

Comparison of Arterial Systolic Pressure Variation with Other Clinical Parameters to Predict the Response to Fluid Challenges during Cardiac Surgery

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Abstract

Prophylactic optimization of stroke volume during surgery has been thought by some to reduce complications following surgery. Mechanical ventilation has been shown to induce variations in systolic systemic arterial blood pressure. Measuring such variations in systolic pressure (SPV) might serve as an attractive method for guiding fluid therapy intraoperatively. It is unknown if variations in systolic pressure following the rapid intravenous administration of a specific volume of fluid would lead to changes in pressure measurements obtained from a pulmonary artery with sufficient sensitivity to predict or guide the need for expansion of the intravascular volume to optimize stroke volume as an index of cardiac function. The purpose of this study was to determine if such measurements of changes in systolic pressures would be useful in optimizing stroke volume.

Nineteen patients undergoing cardiac surgery were enrolled in a prospective cohort study. Following induction of general anesthesia, one or more 250 mL boluses of 6% hetastarch were administered. Stroke volume was calculated from the cardiac output obtained by thermodilution using a pulmonary artery catheter. If the patient's stroke volume increased by less than 10% as a result of a given fluid challenge, the patient was classified as a non-responder. However, if the stroke volume increased by more than 10%, the patient was classified as a responder. The variations in systolic pressure and echocardiographic indices were simultaneously measured before and after the administration of each 250 mL fluid bolus.

Pulmonary artery occlusion pressure (PAOP) values were significantly lower in patients who responded to fluid boluses ($p=0.0085$) than in those who did not. Similarly SPV and SPV_{down} values (defined as the decrease in systolic pressure with ventilation) were significantly greater in the responders ($p<0.05$). No significant intergroup differences were observed in SPV_{up} (increase in systolic pressure with ventilation) or echocardiographic-derived left ventricular end diastolic area. APAOP value less than 10 mm Hg predicted a response (sensitivity 68%, specificity 79%). Although significant intergroup differences in the extent of systolic pressure variations were observed, no appropriate threshold values could be determined that would accurately predict the response to a fluid bolus.

There is a relationship between SPV and SPV_{down} values and intravascular volume status. SPV and echocardiographic-derived values did not predict the response to a fluid bolus as well as values obtained from the pulmonary artery catheter.

Key Words: Intravenous fluid administration, hemodynamic monitoring, systolic pressure variation.

Glossary

CABG — coronary artery bypass graft

CO — cardiac output

EDA — end diastolic area (as measured by transesophageal echocardiography)

ESA — end systolic area (as measured by transesophageal echocardiography)

HES — 6% hetastarch in isotonic saline

HR — heart rate, BPM—beats per minute

LVEDA — left ventricular end-diastolic area

(from echocardiogram)

MAP — mean arterial systemic pressure

nRES — non-responder; a less than 10% increase in stroke volume as a result of a 250 mL bolus of 6% hetastarch

PAP — pulmonary artery pressure

PAC — pulmonary artery catheter

PAOP — pulmonary artery occlusion pressure

RES — responder; a greater than 10% increase in stroke volume as a result of a 250 mL bolus of 6% hetastarch

SPV — systolic pressure variation

SPV_{down} — the decrease in systolic systemic arterial pressure that results from the decreased left ventricular preload that occurs during positive pressure ventilation

SPV_{up} — the increase in systolic systemic arterial pressure that results from the transient increase in left ventricular preload that occurs during the early phase of positive pressure ventilation

SPV_{total} — the total arterial systolic systemic pressure variation defined as the sum of SPV_{up} and SPV_{down}

SV — stroke volume

TEE — transesophageal echocardiography

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Introduction

MORBIDITY IS COMMON following moderate- and high-risk surgical procedures (1–6). Prophylactic optimization of stroke volume (SV) and other indices of oxygen delivery in surgical patients have been demonstrated in some randomized clinical trials to reduce complications and post-operative length of stay (7–13). Three randomized clinical trials used the esophageal Doppler to guide the administration of dynamic fluid challenges (7–9). The goal of these stroke volume (SV) guided dynamic fluid challenges was to expand the intravascular volume and thereby avoid hypovolemia. Avoidance of hypovolemia was thought to be an attractive method of preventing systemic inflammation attributed to splanchnic mucosal ischemia (1, 3, 5, 14, 15). Routinely used triggers of fluid therapy, e.g., systemic hypotension and tachycardia, are insensitive measures of hypovolemia (1, 16, 17).

