

Arterial pressure and stroke volume variability as measurements for cardiovascular optimisation

There is a growing interest in the clinical value of the observed variations in blood pressure and cardiac output (CO) that result from the interactions between the heart and lungs during ventilation. This has naturally coincided with the ongoing development and use of pulse contour analysis monitors: a minimally invasive method of measuring cardiac output. This type of technology converts the arterial pressure waveform trace into a beat-to-beat value for stroke volume, records any changes in arterial pressure, and can match these measurements to the respiratory cycle. Consequently, systolic pressure variation (SPV) (Figure 1), pulse pressure variation (PPV) (Figure 2) and stroke volume variation (SVV) for each respiratory cycle are measured and displayed at the patient's bedside. It has become possible for clinicians to use these interactions routinely in their assessment and optimisation of a patient's haemodynamic status.

The intravascular blood volume of a patient is reflected in the magnitude of the SPV, SVV and PPV.¹ These variables will demonstrate and monitor the cardiovascular response to fluid challenges and provide the clinician with alternative indicators of the 'preload' acting on the heart. They probably provide a more accurate measure of cardiovascular status than central venous pressure (CVP) or pulmonary artery occlusion pressure (PAOP) and central venous cannulation is avoided. Only an intra-arterial catheter is required and this is a commonly performed procedure with a low risk of morbidity. There is also evidence, which we will discuss, that these interactions may give an indication of a patient's preload responsiveness. This would be advantageous as optimal oxygen delivery could be achieved whilst avoiding inappropriate and potentially harmful fluid challenges.

The purpose of this article is to examine those mechanisms behind the heart-lung interactions in the ventilated patient that give rise to the phenomena of SPV, PPV, and SVV. We will discuss the evidence for their clinical use as indicators of intravascular blood volume, their limitations and advantages and how they may be developed in the future.

VARIATION IN BLOOD PRESSURE AND STROKE VOLUME DURING THE RESPIRATORY CYCLE

The fluctuations of the arterial pressure waveform during intermittent positive pressure venti-

lation are familiar and the 'swing' of the pressure trace during inspiration and expiration is easily seen on a standard monitor display. These changes are largely the consequence of alterations in intrathoracic pressure (P_{IT}). It is important to recognise that P_{IT} greatly influences the transmural pressure (P_{TM}), which is the actual effective distending pressure of the cardiac chamber, and represents chamber volume (preload) and afterload. As P_{TM} is the difference between the measured (or transduced) pressure inside the cardiac chamber of interest (P_{MEAS}) and the P_{IT} outside the chamber, it follows that as the P_{IT} increases so the P_{TM} falls:

$$P_{TM} = P_{MEAS} - P_{IT}$$

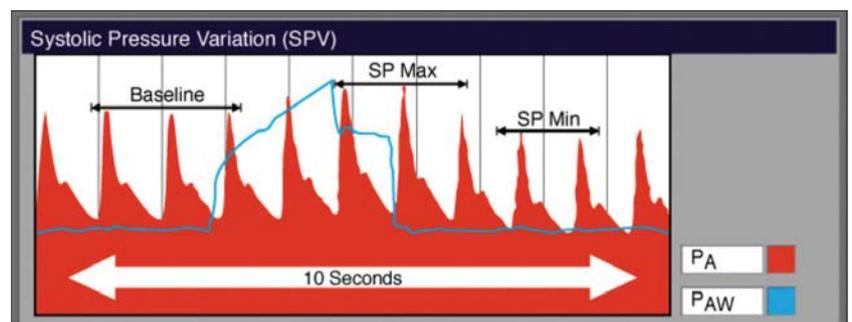
THE INSPIRATORY PHASE OF IPPV

The inspiratory rise in arterial blood pressure seen during intermittent positive pressure ventilation (IPPV) is triggered by several events. A rising P_{IT} whilst decreasing left ventricle (LV) P_{TM} , also increases the drainage of blood from the pulmonary veins into the left atrium. This augmentation of left ventricular end diastolic volume (LVEDV) can be visualised using transoesophageal echocardiography (TOE). The reduction in P_{TM} also reduces LV wall tension (afterload), which results in more efficient ejection of blood into the systemic circulation. The effect of this may be best demonstrated in a failing LV where it is well recognised that IPPV may improve blood pressure as a consequence of reducing LV wall tension and hence cardiac work.

