Cardiac Output Monitoring

K de Vasconcellos

Commentator: J Keshav
Moderator: T Kisten

Department of Anaesthetics
CONTENTS

Introduction................................................................................................3
Rationale for Cardiac Output Monitoring................................................3
Rationale for Noninvasive/Minimally Invasive Cardiac Output Monitors
...........................................................................................................5
Haemodynamic Optimisation.................................................................5
Prediction of Fluid Responsiveness .......................................................7
Statistics, Lies, the “Gold Standard”, and the State of the Literature 10
Ideal Cardiac Output Monitor.................................................................14
Minimally Invasive Cardiac Output Monitors.........................................15
  1) Arterial Waveform Analysis Cardiac Output Monitors ..................15
  2) Doppler Ultrasound.......................................................................31
  3) Transoesophageal Echocardiography...........................................37
  4) Partial Carbon Dioxide Rebreathing Systems ..............................38
  5) Impedance cardiography (Thoracic Electrical Bioimpedance)......41
  6) Miscellaneous .............................................................................44
Conclusion ...........................................................................................45
List of Abbreviations .............................................................................45
References .............................................................................................46


82) CardioQ web resources: www.frca.co.uk/www.e-xclusif.com
83) Hemosonic website: www.hemosonic.com
84) PICCO website: www.pulsion.com
85) LiDCO website: www.lidco-ir.co.uk
86) Vigileo/Flotrac website: www.edwards.com

Introduction

My interest in cardiac output monitors and monitoring was initially piqued while studying for primaries, but with the purchase of the Vigileo/Flotrac monitor at IALCH I decided to look into this topic in more detail. One of the first articles I came across showed 95% limits of agreement for the Vigileo/Flotrac versus pulmonary artery catheter thermodilution of -2.2 to +3.1 l/min: were they trying to tell me that this new device I was keen to use had a 95% chance of being within 5.3 l/min of the “true” cardiac output? Were they actually being serious in trying to market this device? However, as I delved further beneath the surface the waters got murkier and murkier. I began to question the rationale behind monitoring cardiac output, the variables to monitor, which device to use, how to act on the variables, how to interpret the statistics in the articles, how valid were the conclusions in the articles, what was the clinical utility of the conclusions, is the reference method accurate, does any of this effect outcome, what about different patient groups...? I have since scoured the literature and will attempt to answer these and many other questions about this important topic. Any conclusions I have reached are based on the currently available literature. As with much of the medical literature it is fragmented and of vastly differing quality and I am thus certain that we have only uncovered the very tip of the iceberg regarding cardiac output monitoring. We have a long way to go before we can answer these questions with great confidence but hopefully I will be able to provide you with the best available information and thereby provide a platform from which to perform cardiac output monitoring, evaluate the devices, and interpret new information as it emerges.

Rationale for Cardiac Output Monitoring

One of our key roles as anaesthetists is monitoring, interpreting and acting on haemodynamic variables. We assume that by detecting pathophysiological derangements early and acting to correct them we will improve patient outcome. We, however, have a bewildering array of variables to monitor and monitors with which to do this. The first step in effective monitoring is choosing the most appropriate parameter or parameters to monitor. Simply monitoring a parameter though is insufficient and will not improve outcome unless coupled to a treatment strategy that improves outcome. It is thus obvious that haemodynamic monitoring can only improve outcomes for patients with disease processes that have an effective treatment. There can thus be no ‘one size fits all’ approach to haemodynamic monitoring.

When choosing the parameters to monitor and the means to monitor them we need to adopt a rational approach that combines best current evidence with sound basic science and clinical judgement. For example Moller et al showed that intraoperative pulse-oximetry in low-risk surgical patients did not alter outcome; would you be prepared to abandon pulse-oximetry in these patients...?
given its negligible risk? A wealth of evidence supports the view that CVP and PCWP are no better at predicting volume responsiveness than flipping a coin; given their real risks are we justified in continuing to attempt to use them for this purpose? My point is that although I will focus strongly on the available evidence in this talk, the ability to make clinical and value judgements is still essential.

So back to that crucial decision: what variable/s should we monitor? The primary goal of the cardiovascular system is to ensure adequate oxygen delivery to meet the metabolic demands of the tissues. As we know \( \text{DO2} = \text{CO} \times \text{CaO2} \). The key factors determining oxygen delivery are thus cardiac output, haemoglobin concentration, and haemoglobin oxygen saturation. Except in severe hypoxaemia and anaemia, cardiac output is the main variable determining adequate oxygen delivery. It thus makes clear sense to monitor cardiac output in the perioperative and critical care setting as this dynamic variable can easily be optimised to improve oxygen delivery.

But all is not that simple. Firstly, what is a normal cardiac output and how does one control for variables affecting cardiac output? One can control for BSA as a confounder using CI (normal range of 2.5-4.0 l/min/m\(^2\)). Given that \( \text{CO} = \text{HR} \times \text{SV} \) one can control for HR by using SV (normal range 60-130ml/beat), and BSA by using SVI (normal range 33-47ml/m\(^2/\)beat). Despite all this though the question remains: what is a normal cardiac output in reality? What is adequate for an anaesthetised elderly patient will almost certainly not be adequate for a young, pregnant patient in septic shock in ICU. So how does one attempt to get the most out of the cardiac output monitor of choice? One looks to track trends in cardiac output instead of absolute values but more importantly one looks to analyse the determinants of cardiac output and predict or observe their response to possible interventions. In this regard it must be remembered that cardiac output is determined by preload, afterload and contractility and a derangement in cardiac output may be due to any of these variables, either alone or in combination. An abnormal cardiac output reading, no matter how accurate, is thus of limited value unless one is aware of the pathophysiological factors resulting in this abnormality. Thus, most cardiac output monitors provide an index of preload or volume responsiveness e.g. PCWP, SVV, PPV, GEDV, FTc and some also provide information on contractility e.g. peak Doppler velocity and acceleration, and afterload e.g. SVR. The ultimate aim is to incorporate the various haemodynamic variables and possible responses into an integrated, functional haemodynamic monitoring and therapeutic algorithm that improves patient outcome—the essence of goal-directed therapy/perioperative optimisation that I will discuss in due course.

What I hope to have illustrated is that “cardiac output monitoring” is about far more than cardiac output. Thus, when we evaluate or use a cardiac output monitor, although we are interested in how well it measures cardiac output, we corrected flow time in oesophageal Doppler as a predictor of fluid responsiveness. Br J Anaesth. 2007 Sep;99(3):343-8.


70) Hofer C, Muller S, Furrer L, Klaghofer R, Genoni M, Zollinger A. Stroke volume and pulse pressure variation for prediction of fluid responsiveness in patients...
Rationale for Noninvasive/Minimally Invasive Cardiac Output Monitors

The PAC is the traditional gold standard for cardiac output monitoring. It has played a valuable role in improving our knowledge of cardiovascular physiology and pathophysiology and in driving progress in anaesthesia and critical care, e.g. goal-directed therapy. Initially it showed great promise to improve patient care and outcome e.g. Shoemaker's early work. In recent years though it has been dealt what appears to be a fatal blow by studies showing that PAC-guided therapy had no significant effect on outcome or an adverse effect on outcome. Whether this view is based on science or sentiment, whether the studies are flawed or not, whether the adverse outcomes reflect the incompetence of the users of the PAC, rather than the device itself, is largely irrelevant: public opinion against the PAC has swung past the point of no return. The development of an alternative, in the form of minimally invasive cardiac output monitors, has both hastened the demise of the PAC and been driven by concerns over the PAC. The basic rationale for the use of a minimally invasive device is obvious: reducing the potential adverse effects of invasive monitors such as the PAC e.g. valvular damage, pulmonary artery rupture, arrhythmias, sepsis. However, key practical questions are: do they provide at least equivalent haemodynamic data to the PAC; what is the risk benefit analysis; can they improve outcome and if so, in whom; and how are they best used? It is these questions I will attempt to answer in more detail in the rest of this text.

Haemodynamic Optimisation

As alluded to previously, the role of any cardiac output monitor is haemodynamic optimisation. Simply monitoring a parameter, no matter what the parameter, or acting on it in a haphazard manner, will not improve outcome. From this realisation came the concept of goal-directed therapy or haemodynamic optimisation, which may be guided by cardiac output monitoring. There are a number of different strategies that may be employed. I will briefly highlight these in general terms to illustrate some of the potential
applications for cardiac output monitors. More detail will be provided when each of the monitors is discussed individually. Each method has the same end-point: adequate tissue oxygenation and the same starting point: fluid optimisation. How this is achieved is probably not that important as long as it is logical and properly guided. Broadly speaking the two main methods are:

1) Targetting fixed, absolute, physiological/supraphysiological variables
2) An individualised, functional approach
   i) Maximisation of flow-related variables with fluid challenges
   ii) Prediction of fluid responsiveness

1) The first technique targets fixed values of chosen variables. These values are often “supraphysiological”. Directed intravenous fluid and inotropic therapy is used in an attempt to achieve these values. The archetype is Shoemakers “Prospective trial of supranormal values of survivors as therapeutic goals in high risk surgical patients.” Frequently quoted targets are, a CI > 4.5 l/min/m², a DO2 > 600 ml/min, and/or a VO2 > 170 ml/min. Essentially all studies have used the PAC to guide therapy but many minimally invasive cardiac output monitors could theoretically be used to target CI or DO2.

There are many potential flaws in this approach e.g. the magical DO2 and CI figures were merely the median values found in survivors of major surgery and may not apply to the individual patient. In addition driving a patient to reach a value beyond his physiological capability may in itself be deleterious. Unsurprisingly results have been conflicting. However, a metaanalysis by Kern showed that, in high risk patients (mortality risk > 20%), if GDT was instituted early, mortality could be reduced significantly.

2) The second approach is an individualised approach aimed at maximising flow-related parameters (e.g. SV) with fluid challenges, or predicting fluid responsiveness, rather than aiming for predefined absolute values.
   i) The fluid challenge strategy entails repeated fluid challenges (e.g. 200-250ml colloid) until SV no longer increases. This based on the philosophy that normovolaemia is the preload required to produce a maximal SV as per Starling’s law of the heart. Most algorithms require a 10% increase in SV to justify a further fluid challenge. This is to counter the increase in SV that may occur from haemodilution and to minimise the risk of fluid overload. One can also use this approach with other static volumetric markers e.g. GEDV.
   ii) The prediction of fluid responsiveness strategy is an enhancement of this basic functional, individual approach. Here the aim is to predict thermodilution technique in children during heart catheterisation. Anaesthesia. 2008 Aug;63(8):851-5.


25) Compton F, Wittrock M, Schaefer JH, Zidek W, Tepel M, Scholze A. Noninvasive cardiac output measurement in children: comparison of Aesculon transpulmonary thermodilution cardiac output measurements within an up to 6-hour

Page 6 of 50
the response to fluid therapy before it is administered, thus avoiding unnecessary fluid boluses. As the reliable prediction of fluid responsiveness is one of the key potential advantages of the new minimally invasive cardiac output monitors I will discuss this later, as a topic in its own right.

Once fluid status has been optimised one can institute inotropic support if required- this may also be goal-directed and combine elements of the first strategy e.g. aiming for a DO2 > 600 ml/min.