Variables that can be used to guide fluid therapy intraoperatively include those obtained via a pulmonary artery catheter (PAC), such as pulmonary artery diastolic and pulmonary artery occlusive pressures (PAOP). Esophageal Doppler and transesophageal echocardiography (TEE) can be used to measure SV and left ventricular end diastolic area respectively.

SPVs are fluctuations in the systolic arterial blood pressure related to mechanical ventilation. During positive-pressure ventilation, upon inspiration, the increase in intrathoracic pressure propels blood out of the lungs into the left atrium and left ventricle and transiently augments left ventricular preload, SV, and systolic arterial blood pressure. The increased intrathoracic pressure results in reduced venous return to the right atrium, which causes decreased left ventricular filling, preload, SV, and systolic arterial blood pressure. Using the systolic arterial blood pressure at the end of expiration as a reference point, the initial increase of systolic arterial blood pressure above baseline during inspiration is called delta up (SPV_{up}), and the subsequent decrease below baseline during inspiration is called delta down (SPV_{down}). The total systolic pressure variation (SPV_{total}) is defined as the sum of SPV_{up} and SPV_{down} .

SPV can be affected by a variety of factors, including intravascular volume status, cardiac function, chest wall compliance, lung compliance, positive end-expiratory pressure (PEEP), and tidal volume. If these variables remain constant, then changes in the intravascular volume status of the subject are thought to result in

changes in the SPV (18, 19). Perel et al. demonstrated that SPV and delta down are sensitive indicators of hypovolemia in a dog model (20). Rooke et al. found similar results in eight patients, with SPV and delta down increasing with graded hemorrhage (21). Similar results were reported by Ornstein et al. in 15 patients with good ventricular function undergoing coronary artery bypass graft (CABG) surgery who were subjected to hemorrhage (22).

In contrast to previous studies that focused primarily on the response to graded hemorrhage, none have explored whether the optimization of stroke volume (SV) can be correlated with SPV parameters in patients undergoing coronary artery bypass graft surgery (CABG). Our study sought to determine if SPV-derived parameters accurately predicted SV optimization.

Methods

Patients' Inclusion and Intraoperative Management

The clinical investigations described in this manuscript were conducted in accordance with the guidelines of the Declaration of Helsinki. The study was approved by the institutional review board. Patients younger than 18 years old, and patients with an ejection fraction less than 30% or intracardiac shunts were excluded. After obtaining written informed consent, 19 patients undergoing primary CABG surgery were prospectively enrolled. After catheterization of a radial artery, general anesthesia was induced with fentanyl 10–20 $\mu\text{g}/\text{kg}$, etomidate 0.2–0.3 mg/kg , and pancuronium 0.1 mg/kg . After tracheal intubation, a pulmonary artery catheter was introduced via the right internal jugular vein and a transesophageal echocardiography probe (Acuson, Mountain View, CA) was inserted. A transgastric short axis view of the left ventricle was obtained and maintained for measurements of end systolic (ESA) and end diastolic areas (EDA). Patients were ventilated with tidal volumes of 10 mL/kg , and the respiratory rate was adjusted to maintain $P_{a\text{CO}_2}$ between 35 and 40 torr. The patient was then positioned for surgical preparation; however, skin incision did not commence until the conclusion of the study protocol.

Heart rate (HR), mean systemic arterial pressure (MAP), pulmonary artery pressure (PAP), PAOP, intermittent cardiac output (CO) obtained by thermodilution, ESA, and EDA were recorded. SVs were calculated on line by dividing the CO by HR. All arterial pressure

pulse tracings were obtained during a 15-second period of patient apnea followed by five cycles of controlled ventilation. Arterial pressure pulse tracings were analyzed later to determine the extent of SPVs.

After obtaining the aforementioned initial hemodynamic data, 250 mL of normothermic 6% hetastarch in normal saline (HES) was administered via an indwelling intravenous catheter within approximately 5 minutes. Measurements of hemodynamic data were repeated 5 minutes after the conclusion of the fluid bolus. If the patient's SV increased by less than 10%, the patient was classified as a non-responder (nRES) to that bolus of fluid, and the protocol was terminated. If the patient's SV increased by 10% or more, the patient was classified as a responder (RES). In these responding patients, a second 250 mL bolus of HES was then administered, and the hemodynamic measurements were repeated. If the SV now increased by 10% or less, the patient was then classified as a non-responder (nRES) and the protocol was terminated. If, however, the SV increased by 10% or more, the patient was classified as a responder (RES). In this situation, the fluid bolus was repeated for a third and final time during which time the same hemodynamic measurements were repeated. Once again, the patient was classified either as a RES or a nRES. The interval between the start of each fluid bolus was 10 minutes.

