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Change in stroke volume in response to fluid challenge: assessment using esophageal Doppler

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Abstract *Objective:* To compare two methods of assessing a change in stroke volume in response to fluid challenge: esophageal Doppler and thermodilution with the pulmonary artery catheter. *Design:* Prospective study. *Setting:* Department of Intensive Care of a university medical center. *Patients:* 19 adult patients, intubated and sedated, with a pulmonary catheter and a clinical indication for a fluid challenge. *Interventions:* Two examiners independently assessed the effect of a fluid challenge on stroke volume and cardiac output with esophageal Doppler. Thermodilution performed by an independent clinician was used as the reference. Between-method variation and interobserver variability of the Doppler method were assessed. *Measurements and results:* There were no differences in stroke volume and cardiac output before volume

challenge when measured with either of the two methods or by the two examiners using the esophageal Doppler. Despite a small bias between the methods and the two examiners using the esophageal Doppler (overall bias for cardiac output 0.3 l/min), the precision was poor (1.8 l/min). *Conclusions:* The esophageal Doppler method is a non-invasive alternative to the pulmonary artery catheter for the assessment of stroke volume in critically ill patients. Measurement of stroke volume response to fluid challenge using esophageal Doppler shows substantial interobserver variability. Despite the poor precision between methods and investigators, similar directional changes in stroke volume can be measured.

Keywords Cardiac output · Stroke volume · Esophageal Doppler · Thermodilution · Volume challenge

Introduction

Hypovolemia in patients in intensive care units (ICU) is common. The assessment of volume status is not straightforward and must often be based on hemodynamic response to a fluid challenge. The response to a fluid challenge can be assessed by observing changes in stroke volume. While cardiac output measurement using a pulmonary artery (PA) catheter (the thermodilution method) remains the standard in clinical practice [1, 2, 3, 4], stroke volume monitoring with esophageal Doppler provides an attractive, less invasive alternative [5, 6, 7].

Esophageal Doppler was first introduced in the early 1970s and more recently has been successfully approved for optimizing fluid management perioperatively and in intensive care patients [8, 9, 10]. Although stroke volume measurement using esophageal Doppler is simple in principle, several sources of error may interfere with its clinical application. The aim of this study was to assess the hemodynamic changes occurring after a clinically indicated volume load, using both the esophageal Doppler and the thermodilution method. Furthermore, we aimed to assess the inter-investigator variability of the esophageal Doppler method.

Materials and methods

The study was approved by the Ethics Committee of the Canton of Bern, according to the Declaration of Helsinki. Since informed consent by the patients or the family was not considered possible due to the emergency clause, an independent physician was designated to give consent.

Inclusion and exclusion criteria

The indication for inclusion in the study was the treating intensive care resident's decision to give a volume challenge. The inclusion criteria were: age greater than 16 years; patient on mechanical ventilation and sedated; and pulmonary catheter (Edwards Life Sciences, Irvine, Calif.) already in place. The exclusion criteria were: need for an urgent volume infusion (volume load given within 15 min to quickly stabilize a hemodynamically unstable situation); atrial fibrillation or flutter; relevant intra-cardiac shunting; presence of an intra-aortic balloon pump; fluid requirement of >500 ml within the last 2 h or changing requirements of vasoactive drugs (>20% within the last 30 min); coagulation abnormalities (increased thrombin time, thrombocytes $<100 \times 10^3/\mu\text{l}$); and prior enoral or esophageal surgery.

Esophageal Doppler

The esophageal Doppler probe (Cardio Q, Deltex Medical Limited, Chichester, UK) is approved for clinical use, and is routinely used in several institutions [11, 12, 13]. It is placed into the esophagus either through the mouth or the nose. The esophageal probe (90 cm length, 6 mm diameter) holds a 5.1-MHz Doppler device which sends out ultrasound signals at an angle of 45° . Based on the relation between emitted and reflected waves, the blood flow velocity of the descending aorta can be computed. Blood flow velocity is measured at a depth of 35–40 cm after the dental row. Placement is assumed to be correct if well-reproducible, sharply defined wave forms can be seen on the screen of the monitor.

