

Comparing Stroke Volume Variation with Central Venous Pressure Protocol for Fluid Optimization in Patients undergoing Endovascular Aortic Repair: a Randomized Trial

Lampai Polsena, Sirirat Tribuddharat, Thepakorn Sathitkarnmanee, Pathawat Plengpanich, Suparit Silarat, Kriangsak Ngamsaengsirirup, Sarinya Chanthawong, Suangsuda Khanchai

Department of Anesthesiology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand

Abstract

Objectives: To compare postoperative arterial lactate level, as well as hemodynamic parameters and clinical outcomes, between patients undergoing endovascular aortic repair (EVAR) who were managed with either stroke volume variation (SVV) or central venous pressure (CVP) protocol for fluid optimization.

Methods: This is a prospective double-blinded randomized trial. Sixty adult patients underwent elective EVAR, both abdominal and thoracic surgeries in two cardiac centers (Queen Sirikit Heart Center of the Northeast and Srinagarind Hospital, Khon Kaen University). All patients were randomized into two groups with 30 patients each. Intraoperatively, fluid optimization in group CVP was managed using the CVP guided protocol, while the SVV protocol was used for group SVV.

Results: Group SVV had a lower arterial lactate level immediately after surgery (1.2 ± 0.6 vs

1.8 ± 1.0 mg/dL, $P=0.044$). Over the first 48 h postoperatively, there were no significant differences in lactate or creatinine between groups. There was an inverse correlation between SVV and the cardiac index (CI) and between CVP and CI. No correlation was found between SVV and CVP.

Conclusion: Use of the SVV over against the CVP guidance for fluid optimization in patients undergoing EVAR results in a lower arterial lactate level. SVV has a good inverse correlation with CI which confirms that SVV is a useful guide for fluid therapy while CVP has no correlation with SVV and shows a negative instead of positive correlation with CI, and thus should not be used as a guide for fluid optimization.

Keywords: central venous pressure, endovascular aortic repair, fluid therapy, goal-directed therapy, stroke volume variation

Introduction

Perioperative fluid optimization improves clinical outcomes in high-risk patients undergoing major surgeries.¹ Central venous pressure (CVP) has been used as a guide for fluid therapy since 1959² and was still recommended as a goal-equivalent to mixed venous oxygen saturation, in the initial fluid resuscitation of patients with severe sepsis-in the 2004 to 2016 Surviving Sepsis Campaign Guidelines.³⁻⁶ CVP and delta CVP were demonstrated to have the ability to predict fluid responsiveness in patients experiencing hypovolemic shock.⁷ Recent systematic reviews, however, indicated that CVP and delta CVP not only had a poor relationship with the cardiac index (CI) but were also unable to predict fluid responsiveness.^{8,9} By contrast, stroke volume variation (SVV) has been validated as a useful diagnostic tool for predicting fluid responsiveness in various settings including in the intensive care unit and operating room.¹⁰ Pulse pressure variation (PPV) has a strong correlation with SVV and both PPV and SVV are recommended as dynamic parameters for predicting fluid responsiveness.¹¹ Although the SVV derived from the FloTrac/EV1000 system has a higher cost than the PPV derived from standard monitoring, it delivers more valuable parameters such as CI and systemic vascular resistance index (SVRI), which can be extremely useful in the management of complicated cases with derangement of myocardium contractility and afterload.

Endovascular aortic repair (EVAR)-a minimally invasive surgery-has been a popular alternative to the conventional open aortic

aneurysm repair. The goal of anesthesia is to maintain hemodynamic stability and provide adequate perfusion to vital organs including brain, heart, spinal cord, splanchnic vessels, and especially the kidneys to prevent renal impairment.¹² To date, there has been no randomized trial comparing SVV and CVP as a goal for fluid responsiveness in this type of operation. The objectives of the study were to compare postoperative arterial lactate level, hemodynamic parameters, and clinical outcomes 48 h in patients undergoing EVAR managed with the SVV vs CVP protocol; and to assess the correlations between SVV and CI, CVP and CI, and SVV and CVP.