The evidence supporting an individualised approach to haemodynamic optimisation as a viable option is starting to appear. Thus far it has been limited to studies using oesophageal Doppler, and one each using PiCCO and LiDCO (interestingly the PAC has not been used for this approach). These show a reduction in post-operative morbidity, hospital stay, ICU admissions and PONV (with more rapid recovery of gastrointestinal function). A reduction in mortality has been suggested but this was not statistically significant. These studies covered a wide range of surgeries (cardiac, major general, orthopaedic, urological, gynaecological) and patient profiles.

The timing of perioperative haemodynamic optimisation is controversial. It is not within the scope of this text to go into this in much detail, suffice it to say that optimisation before surgery is probably ideal but practically difficult to implement. There is, however, growing evidence to show the efficacy of both intra- and postoperative optimisation and thus these seem to be acceptable alternatives if preoptimisation is not possible.

This is an exciting field with promising early results using a variety of minimally invasive cardiac output monitors. Much further work still needs to be done to define the patient groups most likely to benefit from these interventions, and what variables, targets, and interventions yield the best results.

Prediction of Fluid Responsiveness

As mentioned previously, the greatest systematic improvement in patient outcomes with the use of cardiac output monitors is likely to come from their use in the context of robust, evidence-based goal-directed strategies. Realistically, the most common and clinically useful role, for the practising anaesthetist is likely to be in the area of predicting volume responsiveness, and guiding fluid therapy in the absence of a formal goal-directed algorithm. I thus feel that this important topic deserves further discussion in its own right. As mentioned previously the aim of predicting fluid responsiveness is to identify and optimise patients who are likely respond to fluid therapy without overloading non-responders with unnecessary fluid therapy or fluid challenges.
The prediction of fluid responsiveness has been attempted using a number of parameters:

1) **Static parameters**
   a) Filling pressures e.g. CVP, PAWP
   b) Volumetric parameters i.e. end-diastolic ventricular dimensions
      i) RV and LV end-diastolic volume
      ii) LV end-diastolic area
      iii) Global end-diastolic volume (GEDV)
   c) Flow-related parameters e.g. FTc
   d) Composite parameters e.g. Stroke Output Index (SOI) = SVI/FTc

2) **Dynamic parameters**
   a) Respiratory variation e.g. PPV, SVV
   b) Passive leg raising e.g. ABF, SV

To see the possible utility of cardiac output monitors we need to explore these in more detail:

1) **Static parameters**
   Static parameters attempt to predict preload and fluid responsive based on the Frank-Starling relationship relating preload to stroke volume. A response to fluid/volume is more likely if the preload is low. However, changing ventricular compliance and contractility complicate this relationship greatly. Even if a parameter is a good indicator of preload, preload does not equal preload responsiveness.

   Filling pressures e.g. CVP and PAWP are not only poor markers of preload but have repeatedly been shown to be no better at predicting fluid responsiveness than flipping a coin (AUC of ROC ~ 0.5). Although volumetric parameters are better indicators of preload they are still largely poor predictors of volume responsiveness. Only GEDV (as provided by PiCCO) has been shown to predict volume responsiveness. This was, however, in a single study in a porcine paediatric model (ROC AUC 0.8 vs 0.6 for PPV)\(^\text{67}\). Numerous other studies in a cross-section of adult patients have shown a poor predictive value\(^\text{15;37;70;71}\). Potential explanations for the differences between GEDV and PPV for predicting fluid responsiveness in paediatric patients are differences in heart rate, chest wall compliance, MAP, vasomotor tone and aortic compliance.

   Corrected flow time (FTc) as measured by oesophageal Doppler, although a static variable, has been shown to be a good marker of preload and predict fluid responsiveness in a number studies (e.g. ROC AUC of 0.944 for FTc vs 0.909 for PPV)\(^\text{64;66}\). Other studies have contradicted this finding, with one suggesting that SOI (SOI=SVI/FTc) is a superior parameter for predicting fluid responsiveness – with an SOI > 11% having a 91% sensitivity and a 97% specificity\(^\text{68;69}\).

**Conclusion**

The monitoring of cardiac output and related parameters offers the prospect of exciting advances in patient care. From the above discussion it can be seen that all monitors are not equal, and even within categories, e.g. pulse waveform monitors, there are significant differences between the devices. Thus, before using a device, one needs to be clear about its strengths and weaknesses and have a sound strategy to use the device. We can eagerly await the development of new devices and the improvement of current devices. We also await good quality outcome-based evidence to help us define our target populations and optimal usage strategies.

**List of Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>HR</td>
<td>heart rate</td>
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<tr>
<td>BP</td>
<td>blood pressure</td>
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<td>MAP</td>
<td>mean arterial pressure</td>
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<tr>
<td>CO</td>
<td>cardiac output</td>
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<td>CI</td>
<td>cardiac index</td>
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<td>SV</td>
<td>stroke volume</td>
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<tr>
<td>SI</td>
<td>stroke index</td>
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<tr>
<td>DO2(I)</td>
<td>oxygen delivery(index)</td>
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<tr>
<td>VO2</td>
<td>oxygen consumption</td>
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<tr>
<td>GEDV(I)</td>
<td>global end-diastolic volume (index)</td>
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<tr>
<td>ITBV(I)</td>
<td>intrathoracic blood volume (index)</td>
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<td>EVLW(I)</td>
<td>extravascular lung water (index)</td>
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<td>SVV</td>
<td>stroke volume variation</td>
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<tr>
<td>PPV</td>
<td>pulse pressure variation</td>
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<tr>
<td>SPV</td>
<td>systolic pressure variation</td>
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<td>CVP</td>
<td>central venous pressure</td>
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<tr>
<td>PCWP</td>
<td>pulmonary capillary wedge pressure</td>
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<table>
<thead>
<tr>
<th>Abbreviation</th>
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<tr>
<td>Hb</td>
<td>haemoglobin concentration (g/dl)</td>
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<tr>
<td>CaO2</td>
<td>arterial oxygen content</td>
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<tr>
<td>CvO2</td>
<td>mixed venous oxygen content</td>
</tr>
<tr>
<td>VCO2</td>
<td>CO2 elimination</td>
</tr>
<tr>
<td>CaCO2</td>
<td>arterial CO2 content</td>
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<tr>
<td>CvCO2</td>
<td>mixed venous CO2 content</td>
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<tr>
<td>PaCO2</td>
<td>arterial partial pressure of CO2</td>
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<tr>
<td>ETCO2</td>
<td>end-tidal CO2 concentration</td>
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<tr>
<td>BSA</td>
<td>body surface area</td>
</tr>
<tr>
<td>AUC</td>
<td>area under curve</td>
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<tr>
<td>SVR</td>
<td>systemic vascular resistance</td>
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<tr>
<td>TPR</td>
<td>total peripheral resistance</td>
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<tr>
<td>EF</td>
<td>ejection fraction</td>
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<tr>
<td>CSA</td>
<td>cross-sectional area</td>
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<tr>
<td>ABF</td>
<td>aortic blood flow</td>
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<tr>
<td>Z</td>
<td>impedance</td>
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<tr>
<td>C</td>
<td>compliance</td>
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<tr>
<td>ODM</td>
<td>oesophageal doppler monitoring</td>
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thought not to be affected by changes in low conductivity compartments, such as the lung, and should, in theory, be more accurate than traditional TEB. Initial studies have shown reasonable performance versus ITD, in both haemodynamically stable and unstable postoperative cardiac surgical patients. A study in paediatric patients undergoing catheterisation, however, showed a bias of 0.66 l/min with limits of agreement of -2.26 to 3.58 l/min, and a percentage error of 48.9%. The authors concluded that it was unacceptable for cardiac output measurement but that the device could possibly be used as a cardiac output trend monitor.

A further new development is whole body electrical bioimpedance (WBEB) e.g. NiCaS monitor. Early studies have shown reasonable bias and limits of agreement, but also with a number of practical limitations.

There have been no studies using impedance cardiography in goal-directed therapy, for predicting fluid responsiveness, or demonstrating outcome benefits. Although this technique is highly attractive, as it is completely noninvasive, it cannot be recommended for routine use in the anaesthetic or critical care setting without further advancements in signal processing and further studies of the emerging devices. At the moment there are simply too many sources of noise and potential inaccuracy and the literature that is available is too inconsistent for this device to be used with conviction.

6) Miscellaneous

A variety of other methods of cardiac output assessment have been attempted but none have shown much promise. This includes a number of indicator dilution methods (used as independent techniques, not just as calibration for arterial waveform-based devices), one of which, pulsed dye densitometry, warrants brief further analysis.

This technique allows intermittent cardiac output assessment based on transpulmonary dye dilution, with signal detection occurring transcutaneously, via a technique adapted from pulse-oximetry. Indocyanine green is injected intravenously, and its concentration is estimated in arterial blood via optical absorbance measurements. Cardiac output is calculated from the concentration-time dye dilution curve, using the Stewart-Hamilton principle. A number of factors interfere with signal detection and limit the accuracy of this technique e.g. vasoconstriction, movement, interstitial oedema, and ambient light artefacts. Although an interesting approach, studies have shown only moderate agreement with PAC ITD, and this method is of very limited use for cardiac output assessment in clinical practice.

Possible explanations for these contradictory findings are that FTc is also inversely proportional to afterload (thus is not solely dependent on preload). FTc may also be low in conditions that prevent adequate cardiac filling e.g. pericardial tamponade, mitral stenosis, and these will clearly not respond to fluid administration. In addition if inotropic/vasopressor therapy is instituted prior to establishing volume responsiveness using FTc, the FTc will be low due to vasoconstriction, regardless of preload. FTc may thus best be used in combination with another parameter e.g. SV optimisation or CVP to exclude those conditions that will have a low FTc but not be fluid responsive.

2) Dynamic parameters

These all centre on observing the response of an appropriate variable to a "reversible fluid challenge". This may be induced by cardiorespiratory interactions during positive pressure ventilation or a passive leg raising test. Dynamic variables have almost universally been shown to be superior to passive variables (with the possible exception of FTc and related measures) in predicting fluid responsiveness.

The ability of SVV and PPV to reliably predict fluid responsiveness has been demonstrated in a number of studies,\textsuperscript{5,15,36,37,70,71}.

In theory they are calculated as follows:

\[
PPV(\%)= 100 \times \frac{(PP_{max}-PP_{min})}{(PP_{max}+PP_{min})/2}
\]

and similarly

\[
SVV(\%)= 100 \times \frac{(Sv_{max}-Sv_{min})}{Sv_{mean}}
\]

The values are measured from diastole to systole to eliminate the effect of changes in diastolic filling time between beats. In reality these values are calculated automatically by the cardiac output monitor e.g. SVV and PPV by PiCCOplus and SVV by Vigileo/Flotrac using the above basic principles but different averaging techniques.

