Identifying the impact of hemostatic resuscitation on development of multiple organ failure using factor analysis: results from a randomized trial using first-line coagulation factor concentrates or fresh-frozen plasma in major trauma (retic study).

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Introduction:
to clarify how hemostatic resuscitation affects occurrence of multiple organ failure.

Methods:
analysis of secondary endpoints of the RETIC study [1] (coagulation factors, activated protein C (APC), thrombin generation, ROTEM parameters, syndecan-1, thrombomodulin (TM) and D-Dimer) measured at randomization, and after patients had received FFP or coagulation factor concentrates (CFC) at admission to ICU, 24 and 48 hours thereafter. We used factor analysis to reduce the highly interrelated variables to a few main underlying factors and analysed their relation to MOF before and after hemostatic therapy.

Results:
The factors Concentration, Clot and Hypoperfusion representing trauma-induced coagulopathy (Table 1) were comparable between groups at baseline (Fig 1) and only high Hypoperfusion-score predicted MOF, while after therapy a low Clot-score also predicted MOF. Only the changes of the Clot-score independently affected occurrence of MOF (p=0.0002, adjusted OR 3.40, CI 2.46-4.71), while changes of Concentration (p=0.8979, adjusted OR 0.96, CI 0.68-1.34) and Hypoperfusion (p=0.8098, adjusted OR 1.06, CI 0.84-1.33) did not. A lower Clot-score occurred after FFP transfusion than use of CFC, mainly through persistent thrombocytopenia (platelet count R2-4 FFP vs CFC p<0.02) (Fig 2). The higher Concentration-score after FFP did not affect MOF and FFP had no beneficial effect on fibrinolysis, syndecan-1, TM or APC.

Conclusion:
Hemostatic resuscitation should augment the factor Clot, which is feasible with early fibrinogen administration but not with FFP. The found platelet-saving effect of early fibrinogen administration is important as platelets play a major role in inflammation and transfusion of platelets did not correct thrombocytopenia.

References:

Table 1:

<table>
<thead>
<tr>
<th></th>
<th>Concentration</th>
<th>Clot</th>
<th>Hypoperfusion</th>
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<tbody>
<tr>
<td>coagulation factors</td>
<td>0.56 to 0.91</td>
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<tr>
<td>Fibrinogen</td>
<td>0.69</td>
<td>0.31</td>
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<tr>
<td>Platelets</td>
<td>0.55</td>
<td>0.34</td>
<td></td>
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<tr>
<td>ROTEM</td>
<td>-0.37 to 0.97</td>
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The loading of a variable on one or more of the three factors corresponds to the correlation of that variable and the factor. Coagulation factors = concentrations of coagulation factors FII, FV, FVII, FVIII, FIX, FX, FXI, FXIII antithrombin, protein C, thrombin peak. ROTEM parameters = extrinsically activated coagulation time, alpha angle and and clot firmness at 10 min, fibrin polymerization at 10 min.

Image 1:

Boxplots show the factors Concentration, Clot and Hypoperfusion, extracted from the performed factor analysis (see Table 1) for the CFC (blue, n=46) and the FFP (yellow, n=42) group, as well as for patients without (white, n=40) and with (grey, n=48) multiple organ failure. Each factor is given at the measurement time point baseline (R1) and following haemostatic resuscitation at admission to ICU, 24 and 48 hours thereafter (R2 to R4).

Image 2:
Boxplots show available measurements of extrinsically activated clot firmness at 10 min (ExA10), fibrin polymerization at 10 min (FibA10) and platelet count at baseline (R1) and after therapy at admission to ICU, 24 and 48 hours thereafter (R2 to R4) for the CFC (blue, n=46) and the FFP (yellow, n=42) group as well as for patients without (white, n=40) and with (grey, n=48) multiple organ failure.