Materials and methods

This study is reported according to the CONSORT (Consolidated Standards of Reporting Trials) guidelines. This was a prospective, randomized trial, approved by the Khon Kaen University Human Ethics Committee in Human Research (HE611321) and registered at Clinical-Trials.gov (NCT03218540). All patients gave written, informed consent before being recruited into the study. Based on data from a similar study¹³, a sample size of 30 per group was required to detect a 30% difference in lactate level, with a 20% dropout rate, for a two-sided test with a type I error of 5% and a power of 80%.

The study was conducted between August and December 2018 at two cardiac centers (Queen Sirikit Heart Center of the Northeast and Srinagarind Hospital, Khon Kaen University). We included patients undergoing elective EVAR,

both abdominal and thoracic; between 40-80 years of age; having a New York Heart Association (NYHA) or American society of Anesthesiology (ASA) classification between I and III; and having a BMI between 18-24 kg/m². We excluded patients undergoing redo-surgery; or with any congenital heart disease, cardiomyopathy, rheumatic heart disease, significant arrhythmias, cardiopulmonary dysfunction, or significant liver and kidney disease.

The patients were randomly allocated into two groups (CVP and SVV). Randomization was achieved using computer generated assignments with each being placed in a sealed envelope. Both groups received standard general anesthesia and peri-operative care provided by anesthesiologists with expertise in vascular anesthesia. Standard monitoring consists of electrocardiogram, non-invasive blood pressure (NIBP), pulse oximetry, end-tidal carbon dioxide (ETCO₂), and temperature. The internal jugular vein was cannulated for CVP monitoring. The radial artery was cannulated for invasive blood pressure (IBP) monitoring and connected to a FloTrac transducer with an EV1000 monitor (Edwards Lifesciences, Irvine, CA, USA) to monitor continuous SVV, CI, and SVRI. The screen of the EV1000 monitor in the CVP group was covered with an opaque cloth so that the attending anesthesiologist could not see the information on the screen.

Induction and maintenance of anesthesia

All patients were allowed to drink clear fluid as needed, up to 2 h prior to surgery. Upon arrival at the operating theater, a baseline fluid administration of balance salt solution (2 mL/

kg/h) was started and fentanyl (1-3 µg/kg) given as premedication. Anesthesia was induced with propofol (1-2 mg/kg), etomidate (0.2-0.3 mg/kg) or thiopental (3-5 mg/kg). Intubation was facilitated with atracurium (0.6-0.8 mg/kg) or cis-atracurium (0.2 mg/kg). Anesthesia was maintained with sevoflurane or desflurane at 1 minimum alveolar concentration in oxygen and air. A fentanyl bolus of 1-2 µg/kg was administered when required. Ventilation was controlled using volume-control with PEEP 5 cmH₂O, tidal volume 8 mL/kg, and a ventilator frequency of between 12 and 14 bpm to achieve an ETCO₂ between 30 and 35 mmHg.

For the treatment of anemia, a strict transfusion protocol was followed. Hematocrit was evaluated on an hourly basis. The threshold of hematocrit for blood transfusion was 26% in patients under 65 and 28% in patients over 65 years of age. Patients were kept normothermic using upper forced-air warming (Bair Hugger, Augustine Medical Inc., Eden Prairie, MN, USA).

Fluid therapy protocol

In the CVP group, the goals were (a) a CVP between 8 and 12 mmHg, (b) a mean arterial pressure (MAP) of ≥65 mm Hg, and (c) a urine output of ≥0.5 mL/kg/h. These goals were targeted with the use of 250 mL boluses of crystalloid or colloid over 2-3 min (repeated as necessary), and the use of inotropic and vasopressor agents at the discretion of the attending anesthesiologists. In the SVV group, a bolus of 250 mL of crystalloid or colloid over 2-3 min (repeated as necessary) was administered if SVV was >13%. An inotropic drug was given if the CI was <2.5 L/min/m² when the SVV was

$\leq 13\%$. A vasoactive drug was administered to maintain the SVRI between 2,000 and 2,400 dynes-sec/cm⁻⁵/m² when the SVV was $\leq 13\%$.

After surgery, the patients were extubated when they met the criteria of extubation: arterial blood gas analysis of pH 7.35-7.45, PaO₂ >100 mmHg (with FiO₂ of <50%), and lactate <2 mmol/L. All of the patients were transferred to the ICU, where patient data including any morbidity such as myocardial ischemia, acute kidney injury, or stroke, were recorded at 0, 12, 24, and 48 h, postoperatively. Any derangement was promptly corrected. The primary outcome was arterial lactate at the end of surgery. The secondary outcomes were intraoperative MAP, serum lactate and creatinine as well as complications over 48 h. We also aimed to identify correlations of SVV and CI, CVP and CI, and SVV and CVP. Data were analyzed on an intention-to-treat basis.

