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## **Stroke volume versus stroke volume variations as guidance for fluid therapy in major abdominal surgery**

**Ahmed Mohamed Elsayed Aly**

Assistant Lecturer of Anaesthesia and Surgical Intensive Care, Faculty of Medicine, Alexandria University, Alexandria, Egypt

\*Corresponding author email: [a\\_elsayed142@medalex.edu.eg](mailto:a_elsayed142@medalex.edu.eg)

**Prof. Dr. Mohamed Mohamed El Nakeeb**

Professor of Anaesthesia and Surgical Intensive Care, Faculty of Medicine, Alexandria University, Alexandria, Egypt

**Prof. Dr. Hussein Mohamed Agameya**

Professor of Anaesthesia and Surgical Intensive Care, Faculty of Medicine, Alexandria University, Alexandria, Egypt

**Dr. Moutaz Abdel Mohsen Ghandour**

Lecturer in Anaesthesia and Surgical Intensive Care, Faculty of Medicine, Alexandria University, Alexandria, Egypt

**Abstract**--Background: The aim of the present study was for comparison of stroke volume versus stroke volume variations as guidance for fluid management under guide directions of electrical cardiometry, during major abdominal surgeries. The primary outcome was to compare between two fluid infusion protocols, regarding the haemodynamic changes, whereas secondary outcomes were to evaluate the impact of each protocol on extravascular lung water and oxygenation changes in the post-operative periods, study the effect of each of the adopted method on postoperative complications, incidence of acute kidney injury and intensive care unit staying duration. Settings and Design: This study was a prospective randomized controlled clinical trial. Methods: The study was carried out on 60 patients scheduled for major abdominal surgery. 30 patients, whose intraoperative fluid administration was managed by stroke volume optimization, were compared with 30 patients who received intraoperative fluid therapy guided by stroke volume variation optimization. Results: There was no difference regarding haemodynamic changes in terms of mean heart rate, mean blood pressure, stroke volume, stroke volume variation, and cardiac index.

The first group showed a significant incidence of postoperative pulmonary edema which affected oxygenation process till 24 hours postoperatively. Group II had fewer incidences of complications, acute kidney injury which was reflected upon less intensive care unit stay duration. Conclusion: Application of GDT guided by SVV changes detected by EC achieved more successful aims of optimization of fluid therapy and avoiding complications related to whether hyper or hypovolemia.

**Keywords**--goal directed fluid therapy, stroke volume optimization, stroke volume variation optimization, electrical cardiometry.

**Abbreviations:** GDT: goal-directed therapy; SV: stroke volume; CO: cardiac output; RAP: right atrial pressure; EC: electrical cardiometry.

## Introduction

Yearly, more than 310 million surgical candidates get through major surgery procedures globally, that involve the administration of intravenous fluids.<sup>(1)</sup> In order to compensate for preoperative prohibition of oral intake, anesthesia-induced vasodilation, haemorrhage, and fluid cumulation in extravascular tissues, as well as to improve tissue oxygen allocation and maintain urine output, health-care protocols have traditionally advised for large amounts of intravenous fluids administration perioperatively.<sup>(2)</sup> Contrary, fluid restriction was advised to avoid volume overload, despite the increased risk of hypotension and decreased perfusion in the kidney and other vital organs.<sup>(3)</sup> As a result, the most effective intravenous-fluid regimen is still undefined.<sup>(4)</sup>

The perioperative fluid therapy has recently concentrated on three strategies, fixed high-, low-volume regimens, and individualized optimization strategies, so-called goal-directed therapy (GDT), assisted by routine and advanced cardiovascular monitoring.<sup>(4)</sup> Goal-directed fluid therapy is relayed on a strategic thinking in which perioperative liquids directions ought to augment the oxygen allocation through well-established goals for the therapy, relied on flow-observed measured data. To clarify, an individualized approach has been introduced with aim of optimization of flow-related variables, such as the stroke volume (SV) of the heart, by fluid challenges.<sup>(4)</sup> Standard cardiovascular monitoring of the candidates for surgical procedures involves continuous tracing of blood pressure (invasive or non-invasive) and heart rate. However, blood pressure is not governed by the blood volume intravascularly solely, but by anaesthetic technique and surgical insult as well, turning the detection of hypovolaemia more challenging.<sup>(5)</sup> Though routinely accepted to pilot fluid therapy, blood pressures readings besides heart rate are insufficient indicators of central blood volume.<sup>(5)</sup> Thus, the assessment of blood pressure and heart rate is not sufficient to detect mild hypovolaemia which can lead to compromised tissue perfusion, especially in the splanchnic circulation.<sup>(5)</sup>

