Haemodynamics – Understanding the Relationship

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I maintain that intravenous fluids are drugs. Like any drug they have indications, contraindications, appropriate doses and administration schedules. Amongst other things, haemodynamic monitoring aids us to determine the dose.

Anaesthetists appear as a group to embrace technology and to like numbers. As an inducement to register early for this meeting, the organisers were giving away a Masimo pulse oximeter for your smartphone. Why is pulse oximetry important? Well in 1972, Takuo Aoyagi (figure 1) was trying to develop a non-invasive method to determine cardiac output using cardiogreen dye and an ear oximeter. He found that the light transmission exhibited pulsatile artefacts that made it impossible to compute cardiac output using dye dilution.

He realised the implication and developed a two-wavelength ear pulse oximeter, which made use of heart pulsations to detect and measure arterial blood absorbance. The first commercially successful device was marketed in 1977 by the Biox Corporation (later purchased by Ohmeda).

Fig 1 – Takuo Aoyagi

Few of us would accept monitoring that did not include pulse oximetry and yet when first marketed it took a while for it to be accepted. Severinghaus and Honda[1] explain that "few foresaw its value in anesthesiology, intensive care, and other emergent situations." With concerns over accuracy, it was not until 1986 that the ASA recommended it as standard of care.

Just as with the early story of pulse oximetry, there appears to be a reluctance to monitor cardiac output.[2]

A pivotal goal of anaesthesia and intensive care is tissue oxygen delivery, and this can be related to outcome.[3,4] Haemodynamic monitors are tools that may assist us in this goal by providing information for us to act on. They are not treatments. In the words of Michael Pinsky,[5] "no monitoring tool, no matter how accurate, by itself has improved patient outcome."

Two key requirements for tissue oxygen delivery are perfusion pressure and flow (cardiac output). Advanced haemodynamic monitoring involves –

- Assessment of preload responsiveness (the customary role)
- Cardiac output (CO) monitoring
- Assessment of cardiac contractility
- Assessment of tissue perfusion

Advanced haemodynamic monitoring is an integrative model view of single parameters.

Some Basic Physiology

$$MAP = \mathbf{CO} \times SVR$$

And perfusion pressure is dependent on preload, afterload, rate, rhythm and contractility. If afterload is represented by SVR, then the other four parameters are the determinants of CO.

$$DO_2 = \mathbf{CO} \times [Hb] \times 1.31 \times SaO2$$

$$CO = HR \times \mathbf{SV}$$

Hence stroke volume, the volume of blood ejected by the ventricle per heartbeat, is pivotal in determining flow and oxygenation. It is affected by preload, afterload and contractility. Preload is the end-diastolic ventricular wall tension (/ pressure), or simply how "full" is my patient.

The Frank Starling law (figure 2) holds that the force of myocardial contraction is proportional to initial cardiac muscle fibre length. It describes the relationship of preload to cardiac output.