Introduction of the method

The monitoring of an optimal Doppler signal depends largely on the examiner [14]. According to the manufacturer, reliable results can be obtained after five measurements (Operation Handbook, Deltex Medical Limited, Chichester, UK). In our department, all attending specialists ($n=10$) received a theoretical introduction and a practical demonstration of the method, and felt confident with the method within 8 weeks. The exact number of measurements performed to reach this goal was not registered.

Study protocol

The protocol is shown in Fig. 1. After the resident made the decision for volume administration, the independent physician (a senior specialist of the Department of Anesthesia) rechecked inclusion and exclusion criteria. If appropriate, the patient was included in the study. The study coordinator (one of the co-authors) inserted the Doppler probe. The probe was placed into the esophagus either through the mouth or the nose to a depth of 35–40 cm from the dental row. The sensor was placed in an anterior direction. Correct placement was assumed when well-reproducible, sharply defined wave forms appeared on the screen of the monitor.

The monitor was connected, and two of eight attending specialists not involved in the care of the patient were defined as examiners based on availability. Stroke volume and cardiac output

PROTOCOL

Clinician prescribed a volume challenge

Doppler probe inserted in the esophagus

- **Investigator 1:** correct placement and measurement

Probe displaced

- **Investigator 2:** correct placement and measurement

Thermodilution CO measured by independent clinician



VOLUME CHALLENGE 200 ML COLLOID IN 15 MINUTES

- **Investigator 2:** correct placement and measurement

Probe displaced

- **Investigator 1:** correct placement and measurement

Thermodilution CO measured by independent clinician

Fig. 1 Study protocol

were measured with the esophageal Doppler by the first examiner and then by the second. The study coordinator changed the position of the probe after the first measurement, so that the second examiner was blinded to the results obtained by the first examiner. After the Doppler measurements, the treating resident measured cardiac output with the thermodilution method using a cardiac output monitor (Vigilance TM, Baxter Lab, Santa Ana, Calif.). There were four randomly assigned measurements over the entire respiratory cycle using 10 ml of 0.9% sodium chloride at room temperature [15] with maximal injection speed. The arithmetic mean of these four measurements was calculated. The clinician was blinded to the results obtained by the two examiners who used the Doppler measurement. After all the measurements had been performed, the patient was given 200 ml of a gelatin solution (Physiogel, B. Braun, Emmenbrücke, Switzerland) over 15 min either via a peripheral venous line or through the port of the pulmonary artery catheter. After the volume load, stroke volume measurements were performed by the second examiner, followed by the first examiner, hence in reverse order. Between the measurements, the probe was displaced by the study coordinator and the examiner had to reposition it. Next, the resident repeated the measurements using the thermodilution method. The time interval between two sets of Doppler measurements was a few minutes, depending on how fast the second investigator found the optimal signal. Thermodilution cardiac output was measured immediately after the second Doppler measurement. During each measurement (Doppler and thermodilution method), representative values for systolic and diastolic blood pressure, pulmonary artery pressure, pulmonary artery wedge pressure, and central venous pressure were recorded.

Statistics

With the relatively small number of examinations ($n=20$) we used non-parametric tests. To compare the two methods before volume load, the Kruskal-Wallis Test (heart rate, all pressure values) and the Mann-Whitney U test (cardiac output, stroke volume) were used. For the two latter parameters the mean Doppler values of the two examiners were computed. The effect of the volume challenge for both methods was examined with the Wilcoxon test. The same test was used to analyze the results of both examiners with the Doppler: the Mann-Whitney U test was used to compare the values before the volume challenge, and the Wilcoxon test was used

