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Why the Gray Zone May Shift within the Fog

To the Editor:

We read the article by Cannesson[1] *et al.* and the accompanying editorial[2] with great interest, and praise the effort to better define the clinical utility and applicability of pulse pressure variation (PPV), not only as a tool to predict volume responsiveness but also to move away from a single-threshold value for conducting intraoperative volume optimization and perioperative goal-directed fluid therapy. We would like to make three points.

First, the most commonly used index to assess volume responsiveness, by far in the United States, appears to be stroke volume variation (SVV). Although the area under the receiver-operating curve, in systematic reviews,[3] shows that both PPV and SVV have excellent sensitivity and specificity in patients who are mechanically ventilated with normal tidal volumes and in a regular sinus rhythm, the threshold values discriminating between fluid responders and nonresponders are not the same for these two parameters.[3,4] Thus, although strategies using the "gray zone approach" applied to PPV identify a range of values where volume responsiveness cannot reliably be predicted, this range may not be applicable when SVV is used for determining volume responsiveness. Although it is clear from the work of Joseph Erlanger, the father of the pulse pressure concept,[5] that pulse pressure in man is proportional to left ventricular stroke volume (depending both on arterial tone and cardiac contractility) it is plausible that variations in pulse pressure may also be proportional to variations in stroke volume. To the extent that PPV and SVV are affected differently by changes in arterial tone, given the same degree of volume responsiveness,[4] these values may lose their direct proportionality as vascular tone changes. Pinsky described the potential utility of a SVV-to-PPV ratio to reflect ventricular-arterial coupling that might be helpful when extrapolating PPV threshold data to SVV.[6] Overall, applying PPV's "gray zone" to SVV seems clinically appealing but may be misleading. The "gray zone" defined for PPV should not *simply* be applied to patients who are being optimized using stroke volume variation. The "gray zone" for SVV requires its own definition.

Second, the paper does not address the issue of volume responsiveness *versus* needing to give volume or using a dynamic index to actively restrict fluids or to administer diuretics to patients under certain clinical circumstances. That is, not all patients who are volume responsive require volume therapy. Conversely, there may be untapped utility for SVV- and/or PPV-guided fluid restriction and diuretic use (consider patients with acute lung injury or acute respiratory distress syndrome).[7] The goal would be to identify patients with a PPV that is "too low" who, consequently, should receive restrictive fluid therapy or diuretics.

Third, what is, perhaps, not considered by the author[2] is the fact that PPV goals may vary within individual patients across changing clinical settings in relatively short intervals of time, such as during single lung ventilation for thoracic surgery, laparoscopic pneumoperitoneum, and conditions of pathologic intraabdominal hypertension. For example, the goals for intraoperative PPV during esophagectomy vary during the case, such that the goal during the abdominal part of the procedure is fluid liberal and during the thoracic part of the procedure is fluid restrictive.[8]

In summary, we praise Cannesson *et al.*[1] for their work and we agree that there is a "gray zone" well represented by the picture in the editorial[2] (*i.e.*, the Golden Gate Bridge with fog going across the middle represents "a static view of dynamic indices"). We contend that PPV and SVV "gray zones" are probably better described as the view one gets of the Golden Gate Bridge, with fog going across the middle as one is driving along winding hilly roads. This is a "dynamic view of dynamic indices," such that the gray zone changes at different times depending on one's changing vantage point, an analogy closer to clinical reality.

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This letter and the related letters below were sent to the author of the above-mentioned editorial. The author declined to respond.—James C. Eisenach, M.D., Editor-in-Chief

Drs. Bloomstone and McGee are on the Speakers Bureau of Edwards LifeSciences, Irvine, California. This company manufactures the FloTrac-Vigileo/EV1000 pulse contour analysis system. In addition, the company manufactures the Swan-Ganz Catheter with CCO and the Vigilance monitor.

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How Accurate Is Pulse Pressure Variation as a Predictor of Fluid Responsiveness?

To the Editor:

We read with interest the Perioperative Medicine article "Assessing the Diagnostic Accuracy of Pulse Pressure Variations for the Prediction of Fluid Responsiveness: A 'Gray Zone' Approach" by Cannesson *et al.*[1] and its accompanying editorial: "Insights in a 'Gray Zone.'"[2]

Fluid responsiveness is based on the proposition that an increase in cardiac output by at least a certain amount may be achieved by a specific bolus of a specified fluid, whereas nonresponders will require other means to increase the cardiac output. There are a number of limitations with this definition. The type of fluid used will have an impact on the amount of expansion of the intravascular compartment. In the study, iso-oncotic colloid was used, but even the volume effect of this will depend on the volume status of the patient (context sensitive).[3] Associated with this is the fact that the endothelial glycocalyx is degraded by the release of cytokines during surgery or the release of atrial naturietic peptide caused by hypervolemia.[4] The minimally required increase in cardiac output will have a direct impact on the size of the "gray zone," as was demonstrated in the study, and the utility of bolus fluid therapy has been questioned following the publication of the Feast trial.[5] Fluid responsiveness assessed by pulse pressure variation cannot distinguish between an increase in variation caused by fluid loss from that caused by vasodilation.

The concept of pulse pressure variation is closely related to the respiratory cycle and changes in pleural pressure. Pleural pressure changes are impacted by either smaller tidal volumes or poor lung compliance. As an extreme example, high-frequency oscillation ventilation results in minimal pulse pressure variation irrespective of the volume status of the patient. For patients within the "gray zone," increasing the tidal volume may increase the pulse pressure variation indicating fluid responsiveness.

Although it may be reasonable to give a fluid bolus to patients above the upper limit of the gray zone, a knowledge of the cardiac output is extremely useful to make an informed decision on treatment for patients in or below the gray zone and avoid overloading the interstitial space with fluids. Lichtenstein[6] has suggested that transthoracic ultrasound of the lungs may be useful in the early detection of interstitial syndrome (because of fluid overload, cardiac failure, or increased capillary permeability) by observing a change from A-line predominance to B-line predominance.

There are several limitations of the study that may make it difficult to apply to a more general population, including the male predominance in the study (75%) and the selection of mainly cardiac or abdominal aortic surgery (88%) with only 22% being general surgery.

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The "Gray Zone Approach": Assessing the Accuracy of Pulse Pressure Variation without Considering the Prevalence?

To the Editor:

We read with great interest the article of Cannesson *et al.*[1] regarding the accuracy of pulse pressure variation monitoring to predict fluid responsiveness. We applaud the introduction of "misclassification cost" as a novel approach to evaluate the clinical utility of a widely advocated monitoring technique.