

The physiological basis of arterial pressure variation during positive-pressure ventilation

Bases physiologiques des variations de la pression artérielle systémique lors de la ventilation mécanique

A. Perel * ,¹

Department of Anesthesiology and Intensive care, Sheba Medical Center, Sackler School of Medicine, Tel Aviv University, Tel Hashomer, 52621, Israel

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Abstract

The aim of this communication is to present an overview of the physiological basis of arterial pressure variations during positive-pressure ventilation. The review describes the effects of the mechanical breath on the right and left ventricles, and in particular the vascular waterfall effect and the reduction in venous return and the inspiratory increase in LV preload. A better understanding of the hemodynamic consequences of mechanical ventilation will help the reader to correctly interpret arterial pressure variations and apply their derived parameters into clinical decision-making.

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Résumé

Le but de ce travail est de présenter une large revue des bases physiologiques qui gouvernent les variations de la pression artérielle en ventilation mécanique. Cela nécessite un rappel sur les interactions cardiorespiratoires, et notamment sur les effets des pressions intrathoracique et transpulmonaire sur les fonctions ventriculaires droite et gauche : diminution du retour veineux, augmentation de l'impédance à l'éjection du ventricule droit, amélioration de la précharge ventriculaire gauche. Cette lecture devrait permettre aux lecteurs d'utiliser les variations de la pression artérielle de façon plus rationnelle en pratique clinique.

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Keywords: Arterial pressure; Mechanical ventilation; Heart–lung interactions; Blood volume expansion; dDown; dUp

Mots clés : Pression artérielle ; Ventilation mécanique ; Interactions cardiorespiratoires ; Remplissage vasculaire ; dDown ; dUp

1. Introduction

In recent years we have been witnessing the introduction of a series of new hemodynamic parameters, which are all

based on the analysis of the response of the cardiovascular system to the mechanical breath. These dynamic parameters are unique in that they measure, in various ways, the hemodynamic response to the repetitive increase in intrathoracic pressure during mechanical ventilation, offering insight as to the function of the heart and its predicted responsiveness to fluid loading. Since these parameters have been demonstrated repeatedly and consistently to be superior to the traditionally measured parameters of left ventricular (LV) preload in predicting fluid responsiveness, some of them, like

* Corresponding author.

E-mail address: perelao@shani.net (A. Perel).

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the pulse pressure variation (PPV) and the stroke volume variation (SVV), are already available in commercial hemodynamic monitors.

In order to correctly apply these parameters into clinical decision-making, one has to understand the hemodynamic effects of the mechanical breath during various cardiovascular states, so that interpretation of any abnormal response is clear and preferably immediate. The hemodynamic effects of the mechanical breath are however quite complex, and have been the subject of vast research as well as of various interpretations. The aim of this communication is to review our current knowledge of the physiological aspects of heart–lung interaction during mechanical ventilation that are relevant for the correct use and interpretation of this promising approach to hemodynamic monitoring.

2. Hemodynamic parameters that are based on the response to a mechanical breath

Since the hemodynamic events that occur during the mechanical breath will be discussed in the practical context of how they affect the parameters that have been suggested as clinically useful hemodynamic monitoring tools, a short description of these parameters is warranted at this stage.

- The systolic pressure variation (SPV) is the difference between the maximal and the minimal systolic blood pressure (SBP) values during one mechanical breath [1–3]. It normally consists and is the sum of an early inspiratory augmentation of the SBP, termed dUp (delta up, Δ_{up}), and a later decrease in the SBP, termed dDown (delta down, Δ_{down}) (Fig. 1). The dUp is measured as the difference between the maximal value of the SBP during the respiratory cycle and the SBP during a short apnea. The dDown is measured as the difference between the reference end-expiratory (or apnea) SBP and the minimal SBP value during the respiratory cycle. During hypotension it is recommended that the SPV and dDown be expressed not in mmHg but rather as a percentage of the SBP during apnea, i.e. %SPV and %dDown.
- The PPV is the difference between the maximal and minimal pulse pressures (PP) during the respiratory cycle divided by the mean of these two values [4,5]. When the PP is measured as the difference between the SBP and the diastolic pressure of the preceding beat, it is directly proportional to the stroke volume (SV).

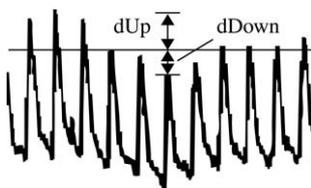


Fig. 1. The normal changes in the arterial pressure during a mechanical breath. The difference between the maximal and minimal values of the SBP is the SPV. The SBP value during a short apnea is used as the reference pressure to measure the dUp (delta up) and the dDown (delta down), which are the two components of the SPV.

