Using cardiac output monitoring to guide perioperative haemodynamic therapy

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Purpose of review
The aim of this study was to review recent advances and evidence for the use of cardiac output monitors to guide perioperative haemodynamic therapy.

Recent findings
There are multiple different cardiac output monitoring devices available for clinical use which are coupled with many different intervention protocols to manipulate perioperative haemodynamics. There is little evidence to demonstrate superiority of any one device. Previous small studies and meta-analyses have suggested that perioperative haemodynamic therapy guided by cardiac output monitoring improves outcomes after major surgery. Despite relatively low-quality evidence several national bodies have recommended 'perioperative goal-directed therapy' (GDT) as a standard of care.
Recent larger trials of GDT have mostly failed to prove a benefit of GDT and one explanation for this is the increased quality of usual care that may be occurring because of initiatives such as enhanced recovery after surgery and the WHO Safer Surgery programmes.

Summary
Perioperative GDT remains an exciting intervention to reduce significant morbidity following major surgery; however, it is not yet a proven standard of care. Further large pragmatic trials are required to demonstrate its effectiveness particularly in the era of enhanced recovery after surgery programmes.

Keywords
cardiac output monitoring, goal directed therapy, haemodynamic optimization, perioperative care

INTRODUCTION

Achieving and maintaining stable haemodynamics has always been a core part of the provision of anaesthesia and critical care. Over recent years, there has been increased interest in the use of monitoring devices to help guide haemodynamic therapy decisions and protocolized treatment strategies particularly in higher risk patient groups. The basic premise is that the preservation of homeostasis and avoidance of tissue hypoxia by the maintenance of adequate blood flow reduces perioperative complications. These goal-directed therapy (GDT) protocols are now being embedded in enhanced recovery after surgery programmes as part of the perioperative surgical home [1▪].

CARDIAC OUTPUT MONITORING

The first studies of perioperative targeted haemodynamic therapy in the 1980s utilized the pulmonary artery catheter (PAC) [2], the only device readily available at the time for bedside cardiac output measurement. Although the PAC is still considered the gold standard cardiac output monitor, its perioperative use is now largely restricted to cardiac surgery [3]. The principal reasons for this are increasing concern about complications from PAC use [4] and the increased availability of alternative less-invasive cardiac output monitors.

Less-invasive technologies to measure cardiac output are now widely available and predominantly utilize analysis of the arterial pressure waveform, Doppler flow measurement or indicator dilution techniques with a variety of indicators. Although

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Curr Opin Crit Care 2015, 21:364–368
DOI:10.1097/MCC.0000000000000212

KEY POINTS

- There are multiple different cardiac output monitoring devices available for clinical use and there is little evidence to demonstrate superiority of any one device.
- Perioperative GDT remains an exciting intervention to reduce significant morbidity following major surgery; however, it is not yet a proven standard of care.
- Appropriately powered large pragmatic trials of perioperative GDT, in the context of enhanced recovery after surgery programmes, are required to determine clinical effectiveness in current practice.

there has been considerable debate as to the absolute accuracy of such devices, there is increasing consensus that absolute accuracy in cardiac output measurements is less important than general trend, particularly changes in measured cardiac output in response to therapeutic interventions [5,6▪]. Of more use to the clinician perhaps, are studies that link the use of these devices and associated GDT protocols with improved patient outcomes.

Cardiac output monitors, both calibrated and uncalibrated, that use arterial waveform analysis are widely used technology in perioperative care. The degree of invasiveness is related to the need for calibration which often involves the presence of a central venous catheter, whereas uncalibrated devices require only an arterial line. How invasive these techniques are is largely related to the perceived risk of the patients – high-risk patients or patients undergoing high-risk surgery are likely to have an arterial catheter and/or a central venous catheter placed as part of their anaesthetic management, and thus have little additional risk if these are used as part of a GDT protocol. The practical application of this technology, including relevant limitations, has been recently reviewed, with the perhaps inevitable conclusion that the less-invasive devices appear to also be less accurate [7].

Esophageal Doppler monitoring (EDM) is a commonly used alternative for cardiac output measurement and has the advantage of being less invasive as it requires the placement of an oesophageal ultrasound probe rather than an intravascular catheter [8]. Although not a new device, its use has increased recently in response to recommendations from the National Institute for Health and Care Excellence in the United Kingdom for use of EDM in high-risk surgical patients [9]. It does require some operator training to obtain and maintain accurate readings and is probably best suited to intraoperative use.

Several newer completely noninvasive devices are now available that utilize bioimpedance or bioreactance [10], plethysmography [11] or suprasternal Doppler [12,13▪]; however, good evidence of improved patient outcomes with their use is not available.