In the right heart converse changes are occurring. Increases in P_{IT} reduce venous return and right ventricular end diastolic volume (RVEDV), whilst increasing right ventricular (RV) work. The latter effect on the RV is the consequence of

AJD Parry-Jones* BSc, MRCP, FRCA,
JAL Pittman† MBBS, BSc, FRCA,
*Department of Intensive Care, University College London Hospitals, London, UK
†Department of Anaesthetics, Royal Devon and Exeter NHS Trust, Exeter, Devon, UK

Figure 1. The fluctuation of the systemic blood pressure (red) with intermittent positive pressure ventilation. The increase and decrease in airway pressure seen in inspiration and expiration is superimposed (blue trace). The increase in blood pressure during inspiration is followed by a decline in expiration before the baseline pressure plateaus during the expiratory pause. A 10 second window is used to reliably capture the maximum and minimum systolic values of a respiratory cycle. P_A is arterial pressure, P_{AW} is airway pressure, SP_{Max} is the maximum systolic pressure and SP_{Min} is the minimum systolic pressure during the respiratory cycle.



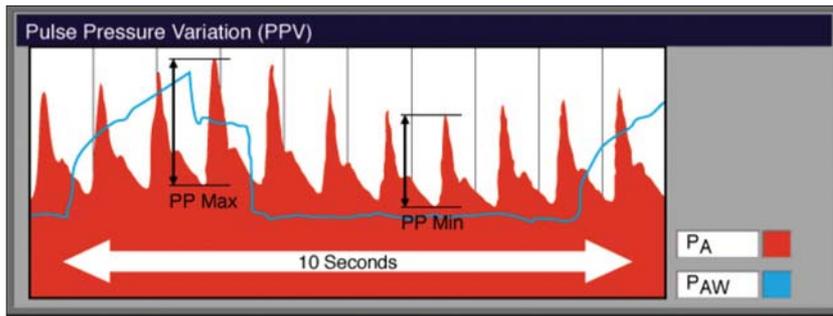


Figure 2. The fluctuation of the Pulse Pressure with intermittent positive pressure ventilation. Pulse pressure is maximal during inspiration (PPmax) and minimal in early expiration (PPmin). A 10 second window is used to reliably capture the maximum and minimum values of a respiratory cycle. The increases and decreases in airway pressure (P_{AW}) during inspiration and expiration are shown in blue. Pulse Pressure variation (PPV) is given as a percentage. P_A is arterial pressure (red).

increased pulmonary vascular resistance, the magnitude of which cannot be offset by the reduction in wall tension that follows the decrease in the radius of the RV chamber. Summaries of the cardiovascular changes that occur in inspiration are shown in Table 1.

THE EXPIRATORY PHASE OF IPPV

When expiration starts, systemic blood pressure begins to fall as the reduced RV output occurring in inspiration feeds through to the systemic side of the circulation. This serial ventricular interdependence is compounded in early expiration by the reduced P_{IT} , which causes a further fall in LVEDV by reducing pulmonary venous drainage. Concurrently, RVEDV is improving due to increasing venous return. If the expiratory phase is extended into an apnoeic period the systemic pressure will rise again to a baseline value as the improved right-sided output begins to feed through to the left heart (Table 2.).

Owing to the restraining effect of the pericardium, the ventricles of the heart also have a

parallel interdependence. Volume dilation of one ventricle shifts the interventricular septum so that it may interfere with the function of the other ventricle. For example, marked increase in right ventricular preload will shift the ventricular septum to the left, decreasing left ventricular compliance and decreasing LVEDV for a given filling pressure. In this manner, the changes in preload that occur during inspiration and expiration could further influence RV and LV performance during the respiratory cycle.

WHAT ARE SPV, PPV AND SVV?

