

# Comparison of Pleth Variability Index and Inferior Vena Cava Distensibility as a Perfusion Indicator in Sepsis Patients: An Observational Study

## Sepsis Hastalarında Perfüzyon Belirteci Olarak Pleth Değişkenlik İndeksi ve Vena Kava İnförör Gerilebilirliğinin Karşılaştırılması: Gözlemsel Çalışma

<sup>1b</sup>Orhan GÖKTÜRK<sup>a</sup>, <sup>1b</sup>Onur AVCI<sup>b</sup>, <sup>1b</sup>Oğuz GÜNDOĞDU<sup>c</sup>, <sup>1b</sup>Ahmet Cemil İSBİR<sup>b</sup>,  
<sup>1b</sup>İclal ÖZDEMİR KOL<sup>b</sup>, <sup>1b</sup>Sinan GÜRSOY<sup>b</sup>, <sup>1b</sup>Kenan KAYGUSUZ<sup>b</sup>

<sup>a</sup>Clinic of Anaesthesiology and Reanimation, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye

<sup>b</sup>Department of Anaesthesiology and Reanimation, Sivas Cumhuriyet University Faculty of Medicine, Sivas, Türkiye

<sup>c</sup>Clinic of Anaesthesiology and Reanimation, Sivas Numune Hospital, Sivas, Türkiye

**ABSTRACT Objective:** The aim of this study was to compare the sensitivity and specificity of Pleth Variability Index (PVI) and distensibility of inferior vena cava (dIVC) in fluid responsiveness of patients with sepsis. **Material and Methods:** Forty patients over 18 years of age who underwent fluid replacement for sepsis in the intensive care unit were included in the study. In our study, the patients were divided into 2 groups as those who had less than 15% increase in cardiac output (CO), and those who had more than 15% increase in CO after fluid replacement (fluid responders and non-responders). Before fluid replacement, demographic data of the patients (age, weight, cause of sepsis, body surface area, SOFA score), vital parameters (systolic arterial pressure, diastolic arterial pressure, mean arterial pressure, heart rate) and measured values (maximum diameter of vena cava inferior, minimum diameter of vena cava inferior, central venous pressure, PVI, CO, and stroke volume) were recorded. After applying crystalloid in a dose of 10 mL/kg for 15 minutes, the recorded parameters were repeated at 15<sup>th</sup> minute. **Results:** When receiver operating characteristic (ROC) analysis was performed for dIVC, the area under the curve (AUC) was found to be 0.833 (0.739-0.926). The threshold value was found to be 17.52%, sensitivity was 77.5%, and specificity was 72.5%. When ROC analysis was performed for PVI, AUC was found to be 0.889 (0.817-0.962). The threshold value was found as 12.50%, sensitivity was 72.5%, and specificity was 92.5%. **Conclusion:** PVI was found to be more specific but less sensitive than dIVC. dIVC is less sensitive and less specific than central venous pressure. However, dIVC and PVI can give useful results in patients who have contraindication of an invasive technique.

**Keywords:** Sepsis; fluid therapy; cardiac output

**ÖZET Amaç:** Bu çalışmanın amacı Pleth Değişkenlik İndeksi (PVI) ve inferior vena kava distensibilitesinin (dIVC) sepsisli hastalarda sıvı yanıtını değerlendirmedeki duyarlılığını ve özgüllüğünü karşılaştırmaktır. **Gereç ve Yöntemler:** Çalışmaya, yoğun bakım ünitesindeki sepsis tanısı almış sıvı replasmanı uygulanacak 18 yaş üstü bireylerden 40 hasta dâhil edildi. Çalışmamızda hastalar, sıvı replasmanı sonrası "kardiyak output"ta [cardiac output (CO)] %15'ten az ve %15'ten fazla artış olan (sıvıya cevap verenler ve vermeyenler) olarak 2'ye ayrıldı. Hastaların sıvı replasmanı öncesi demografik verileri (yaş, kilo, sepsis nedeni, vücut yüzey alanı, SOFA skoru), vital parametreleri (sistolik arter basıncı, diastolik arter basıncı, ortalama arter basıncı, kalp atım hızı) ve ölçüm değerleri (vena cava inferior maksimum çapı, vena cava inferior minimum çapı, santral venöz basınç, PVI, CO, vuruş hacmi) kayıt edildi. Hastalara 15 dk boyunca 10 mL/kg kristaloid uygulandıktan sonra kayıt edilen parametreler tekrarlandı. **Bulgular:** dIVC için alıcı işletim karakteristiği [receiver operating characteristic (ROC)] analizi yapıldığında, eğri altında kalan alan [area under the curve (AUC)] 0,833 (0,739-0,926) bulunmuştur. Eşik değer %17,52 bulunmuş olup; duyarlılık %77,5, özgüllük %72,5 bulunmuştur. PVI için ROC analizi yapıldığında, AUC 0,889 (0,817-0,962) bulunmuştur. Eşik değer %12,50 bulunmuş olup; duyarlılık %72,5, özgüllük %92,5 bulunmuştur. **Sonuç:** PVI'nin, dIVC'den daha spesifik ancak daha az duyarlı olduğu bulundu. dIVC, santral venöz basınçtan daha az duyarlı ve daha az spesifik bulundu. Bununla birlikte dIVC ve PVI, invaziv bir teknik için kontrendikasyonu olan hastalarda faydalı sonuçlar verebilir.