The ability to evaluate intravascular volume is a fundamental part of perioperative care and the management of perioperative hemodynamic instability. Inadequate

intravascular volume can result in a decline in oxygen delivery to tissues, while fluid overburden can result in the occurrence of oedema and organ dysfunction, including respiratory failure.<sup>(6)</sup> The concepts euvolemia and fluid responsiveness are the main concepts relevant to management of fluid status in perioperative and critical care.<sup>(7)</sup> Fluid responsiveness is a strategically concept put to identify patients who will respond with a positive reaction in a physiologic parameter upon fluid administration. surprisingly, a universal fluid responsiveness definition has been not conceived.<sup>(7)</sup> A provisional parameter of a certain size to a standardized volume of a certain type of fluid administered within a certain amount of time and measured within a certain interval.<sup>(7)</sup>

Otto Frank and Ernest Starling explained enhanced ventricular contraction with augmented stroke volume when the ventricular wall was stretched before contraction because of increased venous return. When stroke volume is set off against the sarcomere length of the cardiac muscle, the Frank-Starling curve is generated.<sup>(8)</sup> When cardiac output (CO), the product of stroke volume and heart rate, is put against right atrial pressure (RAP) as a reflection of ventricular preload, the cardiac function curve is constructed. A patient's response upon fluid loading can be explained using the cardiac function curve.<sup>(8)</sup> From the Frank-Starling law of the heart, a rise in preload (infusion of intravenous fluids) will significantly enhance stroke volume only if both major cardiac chambers are on the ascending portion of the curve. If one or both ventricles lie on the flat sector, then the patient will be managed as a non-responder, which means, cardiac output will not rise significantly in response to volume expansion.<sup>(9)</sup>

### **Practical apply of goal-directed fluid therapy and clinical results**

Goal-directed therapy (GDT) has been linked with optimistic clinical results as reported by clinical trials. It seems that the adoption of goal-directed therapy (GDT) for prudence hemodynamic intervention have positive impact on the mortality and surgical complications.<sup>(9)</sup> Although it was found that subgroup analysis of the data suggested non-significant difference in mortality either utilizing a pulmonary arterial floating catheterization, above-normal resuscitation aims, or algorithms using cardiac index or oxygen distribution as targets in GDT, and the incorporated use of fluids and inotropes or fluids solely, still the answer for the optimized strategy in terms of morbidity and maximization patient's outcome. Thus, it has been presumed that the implication of a preemptive strategy as a broad title of hemodynamic monitoring along with GDT can minimize perioperative mortality and morbidity.<sup>(10)</sup> GDT ought not to be focused on solely, illustratively; perioperative hemodynamic inclinations and the fluid requirements of the patient along with management plan should always be considered during their course of hospital stay.<sup>(10)</sup> The concept beneath GDT strategy aiming for optimization of tissue oxygen allocation by reaching a balanced hemodynamic status with the fluid therapy with individualized dosage. For that GDT research, a paramount insight is that an individualized GDT algorithm implies an optimization of blood flowing-measuring tools.<sup>(10)</sup>