Both SVV and PPV have AUC’s under the receiver operating characteristic curves for predicting volume responsiveness of between 0.8 and 0.871, depending on the study. The optimal threshold values for discriminating between responders and non-responders, as given by the ROC curves differ depending on the magnitude of response chosen to discriminate between responders and non-responders and the method used:

For example, the optimal threshold value for predicting a 25% increase in SV was 9.6% for SVV using Flotrac/Vigileo (sensitivity 91% / specificity 83%) and 12.1% for SVV using PiCCO (sensitivity 87% / specificity 76%) in one study.\textsuperscript{19}

In another study the values for a 25% increase in SVI were 12.5% for SVV using PiCCO (sensitivity 74% / specificity 71%) and 13.5% for PPV (sensitivity 72% / specificity72%)\textsuperscript{19}. Of note, one study demonstrated that under open-chest conditions (cardiac surgery) the change in PPV or SVV after sternotomy was a better predictor of fluid responsiveness than the absolute values of either of these variables.
This brings me to the limitations of using SVV/PPV. As mentioned above, these are based on cardiorespiratory interactions and are only validated in mechanically ventilated patients. In fact, they have been shown to be poor predictors of volume responsiveness in spontaneously breathing patients—whether this be triggering breaths in SIMV or PS, or in non-intubated patients. Even altering tidal volume or PEEP can significantly alter the measured values. Thus, one needs to maintain constant, very specific, ventilatory parameters to use these values accurately. In addition, cardiac arrhythmias can invalidate the readings and the patient must be in sinus rhythm or a fixed, paced rhythm. One also needs to ensure there are no technical confounders interfering with the arterial tracing e.g. air bubbles, kinks or clots. Although more difficult to control for, one should be aware that changes in arterial compliance can directly affect PPV. Also worth noting is that a low heart rate reduces the respiratory variation in arterial pressure and may reduce PPV.

In an attempt to overcome these limitations, the effect of passive leg raising on various haemodynamic parameters is being studied. This will allow the use of a dynamic index of volume responsiveness in spontaneously breathing patients and those with arrhythmias. The current controversy is, what is the best variable to monitor? Because of the brief response to passive leg raising one needs a real-time measurement with rapid response. It appears that aortic blood flow (ABF) measured with oesophageal Doppler is the most accurate. An increase in ABF ≥ 10% reliably predicts volume responsiveness and does so more accurately than an increase in SV ≥ 12.5% as measured by transthoracic echocardiography, or a PPV > 12%.

**Statistics, Lies, the “Gold Standard”, and the State of the Literature**

Before one can pass judgement on individual cardiac output monitors a few key concepts need to be clarified. Firstly, some useful definitions:

- **Accuracy:** the degree of closeness of a measurement to its true value
- **Precision** (or reproducibility or repeatability): the degree to which further measurements show the same/similar results (often described as the reciprocal of the variance).
- **Variance:** a measure of the average distance between each of a set of data points and their mean; equal to the sum of the squares of the deviation from the mean value. Simply variance = SD²

A measurement system is valid if it is both accurate and precise.

The usual research question posed in the cardiac output monitoring literature is: “can new device x or y be used interchangeably with, or replace, the gold standard?” Although seemingly rational this approach to evaluating new cardiac output monitors is potentially flawed on a number of levels.

- It thus has potential for use in a wide variety of clinical fields
- Provides, not only continuous CO and SV, but also with estimates of contractility e.g. contractility index, LV ejection time, preejection period (PEP), systolic time ratio, total thoracic fluid volume or index, SVR, LV stroke work index.

There are, however, numerous disadvantages:

- Methodology relies on a large number of assumptions
- Thoracic bioimpedance is not solely dependent on aortic blood flow but is affected by changes in thoracic tissue fluid volume e.g. chest wall oedema, pulmonary oedema, pleural effusions. It is also affected by respiratory changes in pulmonary and venous blood flow.
- Alterations in myocardial contractility, such as those induced by anaesthetic agents, and ischaemia and haemodynamic instability, may also cause errors in cardiac output measurements—limiting its usefulness in precisely the patients one is most likely to need it most.
- Arrhythmias can also result in inaccurate measurements.
- The intraoperative environment is not conducive to the use of TEB devices because of the high likelihood of interference by “noise” from electrocautery, mechanical ventilation and surgical manipulation.

Initial clinical studies showed this to be a reliable device for monitoring cardiac output. These were, however, done in young, healthy volunteers. Subsequent studies, in a wide spectrum of patients, have shown inconsistent results. Early devices fared especially poorly.

The only metaanalysis of TEB studies showed a poor correlation with reference devices: due to the poor statistical analysis it is difficult to reach solid conclusions from these data though. Subsequently, second-generation devices (e.g. BioZ, Cardioscreen, Aesculon, NiCas) have been developed. The new TEB devices e.g. BioZ have faster signal processing; better signal filtering; improved ECG triggering; improved arrhythmia detection; and respiratory filtering, in an attempt to overcome some of the limitations of the original devices. These new-generation devices appear to perform better than the first-generation devices but the results are still inconsistent, especially during dynamic conditions.

An illustrative example is a study of patients who underwent coronary artery bypass grafting. Post induction (haemodynamic stability and minimal “noise”), the bias was -0.02 l/min (CI), with LOA of -0.6 to 0.56 l/min, and a percentage error of 26%. After closure of the sternum, however, the bias was -0.67 l/min, the LOA -2.15 to 0.81 l/min, and the percentage error 53%. The causes of this discrepancy have not been fully elucidated but illustrate the potential for significant inaccuracy.

Another new impedance cardiography device mentioned above is the Aesculon monitor. This utilises the principle of electrical velocimetry, which interprets the maximum rate of change of TEB to calculate cardiac output. The algorithm is...
 Firstly, there is no true gold standard against which to compare new devices. Intermittent thermodilution (ITD) via the PAC has become our default diastole. Blood is thought to be the main contributor to the changes in gold standard because it was the first device to feasibly allow bedside cardiac output measurement, and because of years of experience and familiarity with its use. It, however, has well documented problems with accuracy and precision. Even if performed well, it has a Coefficient of Variation (SD/mean) of approximately 10% or, as also quoted, an inherent accuracy of +/- 20%. As discussed later, if we cannot be certain about our reference method, how can we accept or reject a new method with any conviction. Another factor to consider is the intermittent, averaged nature of ITD measurements. C.O. is, however, a dynamic variable, especially during periods of haemodynamic instability. The implications are that a new device that provides a "continuous" measure of cardiac output could be more accurate than ITD, especially during periods of haemodynamic instability, but appear less accurate on statistical analysis.

Second, there are multiple potential problems with the statistical analysis of many recent studies comparing new devices to ITD. Most early studies and many recent studies still attempt to measure agreement between devices using correlation. By definition correlation indicates the strength and direction of a linear relationship between two random variables. Thus two methods of measuring the same parameter will almost invariably have good correlation, unless there are serious problems with the device or the operator of the device. Correlation thus says very little about whether two devices are interchangeable.

A significant advancement in describing the agreement between two methods of measuring the same physiological variable was provided by Bland and Altman. Bland-Altman analysis and plots are now commonly found in the cardiac output monitoring literature. Basically, the difference between each set of measurements from two different devices is plotted on the y-axis, against the average of the measurements of the two devices for that set, which is plotted on the x-axis. If a true reference method is available e.g. aortic flow probe then that value can be used on the x-axis but if, as in this case, no true reference is available, the average of the two measurements is used and no conclusion can be made about accuracy; one can only comment on agreement. Once plotted one can make a visual assessment of the agreement between the two devices. However, further useful information can be calculated using this method. The bias is the mean difference between the two methods. This quantifies any systematic, non-random deviation of the new method from the mean. Also calculated is the standard deviation of the bias. +/- 1.96 SD of the bias gives the 95% limits of agreement. 95% of the differences between the methods will thus, by definition, fall within these limits of agreement (if normally distributed). Even if the bias is minimal (as is often the case), if the limits of agreement are too wide the new device may not be accurate enough to replace the old device ("gold standard"). The key problem lies in assessing how wide or narrow these
limits of agreement should be, for a new device to be acceptable for clinical use. This is largely a subjective clinical judgement, dependent on many factors, including the population being studied e.g. paediatrics vs adults, and has led to much confusion in interpreting the available literature.

Critchley and Critchley attempted to overcome this by introducing the concept of the percentage error to standardise interpretation of the Bland-Altman data. The percentage error is the limits of agreement/mean of the population. In their original work the coefficient of variation for ITD was 10%. They argued that if the coefficient of the new technique was ≤ 10% then it could be used interchangeably with ITD. If the coefficient of variation for both devices was hypothetically 10% then the percentage error would be 28.4%, which has been rounded off to 30%. Thus, because of this statistical wizardry, it is now often assumed that if the percentage error is less than the magical +/- 30% then the two methods are interchangeable. This is, however, flawed. If the Coefficient of Variation (CoV) for ITD is < 10% in a particular study, and we still use the 30% cut-off, we run the risk of inappropriately accepting the new device. And similarly, if ITD is poorly performed and the CoV is >10%, we may incorrectly reject an acceptable new device if we stick to the 30% percentage error. Thus any study that uses percentage error needs to state the coefficient of variation of their reference method and ideally state the relative contribution to the percentage error from the new device by using the formula \( CV_{b} = \sqrt{(CV_{a-b})^2 - (CV_{a})^2} \). \( CV_{a} \) = CoV of method A (reference method); \( CV_{b} \) = CoV of method b (new method) and \( CV_{a-b} \) = difference in CoV between the two methods. If we accept a CoV of 10% for the reference device we should accept 10% for the new device and if it offers other advantages e.g. less invasiveness or continuous monitoring, we may even accept 15-20%. Again, a judgement call.

5) Impedance cardiography (Thoracic Electrical Bioimpedance)

This technique was initially developed by NASA for research into the haemodynamic effects of zero gravity. Thoracic electrical bioimpedance is, essentially, the electrical resistance to a current transmitted through the thorax. This technique measures the pulsatile changes in electrical impedance through

between 2-11.5 kPa, the cardiac output values will only be accurate if the PaCO2 is >4kPa, as this is when the CO2-Hb dissociation curve is linear, and the assumed relationships between PaCO2 and PvCO2 hold true. We are unlikely to ventilate patients to a PaCO2 below 30mmHg, however.

- Different levels of intrapulmonary shunt, as mentioned earlier, may alter the calculated cardiac output. It is for this reason that poor results have been shown when used in critically ill patients with significant intrapulmonary shunts and haemodynamic instability. It is interesting to note, though, that it was found to be acceptable for use in the lateral decubitus position, and in patients undergoing thoracic surgery with one lung ventilation.

- Shunt fraction may be miscalculated if large changes in haemoglobin concentration occur.

What information can be gleaned from current studies using this advice? Results are conflicting: bias ranges from -1.75 l/min to as little as -0.1 l/min and LOA from -2.5 to 1.9 l/min to -0.5 to 0.3 l/min.

Of interest is a study in cardiac surgical patients that found better results with NICO versus ultrasonic flowmetry (the closest to a true gold standard we have) then with PAC ITD versus ultrasonic flowmetry. Thus comparisons between NICO and ITD must be viewed with caution. Despite this confusion, the key messages that appear to emerge from the literature are:

- NICO is potentially inaccurate in critically ill patients with large intrapulmonary shunts and significant haemodynamic instability.

Even in patients for elective surgery its accuracy has been called into question with a quoted percentage error in the region of 55%. It is most accurate when measuring cardiac output below 3 l/min which is probably the region of most interest to us (interestingly a study showed a percentage error of only 16% when CO < 2 l/min).

