**Registry for invasive treatments for massive pulmonary embolism in pregnancy and postpartum period**

SSC Women’s Health Issue in Thrombosis and Haemostasis

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Description Abstract

Pulmonary embolism (PE) occurs in about 1 in 1000-3000 pregnancies, and is one of the most common cause of maternal mortality in Europe and North America [1]. Whereas the treatment of hemodynamically stable PE during pregnancy is well documented, that of hemodynamically unstable (“massive”) PE, comprising about 5% of all PE, is not. In a recent systematic review, we collected 127 cases of massive and submassive PE during pregnancy and the postpartum period, published between 1967 and 2016 [2]. With thrombolysis (n=83), maternal and fetal survivals were high (94% and 88%). Major bleeding occurred in 17% in the antepartum but was very common (58%) in the postpartum. However, the inference from such data is tempered by the heterogeneity of cases and the risk of publication bias, with a greater likelihood of publication of positive cases with good outcomes. Further, we identified only 3 cases of massive PE treated with extracorporeal membrane oxygenation (ECMO) and 7 cases treated with percutaneous thrombectomy without thrombolytics.

Given this lack of strong evidence, current guidelines consider pregnancy as a relative contraindication to the use of thrombolytics [3] and advise to best reserve thrombolytic therapy for life-threatening maternal thromboembolism [4]. The use of ECMO and percutaneous thrombectomy is not discussed. Clinicians are therefore faced with uncertainty while taking care of pregnant and postpartum women with massive PE.

The objective of this international registry is to explore the maternal effectiveness and maternal/obstetrical safety of thrombolysis, mechanical thrombectomy and ECMO for massive PE in women during pregnancy and the postpartum period (6 weeks). Such data would help inform the care of these very ill patients and future guidelines.

Design and methodology (Data expected to collect, sample size and statistical analysis):

The proposed design is an online registry of massive PE and their treatment during pregnancy and the postpartum period, in English, sponsored by the International Society on Thrombosis and Haemostasis.
The following data will be collected for each reported case, anonymously for the patient.

- Date, hospital and name/email address of reporting clinician
- Maternal characteristics: age, weight, BMI, history of VTE
- Obstetrical characteristics: gravidity/parity, gestational age (at diagnosis of PE), other pregnancy complication; if postpartum: date of delivery, type of delivery
- PE characteristics: diagnostic imaging type, hemodynamic instability, cardiac arrest, use of vasopressors, RV dilation, concomitant DVT
- Treatment options (several modalities are possible) and order of use
  - Thrombolytics: drug (alteplase, reteplase, tenecteplase, monteplase, streptokinase, urokinase), dose, duration of administration, method of administration (iv, pulmonary artery)
  - ECMO: type (a-v, v-v), duration.
  - Percutaneous thrombectomy: type (aspiration, catheter fragmentation, rheolytic devices)
  - Anticoagulation: drug (unfractionated heparin, LMWH, other)
- Maternal outcomes
  - Hemodynamic improvement within 12h of treatment
  - Necessity for further invasive treatment
  - Survival at 7d and 30d.
  - Major bleeding (ISTH definition), location, timing.
- Obstetrical outcomes (if treatment during pregnancy)
  - Fetal survival at 7d and until delivery
  - Fetal bleeding, location and timing.
  - Premature delivery
- Neonatal outcomes
  - Survival at 30d post-delivery
  - Any concomitant neonatal medical problem

Study population

Inclusion criteria: women during pregnancy or the postpartum period (6 weeks), with

- An objectively diagnosed PE: chest angio-CT, ventilation/perfusion lung scintigraphy or tomo-scintigraphy, pulmonary angiography, objectively diagnosed proximal DVT with a clinical PE, echocardiography with RV dilation and clinical PE, and
- Criteria for massive PE, as defined by a SBP <90mmHg, an acute drop of blood pressure >40mmHg, the need for inotropic support or cardiac arrest, and
- Treatment with percutaneous or i.v. thrombolysis, percutaneous thrombectomy, and/or ECMO.

The recruitment will be open to all. Advertisement for this registry will occur through the ISTH, the SSC for Women’s Health Issues, and through national thrombosis societies. The principal
The investigator will continue to screen the literature (Pubmed and conference proceedings) prospectively for published relevant cases, and invite the authors to participate in the registry.

The primary aim of this registry is the description of maternal, obstetrical and neonatal outcomes. For such descriptive purposes, the minimum sample size is determined by the minimum precision of proportions of these outcomes. A sample size of 80 women would allow a precision of ±10% for a proportion of 10%, with a power of 80% and a two-sided alpha of 0.05.

We anticipate a slow recruitment for this rare event in pregnant women. Between 2013 and 2016, there were 8-10 case reports of massive PE during pregnancy or the postpartum period [2]. We anticipate that a recruitment of 10-15 cases per year, with an achievement of 80 included women within 5-8 years.

Expected timeline

<table>
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<tr>
<th>Project design and SSC presentation</th>
<th>Jan 2018-July 2018</th>
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<tr>
<td>Development of the online registry</td>
<td>August 2018-December 2018</td>
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<td>Launch of the registry</td>
<td>January 2019</td>
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<td>Registry duration</td>
<td>Until 2024-2027</td>
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<tr>
<td>Finalization/analysis and reporting</td>
<td>2024-2027</td>
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Expected outcomes (ie. publications):

We intend to publish the results of the registry as an original article in peer-reviewed medical literature at the end of data collection. Thereafter, a guidance document from the SSC for the medical care of pregnancy-related massive PE may be proposed.

Intermediate findings will be regularly presented to the SSC Women’s Health Issues in Thrombosis and Haemostasis during ISTH congresses.

Description of project set/up and management, needed infrastructure and resources (summary):

The needed infrastructure and resources for this project are:

- The development of the online registry, using a dedicated platform such as RedCap©
- A secure electronic environment to store the registry
- The promotion of the registry through the ISTH newsletter, SSC sessions and the ISTH congresses.

The principal investigator is willing to dedicate time to manage the registry, including audits for data quality, missingness, and contact with reporting clinicians if needed.
References