Statistical analyses

The continuous data were presented as mean $\pm$ SD or median (interquartile range) and tested with the unpaired t-test or Mann-Whitney U test. The categorical data were presented as numbers (%) and evaluated using the χ^2 of Fisher's exact test. Changes in the hemodynamic variables (MAP, lactate, and creatinine levels) over time were compared using an ANOVA on repeated measurements. Correlation between two variables was computed as the Pearson coefficient *r*. A *P* <0.05 was considered statistically significant. All calculations were performed using SPSS for Windows version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

Sixty patients were recruited with 30 patients in each group. The study flow is presented in Figure 1. The two groups were comparable with respect to the demographic and clinical data, including baseline hemodynamic parameters (Table 1). Throughout the surgical procedure, the SVV group experienced slightly greater blood loss compared to the CVP group. However, both groups exhibited similar patterns in crystalloid and colloid infusion, fresh-frozen plasma (FFP) transfusion, and urine output. More patients in the SVV group received red blood cell (RBC) transfusion. The administration of vasoactive/vasodilator agents was consistent between the two groups, as depicted in Table 2. Additionally, the intraoperative mean arterial pressures (MAPs) demonstrated comparable trends in both groups, as illustrated in Figure 2.

Immediately after surgery, group SVV had a significantly lower lactate level. The creatinine, hemodynamic parameters, urine output, and hemoglobin were comparable for both groups (Table 3). In the first 48 h postoperatively, there were no significant differences in lactate and creatinine between the groups (Figure 3 and 4). No serious complications were found in either group. There was a significant inverse correlation between SVV and the CI (Figure 5). Instead of a positive correlation, there was a significant negative correlation between CVP and the CI (Figure 6). No correlation was found between SVV and CVP (Figure 7).

Table 1 Patients demographics and baseline hemodynamic parameters

Characteristics	Group SVV (n=30)	Group CVP (n=30)	P-value
Age (yr)	67.1±13.4	64.7±13.8	0.595
Sex			0.781
Male	20 (66.7)	21 (70.0)	
Female	10 (33.3)	9 (30.0)	
Body mass index (kg/m ²)	21.5±2.6	21.7±4.8	0.855
ASA classification			0.791
I/II	0/11 (36.7)	1 (3.3)/11 (36.7)	
III	19 (63.3)	18 (60.0)	
NYHA classification			0.795
I/II	0/17 (56.7)	1 (3.3)/15 (50.0)	
III	13 (43.3)	14 (46.7)	
Ejection fraction			0.718
< 40%	5 (16.7)	4 (13.3)	
40-60%	25 (83.3)	26 (86.7)	
Preoperative comorbidities			0.987
Hypertension	27 (90.0)	26 (86.7)	
Diabetes mellitus	7 (23.3)	6 (20.0)	
Myocardial infarction	6 (20.0)	7 (23.3)	
Dyslipidemia	8 (26.7)	9 (30.0)	
Atrial fibrillation	2 (6.7)	1 (3.3)	
Congestive heart failure	5 (16.7)	4 (13.3)	
Preoperative creatinine value (mg/dL)	0.95±0.23	0.95±0.29	>0.999
Type of operation			0.177
Thoracic	13 (43.3)	7 (23.3)	
Abdominal	15 (50.0)	22 (73.4)	
Combined	2 (6.7)	1 (3.3)	
Operative time (min)	165.8±68.6	152.4±61.8	0.530
Baseline of monitoring			
Mean arterial pressure (mmHg)	74.5±18.6	72.9±9.2	0.742
Cardiac index (L/min/m ²)	2.6±0.8	2.6±0.6	0.994
Stroke volume index (mL/min/m ²)	36.8±9.4	39.5±14.8	0.530
Stroke volume variation (%)	9.8±4.5	9.9±3.7	0.850
SVRI (dynes-sec/cm ⁻⁵ /m ²)	2,218.4±896.3	2,614.2±864.7	0.180
Central venous pressure (mmHg)	7.8±3.6	9.3±3.9	0.230
Hemoglobin (g/dL)	12.2±1.9	11.5±1.4	0.164
Hematocrit (%)	36.9±5.7	34.4±4.1	0.124
Lactate (mmol/L)	0.9±0.5	0.7±0.3	0.312

