Author’s response to reviews

Title: Acceleration sensors in abdominal wall position as a non-invasive approach to detect early breathing alterations induced by intolerance of increased airway resistance

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Reviewer reports:

Reviewer #1: In the present feasibility study Thomas Breuer and colleagues evaluated thoracic and abdominal wall acceleration sensors with the aim to detect respiratory alterations due to increased respiratory workload in healthy volunteers. As a main result, acceleration decreased in abdominal wall position in 15 volunteers with intolerance of increased respiratory workload in comparison to 14 volunteers without intolerance of increased respiratory workload. The authors hypothesized that acceleration measurement could potentially be used to detect respiratory failure prior to clinical impairment in weaning patients.

The study is quite interesting and the manuscript is well written. However, I have some comments regarding study design and conclusions:

* Increased respiratory resistance was implemented to increase respiratory workload. However, the rationale for a further increase of resistance by changing tube diameters is unclear. Wouldn't it be easier to extend the duration of the trial with one tube size until clinical intolerance?
Answer: Thank you for this interesting hint. The decision to test respiratory work load in this predefined and standardized sequence of decreasing tube sizes intended to exclude subject-specific origins of tube-intolerance. Our method aimed to illuminate the acute onset of chest and abdominal wall changes and their predictive value to the development of respiratory failure.

* Intolerance of increased resistance was accompanied by a decrease of abdominal wall acceleration. However, this result does not prove that acceleration decreased prior to intolerance as the title of the manuscript suggests.

Answer: Thank you for your helpful comment. We adapted the title of the manuscript according to your suggestion:

“Acceleration sensors in abdominal wall position as a non-invasive approach to detect early breathing alterations induced by intolerance of increased airway resistance”

* Volunteers were instructed not to change respiratory frequency. Thereby, rapid shallow breathing as an early sign of respiratory failure has been stifled significantly. Thus, calculation of the rapid shallow breathing index might be not reliable.

Answer: Thank you for your comment. According to your important hint, we could not exclude an underestimated Rapid shallow breathing index in our described method, and therefore we did not measure the RSBI in our setting.

* Results must be presented more clearly: Which values were significantly different? As far as I understand, abdominal wall acceleration was different between the two groups of patients but not within groups? At which timepoint? Please provide a table with values and standard deviations.

Answer: We apologize for having confused you. Hopefully our new added Supplemental data lead to more clarity. Since a two-way-ANOVA was performed analyzing effects of two dependencies, it is a bit difficult visualizing the results by a table (it would need a 3-dimensional graph).

* I suggest shortening the discussion: The first paragraph should be part of the introduction.

Answer: Thank you for this important suggestion. We moved the mentioned paragraph to the introduction:
“Respiratory failure manifesting as inadequate gas exchange is raised by a variety of pathophysiological alterations like airway obstruction, chest wall pathologies, muscular or innervation insufficiency, disturbance of alveolar-capillary units or cerebral pathologies. Especially after thoracic and abdominal surgery the respiratory function is hampered due to interventional changes [1, 2]. The resulting pathological breathing patterns are influenced by the workload of the respiratory system, leading to respiratory muscle dysfunction. This well-described phenomenon is determined by the duty cycle of the inspiratory muscle and the ratio of inspiratory pressure to its maximal capacity (P/Pmax) [3, 4]. Fatigue is evident by a reduced muscular force after exercise compared to prior baseline conditions. Due to the fact that the resulting force of respiratory muscles is inaccessible to direct measurements, several indirect methods have been established to predict respiratory muscle work like trans-diaphragmatic pressures, diaphragmatic sonography or the rapid shallow breathing index (RSBI) [5-7].

Breathing depends on continuous synchronized work of respiratory muscles. Especially the function of the diaphragm, as it is the main respiratory muscle, is vulnerable to attenuation [8]. This diaphragmatic dysfunction originated by increased respiratory load leads to muscular injury and disturbance of cellular homeostasis [9-11]. Due to the resulting functional diaphragmatic weakness auxiliary respiratory muscles need to be activated and thereby alter resulting breathing excursions [12].”

Reviewer #2:

Title: Acceleration sensors in abdominal wall position as a non-invasive approach to detect early breathing alterations prior to intolerance of increased airway resistance


In their manuscript „Acceleration sensors in abdominal wall position as a non-invasive approach to detect early breathing alterations prior to intolerance of increased airway resistance“ Breuer and colleagues report the findings in the detection of alterations in breathing excursions with abdominal and thoracic wall acceleration sensors. The results show an interesting approach to predict respiratory failure. Although the manuscript is well written I have some remarks:

Methods:

1. The measurements were made in supine position. It is relevant whether the volunteers were in a position with elevated or flattened torso. Please clarify.