Table 1 Patient profiles. *NPT* natrium–nitroprusside, *NE* norepinephrine, *E* epinephrine, *DOB* dobutamine, *SAPS* Simplified Acute Physiologic Score, *ARDS* adult respiratory distress syndrome, *MODS* multiple organ dysfunction syndrome

Patient no.	Age (years)	SAPS	Gender	Diagnosis	Vasoactive agents
1	73	54	M	Sepsis	NPT 4 mg/h
2	51	33	M	Septic shock	None
3	78	55	M	Sepsis	DOB 20 mg/h
4	21	46	M	Multi-system trauma	DOB 20 mg/h; NE 120 mcg/h
5	67	32	M	Aortic dissection	NE 1300 mcg/h
6	66	43	F	Cardiogenic shock	None
7	71	39	M	Pancreatitis, MODS	NE 300 mcg/h
8	42	39	M	Sepsis	NE 50 mcg/h
9	62	51	F	ARDS	None
10	63	50	F	Mitral insufficiency	NE 200 mcg/h
11	68	25	M	Myocardial revascularization	DOB 15 mg/h
12	47	43	M	Head injury	NE 800 mcg/h
13	75	47	M	Myocardial revascularization	NE 200 mcg/h
14	42	65	F	Cardiogenic shock	None
15	67	63	M	Cardiogenic shock	E 160 mcg/h
16	64	87	F	Aortic dissection	DOB 6 mg/h
17	64	87	F	Aortic dissection	None
18	78	38	M	Sepsis	DOB 6 mg/h; NE 500 mcg/h
19	61	61	M	Sepsis	DOB 10 mg/h
20	69	46	M	Aortic-valve replacement	None
Median (range)	65 (21–78)	47 (25–87)	–	–	–

Table 2 Hemodynamic parameters

	Esophageal Doppler Investigator 1	Esophageal Doppler Investigator 2	Thermomodulation	<i>p</i> ^a	<i>p</i> ^b
Heart rate before volume (b/min)	102 (15)	102 (16)	102 (16)		
After volume (b/min)	101 (16)	102 (17)	101 (16)		
Mean arterial pressure before volume (mm Hg)	65 (8)	65 (7)	64 (6)		
After volume (mm Hg)	67 (7)	66 (9)	66 (8)		
Mean pulmonary–arterial pressure before volume (mm Hg)	26 (5)	26 (5)	26 (5)		
After volume (mm Hg)	28 (6)	28 (6)	28 (5)	<0.01	<0.01
Central venous pressure before volume (mm Hg)	12 (4)	11 (4)	11 (4)		
After volume (mm Hg)	12 (4)	12 (4)	12 (4)	0.03	<0.01
Pulmonary capillary wedge pressure before volume (mm Hg)	14 (3)	14 (3)	14 (3)		
After volume (mm Hg)	15 (4)	15 (4)	15 (4)	<0.01	<0.01

^a *p*: Effect of volume load (Wilcoxon test): esophageal Doppler

^b *p*: Effect of volume load (Wilcoxon test): thermomodulation

to assess the effect of volume administration. Statistical significance was assumed at a *p* value <0.05. Results are given as mean values (±SD), if not stated otherwise.

Results

Between September 2000 and April 2001, 19 patients participated in the study and 20 measurements were performed (1 patient had measurements on two different days). There were 6 women and 13 men with a median age of 62 years (range 21–78 years) and a median Simplified Acute Physiologic Score II (SAPS II) [16] of 47 (range 25–87; Table 1).

Thirteen of the 19 patients were on one or more continuously infused vasoactive drugs (see Table 1). Ta-

bles 2 and 3 summarize the results of the hemodynamic parameters.