Data are presented as number (%) or mean±SD. ASA = American Society of Anesthesiologists, NYHA = New York Heart Association, SVRI = systemic vascular resistance index

Table 2 Intraoperative clinical data

	Group SVV (n=30)	Group CVP (n=30)	P-value
Blood loss (mL)	400 (165-550)	110 (50-500)	0.019*
Fluid administration			
Crystalloid (mL/h)	633 (580-1000)	800 (667-900)	0.892
Colloid (mL/h)	225 (105-500)	167 (150-420)	0.724
Number who received RBC (units)	11 (36.7)	3 (10.0)	0.007
Number who received FFP	1 (3.3)	0	0.486
Vasoactive support (n)			
Ephedrine	13 (43.3)	7 (23.3)	>0.999
Dopamine	1 (3.3)	2 (6.7)	0.554
Vasodilators (n)			
Nitroglycerine	9 (30.0)	5 (16.7)	0.222
Diltiazem	3 (10.0)	2 (6.7)	0.640
Urine output (mL/h)	54 (38-170)	70 (44-112)	0.845
Furosemide (mg)	6.0±2.0	6.0±1.3	0.995
Contrast media (mL)	104.7±44.9	80.1±30.6	0.055

Data are presented as number (%), mean±SD or number, or median (interquartile range). RBC = red blood cell, FFP = fresh frozen plasma

Table 3 Immediate post-operative primary and secondary outcomes on admission to ICU

	Group SVV (n=30)	Group CVP (n=30)	P-value
Lactate level (mg/dL)	1.2±0.6	1.8±1.0	0.044*
Creatinine level (mg/dL)	1.0±0.4	1.2±0.7	0.290
Mean arterial pressure (mmHg)	74.5±18.6	72.9±9.2	0.742
Cardiac index (L/min/m ²)	2.6±0.8	2.65±1.1	0.994
Stroke volume variation (%)	9.6±3.6	9.37±4.8	0.850
Central venous pressure (mmHg)	7.8±3.6	9.3±3.9	0.230
Urine output (mL/h)	100.3±79.3	106.7±116.3	0.845
Hemoglobin (g/dL)	10.6±0.8	10.1±1.4	0.184
Hematocrit (%)	31.9±2.2	30.4±4.0	0.158

Data are presented as mean±SD.

