Author's response to reviews

Title: Safety, Feasibility and Complications during Resective Pediatric Epilepsy Surgery: A Retrospective Analysis

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Author's response to reviews: see over
Dear Dr. Rowles,

On behalf of my co-authors, I am again resubmitting the enclosed manuscript with the changed title „Safety, Feasibility and Complications During Resective Pediatric Epilepsy Surgery: A Retrospective Analysis“ for possible publication in BMC Anesthesiology. We hope that all concerns have now been addressed. We thank the reviewers for the constructive comments and we think that the manuscript was improved thus. Changes in the manuscript are highlighted in blue.

Please find the responses to the reviewers on the following pages.

Yours sincerely,

Marcus Thudium
Corresponding author
Dear Dr. Passariello,

thank you very much for reviewing our manuscript. 
Your concerns are answered as follows:

Major Compulsory revisions:
The manuscript is a retrospective analysis of forty-five patients undergoing resective epilepsy surgery. This is an interesting topic and the experience of a center dealing with this kind of surgery may be of interest. However the manuscript is very poor in details that may be very important in the analysis:

1. The authors describe significant blood loss. There is no detail regarding preoperative values for Hb and coagulation tests. Any coagulation abnormalities or low Hb preoperatively?
   We analysed our data accordingly: The preoperative values for Hb, prothrombin ratio (Quick) and partial prothrombin time (PTT) were 12.6 ± 1.6 g/dl, 99.8 ± 10.7 %, 27.6 ± 1.9 s, respectively, as assessed in 33 patients. In the remaining 12 patients, preoperative values were assessed, but untraceable. However it has been common practice in our hospital, not to perform surgery until coagulation abnormalities have been treated and Hb has been corrected to a concentration above 10 g/dl. We modified our manuscript and included the above mentioned preoperative data.

2. Where there blood saving strategies in place? i.e. tranexamic acid, normovolemic hemodilution, controlled hypotension, preoperative erythropoietin etc. Authors should discuss if they tried to minimize blood loss and how they did this. Strategies may have changed over the years.
   The main blood saving strategy was to meticulously control intraoperative bleeding by bipolar electrocautery. However, neither tranexamic acid, normovolemic hemodilution, controlled hypotension, nor preoperative erythropoietin were applied. Controlled hypotension was discussed but not applied, since maintenance of a sufficient cerebral perfusion pressure was deemed as more important.

3. What about the surgical team? Was the team the same for all surgeries? The experience of the surgical team may correlate with length of surgery and blood loss. Authors should discuss this issue.
   During the observed time period of 22 years, part of the surgical team changed. We agree that the experience of the surgical team will likely have an impact especially on the length of surgery and presumably on blood loss. However, an analysis with respect to individual surgeons was not desired due to internal affairs.
   We modified our manuscript stating that the experience of the surgical team may correlate with length of surgery and blood loss.

4. There is no mention about comorbidities. Syndromic patients may have poorer outcomes and higher risk of bleeding.
   Most patients were diagnosed with temporal lobe epilepsy (18) caused by dysplasia, Ganglioglioma or hippocampal sclerosis. 16 patients had isolated frontal lesions, 8 had lesions in other regions of the brain, tumors or dysplasia.
   One patient suffered from a Sturge-Weber-Syndrome and another two from Tuberous Sclerosis Complex. These did not differ in their blood loss from non-syndromic patients.
5. The authors should discuss their relatively high threshold for transfusion (hb 9.5 gr/dL). How was blood loss measured? How accurate was this technique?

The relatively high transfusion threshold was chosen mainly due to safety reasons, e.g. to avoid haemorrhagic shock and severe anemia: Following massive blood loss, a given haemoglobin concentration will not accurately reflect the true degree of anemia, since Hb concentration will decrease with some time lag. Blood loss was measured as the volume within the suction container minus the volume of the irrigation fluid used. Dedicated suction containers were used for pediatric neurosurgery which allowed us to measure blood loss with an estimated accuracy of approximately 20 ml. We modified our manuscript accordingly.

6. Median and range are needed for numerical values

Data are now shown as mean ± standard deviation in case of normal distribution, or as median [25%; 75% percentile] otherwise. In addition, the range is shown in tables 1 and 2.

7. Hypothermia was very mild (minimum 35.7°C-again, range is important here) thanks to the good intraoperative management of the authors and is unlikely to have caused intraoperative coagulation impairment.

We inserted the range of the minimum temperature into our manuscript.

In fact the authors didn’t find any correlation between temperature and blood loss. I suggest the authors change the title of the manuscript. This is a retrospective analysis about safety, feasibility and complications of this kind of surgery and does not focus on hypothermia-related blood loss.

We changed the title of our manuscript into:

“Safety, feasibility and complications during Resective Pediatric Epilepsy Surgery: A Retrospective Analysis”
Dear Dr. Stoppa,

thank you very much for reviewing our manuscript.
Your concerns are answered as follows:

**The author suggestes Hb 9.5 gr/dl as a trigger for blood transfusion.**
In the work is not mentioned as the haemodynamic parameters. The blood transfusion need to be associated to the haemodynamic parameters and not only to Hb values.
We agree. However, after reviewing the raw data we found that fluids were constantly replaced during surgery so that blood pressure and heart rate could be kept within physiological limits. Therefore in our patient collective Hb seems to represent the only trigger for transfusion. We added this to our manuscript.

**Then the total amount during surgery is not reported.**
We apologise for not completely understanding this sentence. Please find the total amount of blood loss in the results section.

**All the patients have been considered with normovolemic emodiluion before the surgery. Pietrin at al. suggest this procedures to reduce blood loss in pediatric patient.**
Normovolemic hemodilution has not been performed in our patients, although we agree that this procedure might have reduced blood loss. However, normovolemic hemodilution was neither a commonly accepted nor a mandatory procedure during the 22-years period described in our study.

**Was the alteration of coagulation blood test associated with increase of FDP the indication to use fresh forzen plasma? It is no reported in the paper.**
Transfusion of fresh frozen plasma (FFP) according to coagulation test abnormalities is a reasonable and rationale approach. However, it is often not feasible (though desirable) in the pediatric setting, where small blood losses can result in disseminated intravascular coagulopathy (DIC). Performing a coagulation test and defrosting of FFPs takes approximately 60 to 90 minutes (including transportation of blood sample and FFP) in our hospital. Given the fast dynamic of DIC, awaiting the coagulation test results in a situation of profound blood loss would have put the children in jeopardy. Therefore, fresh frozen plasma was given, whenever the estimated blood loss exceeded one third of the total blood volume. We added this to the manuscript.

**It is important to considered normothermia during surgery in Pediatric patient. The author considered also hypothermia but they did not describe time to rich temperature and also how was rewarming.**
The temperature nadir was reached approximately one hour after induction of anaesthesia. Rewarming was performed via a heating blanket.

Marcus Thudium,
Corresponding author

May 26, 2014