

Worldwide Assessment of Separation of Patients From ventilatory assistance

WEAN SAFE



Study protocol

Proponent:

The study is proposed by the Acute Respiratory Failure Section of the European Society of Intensive Care Medicine (ESICM), is endorsed by ESICM and supported by ESICM Trials Group.

Study design:

Prospective, observational, multi-centre, international cohort study

Steering committee:

Giacomo Bellani (Co principal-investigator)

John Laffey (Co principal-investigator)

Tai Pham

Fabiana Madotto

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Gaetan Beduneau

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Frank van Haren

Laurent Brochard

Antonio Pesenti

+ prospectively: top 2 recruiting countries (normalized by population), top 2 recruiting countries (absolute value) will be invited to join the SC for data analysis, manuscript drafting etc etc.

Executive committee:

Giacomo Bellani, John Laffey, Tàì Pham, Leo Heunks

National coordinators: National coordinators are will be that of recruiting centers in your country, facilitating communication of centers with the steering committee (and vice-versa), supporting centers with site activation, eCRF access and patient's recruitment.

A complete list of National coordinators can be found in the Annex.

Key Achievements to Date:

- Oct 2016: Presentation of the study @lives2016 in Milan during the ARF section meeting
- November 2016: application to ESICM for endorsement and use of eCRF
- Oct – Dec 2016: Finalization of study protocol/paper CRF
- March 2017: Inaugural Investigator meeting at ISICEM 2017
- May 2017: Confirmation of ESICM Trials Group support for WEAN SAFE
- May 2017: Confirmation of National coordinators; Start of center recruitment

Next steps - Projected Timeline

- Spring 2017: Development of eCRF
- October 2017: Formal study launch, at LIVES 2017; Second investigator meeting
- Oct 2017 – Mar 2018: Patient's recruitment window period
- Summer 2018: Initial Data analysis
- October 2018: Presentation of initial analyses at LIVES 2018

Background

Successful weaning of patients from invasive mechanical ventilation represents a crucial step in the recovery process following severe respiratory failure [1-3], and is a key clinical challenge for ICU clinicians. Many of the serious complications of IMV are directly related to the duration of ventilation [4, 5]. Failure to successfully separate patients from IMV contributes directly to poorer patient outcomes: including longer duration of ventilation, longer length of stay in the ICU and in the hospital, and higher patient mortality [6, 7]. Patients spend a considerable amount of time in being liberated from invasive mechanical ventilation. The systematic utilization of approaches to reduce the duration of ventilation are therefore of fundamental importance [8-10].

Despite the importance of the weaning period, this process is not rigorously defined, with wide variations in definitions and practices. In addition, the specific impact of weaning difficulties on patient outcomes is still poorly understood. While guidelines do exist on the classification of weaning, a key recent study has shown that these are not applicable to all patients [11]. Moreover different practices exist in regard to weaning procedures and some confusion exists even in what should be considered the beginning of weaning process. This is an important problem, because general recommendations regarding the entire weaning process may encompass completely different causes and consequences of its prolongation and therefore may be totally inappropriate for individual patients.

The WEAN SAFE study will aim to address key issues relating to weaning from invasive MV. WEAN SAFE will have a structure similar to LUNG SAFE [12], in that a large set of patients receiving invasive MV will be enrolled, without setting "weaning" as an inclusion criterion, but rather attempting to identify the weaning process "retrospectively".

Study objectives

Although there are published guidelines about when and how to start the weaning process, we do not know whether these recommendations are used or are feasible, what are the barriers for their implementation and what is the real life impact of an early or late weaning process for the patient.

There is also significant uncertainty about when the process of weaning from IMV is really starting, in our understanding of the impact of sedation management, and knowledge regarding current weaning practices and how this is associated with outcomes.

WEAN SAFE aims to describe, in a large population of ICU patients the current procedures for weaning, the applicability of existing classification systems to 'real world;' weaning from IMV, to describe centers/management/patients characteristics associated to duration of weaning. It will answer the following questions:

- What is the frequency of delayed weaning from invasive mechanical ventilation?