The definitions for these measurements are given in Table 3. The systolic blood pressure during an apnoeic period following expiration is the base line for measuring delta Up (ΔUp) and delta Down ($\Delta Down$) (Figure 3). Delta Up increases in proportion to the increases in LV preload and a reduction in LV afterload. Delta Down reflects the degree of RV preload reduction due to reduced venous return and hence indicates volume responsiveness in a patient. SPV is calculated from the minimum and maximum systolic pressure across a respiratory cycle. The maximal and minimal P_{IT} during a respiratory cycle is unknown and will have a variable effect on SPV, with SPV possibly reflecting transmitted airway pressure rather than cardiac preload. In contrast, when measuring PPV, the systolic and diastolic blood pressures are measured simultaneously at the same P_{IT} . The variable effect of P_{IT} is therefore removed, possibly making PPV a more reliable indicator of preload than SPV.² Left ventricular output will move up and down the Starling curve as preload and afterload change during the respiratory cycle (Figure 4). The magnitude of these movements determines the SVV (Figure 5) with the beat-to-beat SV measurement acquired from pulse contour analysis. SVV relies on the robustness of the algorithms and assumptions used in this technology, and concerns have been expressed about their validity.³ For example, changes in the arterial pressure wave due to arrhythmias, the site of pressure wave sampling or large changes in arterial compliance may erroneously be represented as changes in SV and therefore SVV. Further research is needed to clarify these problems, but current studies support the reliability of pulse contour analysis measurements of SV.⁴⁻⁶

Table 1. A summary of the possible reasons and causes behind the systolic blood pressure rise seen during the inspiratory phase of positive pressure ventilation

Reason	Cause
Increase in left ventricular end diastolic volume	<ul style="list-style-type: none"> • Increase in drainage from pulmonary vessels • Increase in drainage from left atrium into left ventricle • Improved right ventricular output during expiration arriving at the left ventricle owing to pulmonary transit time
Improved left ventricular function	<ul style="list-style-type: none"> • Reduced right ventricular end diastolic volume may improve left ventricular function because of a ventricular interdependence favouring the left ventricle
Transmitted pressure	<ul style="list-style-type: none"> • Increase in intrathoracic pressure increases systolic pressure, as referenced to atmospheric pressure
Decrease in systemic afterload	<ul style="list-style-type: none"> • Reduction in transmural pressure reduces left ventricular afterload

Table 2. The changes in ventricular volume and afterload that occur in the early phases of inspiration and expiration during intermittent positive pressure ventilation (IPPV)

Early inspiration in IPPV	Early expiration in IPPV
↑ Left ventricular end diastolic volume	↓ Left ventricular end diastolic volume
↓ Systemic afterload	↑ Systemic afterload
↓ Right ventricular end diastolic volume	↑ Right ventricular end diastolic volume
↑ Pulmonary afterload	↓ Pulmonary afterload
↑ Systemic blood pressure	↓ Systemic blood pressure

THE EVIDENCE FOR SVV, SPV AND PPV

The existing evidence in favour of using heart-lung interactions as a tool in cardiovascular monitoring falls broadly into two categories. Firstly, an orthodox role in *evaluating* the improved flow in response to a fluid challenge and, secondly, their value in *predicting* whether increasing the preload on the heart will improve CO.

Table 3. The definitions of systolic pressure variation (SPV), pulse pressure variation (PPV) and stroke volume variation (SVV). Maximum systolic blood pressure (SBPmax), minimum systolic blood pressure (SBP min), systolic blood pressure (SBP), diastolic blood pressure (DBP), maximum pulse pressure (PP max), minimum pulse pressure (PP min), maximum stroke volume (SVmax), minimum stroke volume (SV min) and left ventricular end diastolic volume (LVEDV)