Its accuracy is not significantly affected by position or one-lung ventilation. It is more accurate when shunt fraction is frequently recalibrated with arterial blood gas PaCO2 readings. It may be used to assess SV or CO response to fluid challenges but has not been shown to predict fluid responsiveness.

It has also not been studied in any outcome-based studies.

In view of these last two factors, and concerns over a potentially large bias and limits of agreement, the NICO system, despite its appeal, cannot be recommended for routine use on the basis of the current evidence.
Another common problem encountered in the literature with respect to Bland-Altman analysis is its use with repeated measures in the same patient. Bland-Altman analysis was originally designed only for use with a single set of measurements per patient. Thus if studies use repeated measurements in the same patient/s then they need to use a modification of the Bland-Altman method or random effects modelling—this must be stated clearly in the methods before one accepts data from the study, otherwise, the variation of the differences may be underestimated.

In addition, Bland-Altman analysis usually provides a summary of the available data over the entire range of measurements. It is, however, often at the extremes of measurements that clinical decisions need to be made, and the overall bias and limits of agreement may not tell us how reliable the information is at these extremes. We thus need appropriate calculations of bias and limits of agreement for the range/s of interest to us. Or even better, we need to adopt the approach discussed below.

Third, we are mostly asking the wrong question and thus using the incorrect statistical tool. The key question/s should not be “can the new device be used interchangeably with PAC ITD?” We should be asking if the new device can yield useful clinical data to guide therapy, and ultimately improve patient outcome. Once we begin to ask these questions, receiver operator characteristic (ROC) analysis becomes the most appropriate statistical tool. ROC curve was initially designed for use in radar development. We can now use ROC analysis medically, to assess the quality of a new decision making tool, its sensitivity and specificity, and the optimal decision-making point. One plots the sensitivity (true-positive rate) on the y-axis against 1-specificity (false-negative rate) on the x-axis, for different decision-points, thus generating a curve for each tool. For example, one could plot the sensitivity and 1-specificity rates for a SVV of 8%, 10%, 12%, 14%...to predict fluid responsiveness. A useful test will have the plot in the upper left quadrant. This can be quantified by determining the area under the curve (AUC) for the test. An AUC of 0.5 or less suggests the test is no better than chance at predicting the stated outcome, whereas an AUC of close to 1.0 indicates excellent predictive value. By identifying the point on the curve with the best combination of sensitivity and specificity one can also use ROC analysis to determine the optimal decision-making threshold for a particular test. For example, a study mentioned in this text used ROC analysis to determine that the optimal decision-making threshold for predicting fluid responsiveness, with SVV, was 9.6% for SVV using Flotrac/Vigileo as this resulted in the best combination of a sensitivity of 91% and a specificity of 83%. ROC analysis thus offers us the ability to compare the impact of different methods of measuring cardiac output and related parameters, and different threshold values, on clinical decision making and, ultimately, on patient outcome. This is ultimately the purpose of any new
device, and is how new devices and techniques should be evaluated.

**Fig 2: ROC curve for predicting fluid responsiveness**

Hopefully new cardiac output monitoring studies will show a move away from mangled statistics and merely comparing devices against a flawed “gold standard”, and will begin to evaluate these new tools on their ability to influence clinical decision making and patient outcome, and will assist us in determining optimal decision-making thresholds. In addition, we need to ensure that appropriate patient populations are studied and the range of values that would dictate decision making are focused on specifically. In the interim we have to make do with what is available and I will endeavour to extract as much of value from the current literature as possible.

**Ideal Cardiac Output Monitor**

- Noninvasive or minimally invasive
- Appropriate for use in a wide variety of clinical settings e.g. theatre, ICU, labour ward, recovery room, ambulance, emergency room
- Appropriate for conscious or anaesthetised/sedated, intubated or nonintubated patients
- Appropriate for adult or paediatric patients
- Accurate and reproducible
- Continuous
- Provide real-time data
- Allow response to interventions to be tracked and targeted
- Reliable under different physiological conditions
- Minimal specialised training

remains constant during both measurement periods the Fick equations for the non-rebreathing (n) and rebreathing (r) periods can be combined:

\[
CO = \frac{VCO_2n}{CvCO_2n - CaCO_2n} \quad \text{and} \quad CO = \frac{VCO_2r}{CvCO_2r - CaCO_2r}
\]

therefore

\[
CO = \frac{VCO_2n - VCO_2r}{(CvCO_2n - CaCO_2n) - (CvCO_2r - CaCO_2r)}
\]

Because the body has large CO2 stores and CO2 diffuses very rapidly in blood (22 times faster than O2), and thus equilibrates very rapidly, it can be assumed that CvCO2 will remain essentially constant during rebreathing and non-rebreathing periods. Therefore:

\[
\Delta VCO_2 = \text{change in CO2 elimination between non-rebreathing and rebreathing periods.}
\]

\[
\Delta CaCO_2 = \text{change in arterial CO2 content between non-rebreathing and rebreathing periods.}
\]

\[
\Delta CaCO_2 \text{ can be approximated to the change in ETCO2 (dETCO2) multiplied by the slope (S) of the CO2 dissociation curve. Therefore:}
\]

\[
CO = \frac{\Delta VCO_2}{S \times \Delta ETCO_2}
\]

Only non-shunted blood (pulmonary capillary blood flow) is measured using this technique. In order to obtain an accurate cardiac output measurement, one then needs to estimate the shunt fraction. This can done accurately, and relatively non-invasively (only requiring an arterial blood gas), using PaO2, FiO2 and Nunn’s iso-shunt plots. SpO2 can also be used; this is less accurate but obviates the need for an arterial blood gas.

The only commercially available product that uses this principle is the NICO system. This consists of a disposable rebreathing loop, with a rebreathing valve, and a mainstream infrared CO2 analyser and airflow sensor. The rebreathing valve and loop is used to create intermittent partial rebreathing states in cycles of 3min, during which cardiac output is calculated. During a baseline period of 60 seconds the valve is in non-rebreathing mode. This is followed by a partial rebreathing phase of 35 seconds (previously 50
offered by a number of the other monitors discussed. The first obstacle is the extensive training required to become proficient with TOE. Following from this is the fact that TOE is highly operator dependent, limiting inter-observer reliability. The little matter of the never-ending march of time also comes into play: simply put, TOE takes too long to be used as a cardiac output monitor in the ways proposed in this text. As an example, a study of 3-D TOE cardiac output determination reported an acquisition time of 43 seconds, with postprocessing taking 7 minutes before a cardiac output was available. In addition the devices are costly and the probes a large and uncomfortable and preclude continuous monitoring. The development of automated cardiac output assessment may make this device somewhat more user-friendly as a cardiac output monitoring tool. So, although TOE has great clinical utility in other settings, this is currently not the setting for it.

4) Partial Carbon Dioxide Rebreathing Systems

These use a modification of the Fick principle- the differential Fick partial rebreathing method- to calculate cardiac output. The Fick principle is based on the conservation of mass, with the total uptake or release of a substance by an organ being the product of the blood flow to that organ multiplied by the arteriovenous concentration difference of the substance. One may use this principle, with respiratory gases as the indicator, to calculate pulmonary capillary blood flow and cardiac output, if one knows or assumes the shunt fraction. Traditionally oxygen has been used as the indicator with

\[
CO = \frac{VO2}{CaO2 - CvO2}.
\]

This is, however, restricted to research/ catheterisation laboratories as it is invasive and prone to methodological error. With the aid of modern technology CO2 can, far more conveniently, be used as the indicator, with the new equation reading:

\[
CO = \frac{VCO2}{CvCO2 - CaCO2}.
\]

CaCO2 can be calculated from PaCO2 or, more conveniently, estimated from ETCO2. VCO2 can be calculated from the difference between inspired and expired gas CO2 content. CvCO2 is much more difficult to measure. It can, however, ingeniously, be estimated non-invasively with a partial rebreathing technique: the differential CO2 Fick partial rebreathing method. This involves adding approximately 150ml (on average-volumes vary according to instrument settings) of dead-space to the breathing circuit by opening a rebreathing valve and measuring the change in VCO2 and ETCO2 measured during a period of non-rebreathing and a subsequent period of rebreathing. If cardiac output

- Easy to use
- Assess preload or predict volume responsiveness
- Assess contractility
- Not require calibration
- Safe

Minimally Invasive Cardiac Output Monitors

The specific minimally/noninvasive cardiac output monitors will now be discussed individually. I will focus on those monitors in current clinical use, although others may be alluded to briefly. The monitors will be discussed in the following categories:

1) Arterial Waveform Analysis
   a) Calibrated
      i) Transpulmonary thermodilution (PiCCO)
      ii) Lithium dilution (LiDCOplus)
   b) Non-calibrated
      i) Vigileo/Flotrac
      ii) PRAM
   c) Non-invasive
2) Doppler Ultrasound
   a) Transoesophageal doppler
   b) Suprasternal/Transthoracic doppler
3) Transoesophageal Echocardiography
4) Partial Carbon Dioxide Rebreathing Systems
5) Electrical Impedence
   a) Thoracic Electrical Bioimpedance
   b) Electrical Velocimetry
6) Miscellaneous

1) Arterial Waveform Analysis Cardiac Output Monitors

This category represents a variety of monitors that attempt to measure cardiac output and related parameters from analysis of the arterial pressure wave, measured invasively or non-invasively. They use a number of different techniques and proprietary algorithms of varied secrecy and complexity. Some are calibrated against an intermittent reference method of cardiac output determination, while others are uncalibrated and rely on increasingly complex algorithms and reference databases. Thus, despite many similarities, they are a heterogenous group of devices and must be viewed individually with regards to their basic science and clinical data. Despite this they do share a common origin, philosophy, and obstacles that have to be overcome to generate a reliable cardiac output.
The original premise that cardiac output could be calculated from analysis of the arterial pressure waveform was developed by Otto Frank in 1899. \( \text{CO} = \frac{\text{MAP}}{\text{TPR}} \) and TPR could be calculated from the time constant of diastolic aortic pressure decay and arterial compliance (estimated from the aortic pulse wave velocity). Wesseling subsequently determined that the area under the systolic portion of the arterial pressure-time curve divided by aortic impedance (AUCsys/Zao) was a better determinant of cardiac output than MAP, thus pulse contour analysis (and its offshoots) was born. Unfortunately, despite the theoretical elegance, the reality of generating a cardiac output from a pressure waveform has proven extremely complicated as the determinants of the pressure waveform are complex, interrelated physiological parameters that are difficult to model accurately. These include arterial impedance, compliance and peripheral vascular resistance.

**Aortic impedance** represents the opposition to pulsatile aortic inflow. Impedance is influenced by aortic cross-sectional area and compliance.

**Compliance** represents the resistance of the aorta to volume increases, correctly speaking the change in aortic volume per unit change in pressure (dV/dP). Compliance exhibits non-linear behaviour, roughly exponential, with a substantial decrease when arterial pressure increases significantly. Langewouters studied this non-linear behaviour in vitro (in fresh cadavers) and mathematically described how compliance varies with age, gender and height.

**Systemic vascular resistance** is the opposition of the systemic vascular beds to the drainage of blood. It is a dynamic factor and depends on many factors, including circulatory filling, sympathetic tone, temperature, and vasoactive drugs. Cross-sectional area (CSA) is also dependent on age, sex and height, but individual patients may deviate 30% from Langewouters’ population, a possible source of error in any model using this data.