- The SVV is the difference between the maximal and minimal SV during the respiratory cycle divided by the mean SV value [6,7]. The continuous measurement of SVV is made available by the pulse contour method following a necessary measurement of cardiac output (CO) for calibration.
- The respiratory changes in the aortic blood velocity [8] and in the aortic velocity–time integral [9,10] calculated as the difference between the maximal and minimal value during the respiratory cycle divided by the mean of these two values.
- The respiratory collapsibility of the superior vena cava (SVC) is calculated as the difference between the maximal expiratory and minimal inspiratory SVC diameter, divided by the expiratory diameter [11,12].
- The distensibility index of the inferior vena cava (IVC) [13,14] has been calculated as either (a) the difference between the maximal end-inspiratory and minimal end-expiratory IVC diameters, divided by the minimal expiratory diameter [14]; or (b) the difference between the maximal and the minimal IVC diameters divided by the mean of the two values [13].
- The respiratory changes in the plethysmographic signal is calculated as the difference between the maximal and minimal peaks of waveform and expressed as a percentage of the signal amplitude during apnea [15].
- The respiratory changes in the preejection period is defined as the time interval between the beginning of the Q-wave on the electrocardiogram and the upstroke of the arterial pressure [16].
- The respiratory systolic variation test (RSVT) is a measure of the response of the systolic pressure to a respiratory maneuver consisting of three successive incremental pressure-controlled breaths [17]. The slope of the RSVT is calculated by plotting the lowest SBP values after each of the three breaths against their respective airway pressures.

3. The hemodynamic effects of the mechanical breath

Although the changes that occur in the heart due to the increase in the intrathoracic pressure and in lung volume during the mechanical breath have been discussed numerous times in recent year [18–23], this topic is still a source of controversy, as attested by the intense correspondence that appeared in recent literature [24–27]. Although there is still no consensus on some of the aspects of the hemodynamic effects of the mechanical breath, our current understanding does allow us to explore the mechanisms responsible for the respiratory variations in the arterial pulse to take advantage of the clinical benefits that they offer in the hemodynamic monitoring of ventilated patients.

The simplistic approach to arterial pressure waveform analysis during mechanical ventilation is based on the fact that, normally, the main hemodynamic effect of the mechani-

cal breath is a reduction in venous return, as pointed out by earlier observations [28,29]. This normal decrease in right, and after a few beats, LV preload, results in a decrease in the left ventricular stroke volume (LVS_V) when the heart is operating on the steep portion of its function (Frank–Starling) curve. Hence, a decrease in LVS_V (or its surrogates) following the mechanical breath implies that the heart is fluid responsive, while its absence normally reflects a lack of such responsiveness [30]. This physiological principle can be compared to testing the function of a sprinkler system (i.e. the cardiovascular system) that is composed of a compliant feeding hose (i.e. the great veins) and a sprinkler mechanism (i.e. the heart). By applying pressure on the feeding hose (i.e. the mechanical breath) and observing the change in the water stream that comes out of the system (i.e. the LVS_V) one can tell that if the water stream is decreased or unchanged. If the water stream decreases then, logically, increasing the flow (i.e. fluid loading) will most probably result in increasing the output of the system (i.e. fluid responsiveness). If the water stream does not decrease, then one can assume that the output of the system is not dependent on the feeding flow (i.e. no fluid responsiveness), and/or that there may be a problem with the sprinkler mechanism itself (impaired cardiac function). This simple test can offer valuable information especially when the output of the system seems inadequate. Unfortunately, the hemodynamic effects of the mechanical breath are more complex, and need to be further elucidated before attempting to use the respiratory-induced variations in the arterial pressure for clinical decisions.

4. The mechanical breath and the right ventricle (RV)

4.1. The venous return

The main hemodynamic effect of the increased intrathoracic pressure during positive-pressure ventilation is normally a decrease in RV filling due to a decreased venous return. In calves with artificial hearts the mechanical breath was found to produce about a 20% decrease in right ventricular filling [31]. A similar decrease was found in RV stroke output in patients ventilated with tidal volumes of 10–15 ml/kg [20]. During hypovolemia the inspiratory decrease in RV outflow may reach 70% and can be normalized (to about 25%) by volume expansion [32]. Following Guyton's earlier observations, it was traditionally assumed that the venous return is determined by the pressure gradient between the mean systemic filling pressure (P_{ms}, the forward pressure that drives the venous blood back to the heart) and the right atrial pressure (RAP) that serves as a backpressure to venous return. The inspiratory rise in RAP has therefore been implicated as the main direct cause for the associated decrease in venous return [18,19]. This view has been challenged following more recent experiments in which the increase in intrathoracic pressure was not found to be associated with a significant change in the pressure gradient for venous return [32–34]. For a more

in-depth critical analysis of the view that RAP determines venous return the reader is referred to a recently published invited commentary by Brengelmann [35].

