



Prospective Study: Optic Nerve Sheath Diameter in Prediction of Fluid Responsiveness in Sepsis Patients

**Hadeel Ibraheim Elsagheir^{1*}, Abd Elaziz Hamed El badawy¹,
Reda Sobhi Salama Abd Alrahman¹ and Mohamed Samir Abd El Ghafar¹**

¹Anesthesiology, Surgical Intensive Care and Pain Medicine, Faculty of Medicine, Tanta University, Egypt.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2021/v33i1931083

Editor(s):

(1) Dr. Rameshwari Thakur, Muzaffarnagar Medical College, India.

Reviewers:

(1) Charis Liapi, University of Athens, Greece.

(2) Govinda Vittala, Udayana University, Indonesia.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/73263>

Original Research Article

Received 30 June 2021
Accepted 10 September 2021
Published 25 September 2021

ABSTRACT

Background: Sepsis is a life-threatening disease caused by the body's reaction to infection, which results in tissue destruction, organ failure, and death. Sepsis affects at least 30 million people worldwide each year, with 6 million people dying as a result. The goal of the research was to see whether the measurement of the Optic Nerve Sheath Diameter (ONSD) could be used to predict fluid responsiveness in hemodynamically unstable individuals.

Patients and Methods: This prospective observational (cohort) study was conducted at Tanta University Hospitals in the Surgical Intensive Care Unit for 6 months at least after approval from institutional ethics committee.

Results: Demographic data (sex, illiteracy, height, BMI) in our patients of the study there were 34 (81%) male, 8 (19%) female, the age was average from 50.33 (± 8.63 SD) with range (25-65), 9 (21.4%) illiterate, 10 (23.8%) primary, 18 (42.9%) secondary, 5 (11.9%) university, the mean value of weight 80.29 (± 9.45 SD) with range (60.7-98.8), the mean value of height 170.57 (± 7.24 SD) with range (157-182), the mean value of BMI 27.54 (± 2.19 SD) with range (24.3-32).

Conclusion: In patients with sepsis, ocular ultrasonography appears to be a non-invasive and simple-to-learn technique for assessing overall fluid status. It may be particularly effective in finding those septic individuals who should avoid further fluid intake since it could cause pulmonary edema or other fluid-related problems.

Keywords: *Optic nerve sheath diameter; operating room; intensive care unit; goal-directed fluid therapy; stroke volume variation.*

1. INTRODUCTION

Sepsis is a life-threatening disease caused by the body's reaction to infection, which results in tissue destruction, organ failure, and death. Every year, an estimated 30 million individuals acquire sepsis as 6 million people die as a result of sepsis throughout the world [1].

In critical care, intravenous fluid resuscitation is the initial line of acute circulatory support [2]. The present approach and assessment of fluid difficulties in critically sick patients seems arbitrary, does not appear to be evidence-based, and may be detrimental [3].

The choice to give fluid should not be taken carelessly due to the danger of fluid excess. Volume responsiveness may be determined using a variety of techniques and tests. All of these methods have certain drawbacks. The method to use is determined on the patient's condition and the monitoring technology available [4].

In nonpregnant critically sick patients, ultrasound assessment of optic nerve sheath diameter (ONSD) has been reported as a straightforward and accurate method of detecting increased intracranial pressure owing to cerebral edema [5].

Increased ONSD, on the other hand, isn't clear if it may be utilized as a measure of systemic tissue edema and fluid overload. Optic ultrasonography may be utilized to evaluate fluid status and guide peripartum fluid treatment in patients with severe preeclampsia, according to Simenc [6].

As a result, further research on the relationship between ONSD and other fluid status indicators is required before ONSD measures may be suggested as a fluid management guidance in septic patients.

1.1 Aim of the Work

The goal of this study was to see whether ONSD measurement could be used to predict fluid

responsiveness in hemodynamically unstable individuals.

a) Primary outcome:

To detect cut off value of ONSD measurement for prediction of fluid responsiveness.

b) Secondary outcome:

- 1- To correlate Stroke Volume Variation with ONSD.
- 2- To detect sensitivity and specificity of ONSD in prediction of fluid responsiveness.