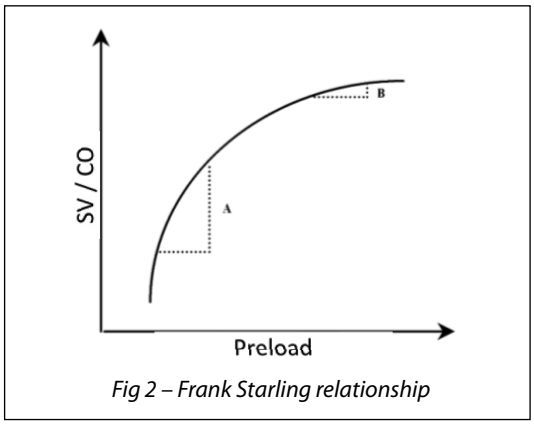


Fig 2 – Frank Starling relationship

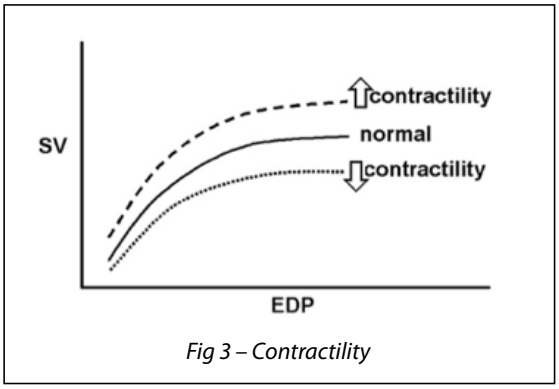


Fig 3 – Contractility

Contractility (figure 3) is the inherent ability of the cardiac muscle to contract regardless of preload or afterload status. It is estimated by analysis of the arterial waveform – maximum speed of the arterial pressure curve during ejection.

So DO_2 depends on CO. And CO depends on SV. And SV depends on preload. So the question for anaesthetists is will SV / CO improve with fluid resuscitation (aka fluid responsiveness)? To increase stroke volume is the *only* reason to give a patient a fluid challenge. However –

- Being fluid responsive does not mean the patient needs fluid
- Measurements of fluid responsiveness do not indicate what type of fluid is most suitable

Fluid therapy is a difficult balance –

- Too little fluid leads to –
  - Tissue hypoperfusion and organ dysfunction
  - Uncorrected hypovolaemia and inappropriate use of vasoconstrictors may worsen hypoperfusion and tissue ischaemia
  - We have evolved to cope with hypovolaemia[6]
- Too much fluid causes –
  - Tissue oedema, impaired wound healing
  - Bowel oedema, reduced motility, ileus, anastomotic leak, abdominal compartment syndrome
  - Lung oedema with increased respiratory complications
  - Impaired oxygen uptake and delivery
  - Worse outcomes, increased LOS
  - Volume overload is a recent phenomenon, usually iatrogenic, and humans lack compensatory mechanisms

Central Venous Pressure

Central venous pressure (CVP) is the pressure within the right atrium and great veins of the thorax. Whilst as a profession we were slow to adopt pulse oximetry and there is a reluctance to embrace advanced haemodynamic monitoring, CVP measurements are near universally used to make clinical decisions. Indeed a 2007 European survey of anaesthetists / intensivists[7] demonstrated that more than 90% used the CVP to guide fluid management.

Whether CVP is predictive of preload and fluid responsiveness has been questioned since 1971.[8] In 1984 Shipley et al[9] made over 1,500 simultaneous measurements of blood volume and CVP in 188 ICU patients. They were able to demonstrate no relationship between CVP and blood volume.

Receiver operating characteristic (ROC) plots compare different clinical tools with different diagnostic accuracies – figure 4. Plots located in the upper left-hand quadrant have better sensitivity and specificity.

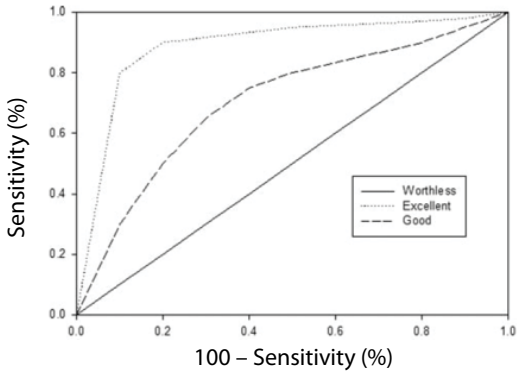


Fig 4 – Receiver operating characteristic (ROC) plot

In 2008 Marik et al published a review of 24 studies involving 803 patients.[8] They were able to show the correlation coefficient between CVP and measured blood volume was 0.16 (95% confidence interval [CI], 0.03-0.28). The area under the ROC curve was 0.56 (95% CI 0.51-0.61) – little better than a coin toss in determining fluid responsiveness. A patient has the same probability of being fluid responsive with a low or a high CVP. CVP is often used to follow 'trends.' In this paper, the correlation between ΔCVP and change in cardiac index was 0.11 (95% CI 0.015-0.21). The authors concluded that there is a very poor relationship between CVP and blood volume and that "CVP should not be used to make clinical decisions regarding fluid management."