Systolic pressure variation is defined as the difference between the maximal and minimal values of systolic arterial pressure recorded over a respiratory cycle. $SPV = \Delta Up + \Delta Down$ Sometimes calculated as a fraction by the equation: $SPV = SBP \text{ max} - SBP \text{ min} / (SBP \text{ max} + SBP \text{ min} / 2)$	Normal value <10 mmHg
$\Delta Up = SBP \text{ max} - \text{Apnoeic baseline}$ (Represents the augmentation of systolic pressure due to the increase in LVEDV and the decrease in LV afterload during inspiration.)	Normal value <5 mmHg
$\Delta Down = \text{Apnoeic baseline} - SBP \text{ min}$ (Represents the fall in LVEDV and the increase in Left Ventricular afterload during early expiration.)	Normal value <5 mmHg
Pulse pressure variation is the maximal difference in pulse pressure seen over a respiratory cycle, where pulse pressure equals systolic blood pressure minus diastolic blood pressure. $PPV = [(SBP - DBP)_{\text{max}} - (SBP - DBP)_{\text{min}}] / [(SBP - DBP)_{\text{max}} + (SBP - DBP)_{\text{min}} / 2]$ $= PP \text{ max} - PP \text{ min} / (PP \text{ max} + PP \text{ min} / 2)$	Normal value <13%
Stroke volume variation is the percentage of change between the maximal and minimal stroke volumes divided by the average of the minimum and maximum over a floating period of 10 seconds. $SVV = SV \text{ max} - SV \text{ min} / (SV \text{ max} + SV \text{ min} / 2)$	Normal value <10%

Evaluating the response to preload challenges

The greatest clinical use of SPV to date has been in the diagnosis of hypovolaemia and the subsequent monitoring of volume resuscitation.^{7,8} Analysis of the arterial waveform of ventilated dogs undergoing stages of normovolaemia, hypovolaemia and hypervolaemia showed that SPV and its components are useful in evaluating intravascular volume status.⁹ Importantly, SPV and $\Delta Down$ more effectively identified hypovolaemia than CVP or mean arterial blood pressure with a blood loss of approximately 500 and 1,000 ml resulting in an SPV of 5 and 10 mmHg respectively.¹⁰ Results are consistent in humans, with haemorrhage increasing SPV and volume administration reducing it.¹¹ When referenced against echocardiography, SPV and $\Delta Down$ correlated well in the detection of hypovolaemia.¹² Even when arterial pressure is maintained at near normal levels by compensatory vasoconstriction, SPV still heralds hypovolaemia.¹³ Coriat *et al.* found $\Delta Down$ to be a better predictor of left ventricular preload than PAOP.¹⁴ If SPV is expressed as a percentage change, this may be a more sensitive parameter than using absolute values but currently it is unknown which is more reliable.

In patients with sepsis-induced hypotension, SPV also showed a significant response to volume loading that was mirrored by end-diastolic area measured by echocardiography.¹⁵ In drug-induced hypotension for spinal surgery, an increased $\Delta Down$ revealed hypovolaemia with again no change in PAOP or CVP.⁷ Despite these studies in a wide range of clinical settings, it is still unanswered if SPV, PPV and SVV are good monitors of hypovolaemia in all patient groups. For example, no studies have been published in which the researchers have looked at these interactions in patients for whom low tidal volume ventilation for acute respiratory distress syndrome (ARDS) has been recommended.¹⁶

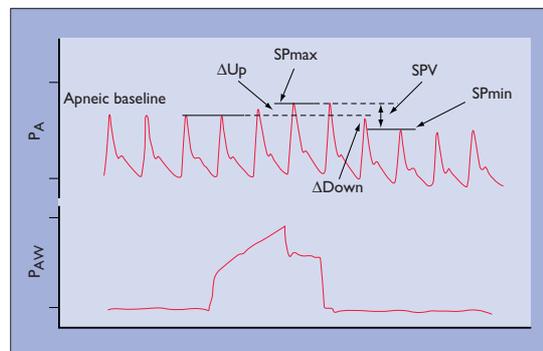


Figure 3. The changes in arterial blood pressure during the respiratory cycle. Systolic Pressure Variation (SPV) is the sum of delta Up (ΔUp) and delta Down ($\Delta Down$) as measured from the apnoeic baseline. P_A is arterial pressure, P_{AW} is airway pressure, SP_{Max} is maximum systolic pressure, SP_{Min} is minimum systolic pressure.