To further complicate matters, the arterial pressure wave is composed not only of the incident wave but also of reflected waves, a source of interference which must be accounted for. In addition most invasive arterial catheters are sited peripherally, leading to distortion of the aortic pressure wave. There are also a number of potential technical issues with arterial catheters and transducers that may come into play e.g. damping, kinking, clots.

Whatever model used, a “relative” cardiac output is calculated. This is then converted to an “actual” cardiac output by comparing the initial calculated value with a calibration cardiac output or a calibration factor derived from a stored algorithm.

Despite the above challenges, a number of cardiac output monitors based on the above principles have, fairly recently, become available for clinical use.

Advantages include:
- Completely noninvasive, which lends itself to widespread use in a variety of patients and settings
- It is safe, usually well tolerated, quick, and cost-effective.
- Entire CO measured with no need for K factor

Major disadvantage are:
- Not a continuous method. Because of the instability of the chest, and the nature of the probe, it is best suited to intermittent assessment of haemodynamic status, unless one is going to stand manning the probe for hours on end.
- Some patients, e.g. those that are breathless, may not tolerate the technique because it requires use in the supine position, and others may find the probe uncomfortable—especially in the suprasternal position.
- Concerns regarding the learning curve required. Finding the correct acoustic windows and signal may be challenging.
- Accuracy may be affected by the presence of a haemothorax or pneumothorax, intracardiac shunts, arrhythmias, and regurgitant lesions.
- Difficulty to accessing the acoustic windows in certain forms of surgery e.g. cardiothoracic, head and neck.

There are no studies documenting its use in predicting volume responsiveness, goal-directed therapy, or influencing outcome. More studies are needed to define its possible future role in patient care.

3) **Transoesophageal Echocardiography**

This technique offers the closest to a complete assessment of cardiac anatomy and physiology we have. It allows us to assess cardiac anatomy, including valvular function; preload (including the possibility of fluid optimisation and assessing volume responsiveness); left ventricular function; and presence of ischaemia/infarction e.g. development of ventricular wall motion abnormalities. Although the reported accuracy of TOE assessment of cardiac output vs PAC ITD varies considerably, new techniques such as 3-dimensional TOE offer the possibility of much improved accuracy.

Many factors, however, prevent this from being a practical alternative as a cardiac output monitor for routine use in a variety of settings—a possibility that is
monitor; the optimal therapeutic strategies; to validate the use of oesophageal Doppler optimisation in further patient populations (especially those who are haemodynamically unstable/requiring vasopressor support and those with dynamic changes in SVR); and to determine which groups, if any, will show a convincing mortality benefit.

b) Suprasternal/Transthoracic Doppler

Based on the same principles as oesophageal Doppler monitoring devices, but using either a suprasternal or a transthoracic acoustic window, these monitors offer a completely noninvasive alternative to oesophageal Doppler. Determinations may be done with the special ultrasound probe in the suprasternal position, in which case the ascending aortic VTi is obtained, and aortic valve area is derived, from a proprietary nomogram, to allow calculation of CO and associated Doppler variables. The 3rd or 4th parasternal intercostal space may also be used, with resultant determination of pulmonary outflow VTi and use of the pulmonary valve CSA (also derived from a proprietary nomogram). Whichever method is used the optimal signal needs to be obtained, as per oesophageal Doppler, before any haemodynamic readings are made.

An advantage of this method vs oesophageal Doppler is that the entire right- or left-sided output is measured and the displayed result is not affected by changes in distribution of blood flow between upper and lower body (cf. K factor in oesophageal Doppler monitoring). Obtaining an optimal signal is, however, potentially more challenging with this technique and thus interobserver variability may be higher, and the learning curve may be longer. A study that specifically looked at interrater reliability in children showed an interrater bias of 0.06 l/min in CI calculation, with LOA of -1.91 to 2.02 l/min.

The most commonly used device is the USCOM (Ultrasonic Cardiac Output Monitor). Results have again been conflicting. A study on postoperative cardiac surgical patients showed a bias of 0.22 l/min for CI vs PAC ITD, with LOA of -1.17 to 1.62 l/min and a percentage error of 52%

Another study in postoperative OPCAB patients showed a bias of -0.13 l/min for cardiac output versus PAC ITD, with LOA of -0.86 to 0.59 l/min and a percentage error of 31%

An interesting study looked at cardiac output measurement using USCOM in heart failure patients with an orthotopic total artificial heart (TAH). The total artificial heart has a known cardiac output and when compared with this the USCOM cardiac output showed a bias of -0.01 l/min, limits of agreement of...
calculated from the area under the thermodilution curve using the modified Stewart-Hamilton equation:

\[ CO = \left[ (T_b - T_i) \times V_i \times k \right] / \int dT_b(\text{d}t) \]

\( T_b \) = blood temperature
\( T_i \) = Injectate temperature
\( V_i \) = Injectate volume
\( k \) = correction constant taking into account specific weight and specific heat of blood and injectate
\( \int dT_b(\text{d}t) \) = Area under thermodilution curve

The thermodilution curve is compromised of a number of exponential decay curves which are generated as the injectate passes through the various compartments of the circulation. Most of the temperature change occurs in the intrathoracic compartment because the thermistor is fairly proximal. Analysis of the different curves thus allows calculation of parameters such as intrathoracic blood volume (ITBV) and extravascular lung water (EVLW).

As alluded to above, the arterial catheters used to measure the thermodilution curve and the pressure waveform are specific PICCO catheters (7cm-22cm). These are inserted in a proximal artery—preferably the femoral artery, but brachial and axillary catheters are also available. It appears that using the femoral site is preferable, and that the longer the catheter, the better the accuracy (possibly from better approximating aortic pressure waveform)\(^ {34} \).

Once calibrated the PICCO system allow continuous cardiac output. It is recommended that calibration is performed every 8 hours but a study by Hamzaoui in critically ill medicated patients showed an increased percentage error 1 hour after calibration\(^ {33} \). Thus, calibration should perhaps be performed more frequently, even hourly, especially in the setting of rapidly changing haemodynamics. In fact, calibration should be performed routinely if there is any major haemodynamic change e.g. in various phases of cardiac surgery—post-induction vs open chest vs post-bypass for instance.

After entering demographic data (height, weight, age, gender) the following parameters are measured or calculated by the PICCOplus system (normal range in brackets where relevant):

- **Flow**: CO/CI
- **Preload**: GEDV/GEDVI (680-800ml/m\(^2\))
- **Predictors of volume responsiveness**: SVV
- **PPV**

Device, the CardioQP, has been designed for use in children. This is an advance in paediatric cardiac output monitoring which is traditionally fraught with difficulty. A study comparing CardioQP to IDT showed a large bias of 0.66 l/min and LOA of -1.13 to 2.45 l/min. Despite this, the authors concluded that this device was a rapid, bed-side, minimally invasive, less expensive, user-friendly tool for cardiac output measurement over a wide range of patient size, and should be used primarily for differentiating whether the child is in a low, medium, or high cardiac output range.

Despite these inconsistent results (largely in comparison to PAC ITD), the true test of a device is whether it can influence patient outcome. This is where oesophageal Doppler cardiac output monitors come up trumps. This is the form of minimally invasive cardiac output monitor with the most convincing evidence of outcome benefit when used as part of a goal-directed strategy. Whether fluid optimisation was achieved using SV, FTc or a combination of these variables, the available studies have consistently shown improved outcomes with oesophageal Doppler-guided fluid optimisation.

A systematic review of the literature for the use of oesophageal Doppler monitoring for fluid replacement in major abdominal surgery showed significant reductions in hospital stay; complications (cardiovascular—including less CCF, renal, respiratory and GIT); ICU admissions; and use of inotropes in the intervention group (oesophageal Doppler optimisation). In addition a more rapid return of gut function was demonstrated. This review also showed a trend toward a reduction in mortality but this was not statistically significant. Of note, significantly greater volumes of colloid were used in the intervention groups and traditional markers of fluid status e.g. BP, HR, CVP, urine output were not significantly different between intervention and control groups\(^ {35} \). Similar benefits have also been shown in cardiac surgery, orthopaedic surgery and urological and gynaecological surgery\(^ {1,61} \).

As an example of a possible optimisation strategy I have included the protocol used by Sinclair in his study of patients undergoing femoral fracture repair\(^ {64} \):

If FTc < 350 ms (suggesting hypovolaemia), a fluid challenge of 3ml/kg is given over 5-10min with 3 possible outcomes and responses:

1) SV same or increased, FTc < 350ms-repeat fluid challenge
2) SV increases > 10%, FTc > 350 ms -repeat fluid challenge till no further increase in SV
3) FTc > 400 ms – no further fluid till FTc or SV decreased.

As discussed under fluid optimisation strategies FTc can be reduced in situations other than hypovolaemia, thus a strategy that combines its use with that of another variable e.g. SV is probably optimal.

While the details remain to be decided, the use of oesophageal Doppler monitoring to guide haemodynamic optimisation has already shown clear benefit. What still needs to be done is to define the optimal variables to...
A degree of operator dependency, as discussed above.

Some core methodological limitations: The oesophageal Doppler only measures descending aortic blood flow. The K factor is assumed to be approximately 30% (CardioQ uses a more complex algorithm). This, however, only applies to young, stable patients and there are many potential confounders. For example, the ratio changes with age, hypovolaemia (preferential diversion of CO to coronary and cerebral circulations, with less descending aortic blood flow), neuraxial blockade (vasodilation results in a greater proportion of blood flow to descending aorta), and other disease states such as atherosclerotic aortic disease and aortic coarctation. In addition aortic cross-sectional area is not constant and is a dynamic variable that changes with pulse pressure, vascular tone, aortic compliance, volume status, and catecholamine administration. Even when measured, the assumption that the aorta is round is not strictly valid, and using $\pi r^2$ to calculate CSA from measured width can result in error.

Since the radius is squared any error in measurement, or assumption of radius, can result in a significant error in cardiac output.

So what is the clinical experience with oesophageal Doppler monitoring (ODM)?

With regards to comparisons of oesophageal Doppler CO/SV performance with a gold-standard, the results have been inconsistent as usual. A metanalysis of 11 ODM studies vs PAC ITD showed a bias of 0.19 l/min with wide LOA of -2.21 to 2.33 l/min, and a percentage error of 52%.

The bias was viewed as acceptable, but the wide LOA was noted with concern, and was interpreted as being contributed to by both the ODM devices and inaccuracies with PAC ITD. A study specifically focusing on CardioQ measurements of CO during OPCABs showed a large bias of -0.56 l/min and wide LOA of -1.84 to 0.72 l/min.

However, a very interesting study showed that with appropriate training (12 insertions of CardioQ) bias was reduced from 1.2 l/min to 0.1 l/min and LOA from 3.2 to 2.2 l/min. This suggests operator dependency and an important role for appropriate training in improving accuracy with this device. Similarly inconsistent results were found for the Hemosonic device. A post-operative cardiac surgical study found a bias of -0.23 l/min with wide LOA of -2.35 to 1.89 l/min. However, another study using an aortic flow probe found that under steady state conditions the SV as measured by the Hemosonic probe differed by < 4% from that measured by the aortic flow probe. The same study found that under dynamic conditions the Hemosonic monitor closely tracked changes in SV but occasionally differed with regards to absolute values.

