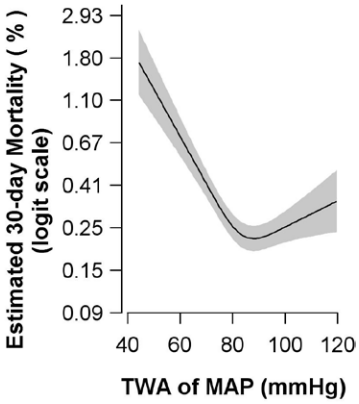

Fig. 3. Estimated mortality for time weighted average (TWA) of mean arterial pressure (MAP). The figure shows that estimated mortality decreased to MAP of 80 mmHg and then increased sharply at lower pressures. Reprinted with permission from Anesthesiology.[2] Copyright 2015, American Society of Anesthesiologists, published by Wolters Kluwer.

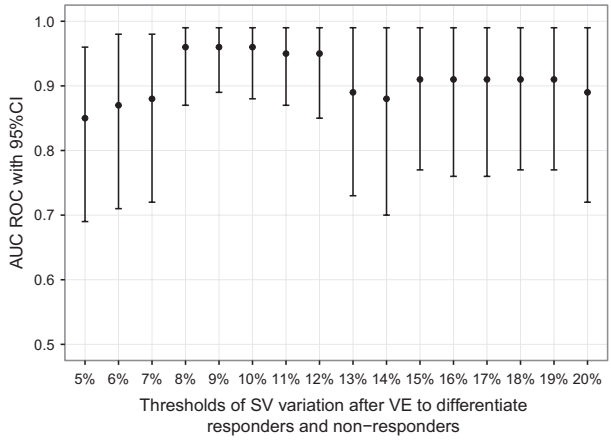

Fig. 1. Relationship between the areas under the receiver operating characteristic (AUC ROC) curves (*points*) with 95% CI (*error bars*) of the lung recruitment maneuver and the thresholds of stroke volume (SV) variation after volume expansion (VE) between 5% and 20% to differentiate between responders and nonresponders.

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Diagnostic Accuracy Studies: The Methodologic Approach Matters!

To the Editor:

With regard to the recent Anesthesiology article by Biais *et al.*,[1] we acknowledge the overall quality of the report and consider the relevancy of the topic of underlying research. However, we have found several methodologic concerns that we would like to address.

First, Standards for Reporting Diagnostic Accuracy Studies have been developed as a list of items[2,3] that contribute to the completeness, transparency, and quality of reporting of diagnostic accuracy studies. We found that key items were lacking in the study from Biais *et al.*[1] The study should have included a degree of blinding that describes whether clinical information and index test results were available to the assessors of the reference standard. A flow diagram is also required to evaluate the risk of selection bias. The reproducibility of the index test and the reference standard should also have been reported. Moreover, the studies cited in the article that support the rationale of the reference standard and its cutoff do not to support an increase of 10% of stroke volume after volume expansion measured by proAQT (Pulsion Medical Systems, Germany) that defined fluid responders.

Second, the threshold to differentiate between responders and nonresponders should be chosen above and close to the least significant change (LSC) of the stroke volume measurement by their considered device. The LSC is defined as the minimum change that can be recognized as a significant change, not a measurement of random variation. Although LSC has been reported previously with transpulmonary thermodilution,[4] no data were reported using the proAQT system. Therefore, LSC for the proAQT system should have been calculated and reported by the authors. Because there was no threshold of stroke volume variation after a volume expansion to differentiate responders and nonresponders that can be supported by a solid clinical or physiologic background, another strategy would have been to provide data for several thresholds.[5] To address this last point, we collected data of the scatterplot given in figure 2 of the article by Biais *et al.*[1] using the software ImageJ (https://imagej.nih.gov/; open source, National Institutes of Health, Bethesda, Maryland). This allowed us to recover raw data of variations of stroke volume after lung recruitment maneuver and after volume expansion and enabled us to perform subsequent analysis. We explored 16 thresholds between 5% and 20% using the R software and pROC package (https://www.r-project.org/; R-3.3.0; accessed May 3, 2016). We computed 95% CI using the bootstrap technique with thousand repetitions. In our point of view, the area under the receiver operating characteristic curve was overestimated with the chosen threshold of 10% (fig. 1). Because the threshold increases beyond the LSC of the measurement system, the area under the receiver

operating characteristic curve should remain constant or increase with the threshold, which was not the case in the study by Biais *et al.*[1] For all of these reasons, we strongly suspect that some recruitment biases could have occurred.

Finally, some studies have previously evaluated the diagnostic accuracy of a transient positive end-expiratory pressure elevation, identified as a recruitment maneuver, to diagnose preload responsiveness. Such diagnostic approaches were similar to those proposed by the authors and should have been discussed.[6–8] Diagnostic studies are at a high risk for biases,[9] and the methodologic considerations above highlight a risk of bias in the study by Biais *et al.*[1]

Competing Interests

The authors declare no competing interests.

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In Reply:

We thank Dr. Jacquet-Lagrèze *et al.* for their interest in our recent article[1] and are happy to respond to their comments.

We fully agree with Dr. Jacquet-Lagrèze *et al.* on the pivotal value of Standards for Reporting Diagnostic Accuracy Studies[2] to improve the quality of diagnostic accuracy studies. As clearly mentioned in the article, inclusions were conducted over a 1-yr period among nonconsecutive patients, and only 28 patients were included. As stated in the Discussion section, we therefore cannot exclude the possibility of selection bias.

We respectfully fully disagree with Dr. Jacquet-Lagrèze *et al.* when they claimed that the studies cited in the article do not support the rationale to define responders to volume expansion as an increase of stroke volume of 10% or more. We invite the authors to read these recommendations[3,4] carefully and many other publications on the subject.[5]

The least significant change has not been yet evaluated for proAQT system (Pulsion Medical Systems, Feldkirchen, Germany). However, the algorithm for pulse contour analysis of the proAQT system is the same as that of the PiCCO system (Pulsion Medical Systems). The main difference between these two devices lies in cardiac output calibration (*i.e.*, transpulmonary thermodilution for the PiCCO and specific algorithm without external method for the proAQT system). Previous studies demonstrated that the proAQT pulse contour analysis algorithm was able to detect changes in cardiac output as small as 5.0% during an end-expiratory occlusion test,[6] 10.0% during a passive leg raising test,[7] 9.5% during a respiratory cycle,[8] and, even more recently, 6.0% during a mini-fluid challenge.[9] Although we fully concur with the authors that additional research is warranted, our data remain nevertheless in line with most recent literature.

Finally, we apologize to the authors for having omitted some significant contributions. However, most of them were unavailable at the time of the submission process without, from our point of view, providing added value (postoperative setting, positive end expiratory pressure elevation in septic patients, mean arterial pressure monitoring, pulmonary elimination of carbon dioxide, *etc.*).

Competing Interests

Dr. Biais received honoraria from Edwards Lifesciences (Irvine, California) and Pulsion Medical Systems (Feldkirchen, Germany) as a lecturer. Dr. Futier received honoraria from Dräger AG (Lübeck, Germany), GE Healthcare (Little Chalfont, United Kingdom), and Fresenius Kabi (Bad Homburg vor der Höhe, Germany) as a lecturer and travel reimbursement by Fisher & Paykel Healthcare (Auckland, New Zealand). The other authors declare no competing interests.

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