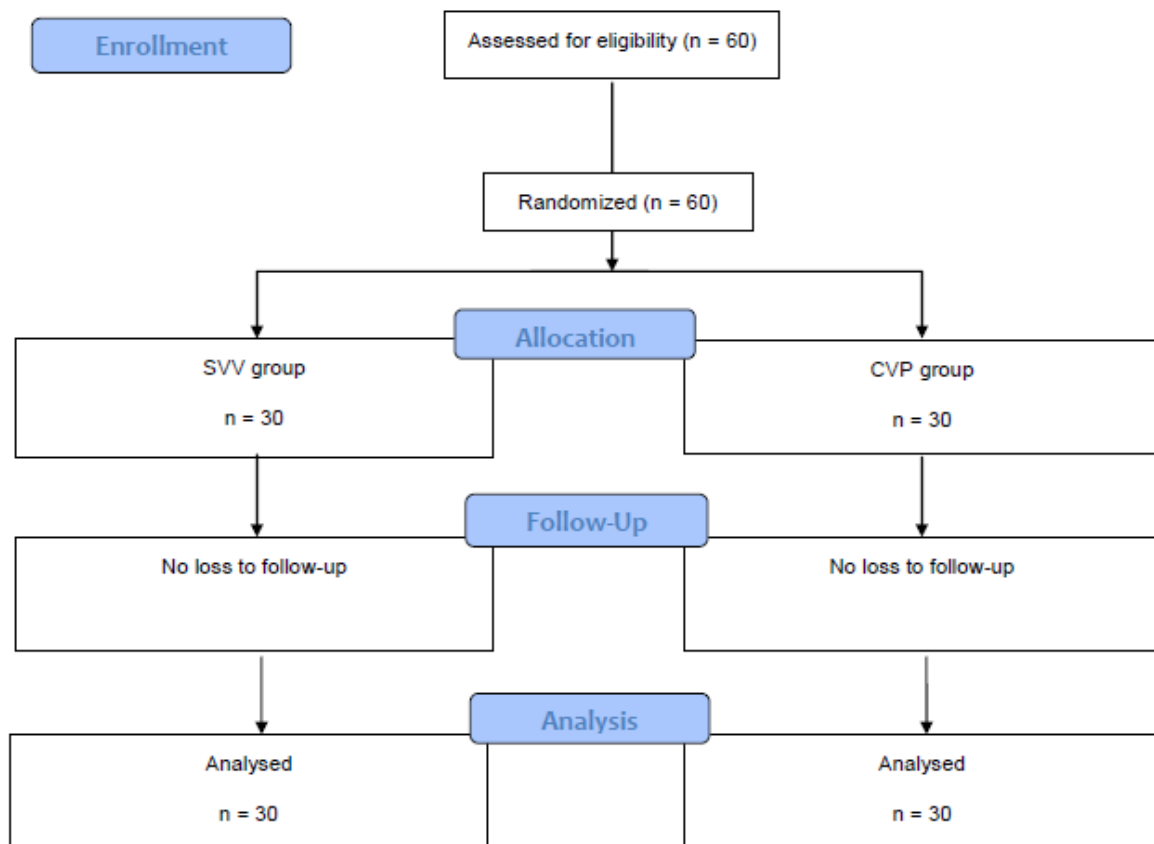


Figure 1 CONSORT diagram

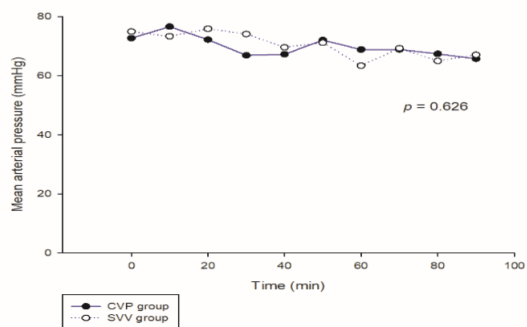


Figure 2 Intra-operative mean arterial blood pressure

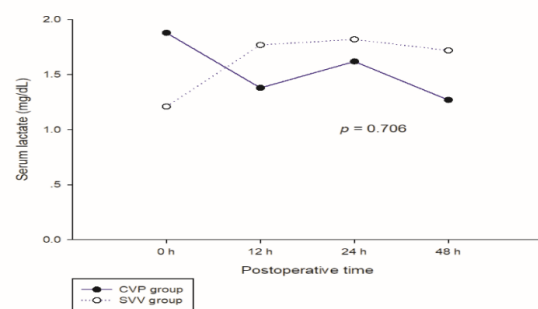


Figure 3 Serum lactate levels during 48-hour post-operatively

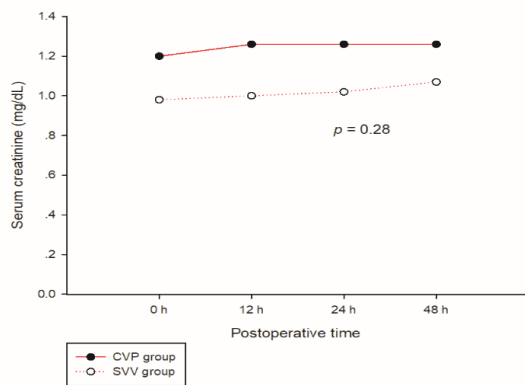


Figure 4 Serum creatinine level during 48-hour post-operatively

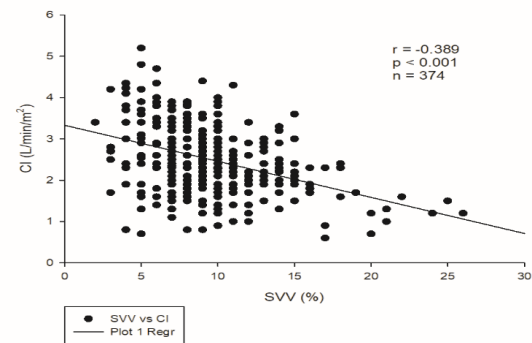


Figure 5 Correlation between SVV and CI

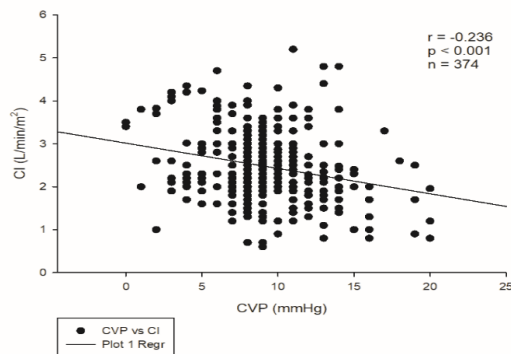


Figure 6 Correlation between CVP and CI

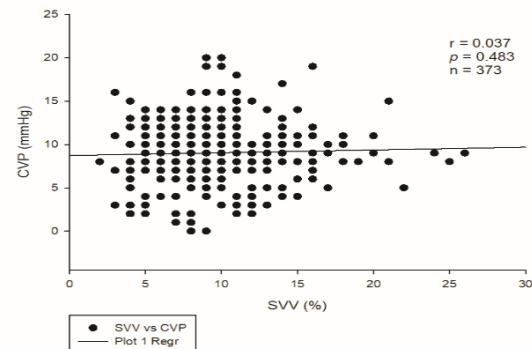


Figure 7 Correlation between CVP and SVV

Discussion

Since EVAR is a 4- to 12-hour procedure with potential for bleeding and acute kidney injury (AKI) (because of frequent contrast load)¹², optimization of the intravascular volume is crucial to positive outcomes. Until recently, CVP has been recommended as a guide for fluid administration²⁻⁶ but new researches have demonstrated it is un dependable.⁷⁻⁹ By contrast, early goal-directed therapy (EGDT)-using dynamic parameters such as SVV and PPV-has been widely validated and accepted as accurate guides

for fluid optimization resulting in improved clinical outcomes.^{10,11,13-16}

The current study revealed that patients managed using the SVV protocol had a lower arterial lactate level-reflecting better tissue perfusion and oxygenation at the end of surgery-compared with the CVP protocol. This finding agrees with previous studies.^{13,15} Even though the patients in group SVV had more bleeding and needed transfusion more often, they still had a lower lactate level; indicating that the SVV protocol facilitates prompt fluid and blood replacement in these patients, and

supports anesthetic goals in EVAR.¹²

