Author's response to reviews

Title: A Prospective Study To Evaluate The Accuracy Of Pulse Power Analysis To Monitor Cardiac Output In Critically Ill Patients.

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Version: 2 Date: 28 June 2007

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Dear Editor

Re: 'A Prospective Study To Evaluate The Accuracy Of Pulse Power Analysis To Monitor Cardiac Output In Critically Ill Patients.'

We would like to thank the reviewers for their obvious hard work that they have put into our manuscript. There points have helped to significantly improve our paper. We feel that we have agreed and changed the paper accordingly with all of their comments. We feel that our paper is important to all clinicians who utilize these forms of cardiac output monitoring and is therefore worthy of publication in your journal.

With kind regards
"This study, therefore seeks to investigate the duration that the two methods remain sufficiently similar to be acceptable for clinical use."

The authors have previously stated that "the calibration will be valid so long as there are no significant changes in the haemodynamic status of the patients". I agree that it is prudent to check the calibration of PulseCO at regular intervals. However, it is not the duration of use, per se, that influences accuracy - it is changes in the state of the patient, and these are more likely to occur in longer periods of time. A recommendation for recalibration based only upon time does not seem sufficient.

We agree entirely with what the reviewer has stated in this comment, and have amended our manuscript accordingly. However it is important to realize that for the routine use of these devices some recommendations with regards time intervals between calibrations must be made. Although this is not absolutely scientifically correct, it is absolutely necessary for normal practice. This is in deed exactly what the manufacturers of this device now do.

"Comparison between these measurements was performed by linear regression analysis and the technique described by Bland and Altman [8]."

This is a fundamental error: the wrong variables are being compared. PulseCO estimates changes in cardiac output (absolute values being displayed after calibration). Therefore, changes in cardiac output estimated by LiDCO and by PulseCO should be compared - not the absolute values. Preferably, proportional changes should be assessed because a change from 2-4L/min is more clinically significant than a change from 12-14L/min.

In figure 1, the correlation coefficients are high because of the large variation in cardiac output between different patients rather that within individual subjects. The method of analysis used by the authors can yield 'good results' even with artificial PulseCO data, where changes in cardiac output have been generated randomly with a computer. See - Br J Anaesth 2002; 89: 336-9
Although the reviewer is strictly correct that this monitor measures changes in cardiac output, this is not how it is used widely around the world, or how it is marketed by the company that makes it. It is sold as a monitor of cardiac output and this is what we have tested. We have used the same statistical analysis as many if not all previous authors in this field including some of the reviewers of this article own work. We feel that it is difficult to simply analyze changes in the variable between two different machines each with their own inherent error, as this is not possible without knowing the exact precision of the reference technique in order to understand the ability of the reference to reliably detect a change. As this work has never been published, the analysis is not possible. We have adjusted the manuscript to acknowledge these points.

Is there sufficient good quality data?

We acknowledge that our data set is not big, although interestingly it is larger than many previous published studies. We have observed a problem with the system in 14 patients- this is what we are reporting. The problem if true is very clinically relevant. It is for other authors to confirm or refute our findings, perhaps in larger groups of patients. We have amended the manuscript to reinforce these points.

"The LiDCOplus monitor (LiDCO, Cambridge, UK) is a device that combines a pulse power algorithm (PulseCO) with an independent form of calibrating the pulse power algorithm via lithium dilution (LiDCO) [7]." Reference [7] does not contain any information about the "pulse power algorithm". Please include an appropriate reference.

This has been changed appropriately.

"This error rate was quantified by dividing twice the standard deviation of the bias by the mean cardiac output for both techniques."

The bias is the mean of the differences. Did you intend: "This error rate was quantified by dividing the twice the standard deviation of the differences by the mean cardiac output for both techniques."

We have checked our wording and ensured that it is correct.

"It has been demonstrated to be accurate so long as recalibration is performed whenever there is major haemodynamic change [1-6]." References [2] and [5] are the same. They showed that the method was grossly inaccurate after phenylephrine infusion.
This has been changed to correct the error.

"At baseline the PulseCO was calibrated using the lithium dilution technique as previously described and according to manufacturer's instructions [9]."

Reference [9] is a study on children and the dose of lithium was not always 0.3 mmol.

This has been corrected in the manuscript.

Reviewer 2

The heterogeneity of the population studied, especially regarding age and pathologies, might compromise the results obtained in consideration of the different vascular tone of these patients. Can the Authors better underline these differences? Authors have to stress the concept that results must be confirmed and actually have to be taken prudentially.

in the Abstract line 10: indwelling instead of in-dwelling

in the Background line 16: veterinary instead of vetinary

in the Discussion: Title: Discussion instead of Conclusions

All of these points have been corrected in the manuscript.

Reviewer 3

Although the bias is good, the precision between the two techniques is poor, especially as the techniques were calibrated together as little as one hour prior to the first comparator measurements being taken. The authors comment "there was considerable variability in these changes between patients and overall the percentage errors tended to increase in individual patients over time" - I agree and feel this point needs to be stressed both in the abstract and covered in the discussion. This individual variation is 'diluted' by averaging all the values taken at each timepoint - this highlights a problem with the Bland-Altman technique i.e. if neither technique consistently over- or under-estimates, then the bias will be good. Even though the precision is poor, this also does not reflect changes over time in the individual patient.

We fully agree with this point and have altered the manuscript accordingly.

There are numerous grammatical and spelling mistakes and typos that will need
correcting.

We thank the reviewer for pointing this out and have corrected the paper as appropriate.

Abstract Concluding paragraph: I'm not sure 'accurate and precise' are the correct descriptors that should be used to describe the agreement between LiDCO and the pulse power algorithm when limits of agreement average 27%. 'Acceptable' is probably a better term, as is used in the last sentence of page 4. However, the weak ability to monitor changes in the individual patient should be mentioned.

We accept this point and have changed the paper where appropriate.

P12: "Until further data become available we would recommend re-calibration is performed utilizing at least two lithium dilution curves in order to reduce variability in the technique and improve accuracy" - this may indeed be the case but it cannot be a recommendation in the absence of any data from the authors to verify this does improve accuracy.

We accept this point and have changed the conclusions to go along with the reviewers point of view.