Despite this the "Surviving Sepsis Campaign" publish internationally endorsed clinical guidelines[10] recommending a CVP target to guide fluid resuscitation. Miller's anaesthesia text[11] states that "the most important application of CVP monitoring is to provide an estimate of the adequacy of circulating blood volume," and that "trends in CVP during anesthesia and surgery are also useful in estimating fluid or blood loss and guiding replacement therapy."

There are now over 100 papers showing no relationship between CVP (or change in CVP) and fluid responsiveness.[12] Marik and Cavallazzi[13] updated their meta-analysis in 2013 to include 43 studies and compare ICU and operating room studies. Once again the area under the curve was 0.56 (95% CI 0.54-0.58) irrespective of whether the patient was in ICU or OR.

CVP may be useful in early detection of impaired cardiac function or high intra-thoracic pressure (not volume status) in –

- Heart transplant patients
- Right ventricular infarction
- Pulmonary hypertension
- Severe LV dysfunction
- Acute PE
- Tamponade
- Tension pneumothorax

Pathological CVP waveforms may assist in diagnosis.

Dynamic Parameters

Static parameters (CVP, PCWP) are insufficient to predict fluid responsiveness. More subtle changes in volume status need to be detected, and targeted endpoints need to be more sensitive and specific to allow for optimisation and possibly better outcomes.

Dynamic techniques rely on the change in preload resulting from mechanical ventilation and allow assessment of whether a patient is on the ascending portion of the Frank Starling Curve and has "recruitable" cardiac output – table 1.

The "swing in the trace" is better referred to as arterial pressure variation or inverse pulsus paradoxus. Intermittent positive-pressure ventilation induces cyclic changes in the loading conditions of the left and right ventricles –

Table 1 – Techniques for assessing fluid responsiveness. ROC, area under receiver operator characteristic curve; IVC, inferior vena cava; SVC, superior vena cava

Static pressure and volume parameters (ROC ~0.5–0.6) ▪ CVP ▪ PAOP ▪ IVC/SVC diameter ▪ Flow corrected time ▪ Right ventricular end-diastolic volume ▪ Left ventricular end-diastolic volume ▪ SVC/IVC variation during mechanical ventilation
Dynamic techniques based on heart–lung interactions during mechanical ventilation (ROC ~0.7–0.8) ▪ PPV ▪ SVV ▪ Pleth variability index ▪ Aortic blood flow (Doppler or echocardiography)
Techniques based on real or virtual fluid challenge (ROC ~0.9) ▪ PLR ▪ Rapid fluid challenge (100–250 cc)

- Mechanical insufflation →
  1. ↓ RV preload due to ↑ pleural pressure and ↓ venous return pressure gradient
  2. ↑ RV afterload due to ↑ transpulmonary pressure

- ↓ RV preload and ↑ RV afterload → ↓ RV stroke volume, which is at a minimum at the end of the inspiratory period

- ↓ RV ejection → ↓ LV filling (after a phase lag of two or three heart beats because of the long blood pulmonary transit time)

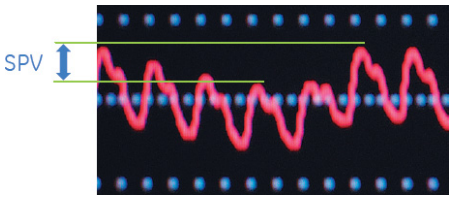
- ↓ LV preload → ↓ LV stroke volume, which is at its minimum during the expiratory period

The magnitude of these changes is dependent on the fluid status of the patient being of greater amplitude in hypovolemic patients where the ventricles operate on the steep portion of the Frank-Starling curve.

