Minimally invasive cardiac output monitoring: what evidence do we need?

M. Chikhani and I. K. Moppett*

Division of Anaesthesia and Intensive Care, University of Nottingham, Queen’s Medical Centre Campus, Nottingham University Hospitals NHS Trust, Nottingham NG7 2UH, UK

* E-mail: iain.moppett@nottingham.ac.uk

Minimally invasive cardiac output monitoring is a hot topic. Recent articles have been published in the British Journal of Anaesthesia and elsewhere attesting to its safety, questioning its validity, and using minimally invasive monitoring in clinical trials. Studies have demonstrated that less-invasive cardiac output monitoring combined with a goal-directed fluid administration protocol is associated with favourable perioperative outcomes in surgical patients deemed to be at high risk of morbidity and mortality.1–4 Recommendations from the Enhanced Recovery after Surgery Group have included specific reference to perioperative fluid optimization with respect to goal-directed targets in high-risk patients.5–6 Despite these studies, questions remain about the role of minimally invasive monitoring. What message can anaesthetists take from these studies?

First, is this monitoring technique valid? Central to this question is what the monitor is supposed to be measuring. In broad terms, the monitors all aim to estimate stroke volume, either as an absolute value or in terms of relative changes. In addition, some use derived indices to predict whether stroke volume is likely to increase in response to a fluid challenge. In clinical practice, however, the clinician is really more interested in what the appropriate treatment should be for a particular patient, rather than stroke volume per se. There is no single best method for validating minimally invasive cardiac output monitoring and recent articles demonstrate the different approaches. Reisner and colleagues7 have compared, in an elegant study, different approaches to estimation of stroke volume using graded lower body negative pressure (LBNP) to simulate haemorrhagic hypovolaemia in healthy volunteers. Their results are moderately reassuring. Each of the techniques demonstrated a progressive reduction in stroke volume with increasingly negative LBNP. On release, the stroke volume returned to baseline with both bioimpedence and the relatively newly described long-time interval analysis of the arterial pressure waveform. Modelflow, the technique used by the non-invasive Finometer, failed to return to baseline after release of LBNP, suggesting that some part of its algorithm is sensitive to a factor not related to stroke volume. However, these results need to be taken in context. LBNP is only a model for haemorrhagic hypovolaemia and the study was performed in healthy volunteers. The clinical scenario is rather more complicated, with vasoactive drugs, ongoing resuscitation, and acute and chronic comorbidities all contributing.

Paarmann and colleagues8 have taken a more traditional approach to validation; a new technique, in this case the ‘pressure recording analytical method’ (PRAM) is compared in relatively stable clinical conditions with the gold standard (thermodilution measurement of cardiac output). On the basis of the Bland–Altman analysis of measured stroke volume, they conclude that PRAM and thermodilution cardiac output are not interchangeable. However, it may again not be so simple. What is not reported is the response to interventions, particularly fluids, which is clinically more relevant. By and large, anaesthetists and critical care physicians are much more interested in the dynamic response to intervention than any absolute values. This study gives us more information about the validity of PRAM but does not answer the question of its clinical utility. Numerous previous studies have questioned the accuracy of different minimally invasive techniques, but few have addressed whether the monitors will provide appropriate information to guide clinical management in the real world. Future studies could usefully provide data on the sensitivity, specificity, and positive and negative predictive values of observed changes in stroke volume. It is important to note that the studies which report the degree of concordance between changes in stroke volume do not report the degree of misclassification between responders and non-responders to fluid challenge.

Ultimately, whatever the technique used, minimally invasive cardiac output monitoring is simply a tool to assist the anaesthetist in deciding on an appropriate course of action. As with any equipment, we use there is variability in quality but what really matters is the person using them, the same is true for minimally invasive cardiac output monitoring.

The evidence base for use of this technology is less robust than it first appears. Optimal volume loading is usually now defined as a lack of a sustained response in stroke volume.
to an adequate fluid challenge. This is predicated on the Frank–Starling physiology of the heart; subjects nearer the top of the curve will not be able to increase stroke volume further. However, what is a sustained response and what is an appropriate fluid challenge? A variety of bolus volumes have been used in different studies with little evidence to justify the choice. The increment in stroke volume needs to be sufficient to be discernible from underlying variation in the patient’s cardiac output and discernible from measurement variation. It will of course be affected by the gradient of the preload–stroke volume relationship. Some patients will be classified as non-fluid responsive because their response to a fluid challenge is below the observable threshold. The consequence of these factors would suggest that however the protocols are written, fluid optimization remains something of an art. The clinician still needs to interpret the cardiac output monitoring in the light of all the available data.