There may be a tendency to reduced accuracy (compared to PAC) in low CO situations.

As mentioned above, ODM is suitable for use in paediatrics, with clinical experience with both forms of devices. A specific version of the CardioQ

- **Contractility**: Global EF
  - Cardiac Function Index (4.5-6.5/min)
  - Index of LV contractility
- **Afterload**: SVR/SVRI
- **Pulmonary oedema**: EVLW/EVLWI (< 10ml/kg)
  - Pulmonary vascular permeability index

It is proposed that an increased EVLW is an important cause of respiratory failure in critically ill patients and studies suggest that using EVLW as a guide to fluid and haemodynamic management may improve outcome. It is calculated as follows: the intrathoracic thermal volume (ITTV) represents the volume of distribution of the thermal indicator. It is calculated from ITTV = CO x mean transit time (Mtt) of thermal indicator. The pulmonary thermal volume (PTV) = CO x downslope time (Dst). GEDV = ITTV – PTV (ml). ITBV has a linear relationship to GEDV with GEDV/ITBV = 1.25GEDV – 28.4 (ml). EVLW = ITTV – ITBV. In other words, EVLW is the difference between thermal indicator distribution in the chest and blood volume in the chest. Whether this parameter (or, in fact, many of the parameters above) will prove useful in clinical practice remains to be seen, but they are interesting prospects, even if mired in mathematics.

There are a number of potential benefits to the PICCO system:
- Transpulmonary thermodilution is a well validated reference method.
- The thermal indicator obviates the need for a chemical indicator (which may be associated with adverse effects, and recirculation and accumulation)
- Loss of the thermal signal is not significant with the long catheters and central monitoring site
- Not influenced by the ventilatory cycle
- Continuous cardiac output monitoring.
- Offers predictors of fluid responsiveness (SVV, PPV), for fluid optimisation strategies.
- Numerous other variables offered - allows a comprehensive cardiac assessment
- Offers assessment of EVLW.
- Suitable for use in awake or anaesthetised patients
- Suitable for ventilated or spontaneously breathing patients (except SVV, PPV)
- Appropriate for use in paediatric patients

**Disadvantages** include:
- The need for central venous access and proximal arterial access (is it in fact truly noninvasive?)
- The use of specific arterial catheters often requires insertion of a second catheter-increasing cost and risk to patient (if preexisting A-line was present)
- The utility of many of the extra parameters offered by PICCO has yet to be proven
The potential need for frequent recalibration is time-consuming and inconvenient.

- It is unsuitable for use in patients with intracardiac shunts, intraaortic balloon pumps, significant aortic valve disease, and significant arrhythmias.

- Technical difficulties with the arterial line or transducer, e.g., damping, will result in inaccurate readings. The system is thus highly dependent on the quality of the arterial pressure trace.

The clinical experience with PiCCO has been conflicting:

- Studies using an old algorithm showed a bias of -0.04 to 1.2 l/min vs PAC ITD CO, and limits of agreement (LOA) ranging from +/- 2.02 to +/- 3.75 l/min. The worst values were obtained with the use of phenylephrine (altered vascular characteristics).

- Two studies using newer versions of the software showed a bias of -0.05 l/min/m² (CI) and LOA of only +/- 0.24 l/min/m² (ICU patients with rapid preload changes) and a bias of -0.07 l/min/m² (CI) with LOA of +/- 0.92 l/min/m² (intraoperatively in cardiac surgery).

A further intraoperative study in OPCAB patients showed a bias of 0.13 l/min vs PAC ITD CO with excellent LOA of +/- 0.2 l/min. What was also interesting to note, was that in this study PiCCO tended to underestimate CO when ITD CO was < 4.0 l/min, and overestimate Co when ITD CO was > 6l/min.

With reference to the Hamzaoui study mentioned above, the overall bias was 0.12 l/min/m² (CI) with LOA of +/- 1.22 l/min/m², and a percentage error of 35%. Within the first hour after calibration the percentage error was only 26-27%, even with large changes in vascular resistance. After the first hour the percentage error was 36%.

The literature seems to suggest that this is an acceptable method of cardiac output monitoring but may be less reliable with rapidly changing haemodynamics, at the extremes of cardiac output, and if not calibrated frequently enough. Recently PiCCO has even been used as the reference method in cardiac output monitor studies, notably in evaluation of the Vigileo/Flotrac device.

The other major clinical use for the PiCCO system is in the prediction of fluid responsiveness and fluid status assessment. This has been discussed above.

The key points emerging from the literature are that, although GEDV and ITBV may have some utility, SVV and PPV are the most promising variables with regards to fluid optimisation. It is important to note that the applicable thresholds differ depending on the device used, the parameter used, and the % SV increase one is aiming for. The PiCCO technical specifications list a SVV and PPV of < 10% as being normal. However, as discussed above the optimal threshold values for predicting a 25% increase in SV with PiCCO are > 12.0% for SVV and > 13.5% for PPV.

There have been no prospective, randomised, controlled studies published to date, as an index of afterload. Corrected flow time (FTc), can be used as a marker of preload or fluid responsiveness. The flow time, or LV ejection time, is the time from the beginning of the aortic pulse wave upstroke to its return to baseline. The FTc is the systolic flow time, corrected for a heart rate of 60bpm-to allow easier comparison of values. Normal FTc is quoted as 330-360ms; however, a value < 350ms is often used to suggest hypovolaemia.

SV ÷ maximum acceleration may also be used as a preload parameter

Irrespective of the model chosen, oesophageal Doppler monitors consist of a flexible probe, approximately the thickness of a nasogastric tube. This is inserted into the oesophagus, either nasally or orally, in an anaesthetised or sedated patient. The ideal location for the probe tip is between the fifth and sixth thoracic vertebrae (3rd intercostal space), which is approximately 35cm at the incisors in the average adult patient. Once at the anticipated depth, the probe is slowly rotated to provide the optimal signal: highest peak velocity; optimal M-mode signal; sharp crisp sound; well-defined waveform. The probe may be left in for days, if required, but frequent adjustment to maintain optimum positioning may be needed. It is contraindicated in patients with oropharyngeal or oesophageal pathology or those who are to undergo surgery in the region of the probe. Severe aortic coarctation and the presence of an intraaortic balloon pump are also contraindications.

Key advantages of the oesophageal Doppler monitor are:
- Only as invasive as a nasogastric tube, and no invasive haemodynamic access required
- Quick and easy to insert
- Continuous, real-time assessment of key cardiovascular parameters
- Measures not only CO/SV, but also offers a total haemodynamic assessment (barring visual assessment of the heart), including preload, contractility, afterload, and heart rate and rhythm.
- Although some specialised training is required, the learning curve is steep, and proficiency is obtained in 10-12 insertions. It is still, however, somewhat operator dependent.
- Proven role in goal-directed therapy/fluid optimisation
- Well documented use in paediatrics

Disadvantages include:
- Patient discomfort from the probe.
- This limits its use to anaesthetised or sedated patients, and thus, mainly to the intraoperative period or ICU patients. Softer probes are being developed which could well expand its indications into the entire perioperative period and to other areas of the hospital.
- May need for frequent repositioning,
- Requires some specialised training,
analysis. The area under the velocity time curve, mathematically determined as the integral of the derivative of velocity over time (dV/dt), from T0 (the start of aortic blood flow) to T1 (the end of flow), is known as the velocity time integral (VTi). The VTi (velocity x time = distance) gives the stroke distance i.e. the distance a column of blood travels along the aorta during ventricular systole. Since length x area = volume, multiplying the VTi (stroke distance) by cross-sectional area (CSA) of the descending aorta will give stroke volume. The CSA is estimated from nomograms based on age, sex, height, and weight as in the CardioQ/QP monitor. More recently it can be calculated from \( \pi r^2 \) via direct measurement of the aortic radius by M-mode ultrasound as in the Hemosonic monitor. CO is then calculated from \( CO = SV \times HR \). This is, however, only descending aortic SV/CO and does not take into account coronary and brachiocephalic blood flow, which accounts for approximately 30% of actual cardiac output. Thus a correction factor (K) of 30%, must be applied by the device, to descending aortic blood flow, to estimate actual SV/CO.

![Fig 5: Typical doppler velocity time curve.](image)

A number of parameters other than SV/CO are calculated, or can be inferred, from the shape of the displayed oesophageal Doppler waveform: The peak velocity, \( PV(\text{cm/sec}) \), is an indicator of LV contractility. PV declines with age. A low PV suggests poor LV contractility e.g. LVF. Afterload influences PV to some degree. Normal PV varies with age, e.g. 90-120cm/sec at age 20; 70-100cm/sec at age 50; 50-80cm/sec at age 70. Maximum acceleration (Hemosonic) and mean acceleration (CardioQ), are also indicators of LV contractility. There has been shown to be a linear relationship between maximum acceleration and ejection fraction. This variable may be affected by preload and afterload. Total systemic vascular resistance can be calculated, if MAP is entered into the support the use of PICCO as part of a goal-directed strategy. However, a prospective study in CABG patients was conducted by Goepfert, which compared GDT using PICCO-derived CI, GEDV and EVLW, with historical controls. The GDT was instituted from induction, and continued for 48 hours, or discharge from ICU \(^{19,84}\). The study utilised a complex algorithm to guide IV fluid, vasoactive, and inotropic therapy. The GDT patients were deemed fit for ICU discharge earlier, and had a shorter duration of mechanical ventilation. The clinical significance of these findings is questionable. PICCO, however, has great potential as a tool for GDT/fluid optimisation strategies and requires further investigation.

### ii) Lithium Dilution

The LiDCOplus monitor combines continuous arterial waveform analysis using the pulse power (as opposed to traditional pulse contour analysis) method of the PulseCO system, with calibration via lithium dilution, using the LiDCO system.

**Pulse power analysis** is based on the principle of conservation of mass, or in this case power. The net power change in the arterial tree is the amount of blood entering the system (the SV) minus blood lost to the periphery during the beat. Following calibration for compliance there is theoretically a linear relationship between nett power and nett flow (SV).

The first step in the algorithm transforms the pressure waveform into a volume waveform using the formula:

\[
\frac{dV}{dP} = \text{Cal} \times 250e^{-kp}
\]

Where:
- \( V \) = volume
- \( P \) = blood pressure
- \( \text{Cal} \) = calibration factor
- \( k \) = curve coefficient
- 250 = the saturation value (ml) i.e. the maximum above the starting volume at atmospheric pressure that the arterial tree can fill

The next step is autocorrelation, to determine what proportion of the change in power is due to the stroke volume. This takes the RMS of the waveform, derives the beat period, and derives a nett effective beat factor which is proportional to the nominal SV. This algorithm overcomes the problem of reflected waves as it takes into account the entire beat and thus is independent of the position of the sampling site. The nominal stroke volume is converted to actual stroke volume by calibration with the lithium dilution technique-allowing compliance, among other factors, to be taken into account.