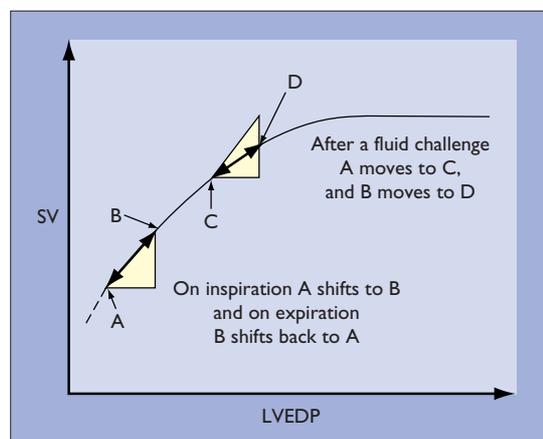


Figure 4. A Starling Curve of Left Ventricular Stroke Volume (SV) against Left Ventricular End Diastolic Pressure (LVEDP) demonstrating the change in stroke volume that occurs with positive pressure ventilation (A-B-A). The starting position on the curve determines the magnitude of the change in SV, and hence the stroke volume variation. Following intra-vascular volume expansion and movement up the curve, the magnitude of change in SV decreases during the respiratory cycle (C-D-C).

Since the recommendations of those studying heart-lung interactions are that patients should be ventilated with tidal volumes of 10 ml/kg, these studies need to be done.

Predicting preload responsiveness

It is widely reported that intravascular filling pressures are unreliable indicators of a patient's cardiovascular status.¹⁷ It is therefore surprising that most clinicians still optimise intravascular volume with the use of fluid challenges guided by pressure (BP, CVP or PAOP). As pressure readings are influenced by compensatory physio-

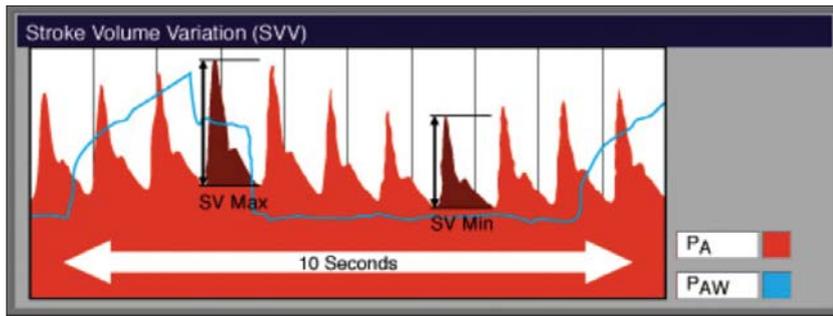


Figure 5. Pulse contour analysis of the arterial pressure wave provides beat-to-beat measurement of the stroke volume. The change in stroke volume over the respiratory cycle (taken from maximum and minimum values over 10 seconds) is the stroke volume variation. SV max is the maximum stroke volume, SV min is the minimum stroke volume, P_A arterial pressure (red), P_{AW} airway pressure (blue). Different pulse contour analysis devices will use all or part of the pressure wave in their algorithms for the calculation of stroke volume.

logical mechanisms that preserve pressure at the expense of flow, this may result in the inadvertent over- or, more commonly, under-administration of fluid. Tailoring fluid challenges to flow-based readings (CO) should theoretically offer an improvement but may still result in the worsening of gas exchange and peripheral oedema if the circulation is not preload sensitive. Preload insensitivity will not be recognised until the fluid has already been administered.

SPV, SVV and PPV are convenient dynamic 'virtual' preload challenges, occurring each respiratory cycle, without the actual administration of fluid. There is evidence that these changes can predict when a patient would respond favourably to fluid administration. In hypotension induced by sepsis, Δ Down was a more sensitive predictor of a favourable response to a preload challenge than PAOP or left ventricular end-diastolic area index measured by echocardiography.¹⁵ Ornstein *et al.*¹⁸ reported that SPV was a better predictor than CVP, pulmonary artery diastolic pressure and PAOP at predicting the percentage drop in CO that occurred in cardiac surgery patients who had 500 ml of blood venesected. Michard *et al.*² found that PPV was even better than SPV at predicting a response to fluid administration, but both were better than right atrial pressure and PAOP. A threshold value of a PPV <13% allowed discrimination between responding (cardiac index increasing by >15% to volume expansion) and non-responding patients. Berkenstadt *et al.*¹⁹ examined SVV as a predictor of fluid responsiveness in patients undergoing brain surgery and found it statistically better at predicting a response to a 100 ml colloid challenge than heart rate, CVP and systolic blood pressure. They found that an SVV of 9.5%, or more, would predict an increase in SV of at least 5% with a sensitivity of 79% and a specificity of 93%. Michard and Teboul looked at studies investigating predictive factors of fluid responsiveness in ICU patients. They concluded that dynamic parameters, including PPV and Δ Down, should be used in preference to CVP, PAOP, RVEDV and left ventricular end diastolic area in predicting fluid responsiveness in ICU patients.²⁰