**Anahtar Kelimeler:** Sepsis; sıvı tedavisi; kardiyak output

Static and dynamic tests can be used to assess fluid responsiveness. Although central venous pressure (CVP) and pulmonary artery wedge pressure

measurements are static measurements, they are invasive methods for the evaluation of responsiveness to fluid replacement.<sup>1,2</sup> All static hemodynamic pa-

**Correspondence:** Oğuz GÜNDOĞDU

Clinic of Anaesthesiology and Reanimation, Sivas Numune Hospital, Sivas, Türkiye

**E-mail:** droguzgundogdu@gmail.com

Peer review under responsibility of Türkiye Klinikleri Journal of Medical Sciences.

**Received:** 06 Aug 2021

**Received in revised form:** 05 Jan 2022

**Accepted:** 03 Feb 2022

**Available online:** 14 Feb 2022

2146-9040 / Copyright © 2022 by Türkiye Klinikleri. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



rameters are generally influenced by individual changes, intrathoracic pressure, ventricular adaptation, complex interactions between vasomotor tone and intravascular volume. Some dynamic indicators, such as stroke volume (SV) changes and pulse pressure changes, have a better diagnostic value for predicting fluid response. However, these 2 indices can be used in patients with sinus rhythm, but limit their benefits in patients with arrhythmias. Distensibility of inferior vena cava (dIVC) with respiration, measured by ultrasound, are another dynamic indicator commonly used to predict the fluid-response.<sup>3</sup> Arrhythmia is not a contraindication in inferior vena cava (IVC) diameter changes in contrast to changes in SV and pulse pressure. It is widely used as a simple, non-invasive, bedside, practical and low-cost tool to guide fluid resuscitation.<sup>4</sup>

Goal directed fluid therapy aims to determine the optimal amount of fluid for an individual patient, and meta-analyses point out its clinical benefits, especially in patients not participating in an enhanced recovery program.<sup>5,6</sup> Hemodynamic optimization has mostly been guided by SV, commonly measured via esophageal Doppler, or by dynamic parameters such as SV variation, pulse pressure variation or the pulse oximetric Pleth Variability Index (PVI), which all are based on cardiopulmonary interactions. PVI is also used in non-septic patients to monitor the hypotension and fluid condition in patients in example hypotension due to general anesthesia induction and major surgeries with fluid lost due to major bleeding.<sup>7,8</sup>

We compared PVI and dIVC, 2 of the dynamic tests, for the evaluation of fluid responsiveness in our intubated patients. The aim of this study was to compare the sensitivity and specificity of PVI and dIVC in fluid responsiveness of patients with sepsis.

## MATERIAL AND METHODS

This is a single-center, prospective, and observational clinical study. The study was started after February 19, 2019; and the 2019-02/03 numbered decision was taken from the Clinical Research Ethics Committee of Sivas Cumhuriyet University. The study was conducted on sepsis patients hospitalized in the intensive care unit (ICU) between June 26, 2018 and July 1, 2019.

The patients were informed about the study if they were conscious, and their relatives were informed if the patients were unconscious. An informed consent form was obtained from the participants and permission was obtained for the study. This study was designed in agreement with the principles of Helsinki Declaration.

This study was carried out on 40 adult patients aged between 18-90 years. Sepsis patients newly admitted to the ICU or developed sepsis in the ICU during their hospitalization were included in the study. All the patients in this study had quick Sequential Organ Failure Assessment score (qSOFA)  $\geq 2$  and SOFA score  $\geq 2$ .

Critical patients requiring urgent resuscitative treatment, patients with increased intracranial pressure and likely to have increased intracranial pressure (intracranial hemorrhage, embolism, head trauma, intracranial mass, etc.), chronic renal failure patients with dialysis-dependent patients, severe heart failure patients with ejection fraction  $< 40\%$  on echocardiography, cardiac index (CI)  $< 2$  L/min/m<sup>2</sup>, patients who did not consent to the study, patients with respiratory activity and pregnant women were excluded from the study. Also, patients that have vasopressor or positive inotropes were not included in this study. Patients who needed neuromuscular blockers and sedation were also excluded from the study.