In current study, the SVV protocol failed to demonstrate better results vis-à-vis secondary outcomes (lactate and creatinine over 48 h postoperatively) compared to the CVP protocol in contradistinction to previous studies.^{13,17,18} The rationale is that the sample size for this study was determined based on the primary outcome, potentially rendering it inappropriate for the secondary outcomes. The most important factor associating with the improved outcomes in EVAR was the expertise of the attending anesthesiologist in vascular surgical procedures.¹⁹ In the current study, competence in vascular anesthesia plus vigilant staff achieved satisfactory secondary outcomes (MAP, serum lactate and creatinine over 48 h) without serious complications in group CVP compared to group SVV.

The results of the correlation analysis show that SVV has a negative correlation with the CI, confirming the usefulness of SVV as a tool for fluid optimization. Meanwhile, the CVP-apart from showing no correlation with SVV-had a significant negative correlation with the CI which can result in inappropriate fluid management. These findings confirm that CVP is not appropriate as a guide for fluid administration.^{8,9,20}

Limitations

Due to the limited sample size, the current study could not parse the low incidence complications such as pneumonia, AKI, or acute congestive cardiac failure; thus, further study with a larger sample is recommended.

Conclusion

The SVV guidance for fluid optimization in patients undergoing EVAR results in lower arterial lactate levels at the end of surgery compared to CVP. Expertise in vascular anesthesia plus the vigilance of the attending anesthesiologist can help to achieve satisfactory secondary outcomes over the first 48 h post surgery (serial lactate and creatinine). The SVV has a good inverse correlation with the CI confirming SVV as a useful guide for fluid therapy. In summary, CVP had a negative correlation with the CI and no correlation with SVV, so CVP should not be used as a guide for fluid optimization. Importantly, there were no serious complications in either group SVV or group CVP.

Potential conflicts of interest

None declared.

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