Abstract

Introduction: Lung-protective ventilation strategy and prone positioning are the strategies practiced to manage patients suffering from acute respiratory distress syndrome (ARDS). Inferior Vena Cava Distensibility (dIVC) Index has been used for predicting fluid responsiveness (FR) in supine position. We conducted this study to observe the utility of dIVC in prone position in ARDS patients and compare it with esophageal Doppler (ED) parameters. Materials and Methods: After ethical clearance, a prospective observational pilot study was conducted in a 12-bedded tertiary care hospital. Adult ARDS patients who were treated with prone ventilation were included. Informed consent was taken from the relatives. IVC was visualized through right lateral approach both in supine and prone positions. We compared IVC distensibility and ED parameters, first in 45° head up and then in prone. FR was defined as an increase in the stroke volume of ≥15% as measured by ED. The patients with dIVC >18% were assumed to be fluid responsive. Statistical analysis was done using SPSS software version 20. Results: Twenty-five patients met the inclusion criteria. ARDS was (mean P/F ratio 116.64 ± 44.76) mostly due to pulmonary etiology. Out of 25 patients, 10 patients were fluid responsive based on dIVC (cutoff >18%) in supine position. When compared to ED values after passive leg raising, dIVC had a sensitivity and specificity of 77.78% and 81.25%, respectively, in predicting FR with a moderate-to-absolute agreement between the two methods. IVC distensibility showed statistically significant negative correlation with corrected flow time (FTc) values both in supine and in prone positions. Conclusion: IVC variability can be observed in acute respiratory distress syndrome patients in prone position. Inferior Vena Cava Distensibility correlates with flow time in both the positions.

Keywords: Acute respiratory distress syndrome, esophageal Doppler, inferior vena cava, prone
response to fluid with variable accuracy. Passive leg raising (PLR) is a reversible fluid challenge without much harm of the actual fluid bolus. Assessing FR in prone position is more complicated, as proning itself may have variable effects on hemodynamics. Some studies suggest increased cardiac output,[8] whereas some show a decrease in cardiac output[9] after turning the patient to prone. Further on, proning may affect the respiratory parameters and abdominal pressures as well. Various technologies for assessing FR are less well tested in prone position.

Pulmonary artery catheter (PAC) monitoring has been the gold standard for hemodynamic monitoring for almost four decades. However, its use is on the decline due to its complications, especially in the ICU. There has been a shift from invasive to minimally invasive or noninvasive techniques for hemodynamic monitoring in critically ill patients.[10-12]

Esophageal Doppler monitoring (EDM) is a minimally invasive technique with high validity as a hemodynamic monitoring tool. Its clinical utility is well tested for assessing hemodynamic perturbations in both operation theater[13,14] and ICU.[15] It has also been used with reliable accuracy in prone patients intraoperatively.[16,17] A change of stroke volume (SV) (10%–15%) in response to fluid challenge or PLR is used for the prediction of FR. Corrected flow time (FTc) has been described to be an indicator of preload.[16,18] It has been utilized for accurate prediction of FR, even in prone position.[14]

Inferior Vena Cava Distensibility Index (dIVC), measured by ultrasonography, is one of the much studied tools for predicting FR.[19-23] in ICU. It is completely noninvasive and with an easy learning curve. This technique utilizes the principle of heart–lung interactions induced by mechanical ventilation in closed chest condition. IVC is usually visualized at subxiphoid region. However, lateral approach at the right midaxillary line is associated with an equivalent measurement.[24,25] Respiratory variation of IVC diameter during positive pressure ventilation has been suggested as an indicator of FR. dIVC cutoff of >18% was found to correlate with FR.[19] However, its role has so far not been studied in ARDS patients or in prone position.

Fluid resuscitation septic shock, with ARDS, is challenging due to hypoxia and associated cardiac dysfunction. Turning the patient to prone may further complicate the scenario by an inability to use tools such as echocardiography and PLR test. Intensivists use dIVC in supine position for predicting FR, but its (dIVC) utility in prone position remains unexplored.

The aim of this prospective observational study was to observe the utility of dIVC in prone position in ARDS patients for predicting FR in reference to EDM parameters.

Our primary objective was to observe the feasibility of measuring dIVC in prone position. The secondary objective was to observe its correlation with EDM-derived parameters. For this purpose, the authors compared dIVC with corrected flow time (FTc) in supine and prone positions.

**Materials and Methods**

This was a prospective observational pilot study conducted in a tertiary care 12-bedded medical surgical ICU over a period of 12 months from February 2016 to January 2017. The study was approved by the institutes’ Ethics Committee. Informed consent was taken from the relatives of the patients. All adult patients with ARDS, who required proning, were included. Patients who had contraindication to proning or application of transesophageal Doppler were excluded. We also excluded all those patients who required any change of ventilatory or vasopressor support during the study period. The standard treatment protocol was not influenced by the study observations.