The main exclusion criteria were as follows: patients that were not intubated, patients who were  $< 18$  years, had high intraabdominal pressure findings, had severe right heart failure (tricuspid insufficiency), could not lie in a supine position, had severe tachypnea, whose present peripheral oxygen saturation (SpO<sub>2</sub>) was below 88%, were morbidly obese, and had no clear images obtained via ultrasonography.

The patients who were candidates for the study were diagnosed with sepsis by the physician in the follow-up and treatment of the department, and the decision of the fluid resuscitation was made by the physician in the department. Methods used for the diagnosis of sepsis (anamnesis, laboratory values, clinical evaluation, physical examination, pulse, blood pressure, respiratory rate, skin color changes, radiological imaging, etc.) are left to the department's diagnosis and treatment protocol. As a result of the

evaluation, if the patient was suspected to have sepsis, intravenous fluid replacement therapy was planned, and the investigator was informed. The researcher informed the patients about the study and patients who gave consent to the study were included.

The demographic (age, weight, gender) and clinical data (cause of sepsis, SOFA score, medical history) of the included patients were recorded. Vital parameters [systolic blood pressure (SBP), mean arterial pressure (MAP), diastolic blood pressure (DBP), CVP] were measured with Dräger Infinity® Delta (©Drägerwerk AG & Co. KGaA, Germany). As an indicator of renal hypoperfusion, blood urea nitrogen/creatinine (BUN/Crea) ratio was calculated and recorded for each patient.

The perfusion index (PI) is calculated by proportioning the infrared rays absorbed by the 2 components in the peripheral circulation by the pulse oximetry plethysmographic (POP) waveform. These components are the amount of radiation absorbed by pulsatile arterial blood flow [alternating current (AC)] in peripheral tissues and the amount of radiation absorbed by static tissues [eg skin, bone, tissue, non-pulsatile blood flow; direct current (DC)]. PI is the percentage expression of the ratio of these 2 components. It is calculated by the formula  $[PI=(AC/DC)\times 100\%]$  and reflects the amplitude of the POP. PVI is an automatic and continuous measurement of dynamic changes in PI during the respiratory cycle.

Formula:

$$PVI: [(PI_{\max}-PI_{\min})/PI_{\max}]\times 100\%.$$

Depending on the oxygenated blood flow in the measurement area, the change in the microvascular structure is reflected in the change in PI. While PI decreases in the case of local vasoconstriction, it increases in the case of local vasodilation.

PI and PVI values were measured at the bedside with radical 7 pulse co-oxymeter. Before the protocol was performed, the monitor was calibrated for a PVI calculation that measured changes in PI occurring at 15-second intervals to capture at least one respiratory cycle. The PVI value was obtained from approximately 2 minutes of data. The screen refresh rate was 1 sec. The sensor that permits continuous evaluation of PVI was attached to the patient's finger and the

best analyzable signal was received by the monitor. Measurements began after a stable PVI value. A value that did not change for at least 5 minutes or changed to a maximum of one point was obtained.

Left ventricular outflow tract diameter (LVOD), velocity time integral (VTI), heart rate (HR) and IVC measurements were performed with Esaote MyLab30Gold cardiovascular ultrasonography device (Esaote SpA, Genova, Italy) and PA240 Esaote 1-4 MHz sector cardiac probe (Esaote SpA, Genova, Italy). For IVC diameter measurement, the right atrium was found primarily on the left lobe of the liver in the anterior midline of the abdomen, with the probe pointer facing the patient's feet. After the sagittal image of the liver, heart, hepatic veins and IVC was obtained in B-Mode, the change of IVC with inspiration and expiration from approximately 2 cm distal to the right atrium was recorded in M-Mode. The maximum diameter during expiration ( $IVC_{\max}$ ) and the minimum diameter during inspiration ( $IVC_{\min}$ ) were recorded in the patient form. The dIVC was then calculated manually by substituting  $IVC_{\max}$ , and  $IVC_{\min}$  in the following formula.

$$dIVC=(IVC_{\max}-IVC_{\min})/IVC_{\min}\times 100$$

The cardiac output (CO) value was calculated automatically using LVOD, VTI, and HR values measured by the transthoracic echocardiography device. Body surface area values that were automatically calculated by the ultrasonography device using height and weight values were entered during patient registration. CI value was calculated automatically by the ultrasonography device with the help of body surface area. Ultrasonographic measurements were recorded on patient follow-up form together with patient information.