4.2. The vascular waterfall and venous return

The main phenomenon that seems to be responsible for the inspiratory decrease in the venous return is the 'vascular waterfall', described more than 40 years ago by Permutt and Riley [36]. Vascular waterfall conditions occur when the surrounding pressure of a collapsible vessel exceeds the intravascular pressure, causing significant obstruction of that vessel. Such waterfall phenomenon has been clearly shown in the recent studies describing the collapsibility of the intrathoracic SVC during the mechanical breath [11,12]. Increased respiratory collapsibility of the SVC ('zone 2' conditions) was shown to be associated with decreased RV outflow, which improved following volume expansion [11], and with significant fluid responsiveness [12]. In this latter study, patients showed either very low or very significant respiratory SVC collapsibility, a bi-modal distribution being characteristic of a vascular waterfall.

Similar vascular waterfall conditions were shown in the IVC in mechanically ventilated dogs [37] and in spontaneously breathing asthmatic patients [38]. Since in humans the collapsible IVC segment is very close to the diaphragm, the abdominal IVC normally distends during the mechanical breath. The degree of the IVC distensibility during the mechanical breath has been shown to be a sensitive indicator of fluid responsiveness in two recent studies [13,14]. In fluid responsive patients, the IVC is less filled and its compliance is relatively high, allowing considerable inspiratory distension. In hypervolemic, non-fluid responsive, patients the IVC is maximally dilated and does not expand significantly more during the mechanical breath [27]. Moreover, in the presence of hypervolemia or congestive heart failure (CHF) the inspiratory diaphragmatic descent and the associated increase in abdominal pressure may cause squeezing of the abdominal venous compartment and the congested liver (which are in "zone 3" conditions), causing an increase in the venous return during the mechanical breath [39,40].

This mechanism may be responsible in part to the lack of the decrease in CO when a positive end-expiratory pressure (PEEP) is applied to hypervolemic patients. However, it is only the respiratory variations in the IVC diameter and not the absolute IVC diameter itself that can differentiate between fluid responders and non-responders [13]. Using the respiratory changes in the IVC as a predictor of fluid responsiveness may be complicated by the presence of tricuspid regurgitation and vena cava backward flow, which have been observed to be prevalent in mechanically ventilated patients [41]. This high incidence of IVC backward flow was explained by the fact that these patients were well filled and that the tidal volumes employed were high [27]. Others have suggested that the impact of this regurgitation can be avoided if the respiratory change in the IVC is measured at end-diastole (R wave

on ECG) period when vena cava backward flow is not possible [26]. In addition, an increased intraabdominal pressure may affect the dimensions and distensibility index of the IVC as well.

The concept of the vascular waterfall between the right atrium and the extra-thoracic IVC and intrathoracic SVC offers a most plausible explanation for the fact that hypovolemic patients have a greater decrease in venous return and RV filling during the mechanical breath. It also explains the observed linear relationship between the SPV and dDown to changes in intravascular volume [1] which, as noted by Magder [19], cannot be easily understood based on the traditional venous return function. Obviously, an inspiratory venous collapse increases the respiratory variations in venous return in ‘zone 2’ conditions and contributes to arterial pressure variations [42].

4.3. RV outflow impedance

Some investigators regard the inspiratory increase in RV outflow impedance to be the main reason for the observed decrease in RV outflow during the mechanical breath [20,43–45]. This is based on observations that an inspiratory reduction in the pulmonary artery velocity–time integral occurs with tidal ventilation before any decrease in RV inflow, and that an inspiratory increase in RV systolic dimension is not accompanied by a decrease in either right atrial diameter or in RV end-diastolic area [43]. Further observations by the same group have shown that in septic patients with RV dysfunction (cor pulmonale) the presence of significant arterial pressure variation was not associated with fluid responsiveness and therefore could not be explained as resulting from transient inspiratory decrease in RV preload but rather as a result of increase in RV afterload [44]. In addition it was suggested that when the RV is very dilated, the inspiratory decrease in venous return and in RV end-diastolic volume, by ventricular interdependence, will increase LV diastolic compliance, LV end-diastolic volume and LVSV [18]. The importance of these observations is in alerting the users of arterial pressure variation that patients with severe RV failure may show false positive signs of fluid responsiveness [20,44]. Normally, however, in the absence of right heart failure, there are a number of reasons to believe that the main mechanism responsible for the inspiratory decrease in RV outflow is the reduction in venous return and not the increase in RV impedance. These include: (a) nearly all of the experimental and clinical studies that have shown the value of arterial pressure variations in predicting fluid responsiveness were done in the absence of severe RV dysfunction. In these studies it was repeatedly shown that this variation, and the dDown segment in particular, increases when venous return is decreased; (b) the increased IVC distensibility and SVC collapsibility during inspiration serve as a living illustration of the inspiratory decrease in venous return; (c) there is a striking similarity in the LV pressure–volume relationship during the mechanical breath and during occlusion of the IVC [46]. This similarity

