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Could prone positioning increase lung function for patients with severe COVID-19 infection?

Submission date
08/06/2020

Recruitment status
No longer recruiting

Registration date
15/06/2020

Overall study status
Completed

Last Edited
28/11/2022

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
COVID-19 is a condition caused by the coronavirus (called SARS-CoV-2) that was first identified in late 2019. This virus can infect the respiratory (breathing) system. Some people do not have symptoms but can carry the virus and pass it on to others. People who have developed the condition may develop a fever and/or a continuous cough among other symptoms. This can develop into pneumonia. Pneumonia is a chest infection where the small air pockets of the lungs, called alveoli, fill with liquid and make it more difficult to breathe.
In 2020, the virus has spread to many countries around the world and neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed. As of April 2020, it is advised that people minimize travel and social contact, and regularly wash their hands to reduce the spread of the virus.
Groups who are at a higher risk from infection with the virus, and therefore of developing COVID-19, include people aged over 70 years, people who have long-term health conditions (such as asthma or diabetes), people who have a weakened immune system and people who are pregnant. People in these groups, and people who might come into contact with them, can reduce this risk by following the up-to-date advice to reduce the spread of the virus.
COVID-19 infection can lead to severe pneumonia with acute hypoxemic respiratory (breathing) failure and need for supply of extra oxygen or even treatment with invasive mechanical ventilation. An overwhelming influx of patients has led to a ventilator shortage in some centres. Further, invasive mechanical ventilation is associated with a high mortality rate. Therefore, strategies to reduce the risk of intubation and mechanical ventilation are needed. Humidified oxygen at different concentrations can be supplied with high flow to a patient through a nasal cannulae, called HFNC. This method has become a mainstay in the treatment of acute respiratory failure in ICUs, reducing the need for mechanical ventilation. HFNC increases airway pressure and may thereby open collapsed parts of the lungs, which eases oxygen delivery to the blood. Another way of increasing oxygen delivery for patients treated with mechanical ventilation can be to lie in a prone position on the belly, or at least in a semirecumbent position. Even for awake patients with respiratory failure but not on mechanical ventilation the prone position seems to improve oxygenation. The aim of this study is to determine if prone positioning could decrease the need for mechanical ventilation in patients treated with oxygen supply by HFNC due to COVID- 19 pneumonia.

Who can participate?
Patients aged 18 or older with COVID-19 infection and pneumonia admitted to hospital, is in need of oxygen supply with high flow nasal cannulae and yet not reaching enough oxygen saturation.

What does the study involve?
This study compares two groups of patients with pneumonia due to COVID-19 infection; one group treated with HFNC and encouraged to lie in the prone position for up to 16 hours per day and night, and one group, also treated with HFNC, who are neither prohibited nor encouraged to lie in the prone position. For a small number of patients from both groups, lung volume will be measured by electrical impedance tomography (EIT) for 2 hours. For all patients, measures are included in the ordinary treatment and according to local regulations. For the patients in the EIT subgroup, an elastic EIT band will be placed around the lower thoracic wall and connected to an EIT device. Five arterial blood gas samples will be collected every 30 minutes during the 2 hours duration. At the same timepoints EIT measurements are collected.

What are the possible benefits and risks of participating?
Possible benefits are less severe respiratory failure and decreased risk of needing intubation and mechanical ventilation. Risks are pressure wounds caused by the prone position or back pain.

Where is the study run from?
Uppsala University Hospital (Sweden)

When is the study starting and how long is it expected to run for?
April 2020 to June 2021

Who is funding the study?
Uppsala University (Sweden)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
1

Study information

Scientific Title
Awake prone positioning with high flow nasal cannula in critically ill COVID-19 patients

Acronym
PROFLO

Study objectives
Prone positioning in awake patients with moderate to severe hypoxemic respiratory failure due to COVID-19 treated with high flow nasal cannula or noninvasive ventilation support will reduce the intubation rate.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/05/2020, Swedish Ethical Review Authority (Box 2110, 750 02 Uppsala, Sweden; +46 (0)10 475 08 00; registrator@etikprovning.se), ref: 2020-02743

Study design
Multicentre open labelled interventional randomized controlled study with two parallel groups

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Respiratory function in patients with respiratory failure due to COVID-19 infection

Interventions
Current interventions as of 24/11/2022:
Patients with a defined respiratory failure due to COVID-19 infection are randomly included in a standard care arm and a prone positioning arm in 1:1 blocks of four. Randomization will be provided using app.studyrandomizer.com. Patients in the prone positioning arm should lay in a prone position or semi-recumbent position with the head of the bed elevated to 30 degrees with the target of 16 hours per day and night. For patients in the standard arm prone or semi-

recumbent position is neither prohibited nor encouraged and may be prescribed by the treating physician at their discretion. All other treatment or interventions for all included patients will follow ordinary local guidelines at the present hospital and are not affected by the study protocol.

For a subgroup of up to 60 patients, electrical impedance tomography will be used to evaluate the effects of prone positioning. Measurements will be performed as a baseline before the patient is placed in the prone position, intermittently during prone position and then 30 minutes after supine repositioning. Samples of arterial blood gases will be collected and respiratory rate, as well as hemodynamic parameters, will be registered. Dyspnea is assessed with the modified Borg scale and discomfort with a visual analogue scale.