There were no significant differences in heart frequency or in the measured pressure values between the Doppler and thermomodulation methods (Table 2). While heart rate and systemic blood pressure remained constant during the whole procedure, mean pulmonary artery pressure and central venous pressure increased slightly. Stroke volume and cardiac output values are displayed in Table 3. The coefficient of variation of all four bolus measurements using the thermomodulation method was 7% (4%) before and 8% (6%) after volume load. There were no differences in stroke volume and cardiac output before volume challenge when measured with either of the two methods or by the two examiners using the esopha-

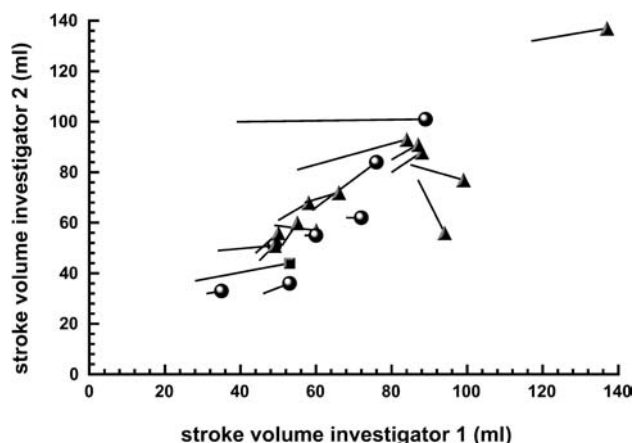


Fig. 2 Esophageal Doppler: investigator 1 vs investigator 2. Comparison of changes in stroke volume in association with volume application. Each *line* shows the data of 1 patient. *Data markers*: values after volume load; *triangles*: patients with catecholamines (epinephrine, norepinephrine, dobutamine); *squares*: patients with natrium-nitroprusside; *circles*: patients without vasoactive agents

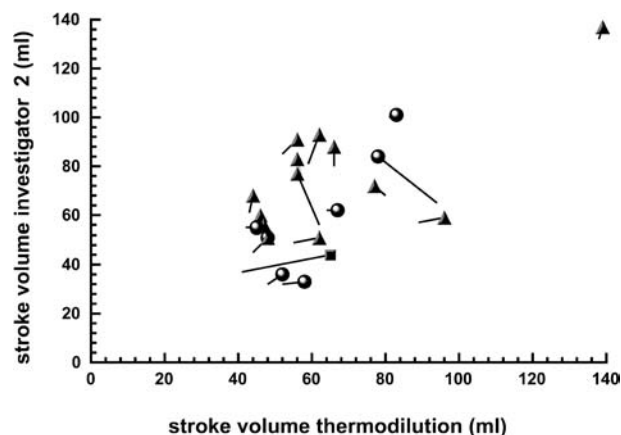


Fig. 4 Esophageal Doppler: investigator 2 vs thermidilution. Comparison of stroke volume change after volume application. Each *line* shows the data of one patient. *Data markers*: values after volume. *triangles*: patients with catecholamines (epinephrine, norepinephrine, dobutamine); *squares*: patients with natrium-nitroprusside; *circles*: patients without vasoactive agents

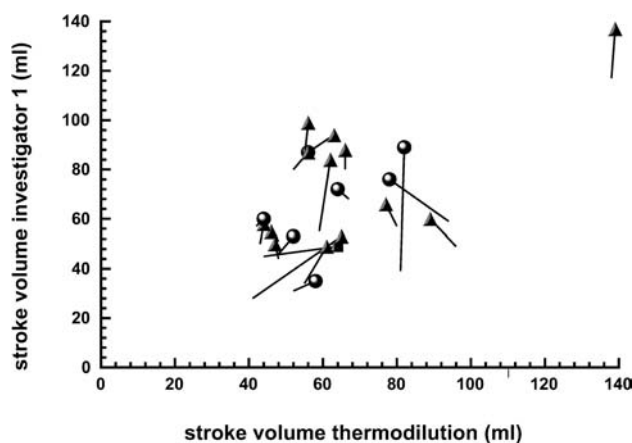


Fig. 3 Esophageal Doppler: investigator 1 vs thermidilution. Comparison of stroke volume change after volume application. Each *line* shows the data of one patient. *Data markers*: values after volume; *triangles*: patients with catecholamines (epinephrine, norepinephrine, dobutamine); *squares*: patients with natrium-nitroprusside; *circles*: patients without vasoactive agents