The patients of the study were divided into two groups as those with less than 15% increase in CO after fluid replacement as "nonresponsive to fluid" (n=17), and those with a 15% or greater increase in CO as "responsive to fluid" (n=23).

Crystalloid infusion at a dose of 10 mL/kg was administered to the patients after the measurements. All measurements of the patients were performed twice, baseline and 15<sup>th</sup> minute of fluid replacement and then fluid replacement was continued with the recommended standard dose of 30 mL/kg/h. During

the whole procedure, ventilator settings were not changed. The ventilator settings of the patients were adjusted in volume-controlled mode with a tidal volume of 8 mL/kg, plateau pressure <30 cmH<sub>2</sub>O, positive end-expiratory pressure of 5 cmH<sub>2</sub>O, and inspiratory/expiratory ratio as 1/2.

## STATISTICAL ANALYSIS

The power analysis of the test was found to be  $p=0.90984$ .

The number of samples taken from the patients included in the study group was determined according to the 95% confidence level and 5% error parameters. Accordingly, the power of the study, which is conducted with 40 patients whose data were obtained for use in the study, was calculated to be 90.984%.

As a statistical method, the data obtained from our study were analyzed by SPSS [ver: 22.0, International Business Machines (IBM), Turkey] program. In evaluating the data, the parametric test assumptions were examined with Shapiro-Wilk test; when the parametric test assumptions were not fulfilled, the Mann-Whitney U test and Wilcoxon test were used. Receiver operating characteristics (ROC) curve analysis was performed to the tests to compare their sensitivity and specificity. ROC curve analyses for the estimation value of the parameters was carried out. The area under the curve (AUC), sensitivity and specificity were used to evaluate the performance of diagnostic tests. ROC was used when determining the estimation value of the parameters with the highest likelihood ratio (sensitivity/1-specificity). By finding the point closest to the (0, 1) coordinate, the cutting point was decided. By calculating the Euclidean distance to the coordinates of all the points on the line (0, 1), it was decided that the closest value is the intercept point. A p value of less than 0.05 was considered statistically significant. All statistical analyzes were interpreted at a 95% confidence level.

## RESULTS

The demographic characteristics, sepsis etiology, lactate clearance, 28-days mortality, CO increase, BUN/creatinine ratio values of the patients are shown in [Table 1](#).

**TABLE 1:** Demographic data of the patients and parameters related to sepsis.

| Demographic data        |                       | Mean  | ±SD    |
|-------------------------|-----------------------|-------|--------|
| Age (year)              |                       | 70.37 | ±18.31 |
| BSA (m <sup>2</sup> )   |                       | 1.69  | ±0.18  |
| SOFA score              |                       | 11.15 | ±4.83  |
| Weight (kg)             |                       | 64.73 | ±12.85 |
| BUN/creatinine          |                       | 29.64 | ±19.42 |
| Lactate clearance (1 h) |                       | 19.2  | ±19.99 |
|                         |                       | n     | %      |
| Causes of sepsis        | Pneumosepsis          | 17    | 42.5   |
|                         | Urosepsis             | 10    | 25     |
|                         | Wound infection       | 5     | 12.5   |
|                         | Catheter              | 4     | 10     |
|                         | Cholangiosepsis       | 3     | 7.5    |
|                         | Necrotizing fasciitis | 1     | 2.5    |
| Gender                  | Female                | 23    | 57.5   |
|                         | Male                  | 17    | 42.5   |
| CO increase             | <15%                  | 17    | 42.5   |
|                         | >15%                  | 23    | 57.5   |
| Monthly mortality       | <28 days              | 23    | 57.5   |
|                         | >28 days              | 17    | 42.5   |
| BUN/creatinine          | <20                   | 16    | 40     |
|                         | >20                   | 24    | 60     |
| Lactate clearance (1 h) | <10                   | 15    | 37.5   |
|                         | >10, <20              | 9     | 22.5   |
|                         | >20, <30              | 8     | 20     |
|                         | >30                   | 8     | 20     |

SD: Standard deviation; BSA: Body surface area; SOFA: Sequential Organ Failure Assessment; BUN: Blood urea nitrogen; CO: Cardiac output.

The mean basal PVI value was  $11.59\pm 2.29$  in the nonresponsive group. The mean PVI value of the non-responsive group after the fluid replacement was  $8.88\pm 1.76$ . The difference was found to be significant when PVI values before and after fluid replacement were compared in the nonresponsive group ( $p=0.001$ ).