has served as a basis for using large tidal volumes for the assessment of LV systolic function [46]; (d) The mechanical breath is normally producing a decrease in the transmural RAP [47–49], a fact which is hardly consistent with significant increase in RV impedance, which would be expected to increase transmural CVP.

5. The mechanical breath and the left ventricle (LV)

5.1. The early inspiratory augmentation of the LVSV

Normally, the increase in intrathoracic pressure during the mechanical breath causes an early augmentation of the LVSV that is expressed as an increase in the arterial blood pressure (Fig. 1). Although this phenomenon has been repeatedly described many years ago [47,50,51], it has not received a lot of clinical attention. It seems in retrospect that the main reason for this relative inattention is the fact that this early increase in SBP, termed ‘reversed pulsus paradoxus’ [52] and later quantified as the dUp [1,53], is normally the minor variation in the arterial pressure during mechanical ventilation and does not seem at first glance to be of clinical importance. However, with the growing number of publications that examined arterial pressure variation during mechanical ventilation, the dUp was consistently found to be very small during hypovolemia and to increase significantly during hypervolemia and/or CHF [1,54–57], when it often becomes the dominant respiratory variation in the arterial pressure [1,3,54,55,57] (Fig. 2). Hence, the presence of moderate respiratory variations in the arterial pressure may be due to a dUp phenomenon only [3,49,58], a fact that cannot be easily appreciated without close observation of the relationship between the peak arterial pressure and the pressure during a short apnea.

A number of different factors have been proposed to explain this early inspiratory augmentation of the LVSV [19,47,51,59]. These include (a) an increased pulmonary venous return and in LV preload due to squeezing of pulmonary blood volume (PBV); (b) decrease in LV afterload; (c) an inspiratory decrease in RV volume with a concomitant increase in LV diastolic compliance; (d) external compression of the heart by the inflating lungs; (e) improved myocar-

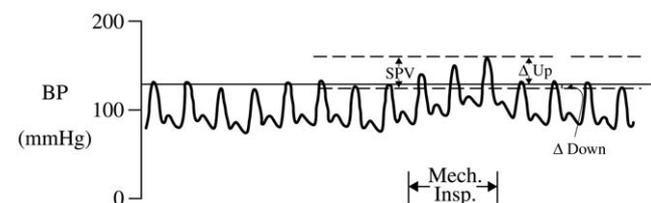


Fig. 2. The arterial pressure waveform of a septic patient in which a dominant dUp is the main respiratory variation. Note that the inspiratory increase in the SBP is accompanied with an increase in the PP (systolic minus *previous* diastolic) as well, reflecting the increase in LVSV due to the increased intrathoracic pressure. Figure supplied by Dr. Eran Segal.

dial systolic function; (f) initiation of neurocirculatory reflexes; (g) an earlier and longer opening of the aortic valve. Although there is still no consensus about the exact mechanism responsible for this inspiratory increase in LVSV, it would seem reasonable to assume that it is a result of a number of forces, some of which may be more important than others in specific clinical situations. Since the presence of an isolated dUp is quite prevalent in critically ill patients [49], a better understanding of its possible physiological origins may be helpful in understanding its clinical significance.