2. PATIENTS AND METHODS

This prospective observational (cohort) research was conducted at Tanta University Hospitals in the Surgical Intensive Care Unit for 6 months at least after approval from institutional ethics committee.

An informed written consent was filled by all patients' relatives. Everyone was given an explanation of the study's aim as well as a secret code number. Research results were only used for scientific purpose. There was no risk on the patients as it is an observational study.

Any unanticipated hazards that arose throughout the study were promptly communicated to the patients and the ethics committee. Waste materials were disposed according to standards of infection control in Tanta university hospitals.

A- Inclusion criteria:

Mechanically ventilated patients with mean arterial blood pressure lower than 65 mmHg and are 18 years old or older.

B- Exclusion Criteria:

- Patients breathing spontaneously.
- History with intracranial illness, such as Alzheimer's disease, should be evaluated

(stroke, TBI, causes of increase intracranial pressure).

- Local ophthalmologic disease: (Glaucoma, Single eye).
- High PEEP need.
- Known history of cardiovascular disease.
- Organ/s failure at admission.

C- Sample size calculation:

G*Power 3.1.9.2 for sample size calculation (Universitat Kiel, Germany). The sample size (N42) got determined based on the following factors:

- α error 0.05
- Power of the study 95%
- Area under the curve (AUC) of SVV to predict fluid responsiveness was 0.927 according to a previous study [7] at ONSD > 5.8 mm.

To overcome the drop-out, 8 cases were added. Therefore, 50 cases were recruited.

D- Study design:

The patients who met the preceding requirements were recruited in the research. Patients were also monitored (pulse oximetry, 5 lead ECG, non-invasive blood pressure, end tidal CO₂ and temperature).

2.1 Measurements

Optic nerve sheath diameter measurement:

Statistical analysis of the data

The IBM SPSS software program version 20.0 was used to examine the data that was input into the computer. (IBM Corporation, Armonk, NY) Number and percent were used to describe qualitative data. The Kolmogorov-Smirnov test was performed to ensure that the distribution was normal. Range (minimum and maximum), mean, standard deviation, and median were used to characterize quantitative data. The significance of the acquired findings was assessed at a 5% level.

3. RESULTS

Descriptive analysis of the studied cases according to ONSD ranged between (4.9-6.2), (5.1-8.5), (5-7.5), (5-7.5), (4.8-7.5), and (4.8-7.5) with a mean (\pm) value 5.59 \pm 0.41, 6.85 \pm 0.84, 6.43 \pm 0.67, 6.27 \pm 0.74, 6.22 \pm 0.81 and 6.23 \pm 0.81 at attendance, during stroke volume changes, 1st day, 2nd day, 3rd day and 4th day respectively.

There was significant increase in ONSD during stroke volume changes compared to attendance, during stroke volume changes, 1st day, 2nd day, 3rd day and 4th day [Table 1, Fig. 1].

Correlation between Stroke volume change and ONSD at 1st day There was negative correlation between the SVV and ONSD at 1st day [Table 2, Fig. 2].

Comparison between Stroke volume variation <10 and \geq 10 according to ONSD when SVV<10 the number of cases was 13 and ONSD was 5.52 \pm 0.39, 5.60 \pm 0.42, 5.78 \pm 0.42, 5.68 \pm 0.49, 5.44 \pm 0.46 and 5.29 \pm 0.46 and when SVV was \geq 10 the number of cases was 29 and the ONSD was 5.62 \pm 0.42, 6.49 \pm 0.70, 6.52 \pm 0.73, 6.53 \pm 0.67, 6.57 \pm 0.67 and 6.66 \pm 0.52 during attendance, resuscitation, 1st, 2nd, 3rd, and 4th day respectively there was no significant between stroke volume variation <10 and \geq 10 groups as regard ONSD at attendance, also there was no significant correlation between ONSD and, During resuscitation, 1st, 2nd, 3rd and 4th day when SVV <10, also there was significant increase between ONSD and during resuscitation, 1st, 2nd, 3rd and 4th day when SVV \geq 10 [Table3, Figs. 3-4].