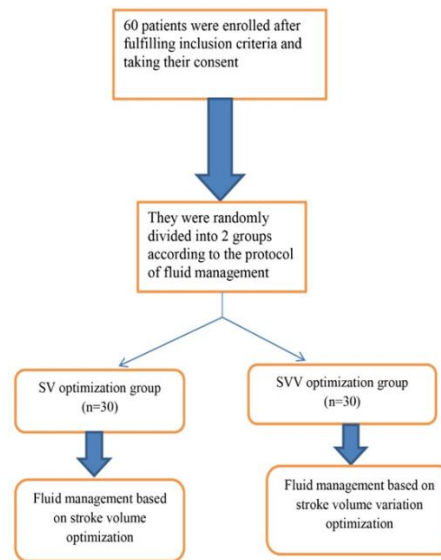
### **Electrical cardiometry**

EC is a recent monitoring technique for measuring continuous cardiac output non-invasively. It is relayed on continuous assessment of transthoracic electrical bio-impedance (TEB).<sup>(11)</sup> EC is able to isolate the changes in impedance created by the circulation, partly caused by the change in orientation of the erythrocytes during the cardiac cycle. 2 electrodes are placed on the left base of the neck and 2 on the left inferior side of the thorax at the level of the xiphoid process. The inter-electrode gap of the lower electrodes should be 15 cm in adults. The electrodes are connected to the ICON<sup>®</sup> monitor. The device derives stroke volume, heart rate and CO from the impedance values.<sup>(12)</sup>

It differs from the traditional bio- impedance or ICG methods which rely on the assumption of periodical volumetric changes in the aorta to determine SV and cardiac output (CO). The primary aim of this study was to compare between two fluid infusion protocols, regarding the haemodynamic changes, in addition, the secondary aim was to evaluate the impact of each protocol on extravascular lung water, oxygenation changes in postoperative period, complications rate, incidence of acute kidney injury, and estimated period of postoperative intensive care course.

### **Patients and Methods**

After complete informed consent and approval from the ethical committee of Alexandria Faculty of Medicine, 60 patients were subjected to complete history taking, physical examination, and routine laboratory investigations at Alexandria Main University Hospital. Inclusion criteria were American Society of Anesthesiologist (ASA) status II-III, who were scheduled for elective major abdominal surgery (defined as procedures expected to last more than 2 hours, or with an anticipated blood loss greater than 500 mL), and a planned postoperative ICU admission while exclusion criteria were patient refusal, perioperative haemodynamic instability, emergency abdominal operations, Cardiac arrhythmia, and distant metastatic malignancy.



Flow chart of patients

Candidates were assorted at random, by closed envelope process, into 2 groups: group I: stroke volume optimization group,  $n = 30$ : they received a fluid therapy based on stroke volume response to fluid boluses as shown in chart (1). Group II: stroke volume variation optimization group,  $n = 30$ : they received fluid therapy according to the stroke volume variation as shown in chart (2). In both groups replacement of blood losses with packed red blood cells if the blood haemoglobin level were to be lower than 7 g/dL.

