

may cancel each other. Other factors that may theoretically influence the SPV are the arterial elastance and the presence of vasoactive drugs. However, Tavernier *et al.*¹ showed for the first time that the SPV is a useful parameter for a wide range of systemic vascular resistances and drug therapy.

Using the tidal volume as a challenge of the cardiovascular system enables the clinician to easily measure dynamic parameters that reflect volume status and predict the response to volume load. Such true linkage of ventilator and monitor should be automated in the future, possibly contributing to a reduced use of more invasive or expensive, or both, monitoring techniques.

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Blood Volume Measurement

The Next Intraoperative Monitor?

THIS month's issue of *ANESTHESIOLOGY* features two independent investigations of a new method for measuring circulating blood volume (CBV) at the bedside. In Haruna *et al.*¹ and Iijima *et al.*² the new noninvasive method of pulse dye densitometry is postulated as a more practical alternative to traditional measurements of blood volume. This method is "seminoninvasive" be-

cause it necessitates the intravenous injection of indocyanine green dye for each CBV measurement. Indocyanine green dye is rapidly distributed to the circulating compartment and then eliminated by the liver within approximately 20 min. The pulse dye densitometer measures circulating dye concentration *versus* time using two-wavelength light absorption, similar to pulse oximetry. (One of the coauthors is the original inventor of the pulse oximeter: Takuo Aoyagi) The dye elimination curve is back-extrapolated to the "first-pass" time, and the blood volume is calculated as the total dye dose divided by the initial concentration.

In both studies, the new method is compared with two "gold-standard" methods, one of which involves injection of radioactive iodine-labeled albumin. The goal is to compare simultaneous measurements of CBV using the new and old methods and decide whether the new dye method can replace the old gold standard. This is the format of a typical methods comparison study. Whenever we read a methods comparison study, we should

This Editorial View accompanies the following articles: Haruna M, Kumon N, Yahagi N, Watanabe Y, Ishida Y, Kobayashi N, Aoyagi T: Blood volume measurement at the bedside using ICG pulse spectrophotometry. *ANESTHESIOLOGY* 1998; 89:1322-8; and Iijima T, Iwao Y, Sankawa H: Circulating blood volume measured by pulse dye densitometry: Comparison with ¹³¹I-HSA analysis. *ANESTHESIOLOGY* 1998; 89:1329-35.

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EDITORIAL VIEWS

ask three questions: (1) What is the nature and accuracy of the gold standard? (2) Are the two methods compared by the proper statistical methods? (3) Do I really want to know the values of the variable being measured? We shall look at each of these questions in turn.

The first question regarding the accuracy of the gold standard method should be the easiest to answer, yet it is often ignored. Haruna *et al.*¹ and Iijima *et al.*² both make general reference to the uncertainty of the radioactive tracer technique, but neither provides a quantitative assessment of its accuracy. This common problem in methods comparison studies is not always the fault of the authors. We often accept as gold standards measurement methods in which accuracy is not well known or documented.

As to the second question, methods comparison studies suffer from widespread use of inappropriate statistical methods. The most common is the use of the correlation coefficient, or *r* value, as a measure of agreement. The correlation coefficient measures the degree of association of two independent variables. For example, it would be appropriate to measure the correlation of weight with daily caloric intake. However, in a methods comparison study we are comparing two measurements of the same variable. It is obvious that the two measurements will be highly associated, but the correlation coefficient does not really tell us how well they agree. Correlation depends strongly on the range of values included in the data. If we compare two methods of measuring blood volume and if all of the data are clustered near the same CBV value, the correlation will be low, despite good agreement of the methods. Iijima *et al.*² and Haruna *et al.*¹ both present correlation coefficients, which can only add confusion to the interpretation of their data.

What are the right statistics for methods comparison studies? The most logical and popular is the bias and precision method, as described by Altman and Bland.³ *Bias* is defined as the mean error, or average, of the difference between simultaneous measurements by the two methods. The *precision* is the standard deviation of these differences. I have suggested that the latter should be called "imprecision" because the larger its value, the less precise the measurement. Bias measures the systematic error or tendency of one method to read consistently higher or lower than the other. Imprecision measures the random error or lack of reproducibility of the measurements. Iijima *et al.*² and Haruna *et al.*¹ have presented bias and imprecision values, both in terms of absolute values (liters of blood volume) and percentage

errors. This must be clear to the reader: The *absolute bias* is the average of the differences between the two measurements, in liters, whereas the *percentage bias* is the average of the percentage differences between the two measurements.

Although bias and imprecision are useful statistics, they often do not tell the whole story. What if the new method tends to underestimate at low values and overestimate at high values? Depending on the range of our data values, the bias could be zero, with the positive and negative errors canceling out. Yet there is clearly a systematic error at play. For this reason, bias and imprecision alone are not sufficient to describe agreement; we must see a plot of the raw data. A very useful form is the "bias plot," as described by Altman and Bland.³ Here we plot the differences between the two methods *versus* their mean. Iijima *et al.*² show bias plots in their figures 2, 3, 4, and 5, although they plot the measurement differences *versus* the gold standard values rather than the mean of the two. Unfortunately, Haruna *et al.*¹ show no data plots. Consider figure 4A in Iijima *et al.*² This bias plot shows a slight tendency (perhaps insignificant because of the small number of data points) to exhibit positive errors at low CBV and negative errors at high CBV. This is the type of important information that will be missed without presentation of the raw data.

And now to the final question: Do we really care? That is, is the noninvasive measurement of blood volume something that should be of interest to the clinical anesthesiologist? Circulating blood volume would be another new variable to add to our monitoring armamentarium. Each time technology presents a new variable for inclusion in the increasing complex "instrument panel" of the anesthesiologist, we should ask whether this variable provides information that is (1) distinct from that which we already have and (2) important to us in that it can affect patient treatment. Regarding the first, CBV is arguably distinct from all current hemodynamic variables. It is related to preload, which we estimate in a number of ways, but it is also different. For example, a septic patient can have constant CBV despite decreasing preload. Conversely, a trauma patient who is slowly exsanguinating can maintain constant preload until he has lost much of his CBV. In fact, Shoemaker⁴ has shown, in critically ill patients, that CBV is very poorly correlated with other hemodynamic variables, including hematocrit, CVP, pulmonary artery wedge pressure, mean arterial pressure, and heart rate. Thus, the information presented by CBV satisfies the test of being new and distinct.

The final question is as follows: How would CBV data obtained every 20 min (the limitation of the proposed test) influence patient management? Consider again the young, previously healthy, trauma patient with an occult intraabdominal hemorrhage. Cardiac preload, as determined by either right- or left-sided filling pressures or even transesophageal echocardiography, can remain nearly constant because of sympathetic compensation for volume loss.⁴ When the limits of this compensation finally are exceeded (blood loss of 25% or more), the patient may rapidly become profoundly hypotensive and "crash." Presumably, sampling CBV every 20 min would detect the downward volume trend well before this hemodynamic decompensation. In this case then, CBV monitoring would change patient treatment. Many other realistic examples can be easily developed.

My conclusion is that CBV monitoring, if sufficiently practical and accurate, may be a useful addition to our monitoring repertoire and could affect patient treatment and therefore outcome. The two articles presented in this issue are a real step toward the development of such a monitoring method. The next questions to be an-

swered are as follows: How accurate must CBV monitoring be and can this dye-dilution technique meet our clinical requirements? That should be the subject of further studies.

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