Correlation between ONSD and fluid on different SVV.

There was positive correlation between ONSD and fluid when SVV \geq 10 with significance increase, also no significance between ONSD and fluid when SVV<10 [Table 4, Fig. 5].

Table 1. Descriptive analysis of the studied cases according to Optic nerve sheath diameter ONSD (n=42)

Optic nerve sheath diameter ONSD	Min. – Max.	Mean ± SD.	p1
At attendance	4.9 – 6.2	5.59 ± 0.41	
During stroke volume changes	5.1 – 8.5	6.85 ± 0.84	<0.001*
1 st day	5 – 7.5	6.43 ± 0.67	<0.001*
2 nd day	5 – 7.5	6.27 ± 0.74	<0.001*
3 rd day	4.8 – 7.5	6.22 ± 0.81	<0.001*
4 th day	4.8 – 7.5	6.23 ± 0.81	<0.001*

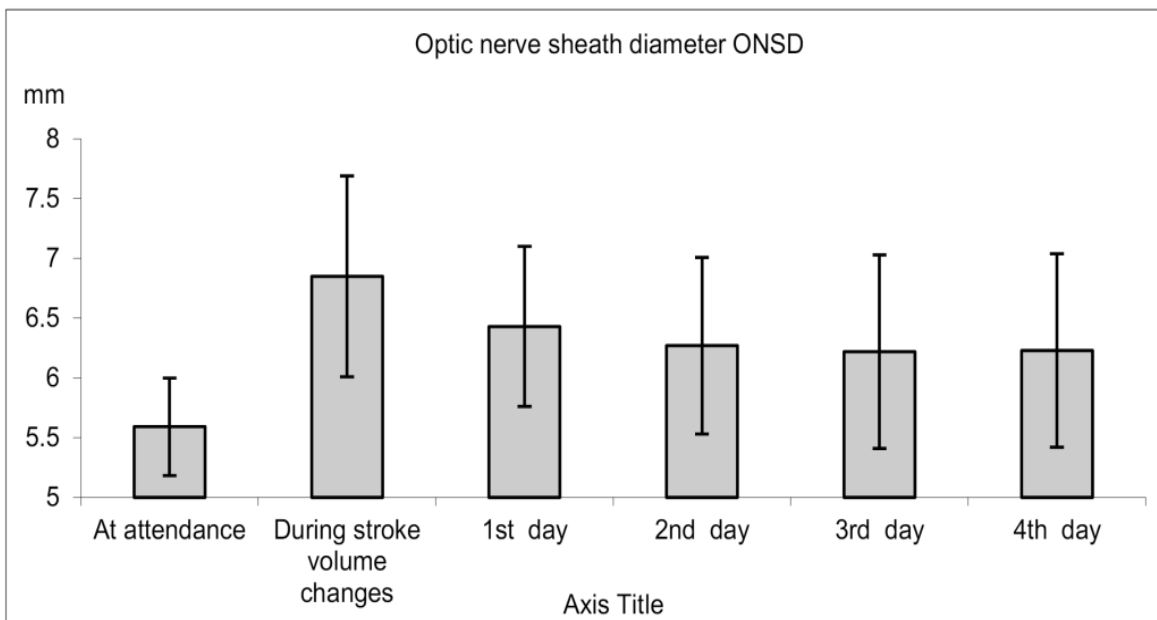


Fig. 1. Descriptive analysis of the studied cases according to Optic nerve sheath diameter

Table 2. Correlation between Stroke volume change (%) with ONSD 1st day (n=42)