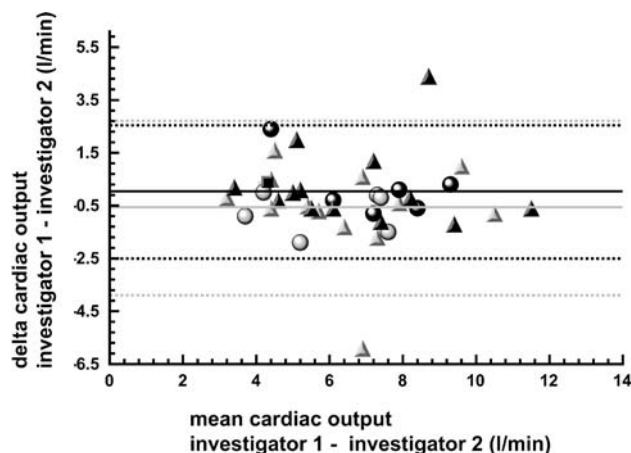


Fig. 5 Bland-Altman graph: investigator 1 vs investigator 2. *Grey data points*: value before volume; *black data points*: value after volume; *triangles*: patients with catecholamines (epinephrine, norepinephrine, dobutamine); *squares*: patients with natrium-nitroprusside; *circles*: patients without vasoactive agents; *solid line*: mean values; *dotted lines*: mean values ± 1.96 standard deviation

Table 3 Stroke volume and cardiac output before and after volume challenge

	Esophageal Doppler			Thermidilution	p^a	p^b
	Investigator 1	Investigator 2	Mean			
Stroke volume before volume (ml)	60 (23)	65 (24)	62 (22)	63 (24)		
After volume (ml)	69 (24)	69 (25)	69 (24)	66 (22)	<0.01	0.02
Cardiac output before volume (l/min m ²)	5.96 (2.12)	6.52 (2.17)	6.24 (1.97)	6.35 (2.30)		
After volume (l/min m ²)	6.85 (2.03)	6.81 (2.12)	6.83 (1.97)	6.57 (2.26)	0.01	0.09

^a p : Effect of volume load (Wilcoxon test): esophageal Doppler

^b p : Effect of volume load (Wilcoxon test): thermidilution

geal Doppler. With both methods, and with both examiners using the esophageal Doppler method, there was a significant increase in the stroke volume after a volume challenge, while the increase in the cardiac output measured by thermodilution was not significant (Table 3). While the overall correlation between the two methods was relatively good both before and after volume load (correlation coefficients between 0.6 and 0.9; $p < 0.01$), individual differences between the methods and the examiners using esophageal Doppler were obvious (Figs. 2, 3, 4). The Bland-Altman analysis (Fig. 5) demonstrates that the bias is small (overall bias for cardiac output 0.3 l/min) but the precision is poor (1.8 l/min).

Discussion

The main finding of this study was the great variability in the measured changes in stroke volume after a volume load, as assessed by two different methods – thermodilution and esophageal Doppler – as well as by two different examiners both using the esophageal Doppler method.

There are several possible explanations for these discrepancies. Firstly, the differences could be real, i.e., they could reflect an unstable hemodynamic situation. We investigated critically ill, mechanically ventilated and sedated patients, who were often dependent on vasoactive drugs. Their cardiac function may well have shown greater variance than is normally expected. Consequently, the examiners could have measured correct values. We could not find differences between patients with or without vasoactive agents (Figs. 2, 3, 4). Secondly, the differences could be due to stimulation of the patient. The placement and manipulation of the esophageal probe could have provoked an adrenergic stimulation in the patient so that the examiners again correctly measured a change in the hemodynamic situation. The greater difference between the examiners using the Doppler method before the volume load as compared with afterwards supports this hypothesis. The esophageal probe had to be placed before the volume load, whereas after the volume load, the probe remained in situ with a smaller manipulation. A third explanation could be a study bias of the examiners, who eventually were convinced that they would measure a higher stroke volume at the second measurement because they were aware that the patients received additional volume between the two measurements; thus, it is possible that the search for the optimal signal lasted longer during the second measurement. Another explanation for the inter-individual differences in the obtained hemodynamic parameters is the fact that the measurements after volume load were performed over a relatively wide time frame for medical reasons (mean after-fluid loading: 8.6 min; range 1–32 min). Early measurements may not have included