Answer: Thank you for your important suggestion. We clarified the position in the method section:
“The volunteers were turned into a 30-degree elevated supine position and then connected to the clinical monitor equipment to continuous...”

2. The participants had to breathe through orally administered tubes of different diameters. Usually the pre-assembled tubes have different length according to the diameter. Based on the length and the diameter, did you estimate the resistance? Please add the resistance-values of each used endotracheal tube into the method section.

Answer: Based on your suggestions we calculated the flow-resistance in accordance with the Hagen-Poiseuille-Law. Therefore, we added the following paragraph in the results section:

“In accordance to the Hagen-Poiseuille-Law the calculated relative flow resistance of the used 5mm tube was 15.0/mm3, for the 4mm tube 36.6/mm3, for the 3mm tube 83.0/mm3 and for the 2mm tube 420.2/mm3.“

Results:

3. The authors present the changes in abdominal and thoracic wall acceleration. They point out that increased respiratory workload led to a significant decrease of acceleration in the abdominal wall position. The thoracic acceleration sensors did not detect any changes during increased respiratory workload. Are there any significant differences between the 3 abdominal wall sensors? Please add the comparison between the different abdominal positions in the results.

Answer: Thank you for this comment. We analyzed all acceleration sensors in abdominal and thoracic wall position and afterwards focused on the most enhanced acceleration for each position to identify the differences between abdominal and thoracic wall position.

4. The text in combination with Figure 4 is hardly understandable. This is especially because the Figure-legend is wrong concerning description of colors. According to the legend colors differentiate between "completed" (blue circles) and the "abandoned" group (green circles), according to the Figure colors differentiate between thoracic and abdominal sensor position.

Since Figure 4 approaches the main topic of the manuscript it should be overworked and its statement should be made clearer in the results-section as well as in the Figure. Even since "artificial units" are used a table would be very useful to demonstrate the authors arguments (especially concerning statistical significance).
Answer: Thank you for this important comment. We adapted Figure 4 to clarify our findings in the completed and abandoned group, each with thoracic and abdominal wall accelerations sensors:

Figure 4: Measured acceleration difference between inspiration and expiration in the “completed” group and the “abandoned” group in the first 2 minutes without tube connection, from minute 2 to minute 4 orally connected to an endotracheal tube of 5mm internal diameter, from minute 4 to minute 6 connected to a 4mm tube, from minute 6 to minute 8 connected to a 3mm tube and from minute 8 to minute 10 connected to a 2mm tube.

Panel A displays acceleration sensor measurements in abdominal wall position of the “completed” group.

Panel B displays acceleration sensor measurements in abdominal wall position of the “abandoned” group.

Panel C displays acceleration sensor measurements in thoracic wall position of the “completed” group.

Panel D displays acceleration sensor measurements in thoracic wall position of the “abandoned” group.

Data are displayed as means of artificial units ± CI.

Discussion:

5. The authors show that increased workload lead to changes in abdominal wall movement. Possible explanations were included into the discussion. Additionally no changes in thoracic wall movement were reported. The explanation of this finding is missing. Please add an explanation of this fact into the

Answer: Your statement that an explanation of the missing thoracic wall movement is missing is right. We added a possible explanation of this nonexistent thoracic movement into the discussion- section:

“In our measurements, we also found no movement in the thoracic wall during increase workload. A possible explanation of this fact could be a different force of the thoracic wall compared with the abdominal wall during the attempt to compensate an increased respiratory resistance. It could be suggested that the breathing support by abdominal wall muscles has a higher impact than the thoracic muscles.”
6. The authors mention that "Especially after thoracic and abdominal surgery the respiratory function is hampered due to interventional changes [10, 11]." And "In contrast to recent and/or established methods to assess the respiratory muscle function we investigated a non-invasive, economical and practical approach that demonstrates the valid detection of breathing excursions by accelerator sensors in presence of gradually increased airway resistance."

Most probably behavior of thoracic and abdominal excursions are completely different after a) thoracic or b) abdominal surgery and c) in healthy persons. Even more, the type of thoracic surgery (thoracotomy, sternotomy) will have a different response. Please comment!

Answer: Thank you for this important hint. We added your arguments to the limitations section.

“Especially different surgical approaches, e.g. thoracic or abdominal surgery, may have a significant and independent impact on the ratio of abdominal to thoracic breathing excursions and may differ from our findings in healthy volunteers, who did not undergo any surgery.”

In conclusion, if the authors can comment sufficiently to the aforementioned remarks the manuscript would introduce a new and interesting non-invasive approach to predict respiratory failure.