	Stroke volume change (%)	
	r	p
ONSD 1 st day	-0.823	<0.001

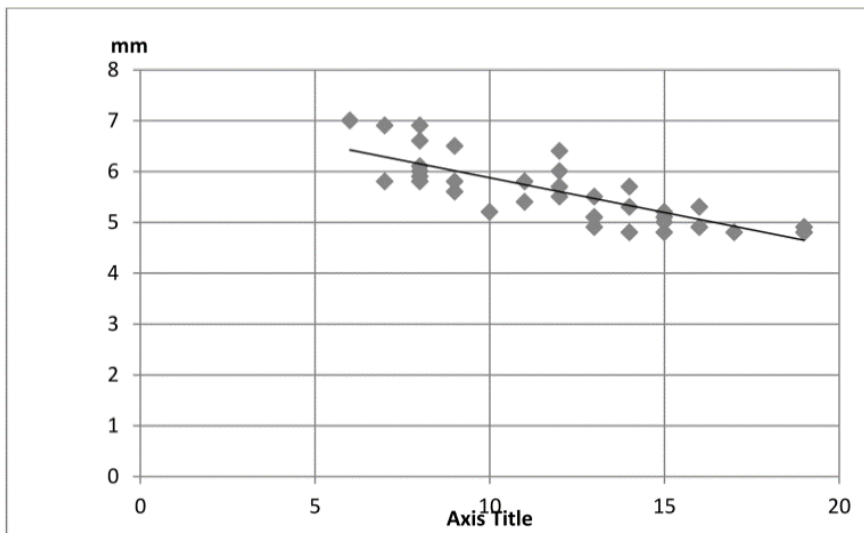


Fig. 2. Correlation between Stroke volume change (%) with ONSD 1st day

Table 3. Comparison between Stroke volume variation <10 and ≥10 according to ONSD (n=42)

ONSD	Stroke volume variation <10 (n = 13)	P value	Stroke volume variation ≥10 (n = 29)	P value
At attendance	5.52 ± 0.39		5.62 ± 0.42	
During resuscitation	5.60 ± 0.42	0.658	6.49 ± 0.70	< 0.001*
1 st day	5.78 ± 0.42	0.135	6.52 ± 0.73	< 0.001*
2 nd day	5.68 ± 0.49	0.376	6.53 ± 0.67	< 0.001*
3 rd day	5.44 ± 0.46	0.626	6.57 ± 0.67	< 0.001*
4 th day	5.29 ± 0.46	0.186	6.66 ± 0.52	< 0.001*

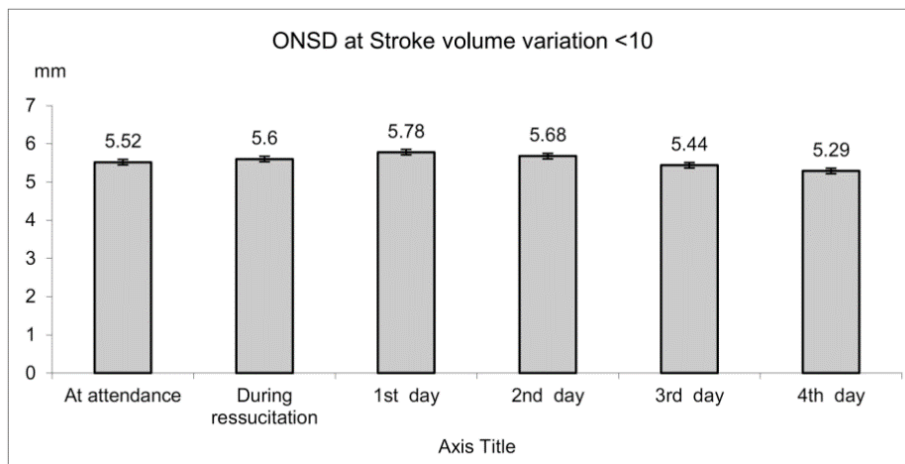


Fig. 3. Correlation between ONSD at attendance, during resuscitation days when stroke volume variation <10

