Objectives: to evaluate the current diagnostic and therapeutic approaches for sepsis-associated disseminated intravascular coagulation (DIC) in a large prospective registry.

Design: prospective, multicenter, international registry.

Study population: patients 18 years or older with severe infection to be potentially associated with DIC will be eligible for the study. The clinical visits and monitoring of the patients will follow local routine practices. No specific imaging tests or laboratory evaluations will be required and patients will be evaluated and treated according to local policy. All the involved centers will be asked to update information on included patients at 2, 4, 6, 8, 10 and 28 days after inclusion (see flow-chart).

Study outcomes: The primary outcome of the study is the development of DIC. Secondary outcomes are thrombotic (arterial and venous) and bleeding events, overall mortality at 28 days.

Study sample, feasibility, and analysis plan: We plan to enroll a minimum of 1000 patients in approximately 30 centers. With an expected rate of about 20 patients/year/center the recruitment phase should last about 2 years. Preliminary information on baseline characteristics, risk factors, and treatments will be analyzed by means of descriptive statistics. Variables with a non-parametric distribution will be presented as medians (range) and those with a parametric distribution as means (± standard deviation). Between group differences will be tested with the Mann-Whitney U test or the T-test, as appropriate. Risk factors for death, thrombosis and bleeding will be evaluated by logistic regression. Variables with a statistical significance corresponding to a p ≤ 0.15 in univariate analysis will be assessed in multivariate logistic regression analysis. Variables with a statistical significance p ≤ 0.05 in multivariate analysis will be consider as independent predictors.
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Design and methodology (Data expected to collect, sample size and statistical analysis):

Describe concisely the research design and methods for achieving these goals. Suggested length 2-3 paragraphs

Design: prospective, multicenter, international registry.

For each patient the following data will be collected:

- Age, gender, and race;
- Clinical signs and symptoms (e.g. blood pressure, heart rate);
- Scores and laboratory tests to diagnose DIC;
- Type and main characteristics of the severe infection
- Personal history of thrombotic (arterial and venous) or bleeding events;
- Available laboratory parameters results (e.g. blood count, liver and kidney function, inflammatory and coagulation parameters) assessed at the time (within 24 hours) of the diagnosis of DIC;
- Type, dose, and duration of any treatment provided for severe infection;
- Type, dose, and duration of any treatment provided specifically for DIC;
- Any other concomitant treatments (e.g. prophylactic heparin for venous thromboembolism prophylaxis);
- Mortality and other significant morbidities;
- Thrombotic and bleeding events;
- Treatment provided for the thrombotic and bleeding events.

A web-based database will be available to all participating centers for data collection.

Study outcomes

The following outcomes will be recorded during the study:

- DIC diagnosed by the ISTH or JAAM score;
- Death;
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- Venous thromboembolic events (symptomatic and unsuspected), including pulmonary embolism and deep vein thrombosis (DVT) of the upper and lower limbs, visceral DVT, and cerebral DVT;
- Arterial thromboembolic events (myocardial infarction, stroke, peripheral embolism);
- Major and clinically-relevant non-major bleeding.

Follow-up

All the involved centers will be asked to update information on included patients at 2, 4, 6, 8, 10, and 28 days after inclusion (Flow-chart). The clinical visits and monitoring of the patients will otherwise follow local routine practices. During each patient contact, the following will be systematically checked:

- Occurrence of study outcomes;
- Changes in concomitant medications;
- If available, results of laboratory parameters (e.g. blood count, liver and kidney function, inflammatory and coagulation parameters) and change in diagnostic/dynamic scores since inclusion;

No specific imaging tests or laboratory evaluations will be required and patients will be evaluated and treated according to local policy.

Study sample, feasibility, and analysis plan: Almost 5% of all patients admitted to the Intensive Care Unit develop DIC. In particular, DIC occurs in more than 30% of patients admitted to ICU with severe sepsis. As we planned to enroll prevalently patients with sepsis, we estimate a minimum incidence of DIC of 20%. Therefore, we plan to enroll a minimum of 1000 patients in approximately 30 centers to evaluate at least 200 patients with DIC. With an expected rate of about 20 patients/year/center the recruitment phase should last about 2 years. Preliminary information on baseline characteristics, risk factors, and treatments will be analyzed by means of descriptive statistics. Variables with a non-parametric distribution will be presented as medians (range) and those with a parametric distribution as means (±standard deviation). Between group differences will be tested with the Mann-Whitney U test or the T-test, as appropriate. Risk factors for death, thrombosis and bleeding will be evaluated by logistic regression. Variables with a statistical significance corresponding to a p ≤ 0.15 in univariate analysis will be assessed in multivariate logistic regression analysis. Variables with a statistical significance p ≤ 0.05 in multivariate analysis will be consider as independent predictors.
Study population: patients 18 years or older with a severe infection potentially associated with DIC, admitted to ICU, will be eligible for the study. The maximal time-window allowed between the diagnosis of the disease and inclusion in the study will be 72 hours. Investigators will note all relevant laboratory tests measured.

Participating Centers (still

Italy
University of Insubria – ASST Settelaghi, Varese (ICU, Paolo Severgnini; Thrombosis Unit, Alessandro Squizzato)
University of Chieti, Chieti (Thrombosis Unit, Marcello Di Nisio)
Padova (ICU, Sabrina Boraso)
Brescia (Fondazione Poliambulanza, ICU, Ferretti Pierluigi)

England
Manchester Royal Infirmary, Manchester (Jecko Tachil)

The Netherlands
Amsterdam (Academic Medical Center, ICU, Marcella Muller)

Japan
(Juntendo University, Department of Emergency and Disaster Medicine, Toshiaki Iba)

Expected timeline:
Ethical committee submission: November 2017
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Launch: February 2018
Duration: 2 years
Finalization/analysis: February 2020
Reporting: May 2020

Publication type (SSC Communication, Guidance document or original article):

Original article

References:


