (3%)      |
| - COPD                          | 4 (10%)       | 2 (6%)      |
| - Fibrosis                      | 0 (0%)        | 1 (3%)      |
| - Sarcoidosis                   | 1 (3%)        | 0 (0%)      |
| Diabetes mellitus               | 11 (28%)      | 14 (39%)    |
| Renal disease$^a$               | 2 (5%)        | 3 (8%)      |
| Active cancer                   | 1 (3%)        | 4 (11%)     |
| Liver disease                   | 1 (3%)        | 0 (0%)      |
| Enrollment outside ICU          | 20 (51%)      | 19 (53%)    |
| HFNO                            | 29 (74%)      | 31 (86%)    |
| Flow rate (HFNO)                | 50 [40–50]    | 50 [40–50]  |
| PEEP (NIV)                      | 8 [6–8]       | 7 [6–10]    |
| FiO$_2$                         | 0.6 [0.55–0.70] | 0.6 [0.55–0.70] |
| SpO$_2$                         | 94 [92–95]    | 93 [91–94]  |

$^a$ Creatinine clearance $< 60$ ml min$^{-1}$

Categorical parameters are presented as n (%), continuous variables as median (interquartile range [IQR]); COPD, Chronic obstructive pulmonary disease; BMI, Body Mass Index; ICU, Intensive Care Unit; HFNO, High-flow Nasal Oxygen; PEEP, Positive End Expiratory Pressure; NIV, Noninvasive ventilation; RR, Respiratory Rate; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure.
| Variable                  | Control group | Prone group |
|--------------------------|---------------|-------------|
| PaO₂                     | 9.2 [8.2–10]  | 8.8 [7.7–9.7] |
| RR                       | 26 [23–32]    | 24 [21–29]  |
| PaO₂/FiO₂ ratio          | 15.4 [12.5–17.3] | 15.4 [11.5–17.4] |
| SpO₂/FiO₂ ratio          | 157 [136–175] | 151 [131–174] |
| SBP                      | 130 [120–140] | 130 [120–140] |
| DBP                      | 70 [60–80]    | 69 [62–75]  |

*a Creatinine clearance < 60 ml min⁻¹*

Categorical parameters are presented as n (%), continuous variables as median (interquartile range [IQR]); COPD, Chronic obstructive pulmonary disease; BMI, Body Mass Index; ICU, Intensive Care Unit; HFNO, High-flow Nasal Oxygen; PEEP, Positive End Expiratory Pressure; NIV, Noninvasive ventilation; RR, Respiratory Rate; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure.

Level of respiratory support, oxygenation and hemodynamic status were balanced between the two groups at inclusion. More patients allocated to the prone group had HFNO at randomization compared to the control group (86% vs 74%).

**Primary endpoint**

Within 30 days after enrollment, 13 patients (33%) in the control group and 12 patients (33%) in the prone group were intubated (HR 1.01 (95% CI 0.46–2.21); P = 0.99) (Fig. 2).

**Secondary endpoints**

Duration of early APP (first three days after enrollment) and total APP (all days from enrollment to protocol discontinuation) were longer in the prone group compared with the control group (Table 2).
| Variable                                      | Control group | Prone group   | P value |
|----------------------------------------------|---------------|---------------|---------|
| Count                                        | 39            | 36            |         |
| Daily total prone time, hours                | 3.4 [1.8–8.4] | 9.0 [4.4–10.6] | 0.014   |
| Total protocol duration, days                | 4.9 [2.3–8.1] | 4.2 [1.7–5.7] | 0.33    |
| Daily prone time day 1–3, hours              | 2.6 [0.3–8.1] | 8.5 [5.2–12.2] | 0.001   |
| 30-Day Mortality                             | 3 (8%)        | 6 (17%)       | 0.30    |
| VFD\(^a\), days                             | 2 [1–10]      | 7 [0–20]      | 0.38    |
| Days free from HFNO/NIV\(^b\)                | 24 [22–26]    | 26 [23–28]    | 0.15    |
| Enrolment to IMV, days                       | 2 [1–6]       | 2 [1–5]       | 0.59    |
| Use of NIV                                   | 27 (69%)      | 21 (58%)      | 0.33    |
| Enrolment to NIV, days                       | 0.25 [0.1–1.1]| 0.23 [0.05–1.2]| 0.63 |
| Admitted to ICU                              | 27 (69%)      | 27 (75%)      | 0.58    |
| ICU LOS, days                                | 11 [3–22]     | 5 [4–13]      | 0.25    |
| Hospital LOS, days                           | 18 [11–30]    | 16 [11–22]    | 0.44    |
| Vasoactive drugs                             | 17 (44%)      | 13 (37%)      | 0.57    |
| Sedation by continuous infusion\(^c\)        | 14 (36%)      | 16 (44%)      | 0.45    |
| Renal replacement therapy                    | 1 (3%)        | 1 (3%)        | -       |
| ECMO                                         | 1 (3%)        | 0 (0%)        | -       |
| WHO Clinical Progression Scale day 7, (0–10) | 6 [6–7]       | 6 [5–7]       | 0.35    |
| WHO Clinical Progression Scale, day 30, (0–10)| 2 [2–6]       | 2 [2–4]       | 0.28    |

\(^a\)Ventilator-free days were calculated for intubated patients and defined as days free from invasive mechanical ventilation from enrollment until day 30. Control n = 13, Prone n = 12.