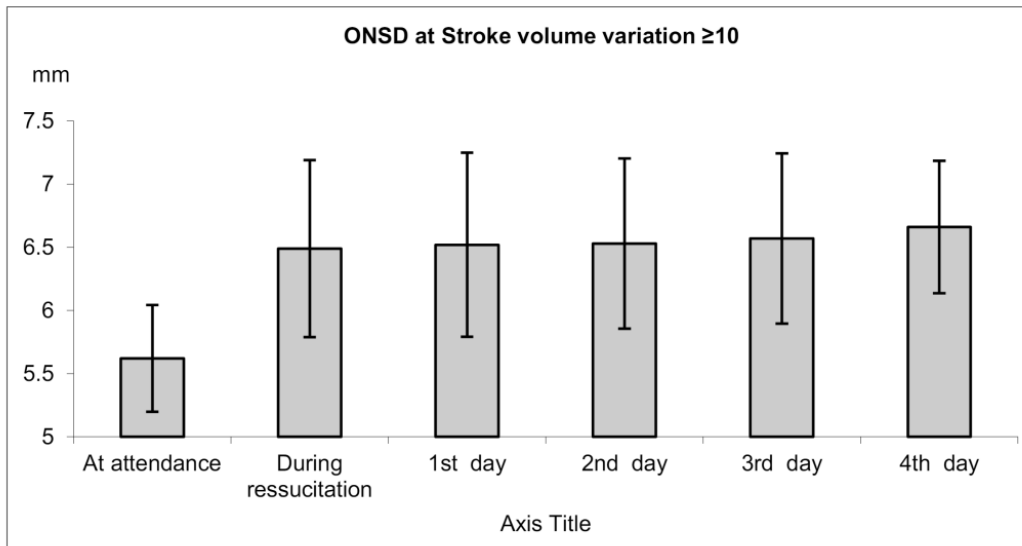


Fig. 4. Correlation between ONSD at attendance, during resuscitation days when stroke volume variation and ≥ 10

Table 4. Correlation between ONSD with Fluid on different SVV (n=42)

Patient Number	13		29	
	SVV<10		SVV ≥ 10	
	Fluid amount (ml/kg)		Fluid amount (ml/kg)	
	r	p	r	P
ONSD	0	1	0.954	<0.001

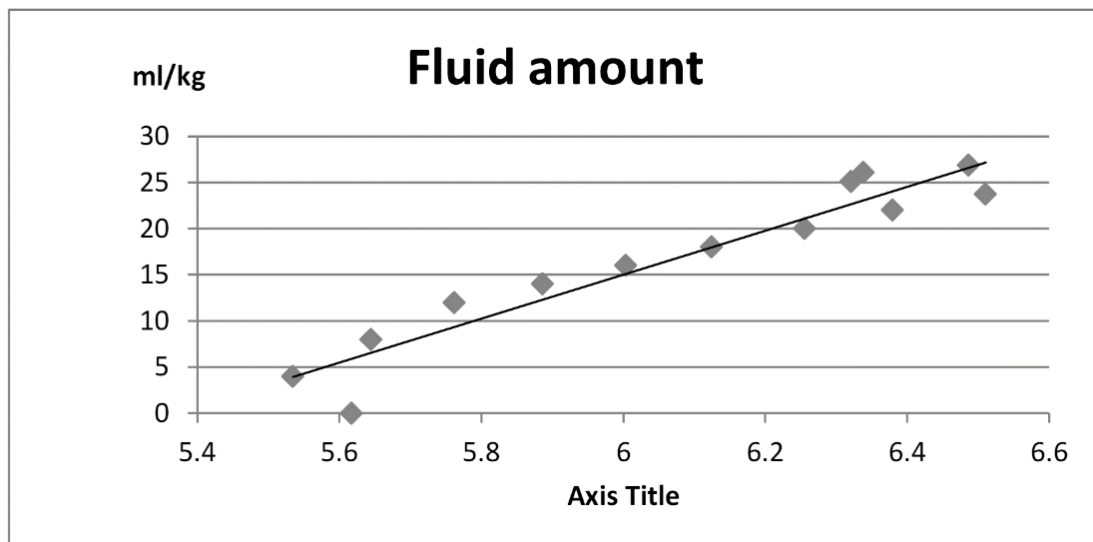


Fig. 5. Correlation between ONSD with Fluid on different SVV

4. DISCUSSION

As with stroke and severe myocardial infarction, sepsis and, in particular, septic shock, recognized as health emergencies. The importance of early detection and prompt implementation of resuscitative procedures cannot be overstated. However, identifying sepsis may be difficult, and optimal treatment techniques are always changing [1].

