Suggestions for future observational studies:

| | |
|---|---|
| Definitions | 1) Do not define bleeding severity according to the number of PBRC units transfused in a specific timeframe. Definition should be based on parameters collected on admission<br>2) Define coagulopathy |
| Case mix selection | 1) Bleeding without coagulopathy<br>2) Bleeding with coagulopathy<br>3) Bleeding without coagulopathy and timely surgical/interventional haemostasis<br>4) Bleeding with coagulopathy and delayed surgical/interventional haemostasis<br>5) Terminal bleeding with consequent coagulopathy |
| Methodology and statistics | 1) Dataset: high quality database collecting items predefined to address specific queries<br>2) Design: Availability of a control group (e.g. patients not receiving a specific treatment) for comparisons with the study group<br>3) Statistics: control for confounding using appropriate statistical models methods (e.g. logistic regression, propensity score matching)<br>4) Design and statistics: large cohorts should be analysed to avoid overfitting; at least 10 outcomes should be available for each variable included in the models (including the initial models before further variable selection)<br>5) Dataset and statistics: the number of variables should be sufficient to develop *explanatory* models (i.e. most known important predictors should be included), avoid underfitting<br>6) Statistics: avoid bivariate methods to select variables to be included in the model<br>7) Statistics: be cautious in the use of automatic selection procedures for covariate selection, particularly when the sample size is not large<br>8) Statistics: account for the immortal-time bias when dealing with time-dependent treatments<br>9) Statistics: account for treatment selection bias (balance the probability of receiving treatment between study and control group) |
| Treatment side effects | Collect data concerning potential side effects (e.g. ALI after transfusion, deep venous or thrombosis after fibrinogen administration, etc.) |
| Outcome | Besides short-term outcomes (such as 6-24 hours, 28-days) middle-long term outcomes should be preferred (at least hospital outcomes; 6-months outcomes could be indicated in specific conditions: elderly, head trauma) |
| External validation | Dataset: the number of patients and centres participating should be sufficiently large to allow the generalizability of the results |