Follow-up is at 2 months after the end of inclusion.

Previous interventions:
Patients with a defined respiratory failure due to COVID-19 infection are randomly included in a standard care arm and a prone positioning arm in 1:1 blocks of four. Randomization will be provided using app.studyrandomizer.com. Patients in the prone positioning arm should lay in a prone position or semi-recumbent position with the head of the bed elevated to 30 degrees with the target of 16 hours per day and night. For patients in the standard arm prone or semi-recumbent position is neither prohibited nor encouraged and may be prescribed by the treating physician at their discretion. All other treatment or interventions for all included patients will follow ordinary local guidelines at the present hospital and are not affected by the study protocol.

For a small subgroup of 30 patients, 15 from each group, electrical impedance tomography will be measured during one occasion. Measurements will be performed before placed in a prone position, intermittent during 2 hours in a prone position and during 1 hour in a semi-recumbent position. During this part samples of arterial blood gases are collected and respiratory rate, as well as hemodynamic parameters, are registered. Dyspnea is assessed with the modified Borg scale and discomfort with a visual analogue scale.

Follow-up is at 2 months after the end of inclusion.

Intervention Type
Other

Primary outcome(s)
Rate of intubation for mechanical ventilation support, recorded in EHR at inclusion and once if applied. Timeframe 30 days after inclusion.

Key secondary outcome(s))
All measures are included in the ordinary treatment and according to local regulations registered or automatically collected in the EHR or PDMS from where data is exported to a database protocol:
1. Time in prone position (pp); every time the patient changes position the timepoint will be recorded in a preprinted protocol (CRF) or the PDMS if available, total time measured once per day and night in hospital
2. Need for vasoactive drugs, day and time for start, change of infusion rate or stop of vasopressor infusion, recorded in PDMS or EHR, evaluated once per day and night in hospital
3. Days on ventilator support, day and time of intubation and start of ventilator support, day and

time of extubation and end of ventilator support, recorded in PDMS or EHR, checked once a day in hospital
4. In-hospital and ICU length of stay: timepoint recorded in the EHR when enrolled and discharge at hospital/ICU
5. Rate of complications reported in a preprinted protocol (CRF) every 24th hour after inclusion
6. 7- and 30-day mortality: day and time of death recorded in the EHR, checked once within a month after discharge from the hospital
7. Clinical improvement measured using WHO ordinal scale at baseline, day 7 and day 30

Completion date
25/06/2021

Eligibility

Key inclusion criteria
1. Age 18 year or older
2. Admission to a hospital with confirmed or strongly suspected COVID-19 infection
3. Hypoxic respiratory failure defined as a PaO2/FiO2 ratio ≤ 20 kPa (150 mmHg) and/or a FiO2 of ≥ 0.5 to reach a SpO2 of 94% for more than 1 hour
4. Oxygen supplementation (ongoing or planned) with high flow nasal cannuale or noninvasive ventilating support

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
75

Key exclusion criteria
1. Severe nasal obstruction or other contraindication to high flow nasal cannulae
2. Patient unable to lay prone or in the face forward position
3. Immediate need for intubation
4. Severe and/or uncontrolled hemodynamic instability
5. Previous intubation for COVID-19 pneumonia (i.e. step down patients)
6. Pregnancy
7. Known terminal illness with life expectancy less than 1 year
8. Decision not to intubate
9. Inability to understand oral or written study information and/or to cooperate with instructions

necessary to complete the allocated intervention
10. Inability to understand oral or written study information

Date of first enrolment
25/06/2020

Date of final enrolment
08/06/2021

Locations

Countries of recruitment
Sweden

Study participating centre
Uppsala University Hospital
Sjukhusvägen
Uppsala
Sweden
751 85

Study participating centre
Karolinska University Hospital
Eugeniavägen 3
Solna
Sweden
17176

Study participating centre
Ryhov Hospital
Sjukhusgatan
Jönköping
Sweden
55305

Sponsor information

Organisation
Uppsala County Council

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Akademiska Sjukhuset

Alternative Name(s)
Uppsala University Hospital

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Results and Publications

Individual participant data (IPD) sharing plan
Measurements and recordings concerning ordinary health care are stored in the EHR according to Swedish healthcare legislation. For measurements recorded in preprinted protocols (CRF) the protocols will be stored in an Investigator Site File in a locked room before being transformed into a database via webform (OpenClinica). All digital data is stored for at least 10 years after publication in a password-protected server. Participants in the trial group will have access to the data. Every study participant can request to take part of only their own data. Data on an aggregated, not individual, level will be published in a peer-reviewed journal, this with consent from participants. On request of authorities, if any doubt's of the trail's integrity according to GCP and becoming subject for investigation, data will be shared without consent from participants. No other sharing is allowed.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		14/06/2021	13/08/2021	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version V1.5	15/05/2020	03/07/2020	No	No
Protocol file	version 1.5	15/05/2020	01/04/2021	No	No
Protocol file	version 2.6	11/02/2021	24/11/2022	No	No