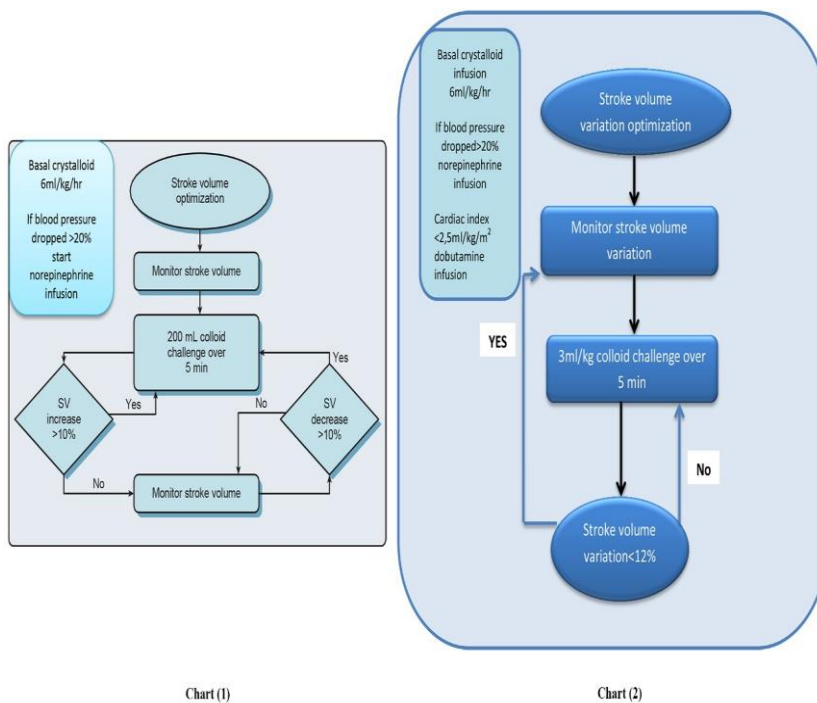


Chart (1)

Chart (2)

In both groups, EC device, The ICON™ monitor, manufactured by Cardiotronc, Inc., was attached to the candidate by 4 ECG electrodes, 2 of them were attached to the left side of the neck and the other 2 electrodes were attached to the left aspect of the thoracic wall intersecting the mid-axillary line at the plane of xiphisternum. The variables studied were sex, age, body mass index (BMI), type and duration of the interventions, hemodynamic parameters in terms of Invasive MAP, heart rate, stroke volume, stroke volume variation, and cardiac index. Variables for intra-operative and postoperative organ perfusion included Hb level, central venous oxygen saturation, and serum lactate. Also, total intraoperative infused crystalloid and colloid volume, total dose of vasopressor (noradrenaline) and inotrope (dobutamine), total amount of blood loss and units of intraoperative, and postoperative transfused RBCs were evaluated. Urine output was assessed as well. Postoperatively, lung perfusion indices (hypoxic index and arterial blood gases) and lung ultrasound were investigated. Also, renal perfusion indices (serum creatinine, creatinine clearance, and urine output and serum neutrophil gelatinase-associated lipocalin) were estimated. Time to return of bowel function, ICU, and postoperative complications were recorded.

### **Statistical analysis**

A sample size of 60 patients was calculated using Epi Info 7 Software for the calculated size of sample and based on 39% exposed with outcome, to achieve 80% study power and 95% confidence limit.<sup>(13)</sup> Data were anatomized using IBM SPSS software package version 20.0 for statistical analysis. Qualitative data were expressed as numerical and percentage outcomes. The Kolmogorov-Smirnov test was adopted to establish the normality of distributed data. Quantitative data were expressed as range (minimum and maximum), mean, standard deviation and median. The significance of the gained outcome was stated at five percentage level. Chi-square test was adopted for categorical data, for comparison between different groups), Fisher's Exact or Monte Carlo correction (correction for chi-square when more than twenty percentage of the cells have expected count less than five), McNemar (recognized to anatomize the significance between the several phases), Student t-test (for classically distributed quantitative data, for comparison between two studied groups), Paired t-test (for normally distributed quantitative variables, for comparison between 2 periods), ANOVA with recurrent measures (for classically distributed quantitative data, for comparison between more than 2 durations or phases, and Post Hoc test (Bonferroni adjusted) for pairwise comparisons), Mann Whitney test (for unclassically distributed quantitative data, for comparison between two studied groups).

