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EDITORIALS

Academic assessment of arterial pulse contour analysis: missing the forest for the trees?

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In this issue of the *British Journal of Anaesthesiology*, Montenij and colleagues[1] provide a thoughtful review of analytic methods for comparing cardiac output measurement methods, with focus on arterial pulse contour analysis methods that are intended to measure cardiac output. This review is a welcome addition to the literature, as such comparative investigations are commonplace, and often without optimal rigor.

At the same time, I hold a concern about another deficiency in pulse contour investigations. Despite 414 'pulse contour' AND 'cardiac output' articles currently indexed by PubMed, a century of academic reports describing various pulse contour methods[2] and decades of commercial sales, it remains uncertain whether pulse contour methods provide more sensitive and specific indicators about circulatory decompensation than routine use of blood pressure (bp) and heart rate monitoring – let alone whether such technology leads to improved patient outcomes. It can be argued that conducting future studies that continue to merely compare one cardiac output measurement technique against another, risks missing the forest for the trees.

To be sure, management of the tenuous patient – stable but with minimal physiological reserve, and with a high risk of decompensation, as might occur after haematemesis from esophageal varices, or during an invasive procedure – is a challenge. The vigilant clinician monitors tenuous patients carefully, to respond to any deterioration while avoiding unnecessary and excessive intervention. A conundrum may occur when the arterial bp drifts down, which might indicate deterioration, such as new, dangerous blood losses. Yet as often as not, this is relatively benign, a lessening of vasoconstriction as the patient becomes more relaxed as a result of medication or time. The vigilant clinician must distinguish between these two very different physiological circumstances, and the stakes are high. Accordingly, there has been interest in techniques for non-invasive monitoring cardiac output, such as pulse contour analysis, as cardiac output is a cardinal metric of circulatory adequacy and, as the dividend of the bp–to–central venous pressure gradient, also yields total peripheral resistance (TPR), a measure of vasoconstriction.[3]

If pulse contour analysis for measuring cardiac output is truly reliable, then it should be uniformly used as the standard-of-care for tenuous patients. If the technique is inaccurate, then it is only an illusion that the patient's cardiac output and vascular tone are being carefully monitored, unreliable information that gives a false – and possibly dangerous – sense of security when managing tenuous patients.

The rationale behind pulse contour analysis

For a masterly treatment of the principles underlying pulse contour analysis, one may consult the textbook 'McDonald's Blood Flow in Arteries'.[4] The vast majority of pulse contour methods estimate volumetric flow in the aortic root, which equals cardiac output. As a matter of basic physics, note that it is not the pressure wave but the *pressure gradient* that impels fluid to flow in blood vessels. In other words, it is the *difference* of pressures in a segment of artery, upstream vs downstream, that accelerates/decelerates the pulsatile blood within that segment. It is simply

impossible to compute flow with only one pressure wave: computing the gradient cannot be done precisely without a second pressure measurement. Most pulse contour methods address this conundrum by relying on probabilistic relationships between the upstream pressure wave and the downstream pressure wave. For instance, one method of calculating flow would be to assume that the downstream pressure waveform is similar to the upstream pressure, aside from a small time delay. From this assumption, pressure gradients can be estimated and flow computed.

The first challenge for pulse contour analysis is that the downstream waveform is not, in fact, the same shape as the upstream waveform, because the entire pressure waveform is not wholly moving downstream. Instead, there is a primary wave moving downstream, while there are smaller pressure waves that move upstream: reflected pressure waves from distal vascular junctures that travel in the retrograde direction. These reflected waves increase the amplitude of an arterial waveform, but they actually create retrograde pressure gradients that decelerate the blood and retard flow. Larger bp waveforms do not always correspond to greater forward flow! This is one fundamental challenge to pulse contour analysis, and different pulse contour methods use different techniques, usually statistical corrections based on either patient characteristics or some property of the shape of the bp waveform, to try to circumvent this complication.

There is a second challenge. While the gradient of pressure determines the magnitude of acceleration/deceleration, it is the diameter of the vessel that dictates the actual volume of blood. Pulse contour methods must use some technique to address this complication, such as a calibration of volume against another reference, or relying on probabilistic relationships between age and gender and the likely size and pulsatile compliance of the arterial vessel.