the volume effect, whereas during late measurements the volume effect may have been abated. Nevertheless, we could not find a time dependency of changes in stroke volumes. Moreover, in a few patients the thermodilution method may well have been incorrect, since the differences between the four bolus measurements was greater than the predicted 10% [17]. Finally, when supra-aortic branches are preferentially perfused, for some reason, cardiac output and descending aortic blood flow may not change in parallel.

Several authors have demonstrated that optimizing cardiac function, i.e., increasing the oxygen delivery to the tissues perioperatively and in the ICU, improves the outcome of the patients [18, 19, 20]. In order to increase stroke volume and cardiac output, preload has to be optimized. The clinical diagnosis of an insufficient preload is easy in hypovolemic patients but is difficult when myocardial dysfunction, altered vessel reactivity, and increased endothelial permeability co-exist, e.g., in septic patients [21, 22] and in patients after cardiac surgery [23]. The preload and the effect of a volume challenge can be measured with echocardiography in these patients, but this technique is not suitable for continuous monitoring. In these patients, the pulmonary artery catheter is generally used to obtain continuous or semi-continuous values of cardiac output and other hemodynamically relevant values. This method is invasive and the overall benefit has been questioned [1,3,4, 24, 26, 27, 28, 29, 30].

As an alternative, esophageal Doppler allows a noninvasive estimation of cardiac output. Since esophageal Doppler measures aortic blood flow but not the flow to supra-aortic arteries, the absolute value underestimates total cardiac output. Furthermore, esophageal Doppler measures beat-to-beat flow velocity, which is then converted to cardiac output, whereas thermodilution measures an average cardiac output over a certain time (a mean value of several measurements is calculated). Esophageal Doppler has been used to estimate the prognosis in cardiac surgery patients [31]. Furthermore, initial hemodynamic values can be obtained faster than with pulmonary artery catheterization [32]. The use of the Doppler method has been associated with improved perioperative morbidity and shortening of hospital stay [33].

The great inter-individual differences we found between the measurements of the two examiners using the Doppler are inconsistent with the results obtained by others [6, 10, 34]. These authors found a closer inter-individual correlation between the esophageal Doppler and continuous thermodilution methods. The most probable explanation for the difference, however, is lack of experience with the esophageal Doppler technique. There is a correlation between the accuracy of the obtained signal and the training time [14].

Since the aortal diameter is not measured, variability in accuracy in the absolute values can be expected. A

significant pathology, such as a rigidity or manifest sclerosis of the aorta, results in a discrepancy between estimated and real cardiac output values. There are esophageal Doppler devices with integrated ultrasound that allow the aortic diameter to be measured individually. Using these devices increases the reliability of the cardiac output value [35]; however, since the esophageal Doppler signal is highly position dependent, and the method used to define the best signal and its drift over time may be different both among and between individuals, the accuracy of this method remains limited. On the other hand, poor contractility in some patients may also have limited the accuracy of the "gold standard" thermodilution method.

Conclusion

We conclude that the esophageal Doppler method is a non-invasive method for the monitoring of some cardiac functions. Its use, however, is not as easy as described in the literature. If the method is not learned systematically, the probability of obtaining non-reproducible data is great. Future studies should evaluate the reproducibility of this method after a standardized teaching period with final examinations. Nevertheless, this study demonstrates that a clinically indicated volume load often, but not always, leads to an increase in stroke volume.

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