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Testing of a machine which monitors ventilator settings and advises the caregiver to try and improve breathing in patients with respiratory failure (ARDS)

Submission date
30/06/2020

Recruitment status
No longer recruiting

Registration date
03/07/2020

Overall study status
Completed

Last Edited
22/05/2025

Condition category
Respiratory

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background
Patients admitted to the intensive care unit with respiratory failure related to acute respiratory distress syndrome (ARDS) receive invasive mechanical ventilation. There are numerous causes of ARDS including pneumonia as a result of bacteria, flu; but also, other non-infectious causes including trauma. During the current pandemic, coronavirus (COVID-19) has become the commonest cause of ARDS worldwide leading to many people being placed on ventilators. Mechanical ventilation is the medical term for a breathing machine used to assist or replace spontaneous breathing. Whilst this type of ventilation is a life-saving intervention, it can also cause lung damage if not implemented carefully. The ventilator forces a volume of air under pressure into the lungs like a bellows. Often the lungs of ARDS patients are already stiffer and the ventilator can cause further damage by over pressuring and over stretching part of the patient's lungs. Patients may also be on extracorporeal membrane oxygenation (ECMO) if the lungs are severely injured and cannot be oxygenated with conventional ventilation. When ECMO is stopped and there is a return to mechanical ventilation the lungs are still injured and susceptible to further injury. Hence, reducing the delivered pressure of mechanical ventilation should reduce complications such as ventilator-associated lung injury, ventilator-acquired pneumonia, and patient discomfort.
For mechanical ventilation, selecting the correct oxygen, pressure and volume levels is important, as incorrect levels can harm the patient, and result in an increased time connected to the ventilator. Selecting the correct levels may be difficult and depends upon the individual patient and their condition. Recently, a system has been developed (the Beacon Caresystem©) which advises the doctor/nurse/physio/respiratory specialist as to how to best set the ventilator. The Beacon Caresystem© is the first system to continuously advise on settings for mechanical ventilation which best suit the individual patient by using a mathematical model based on the patient's physiological responses at any particular point in time. It is attached to the patient circuit, which is linked to the ventilator and assesses how their lungs are working and through this model gives advice on how to change the ventilator. This advice can then be taken (or not taken) by the clinical team to change the ventilator settings. The advice of the Beacon

Caresystem© has been shown to be safe and improve the patients' condition, even when attached for just a few hours in stable post-operative patients. This study is necessary to see if the Beacon Caresystem© can improve patient care in more complex ICU patients i.e. in patients admitted with ARDS as currently, the ventilator setting is solely determined by the decision of the clinical team.

Aims
Aim 1: To investigate if the ventilator setting managed by the doctor's decision aided by monitoring and advice from the Beacon Caresystem© results in improved ventilation in patients suffering from ARDS compared to the decision of the doctor alone.
Aim 2: To examine the biological and physiological factors that determine the worsening of ARDS and the processes involved in recovery from ARDS with the aim to develop new therapies to help detect and speed recovery.
Aim 3: To examine differences between ARDS caused by COVID-19 and non-COVID-19 causes.

Who can participate?
Patients are eligible to participate in this study because they have had a diagnosis of ARDS and are receiving invasive mechanical ventilation. They need to be identified by the consultant and /or ICU nurse / research team by checking medical notes and looking at the clinical condition.

What does the study involve?
Patients can just consent to Aim 1 of the study or Aim2 also – they have the option on the consent form.
Aim 1: If the patient agrees to participate in the study, they will be assigned to one of two groups by chance (like flipping a coin). They will not know which group they were allocated, but the study doctor and team will know. For the two groups, ventilator settings are decided by either the ICU team alone or through advice given by the Beacon Caresystem©. For each of these groups, the management of the ventilator and a number of clinical parameters will be measured to assess whether using the Beacon Caresystem© improves care.
Aim 2 and 3: In this part of the study we would like to take samples to try to determine the biological processes involved in ARDS. These will include samples from the lungs (through a bronchoscope inserted into the airways), blood samples, and urine samples, which are all part of routine ARDS management. From these samples, if permission is given, immune cells as well as DNA and RNA extracts may be analysed to examine genes that are associated with ARDS progression and recovery. Furthermore, it hopes to find important differences between COVID-19 and other causes of ARDS.

What are the possible benefits and risks?
Potential benefits:
We cannot promise that the study will help the patient personally. If ventilator settings are decided by the BEACON Caresystem© then it may be the case that the patient spends a shorter period of time connected to the ventilator. If so, this may reduce the risk of possible complications associated with mechanical ventilation such as ventilator-associated lung injury, ventilator-acquired pneumonia, respiratory and skeletal muscle wasting, and patient discomfort.
However:
• The patients involvement in the study may help us understand and reduce the possible complications associated with mechanical ventilation in the future.
• The biological samples could improve our understanding of ARDS to enable us to personalise treatments for patients in particular, differences between ARDS caused by COVID-19 and other non-COVID-19 causes.
Potential risks:
The Beacon Caresystem© may advise on the settings of the ventilator connected to the patient.

