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Comparison of lung water in COVID-19 patients and other patients with acute respiratory failure

Submission date	Recruitment status	[_] Prospectively registered
05/04/2020	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
07/04/2020	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
12/06/2023	Infections and Infestations	

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 March 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.

Rapid progression of inflammation results in a substantial number of COVID-19 patients requiring mechanical ventilation. In these most severely ill patients, computed tomography of the chest demonstrates a typical pattern which is suggestive to a degree that it is disease-defining, even if the SARS-COV-2 PCR test is negative.
Extravascular lung water index (EVLWI) is a marker of pulmonary oedema. Single indicator transpulmonary thermodilution (TPTD) provides bedside measurement of EVLWI. Several studies demonstrated significant and independent association of EVLWI and its changes over time with mortality. A recent study in a non-COVID-19 cohort with ARDS (see ISRCTN32938630) suggests better and earlier prediction of 28-days-mortality compared to traditional scores grading the severity of ARDSARDS. Furthermore, TPTD-monitoring „per se“ was independently associated with a lower mortality.
However, pathology of COVID-19 is not fully understood, and there is a lack of data on EVLWI and other TPTD-parameters from COVID-19-patients.

Therefore, it is the aim of this study to measure EVLWI in patients with COVID-19 and to compare these findings to EVLWI from a recent non-COVID-19 cohort with ARDS.
As secondary endpoints we will also compare other haemodynamic parameters between COVID-19 and non-COVID-19 patients.

Who can participate?
Adults with COVID-19 and ARDS according to the Berlin definition

What does the study involve?
From the day of intubation, TPTD (PiCCO, Pulsion Medical Systems, Germany) will be performed daily to derive EVLWI, Cardiac Index CI and the preload marker global end-diastolic volme index GEDVI. Furthermore, all other parameters derived from the PiCCO-measurement will be documented.

What are the possible benefits and risks of participating in the study?
The possible benefit is a very thorough analysis and monitoring of pulmonary and haemodynamic parameters. There are no additional risks to participants due to the observational design of the study.

Where is the study run from?
General Intensive Care Unit R3a (2/11) of Munich University Hospital (Germany)

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

Who is funding the study?
Technical University of Munich (Germany)

Who is the main contact?
Prof. Wolfgang Huber
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
EVALUATION: Extravascular lung water index in patients with COVID-19: A prospective comparison to a recent cohort with non-COVID-19 ARDS

Acronym
EVALUATION

Study objectives
The aim of this study is to measure EVLWI and other haemodynamic monitored parameters (Cardiac Index CI, global end-diastolic volme index GEDVI) in patients with COVID-19 and to compare these findings to EVLWI from a recent non-COVID-19 cohort with ARDS. We hypothesize that EVLWI is higher in OVID-19-ARDS-patients compared to the non-COVID-19-ARDS-patients (control group).
Main questions addressed by the study:
1) Is there a difference of abovementioned parameters for the two cohorts?
2) Does measurement of extravascular lung water index (EVLWI) provide additional therapeutic /prognostic information?
3) Is pulmonary oedema in COVID-19 patients also due to cardiac impairment?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/03/2020, Ethikkommission der Technischen Universität München (Ismaniger Str. 22, Munchen, 81675, Germany; +49 (0)89 41404371; ethikkommission@mri.tum.de), ref: 178/20 S

Study design
Observational single-centre cohort study; comparison to a recent cohort of non-COVID-19 patients with ARDS (see ISRCTN32938630)

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
See additional files (in German)

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection) and acute respiratory distress syndrome (ARDS)

Interventions
According to the standard of the ICU for COVID-19 and non-COVID-19 patients, routine data of patients with COVID-19 and ARDS including PiCCO-monitoring will be documented from the day of intubation until extubation. All measurements were repeated at least once per day.

Intervention Type
Other

Primary outcome measure
Extravascular lung water index EVLWI measured using TPTD (PiCCO; Pulsion Medical Systems; Feldkirechen Germany) daily from intubation until extubation

Secondary outcome measures
Measured daily using TPTD from intubation until extubation:
1. Cardiac index CI
2. Preload marker global end-diastolic volume index GEDVI
3. Pulmonary vascular permeability index PVPI

Overall study start date
11/03/2020

Completion date
30/04/2020

Eligibility

Key inclusion criteria
1. Aged 18 or older
2. Critically ill
3. COVID-19 and acute respiratory distress syndrome (ARDS) according to Berlin-Definition
4. No contra-indication to PiCCO-monitoring

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
25

Key exclusion criteria
1. Pregnant

Date of first enrolment
19/03/2020

Date of final enrolment
30/04/2020

Locations

Countries of recruitment
Germany

Study participating centre
Medizinische Klinik und Poliklinik II
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Sponsor information

Organisation
Klinikum der Universität München

Sponsor details
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Sponsor type
University/education

Website
http://www.gdit.edu.cn/

ROR
https://ror.org/02jet3w32

Funder(s)

Funder type
University/education

Funder Name
Technische Universität München

Alternative Name(s)
Technical University of Munich, TUM

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Germany

Results and Publications

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

Intention to publish date
01/05/2020

Individual participant data (IPD) sharing plan

The datasets generated during the current study are available upon request from Paul Schmidle (paul.schmidle@mri.tum.de) and Wolfgang Huber (wolfgang.huber@mri.tum.de). The data will be available following permission from the Institutional Review Board.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			18/05/2020	No	Yes
Preprint results	non-peer-reviewed results in preprint	11/09/2020	16/03/2021	No	No
Results article		01/06/2021	12/06/2023	Yes	No