**Transpulmonary lithium indicator dilution** involves the intravenous injection of a......
bolus of 0.15-0.3 mmol of a 150mmol/l lithium chloride solution. This meets many criteria for an ideal indicator and may be injected centrally or via an antecubital vein (cf. PiCCO). The lithium concentration is then measured by a sensor attached to a standard arterial line, which may have been inserted at any site. Blood is aspirated (3ml per calibration) into the sensor assembly at a constant rate by a battery operated pump. The voltage across an ion-selective membrane in the sensor is related to the lithium concentration in plasma by the Nernst equation.

A lithium concentration-time curve is constructed and the reference cardiac output is calculated from the AUC and lithium dose, using a modified Stewart-Hamilton equation:

\[
CO = \frac{(Li \times 60)}{[AUC \times (1-PCV)]}
\]

\(Li\) = lithium dose

\(AUC\) = area under lithium concentration-time curve prior to recirculation
\(PCV\) = packed cell volume

The correction, 1-PCV, is required as lithium is only distributed in plasma, and not in RBC, during the first pass. It is calculated from Hb(g/dl)/34 and is why the Hb has to be entered into the LiDCO monitor at the time of calibration. A correction also needs to be applied for plasma sodium, because, in the absence of lithium, the baseline voltage is determined by the sodium concentration in plasma. Severe hyponatraemia may render calibration unreliable.

This dose of lithium has no known pharmacological effect, and calibration is considered safe, even in patients with non-functioning kidneys, if they weigh 40kg or above. Use of this method is contraindicated in patients on lithium therapy, due to the poor signal-to-noise ratio. It is also contraindicated in the first trimester of pregnancy. Non-depolarising muscle relaxants may interfere with the lithium sensitive electrode and calibration should be performed prior to administration of a non-depolarising neuromuscular blocker.

Calibration should be performed at least 8 hourly, and more frequently if there is haemodynamic instability or evidence of any change in arterial compliance or resistance. The number of calibrations is theoretically time-limited by the lithium dose, but there is very little in the literature to support this.

Lithium dilution has been shown to be comparable to intrapulmonary thermodilution over a wide range of cardiac outputs.

The parameters displayed include: continuous CO, CI, SV, SVI, SBP, DBP, MAP, PPV, SVV, SPV, SVR, SVRI and ITBV. One can thus make a continuous assessment of flow variables i.e. CO/SV as well as preload/fluid monitoring and reduce the potential for complications. Unfortunately, current techniques have performed poorly. Examples include applanation tonometry-derived radial artery pulse contour analysis. This technique involves obtaining radial artery pressure waveforms noninvasively using a tonometer applied to the skin of the distal forearm over the radial artery. A recent study in critically ill patients showed a large bias of 2.03 l/min vs cardiac output determination via transpulmonary thermodilution, with a percentage error of 85%39. It was concluded that this device is not suitable for use as a cardiac output monitor in haemodynamically unstable critically ill patients. Another technique uses the volume-clamp method with a small pressure cuff placed on the finger. An aortic flow waveform is modelled from this input and integration of this waveform allows calculation of SV and CO. This technique does not compare well to PAC ITD but may have a limited role in outpatient care and medical research39.

2) Doppler Ultrasound

a) Transoesophageal doppler
b) Suprasternal/Transthoracic doppler

a) Transoesophageal doppler

Oesophageal Doppler cardiac output monitors use an ultrasound transducer mounted in a flexible oesophageal probe. Because of the proximity of the oesophagus to the descending aorta, an excellent acoustic window is created for relatively noninvasive monitoring of a number of aortic haemodynamic parameters. When ultrasound encounters tissues of different acoustic density a fraction of the emitted signal is reflected. When this ultrasound signal is directed along the path of blood flow in the aorta, a fraction of the ultrasound is reflected by the moving red blood cells. There is a shift in frequency of the reflected waves which is proportional to the velocity of the blood flow. This Doppler shift is the basic operating principle of all these devices and is expressed as follows:

\[
f_d = 2\left(\frac{f_t}{C}\right) \times V \times \cos \theta
\]

\(f_d\) = change in frequency (Doppler shift)
\(f_t\) = transmitted frequency
\(V\) = velocity of moving blood
\(C\) = velocity of ultrasound in blood
\(\cos \theta\) = cosine of the angle of insonation i.e. angle between the direction of the ultrasound beam and blood flow

By solving for V, the oesophageal Doppler monitor determines the velocity of blood flow in the descending aorta. As aortic blood flow is pulsatile and velocity changes with time, the velocity is plotted against time for further
minimally invasive cardiac output monitor. If questions over its performance in different clinical settings and patient populations can be satisfactorily answered with the new, or future, software versions it will represent a significant advance in cardiac output monitoring, and will pave the way for its widespread use in a variety of settings. Outcome studies are needed and if positive will cement its role in our armamentarium. As it currently stands, we need to be aware of the apparent strengths and limitations of this device, and use it sensibly, with these in mind at all times.

ii) Pressure Recording Analytical Method (PRAM)

This is a new pulse waveform method of cardiac output monitoring that does not require calibration or the use of demographic data. The arterial pressure waveform is sampled at a very high frequency of 1000Hz, via a standard femoral or radial arterial line. Analysis of the pressure profile changes is based on the theory of perturbations, in which any physical system under the influence of a perturbation tends to react to achieve its own state of minimum energy. The basic principle of PRAM is that, in any given vessel, volume changes occur mainly from radial expansion of the artery in response to changes in pressure. PRAM measures absolute stroke volume, without external calibration, by determining the parameters that characterise the elastic properties of the arteries from the analysis of the pressure wave profile over the entire cardiac cycle (systole and diastole). SV is calculated from:

\[ SV = \frac{AUC}{P(t)} \times K \]

- \( AUC \): area under systolic portion of pressure time curve
- \( P(t) \): pressure wave profile, expressed as the variation of pressure over time throughout the cardiac cycle
- \( K \): a calibration factor obtained from comparison of measure MAP with predicted MAP

Very few studies using this new technique are available, thus no conclusions as to its performance and future role can be really be reached. It does seem to be generating some interest in the paediatric community, however. A recent study in Pediatric Critical Care Medicine reported bias of 0.12 l/min, limits of agreement of -0.54 to 0.77 l/min, and a percentage error of 21% vs CO measurements by transthoracic echocardiography, in paediatric ICU patients. Thus, although there is early promise, it remains a case of watchful waiting for more studies to emerge before one can reach a reasoned opinion on PRAM.

c) Noninvasive Arterial Pressure Waveform Analysis

Noninvasive arterial pressure cardiac output determination is a theoretically attractive prospect as it would broaden the applicability of cardiac output responsiveness and afterload. If one enters SpO2/PaO2, DO2 is calculated intermittently and similarly, if central venous saturation is entered, the device will calculate VO2.

Advantages of the LiDCOplus system are:
- Central venous access is not required
- It does not require specific arterial catheters, of for the catheter to be inserted at a proximal site.
- It is thus truly minimally invasive
- It is quick to set up, easy to use and requires minimal training.
- A number of user-friendly interfaces and data presentation screens are available.
- It provides continuous cardiac output monitoring and allows assessment of fluid responsiveness
- Lithium dilution calibration has the advantages listed above, and, in addition, there is no possibility of thermal interference with calibration, especially in situations of rapid temperature changes e.g. coming off CPB (cf. PICCO).
- It is applicable for use in patients who are anaesthetised or awake; ventilated or not ventilated; and may be used in the pre-, intra- or postoperative setting and in a wide variety of other hospital settings.
- It has been used in paediatric patients.

Disadvantages include:
- Those associated with the lithium indicator, as discussed above.
- It is also subject to the limitations of all pulse waveform devices: the need for a good quality arterial trace.
- It is not suitable for use in patients with intracardiac shunts, intraaortic balloon pumps, severe aortic valve disease, significant arrhythmias and severe peripheral vascular disease or vasoconstriction.

Again, actual comparisons with PAC ITD CO measurement have proven conflicting. A study by Kim, in paediatric patients undergoing cardiac catheterisation, reported bias of 0.19 l/min/m² (CI) vs PAC ITD; the LOA were -0.09 to 0.47 l/min/m², resulting in a percentage error of 17.5%. This very favourable result is, however, in conflict with that reported by Yamashita in OPCAB patients, where a large bias of 0.71 to 0.76 l/min and wide LOA of +/− 2.26 to +/- 2.68 l/min were found. The conclusion in this study was that cardiac output by PulseCo is not interchangeable with thermodilution in patients undergoing OPCAB.

A further study, in cardiac surgical patients, showed bias of -0.17 l/min for CO, with LOA of -1.55 to 1.20 l/min. This study looked at the precision of the cardiac output monitor given different assumed precisions of PAC ITD. If the precision of PAC ITD was taken as 10% then the precision of LiDCO in this study was 10.2% which compares favourably with the criteria of Critchley and...
Critchley discussed in the statistics section. The authors felt their ITD may have a better precision, closer to 5%, and when this value was used the precision of LiDCO was 13.4% which may still be acceptable given its noninvasive nature. Interestingly, the values for PiCCO were 15.2% and 17.5% respectively. This study also revealed that LiDCO correctly tracked significant changes in cardiac output in 88% of cases (PiCCO 84%). Another interesting study showed that LiDCO was able to reliably track rapid changes in LVSV in comparison to aortic flow probe and appeared superior to oesophageal doppler in this instance. It was also noted that LiDCO tended to underestimate SV at higher SV's.

LiDCO offers the potential for fluid status assessment. As mentioned previously SVV and PPV variation are useful predictors of fluid responsiveness. ITBV may be used as a static marker of volume status. The LiDCO product information states that a SVV or PPV <10% is normal while values over 13-15% predict fluid responsiveness. Belloni reported that a SVV or PPV > 12% predicted an increase in CI by > 15%.

LiDCO has been used in goal-directed strategies. A study by Pearse in 2005 looked at a postoperative optimisation in 122 high-risk general surgical patients, assigned to either a control group, with fluid therapy guided by CVP, or a GDT group, guided by LiDCO monitoring. In the GDT group a concerted effort was made to achieve a DO2I of 600ml/min/m² within the first hour of reaching ICU. This was initially through fluid optimisation based on a SV optimisation approach. If the target DO2I was not reached with fluid alone dopexamine was introduced, up to a maximum of 1ug/kg/min. The protocol was maintained for 8 hours and then discontinued regardless of whether the target DO2I had been reached. The results showed a reduction in complication rate (68% in control group and 44% in the protocol group) and length of hospital stay (17.5 vs 29.5 days).

LiDCO is thus another device that appears to offer much potential as a cardiac output monitor and haemodynamic optimisation tool. As with all these devices, there remain concerns over performance in dynamic conditions. Therefore, in order to improve the accuracy of the device, more frequent calibration should be performed during changing haemodynamic conditions.

b) Non-calibrated Arterial Pressure Waveform Analysis
The ability to derive cardiac output from the arterial pulse waveform without the need for calibration is an attractive prospect as it removes the inconvenience and time consumption of calibration, it also eliminates the risk of adverse effects associated with the calibration method. In addition, it offers the prospect of eliminating the time-related decline in accuracy of calibrated methods as one moves further from the last calibration. There is also a reduced risk of an operator error, as can occur with calibration. Attaining this simplicity and ease

*1 Vigileo/Flotrac was found to track magnitude and direction of significant changes in cardiac output in 96% of cases.

