Author's response to reviews

Title: Non-invasive pulse wave analysis for monitoring the cardiovascular effects of CO2 pneumoperitoneum during laparoscopic cholecystectomy

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Author's response to reviews: see over
Dear Ms. Costoy,

Thank you very much for allowing us to revise our manuscript entitled „Noninvasive pulse wave analysis for monitoring the cardiovascular effects of CO₂ pneumoperitoneum during laparoscopic cholecystectomy”.

We revised the manuscript according to the suggestions of the reviewers, we marked the with red color changes we made. In the following we respond point-by point to the reviewer’s comments and suggestions.

We hope that in its present form the manuscript will meet the requirements of BMC Anesthesiology.

Yours sincerely

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RESPONSES TO 1247951574129658 COMMENTS

• "The major drawback of this paper is the lack of a control monitoring technique." Thank you for this comment, we do agree. However, this study may be considered as a pilot investigation of a new technique and in fact, in further studies a sophisticated hemodynamic monitoring should be used as control. We addressed this issue within the limitations section as follows: Finally, the main limitation of this study is the lack of a control group, i.e. other hemodynamic measurements were not used. However, this trial is a pilot application of applanation tonometry in this field. As this is a non-invasive method, in this first, pilot step of our investigations we intended to compare hemodynamic changes with those that used invasive monitoring techniques reported in the literature.

• "The applanation tonometry is only superficially presented and discussed in the last part of the discussion section, without any explanation of its pro-and con." Thanks for this comment. In the discussion section the pro-con’s and the limitations of the method are discussed in more detail: Limitations: The intraoperative use of the device is limited by the position of the radial artery, i.e. in some surgical scenarios it may disturb the surgical team, making monitoring impossible. Another limitation to be mentioned is operator-dependency: for reliable monitoring it is necessary to have previous experience with the technique.

• "from tables and figures it is not evident if these changes are really of clinical interest". We agree with this comment. To take a position of the changes, we added to the discussion section: "It has to be noted that hemodynamic parameters in this phase returned to the baseline, preinduction values (Table 3.). It seems that the effect of inducing pneumoperitoneum counteracts the hemodynamic depressant effects of the anesthetics suggesting that changes in ASA I-II patients are clinically most probably not relevant. In a recent study, Cinnella and co-workers also demonstrated that hemodynamic stability after administering pneumoperitoneum is maintained even if moderate (5 cm H2O) is applied." and "Further studies are needed to prove whether the method may be helpful in delineating critical situations in patients with limited cardiovascular reserve (ASA III-IV patients) by defining cut-off values of safety"

• "The bibliography cited is partly outdated" We updated it, thank you for this comment.

• "The English should be reviewed and decimal numbers in tables should be correctly written with a full stop instead of a comma." Done, thank you.

Thank you for the thorough reviewing work of this reviewer.
RESPONSES TO 1519406995127771 COMMENTS

- “The study is correctly designed with one major weakness that SphygmoCor was the only method of measurement used. However if we consider this trial as the pilot investigation this weak point is less important.” Thank you for this comment, we also see this limitation. Accordingly, we added to the limitations in the discussion section: “Finally, the main limitation of this study is the lack of a control group, i.e. other hemodynamic measurements were not used. However, this trial is a pilot application of applanation tonometry in this field. As this is a non-invasive method, in this first, pilot step of our investigations we intended to compare hemodynamic changes with those that used invasive monitoring techniques reported in the literature.”

- “The introduction section should be shortened; the first paragraph concerning the surgical aspect of laparoscopic cholecystectomy can be deleted.” We did it accordingly, thank you for this comment.

- “The methods are correctly described excepted the definition of “Time 4”, which should be clarified.” We added the definition of Time 4.

- “...one figure, which in my opinion is not complete. The data on significant changes observed during the study should be included.” We completely agree with this comment, and changed the Figure accordingly.

- “The authors should take some position concerning the clinical relevance of observed changes...” To the discussion section we added: It has to be noted that hemodynamic parameters in this phase returned to the baseline, preinduction values (Table 3.). It seems that the effect of inducing pneumoperitoneum counteracts the hemodynamic depressant effects of the anesthetics suggesting that changes in ASA I-II patients are clinically most probably not relevant. In a recent study, Cinnella and co-workers also demonstrated that hemodynamic stability after administering pneumoperitoneum is maintained even if moderate (5 cm H₂O) is applied.

- “The abstract needs several changes notably the expressions like “moderate increase” and “marked increase” should be replaced by the data with mention of significant differences (P values included).” We changed it accordingly. thank you for the comment.

The authors wish to express their gratitude for this reviewer for this thorough review.
RESPONSES TO 1995706530130816 COMMENTS

• „Pag. 5 line 10 Please specify the value of PEEP if you had. Associated PEEP can modify the results“ We did not administer PEEP. To the methods section we added: „PEEP was not administered (ZEEP).“

• „Pag.5. line 11. Please change the term of" CO2 insufflation" with "CO2intra-peritoneal pressure". Insufflation means " the introduction of a flow of gas into a body cavity " Thank you for the comment. We have changed it accordingly.

• „Pag.6. line 4.b Please provide results for the ejection duration hemodynamic parameter. Even if it’s possible to calculate the ejection duration and ejection duration index from the PWA I didn’t see any sustainable results about this parameter.” Data on ejection duration are now provided in the tables.

• „Pag. 7 line 2. I consider it would be better to evaluate the hemodynamic results also after the period when the gases were closed.” We do agree with this comment. Unfortunately we do not have data on this. We take this comment into account in further studies.

• „Pag.7. line 14 Please consider if the number of females (much more than man) and the age (50 years) could influence the results.” It may well possible but we did not adress this question in this present study.

• „Pag.8. line 1. Please consider if the central aortic pressure values increases only because of the peripheral arterial stiffness or also because blood is squeezed from the splanchic venous and preload (return) is augmented ( IAP levels below 15 mm Hg) and Pag. 8. line 22, 23. Please reconsider the affirmation that "The decrease of augmentation index reflecting the stiffness of the peripheral vessels " In my opinion the decrease of augmentation index was about vasodilatatory effect of the anesthetic and ...” We agree with this this comment. Accordingly, we added to the discussion section: It has to be noted that hemodynamic parameters in this phase returned to the baseline, preinduction values (Table 3.). It seems that the effect of inducing pneumoperitoneum counteracts the hemodynamic depressant effects of the anesthetics suggesting that changes in ASA I-II patients are clinically most probably not relevant. In a recent study, Cinnella and co-workers also demonstrated that hemodynamic stability after administering pneumoperitoneum is maintained even if moderate (5 cm H₂O) is applied. [16]

• „Pag.9. line 20-25 please let me suggest to the author another point of view about the pneumoperitoneum hemodynamic effects: the results from this study show that the hemodynamic modifications, produced by the pneumoperitoneum, were good for the patients, because after the insufflations they were similar with the initial values before the induction of anaesthesia. That means the modification of pneumoperitoneum antagonized (cancelled) the decrease of the peripheral and central pressure and also decrease of the augmentation pressure produced by the induction of anaesthesia.” We do agree, see previous comments added.

• „Maybe it would be interesting for the author to compare the values before induction with the results obtained after insufflations.” To meet this requirement, we added a new table (Table 3.).

The authors do thank very much for the thorough reviewing work of this reviewer.