Early PReserved SPONtaneous breathing activity in mechanically ventilated patients with acute respiratory distress syndrome - The PReSPON Randomized Controlled Trial

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To evaluate the efficacy and safety of preserved spontaneous breathing activity in the early phase of moderate to severe ARDS.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Interventional

Summary

ID

NL-OMON53874

Source
ToetsingOnline

Brief title
PReSPON

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
ARDS

Research involving
Human

Sponsors and support

Primary sponsor: University Hospital Bonn
Source(s) of monetary or material Support: Zorggroep Acuut van Maxima MC

Intervention

Keyword: ARDS, Controlled ventilation, Mechanical ventilation, Spontaneous breathing

Outcome measures

Primary outcome

Primary efficacy endpoints:

• All-cause mortality at study day 28 (D28)

• Number of ventilator free days (VFD) until D28

Secondary outcome

Key secondary endpoint(s):

• All-cause mortality at study day 90 (D90)

• Number of vasoactive drug free days until D28

• Number of renal support free days until D28

• Number of ICU free days until D28

• Sequential Organ Failure Assessment (SOFA) score during ICU stay

Study description

Background summary

The potential benefits of preserved early spontaneous breathing activity during mechanical ventilation are an increased aeration of dependent lung regions, less need for sedation, improved cardiac filling, and better matching of pulmonary ventilation and perfusion and thus oxygenation. Two small randomized controlled trials (RCTs) in patients with acute respiratory distress syndrome (ARDS) reported less time on mechanical ventilation and in the intensive care unit (ICU) with preserved early spontaneous breathing activity during Airway

Pressure Release Ventilation (APRV).
Debate exists over the net effects of preserved early spontaneous breathing activity with regard to ventilator-associated lung injury (VALI). In fact, by taking advantage of the potential improvement in oxygenation and recruitment at lower inflation pressures associated with APRV, physicians could possibly reduce potentially harmful levels of inspired oxygen, tidal volume, and positive end-expiratory pressure (PEEP). However, spontaneous breathing during mechanical ventilation has the potential to generate less positive pleural pressures that may add to the alveolar stretch applied from the ventilator and contribute to the risk of VALI. This has led to an ongoing controversy about the question whether an initial period of controlled mechanical ventilation with deep sedation and neuromuscular blockade or preserved early spontaneous breathing activity during mechanical ventilation is advantageous with respect to outcomes in ARDS patients. A RCT investigating the effects of early spontaneous breathing activity on mortality in moderate to severe ARDS has been highly recommended in the research agenda for intensive care medicine.

Study objective

To evaluate the efficacy and safety of preserved spontaneous breathing activity in the early phase of moderate to severe ARDS.

Study design

Confirmatory, prospective, randomized, open controlled international multi-centre trial.

Intervention

After inclusion, a lung-protective ventilator strategy will be applied (if this has not yet been implemented) and patients will be randomized to:
Spontaneous Breathing Group
Spontaneous breathing activity will be allowed during APRV within one hour after randomization throughout the first 48 hours.
Controlled Mechanical Ventilation Group
Pressure controlled mechanical ventilation will be applied throughout the first 48 hours.
After 48 hours, standard routine care should be provided in both groups, although we suggest moderate sedation while spontaneous breathing is maintained with APRV, pressure support ventilation (PSV), or other assisting ventilator modes. Weaning off mechanical ventilation will be performed after 48 hours according to a protocol using spontaneous breathing trials.

Study burden and risks

Two standard treatments are compared with similar risks and complications. Our

expectation is that there will be no difference.

Contacts

Public
University Hospital Bonn

Venusberg-Campus 1
Bonn 53127
DE
Scientific
University Hospital Bonn

Venusberg-Campus 1
Bonn 53127
DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Moderate to severe ARDS for <= 48 hours according to the Berlin definition is defined by acute onset of:
a. PaO2/FiO2 <= 200 mmHg (equivalent to <= 26.7 kPa) under invasive mechanical ventilation with PEEP >= 5 cmH2O
b. Bilateral infiltrates documented by chest radiograph
c. Not fully explained by cardiac failure or fluid overload (e.g. echocardiography)
2. Requirement for positive pressure ventilation via an endotracheal tube/ tracheotomy

3. Informed consent according to local regulations
4. Age >= 18 years
5. Expected duration of invasive mechanical ventilation > 48 hours at randomization

Exclusion criteria

1. Need of extracorporeal lung support, high frequency oscillation and/or inhaled vasodilators for severe hypoxemia at randomization
2. Woman known to be pregnant, lactating or having a positive or indeterminate pregnancy test
3. Neuromuscular disease that impairs ability to ventilate spontaneously
4. Severe chronic respiratory disease (e.g. COPD, pulmonary fibrosis, and other chronic diseases of the lung, chest wall or neuromuscular system) requiring home oxygen therapy or mechanical ventilation (non-invasive ventilation or via tracheotomy) except for Continuous Positive Airway Pressure (CPAP) or non-invasive Biphasic Positive Airway Pressure (BiPAP) used solely for sleep-disordered breathing
5. Chronic kidney disease stage V (requirement of dialysis) according to the K/DOQI definition of chronic kidney disease
6. Massive diffuse alveolar haemorrhage
7. Recent lung transplant < 12 months
8. Morbid obesity defined as weight greater than 1 kg / cm
9. Burns > 70% total body surface
10. Suspected or known elevated intracranial pressure
11. Chronic liver disease (Child-Pugh grade C)
12. Ongoing chemotherapy and/or bone marrow transplantation within the last 3 months
13. Moribund patient not expected to survive 48 hours
14. Patients not expected to survive 90 days on the basis of the premorbid
15. Patient, surrogate, or physician not committed to full life support.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-04-2024
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	13-07-2023
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04228471
CCMO	NL82657.015.22