Measurement

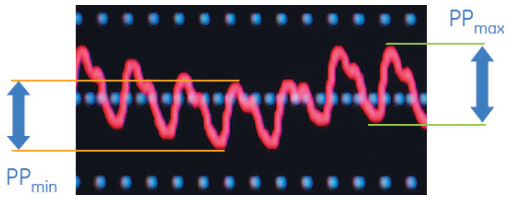
Systolic pressure variation (SPV, in mmHg) is a numerical quantification of the degree of swing in the arterial trace. Whether SPV is useful in spontaneously ventilating patients, whose respiratory physiology differs, is a matter of debate.

$$SPV = SBP_{max} - SBP_{min}$$



Pulse pressure variation (in %; aka dPP or ΔPP) is the ratio of the change in pulse pressure to the mean pulse pressure.

$$PPV = \frac{PP_{max} - PP_{min}}{(PP_{max} + PP_{min})/_2} \times 100$$



SPV and PPV have the attraction that they are effectively a free "by-product" of invasive arterial blood pressure monitoring. The major equipment manufacturers include software into their monitors which calculate these variables for us. However there are limitations –

- The patient must be mechanically ventilated (7 or 8ml/kg TV)
- They must make no spontaneous respiratory effort
- Cannot be used with an open chest
- High PEEP affects the result
- The patient must not have sustained cardiac arrhythmias as these result in variable cardiac filling time. More advanced standalone devices are able to filter out such arrhythmias to a degree
- Elevated intra-abdominal pressure / laparoscopic procedures
- Readings of invasive BP must be reliable (zeroed, no damping)
- RV failure
- There are questions around the effects of vasoconstrictors

A group based in Virginia[14] have investigated the ability of anaesthesia providers to eyeball SPV. They tasked 50 anaesthetists with estimating SPV as a percentage of SBP. Each was asked to look at 10 traces and determine whether the patient needed fluid. They found that visual estimates are within clinically reasonable limits 82% of the time and that erroneous management decisions were made in association with 4.4% of measurements.

When calculated manually PPV is termed PPV_{man} and is derived over a single mechanical breath. Continuous automated measurements (PPV_{auto}) are calculated over a longer period and hence the two values may differ. Cannesson et al[15]

investigated the ability of both measurements to predict fluid responsiveness during coronary artery bypass grafting. The agreement between PPV_{man} and PPV_{auto} was 0.7% ± 3.4%. In terms of predicting fluid responsiveness, the areas under the ROC curves (figure 5) were 0.923 ± 0.060 for PPV_{man} and 0.919 ± 0.058 for PPV_{auto}, showing that PPV_{auto} can be displayed continuously to predict fluid responsiveness. The authors caution though that a minute of haemodynamic stability is required before the value can be used clinically.

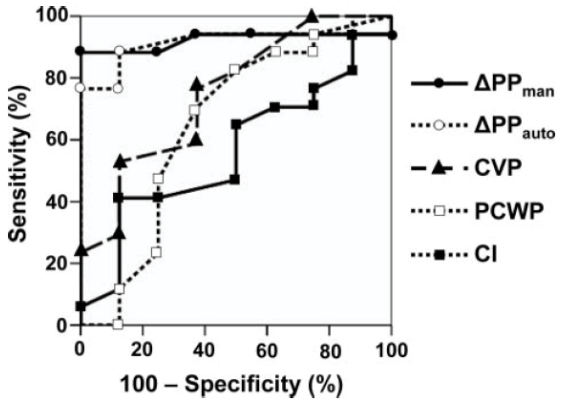


Fig 5 – Receiver operating characteristic curves comparing the ability of PPV_{man}, PPV_{auto}, CVP, PCWP, and CI at baseline to discriminate between responders and nonresponders to volume expansion

Cannesson et al have gone on to clarify the utility of PPV in a multicentre trial[16] and to clarify a "grey zone." This study again showed a strong predictive value with the area under the ROC curve being 0.89 (95% CI 0.86-0.92).