LIMITATIONS

The ventilatory status of a patient must be known before the cardio-respiratory interactions

of SVV, SPV and PPV can be interpreted. The changes in arterial pressure during the respiratory cycle of a self-ventilating patient are in the opposite direction to those seen during IPPV and it is unclear whether in this situation these interactions can be used clinically. They are intrinsically highly variable due to the changing tidal volumes and respiratory rate seen in a conscious patient. It is therefore recommended that, for a reliable measurement, a patient should be ventilated with a constant tidal volume and a fixed respiratory rate, and be in sinus rhythm. Large tidal volumes or high respiratory rates will intermittently increase P_{IT} and may increase intrinsic PEEP, influencing SVV, SPV and PPV. Similarly it has been suggested that changes in chest wall or lung compliance could influence these cardiorespiratory interactions, as could changes in PEEP. In fact, Pizov²¹ used SPV to predict the effect of changes in PEEP on cardiac output. It is also possible that the changes in arterial pressure or stroke volume during inspiration reflect improved contractility in an afterload-dependent LV, rather than hypovolaemia. Arguably it is difficult to differentiate between these very different pathological states that have contrary management using heart-lung interactions. Specific measurement of Δ Up (hypervolaemia and afterload reduction) and Δ Down (hypovolaemia) may be a solution. Other issues relating to the reliability of use of SPV, SVV and PPV include the role of the dynamic response characteristics of the arterial catheter transducer system, the influence of cardiac arrhythmias and the relevance of the site of arterial pressure measurement within the body. These concerns need to be addressed and clarified.

CONCLUSION

Cardio-respiratory interactions are of clinical interest because they provide an assessment of intravascular volume and preload sensitivity, and the evidence repeatedly suggests they are more reliable than CVP or PAOP for this purpose. At present, in terms of clinical value, there is little to differentiate between SPV, PPV or SVV. Using these heart-lung interactions reduces the risks arising from cardiovascular monitoring and central venous cannulation could potentially be avoided. PulseCO (LiDCO Ltd) needs only a radial arterial and peripheral venous catheter to obtain the data to display SVV, SPV and PPV.²² These are commonly performed, low morbidity procedures and allow these measurements to be applied to a wide range of ventilated patients in the operating room, intensive care unit, high dependency area and the emergency department. The significance of these interactions is closely linked to the further acceptance of pulse contour analysis as a method of CO measurement. Indeed, currently it is only via such commercially available technologies that these interactions can be continuously

displayed (either PulseCO by LiDCO Ltd, or PiCCO by Pulsion Medical Systems GmbH).

It has not yet been demonstrated that fluid administration guided by SPV, PPV or SVV improves the clinical outcome of patients when compared to the use of more conventional cardiovascular measurements. This is the challenge to those promoting the clinical use of heart-lung interactions, alongside the need to confirm their applicability in different patient groups. Heart-lung interactions do appear to offer something different. Whilst measurements of perfusion can influence outcome by guiding resuscitation of patients,²³ they cannot accurately predict whether an additional fluid challenge is necessary or could potentially worsen the situation. Heart-lung interactions appear to be able to predict preload-responsiveness. If it was reported that patients with ARDS are best managed 'dry', a predictive tool for preload responsiveness could be very beneficial in monitoring cardiac status whilst reducing the risk of non-cardiogenic pulmonary oedema with inappropriate fluid challenges. This type of evidence is awaited and may be what is required to take heart-lung interactions into routine clinical practice.

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Correspondence to:
Dr James Pittman
Department of Anaesthetics
Royal Devon and Exeter NHS Trust
Barrack Road
Exeter, Devon EX2 5DW
United Kingdom
e-mail: pittmans2000@hotmail.com