In an attempt to make this process more reliable, derived indices are calculated by the monitors which make an estimate of likely fluid responsiveness on the basis of heart–lung interactions: pulse pressure variation (PPV), stroke volume variation (SVV), and systolic pressure variation (SPV) are the best described. Again the evidence base is perhaps not as strong as it first seems. If tidal volume and therefore intrathoracic pressures are not consistent then assessments of SVV, PPV, and SPV are inaccurate. All of these indices are reliant on change in intrathoracic pressure and therefore a tidal volume of 8 ml kg$^{-1}$ has been suggested as a minimum. A study using a pig model of acute lung injury and haemorrhage adds support to this concept, although care must be taken with extrapolation from animal models to clinical practice. Low (6 ml kg$^{-1}$) tidal volume reduced the discriminatory power of SVV and SPV, to diagnose haemorrhagic hypovolaemia, whereas PPV appeared less dependent upon tidal volume (VT). Unfortunately, for methodological reasons, the authors did not provide any data on these indices as predictors of fluid responsiveness. Patient position may also affect PPV and SVV, as demonstrated by an increase in the optimal threshold value for PPV and SVV from the supine to prone positions. The discriminatory ability of the indices did not change, however, suggesting that the clinician can still use the indices but with a different threshold. The obvious practical consequence of these studies is that the clinician cannot take an isolated value from a cardiac output monitor as an absolute indication of optimal intravascular volume. The data have to be interpreted in the appropriate clinical context.

If the evidence base for the monitoring appears to be slightly confusing, at least the monitoring appears to be safe. In this issue of the British Journal of Anaesthesia, Belda and colleagues report prospectively collected data from more than 500 patients mainly undergoing femoral arterial cannulation for transpulmonary thermodilution measurement of cardiac output. Almost all complications were transient with a catheter-related infection rate of 0.78%, comparable with routine intensive care monitoring. However, one patient did develop a femoral thrombosis requiring surgical embolectomy, so the catheters cannot be viewed as risk free. In comparison, the complication rate of following pulmonary artery catheter (PAC) insertion is between 4% and 10% with PAC-related bacteraemia occurring in 0.7–1.8% and arrhythmia requiring treatment in 3%. Complications after oesophageal Doppler placement also seem to be low though not unknown. Inadvertent endobronchial insertions causing incompetence of the cuffed tracheal tube and aspiration pneumonitis has been reported.

Despite these caveats, the evidence base for minimally invasive cardiac output measurement improving patient outcome as part of optimization protocols is reasonably strong particularly for colorectal surgery. There are several ongoing studies comparing minimally invasive cardiac output monitoring-based protocols with standard care which when reported may provide clearer evidence of which patients may benefit from this approach.

Evidence-based manipulation of the cardiovascular system can appear to be arbitrary in nature. Accurate administration of fluids according to a protocol may be difficult to master and can be seen as subjective. The positive outcomes associated with these goal-directed protocols may well stem from the personalization of fluid administration whether or not the endpoints nor their means to achieve them are based on any particular science. It may be that the thought process involved in the practical administration of an optimal fluid regime is enough to make a difference. One US study estimates that just less than one-quarter of surgical procedures met criteria for minimally invasive monitoring. At present, there are few data to demonstrate whether benefits seen in trials translate into patient or healthcare benefits if used in this number of patients in routine clinical practice.

Research will continue on the use of minimally invasive cardiac output monitoring. In order to bring more clarity to the field, we would suggest that there should be some framework for future studies. Validation studies should ideally be performed in relevant populations with a reasonable dispersal of volume status. These studies should report not only absolute relationships between measurement techniques but also the degree of correct identification of response to interventions and the ability to track changes in clinical conditions. The definition of responders and non-responders to fluid challenge should be based on endpoints which have been used successfully in clinical studies. The choice of 10% increase in SV at 5 min after fluid challenge may have been arbitrary, but the empirical evidence is that it seems to be associated with benefit. Studies are required urgently to assess the practical ability of clinicians to deliver the protocols used in research studies. As with other practical skills, we need evidence of how to teach its safe use, and also evidence of the inevitable complications of its use in routine practice.

Meanwhile, minimally invasive cardiac output represents another numerical trend monitor for anaesthetists and intensivists to use, alongside medical history, clinical examination, situational awareness, and other monitoring.
modalities in the delivery of personalized fluid regimes to improve patient outcome.

**Conflict of interest**

I.K.M. has received honoraria from Schering-Plough in the past 5 yr. He is an investigator in the OPTIMISE study which receives equipment support from LiDCO Group Plc. He is the chief investigator for a study using LiDCO in hip fractures (no commercial support). He received consumables support from Deltax Medical (CardioQ) for a study in 2004. He is a member of the editorial board of the *British Journal of Anaesthesia*. M.C. is an investigator in the OPTIMISE study which receives equipment support from LiDCO Group Plc.

**References**