In USA, sepsis affects 750,000 individuals each year and stands as the top mortality cause in severely sick patients with about 210,000 annual deaths [2]. Septic shock accounting for approximately 10% of admissions to intensive care units with a mortality over 50%, affects roughly 15% of sepsis patients. Between 2000 and 2008, the sepsis incidence in USA more than quadrupled [3], Perhaps as a result of the increasing use of invasive surgeries, immunosuppressive medications, and chemotherapy in our ageing population, as well as the development of antibiotic resistance. In the United States, the cost of sepsis-related care is more than \$20.3 billion per year [4].

Fluid resuscitation may be guided in a variety of ways that are both safe and effective. In critically sick patients, conventional cardiac filling pressures don't predict fluid responsiveness (i.e., a rise in cardiac output in response to a fluid challenge) [5]. Fluid responsiveness may be predicted using other techniques that measure active fluctuations in heart stroke volume amid controlled breathing [5].

The measurement of ONSD using ultrasound is a non-invasive technique for ICP monitoring. The cranial dura mater has a direct anatomical extension in the form of the optic nerve sheath. Anatomical continuity refers to unrestricted flow of cerebrospinal fluid between the subarachnoid area around the optic nerve and intracranially. Increased ONSD is caused by an increase in pressure inside the intracranial compartment, which causes swelling of the optic nerve (papilledema) [6, 8].

We aimed to examine ONSD measurement for predicting fluid responsiveness in hemodynamically unstable patients.

To detect cut off value of ONSD measurement for prediction of fluid responsiveness

- To correlate Stroke Volume Variation with ONSD.

- To detect sensitivity and specificity of ONSD in prediction of fluid responsiveness

In our result we found that there was Positive correlation between ONSD and Fluid amount when SVV ≥ 10 with high significance. Using ONSD was shown that more than 4.95 as it cut off value, it can discriminate between improvement cases with level of sensitivity 88.6% and specificity 100%.

In agreement with our study and due to the severity of their illness, Zimmerma evaluated 20 patients (13 males) undergoing elective major abdominal surgery who needed both arterial and CVP monitoring. Patients suffering cardiovascular disease, intracardiac shunts, peripheral vascular disease, regional myocardial asynchrony, preoperative dysrhythmias, and an ejection fraction of less than 30% were excluded from the study. According to their results, both less invasive assessable variables, stroke volume variation and pleth variability index, may be useful indicators of fluid responsiveness in mechanically ventilated patients undergoing major surgery [9].

Also Huang [10] they investigate from many sources about SVV diagnostic value in predicting fluid responsiveness. They found SVV stands as a strong predictor for patients ventilated using tidal volume over 8 ml/kg. Yet, further research is needed into its predictive usefulness in patients ventilated with low tidal volume ventilation. When spontaneous breathing is present, the predictive value of SVV is impaired. In instances of peripheral vascular disease, cardiac arrhythmia, valvular heart disease, intracardiac shunts, and poor ejection fraction, SVV is also ineffective.

Mallat also looked at 49 critically sick, profoundly sedated, and mechanically ventilated patients who didn't have any cardiac arrhythmias and needed a fluid challenge due to circulatory failure. The continuous cardiac index CCI, SVV (PiCCOTM; Pulsion), and pulse pressure variation (PPV) were all measured prior and post patients were given fluid, and it was discovered that the SVV100 and PPV100 predict fluid responsiveness more precisely than CCI100 (PiCCOTM; Pulsion) in patients suffering circulatory failure as well as low volume ventilation [11].

Renata also compared data from 23 patients who underwent posterior spine arthrodesis surgery and had their intraoperative fluid administration

handled via goal-directed fluid therapy (GDFT) protocol based upon SVV with data from 23 matched controls who underwent similar surgery in the same timeframe but were given a placebo [12].

Furthermore, Rathore worked on 50 patients who were having major operations and were observed for PPV and SVV following anesthesia induction and 500 mL of isotonic crystalloid bolus delivery. Patients who had an increase in cardiac output of more than 15% following the fluid bolus were considered responders, whereas those who had a drop of less than 15% were considered non-responders. Both PPV and SVV were helpful predictors of cardiac response to fluid loading. PPV has a stronger link to fluid for both responders and non-responders alike [13].

