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The effects of vasoactive drugs on pulse pressure and stroke volume variation in postoperative ventilated patients☆,☆☆

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Abstract

Introduction: Although pulse pressure variation (PPV) and stroke volume variation (SVV) during mechanical ventilation have been shown to predict preload responsiveness, the effect of vasoactive therapy on PPV and SVV is unknown.

Methods: Pulse pressure variation and SVV were measured continuously in 15 cardiac surgery patients for the first 4 postoperative hours. Pulse pressure variation was directly measured from the arterial pressure waveform, and both PPV and SVV were also calculated by LiDCO Plus (LiDCO Ltd, Cambridge, United Kingdom) before and after volume challenges or changes in vasoactive drug infusions done to sustain cardiovascular stability.

Results: Seventy-one paired events were studied (38 vasodilator, 10 vasoconstrictor, 14 inotropes, and 9 volume challenges). The difference between the measured and LiDCO-calculated PPV was 1% ± 7% (1.96 SD, 95% confidence interval, $r^2 = 0.8$). Volume challenge decreased both PPV and SVV (15% to 10%, $P < .05$ and 13% to 9%, $P = .09$, respectively). Vasodilator therapy increased PPV and SVV (13% to 17% and 9% to 15%, respectively, $P < .001$), whereas increasing inotropes or vasoconstrictors did not alter PPV or SVV. The PPV/SVV ratio was unaffected by treatments.

Conclusion: Volume loading decreased PPV and SVV; and vasodilators increased both, consistent with their known cardiovascular effects. Thus, SVV and PPV can be used to drive fluid resuscitation algorithms in the setting of changing vasoactive drug therapy.

1. Introduction

Positive-pressure ventilation-induced arterial pulse pressure variation (PPV) and left ventricular (LV) stroke volume variation (SVV) are sensitive and specific predictors of preload responsiveness [1-7]. Specifically, threshold variation values exceeding 10% to 15% during 7- to 10-mL/kg tidal volume ventilation predict well cardiac output increases greater than 20% in response to a 250- to 500-mL fluid bolus infusion. Based on these robust findings across several studies, both PPV and SVV have been proposed as

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reasonable parameters to guide resuscitation [8]. Indeed, PPV has recently been showed to be an effective guide in fluid therapy in high risk patients [9].

However, several factors commonly seen in critically ill patients can potentially influence both PPV and SVV independent of preload responsiveness. For example, because the primary driving force causing the variation on LV filling during positive-pressure breathing is the increased lung volume–induced increase in pleural pressure [10], if tidal volume were to vary, then for the same intravascular volume status PPV and SVV would also covary [11–15]. Similarly, if vasomotor tone were to vary, it may alter unstressed circulatory blood volume. Thus, the effective circulating blood volume should also vary inversely with changes in vasomotor tone [16]. One would predict that vasopressors should decrease both PPV and SVV, whereas vasodilators would have the opposite effects. The hemodynamic effects of inotropic agents may have varying effects depending on their impact on LV ejection efficiency, vasomotor tone, and heart rate. Finally, changes in the ratio of PPV to SVV at a constant tidal breath should parallel changes in central arterial compliance. If vasopressor therapy increased arterial stiffness, then PPV/SVV should increase and vasodilators should induce the opposite effect.

Although we recently documented that inotropes do not alter PPV and SVV in an animal model [17], the effect of vasoactive agents and inotropes on PPV and SVV has not been studied in humans [18]. Because critically ill patients are often resuscitated with a combination of agents including fluid and vasoactive and inotropic drugs, these interactions must have clinical relevance if PPV and SVV parameters are to be used to guide resuscitation therapy in these patients. Thus, we examined the impact of selective infusions of vasoactive agents and inotropes as compared with volume loading on PPV and SVV changes and their ratio in post–cardiac surgery patients.

2. Methods

The study was approved by our institutional review board, and all subjects signed informed consent. Twenty post–cardiac surgery patients (54-82 years of age) were studied. Additional inclusion criteria were the presence of both an arterial and pulmonary artery catheter (PAC) (Edwards LifeSciences, Irvine, CA) (either intermittent bolus thermodilution [CO_{TD}] or continuous cardiac output [CCO]). Exclusion criteria were evidence of cardiac contractility dysfunction (ejection fraction <45% by intraoperative echocardiography), pregnancy, pacemaker/automatic internal cardiac defibrillator (AICD), heart/lung transplant, persistent arrhythmias, severe valvular stenosis or insufficiency after surgery, intraaortic balloon pump, or other mechanical cardiac support. Patients were admitted to the intensive care unit (ICU) on assist-control ventilation with 12/min respiratory rate (no patient had a spontaneous respiration >16/min) and 6 mL/kg tidal volume, I/E time of 1:2, and 5 cm H_2O positive end-expiratory pressure. Fentanyl (25-50 μg) was given as needed by nursing staff if patient appeared to have pain or discomfort.

Therapeutic interventions were categorized as vasodilator, vasoconstrictor, inotropic, or volume loading as defined by:

1. Volume: any given volume of at least 250 mL of blood products, colloid, or crystalloid infused in less than 15 minutes
2. Vasodilator: any increase of at least 0.1 μg/(kg min) in nitroprusside infusion
3. Vasoconstrictor: any increase of at least 0.01 μg/(kg min) in epinephrine, norepinephrine, or phenylephrine, or at least 1 μg/(kg min) in dopamine infusion
4. Decrease inotrope: any decrease of at least 0.01 μg/(kg min) in epinephrine or at least 1 μg/(kg min) in dobutamine or dopamine infusion

These vasoactive drugs and volume were given based on a preset postoperative order set that defined that vasopressors and vasodilators were to be given to keep mean arterial pressure (MAP) between 90 and 65 mm Hg (with individual subject adjustments made on a case-by-case basis). Thus, vasodilator agents were given to reverse hypertension, whereas vasopressors were given before hypotension occurred to sustain MAP greater than 65 mm Hg. In practice, subjects rarely received single interventions, with most receiving 2 treatments simultaneously. Because we wished to examine the selective effect of specific treatments, we excluded multitreatment events. Thus, all reported paired pre– to during drug infusion or pre– to post–volume loading events are single treatment events. The *predrug infusion period* was defined as the time immediately before starting treatment, and the *during drug infusion time* was defined as the time after starting the drug at a constant infusion rate once hemodynamic parameters returned to a stable new state, as assessed by measure of continuous cardiac output, heart rate, and blood pressure. Accordingly, we could analyze single therapeutic events in only 15 of the original 20 patients recruited for this study.

Table 1 Patients characteristics

Age (y)	71 ± 10
Sex (M/F)	14/6
Body mass index	29 ± 5
LVEF (%)	51 ± 8
Type of PAC (CO_{TD}/CCO)	12/8
LiDCO calibrated against (lithium dilution/PAC)	12/8
Calibrated against PAC (CO_{TD}/CCO)	6/2
Type of operation	n
CABG	8
Valvular repair	5
CABG + valve repair	3
CABG +/− valve repair +/− TAAR	4

Data are presented as mean ± SD. n = 20. LVEF indicates left ventricular ejection fraction; CABG, coronary artery bypass grafting; TAAR, thoracic aortic aneurysm repair.