Flow versus Pressure Controlled Ventilation in patients with moderate to severe Acute Respiratory Distress Syndrome

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By using advanced respiratory monitoring, we will aim to gain more understanding about the physiological effects and potential benefits of FCV in comparison to PCV in patients with moderate to severe ARDS. We hypothesize that FCV results in a lower…

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

Summary

ID

NL-OMON53828

Source
ToetsingOnline

Brief title
FCV vs PCV in moderate to severe ARDS

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
moderate to severe Acute Respiratory Distress Syndrome and pulmonary inflammatory disease

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Research Grant verkregen van Ventinova Medical B.V. die op hun beurt funding hebben verkregen vanuit het Europese Unie Horizon 2020 wetenschaps- en innovatie programma onder grant agreement nummer 961787,Ventinova Medical B.V.

Intervention

Keyword: ARDS, FCV, PCV

Outcome measures

Primary outcome

Primary endpoint is the difference in Mechanical Power (Joules per minute)

after 90 minutes on FCV compared to after 90 minutes of PCV; obtained from the

Pressure-Volume loops.

Secondary outcome

These following secondary study parameters will be measured at baseline (PCV)

and thereafter every 30 minutes on FCV and PCV for a total of 180 minutes:

- Dissipated energy (Joules per tidal volume) derived from Pressure-Volume

Loops

- EELV assessed by EIT; an important secondary endpoint is the difference

in EELV after 30 minutes on FCV compared to after 30 minutes on PCV.

- Airway pressures (peak airway pressure, plateau pressure, mean airway

pressure, PEEP, intrinsic PEEP, driving pressure) as measured on the airway

pressure tracings

- Transpulmonary pressures (end-expiratory transpulmonary pressure,

end-inspiratory transpulmonary pressure, transpulmonary driving pressure) as

measured using esophageal manometry

- Minute volume as measured using flow tracings

- Ventilatory ratio as a measure of dead space ventilation

- Regional Ventilatory Delay Index (RVDI) assessed by EIT

- Global Inhomogenity Index (GI) assessed by EIT

- P/F ratio

- Hemodynamic parameters (e.g. mean arterial pressure, heart rate)

These following secondary study parameters will be measured at five points during the study, namely at baseline (PCV), two times after a 90 minutes ventilation study period (FCV/PCV) and 90 minutes and 24 hours after the end of the study (PCV). Biomarkers in EBC (exhaled breath condensate) as a measurement for pulmonary inflammation that will be measured are pro-inflammatory cytokines IL-1β, IL-6, IL-12p70, TNF-α, anti-inflammatory cytokine IL-10 and chemokine IL-8 and biomarkers CD14, CD163 and CD25 for monocyt, macrophage and T-cell activation respectively.

Study description

Background summary

During controlled mechanical ventilation (CMV) only the inspiration is controlled by either a set driving pressure (Pressure Controlled Ventilation, PCV) or tidal volume (Volume Controlled Ventilation, VCV). The expiration depends on the passive elastic recoil of the respiratory system and cannot be controlled and lasts until the airway pressure is equal to the positive end-expiratory pressure (PEEP). The exponential decrease in airway pressure during expiration may result in alveolar collapse and hypoxemia. Flow controlled ventilation (FCV) is a mechanical ventilation method that uses a constant flow during both inspiration and expiration. FCV results in a gradual decrease in airway pressure during expiration as flow is controlled. In both

animal and prospective crossover studies, controlled expiration resulted in higher mean airway pressures with reduced alveolar collapse. Besides, FCV resulted in a higher ventilation efficiency measured by a decrease in minute volume at stable arterial partial pressures of carbon dioxide ($PaCO_2$). Where a reduction in alveolar collapse may lead to less atelectrauma, a higher ventilation efficiency may lead to a lower mechanical power (MP), which is the amount of energy that is transferred to the respiratory system by the mechanical ventilator every minute. Both are important determinants of Ventilator Induced Lung Injury (VILI). This makes FCV a very interesting ventilation mode in patients with the Acute Respiratory Distress Syndrome (ARDS) in which VILI is still a major contributor to overall morbidity and mortality.
Two prior prospective cross-over studies have been performed in (COVID-19) ARDS patients that did show a lower minute volume with FCV compared to PCV or VCV. However, these studies did not take into account assessments of the MP or end-expiratory lung volume (EELV), which is a measurement of lung aeration.