Zilcar's study has shown the predicted PPV and SVV values in laparoscopic operations for pneumoperitoneum patients utilizing a LiDCORapid™ hemodynamic monitor, and its results indicate that LiDCORapid™-messed PPV and SVV may be utilized as fluid response predictors for pneumoperitoneum patients [14].

Simenc also looked at female patients suffering severe preeclampsia. In this research, 30 patients were recruited to see whether there was a link between the optic nerve sheath diameter ONSD as well as lung ultrasonography estimations of extravascular lung water in severe preeclampsia. Within 24 hours after birth, ONSD and lung ultrasound were done, and they discovered. In patients suffering severe preeclampsia, ocular ultrasonography has been shown to be a non-invasive and simple-to-learn technique for assessing overall fluid condition. It may be particularly helpful in detecting preeclamptic individuals who should avoid further fluid intake since it could cause pulmonary edema or other fluid-related problems. More research is required to see whether this diagnostic technique is helpful in decreasing maternal problems associated with inadequate fluid management in severe preeclampsia [6].

They studied on patients having neurosurgery operations intraoperatively, in addition to Messina, and discovered that baseline values of dynamic indices are inadequate for evaluating preload dependency. Influences in PPV and SVV generated after tidal volume challenge (VTC) are reliable and comparable in predicting fluid responsiveness to changes in cardiac index CI and stroke volume index SVI generated after end

expiratory occlusion test EEOT performed at 8 ml kg⁻¹. These tests should be seen as complementary, well-tolerated, and helpful tools for determining intraoperative fluid treatment [15].

In addition, Fayed's study was on hemodynamically unstable patient in intensive care units with septic shock and mechanically ventilated aged more than 18 years old and need resuscitation and found that In patients ventilated mechanically with septic shock, SVV may predict fluid response and can be linked to IVC distensibility [16].

Douglas also relied on a multicenter, randomized clinical research involving 13 hospitals in USA and the UK that looked at patients who came to EDs with sepsis, hypotension, and the possibility of ICU admission. and their research found that physiologically guided fluid and vasopressor resuscitation via passive leg raise-induced stroke volume change to direct septic shock treatment is safe, with reduced net fluid balance and decreased danger of renal and respiratory failure. When compared to standard treatment, dynamic evaluations to guide fluid delivery can enhance outcomes for septic shock patients [17].

Perner's research, in contrast to ours, comprised thirty septic shock patients on pressure support ventilation who were monitored via PiCCO system and received 500 mL of colloid based on clinical reasons. Variation in the volume of the arterial pulse contour stroke Before and after the fluid challenge, the SVV and the transpulmonary thermodilution cardiac index were assessed. They discovered that with septic shock patients on pressure support ventilation, SVV failed to predict the response in cardiac output to fluid challenge [18].

Andrews also discovered that in a resource-limited environment, a strategy for early resuscitation with intravenous fluids and vasopressors elevated in-hospital mortality relative to standard treatment among individuals with sepsis and hypotension, the majority of whom were HIV-positive. Further studies are required to develop better explanations on the impact of intravenous fluid boluses and vasopressors in sepsis patients in various low- and middle-income healthcare settings and patient groups [19].

In addition, Rui's research indicates that assessing fluid responsiveness in intra-abdominal hypertension patients is linked to

false-negative instances of passive leg lifting. Variations in pulse pressure and stroke volume are seldom used [20].