One problem with the ROC approach is that it leads to "black or white" decision making, seeking a value above which patients will be fluid responders, and this does not fit clinical practice. As they explain, a "grey zone technique proposes two cut offs that constitute the borders of the grey zone. The first cut off allows exclusion of the diagnosis (fluid responsiveness) with near certainty, whereas the second cut off is chosen to include the diagnosis with near certainty. Intermediate values included in the grey zone correspond to a prediction not precise enough for diagnostic decision making". They identified a grey zone of PPV values between 9 and 13%, between which fluid responsiveness cannot be reliably predicted.

Advanced Standalone Monitors

There exist a plethora of advanced haemodynamic monitors based on different technologies –

- Pulmonary artery catheters (PAC)
- Transoesophageal echo (TOE)
- Bioreactance
  - NICOM
- Continuous wave doppler
  - CardioQ (oesophageal doppler)
  - USCOM
- Pulse contour analysis
  - FloTrac
  - PiCCO
  - LiDCO, LiDCO-rapid
  - PRAM-MostCare
- Nonivasive pulse contour
  - Nexfin
- Partial carbon dioxide rebreathing
  - NICO

These offer an assessment of cardiac output as well as other haemodynamic parameters. Two of the most popular devices will be reviewed.

Pulse contour analysis – FloTrac

Advantages[17] –

- Continuous cardiac output
- Mini-invasive, "self-calibrating"

Disadvantages –

- Accuracy of output has been a concern
- Sensitive to changes in arterial resistance
- Requires a specific arterial pressure sensor

The FloTrac / Vigileo (now EV1000) system (Edwards Lifesciences) was introduced in 2005.[18] It utilises a pulse contour analysis technique that allegedly negates the need for external calibration and is therefore quick to use and less invasive. The proprietary waveform analysis calculates vascular impedance by combining the empirical estimation of large vessel elastance from patient demographic data with the quantitative analysis of the arterial waveform to determine dynamic resistance. These combined values generate a so-called auto-calibration scaling factor (Chi factor). The Chi factor, along

with a whole waveform assessment of pulse pressure, is then used to derive stroke volume. Further derivation provides other haemodynamic variables including stroke volume variability, a useful indicator of volume responsiveness, and cardiac output.

Stroke volume variation (SVV) is expressed as a percentage and is analogous to PPV. Values above 13% are considered to indicate fluid responsiveness. Hofer et al found that SVV reliably predicted fluid responsiveness.[19] The determination of SVV suffers from the same limitations as PPV described above. In determining fluid responsiveness using SVV, the area under the ROC curve has been calculated as 0.84 (95% CI 0.78-0.88).[20]

Slagt et al recently performed a systematic review of 65 CO validation studies with 2,234 patients and 44,592 data points.[18] They examined the performance of the FloTrac / Vigileo in three separate patient groups – general critical care including post-surgical patients and critical care patients with presumed normodynamics, a group of post-cardiac patients with presumed hypodynamics, and a group of patients with liver disease or sepsis with presumed hyperdynamics. They found that SVV predicted fluid responsiveness in 85% of studies examined and that "the accuracy and precision of the FloTrac / Vigileo system can be regarded as sufficient for rountine clinical use in hypo- or normodynamic conditions in the absence of large changes in vascular tone" with percentage errors at 30% or lower.

The relation between pulse pressure (PP) and SV is less fixed in hyperdynamic and vasodilated states such as liver disease, liver surgery, or septic shock. Moving down the arterial tree, PP normally increases, but in hyperdynamic conditions, the opposite occurs, leading to an underestimation of SV. Software releases 3 and 4 have sought to address this. The paper by Slagt et al reviewed software versions up to 3.02 (version 4 was released in 2014) and found performance in hyperdynamic states to be inadequate, that SVV may still be "useful" in predicting fluid responsiveness but that trending capacity "remains affected by changes in vascular tone."