- What are the current approaches taken to wean patients from invasive mechanical ventilation?
- What are the factors that are used to determine when patients are in the weaning phase?
- What are the barriers to effective weaning from invasive MV?
- What factors (patient, institutional, medical practice) contribute to failed attempts to wean from invasive mechanical ventilation?
- What is the impact of sedation management on weaning from invasive MV?
- What is the impact of premorbid conditions and of frailty on weaning from invasive MV?
- What is the utility of existing classifications for weaning from invasive MV?
- What is the impact of early versus delayed and/or failed weaning from invasive MV?
- What regional or geo-economic differences exist regarding weaning from invasive MV?
- What is the therapeutic resource use in patients with delayed weaning from IMV?

Screening

- All patients admitted in the ICU and aged >16 will be screened daily

Inclusion Criteria

- A patient will be included if he/she is undergoing Invasive mechanical ventilation on the second morning (between 6am and 10 am) after initiation of mechanical ventilation or after ICU admission (if ventilation was already in place).

Exclusion criteria

- Lack of informed consent (where required)
- Patients already present in the ICU at the beginning of the study, independently of the form of ventilatory support

Note that previous enrollment in the same study is NOT an exclusion criteria. Data on previous enrollment will be captured by the CRF

Intervention required

Due to its observational design no intervention is required.

Enrollment in concomitant studies

Due to the observational nature of the present study, patients enrolled in other observational/interventional study CAN be enrolled in the present study.

Sample size

We aim to collect a large “convenience sample”, with > 5,000 patients. Based on the LUNG SAFE data, we can estimate to enroll about 11 patients invasively ventilated on Day 2 following intubation per participating ICU in a 4 week period. We are therefore targeting the enrollment of 500 registered ICUs (considering a 10% dropout)

Data collection period

Each one of the participating ICUs will collect the data over a four weeks period, to be selected in a six-months “window” from October 2017 to March 2018.

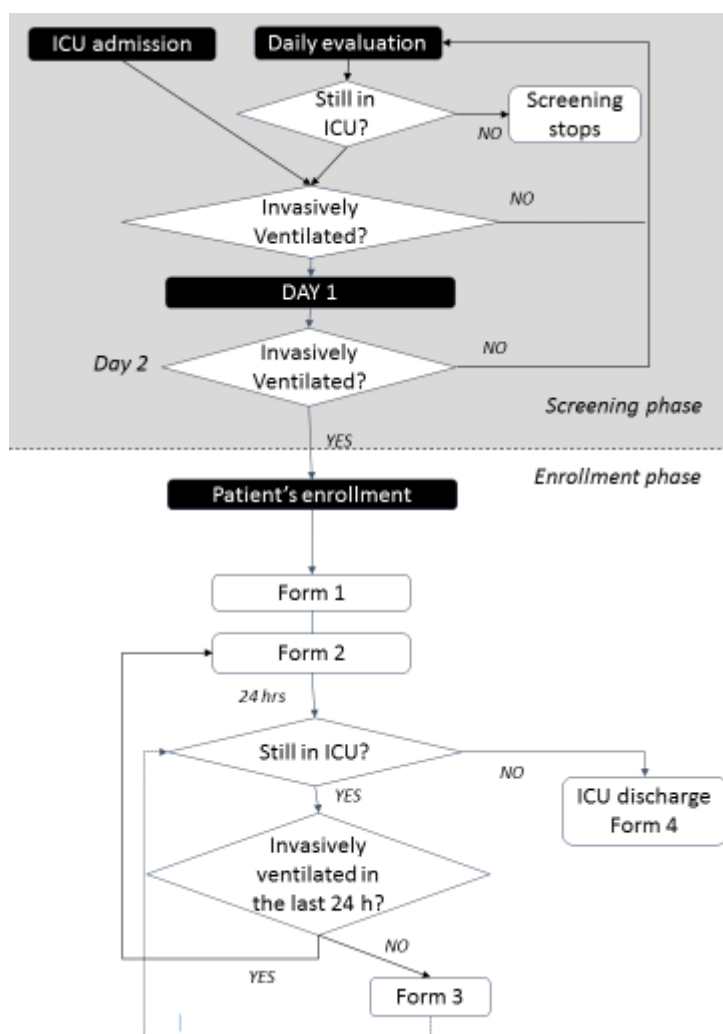
Patients enrollment/study days

Patients will be screened for the study when undergoing mechanical ventilation and admitted in the ICU.

