European Society of Intensive Care Medicine (ESICM) – Acute Respiratory Failure Section

Large observational study to UNderstand the Global impact of Severe Acute respiratory FailurE – ['LUNG-SAFE' study]

Study Protocol and Data Collection Forms

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INTRODUCTION

The original description of Acute Respiratory Distress Syndrome (ARDS) dates back more than 40 years. After the landmark definition provided by the American European Consensus Conference in 1994 [1], the definition was recently updated, by the "ARDS definition task force" (an initiative of the European Society of Intensive Care Medicine endorsed by the American Thoracic Society and the Society of Critical Care Medicine) which proposed and validated the "Berlin definition"[2], with the aim of overcoming some of the limitations which have emerged in regard to the 1994 definition.

Several large observational population studies have been conducted in the last 10 years, with the aim of describing the ICU incidence and outcome of ARDS patients as well as collecting clinical and physiological variables, with a specific focus on mechanical ventilator settings [3-5]. These studies have provided great insights into the understanding of ARDS: far from the carefully controlled settings of randomized controlled trials these studies provide a "real-life picture" of ARDS patients and of clinicians' response.

However, important advances and changes in the management of patients with respiratory failure have occurred. First, the use of non-invasive ventilation to delay/prevent intubation has rapidly increased. The 1994 definition of ARDS required the patient to be supported by mechanical ventilation. Second, protective ventilation has become more established and the use of adjuncts such as ECMO has increased substantially in the last five years. Third, the patient population is also changing, as elderly patients are more commonly admitted into ICUs. Perhaps most importantly, the definition of ARDS itself has recently changed.

For these reasons the Acute Respiratory Failure section of ESICM proposes to undertake the "LUNG SAFE study", in order to prospectively assess the incidence of, and outcomes from ARDS, as defined by the Berlin definition.

In summary, the study will focus on the following items:

- The frequency and disease burden of acute hypoxaemic respiratory failure in winter
- The aetiologies of acute hypoxaemic respiratory failure requiring ventilatory support.
- The incidence of ARDS based on the Berlin definition within this patient cohort
- The mortality from ARDS within this cohort, and how does this vary based on ARDS severity
- Natural history of ARDS (duration and evolution by severity)
- Therapeutic resource utilization
    - Use of treatments, such as recruitment maneuvers, prone positioning, nitric oxide, high frequency oscillation, ECMO, transfer to tertiary hospital from smaller regional ones) according to the severity of the disease
    - Use of non-invasive ventilation in management of ARDS patients (use in different stages: early ARDS versus immediately after extubation)

METHODS

This is a prospective observational study, aimed at collecting an adequate dataset on a large cohort of patients admitted to a large number of ICUs.

ICU RECRUITMENT AND PARTICIPATION

ICUs will be invited to participate on a voluntary basis. ICUs enrolling into existing databases (e.g., ERIC study, ICON audit) will be invited to participate. It is important that participating ICUs commit (by written agreement) to fully comply with the study protocol.

ICU recruitment in each country will be spearheaded by a national coordinator

Each ICU will be requested to recruit for **4 consecutive 'winter' weeks**

a. Northern Hemisphere – 4 week period between February 1st and March 31st 2014.
b. Southern Hemisphere: 4 week period between June 1st – August 31st 2014

There will be 2 data collectors per participating ICU's. Each data collector will undergo an online training program designed to standardize data interpretation [esp. CXR's] and will receive a login authorization following completion of this training.

INCLUSION CRITERIA: All patients admitted to the participating ICUs receiving invasive or non-invasive ventilation will be screened and included in the database.

EXCLUSION CRITERIA: Age < 16

DATA COLLECTION

Data collection will be web based, permitting 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 will be done at 10am each morning.

Form #1: 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.

Form #2: Completed at ICU admission on all patients in participating ICUs

Form #3: Completed on all patients receiving: (1) CPAP > 5cm H_2O, or Assisted ventilation (invasive or non-invasive) with PEEP CPAP > 5cm H_2O and with a P/F ratio <300 [<40 if PO_2 in KPa]. Patients will be reassessed daily and if they fulfill inclusion criteria will have form #3 completed at that point, and be entered into the study at that point. Day 1 is the date of fulfillment of the inclusion criteria. Data will be collected daily for Study Days 1-7 inclusive, then on Study Days 10, 14, 28, and at ICU death or discharge.

Forms #4 and 5: Completed at ICU and at either hospital discharge or day 90 [whichever comes first] respectively.

SAMPLE SIZE

Our aim is to obtain a sample of at least 1000 ARDS patients within the cohort of patients receiving assisted ventilation. The reported incidence of ARDS in ICU patients varies, from 2.2% of ICU admissions develop ARDS in ALIEN [3], 7.1% in ALIVE Study [6], to 17.5% of Ventilated patients in KCLIP [7]. A reasonable projection of the incidence of ARDS among patients admitted in ICUs can be estimated to approximate 5% of ICU admission. As a conservative estimate, if a medium-sized ICU admits 50 patients/month and collects data for four weeks, **500** ICUs will be necessary to achieve this number.

ETHICAL APPROVAL AND PATIENT'S CONSENT

We believe that informed patient consent will not be necessary, as this audit is purely observational, the data collected are part of routine clinical care, and the data will be anonymized. However, each PI will notify the relevant ethics committee, in compliance with the local legislation and rules. The national coordinators will facilitate this process.

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.

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