SPV Calculations

All SPV calculations were performed "off-line" after completion of the study protocol. A systolic systemic arterial pressure was measured during the last five seconds of patient apnea. This measurement served as the baseline from which SPV_{up} and SPV_{down} were calculated. The maximal increase in systolic systemic arterial blood pressure during early inspiration above the apneic systolic pressure was defined as SPV_{up} . The difference between the systolic systemic arterial blood pressure and the maximal decrease in systolic pressure during positive pressure ventilation was defined as SPV_{down} . The sum of SPV_{up} and SPV_{down} was defined as SPV_{total} .

Statistical Analysis

The goal of the present study was to determine whether SPVs accurately reflected changes in SV. Hence, each fluid bolus was considered a separate case and assumed statistical independence. Differences in SPV_{up} , SPV_{down} , SPV_{total} , EDA, and PAOP between RES and nRES

groups were analyzed by the Student's t-tests. Differences in hemodynamic parameters between sequential boluses were analyzed by paired Student's t-tests with correction for multiple comparisons. All analyses were two tailed, and a p value ≤ 0.05 was considered significant.

Results

Demographic data for the 19 patients who were studied are summarized in Table 1. Patients received a total of 36 boluses of HES. Six patients received only 1 fluid bolus (total 250 mL), 9 patients received 2 boluses (total 500 mL), and 4 patients received 3 boluses (750 mL total). Hemodynamic data during pre-bolus conditions and subsequent fluid boluses are summarized in Table 2. In response to the first fluid bolus, there was a statistically significant increase in systolic and diastolic pulmonary artery pressures, PAOP, CO, and SV as well as a significant decrease in SPV and SPV_{down} comparing these values before vs. after the first fluid bolus. There was a significant increase in pulmonary artery diastolic pressures and PAOP while SPV and SPV_{down} decreased in response to the second fluid bolus, while no significant differences were detected in any of these responses to the third fluid bolus.

Only 4 out of the 19 patients met the protocol to receive a third bolus of 250 mL of fluid (total 750 mL). The SVs of these four patients at the 4 time points were: 55/63/68/63; 42/55/69/73; 33/40/47/48; and 35/53/60/63. Only the first of these patients demonstrated a decrease in the SV in response to the third fluid bolus.

The 36 cases of fluid boluses were characterized as RES (n=17) (SV increased by 10% or more) or nRES (n=19) (SV increased by less than 10%). Variables relating to intravascular fluid volume that were assessed in our study, divided into RES versus nRES, are summarized in Table 3. PAOP values were significantly lower in patients who responded to fluid boluses (p=0.0085) compared with those who did not. Similarly SPV and SPV_{down} values were significantly greater in

TABLE 1
Demographic Data of 19 Patients

Age (years)	63 ± 9
Weight (kg)	83 ± 15
Height (cm)	172 ± 9
Number of vascular grafts	median 3 (range 2–5)
History of hypertension	8/19
History of diabetes mellitus	10/19
History of chronic renal insufficiency	1/19

Mean ± SD except where noted

TABLE 2
Hemodynamic Data Summary

	Baseline (n = 19)	250 mL (n = 19)	500 mL (n = 13)	750 mL (n = 4)
HR BPM	63 ± 12	62 ± 12	62 ± 11	64 ± 7
MAP mm Hg	74 ± 10	79 ± 12	83 ± 12	85 ± 11
Systolic PAP mm Hg	28 ± 8**	32 ± 9	32 ± 7	32 ± 6
Diastolic PAP mm Hg	12 ± 6**	15 ± 6 ⁺⁺	15 ± 5	20 ± 6
PAOP mm Hg	10 ± 5**	14 ± 7 ⁺⁺	15 ± 4	20 ± 9
CO L/min	4.2 ± 1.8**	4.8 ± 1.9	5.1 ± 2.1	3.9 ± 0.7
SV mL	64 ± 18**	77 ± 22	81 ± 21	62 ± 10
LVEDA cm ²	17.3 ± 6.9	18.6 ± 6.5	20.2 ± 7.1	21.0 ± 6.0
SPV mm Hg	7.2 ± 4.3**	5.2 ± 2.9 ⁺	4.9 ± 2.6	3.3 ± 1.3
SPV _{up} mm Hg	2.6 ± 1.4	2.6 ± 0.9	2.9 ± 1.0	2.2 ± 1.0
SPV _{down} mm Hg	4.6 ± 4.1**	2.6 ± 3.0 ⁺	2.1 ± 2.5	1.1 ± 1.1

Table columns represent cumulative volume of fluid boluses.