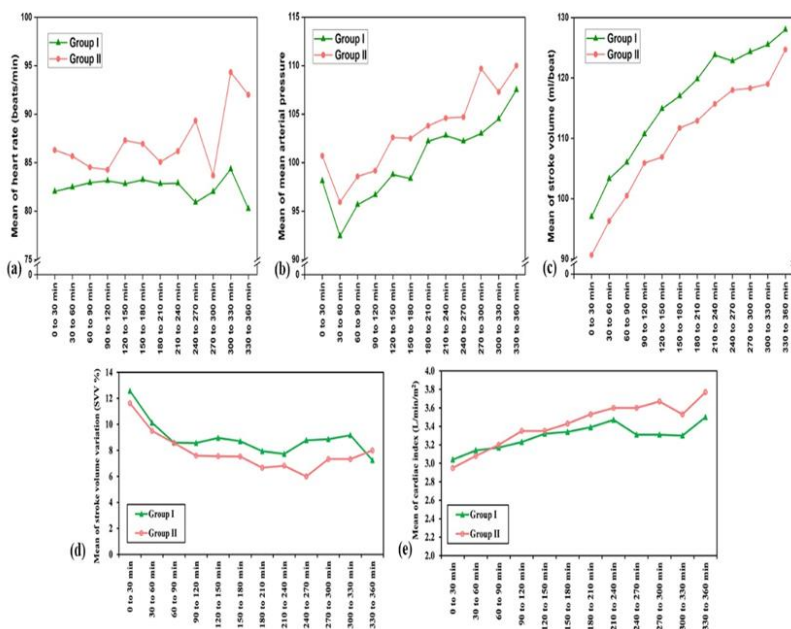
### **Results**

Regarding demographic data (gender, age, and BMI) and operation duration, a statistically considerable divergence was not detected between the two groups as illustrated in table (1).

Table 1  
Demographic data, duration of operation

Demographic data	Group		I Group		II Test Sig.	of p
	(n = 30)		(n = 30)			
	No.	%	No.	%		
Gender						
Male	17	56.7	14	46.7	$\chi^2=$ 0.601	0.438
Female	13	43.3	16	53.3		
Age (years)						
Mean $\pm$ SD.	47.17 $\pm$ 12.33		53.07 $\pm$ 12.06		t= 1.874	0.066
Median (Min. – Max.)	48.50 (19.0 – 77.0)		54.50 (32.0 – 77.0)			
BMI (kg/m <sup>2</sup> )						
Mean $\pm$ SD.	26.13 $\pm$ 3.12		25.60 $\pm$ 2.44		t= 0.738	0.464
Median (Min. – Max.)	26.0 (21.0 – 35.0)		26.0 (22.0 – 35.0)			
Duration of operation (minutes)						
Mean $\pm$ SD.	221.0 $\pm$ 83.18		193.0 $\pm$ 75.44		U= 0.118	0.118
Median (Min. – Max.)	225.0 (120.0 – 360.0)		180.0 (120.0 – 360.0)			

Regarding alternations in haemodynamic results (heart rate and invasive blood pressure monitoring), insignificant differences were recorded between the two groups as shown in figure 1 (a, b). According to the comparison between the two groups in terms of stroke volume, stroke volume variation, and cardiac index, non-significant differences were measured statistically as shown in figure 1(c, d, e).



The difference between the studied groups of patients showed no significant change regarding the haemoglobin levels (Hb), blood loss, and packed red blood units given as shown in table 2. According to the study, amount of intravenous fluids given were differentiated as follows. In terms of crystalloids, there was no significant change. However, the colloid rate of fusion was significantly higher in the first group of the study as demonstrated in table 2. Similarly, the dose of infused drugs (noradrenaline and dobutamine) showed a significant inclination towards the second group (table 2).

Table 2  
Comparison between groups regarding blood loss, total packed RBC, amount of crystalloids and colloids, noradrenaline and dobutamine, and urine output