When PVI values were compared in the fluid-responsive group itself, the mean basal PVI value was found to be  $22\pm 2.76$ . The mean PVI value of the group was found to be  $10.48\pm 3.09$  after the fluid replacement. The difference was statistically significant ( $p<0.001$ ) between the PVI values before and after the fluid replacement in the fluid-responsive group ([Table 2](#)).

Comparing dIVC values within the non-responsive group, the mean basal dIVC value was found to be  $16.35\pm 5.56$ . The mean dIVC value after the fluid

**TABLE 2:** Comparison of hemodynamic parameters of the patients and comparison of dIVC and PVI values that measured at basal and after fluid replacement according to CO.

|               | CO   | dIVC basal | dIVC after fluid replacement | p value |
|---------------|------|------------|------------------------------|---------|
|               |      | Mean±SD    | Mean±SD                      |         |
| Nonresponsive | <15% | 16.35±5.56 | 11.25±4.54                   | <0.001* |
| Responsive    | ≥15% | 36.55±10   | 16.55±5.97                   | <0.001* |
| p value       |      | <0.001*    | <0.001*                      |         |
|               | CO   | PVI basal  | PVI after fluid replacement  | p value |
|               |      | Mean±SD    | Mean±SD                      |         |
| Nonresponsive | <15% | 11.59±2.24 | 8.88±1.76                    | 0.001*  |
| Responsive    | ≥15% | 22±2.76    | 10.48±3.09                   | <0.001* |
| p value       |      | <0.001*    | 0.120                        |         |

\*p<0.05; significant; PVI: Pleth Variability Index; CO: Cardiac output; SD: Standard deviation.

replacement was 11.25±4.54. The difference between the baseline dIVC values and the dIVC values after the fluid replacement was found to be significant in the non-responsive group (p<0.001). When the dIVC values within the fluid responsive group were compared, the mean basal dIVC value was found to be 36.55±10. The mean dIVC value after the fluid replacement of the responsive group was 16.55±5.97. The difference between the baseline dIVC values and the dIVC values after the fluid replacement was found to be significant in the responsive group (p<0.001). When the mean basal dIVC values of fluid-responsive and nonresponsive groups were compared, the difference was significant (p<0.001). When the mean dIVC values after fluid replacement of fluid responsive and nonresponsive groups were compared, the difference was significant (p=0.001) (Table 2).

When the mean CVP, SBP, DBP, MAP, HR, PVI, SV, CO, CI, and dIVC values were compared after basal and fluid replacement, the differences were significant (p<0.05) (Table 3).

In the ROC analysis of the patients, the threshold value for CVP was 9.5 mmHg. The AUC was calculated as 0.831 (0.743-0.919). The sensitivity and specificity of the test were found to be 80% and 75%, respectively, in the evaluation of the responsiveness to fluid replacement in sepsis patients (p<0.001).

In the ROC analysis of the patients, the threshold value for PVI was 12.50. The AUC was calculated to be 0.889 (0.817-0.962). The sensitivity and speci-

**TABLE 3:** Comparison of hemodynamic parameters of the patients.

|      | Basal        | After fluid replacement | p value |
|------|--------------|-------------------------|---------|
|      | Mean±SD      | Mean±SD                 |         |
| CVP  | 8.42±1.95    | 11.40±2.31              | <0.001* |
| SBP  | 92.17±18.64  | 104±24.12               | <0.001* |
| DBP  | 54.27±11.51  | 58.95±14.15             | 0.016*  |
| MAP  | 67.25±13.12  | 75.47±18.11             | 0.001*  |
| HR   | 106.37±20.89 | 99.77±19.64             | 0.001*  |
| PVI  | 17.57±5.79   | 9.80±2.70               | <0.001* |
| SV   | 56.84±23.36  | 76.51±29.11             | <0.001* |
| CO   | 5.82±1.98    | 7.7±3.01                | <0.001* |
| CI   | 3.41±1.13    | 4.51±1.69               | <0.001* |
| dIVC | 28.73±12.37  | 14.37±4.69              | <0.001* |

\*p<0.05; significant; SD: Standard deviation; CVP: Central venous pressure; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure; HR: Heart rate; PVI: Pleth Variability Index; SV: Stroke volume; CO: Cardiac output; CI: Cardiac index; dIVC: Distensibility of inferior vena cava.

ficity of the test were found to be 72.5% and 92.5%, respectively, in the evaluation of the responsiveness to fluid replacement in sepsis patients (p<0.001).

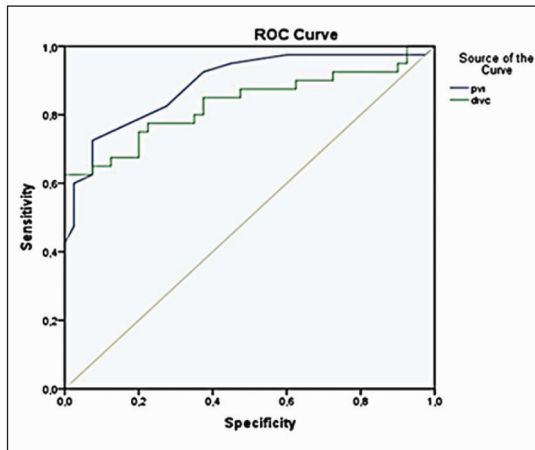
In the ROC analysis of the patients, the cut-off value for dIVC was 17.52. The AUC was calculated as 0.833 (0.739-0.926). The sensitivity and specificity of the test were found to be 77.5% and 72.5%, respectively, in the evaluation of the responsiveness to fluid replacement in sepsis patients (p<0.001) (Table 4).

ROC analysis values of CVP, PVI, dIVC values according to CO change were shown in Figure 1 and Figure 2.

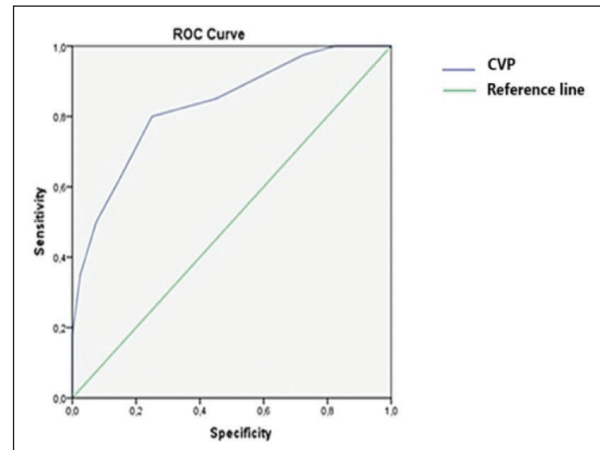
**TABLE 4:** ROC analysis values of CVP, PVI, dIVC values according to CO change.

|      | Threshold | Sensitivity | Specificity | AUC                 | LR+ | LR- | PPV  | NPV  | p value |
|------|-----------|-------------|-------------|---------------------|-----|-----|------|------|---------|
| CVP  | 9.5       | 0.800       | 0.750       | 0.831 (0.743-0.919) | 3.2 | 0.3 | 75.0 | 80.0 | <0.001* |
| PVI  | 12.50     | 0.725       | 0.925       | 0.889 (0.817-0.962) | 9.7 | 0.3 | 92.5 | 72.5 | <0.001* |
| dIVC | 17.52     | 0.775       | 0.725       | 0.833 (0.739-0.926) | 2.8 | 0.3 | 72.5 | 77.5 | <0.001* |

\*p<0.05; significant; ROC: Receiver operating characteristic; CVP: Central venous pressure; PVI: Pleth Variability Index; dIVC: Distensibility of inferior vena cava; CO: Cardiac output; AUC: Area under the curve; LR: Likeness rate; PPV: Positive predictive value; NPV: Negative predictive value.



**FIGURE 1:** Comparison of PVI and dIVC's ability to predict fluid response in ROC curve. ROC: Receiver operating characteristic; PVI: Pleth Variability Index; dIVC: Distensibility of inferior vena cava.



**FIGURE 2:** Ability of CVP to predict the response to fluid therapy in the ROC curve. ROC: Receiver operating characteristic; CVP: Central venous pressure.

## DISCUSSION

We have investigated 2 non-invasive methods (dIVC and PVI) rather than CVP which is invasive to predict the sufficiency of a fluid replacement therapy. To determine the fluid responsiveness in sepsis patients, PVI was found to be the most specific and CVP was found to be the most sensitive method.

In the literature, the dIVC cut-off value for vena cava changes in patients responding after the fluid replacement was 18%.<sup>3</sup> de Oliveira et al. found the area under the ROC curve for dIVC as  $0.84 \pm 0.10$  (0.63-1.0) and a cut-off value of 16% (sensitivity; 66.67, specificity; 100%) in a study performed in patients in need of postoperative fluid.<sup>9</sup> The area under the ROC curve for dIVC in our study was 0.83 (0.73-0.92) and the cut-off value was 17.52% (sensitivity; 77.5%, specificity; 72.5%). Although the 17.52% threshold in our study was consistent with the literature, it was possible to separate patients who could respond to fluid

replacement. When specificity and sensitivity data were examined for dIVC, high selectivity values were found. Since our patient population consisted of sepsis patients, a homogeneous distribution was achieved.

Pişkin and Öz included 72 mechanically ventilated patients in their study.<sup>10</sup> They investigated the effect of passive leg raising test on dIVC and PVI. They found the dIVC with 80% sensitivity and 87.5% specificity at a threshold value of >23.8%, and also in their study; PVI at a threshold value of >14% provided 95% sensitivity and 81.2% specificity. The present study differs from Pişkin and Öz's research in terms of fluid replacement. The sensitivity of PVI and dIVC to fluid replacement were investigated in order to passive leg raising test. So, the present study is more important in revealing the sensitivity of these tests to fluid-response.

It is not surprising that the PVI threshold value varies between studies, as there are many factors such as the degree of disease, respiratory settings (positive

end-expiratory pressure, tidal volume, etc.) or the use of norepinephrine. The fluid needs of the patients should be determined under these conditions.

For volume expansion, vein expanders like 300 mL bolus fluid replacement-like effect with passive leg raise test, 7 mL/kg 30 minute gelatin infusion, 7 mL/kg 30 minute hydroxyethyl starch infusion, 500 mL intravenous crystalloid infusion for 15 minutes were used in studies based on changes in vena cava diameter considering CO as a reference value.<sup>3,11</sup> Since our patient population was sepsis patients, we preferred crystalloid as a vasodilator with the recommendation of the sepsis survival campaign. We started to replace the fluid in a dose of 10 mL/kg for the first 15 minutes, and then fluid replacement was continued with the recommended standard dose of 30 mL/kg/h, and avoided adverse results with a probable aggressive protocol.

The patient population in our study consisted only of adult patients, and the mean age was found to be 70.37 years, and our study, as in many studies, revealed that the elderly population was in the majority in the age spectrum of sepsis patients.<sup>12-14</sup>

Comorbidities and decreased organ reserve in elderly patients lead to an increase in morbidity after intensive care treatment and an increase in mortality during the ICU hospitalization. Although the mortality percentage was not calculated according to the decades in our study, it supports the increase in mortality above the age of 65 in sepsis developing in critically ill patients because of the average age of 70.37 years.<sup>15</sup> Opal et al. found the mortality rate to be 32% in severe sepsis in 2005. They showed that this ratio increased to 54% when septic shock developed.<sup>16</sup>

In the study of Adrie et al., 44% of the patients had pneumosepsis and 12.9 % had urosepsis.<sup>14</sup> In the study performed by Nasir et al., the causes of sepsis were evaluated according to gender and respiratory infections, and urinary tract infections were found dominant in both men and women.<sup>17</sup> In our study, the causes of sepsis were found to be pneumosepsis (42.5%) and urosepsis (25%), which was consistent with the literature in terms of these rates.

In our study, 57.5% of the patients responded to fluid replacement. Since it contains close values in

similar studies conducted in CO monitoring in septic patients, our study was found consistent with the literature.<sup>3</sup>

There were some limitations of this study. One of them was standardizing patients in the critical patient population. Another limitation was the number of the patients. It's obvious that more studies with largest patient numbers are needed to clarify this subject.

## CONCLUSION

In conclusion, PVI was found to be more specific but less sensitive than dIVC. dIVC is less sensitive and less specific than CVP. Because CVP is an invasive technique, searching for a non-invasive method to measure the fluid responsiveness must go on with researches with high number of patients. At this point, dIVC measurement as a simple method by echocardiography and PVI measurement using a PI may give useful results without invasive catheterisation.

### Acknowledgement

*We thank to all the members of anaesthesiology departments.*

### Source of Finance

*During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.*

### Conflict of Interest

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### Authorship Contributions

**Idea/Concept:** Orhan Göktürk, Onur Avcı; **Design:** Orhan Göktürk, Onur Avcı; **Control/Supervision:** Oğuz Gündoğdu, Ahmet Cemil İsbir; **Data Collection and/or Processing:** Oğuz Gündoğdu; **Analysis and/or Interpretation:** İclal Özdemir Kol, Sinan Gürsoy, Kenan Kaygusuz; **Literature Review:** İclal Özdemir Kol, Sinan Gürsoy, Kenan Kaygusuz; **Writing the Article:** rhan Göktürk, Onur Avcı, Oğuz Gündoğdu; **Critical Review:** Ahmet Cemil İsbir, İclal Özdemir Kol; **References and Fundings:** Sinan Gürsoy, Kenan Kaygusuz.