5.2. The inspiratory increased in LV preload

The increase in intrathoracic pressure normally squeezes the PBV into the left atrium, thus increasing LV preload and outflow. Versprille and Jansen [48] had termed the inspiratory decrease in the PBV as the ‘ebb tide’, and its expiratory increase as the ‘flood tide’, stressing the fact that the PBV serves as a reservoir of the LV preload during mechanical ventilation [20,48]. Brower et al. [50] have shown that during ‘zone 2’ lung conditions mechanical inflation caused a decrease in the pulmonary venous flow and an increase in PBV, due to retention of blood in the extra-alveolar vessels. During ‘zone 3’ conditions, however, lung inflation was associated with transient increase in pulmonary venous flow and a decrease in PBV since blood was expelled from the engorged alveolar vessels [50]. Such an inspiratory increase in pulmonary venous flow has been recently shown by echocardiography to occur in septic patients [49], and is responsible for the observed increase in the filling [31] and the dimensions of the left heart chambers during tidal inflation [47,49]. That the increase in LV preload seems to be the main mechanism responsible for the normally occurring inspiratory augmentation of LV outflow is further supported by the fact that, by converting more lung regions from ‘zone 2’ to ‘zone 3’ conditions, fluid administration causes the dUp to increase at the same airway pressure [1,3,54–57]. This is in contrast with Magder’s recent speculation that the outflow from the right heart and inflow to the left heart are not directly affected by the increase in intrathoracic pressure, since both upstream and downstream compartments are equally altered by the change in pleural pressure [19]. Of great significance is the observation that the inspiratory increase in pulmonary venous flow was seen mainly in patients with a prominent dUp, while patients with an isolated dDown showed an inspiratory decrease in pulmonary venous flow [49], supporting the experimental observations of Brower et al. [50].

5.3. Other proposed mechanisms for the inspiratory increase in LVSV

The transient augmentation in LVSV due to the inspiratory increase in LV preload offers a plausible explanation to the dUp in pulmonary ‘zone 3’ conditions and normal LV fluid responsiveness. However, the presence of a more dominant dUp during hypervolemia and CHF, i.e. when the LV is

characteristically not fluid responsive, points to the presence of other forces as well. The inspiratory increase in pleural pressure changes LV pressure relative to the extra-thoracic aorta and therefore produces an effective decrease in LV afterload [18,51]. Such a decrease in afterload may theoretically facilitate LV ejection when contractility is impaired. In addition, the possible greater transmission of the pleural pressure to the LV as compared with the aorta itself, may cause an earlier and longer opening of the aortic valve during inspiration [19]. Other investigators have not found any measurable decrease in LV afterload during the mechanical breath [49,60]. In fact, Vieillard-Baron et al. [49] found recently that LV systolic wall stress, an index of LV afterload, significantly increased during tidal ventilation. In addition, these authors found it difficult to imagine that the small increase in pleural pressure that was observed in their septic patients during lung inflation would have any measurable effect on LV ejection pressure [49]. Other hypothetical mechanisms that have been mentioned as being able to contribute to the early inspiratory increase in LVSV include a possible improved LV contractility [59] and/or a higher external pressure that is exerted on the LV by the expanding lungs [61].

It seems therefore that the inspiratory augmentation in LVSV is produced by a complex combination of mechanisms, the balance of which depends on the state of cardiac contractility [62]. Under normal conditions, the dUp is due mainly to the squeezing of the PBV from the pulmonary vasculature. It seems however that when LV contractility is reduced, and as long as pulmonary ‘zone 3’ conditions and a significant threshold value of LV end-diastolic volume are present, LV ejection is facilitated by the mechanical breath by a combination of reduced LV afterload and external pressure on the heart. This ‘LV-assist’ mechanism accounts for the prominence of the dUp when LV function is reduced experimentally [54,57] and has been used in a number of studies to effectively increase CO in patients with CHF [18].

5.4. The dUp during open-chest conditions

Under complete open-chest conditions, when the hemodynamic effects of the mechanical breath are not expected to be significant, a small but consistent dUp is normally observed. Reuter et al. [63] have recently demonstrated that mid-thoracotomy is associated with an increase in the global end-diastolic volume (GEDV), and with a diminished, though persistent, respiratory-induced SVV and PPV. Our own analysis of arterial pressure variations, including the dUp, in patients undergoing coronary revascularization, is shown in Fig. 3. Shortly after termination of cardiopulmonary bypass (CPB) (Fig. 3, bars A and B), when the sternum is fully retracted, all of the observed pressure variations are due to a dUp component, signifying repetitive augmentation of the LVSV. The concomitant dDown is however insignificant, denoting the fact that the mechanical breath does not hamper venous return when the chest is open. Once chest retractors are removed, and especially after complete chest closure (Fig. 3, bars C