	Group I	Group II	Test of P	Sig.
Blood loss (ml)	(n = 30)	(n = 30)		
Mean ± SD.	453.33 ± 299.01	507.67 ± 283.67	U=	0.168
Median (Min. – Max.)	365.0 (150.0 – 1240.0)	460.0 (200.0 – 1200.0)	357.000	
Total packed RBC (units)	(n = 4)	(n = 4)		
Mean ± SD.	1.75 ± 0.50	1.75 ± 0.50	t=	1.000
Median (Min. – Max.)	2.0 (1.0 – 2.0)	2.0 (1.0 – 2.0)	0.000	
Amount of crystalloid (ml)	(n = 30)	(n = 30)		
Mean ± SD.	1695.0 ± 652.54	1452.27 ± 535.89	U=	0.141
Median (Min. – Max.)	1612.5(840.0–3240.0)	1555.0(840.0–2700.0)	350.500	
Amount of colloid (ml)	(n = 30)	(n = 30)		
Mean ± SD.	1056.7 ± 323.43	488.33 ± 224.09	U=	<0.001*
Median (Min. – Max.)	1000.0(600.0–1600.0)	500.0 (200.0 – 950.0)	68.000*	
Noradrenaline given (micrograms)	(n = 5)	(n = 5)		
Mean ± SD.	142.80 ± 31.27	188.0 ± 19.24	t=	0.025*
Median (Min. – Max.)	131.0 (105.0 – 180.0)	190.0 (160.0 – 210.0)	2.753*	
Duration (minutes)	(n = 5)	(n = 5)		
Mean ± SD.	23.0 ± 4.47	27.0 ± 4.47	t=	0.195
Median (Min. – Max.)	20.0 (20.0 – 30.0)	30.0 (20.0 – 30.0)	1.414	
Dobutamine given (mg)	(n = 0)	(n = 5)		
Mean ± SD.	–	18.70 ± 3.11	–	–
Median (Min. – Max.)	–	20.0 (15.0 – 22.50)	–	–
Duration (minutes)	(n = 0)	(n = 5)		
Mean ± SD.	–	25.0 ± 6.12	–	–
Median (Min. – Max.)	–	25.0 (15.0 – 30.0)	–	–
Urine output(ml)	(n = 30)	(n = 30)		
Mean ± SD.	84.63 ± 13.59	68.07 ± 12.13	t=	<0.001*
Median (Min. – Max.)	85.0 (65.0 – 110.0)	65.0 (50.0 – 100.0)	4.980*	

Regarding the urine output, there was an increase in the urine output in the first group compared to the second throughout intra and post-operatively, similarly, there was a detection of significant difference in level of creatinine, creatinine clearance, and serum neutrophil gelatinase associated lipocalcin at 6 hours postoperatively (table 3).

Table 3  
Comparison between the two studied groups according to serum neutrophil gelatinase associated lipocalcin at 6 hours

Serum gelatinase associated lipocalcin (Ngal ng/ml)	Neutrophil associated	Group (n = 30)	I Group (n = 30)	II t	p
6 hours					
Mean ± SD.		70.0 ± 10.85	29.40 ± 4.08	19.183*	<0.001*
Median (Min. – Max.)		68.50(50.0 – 96.0)	29.0 (21.0 – 41.0)		

Regarding changes related to lung ultrasound in the comparison process between the two groups, the first proved to have significant interstitial edematous tissues along the postoperative period, which resolved after 24 hours later. This was reflected upon the hypoxic index, which was calculated. However, the edematous changes did not affect the carbon dioxide exchange as shown in the analysis of the arterial blood gases. In terms of complication rate (nausea, vomiting, lung atelectasis, and wound infection), the second group proved statistically to have a significant lower incidence of such incidents. This may related to the edematous changes in various tissues, which occurred in the study group table (4). Besides, initial bowel movements were detected earlier in the second group. This may attributed the same progress of crystalloid fluid accumulating in the gastrointestinal wall, which affects its motion table (4). Related to mentioned points, this was echoed on the duration of intensive care course. As less complication rate and less edematous lung changes, the second group patients had to stay fewer days compared to the first group of patients table (4).

Table 4  
Comparison between the two studied groups regarding complication rate, duration to first bowel movement, and duration of ICU stay

	Group (n = 30)		I Group (n = 30)		II Test Sig.	of P
	No.	%	No.	%		
Complication						
Lung atelectasis	6	20.0	0	0.0	$\chi^2=6.667^*$	FEp=0.024*
Nausea	9	30.0	1	3.3	$\chi^2=7.680^*$	FEp=0.006*
Vomiting	9	30.0	1	3.3	$\chi^2=7.680^*$	FEp=0.006*
Wound infection	6	20.0	0	0.0	$\chi^2=6.667^*$	FEp=0.024*
Duration to first bowel movement(days)						
Mean ± SD.	2.17 ±1.22		1.49 ±0.87		U=293.0*	0.016*
Median (Min. – Max.)	2.0 (0.21 –4.0)		2.0 (0.08 –3.0)			