## REFERENCES

1. Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. *Chest*. 2008;134(1):172-8. [Crossref] [PubMed]
2. Osman D, Ridet C, Ray P, Monnet X, Anguel N, Richard C, et al. Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge. *Crit Care Med*. 2007;35(1):64-8. [Crossref] [PubMed]
3. Barbier C, Loubières Y, Schmit C, Hayon J, Ricôme JL, Jardin F, et al. Respiratory changes in inferior vena cava diameter are helpful in predicting fluid responsiveness in ventilated septic patients. *Intensive Care Med*. 2004;30(9):1740-6. [Crossref] [PubMed]
4. Au SM, Vieillard-Baron A. Bedside echocardiography in critically ill patients: a true hemodynamic monitoring tool. *J Clin Monit Comput*. 2012;26(5):355-60. [Crossref] [PubMed]
5. Grocott MP, Dushianthan A, Hamilton MA, Mythen MG, Harrison D, Rowan K; Optimisation Systematic Review Steering Group. Perioperative increase in global blood flow to explicit defined goals and outcomes after surgery: a Cochrane Systematic Review. *Br J Anaesth*. 2013;111(4):535-48. [Crossref] [PubMed] [PMC]
6. Benes J, Giglio M, Brienza N, Michard F. The effects of goal-directed fluid therapy based on dynamic parameters on post-surgical outcome: a meta-analysis of randomized controlled trials. *Crit Care*. 2014;18(5):584. [Crossref] [PubMed] [PMC]
7. Şen G, Düğür C, Avcı O, Gürsoy S, Kaygusuz K, Kol İÖ, et al. Total kalça cerrahisi operasyonunda non-invaziv PVI (Pleth Variability İndeks) monitörizasyonunun sıvı ve kan transfüzyonuna, intraoperatif hemodinami üzerine etkinliğinin değerlendirilmesi [Investigation of the efficacy of PVI (Pleth Variability İndeks) monitorization on intraoperative fluid and blood transfusion, intraoperative hemodynamics in total hip surgeries]. *Van Tıp Derg*. 2018;25(2):138-45. [Crossref]
8. Yüksek A. Utility of the Pleth Variability Index in predicting anesthesia-induced hypotension in geriatric patients. *Turk J Med Sci*. 2021;51(1):134-9. [Crossref] [PubMed] [PMC]
9. de Oliveira OH, Freitas FG, Ladeira RT, Fischer CH, Bafi AT, Azevedo LC, et al. Comparison between respiratory changes in the inferior vena cava diameter and pulse pressure variation to predict fluid responsiveness in postoperative patients. *J Crit Care*. 2016;34:46-9. [Crossref] [PubMed]
10. Pişkin Ö, Öz İİ. Accuracy of pleth variability index compared with inferior vena cava diameter to predict fluid responsiveness in mechanically ventilated patients. *Medicine (Baltimore)*. 2017;96(47):e8889. [Crossref] [PubMed] [PMC]
11. Moretti R, Pizzi B. Inferior vena cava distensibility as a predictor of fluid responsiveness in patients with subarachnoid hemorrhage. *Neurocrit Care*. 2010;13(1):3-9. [Crossref] [PubMed]
12. Kim J, Kim K, Lee H, Ahn S. Epidemiology of sepsis in Korea: a population-based study of incidence, mortality, cost and risk factors for death in sepsis. *Clin Exp Emerg Med*. 2019;6(1):49-63. [Crossref] [PubMed] [PMC]
13. Driessen RG, van de Poll MCG, Mol MF, van Mook WNKA, Schnabel RM. The influence of a change in septic shock definitions on intensive care epidemiology and outcome: comparison of sepsis-2 and sepsis-3 definitions. *Infect Dis (Lond)*. 2018;50(3):207-13. Erratum in: *Infect Dis (Lond)*. 2018;50(3):245. [Crossref] [PubMed]
14. Adrie C, Alberti C, Chaix-Couturier C, Azoulay E, De Lassence A, Cohen Y, et al. Epidemiology and economic evaluation of severe sepsis in France: age, severity, infection site, and place of acquisition (community, hospital, or intensive care unit) as determinants of workload and cost. *J Crit Care*. 2005;20(1):46-58. [Crossref] [PubMed]
15. Fleischmann C, Thomas-Rueddel DO, Hartmann M, Hartog CS, Welte T, Heublein S, et al. Hospital incidence and mortality rates of sepsis. *Dtsch Arztebl Int*. 2016;113(10):159-66. [PubMed] [PMC]
16. Opal SM, Girard TD, Ely EW. The immunopathogenesis of sepsis in elderly patients. *Clin Infect Dis*. 2005;41 Suppl 7:S504-12. [Crossref] [PubMed]
17. Nasir N, Jamil B, Siddiqui S, Talat N, Khan FA, Hussain R. Mortality in sepsis and its relationship with gender. *Pak J Med Sci*. 2015;31(5):1201-6. [Crossref] [PubMed] [PMC]