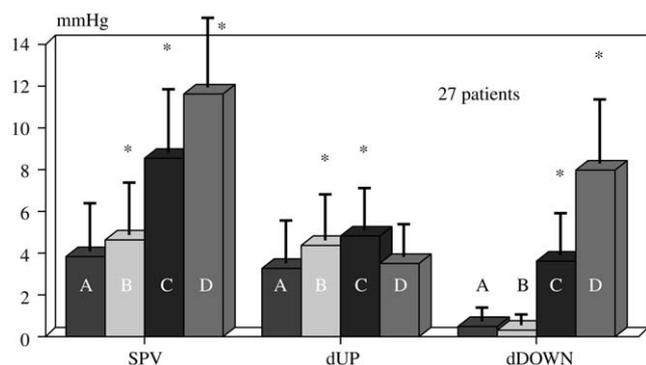


Fig. 3. The mean values (\pm S.D.) of the SPV and its dUp and dDown components, in 27 patients undergoing coronary artery revascularization. A. Three minutes after end of CPB, chest fully opened. B. Fifteen minutes after CPB, chest still fully opened. C. After removal of sternal retractors. D. After chest closure. * $P < 0.05$ compared with end of CPB (A).

Figure supplied by Dr. Eran Segal.

and D), the dDown component becomes much more prominent, reflecting the transient respiratory-induced decrease in venous return and in LVSV. The fact that in the study of Reuter et al. [63] the PPV and SVV were inversely correlated with the GEDV, led the authors to conclude that even under open-chest conditions these parameters reflect preload-dependency and may be used to guide fluid therapy. Such conclusion is seemingly in contrast with our own observations that all of the respiratory arterial variation in open-chest conditions is due to a dUp (Fig. 3), and with the fact that, under closed-chest conditions, a dominant dUp is associated with a lack of fluid responsiveness. However, the few rare occasions in which we have observed the dUp to be absent under open-chest conditions, were always associated with a congested heart that contracted poorly. Hence it seems that, under open-chest conditions, a higher GEDV (and presumably a higher PBV) is associated with a lower (and not higher) dUp. The reason for this is unclear, since the only possible source of the observed dUp is an increase in preload due to squeezing of PBV even when the chest is open. In the meantime, under these conditions, the response of the LVSV to the mechanical breath seems to be more dependent on the LV contractility and filling status than on the amount of PBV that is ‘squeezed’ into the LV. The physiology and clinical usefulness of the SVV and the PPV when the chest is open need to be studied further, bearing in mind that these parameters measure the total respiratory variation of the LVSV and cannot differentiate between the dUp and dDown.

5.5. Is the dUp influenced by the transmission of pleural pressure?

Theoretically the dUp can be influenced by partial transmission of the intrathoracic pressure to the LV and the aorta during the mechanical breath and thus may not be representative of an augmented LVSV [4,64]. This theoretical disadvantage of the SPV has been the background for the introduction of the PPV as a presumably better dynamic parameter of

fluid responsiveness [4,5]. The actual degree of this transmission seems however to be minimal [19,49], which is not surprising in view of the close correlation of the SPV to the PPV [5] and to the SVV [6,7]. However, in a study that was designed to test the hypothesis that changes in the SBP are induced solely by in-phase changes in intrathoracic pressure, and which was done in patients with relatively small SPV values in both closed and open-chest conditions, Denault et al. [64] have not found a consistent relationship between the changes in the SBP and the LV end-diastolic area as determined by an automated border detection software. They, therefore, claimed that “changes in systolic arterial pressure reflect changes in airway pressure better than they reflect concomitant changes in LV hemodynamics” [64]. Moreover, they have concluded that the dDown is not related to a decrease in LV preload [64]. However, although this study is frequently cited, its results have to be treated with caution, since the figure of the analog signals that accompany this publication is strongly suggestive of a possible problem of dys-synchronicity between the arterial pressure and the presumably simultaneous LV area recordings (see Fig. 2 in Ref. [64]). According to this figure, a transient inspiratory decrease in LV area seems to occur simultaneously with an increase in both the SBP and the arterial PP, denoting a simultaneous increase in LVSV. There is however no logical physiological explanation for the occurrence of an increase in LVSV in the presence of such a marked decrease in LV volume, especially when there is ample evidence that at this time exactly the preload to the LV normally increases. Hence it seems that the critique expressed in this article on the physiological basis and potential clinical usefulness of the SPV is based on a possibly erroneous interpretation of the data due to problems of synchronicity of the measured variables.

Although a small degree of transmitted intrathoracic pressure may affect the SPV, the PPV seems to be just a little more accurate than the SPV as a predictor of fluid responsiveness [5], a finding that was corroborated by our own study (Preisman et al., submitted for publication). However, in contrast with the results of Denault et al. [64], the SPV and dDown were repeatedly found to significantly correlate with changes in the LVSV, which were measured by aortic velocity–time integral [8,9,65], by Doppler echocardiography [49], by the arterial PP [5], and by the pulse contour method [7]. A recent study using conductance volumetry has also shown that, in contrast to the Denault study, the arterial pressure decreases simultaneously with the inspiratory decrease in LV volume [46]. It is therefore that for all practical purposes the SPV, dDown and dUp should be perceived as representing true changes in the LVSV during the mechanical breath.