Study objective

By using advanced respiratory monitoring, we will aim to gain more understanding about the physiological effects and potential benefits of FCV in comparison to PCV in patients with moderate to severe ARDS. We hypothesize that FCV results in a lower mechanical power and an increased EELV (lung aeration) compared to PCV, thereby potentially reducing the risk of VILI. To explore whether FCV could decrease pulmonary inflammation by providing ventilation at a lower mechanical power compared to PCV we will measure inflammatory biomarker levels in exhaled breath condensate. Insights from this study allow the optimization of personalized lung protective mechanical ventilation.

Study design

Randomized crossover physiological pilot study comparing FCV and PCV.

Intervention

Patients are mechanically ventilated with PCV mode at baseline. Upon inclusion the EIT-belt and an esophageal balloon are placed to assess the EELV and transpulmonary pressures respectively. Besides, patients are randomized between the sequence of ventilation mode, namely 90 minutes of PCV followed by 90 minutes of FCV or 90 minutes of FCV followed by 90 minutes of PCV. When PCV is switched to FCV the same mechanical ventilator settings are used as in the PCV mode. After half an hour on FCV the PEEP, drivingpressure and flow of FCV are optimised based on the highest compliance and lowest flow matching with a stable $PaCO_2$ thereby not exceeding lung protective ventilation limits (transpulmonary driving pressure <= 12cmH_2O and tidal volumes <= 8 ml/kg ideal body weight (IBW)). PCV is always set according to standard of care. Total time

of measurements / study time is 180 minutes.

Besides, exhaled breath condensate will be collected from the expiratory tubing system from the ventilator by means of the TURBODECCS collecting system. A total of 5 samples will be collected (PCV baseline, after 90 minutes of FCV and after 90 minutes of PCV), 90 minutes and 24 hours after the end of the study (on PCV).

Study burden and risks

All patients are sedated and on CMV, therefore there will be no discomfort for the patient. FCV has been successfully applied during surgery and on the ICU and the patient will be monitored continuously so the clinical team can act directly in case of any adverse event. The mechanical power is calculated afterwards using software on the obtained Pressure-Volume loops (derived from the continuous flow- and pressure measurements). Lung volume is measured with EIT, a non-invasive, radiation-free monitoring tool. Transpulmonary pressures are measured with an esophageal balloon that is placed in a similar manor as a nasogastric feeding tube. During optimisation of FCV no lung protective ventilation limits will be exceeded. Therefore, overall the risks of this study are limited.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- 18 years or older;
- Provided written informed consent;
- Undergoing controlled mechanical ventilation via an endotracheal tube;
- Meeting all criteria of the Berlin definition of ARDS:
o Hypoxic respiratory failure within 1 week of a known clinical insult or new or worsening respiratory symptoms
o Bilateral opacities on X-ray or CT-scan not fully explained by effusions, lobar/lung collapse (atelectasis), or nodules
o Respiratory failure not fully explained by cardiac failure or fluid overload.
o Oxygenation: moderate ARDS P/F ratio between 101-200 mmHg, severe ARDS PF ratio <= 100mmHg, both with PEEP >= 5 cmH2O.
- Development of ARDS <= 72 uur
- Intubated

Exclusion criteria

- Severe sputum stasis or production requiring frequent bronchial suctioning (more than 5 times per nurse shift) - Untreated pneumothorax (i.e. no pleural drainage) - Hemodynamic instability defined as a mean arterial pressure below 60mmHg not responding to fluids and/or vasopressors or a noradrenalin dose > 0.5mcrg/kg/min - High (>15 mmHg) or instable (an increase in sedation or osmotherapy is required) intracranial pressure - An inner tube diameter of 6mm or less - Anticipating withdrawal of life support and/or shift to palliation as the goal of care - Inability to perform adequate electrical impedance tomography (EIT) measurements - Contra-indications for nasogastric tube or inability to perform adequate transpulmonary pressure measurements

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-09-2023
Enrollment:	28
Type:	Actual

Medical products/devices used

Generic name:	Evone ventilator (FCV) and Evita or Servo i ventilator (PCV)
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	30-06-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-04-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL83234.078.23