For abbreviations — see glossary

* p<0.05 after first fluid bolus

** p<0.01 after first fluid bolus

+ p<0.05 after second fluid bolus

++ p<0.01 after second fluid bolus

the RES group (p<0.05). No significant difference between groups was observed with regard to LVEDA or SPV_{up} values. An initial pulmonary capillary wedge pressure value of less than 10 mm Hg was the optimal predictor of responders with a sensitivity of 68% and a specificity of 79%. Although SPV and SPV_{down} values (as a continuous variable) were predictive of likelihood of response to fluid challenge, when comparing RES versus nRES, no appropriate threshold values of either variable could be determined to accurately predict the response to a fluid bolus.

Discussion

Recent studies suggest that occult hypovolemia and hypoperfusion in the perioperative setting may be an avoidable cause of postoperative morbidity (7–13). These studies all had the same overall goal of avoiding occult hypoperfusion. Some of the investigators employed a protocol involving the administration only of fluids (7–9), whereas others employed both fluids and inotropic agents (10–13).

There is no easy way to accurately and quickly measure and monitor changes in intravascular volume. One limitation of our study is that we assumed the PAC to be a “gold standard” for guiding fluid therapy. Clearly, PAOP and PAD are imperfect measures of intravascular volume status. Compensatory arterial and venoconstriction can result in cardiac filling pressures that appear normal despite significant hypovolemia (16, 26).

TABLE 3
Presumptive Indicators of Patient Optimization

	RES (n = 17)	nRES (n = 19)	p value
PCWP mm Hg	9 ± 4	13 ± 4	0.0085
LVEDA cm ²	16.7 ± 5.8	19.0 ± 6.8	NS
SPV mm Hg	8.2 ± 3.9	5.3 ± 2.6	0.0179
SPV _{up} mm Hg	2.8 ± 1.5	2.6 ± 1.0	NS
SPV _{down} mm Hg	5.4 ± 3.9	2.7 ± 2.8	0.0246

Since each fluid bolus was considered a separate case and assumed statistical independence, all boluses are presented as aggregate data.

p values of differences between RES and nRES groups; NS = not significant.

Use of SPV or SPV_{down} values could theoretically be used to enhance stroke volume and cardiac performance. Our data demonstrate that changes occurred in SPV and SPV_{down} values in relation to the intravascular volume status prior to a fluid bolus. In contrast, we found no relationship between echocardiographic-derived parameters (e.g., left ventricular end diastolic area) and intravascular volume status. SPV parameters, however, were poorer predictors of the need for additional fluid than were measurements derived from the PAC. Although esophageal Doppler-guided fluid administration has suggested improved outcome in several clinical studies (7–9), it is not known whether such measurements would better correlate with directly measured SV.

Another limitation of our study is that we measured SPV parameters off line. To be clinically useful, however, a manufacturer of monitoring equipment would need to create an algorithm that provides for real time assessments of SPV and SPV_{down}. This yet to be determined algorithm would ideally detect pulmonary airway pressures and tidal volumes so as to most accurately assess SPV parameters.

Patients excluded from participating in the study, e.g., those younger than 18 years old, and patients with a left ventricular ejection fraction less than 30% or intracardiac shunts, represent another limitation to our study. Yet most patients undergoing cardiac surgery are older than 18 years, do not have intracardiac shunts, and have a left ventricular ejection fraction greater than 30%. Hence, exclusion of these patients does not significantly limit our ability to generalize our results to most adult patients undergoing cardiac surgery.

Summary

In summary, we demonstrated a significant difference in some SPV parameters in patients in whom SV could be increased by the relatively rapid administration of additional fluid. Although significant differences were observed, no threshold values of these SPV parameters could reliably predict, in patients undergoing elective cardiac surgery, the amount of the additional volume to be administered. PAC-derived values best predicted the response to a fluid bolus.

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