5.6. The clinical implications of a dominant dUp

Mere superficial eyeballing of the arterial pressure fluctuations during mechanical ventilation, without relating them to stable SBP values during the end-expiratory pause, may be misleading. Since these variations may be attributed to the

more commonly occurring dDown, one may erroneously assume that the patient is fluid responsive. The identification of a prominent and/or isolated dUp (Fig. 3) is of great clinical value, since this finding implies that the patient is either hypervolemic or having compromised LV function. Since the mechanical breath serves as a repetitive ‘assist device’ to the LV in such conditions, weaning the patient from ventilatory support at this time without improving his cardiovascular function (e.g. diuretics, inotropes or afterload reduction) is probably not advisable. Last but not least, since the SPV, PPV and SVV measure the difference between the maximal and minimal beats during the respiratory cycle, they include the dUp as well. The presence of a significant or dominant dUp may therefore decrease their accuracy as predictors of fluid responsiveness. A PPV of 10% for example, may be associated with a variety of combinations of dUp and dDown, which accounts for the higher reported threshold value (13%) necessary for the accurate prediction of positive fluid responsiveness [4,5]. An indirect evidence for this limitation can be found in a recent study where the SVV was shown to be a better predictor of fluid responsiveness in patients with normal cardiac function than in patients with a low preoperative ejection fraction and higher intraoperative LV end-diastolic dimensions [66]. The most probable explanation for the reduced performance of the SVV when cardiac function was impaired is that these patients may have had a characteristically higher dUp, the prominence of which resulted in a lesser predictive ability of the SVV.

5.7. The decrease in LVSV (dDown)

The second phase of the response of the LV to the mechanical breath is normally a decrease in LVSV, which is the result of the earlier decrease in RV output. The reduced LVSV is reflected in the decrease in the arterial systolic (dDown) and PP during late inspiration and/or early expiration. The dDown is normally the main component of the arterial pressure variation, accounting for the many publications that have repeatedly shown that the SPV, PPV and SVV are better indicators of changes in blood volume, of occult hypovolemia and of fluid responsiveness, than static preload parameters. The surprising sensitivity of the dDown to changes in volume status can be explained by, and is testimony of, the vascular waterfall effects of the increased intrathoracic pressure on the venous return, as mentioned earlier. Jardin [20], however, seems to prefer the theory that the dDown is caused mainly by the decrease in RV ejection, due to an increase in RV impedance and a delay in the re-filling of the pulmonary capillary bed, which cause a later decrease in LV filling and outflow. I have already stated previously my reasons to believe that, in the absence of right heart failure, the main mechanism responsible for the inspiratory decrease in RV outflow, and the later decrease in LVSV, is the reduction in venous return and not the increase in RV impedance.

In one study, however, in which pigs were exanguinated to a low mean arterial pressure, the dDown was not considered

to reflect the degree of hemorrhage better than the mean arterial pressure and other hemodynamic parameters [67]. However, when the blood pressure is changing rapidly, or when it is very low, it is highly recommended to express the SPV and the dDown as a percentage of the SBP value during end-expiration, namely as %SPV and %dDown [30]. If, in the above mentioned study [67], the %dDown would have been used rather the absolute dDown in mmHg, then it would have changed much more significantly during the hypotensive period and would have become more significant.

The sensitivity of the SPV and the dDown to changes in intravascular volume can also be seen from their response to passive leg raising (PLR). In patients with acute circulatory failure the changes in the respiratory-induced PPV during PLR were significantly correlated with changes in SV during PLR and following rapid fluid expansion [68]. In another experimental study, Pizov et al. [69] found that the application of PEEP in normovolemic dogs caused a significant reduction of the CO and a significant increases in the SPV and dDown. The same level of PEEP, however, did not affect CO in hypervolemic dogs with induced myocardial depression, nor did it change the SPV and the dDown. Hence the presence of a significant dDown should prevent the augmentation of PEEP without prior fluid loading or without the application of more advanced hemodynamic monitoring, while the absence of the dDown means that the expected hemodynamic effects of PEEP will most probably be negligible. In critically ill patients the PPV values prior to PEEP application were shown to significantly correlate with the PEEP-induced changes in CO, which also correlated with the changes in PPV following PEEP [4].