The system does not automatically change the settings on the ventilator and it only advises the nurse and doctor. It is always up to the doctor to actually make these changes and the chances that incorrect advice is provided and implemented are minimal.
Risk is low from biological sampling –samples are taken alongside routine clinical blood samples using the same vascular lines that have already been connected to the patient's body.

Bronchoscopy is a standard procedure performed on ICU. The potential risk for bronchoscopy is a reduction in oxygen delivery but this is minimal in the ICU as patients are attached to the ventilator and this is much less when a patient is on ECMO. In keeping with standard recommendations, patients who are receiving high levels of inspired oxygen (according to the treating physician) through the ventilator will not undergo bronchoscopy and BAL. Bronchoscopy will also only be undertaken if the ICU consultant has no concerns regarding safety of the procedure.

Where is the study run from?
The Sponsor for this study is Imperial College London. This is a multicentre study with one site in the UK – The Royal Brompton and Harefield NHS Foundation Trust, Sydney Street, London

When is the study starting and for how long?
Recruitment started at the Brompton Hospital in March 2020 and will continue until the end of March 2021.

Who is funding the study?
The study is funded by European Commission Horizon 2020 Fast Track to Innovation programme

Who is the main contact?
The Chief Investigator is Dr Brijesh Patel
The Study Manager is Dr Sharon Mumby
All queries should be directed to DeVENTstudy@imperial.ac.uk who will direct the query to the appropriate person.

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
266521

ClinicalTrials.gov number
NCT04115709

Secondary identifying numbers
CPMS 43529, IRAS 266521

Study information

Scientific Title
Decision support system to evaluate VENTilation in ARDS (DeVENT)

Acronym
DeVENT

Study objectives
To evaluate whether an open-loop physiologic model-based decision support system (Beacon Caresystem) reduces driving pressure during mechanical ventilation in patients with ARDS.
To perform a cross-sectional study to characterize cohorts of subjects with ARDS in terms of clinical features, physiological measurements and non-invasive measurement of biomarkers (including those in BAL and blood)
To perform a longitudinal study in ARDS cohorts, repeating the measurements made during the cross-sectional study.
To use the measurements made as part of the cross sectional and longitudinal studies to develop phenotypic handprints for adults with ARDS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/01/2020, (London) South East Research Ethics Board (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8204; nrescommittee.london-southeast@nhs.net), ref: 19/LO/1606

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Acute respiratory distress syndrome

Interventions
The study is a randomised control trial, comparing the effects of mechanical ventilation in ARDS provided as standard care, with mechanical ventilation set according to the advice of the Beacon Care system. The study will compare if the use of the system results in a better application of PEEP and driving pressure across all severities and phases of ARDS.
The broad timeframe for the study is as follows. The study will be conducted at three sites. Two of these sites are outside the UK, one in France and one in Italy.
The systems will be delivered and installed starting September 2019 in the UK site, followed by France and Austria in October 2019. A one month period of training will then follow where all doctors and nurses involved in using the system will be trained. During this period none of the systems advice will be applied. This training will be supported by study partners, and nurses trained as super users of the system, by Mermaid Care A/S, the company producing the system, and by project investigators who have previously conducted studies using the system.
Patient inclusion and data collection will be performed at in the UK sites over a 15 month period from start October 2019 to January 2020. In both European sites, inclusion and data collection will be performed over a 12 month period from start January 2020 to December 2020. Final data analysis and report writing will be performed by March 2021.
For all study sites, all adult patients diagnosed with ARDS in the cardio-thoracic intensive care unit (ICU) undergoing mechanical ventilation will be considered to see if they are eligible for the study.
Critically ill patients are and often unconscious and may not be able to grant consent. Therefore, the Patient Informed Sheet (PIS) and Consent Form will be requested from a third party acting as a consultee; in most cases this person will be a Personal Consultee, who is someone who knows the person lacking capacity and is able to advise the researcher about that person’s

wishes and feelings in relation to the project and whether they should join the research. This person must be interested in the welfare of the patient in a personal capacity, not in a professional capacity or for remuneration and will mostly likely be family member, carer or friend, etc. Where the personal consultee
is not available on site, the researcher may contact the personal consultee by telephone and seek verbal advice. The verbal agreement will be recorded in the telephone consultee declaration form. The telephone consultee declaration form will be signed by a second member of staff who has witnessed the telephone advice. A copy of the PIS will be emailed to the personal consultee.
Where no Personal Consultee is available, the researcher will nominate a professional person to assist in determining the participation of a person who lacks capacity. A Nominated Professional Consultee is someone who will be appointed by the researcher to advise the researcher about the person's (who lacks capacity) wishes and feelings in relation to the project and whether they should join the research. An independent clinician not treating the patient will be asked to be the nominated consultee. A patient information sheet will be distributed immediately following the patient being identified as eligible for the study.
We will ask the patient if we can use their existing hospital records. Without their consent, no additional information about the patient will be collected for the purposes of the study. However, to maintain integrity of the randomised trial, all information collected up to that time will still be used and analysed as part of the study.