*2 CO was overestimated at low CO and underestimated at high CO. The authors concluded that Vigileo/Flotrac performed well at low CO but was sensitive to changes in vascular tone.

*3 Phenylephrine resulted in a drop in CO with PAC TD but an increase in CO with Vigileo/Flotrac.

*4 Significant differences in performance were noted depending on timing of reading, probably related to differences in haemodynamic stability, with poorer performance during rapidly changing haemodynamic conditions.

*5 Note choice of PiCCO as reference method.

*6 The The significantly better performance of the device in Child-Pugh A vs Child-Pugh B and C patients was interpreted as being due to the pathologically low SVR in severe liver disease.

*7 Note again use of PiCCO as reference method.

*8 Note difference in percentage error between intraoperative and ICU readings, possibly related to fewer acute haemodynamic changes in ICU than intraoperatively.

As can be seen the results vary considerably. It does appear that the latest algorithm offers improved performance, if one excludes the study by Compton which questionably uses PiCCO as the reference method. One, however, cannot reliably claim this on the basis of the available evidence. It appears that the performance of the device is improved in conditions where rapidly changing haemodynamic conditions are less likely, i.e. acute changes in haemodynamics can adversely affect performance. This also appears less marked with the newer software. One also has to consider the possibility that Vigileo/Flotrac may in fact perform better than the reference method in situations with rapidly changing haemodynamics, resulting in the observed differences. The studies also suggest that the patients' underlying pathologies e.g. chronic liver disease need to be taken into account when choosing and evaluating a cardiac output device. More studies are clearly indicated to evaluate the latest software, in a variety of settings, and using a variety of patient populations.

Vigileo/Flotrac SVV has been validated for predicting fluid responsiveness. Using software version 1.07, a SVV > 9.6% predicted an increase in SV > 25% with a sensitivity of 91% and specificity of 83% (vs PiCCO: SVV >12.1%, sensitivity 87%, specificity 76%). A SVV > 10% was found to predict a 15% increase in CI with a sensitivity of 82% and specificity of 88%, using software version 1.10.

No GDT/fluid optimisation outcome studies have thus far been reported.

The Vigileo/Flotrac offers much promise as a simple, easy to use, truly
assessment of this device extremely difficult. One is unable to independently evaluate the algorithm, using stored waveforms or cardiovascular models, because it is not available publicly. In addition, the available clinical studies use a variety of different software versions, which may well not be comparable. So, not only, is there a plethora of studies to evaluate, but there is the added factor of different software versions to consider. It is not surprising then that the literature is confusing and inconsistent.

I have attempted to provide an overview of the current literature regarding the performance of the Vigileo/Flotrac device in following table, which contains key studies published from 2007:

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Software</th>
<th>Setting</th>
<th>Ref</th>
<th>Bias (l/min)</th>
<th>LOA (l/min)</th>
<th>% Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>McGee(^{41})</td>
<td>2007</td>
<td>?</td>
<td>Multicentre, mixed medical surgical ICU</td>
<td>PAC ITD 0.2</td>
<td>-2.36 to 2.75</td>
<td>43%</td>
<td></td>
</tr>
<tr>
<td>Breuker(^{40})</td>
<td>2007</td>
<td>?</td>
<td>Post-cardiac surgery</td>
<td>PAC ITD -0.14</td>
<td>-2.14 to 1.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chakravathy(^{44})</td>
<td>2007</td>
<td>?</td>
<td>OPCAB</td>
<td>PAC ITD 0.15</td>
<td>+/- 0.66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorsomradee(^{43})</td>
<td>2007</td>
<td>1.01</td>
<td>Cardiac surgery</td>
<td>PAC TD 0.12</td>
<td>-3.25 to 3.49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>De Waal(^{23})</td>
<td>2007</td>
<td>1.01</td>
<td>CABG intra-op / postop</td>
<td>PAC ITD 0.0</td>
<td>-1.74 to 1.74</td>
<td>33% after induction 45%</td>
<td></td>
</tr>
<tr>
<td>Zimmerman(^{30})</td>
<td>2008</td>
<td>1.01</td>
<td>CABG intra-op / postop</td>
<td>PAC TD -0.13</td>
<td>-3.13 to 2.86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sakka(^{45})</td>
<td>2007</td>
<td>1.07</td>
<td>Septic shock</td>
<td>PICCO 0.5</td>
<td>+/- 4.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biais(^{22})</td>
<td>2008</td>
<td>1.07</td>
<td>Liver transplant</td>
<td>PAC TD 0.8 (Child-Pugh A 0.025)</td>
<td>-1.8 to 3.5 (Child-Pugh A 0.64) to 0.69</td>
<td>43% (Child-Pugh A 15%)</td>
<td></td>
</tr>
<tr>
<td>Button(^{39})</td>
<td>2007</td>
<td>1.07</td>
<td>Cardiac Surgery</td>
<td>PAC TD 0.1-0.6 intraop 0.1-0.2 ICU</td>
<td>+/- 1.8 to +/- 2.4 intraop +/- 2.4 to +/- 2.6 ICU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mehta(^{31})</td>
<td>2008</td>
<td>1.07</td>
<td>OPCAB</td>
<td>PAC ITD 0.26</td>
<td>+/- 1.33</td>
<td>29%</td>
<td></td>
</tr>
<tr>
<td>Compton(^{37})</td>
<td>2008</td>
<td>1.10</td>
<td>Haemodynamically unstable ICU</td>
<td>PICCO 0.68</td>
<td>+/- 1.94</td>
<td>58.8%</td>
<td></td>
</tr>
<tr>
<td>Mayer(^{38})</td>
<td>2008</td>
<td>1.10</td>
<td>Cardiac surgery</td>
<td>PAC ITD 0.19</td>
<td>+/- 0.6</td>
<td>24.6% Intraop 28.3% ICU 20.7%</td>
<td></td>
</tr>
</tbody>
</table>

of use while maintaining acceptable accuracy has, however, proven challenging because of the difficulties in accurately modelling the circulatory system described above.

i) Vigileo/Flotrac
The device which has shown the greatest promise in overcoming these difficulties and which consequently features most prominently in the literature is the Vigileo/Flotrac system. This consists of the Flotrac sensor and Vigileo monitor and uses an algorithm based on pulse contour analysis.

The Flotrac sensor is attached to an existing peripheral arterial line. The Flotrac algorithm then analyses the pressure waveform at 100Hz for 20-second intervals, capturing 2000 data points per interval. The standard deviation of the arterial pulse pressure (σAP) is then calculated from this set of data points. The standard deviation of the pulse pressure is used, instead of pulse pressure per se, because σAP is independent of the effects of vascular tone. It is proportional to the SV. σAP (mmHg) is then converted to SV (ml/beat) by application of a conversion factor Khi (χ): SV = χ x σAP. CO is then calculated from CO = PR x SV; of note pulse rate (PR) is used instead of heart rate as only truly perfused beats are captured to calculate CO.

χ is a multivariate polynomial equation that assesses the impact of the individuals ever-changing vascular properties e.g. compliance, resistance, impedance on pulse pressure. It can be depicted as:

χ = M (HR, σAP, C(p), BSA, MAP, µ3ap, µ4ap)

M represents the multivariate polynomial equation and the variables in brackets are the multiple determinants of χ. HR and σAP are self-explanatory. Body surface area (BSA) is calculated from Dubois’ equation using entered demographic data of height and weight. Mean arterial pressure (MAP) is calculated by taking the sum of the sampled pressure points over 20 seconds and dividing this by the number of points.

C(p) is the large vessel compliance as a function of pressure. This is calculated based on data obtained from Langewouters’ work. Input demographic data includes age, gender, height and weight. The basic underlying equation is:

\[ C(p) = L \frac{A_{max}}{\pi P1} \frac{aP1}{1 + \left(\frac{P - P0}{P1}\right)^2} \]
L = estimated aortic length
Lmax = maximum aortic cross-sectional area
P = arterial pressure
P0 = pressure at which compliance reaches its maximum
P1 = width of the compliance curve at half maximum compliance

\( \mu_{3ap} \) is a statistical moment determined by skewness, which is a measure of lack of symmetry. The symmetry characteristics of the arterial pressure waveform can indicate a change in vascular tone and/or resistance. Two functions may have the same mean and SD but will rarely have the same skewness. For example, if pressure data points increase quickly during systole and fall slowly during diastole, this represents increased skewness, and suggests vasoconstriction. Decreased skewness suggests low resistance.

\( \mu_{4ap} \) is the statistical moment determined by kurtosis, which is a measure of how peaked or flat the pressure data points are with respect to normal distribution. Pressure data with a high kurtosis has a rapid pressure rise and fall with a distinct peak near the mean and a heavy tail and suggests poor compliance. A low kurtosis has a flat peak and suggests high compliance.

\( \chi \) is recalculated every 60 seconds in the more recent Vigileo software updates. Thus the impact of changing vascular parameters is taken into account every minute. Previous versions of the software only updated \( \chi \) every 10 minutes. As mentioned above \( SV = \sigma AP \times \chi \).

The parameters provided by this system include continuous CO, CI, SV, SVI, SVV, and SVR. Thus, one can make an assessment of flow parameters, as well preload (or more specifically predict fluid responsiveness from SVV), and afterload (from SVR). If SpO2 and PaO2 are entered into the monitor the Vigileo will also display DO2/DO2I thus permitting use with DO2 optimisation strategies.

The key advantages of the Vigileo/Flotrac system are:
- Does not require calibration
- Provides a continuous, essentially real-time, assessment of CO/SV and other relevant haemodynamic parameters
- It can be used with an existing A-line, and does not require proximal arterial access or central venous access. There were, in fact, initial concerns that femoral catheters may reduce the accuracy of this device but subsequent reports have refuted this.
- It is simple to set up, easy to use, and requires minimal extra training.
- This system is truly minimally invasive and is thus applicable for use throughout the perioperative period and in a wide variety of settings, including those beyond the traditional critical care and perioperative period. Its use is warranted across a wide spectrum of patients, but may be especially relevant in patients who are not ill enough to warrant the risk of more invasive devices. Devices such as these may expand the use of cardiac output monitoring into environments such as the emergency department and labour ward.

There are a number of limitations to keep in mind:
- As with all pulse waveform devices, it requires a high fidelity pressure trace to provide accurate results. Damping, kinking, clots or air bubbles in the system can render the displayed values inaccurate. The Flotrac sensor kits are configured to optimise the frequency response, and addition of any extra pressure tubing or stopcocks is discouraged by the manufacturer. Good care of the arterial line and transducer system is mandatory.
- This system is not indicated for use in patients with severe arrhythmias, intraaortic balloon pumps and ventricular assist devices.
- Absolute values in aortic regurgitation may be inaccurate, but it is claimed that trending remains accurate.
- Severe peripheral vasoconstriction e.g. hypothermia, hypovolaemic shock or vasopressor use may affect accuracy, especially with use of the radial artery. One may consider the use of a femoral catheter where this is anticipated.
- According to the manufacturer, the Flotrac sensor is currently only indicated for adult use.
- From a technical, and philosophical view, the fact that the algorithm used to derive cardiac output is, not only extremely complex, but also a guarded, proprietary secret that is constantly being updated, makes an objective