Duration of ICU stay  
(days)

Mean $\pm$ SD.	3.47 $\pm$ 1.20	2.93 $\pm$ 1.05	U=312.5*	0.036*
Median (Min. – Max.)	4.0 (1.0 –5.0)	3.0 (1.0 –5.0)		

## Discussion

In terms of optimized care of population planned for surgical interventions, hemodynamic evaluation is pivotal for both recognition and management.<sup>(14)</sup> The thermo-dilution Swan-Ganz catheter has long been classically used as a routine CO measurement in critical surgical patients, but the invasiveness and clinical impracticability restrain its routine usage.<sup>(15)</sup> As a result, Electrical cardiometry (EC) has been presented as a non-invasive, reliable and simple technique for hemodynamic evaluation.<sup>(7, 16)</sup> The clinical judgment relies heavily on evaluating the trends and not absolute data.<sup>(17)</sup> Thus, this study was conducted to delineate the ideal methodology for administration of intravenous fluids intra-operatively. Optimization of the stroke volume ejected from the heart with each beat was the suggested the cause of insignificant difference in the mean heart rate changes among the two groups in accordance with the study of Johnson, et al.<sup>(18)</sup>. As this creates non-significant change in cardiac output, along with the systemic vascular resistance, an insignificant change in the mean arterial blood pressure as was explained by Benes, et al.<sup>(19)</sup>

Both methods proved to be efficient as an estimate for the stroke volume, stroke volume variations, and cardiac index as suggested by Kadafi, et al.<sup>(20)</sup>. Importantly noticed result was the negative correlation between SVV and CI before and after administration of fluid boluses in group II. This finding was also suggested by Daniel A Reuter et al., who hypothesized that measuring SVV during mechanical ventilation allowed the accurate prediction of changes in CI in response to volume loading.<sup>(21, 22)</sup> The haemoglobin level (Hb) along with, total amount of estimated blood losses and number of packed red blood cells (RBC's) given showed an insignificant difference as was found by Yu-Gyeong Kong, et al.<sup>(23)</sup>. Regarding the systemic perfusion indices and serum lactate, the comparison showed an insignificant difference along with findings suggested by Jan Benes, et al.<sup>(24)</sup> In contrast, the central venous oxygen saturation showed a statically significant change but it should be clarify that these values still present in the normal physiological variations for such values.

Regarding the usage of the vasopressors and inotropes, the second group showed a statistically difference in the administration of these drugs. This was attributed to the guidance of the second method by the stroke volume variation. As regarding amount of fluids given the first group showed a significant increase in the infusion of colloid fluids relatively to the second group. Similarly, Gerard R., et al.<sup>(24)</sup> demonstrated that an algorithm based solely on the patient's SV response to fluid bolus is attractive because of its simplicity but it can be associated with fluid overload due to more crystalloid fluids given. This trend was associated with multiple outcomes. Firstly, increased rate of interstitial lunge edema, and decreased hypoxic index. Secondly, the effect on renal profile, namely increased levels of creatinine, creatinine clearance, and the serum neutrophil gelatinase associated lipocalcin level. Thirdly, the complication's incidence (nausea,

vomiting, lung atelectasis, and wound infection) was more obvious in the first group. Fourthly, the first intestinal movements were detected significantly in the second group. This could be attributed to tissue edema caused by more fluid boluses given in the first algorithm of the fluid management therapy, which affects organs such as the lungs and the gastrointestinal tract (including the surgical manipulation sites).<sup>(25)</sup> Lastly, these were associated with less intensive care unit days in the second group.<sup>(26)</sup>

## Conclusion

Application of GDT guided by SVV changes detected by EC achieve more successful aims of optimization of fluid therapy and avoiding complications related to whether hyper or hypovolemia.

## Limitations

The major limitation in the present study was sample number being small, single-center study, and exception of patient with as the adopted protocols could not to be applied to these population.

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## Disclosure of potential conflicts of interest

No potential conflict of interest was reported by the author(s).

**ORCID** <https://orcid.org/0000-0001-7818-8478>

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