In humans the reported values for the SPV vary between 7–16 mmHg and 2–11 mmHg for the dDown [2,3,5,7,9,15,16,49,70–72]. This large spectrum of ‘normal’ values is due to a variety of filling conditions and of tidal volumes. However, in humans, a decrease of 500 ml (or 10%) in the blood volume resulted repeatedly in an increase of about 5 mmHg in the SPV and dDown [15,70,71]. Varying degrees of fluid expansion in humans have always shown the SPV to decrease significantly by anywhere from 2.5 to 10 mmHg [2,3,5,7,9]. For the PPV and SVV parameters, values above 10–13% indicate, with very high sensitivity and specificity, that fluid loading will cause an increase in CO.

6. Limitations of functional hemodynamic parameters

The main limitation of functional hemodynamic parameters is that their use is limited to patients who are on fully controlled mechanical ventilation. In patients that are breathing spontaneously or on partial ventilatory support, quantification of the respiratory changes in pulsatile parameters may be inaccurate and difficult to interpret. Other potential inaccuracies may be due to the lack of standardization of the magnitude of the tidal volume employed, an exaggerated variation being observed in the presence of large tidal volumes,

and a small variation when low tidal volumes are being used [73]. Others have recently claimed that the size of the tidal volume influences not only the arterial respiratory variations but also the hemodynamic response to a fluid load, since larger tidal volumes increase the mean airway pressure and may shift the LV function curve to the left [74]. A change in the tidal volume itself, within the accepted clinical range, has however, very little effect on the mean airway pressure. In addition we have previously shown that the increase in tidal volume affects the SPV and its components in a similar and consistent fashion in all volume states [55]. This is one of the main reasons for the recently introduced RSVT, which employs a standardized respiratory maneuver consisting of three successive incremental pressure-controlled breaths for the evaluation of fluid responsiveness [17]. Exaggerated arterial pressure variations can also be seen in the presence of air-trapping or reduced chest wall compliance [19,30]. Decreased lung compliance by itself should not affect the usefulness of the SPV and its derivatives if the tidal volume is unchanged, since the effects of increased airway pressure and its reduced transmission may cancel each other out. In fact some of the major clinical studies on functional hemodynamic parameters have been done in patients who were in respiratory failure [3–5,49].

Since functional hemodynamic parameters rely on individually measured beats, any arrhythmias may cause significant inaccuracies. Nodal rhythm, however, may increase the SPV by effectively decreasing preload due to the loss of the ‘atrial kick’. As mentioned before, the PPV, SVV and PPV include the dUp, a component that is unrelated to fluid responsiveness and, when prominent, may reduce their ability to accurately reflect fluid responsiveness. In addition, the presence of right ventricular dysfunction may cause falsely high SPV and PPV values even though these patients may not be fluid responsive [20,44]. Since the normal healthy heart is fluid responsive, the presence of fluid responsiveness is not an indication by itself to administer fluids. In addition, functional hemodynamic parameters do not offer an answer to the dilemma of cardiovascular ‘optimization’.

7. Conclusions

The physiology of the hemodynamic effects of the mechanical breath is quite complex, since the increase in intrathoracic pressure affects the inflow, outflow and function of both cardiac chambers. The normal response to a mechanical breath is characterized by an initial decrease in RV preload, due to the vascular waterfall phenomenon, and in RV output. At the same time, LV filling is increased due to squeezing of PBV into the left atrium, leading to an initial increase in the LVSV. Later on in the respiratory cycle, RV output increases and LV output decreases. However, various factors are involved in this complex process, some of which are still under debate. In addition, the hemodynamic effects of the mechanical breath are greatly dependent on the prevailing conditions of cardiac

filling and function. Since the resulting changes in the LV outflow are reflected in the arterial pressure, analysis of the response of the arterial pressure may offer significant insight as to the cardiovascular status, and more specifically as to the fluid responsiveness of the patient. Finer analysis of the arterial pressure waveform may help the identification of those patients in which the mechanical breath results in an increase in CO. This augmentation of LV output is a result of a combination of factors, among which a reduction in afterload and external pressure on the heart by the expanding lungs seem to be of importance especially in patients with reduced LV function.

The clinical use of functional hemodynamic parameters that are derived from respiratory-induced variations in the arterial pressure is gaining wider popularity in the hemodynamic monitoring of ventilated patients. In order to correctly measure and interpret these parameters, one must have a basic knowledge of the normal and abnormal physiology of heart–lung interaction during mechanical ventilation. In addition, the inherent limitations, and the associated confounding factors, of these parameters have to be clearly recognized. Nevertheless, these functional hemodynamic parameters offer immediate, dynamic, and essential information about the cardiovascular function of ventilated patients, in which hemodynamic uncertainty and potential instability are often present.

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