If consent is obtained and the patient is still eligible, then they will be randomly allocated to one of two groups. This random allocation will be performed according to the randomisation template with random block allocation. If the patient is allocated to the standard care group then all care will be according to usual practice. If the patient is allocated to the Beacon group, mechanical ventilation will be set with advice from the system. In either case, the study ends for the individual patient either with successful transfer of the patient to another department, or patient death. All other care will be according to usual practice.

110 patients will be included in the study, with 55 patients in each of the groups. 55 patients per group will allow to detect a difference of 3cmH2O in driving pressure between the groups with 90% power and a two sided alpha of 0.05 assuming a control group driving pressure of 15 cmH2O with a standard deviation of 2.5 cmH2O and including a 40% dropout. We have used data from the MIMIC dataset (as published in Serpo Neto et al) for the estimation of the driving pressure. In view of the longitudinal analysis, loss to follow up has taken account of an average mortality of 34% and a 6% drop out.

Intervention Type
Procedure/Surgery

Primary outcome measure
Driving pressure will be measured once a day, using end inspiratory and expiratory pauses Respiratory pressures at the end of inspiratory (Pplat) and expiratory (PEEP) pauses are known to approximate average pressure in the alveoli at these points, such that their difference, Pplat-PEEP, is the correct measure of driving pressure applied to the lungs. This measurement will only be performed in breaths where no spontaneous breathing activity occurs. In addition to the measurement of driving pressure performed, surrogate measurements of driving pressure will be obtained continuously by approximating Pplat with peak inspiratory pressure (Ppeak), and PEEP with PEEP values set on the ventilator (PEEPset).

Secondary outcome measures

1. Daily average calculated delivered pressure over time, for periods of spontaneous breathing
2. Daily average calculated mechanical power over time
3. Daily average calculated oxygenation index over time
4. Daily average ventilatory ratio over time
5. Incidence and duration of proning events and pre- and post- respiratory physiology
6. Ventilator free days at 28 days
7. Composite endpoint including any cause of death at 28 days and days free of mechanical ventilation within 28 days among survivors
8. Time from control mode to support mode
9. Proportion of breaths dysyncronous with the ventilator
10. Number of changes in ventilator settings per day
11. % of time in control mode ventilation
12. % of time in support mode ventilation
13. Total duration of mechanical ventilation
14. Changes in tidal volume over time
15. Changes in PEEP setting over time
16. Timing, incidence and duration of neuromuscular blockade
17. Mortality at 28 days, 6 months and 1 year
18. Organ failure free days in the first 28 days, assessed using the sequential organ failure assessment (SOFA) score and/or delta SOFA
19. Ventilation related complications e.g. pneumothorax and/or pneumomediastinum
20. Device malfunction event rate
21. Device related adverse event rate
22. Number of times the advice from the Beacon system is followed through the duration of the study
23. Daily Radiographic Assessment of Lung Oedema (RALES score over time)

Overall study start date
01/04/2019

Completion date
30/09/2021

Eligibility

Key inclusion criteria
1. Invasive mechanical ventilation
2. A known clinical insult with new worsening respiratory symptoms
3. Chest radiograph with bilateral infiltrates consistent with evidence of pulmonary oedema but not fully explained by cardiac failure
4. Hypoxaemia as defined by PaO2/FiO2 of ≤300mmHg (or ≤40kPa) (pre-ECMO PaO2/FiO2 will be used should the patient be placed on extracorporeal support)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 110; UK Sample Size: 50

Total final enrolment
95

Key exclusion criteria
1. Aged <18 years
2. The absence of an arterial catheter for blood sampling at study start
3. Consent declined
4. Over 7 days of mechanical ventilation
5. Treatment withdrawal imminent within 24 h
6. DNAR (Do Not Attempt Resuscitation) order in place
7. Severe chronic respiratory disease requiring domiciliary ventilation and/or home oxygen therapy (except for sleep disordered breathing)
8. Veno-ArterialVA ECMO ECMO
9. Head trauma or other conditions where intra-cranial pressure may be elevated and tight regulation of arterial CO2 level is paramount

Date of first enrolment
17/03/2020

Date of final enrolment
31/03/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Brompton Hospital
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Sponsor information

Organisation

Imperial College London

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Sponsor type
University/education

Website
http://www.imperial.edu/

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
European Commission

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, Ευρωπαϊκής Επιτροπής, Европейската комисия, Evropské komise, Commission européenne, Choimisiúin Eorpaigh, Europskoj komisiji, Commissione europea, La Commissione europea, Eiropas Komisiju, Europos Komisijos, Európai Bizottságról, Europese Commissie, Komisja Europejska, Comissão Europeia, Comisia Europeană, Európskej komisii, Evropski komisiji, Euroopan komission, Europeiska kommissionen, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
30/09/2022

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version v2.0	15/05/2020	03/07/2020	No	No
HRA research summary			28/06/2023	No	No
Protocol article		17/01/2022	22/05/2025	Yes	No