- Day 1 will be defined as the first day when IMV commences
- Day 2 commences at 6-10am (fixed time point each day per ICU practice) after IMV commences. Patients undergoing invasive mechanical ventilation on the morning of day 1 will be screened for the study
- Patients still undergoing IMV on Day 2, will be enrolled in the study
- Patients not undergoing invasive mechanical ventilation or liberated from invasive mechanical ventilation on day 1 will be re-evaluated daily for the presence of inclusion criteria.

Data collection

Data collection will be web based, using conditional Data Collection screens, i.e. data collectors will be automatically guided as to which sections to complete based on data entered indicating whether Inclusion Criteria are met. Data collection must be done **at a fixed time for that particular ICU, which can be between 6 and 10am** each day.



ICU Participation Form (Form 0): This is completed by each participating ICU just prior to study commencement. It will provide a set of data concerning its own size, staff, case-mix.

Screening Form: Completed for all patients, over 16 years of age, admitted in participating ICUs

Study Form 1: Completed on all patients that are still in receipt of invasive MV on day 2.

Daily Form 2: Completed daily on all patients enrolled into the study who received invasive MV over the last 24 hours.

Daily Form 3: Completed daily on all patients enrolled into the study who have not received invasive MV over the last 24 hours.

Outcomes Form 4: Completed on patients at ICU discharge and finalized at either hospital discharge or day 90 [whichever comes first] respectively.

Ethical Approval and Patient Consent

As this study is purely observational, the data collected are part of routine clinical care, and the data will be anonymized, then informed patient consent may well not be necessary. However, there are considerable variations by country in regard to this. Each PI will notify their relevant ethics committee, in compliance with the local legislation and rules, and complete any required ethics committee processes. In most countries, a National coordinator will liaise with participating centres, helping to obtain IRB approval.

Data Anonymization and De-identification

The study will not store electronically any data which allow direct patient's identification (such as name and/or date of birth). Only initials and age are collected and the patient is then assigned a unique identifier number, generated by the eCRF, used to identify the data, but investigators are allowed not to enter patient's initials in the eCRF. Upon enrollment in the eCRF, the patient is assigned a unique identifier number, termed the Study ID, which is used subsequently to identify the data. If initials are not inserted in the eCRF a record connecting patient's initials and Study ID can be retained locally, to facilitate data collection. At the end of the study, a verification of all data in the database is carried out, and the local site coordinator asked to verify specific data as needed. Once this is done, the database is locked and before the beginning of the statistical analysis the patients' initials will be erased from the dataset. The individual site coordinators are then asked to destroy all identifying information, including the record linking the patient's initials to their Study ID. Thereafter, data will only be identified with the unique Study ID. The data is stored securely and all procedures regarding data management will comply with EU directive on data protection 95/46/EC. Further details can be found in the document signed by Clinfile, provider of the electronic CRF. After study completion the database will be securely stored to avoid accidental or unauthorized disclosure or access. Access to the database will be granted to the "Lung Safe" investigators only, to perform the statistical analysis described in the attached plan. Lung safe investigators have the right to propose additional analysis of the collected data, subject to approval of the Principal investigators.

Publication and Authorship

The data collected belongs to the WEAN SAFE Investigators, and substantial authorship opportunities are available to participants. A more detailed policy will follow, but the very successful principles as for LUNG SAFE will be followed. Results from the trial will be published by the WEAN SAFE nominated Executive Committee. Each participating centre and its lead investigator will be named as collaborator on the published manuscript. Of importance, this collaborator credit will also appear in PubMed, when searches are made for your name.

In addition, the top 2 recruiting countries (normalised by population), and the top 2 recruiting countries (absolute value) will be invited to participate in manuscript drafting and offered authorship. There will also be opportunities as a 'WEAN SAFE Investigator' to propose sub-studies, and where these proposals are accepted, to receive authorship credit on these.

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