

Title: EPVent 2 – A Phase II study of Mechanical Ventilation Directed by Transpulmonary Pressures.

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Sponsor: NIH

Purpose of Research

The goal of this research is to see if there is a better way to adjust the air you get while on a mechanical ventilator. We are testing a new method of adjusting your ventilator settings based on the amount of pressure in your throat, chest, and lungs. We will be comparing this to the standard method of adjusting your ventilator settings based on the amount of air going in and out of your lungs.

Usually mechanical ventilation is guided by measuring the pressure in your lungs. For this study we will also measure the pressure in your esophagus (swallowing tube) using a small balloon. For half of the patients in this study, we will use the pressure in your esophagus to guide the settings of your ventilator. For the rest of the patients in this study we will use measurements of the pressure in your lungs to set your ventilator. The purpose of this study is to see whether measuring pressure in your esophagus will allow us to choose the best method of mechanical ventilation in patients with ARDS.

Approximately 30 people will take part in this study at this facility. A total of 200 people will take part in this study at all study sites in the United States and Canada.

Subjects are invited to volunteer for a research study about mechanical ventilation in patients with acute respiratory distress syndrome (ARDS). You are being asked to take part in this study because you have a lung disorder and need to be on a machine to help you breathe.

- **Acute respiratory distress syndrome (ARDS)** is a life-threatening lung condition that prevents enough oxygen from getting into the blood. It is caused by any major harm to the body or injury to the lung itself.
- **Mechanical ventilation** is a life support treatment. A mechanical ventilator is a machine that helps people breathe when they are not able to breathe enough on their own. The mechanical ventilator is also called a ventilator, respirator, or breathing machine.

Since no one knows yet which of the treatments in this study will be better for you, not everyone in the research study will be receive the same treatment. The decision as to which treatment you receive will be made by chance, like the flip of a coin, not by your doctor or based on your medical condition. Neither you nor the doctors will be able to decide which treatment will be used. You have a 50/50 chance of receiving either treatment. This way of studying treatments provide more objective information about the treatments and allows better comparisons to be made. After the randomization, you will be assigned to one of the following groups:

- Intervention Group** – If you are assigned to the intervention group, your breathing machine settings will be guided by the pressures measured in your esophagus. The breathing machine will be adjusted to keep enough inflating pressure in your lungs to prevent them from collapsing but not so much pressure to cause your lungs to overstretch.
- Control Group** – If you are assigned to the control group your breathing machine will be adjusted to give you low tidal volume mechanical ventilation, which is our standard of care. Your breathing machine will be set to give you enough small breaths to keep the oxygen levels in your blood at an adequate level without using the pressure measurements in your esophagus. We will measure the pressures in your

esophagus over the next few days, but your doctors will not use that information to change the ventilator settings.

If one treatment arm is found to be less effective than the other while you are taking part in the study, you will be informed and further treatment will be discussed.

Your breathing machine settings will be guided by your study treatment assignment until you are able to breathe by yourself for at least two days.

Inclusion Criteria:

Acute onset of ARDS as defined by the Berlin Consensus Conference definitions:

1. Hypoxemic respiratory failure with PaO₂ / FIO₂ ratio < 200 mmHg
2. Bilateral alveolar/interstitial infiltrates on chest x-ray, with opacities not present for more than 7 days
3. Respiratory failure not fully explained by cardiac failure or fluid overload
4. Intubation on controlled ventilation and receiving PEEP ≥ 5 cm H₂O
5. Age 18 years or older
6. Duration of ARDS 36 hours or less from meeting final Berlin criterion.

Exclusion Criteria:

1. Received mechanical ventilation more than 96 hours
2. Recently treated or bleeding varices, esophageal stricture, hematemesis, esophageal trauma, recent esophageal surgery or other contraindication for nasogastric tube placement
3. Severe coagulopathy (platelet count < 5000/microliter or INR > 3)
4. History of lung or liver transplantation
5. Elevated intracranial pressure or conditions where hypercapnia-induced elevations in intracranial pressure should be avoided
6. Evidence of active air leak from the lung
7. not committed to full support
8. Participation in other intervention trials for ARDS or for sepsis within the past 30 days.
9. Neuromuscular disease that impairs ability to ventilate spontaneously
10. Severe chronic liver disease, defined as Child-Pugh Score of ≥12
11. Treating clinician refusal, or unwillingness to commit to controlled ventilation for at least 24 hours
12. Inability to get informed consent from the patient or surrogate.
13. Use of rescue therapies for prior to enrollment (e.g. nitric oxide, ECMO, prone positioning, high frequency oscillation). This does not exclude cases where these therapies were used as the initial mode of ventilation