There is also a third major analytic challenge. It is only within the aortic root that flow equals cardiac output, whereas the arterial waveform is usually measured somewhere in the periphery. Pulse contour methods must use some technique to estimate flow in the proximal aorta using a pressure waveform measured in the periphery. Again, a common approach is to use probabilistic relationships between those waveforms. (One approach is to use a generalized transfer function, which is a mathematical manipulation based entirely on probabilistic relationships between peripheral and central waveforms[5]).

The crux of the matter

There is indeed a physical causal relationship between the arterial pressure waveform and cardiac output. However, taking the three analytic challenges together, it is also clear than quantifying cardiac output from pulse contour analysis must rely on probabilistic relationships (e.g. the *likely relationship* between the central and peripheral arterial waveform; the *likely relationship* between the patient's age, gender, etc. and the size and compliance of the patient's aorta; or the *likely relationship* between the upstream and downstream pressure waves that determine the flow-determining pressure gradient). These 'likely relationships' are purely probabilistic; they are observed in the majority of cases, but not all cases. Conceptually, it is no different from relying on a patient's weight to estimate her height: a reasonable estimate can be made for many individuals, but there is likely a subset for whom the relationship will be invalid. Which means that the estimated cardiac output by pulse contour may be accurate, except when it isn't.

This doesn't invalidate pulse contour analysis. We clinicians are accustomed to relying on probabilistic relationships when we assess our patients' haemodynamics. When mean arterial pressure (MAP) is falling, we know that it typically represents failing circulation. Or when the patient has a large pulse pressure, we assume that the patient probably has a large stroke volume. Yet sometimes these probabilistic relationships are invalid (e.g. patients with low MAP who are not in shock but are merely vasodilated). It is because our routine measures, such as MAP and pulse pressure, can be clinically ambiguous that we seek superior, less ambiguous non-invasive measures.

Returning to pulse contour analysis: the motivation to incorporate this technology into our practice is because we know that routine bp is not always reliable in assessing circulatory state. Yet pulse contour cardiac output also relies on a set of probabilistic relationships that may be invalid for some subset of clinical situations. Is pulse contour analysis superior to routine vital signs monitoring? Or does it provide false reassurance by continuously displaying a cardiac output estimate that is not always reliable? Is it indeed superior to routine monitoring? In my opinion, after more than several decades, this question is not answered.

Open questions within the literature

The academic literature regarding pulse contour analysis is dominated by method comparison studies (i.e. comparing cardiac output from pulse contour analysis vs a reference method). Method comparison studies do not answer the following question: 'should I use technology X for patient Y.' The emphasis on '95% confidence intervals' can mask serious problems that can occur under certain circumstances: pulse contour method, overly reliant on probabilistic relationships, might yield wildly and systematically inaccurate cardiac output in a subset of patients with atypical physical or physiological properties. Focus on the majority of cases who, by definition, fall within the 95% confidence interval, and treating errors as if they are just 'random', means that major failures of these techniques are treated as nothing more than 'outliers' (i.e. unpredictable statistical flukes).

Yet it is very possible that pulse contour analysis fails in a predictable way under predictable conditions (and those conditions may or may not be commonplace in any given published study). It would be valuable to determine if there are patients in whom pulse contour analysis predictably fails so that we may learn the most about the technologies' true capabilities and pitfalls. Consider pulse oximetry, by analogy: we know not to rely on pulse oximetry if there are haemoglobinopathies or after methylene blue, and we know it is less reliable given poor skin perfusion or bright ambient lights. We must focus on defining any non-random sources of error for each and every investigational cardiac output method that we hope to use on patients.

Method comparison studies[1] are only a rudimentary way of assessing pulse contour analysis. Other essential questions include, how frequently does clinical management change when guided by pulse contour analysis rather than routine monitoring, and are overall prospective outcomes improved? Or, can pulse contour analysis predict the patient's future physiological state better than routine methods involving bp and heart rate alone? (A useful schema for diagnostic test assessment includes technical efficacy, diagnostic accuracy efficacy, diagnostic thinking efficacy, therapeutic efficacy, clinical outcome efficacy, and societal efficacy[6]).