5. CONCLUSION

In patients with sepsis, ocular ultrasonography appears to be a non-invasive and simple-to-learn technique to assess overall fluid condition. It may be particularly effective in finding those septic individuals who should avoid further fluid intake since it could cause pulmonary edema or other fluid-related problems.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Nunnally ME, Patel A. Sepsis-What's new in 2019? *Current Opinion in Anesthesiology*. 2019;32:163-8.
2. Long E, Marik PE. Can the Brain Predict Fluid Responsiveness? *Anesthesiology*. 2019;130:674-6.
3. Michard F, Biais M. Predicting fluid responsiveness: time for automation. *Critical Care Medicine*. 2019;47:618-20.
4. Monnet X, Marik PE, Teboul J-L. Prediction of fluid responsiveness: An update. *Annals of Intensive Care*. 2016;6:1-11.
5. Agrawal A, Cheng R, Tang J, Madhok DY. Comparison of two techniques to measure optic nerve sheath diameter in patients at risk for increased intracranial pressure. *Critical Care Medicine*. 2019;47:e495.
6. Simenc GB, Ambrozic J, Prokselj K, Tul N, Cvijic M, Mirkovic T, et al. Optic nerve ultrasound for fluid status assessment in patients with severe preeclampsia. *Radiology and Oncology*. 2018;52:377.
7. Soliman R, Zeid D, Yehya M, Nahas R. Bedside Assessment of Preload in Acute Circulatory Failure Using Cardiac Velocimetry. *J Med Diagn Meth*. 2016;5:2.
8. Soliman R, Zeid D, Yehya M, Nahas R. Bedside assessment of preload in acute circulatory failure using cardiac velocimetry. *J Med Diagn Meth*. 2016;5:2.
9. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 sccm/esicm/accp/ats/sis international sepsis definitions conference. *Intensive Care Medicine*. 2003;29:530-8.
10. Huang L, Zhang W, Cai W, Luo H, Chen Y, Zhang S. The role of stroke volume variation in predicting the volume responsiveness of patients with severe sepsis and septic shock. *Chinese Journal of Emergency Medicine*. 2010;19:916-20.
11. Mallat J, Meddour M, Durville E, Lemyze M, Pepy F, Temime J, et al. Decrease in pulse pressure and stroke volume variations after mini-fluid challenge accurately predicts fluid responsiveness. *British Journal of Anaesthesia*. 2015;115:449-56.
12. Bacchin MR, Ceria CM, Giannone S, Ghisi D, Stagni G, Greggi T, et al. Goal-directed fluid therapy based on stroke volume variation in patients undergoing major spine surgery in the prone position: A cohort study. *Spine*. 2016;41:E1131-E7.
13. Rathore A, Singh S, Lamsal R, Taank P, Paul D. Validity of pulse pressure variation (PPV) compared with stroke volume variation (SVV) in predicting fluid responsiveness. *Turkish Journal of Anaesthesiology and Reanimation*. 2017;45:210.
14. Zlicar M, Novak-Jankovic V, Cecconi M. Predictive values of pulse pressure variation and stroke volume variation for

- fluid responsiveness in patients with pneumoperitoneum. *Journal of Clinical Monitoring and Computing*. 2018;32:825-32.
15. Messina A, Montagnini C, Cammarota G, De Rosa S, Giuliani F, Muratore L, et al. Tidal volume challenge to predict fluid responsiveness in the operating room: an observational study. *European Journal of Anaesthesiology| EJA*. 2019;36:583-91.
 16. Fayed AM, Abd El Hady WS, Abd El MAEA, Melika MEA. Stroke volume variation compared with inferior vena cava distensibility for prediction of fluid responsiveness in mechanically ventilated patients with septic shock. *Research and Opinion in Anesthesia and Intensive Care*. 2020;7:84.
 17. Douglas IS, Alapat PM, Corl KA, Exline MC, Forni LG, Holder AL, et al. Fluid response evaluation in sepsis hypotension and shock: A randomized clinical trial. *Chest*. 2020;158:1431-45.
 18. Perner A, Haase N, Guttormsen AB, Tenhunen J, Klemenzson G, Åneman A, et al. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. *New England Journal of Medicine*. 2012;367:124-34.
 19. Andrews B, Semler MW, Muchemwa L, Kelly P, Lakhi S, Heimbürger DC, et al. Effect of an early resuscitation protocol on in-hospital mortality among adults with sepsis and hypotension: A randomized clinical trial. *Jama*. 2017;318:1233-40.
 20. Shi R, Monnet X, Teboul J-L. Parameters of fluid responsiveness. *Current Opinion in Critical Care*. 2020;26:319-26.

© 2021 Elsagheir et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:
<https://www.sdiarticle4.com/review-history/73263>