ASSESSMENT OF VOLUME RESPONSIVENESS

One of the principal advantages of monitors that utilize arterial waveform analysis is the ability to accurately predict fluid responsiveness, somewhat arbitrarily defined as an increase in cardiac output or stroke volume of 10–15% in response to a fluid bolus administration [14], although the reported volume and rate of fluid administration are variable [15]. The predictive accuracy of these devices is in marked contrast to the ability of clinicians to predict volume responsiveness using clinical criteria alone which is approximately only 50% accurate [15]. Pulse pressure variation (PPV) and stroke volume variation (SVV) are calculated as $(PP/SV_{max}-PP/SV_{min})/(PP/SV_{mean})$and a value of at least 14% accurately predicts fluid responsiveness with reported predictive values of more than 0.85 [16], although a grey area exists between 9 and 13% in which there is variation in predictive performance [17,18]. Pleth variability index and pulse oximetry plethysmographic waveform amplitude use similar principles to PPV and SVV using noninvasive technology and have reasonable predictive ability for fluid responsiveness [19].

All of these methods do, however, have some limitations, including inaccuracy with significant cardiac arrhythmias and a requirement for the patient to be mechanically ventilated with a tidal volume of at least 8 ml/kg [20]. One technique used to circumvent these limitations is the passive leg raise which can accurately predict increases in cardiac output seen with a subsequent fluid bolus. Passive leg raise has limited utility in the operating room; however, it does have a place in the ICU [21].

A recently published substudy from the Optimisation of Cardiovascular Management to Improve Surgical Outcome (OPTIMISE) investigators has cast some doubt on the utility of SVV and PPV to predict volume responsiveness with both variables only performing moderately well during and after surgery (predictive values between 0.64 and 0.70) [22▪▪]. It is perhaps not surprising that the efficacy of these devices when evaluated as part of a pragmatic clinical trial that was primarily focussed on assessing outcomes following the delivery of a clinical intervention was somewhat less than had been observed in studies in which the primary endpoint was assessment of the device itself.

Although early studies of these devices show promise in higher risk patient groups, it is too early

to conclude that the inevitable extension of the use of these technologies into the care of lower risk patients or surgical procedures will have any benefits [23▪].

GOAL-DIRECTED INTERVENTIONS AND PROTOCOLS

Bolus intravenous (i.v.) fluid administration has remained the main intervention studied in clinical trials of GDT. Much of the original research into perioperative GDT focussed on maximizing cardiac output with an emphasis on using titrated bolus of i.v. fluid that is repeated until either no further incremental rise in cardiac output or stroke volume is seen or alternatively until SVV or PPV monitoring indicates that the patient is no longer volume responsive. The logic behind this approach is that maximizing oxygen delivery will reduce tissue hypoxia; however, most studies reported significantly larger fluid volumes being administered to the GDT arms. In a trial of GDT in patients undergoing major colorectal surgery, the subgroup of patients who were aerobically fit had worse outcomes with the intervention [24]. Indeed, the increasing recognition that the administration of i.v. fluid is not innocuous [25,26] has led to one observer remarking that 'the best fluid is probably the one that has not been given to the patient' [27].

Recently, there has been a shift towards 'optimization', that is, the provision of fluid only to patients who are likely to be fluid responsive and for whom the cardiac output is known or suspected to be inadequate, rather than 'maximization'. The assessment of adequacy of cardiac output is not straightforward with clinical methods often unreliable or unusable during the perioperative period because of surgical and anaesthetic interventions. Monitoring of global oxygen balance using venous oximetry has theoretical appeal; however, three recent large multicentre studies in patients with sepsis failed to show improved outcomes with venous saturation monitoring using central venous catheters [28▪▪,29▪,30▪].

Use of vasoactive agents as part of the GDT protocol is controversial. Recent studies that either mandated a fixed dose of drug in addition to a fluid-based GDT regime [31▪▪] or that allowed the introduction of vasoactive drugs if the haemodynamic targets were not being met with fluid alone [32▪] have not demonstrated improved outcomes, although both studies had a similar amount of i.v. fluid administered in both groups. Although theoretically there is an increased risk of adverse events with the use of these agents, a recent meta-analysis demonstrated a decreased risk of cardiac complications in high-risk patients undergoing noncardiac surgery. The review found that the greatest benefit was in regimes that included both fluid and inotrope drugs [33▪▪].