\(^b\)Patients who were not intubated.

\(^c\)Non-intubated patients during protocol

Categorical parameters are presented as n (%), continuous variables as median (interquartile range [IQR]), VFD, Ventilator-Free Days; HFNO, High-flow Nasal Oxygen; NIV, Non-Invasive Ventilation; IMV, Invasive Mechanical Ventilation; ICU, Intensive Care Unit; LOS, Length of Stay; ECMO, Extracorporeal Membrane Oxygenation; WHO, World Health Organization
| Variable | Control group | Prone group | P value |
|----------|---------------|-------------|---------|
| Adverse events | 9 (23%) | 2 (6%) | 0.032 |
| - Skin breakdown | 0 (0%) | 1 (3%) | - |
| - Vomiting during proning | 0 (0%) | 0 (0%) | - |
| - Central or arterial line dislodgement | 1 (3%) | 2 (6%) | 0.51 |
| - Cardiac arrest within 30 days | 0 (0%) | 0 (0%) | - |
| - During proning | 2 (6%) | 0 (0%) | - |

a Ventilator-free days were calculated for intubated patients and defined as days free from invasive mechanical ventilation from enrollment until day 30. Control n = 13, Prone n = 12.

b Patients who were not intubated.

c Non-intubated patients during protocol

Categorical parameters are presented as n (%), continuous variables as median (interquartile range [IQR]), VFD, Ventilator-Free Days; HFNO, High-flow Nasal Oxygen; NIV, Non-Invasive Ventilation; IMV, Invasive Mechanical Ventilation; ICU, Intensive Care Unit; LOS, Length of Stay; ECMO, Extracorporeal Membrane Oxygenation; WHO, World Health Organization

Three patients (8%) died in the control group compared with six patients (17%) in the prone group (HR 2.29 (95% CI 0.57–9.14), P = 0.30). There were no significant differences between groups regarding ventilator-free days for intubated patients, days free of NIV/HFNO for patients not intubated, hospital or ICU length of stay or use of organ support between groups.

**Adverse events**

Nine patients (23%) in the control group had pressure sores, all located in the lower back or gluteal region, compared with two patients (6%) in the prone group that were both related to pressure from the HFNO (difference -18% (95% CI -2% to -33%); P = 0.032). Three cardiac arrests occurred, one in the control group and two in the prone group but none related to APP.

**Exploratory analysis**

Patients with duration of APP shorter than 3 hours (n = 26) versus longer than 9 hours (n = 26) irrespective of allocation (median prone duration 0.46 [IQR 0-2.2] versus 11.9 [IQR 10.4–13.5] hour per day, p = < 0.001) were compared using Cox’s proportional hazards model, but there was no significant difference in the proportion of patients being intubated in unadjusted analysis (HR 1.14 (95% 0.44–2.96), P = 0.79) or in analysis adjusted for age and PaO$_2$/FiO$_2$ at enrollment (HR 0.79 (95% CI 0.29–2.18), P = 0.65) (eFigure 3, Additional File 1).
Sub-analysis of patients with PaO$_2$/FiO$_2$ ratio \( \leq 15 \) kPa did not show any difference the proportion of patients being intubated between groups in unadjusted analysis (HR 0.94 (95% CI 0.35–2.50), \( P = 0.90 \)) or when adjusting for age (HR 0.51 (95%CI 0.25–1.89), \( P = 0.49 \)). Among patients in this sub-cohort, median prone duration per day was 3.8 hours [IQR 2.0–6.5] in the control group (\( n = 13 \)) compared with a median of 8.5 hours [IQR 6.5–10.8] in the prone group (\( n = 14 \)), \( P = 0.021 \) (eFigure 4, Additional File 1).

**Discussion**

This is to the best of our knowledge the first randomized clinical trial investigating prolonged prone positioning in non-intubated spontaneously breathing patients with COVID-19. The main finding was that implementation of a protocol for APP increased the duration of prone positioning but did not affect rate of intubation, the use of other supportive treatments, 30-day mortality or faster recovery patients with moderate to severe hypoxemic respiratory failure compared with standard of care.

The results of this study were consistent also in exploratory post-hoc analyses subgrouping patients according to the duration of APP irrespective of group allocation. Further, no benefit of prolonged APP was found in patients with PaO$_2$/FiO$_2$ ratio < 15 kPa at inclusion between the prone and control group.

