Reviewer's report

Title: Fluid management guided by a novel continuous non-invasive arterial pressure device is associated with decreased postoperative morbidity in patients undergoing total knee and hip replacement - a randomized study

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Reviewer: Tomi Pösö

Reviewer's report:

The authors for this manuscript “Fluid management by a novel continuous non-invasive arterial pressure device...” hypothesize that intraoperative, goal-directed volume therapy by use of dynamic index (PPV) and continuous arterial blood pressure obtained by non-invasive “CNAP”- device may have impact on postoperative morbidity in orthopedic patient population. Some of the aims of the study, per se, are fundamental including high-volume group of patients with overall moderate to high risk for cardiovascular adverse events. Furthermore, non-invasive approach for cardiovascular monitoring is an interesting issue in principle.

Unfortunately, I have multiple major concerns and with regards to this manuscript. Some of these are described in detail in my comments. The manuscript has major weaknesses in study design, structure of the text body, data presentation and scientific objectivity and statistics that jeopardize the conclusions. In addition, this manuscript is not easy to read. The data presented, majority of the results and conclusions of the study are in a major controversy.

Major Compulsory Revisions

Study design, methods, data gathering, data presentation, statistics and conclusions.

1. The study was aiming to optimize intraoperative volume therapy by CNAP device in the intervention groups. In Figure 1 the authors present nice, state-of-art protocols for use of intraoperative fluids and vasoactive drugs. However, no intraoperative dynamic data (PPV), no blood pressures, heart rate or use of vasoactive drugs are presented. Only hemodynamic data available is baseline and end-of procedure MAP, PPV and heart rate that indicate euvolemic patient population with hypertension. In table 1 one may inspect that all study arms include individuals with significantly stressed cardiovascular system. These patients have propensity for hemodynamic instability during GA and are not always that easy to handle in general anesthesia. So, the authors should be able to show mean values of PPV, MAP and HR minimum for statements “maintained hemodynamic stability” (Abstract, lines 15-16 and page 10 lines 3-4 e.g.) and to proof that the device "CNAP" has been utilized during surgery and to carry out a reliable statistical analysis on the whole. In addition, mean values of volatile anesthetics, opiates would have been valuable for comprehensive evaluation of
presented data of fluids infused, drugs injected and hemodynamics.

2. Page 11, lines 12-15. The statements about “liberal approach” and hemodilution in controls are not justified and non-sense. Difference at only 360ml (e.g. controls vs pressure) in total volume infused intraoperatively cannot be labeled as “liberal” approach. In addition, reported 24 h balance was minus 480ml for controls! And, no volume of blood infused is reported.

In addition, page 10, lines 12-13, the statement “A drop of hemoglobin...was significantly more pronounced in the control group..” is not justified. In table 2 end-of-surgery Hb is even higher vs other groups combined to no difference in transfusion frequency intraoperatively. Moreover, no statistical analysis was conducted for Hb values.

3. Moreover; the statement page 11, lines 12-13 and table 2: presented PPV values after induction indicates euvoelma; no need of fluids. It should have been crucial to show how PPV, MAP obtained by CNAP follows volume depletion (bleeding) during surgery and for objective evaluation of the device and need of fluids.

4. Statistics: Table 2 and 3, it seems that more blood was infused in controls. There is no significant difference in blood loss during surgery or the first POP day, i.e., increased blood transfusions may depend on lack of standardization of the management of the control group, not use of the device. In addition, length of hospital stay was quite long (up to 12 d), that is, frequency of blood transfusions may not depend on intraoperative fluid management but surgery per se, medications with impact on thrombocyte aggregation, for example. And no intraoperative values of Hb are presented that reduces reliability of the statistics reported. Only one value of Hb (24h POP) is reported. So, propensity for investigator bias may be a fact and objective statistics cannot be motivated without valid data of Hb.

5. A single modality for intraoperative monitoring was implemented. This increases risk of inappropriate decision making and hence, incorrect fluid therapy, during possible system failure of the device. Some other modality (e.g. arterial line, non-invasive blood pressure, PiCCO, TTE/TEE, FloTrac, ccNexfin) should also have been used for assessment of validity of CNAP data. At last, as the authors state (page 12, lines 17-19) this manuscript is the first one that monitors GDT by CNAP. Without intraoperative hemodynamic, vasoactive and anesthetic drug data it is barely possible to assess reliability of the device. Moreover, as stated in page 12, lines 22-23, that hemodynamic instability may jeopardize reliability of the data – however intraoperative hemodynamic data is no reported. So, once again, the main conclusions are not justified.

6. Methods/aims: This manuscript is a quantitative study. Qualitative, clinic specific outcomes like “before and after” cannot be evaluated with the data presented. This aim cannot be motivated. For the same reason, page 14, lines 1-2, the conclusions are not valid due to quantitative nature of data gathered.

7. Study design; the controls. The manuscript has no valid controls. Fluid therapy should have been standardized as the group “Pressure”. Standardized, non-invasive blood pressure measurements and thresholds for blood transfusion
should have been crucial. Conclusively, in principle, a control group must have a basic treatment protocol for reliable statistical analysis. Now, the management of “no treatment controls” may even be questioned and reassessed by the ethical review board.

For these reasons the authors should not put together a manuscript in the field of “intraoperative goal directed fluid therapy” and the conclusions are not justified. Actually, in my opinion, this controversy can partly be found as well in the previous paper of the authors “Critical Care 2010, 14:R118”; the reference # 16 in this manuscript.

Minor Essential Revisions:
1. Tables: Too much information without significance is provided.
2. Writing: Many typos and grammatical misses.
3. The main headline is too long.
4. Is general anesthesia your standard approach in orthopedic individuals, not spinal anesthesia? Why?
5. Page 11, lines 17-18; the statement that “PRESSURE” group is a “fluid restriction group” is not justified. There is no difference in principles of GDT – one group applies MAP and HR and the other one PPV.

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.