The largest trial of perioperative GDT using a cardiac output monitor was recently published [31▪▪]. The OPTIMISE trial was a pragmatic randomized controlled trial of targeted haemodynamic management in patients undergoing major gastrointestinal surgery that included 734 patients from 17 UK hospitals. The intervention combined bolus doses of intravenous colloid to maximize stroke volume and a fixed dose dopexamine infusion. The primary outcome (a composite of mortality and surgical morbidity at 30 days) was present in 36.6% of intervention patients vs. 43.4% of usual care (95% confidence interval 0.71–1.01; $P = 0.07$). When an *a priori* analysis was performed excluding the first 10 patients from each centre, the result became significant, demonstrating perhaps that a significant learning curve exists for implementation of multifaceted GDT protocols.

When deciding which GDT protocol to use, there is little evidence to guide the clinician as to their relative safety and efficacy [23▪,34▪]. Given this lack of guidance, the choice of which algorithm to follow is principally dependent on the device being used.

Although it is logical to investigate perioperative bundles of care, one of the disadvantages is the inability to establish which individual components of the bundle contribute to any observed clinical benefits. The progressive rapid establishment of enhanced recovery after surgery programmes, which include many of the principles and interventions seen in GDT protocols, has also altered the baseline for usual care thus narrowing the treatment difference between intervention and control groups [35], which is potentially reduced further by a Hawthorne effect from what are inevitably unblinded interventions. Any future studies will have to account for this in their design and sample size calculation.

WHICH PATIENT GROUPS MIGHT BENEFIT FROM GOAL-DIRECTED THERAPY?

The majority of the studies published so far evaluating the use of GDT utilizing a cardiac output monitor have been in patients undergoing gastrointestinal surgery. Although many of these studies have been small and conducted in a single centre, multiple systematic reviews and meta-analyses [36,37▪] have suggested that there are benefits including a reduction in mortality and serious morbidity; however, the effect of publication bias on

these meta-analyses may be significant. The OPTIMISE investigators published an updated meta-analysis alongside the primary study results [31▪▪] and found that in the 38 studies included there was an overall reduction in perioperative complications with GDT (31.5 vs. 41.6%; relative risk 0.71, 95% confidence interval 0.71–0.83) but no significant difference in mortality.

Evidence in other patient groups is much more limited and often contradictory; however, the use of perioperative GDT has shown benefits in major orthopaedic [38], cardiac [39,40] and vascular [41] surgery, although once again the studies are small and usually single centre limiting generalizability. A systematic review of the use of GDT in cardiac and vascular surgery found limited evidence of benefit; however, it included only 11 studies with a total of 1179 patients [42]. The authors called for further larger trials with a low risk of bias to be conducted.

It would seem likely that any benefits of perioperative GDT would be most marked in either higher risk patients or those undergoing major procedures and this has been demonstrated in some reviews [43].

One of the difficulties with evaluating the benefits of perioperative GDT is that usual care is constantly changing and evolving. Initiatives such as enhanced recovery programmes and more recently the concept of the perioperative surgical home that champions the role of the multidisciplinary team in the delivery of best practice care preoperatively, intraoperatively and up to 30 days postoperatively coupled with initiatives such as the WHO safe surgery programme [44] are aimed at improving care and outcomes for surgical patients. Few studies of GDT have been conducted with the usual care arm being 'best practice' according to the above and it is likely that any additional benefit of GDT will be limited in patients already receiving the high-quality care that such programmes provide.

Some commentators have questioned if the primary benefit of perioperative GDT relates to increased attention by the anaesthetist during the intervention and the possible benefits of standardization of care, particularly in relation to fluid administration [35].

FUTURE RESEARCH

It is refreshing to see research is now more directed at assessing the impact of these technologies on patients' outcomes rather than on methodologically flawed comparisons of technical precision between different devices which have little relevance to the bedside clinician. Much larger studies are required to answer the question as to which patient groups will benefit from perioperative goal-directed haemodynamic therapy and which device and associated GDT protocol is most effective.

CONCLUSION

The use of cardiac output monitors to guide perioperative haemodynamic therapy is now widely accepted and practised despite little high-quality evidence of benefit to patients. As with many other areas of clinical practice, the promise of benefit shown in small single-centre studies has not been confirmed in subsequent larger studies. Use of composite endpoints, with all the inherent problems that this brings, is inevitable in clinical trials of surgical patients; however, appropriately powered large pragmatic trials of GDT that compare the intervention with 'current best practice' are required to allow us to fully quantify the role and benefits that perioperative cardiac output monitoring offers to surgical patient populations.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

S.M. has received honoraria and travel expenses from Edwards Lifescience, Baxter Healthcare and Fisher & Paykel Healthcare. R.P. has received travel expenses from Fisher & Paykel Healthcare. Research in the Cardiothoracic and Vascular Intensive Care Unit at Auckland City Hospital is supported in part by an unrestricted grant from Fisher & Paykel Healthcare.

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