Prone positioning in mechanically ventilated patients with COVID-19 improves oxygenation and is associated with reduced mortality[33]. Although APP similarly improves oxygenation in non-intubated patients with COVID-19[3, 16–23], reports have failed to show benefits on patient-centered outcomes[25, 26]. A multicenter observational study, investigating a cohort of 199 patients with COVID-19 found no difference in intubation rates in patients with duration of APP for more than 16 hours per day compared with shorter duration of APP[25]. They reported similar baseline characteristics, degree of respiratory failure and mortality but higher intubation rates (41% in the control group and 40% in the prone group) compared with our investigation. Further corroborating our results, a single center observational study including 166 patients with COVID-19 with respiratory rate \( \geq 24/\text{min} \) who required oxygen supplementation \( \geq 3 \) L min$^{-1}$ found no difference in intubation rates or ICU admission in patients who were treated with APP compared to those who were not[26]. Although the patients in this study were younger and had less severe respiratory failure at inclusion compared to our population, they reported higher overall intubation rates (58% in the prone group and 49% in the control group) compared with our trial.

There are several possible explanations for the neutral result of our investigation. Due to observed beneficial physiological effects, patients with COVID-19 were increasingly treated with APP as part of standard care during the study period at the participating study hospitals, resulting in longer APP duration than expected in the control group. Although the median duration of APP per day was 9.0 hours in the prone group compared with 3.4 hours in the control group, this difference may not have been enough to decrease the rate of intubation. The optimal duration of prone positioning is unknown; however, the mean duration of prone positioning was 17 hours per day in the prone group compared to 0 hours in the supine group in the first study that reported mortality benefit in mechanically ventilated patients[1]. Intubated
patients are often heavily sedated to tolerate prone positioning and it may be difficult to reach a similar duration of prone positioning in awake patients. Sedation with alpha-2-agonists and analgesia with opioids may be necessary to increase the compliance to APP. Sedation itself could have undesired effects and counteract improvements of respiratory mechanics associated with APP[34]. There was no difference in requirement of sedation by continuous infusion between groups in the present investigation, but we did not record the use of intermittent sedative and analgesic drugs. Reduction in lung injury associated with mechanical ventilation may in part explain the mortality benefit in mechanically ventilated ARDS patients[1] and patients with COVID-19[33] undergoing prone positioning[35]. In non-intubated critically ill patients, APP may delay intubation due to temporary improvements in oxygenation[25] which could paradoxically lead to self-inflicted lung injury[36, 37]. This presumed mechanism does not appear relevant in our study as time to intubation was similar between groups.

Patients in the control group had more pressure sores compared with patients in the prone group. Frequent changes in body position may have reduced the risk of lower back and gluteal pressure sores in the prone group. However, this may have been a spurious finding and future studies may provide additional information.

Strengths of the present study included the randomized multicenter design and the well-defined protocol for APP increasing generalizability and reproducibility. This trial was conducted during the second pandemic wave, and physicians, nurses and physiotherapists at the participating ICUs and wards gained extensive experience of prone positioning in non-intubated patients during the first wave, ensuring high quality APP for included patients. No patients were lost to follow up and there was minimal missing data. As the first randomized clinical trial of prolonged APP in COVID-19, this trial provides important new information to bedside clinicians and for future studies.

There are also limitations to this trial. First, due to the nature of the intervention, blinding was not possible, increasing risk of bias. Second, the limited statistical power precluded detailed investigation of subgroups that may benefit of APP. Third as all study sites became overwhelmed by severely ill patients with COVID-19, and research staff was relocated for clinical service, we were not able to identify all patients eligible for inclusion. Fourth, APP was increasingly considered standard of care in COVID-19 related hypoxic respiratory failure attenuating the difference in duration of APP between groups.

**Conclusions**

A protocol for APP and standard care among patients with hypoxemic respiratory failure due to COVID-19 was safe and increased the duration of prone position, but did not reduce the rate of endotracheal intubation compared with standard care alone. Further research is warranted to identify subgroups that may benefit from APP.

**List of abbreviations**

APP - awake prone positioning
Declarations

Ethics approval and consent to participate

The protocol was registered at the ISRCTN registry (ISRCTN54918435) 15 June 2020 (isrctn.com). Ethical approval for this trial (dnr. 2020-02743) was provided by the Swedish Ethical Review Authority 10 June 2020. All research was performed in accordance with national guidelines and regulations. Written informed consent was obtained from all subjects.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

MJF has received travel support and lecture fees from Fisher & Paykel Healthcare, Auckland, New Zealand, however not related to this study. DF has received travel support from Armstrong Medical, Coleraine, Great Britain, to participate in a scientific seminar, however not related to this study. The other authors declare that they have no competing interests.

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Authors’ contributions

JR conceived the study. JR, DF, PF, EvO, MJF, PS, NJ contributed to the design of the study. JR, EvO, KT, LE, GB, FCJ and MJF collected patient data. EvO, JR, PF, DF, KT and MJF performed data analysis. The first draft of the manuscript was written by JR and EvO. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript for publication.

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Figures
Figure 1

Consolidated Standards of Reporting Trials (CONSORT) flow diagram of randomized and analyzed participants
Figure 2

Kaplan-Meier survival analysis. Within 30 days, 13 patients (33%) were intubated in the control group compared with 12 patients (33%) in the prone group, HR 1.01 (95% CI 0.46-2.21), P=0.99

Supplementary Files

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