Oesophageal Doppler – CardioQ

Advantages[17] –

- Less invasive than arterial-based systems

Disadvantages –

- Requires frequent manipulation for proper position
- Operator dependent[15]
- Validation data is old and little on CO trending[21]

Less invasive hemodynamic monitoring systems started in the 1990s.[17] One of the first systems to be described and developed was an oesophageal doppler system allowing for non-invasive monitoring of CO. The CardioQ-ODM (Oesophageal Doppler Monitor; Deltex Medical) utilises a probe placed in the oesophagus and aimed at the descending aorta. The waveform is very dependent on correct positioning and to optimise the signal requires frequent adjustments of depth, orientation, and gain. The CardioQ-ODM calculates the aortic cross-sectional area using a nomogram based on the patient's age, height and weight.[22] Calculation of cardiac output is dependent on five assumptions –

1. The distribution of blood caudally to the descending aorta and rosterally to the great vessels and coronary arteries maintains a constant ratio of 70% to 30%
2. That a flat velocity profile exists within the aorta
3. The estimated cross-sectional area is close to the mean systolic diameter
4. There is negligible diastolic blood flow
5. The velocity of blood flow in the aorta is measured accurately

The monitor offers a number of haemodynamic variables which can be used to guide treatment –

- Peak velocity – the peak velocity of blood in the aorta gives a good estimation of myocardial contractility
- Stroke volume (and thus CO) – stroke distance is the area under the velocity-time waveform; when multiplied by the aortic diameter this gives an estimate of the stroke volume. The stroke volume is usually averaged over a number of beats
- Corrected flow time (FTc) – the flow time is the duration of forward flow in the aorta. The flow time varies with heart rate and can be corrected to 60bpm. Anything that impedes filling or emptying of the left ventricle will cause a reduction in FTc. Most commonly this is seen in hypovolaemia

Unlike pulse contour analysis which require modelling of the circulation to produce an algorithm that converts pressure changes to blood flow, ultrasound measures blood flow directly. However the CardioQ does not measure true CO. Most of its validation data pre-date percentage error.[21] Dark and Singer's meta-analysis of 2004 used a statistic called "percentage of clinical agreement" (PCA) based on the number of data pairs that were within ±15% of mean bias.[23] Re-evaluation of data from this paper using mean CO and limits of agreement shows that the percentage error for many of these oesophageal Doppler studies was 40–50%.[21] However, the CardioQ-ODM does seem to track changes in CO, although there is little published data other than that found in a study by Valtier et al.[24]

Several studies (with small numbers) have shown a positive impact on postoperative complications in patients undergoing high-risk surgery.[17] Based on eight studies (six funded to some extent by the manufacturer) the UK National Health Service's National Institute for Heath and Clinical Excellence (NICE) has recommended the use of the CardioQ-ODM in high-risk surgical patients.25

Passive Leg Raise

A passive leg raise results in the transfer of blood from the legs and abdominal compartments and can be used to assess preload responsiveness. It is essentially a reversible autotransfusion with 45° leg elevation equivalent to a 500ml fluid bolus.12 The manoeuvre has been shown to be highly predictive with an area under the ROC curve of 0.95. It is useful in ED, ward and ICU settings, especially in patients with cardiac arrhythmias and spontaneous ventilation where dynamic parameters lose their predictive ability. It also avoids unnecessary fluids. Obviously utility in theatre is limited. Intra-abdominal hypertension (>16mmHg) impairs venous return and the ability to detect fluid responsiveness.

A Final Word

The use of the parameters and devices described above is often linked to a protocol for fluid and haemodynamic management – goal directed therapy. Despite all the advances in recent years it remains unclear which device to use in which setting.17 Crucially patient outcome data is missing. But can we expect a haemodynamic monitoring system by itself to affect outcome? After all, pulse oximetry has been evaluated in randomised trials including over 20,000 patients26 and has never been shown to improve patient outcome.

Competing Interests

I am a member of the medical advisory board of Edwards Lifesciences. I have previously been contracted for web development for the JAFA Trust, the organisers of this meeting.

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