Author’s response to reviews

Title: Tracheostomy in intensive care unit patients can be performed without bleeding complications in case of normal thromboelastometry results (EXTEM CT) despite increased PT-INR: a prospective pilot study results (EXTEM CT) despite increased PT-INR: a prospective pilot study

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Author’s response to reviews:

Dear editor,

We have done changes in our manuscript. Responses to reviewer 1 are in green color /also in article/ and to reviewer 2 in red color.

We believe that it will be satisfactory for both reviewers.

Best regard,

Miroslav Durila /for all authors/

Reviewer 1

As per my previous comment: “There is no mention of PTT and other standard blood clotting parameters such as platelet counts that clearly influence bleeding”. Although platelet counts are now provided, the individual PTTs are not.

- We put APTT-INR values of our patients in method section (APTT-INR 0.8-1.18). Patients who had APTT-INR higher than 1.2 did not fulfil inclusion criteria for the study and were not taken in the study.

- There were four reasons why we preferred studying PT time and EXTEM before APTT and INTEM:

  1. In practice, in ICU patients after 3-4 days of hospitalisation PT prolongation is much more often than APTT prolongation.
  2. Excintric pathway of coagulation initiation prevails in vivo, as describes cellular model of coagulation.
  3. When APTT is increased, the therapy is only FFP.
4. When PT is prolonged, prothromplex complex (PCC) can be used instead of FFP (we try to avoid FFP as it is accompanied by increased mortality)

Sepsis leading to bleeding is due to a consumption of clotting factors - particularly fibrinogen, factor V and factor VIII, and increased fibrin degradation products (all not measured). The cumulative effect is to prolong PTT. Since according to the authors PTT was normal for all (Methods page 4), I am not convinced that sepsis has anything to do with the prolongation of the INR (for the cases with INR > 1.3) - which could be due to Vit K insufficiency and/or liver problems.

- We agree with reviewer and we put the comment at the end of method section explaining that patients were divided into groups according to admission diagnosis (meaning that the severe sepsis has almost resolved at the time when tracheostomy was performed):

We also identified the cause for which the patients were brought to ICU and accordingly, divided them into two groups as septic (patients who were admitted to ICU because of severe sepsis) and nonseptic (admitted for a reason other than sepsis).

We address the reviewers comment also in the section talking about limitation:

The limitation of the study is the fact that at the time of performed tracheostomy the the primary cause and the reason for admission to ICU had almost resolved (tracheostomy is usually performed after 10th day of artificial ventilation) and patients from both groups were becoming alike, meaning becoming patients with ICU coagulopathy. That might be the reason why there is a little and no statistically significant difference in CT-EXTEM parameters between groups.

- As primary goal of study was to compare PT-INR with EXTEM in ICU patients I think that changing the title of article to ,, Tracheostomy in intensive care unit patients can be performed without bleeding complications in case of normal thromboelastometry results (EXTEM CT) despite increased PT-INR: a prospective pilot study,, would be more appropriate.

Furthermore inclusion of the INTEM would be indicative of the contact pathway of coagulation - readily affected by consumptive coagulopathy during sepsis with factor depletion. Showing the INTEM values would be more convincing to this reviewer. This is further evident since the EXTEM CT values in sepsis and non-sepsis are not significantly different and fall well within the normal range of 38-79 sec.

5. This is addressed previously: We preferred PT and EXTEM as we believe that excintrinsic pathway of coagulation initiation prevails in vivo, as describes cellular model of coagulation and in chronic ICU patients PT prolongation is more common than APTT. However, we admit that a new title would fit better for this article.
Therefore the INTEM values would have been informative. I would not base any clinical decisions on only EXTEM parameters in the absence of a PTT and INTEM using the ROTEM.
- Neither do we. It is necessary to know APTT value because there can be heparin effect or patient can have deficiency of FVIII...
- If any patient was on heparin I would have compared the INTEM with the HEPTEM.”
- And also we would do the same thing.

From the results provided it is unclear who exactly received the 4 units of FFP - what were their exact coagulation parameters.
- Added data in results and discussion section: There was only one case when EXTEM CT was prolonged (CT of 99 seconds, PT-INR was 1.4 and APTT-INR was 1.18) out of 27 ROTEM.

The Figures do not make sense you cannot have values INR 1.2-1.3 in one category and in another INR # 1.3 as in Figure 1 and in other Figures. Where would an INR value of exactly 1.3 go? – corrected in figures

Reviewer 2

Minor Essential Revisions:
Page 4, line 13: delete „maximum“, since A10 is defined as the amplitude in mm 10 min after CT.-done

Page 4, line 13f: Change wording to “maximum clot firmness-MCF”.-done

Page 4, line 14: Change wording to “Lysis index-LI30 and LI60”.-done

Page 4, line 15f: Change wording to “… where ROTEM revealed pathological values in EXTEM CT. ROTEM was not re-assessed after the intervention.” -done

Page 6, line 8: Delete one superfluous bracket. -done

Page 8, line 7f: Change wording to “The normalization of EXTEM CT despite an increased INR value might be due to the presence of sepsis with increased tissue factor expression on circulation monocytes …”.-done

Page 9, line 4: Change wording to “CT – coagulation time (time from starting the test until a clot firmness of 2 mm is reached) -done
Page 14, table 1: Change “LY30 and LY60” to “LI30 and LI60”. (LY30 and LY60 are TEG parameters describing lysis in percentage of MA 30 or 60 min after MA, respectively. LI30 and LI60 are ROTEM parameters describing the residual clot firmness in percentage of MCF 30 or 60 min after CT, respectively). -done

Page 14, table 1 legend: Change wording to “… MCF-maximum clot firmness; LI30 and LI60 …” and Normal values “… LI60 0-15%; …”.-done

Page 14, table 1 legend: I assume you want to point out that * means p<0.05, ** means p<0.01, and *** means p< 0.001.-corrected

Figure 1: Change “INR 1,2-1,3” to “INR 1,21-1,29”.-corrected

Figure 3: Change “INR 1,2-1,3” to “INR 1,21-1,29”.-corrected