**Procedure**

The baseline clinical and laboratory parameters were noted at the start of the evaluation. The demographic data including age, sex, weight, and height were noted. Ideal body weight was calculated for tidal volume delivery (8 mL/kg). All the patients had invasive arterial blood pressure monitoring with transducer at phlebostatic axis and central venous catheter in situ. All the patients were deeply sedated and paralyzed (if required) with muscle relaxation for complete synchronization with the ventilator. Intra-abdominal pressure (IAP) was measured in supine position with transducer at the iliac crest level by revised Kron’s technique by Cheatham and Safcsak.[26]

**Inferior vena cava measurement**

The IVC was assessed by the echocardiography probe (2–5 MHz) of Sonosite machine in the right midaxillary line, with liver being the acoustic media [Figure 1]. The distensibility index (dIVC) was measured during one respiratory cycle. dIVC was calculated as [(maximum diameter − minimum diameter)/minimum diameter] × 100%. We assumed patients with dIVC >18% as fluid responsive based on the results of a previous study.[19]

**Transesophageal Doppler**

A 4-MHz ED probe connected to a spectral analyzer (CardioQ, Deltex Medical, Chichester, UK) was inserted by an experienced operator via oral/nasal route into the esophagus and positioned to obtain proper aortic velocity waveform, by adjusting gain, rotation, and depth on the screen with adequate Doppler acoustics.

**Study protocol**

The parameters (hemodynamic, respiratory, and ED parameters) were measured at 45° head up (T1) in supine position, and then after 1 min of PLR (T2) and again after 5 min of proning (T3) without changing any ventilatory settings or rate of vasopressors (The patients were excluded if any of the above were done for any specific indication.) dIVC was measured at T1 and T3. IAP was measured in supine flat position and again at T3.

Patients with dIVC >18% were assumed to be fluid responsive (dIVC cutoff >18% based on a previous study.[19]) The results of dIVC were compared with FR determined by EDM (SV variation [SVV] >15%) after PLR. The EDM parameters
were measured by a physician who was trained in EDM. All patients were made prone with arms extended using appropriate thoracopelvic supports, minimizing pressure on the abdomen and taking all necessary precautions required for prone positioning. dIVC and EDM values were noted again in prone position.

**Statistical analysis**

Descriptive data were summarized as mean (standard deviation) and median (interquartile range). Data were analyzed using paired *t*-test (if normal) and Wilcoxon test for nonnormal data. Categorical data were presented in number (%). All results were evaluated by Spearman’s correlation analysis. All tests were two tailed, and *P* < 0.05 was considered statistically significant. Data were analyzed using SPSS software version 20 (IBM Inc., Chicago, IL, USA).

**Results**

A total of 25 patients were included in the study [Figure 2]. Table 1 shows baseline demographics and hemodynamic and respiratory parameters at study entry. The mean APACHE II score was 21.56 ± 6.23 and SOFA score was 11.56 ± 3.82. Twenty-four patients had septic shock requiring vasopressor support. All the patients had either moderate or severe ARDS (mean P/F ratio 116.64 ± 44.76). Average fluid balance within 72 h before proning was 1.71 ± 0.91 L. Twelve patients survived at ICU discharge.

In supine position, ten patients were found with dIVC >18%, whereas 12 patients were found to be fluid responsive (PLR responsive) based on the observation of change of SV (>15%) from EDM. When compared with EDM SVV for FR in supine position, dIVC was found to have a sensitivity and specificity of 77.8% and 81.25%, respectively, with an overall accuracy of 79.50%. Kappa statistics was 0.58 (95% confidence interval = 0.25 – 0.91, *P* = 0.004), showing moderate-to-absolute agreement between the two methods.

Table 2 represents clinical, EDM, and dIVC values for all patients in supine (T1), after PLR (T2), and in prone positions (T3).

**Figure 2: Study inclusion design**

**Table 1: Baseline characteristics of the patients**

| Characteristics (n = 25) | Mean ± SD/n |
|-------------------------|-------------|
| Age (years)             | 51.56±16.44 |
| Sex (female/male)       | 4/21        |
| APACHE II at admission  | 21.56±6.23  |
| SOFA at admission       | 11.56±3.82  |
| Septic shock (yes/no)   | 24/1        |
| Type of illness (medical/surgical) | 23/2 |
| Pulmonary/extrapulmonary ARDS | 18/7 |
| Dose of norepinephrine (µg/kg/min) | 0.36±0.54 |
| P/F ratio               | 116.64±44.76|
| Lactate level (mg/dL)   | 17.14±8.71  |
| Fluid balance at last 72 h (L) | 1.71±0.91 |
| Length of ICU stay (days) | 28.00±19.16 |
| Survivor/nonsurvivor    | 12/13       |

APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; SD: Standard deviation; ARDS: Acute respiratory distress syndrome; ICU: Intensive care unit

**Table 2: Comparative representation of hemodynamics, esophageal Doppler monitoring, and Inferior Vena Cava Distensibility index in supine (T1), after passive leg raising (T2), and after proning (T3) in all patients**

| Parameter         | T1          | T2          | T3          |
|-------------------|-------------|-------------|-------------|
| HR                | 116.5±23.42 | 117.14±23.20| 117.09±24.51|
| MAP               | 79.41±5.62  | 79.91±7.28  | 81.50±9.17  |
| SD                | 13.51±6.22  | 14.07±5.12  | 13.05±5.41  |
| SV                | 66.82±22.94 | 69.77±18.12 | 64.36±20.68 |
| SVI               | 33.67±10.63 | 36.47±9.55  | 35.12±11.94 |
| CO                | 7.08±1.54   | 7.69±1.59   | 7.62±2.56   |
| CI                | 3.75±0.83   | 4.14±0.87   | 4.01±1.31   |
| PV                | 90.85±31.10 | 93.82±28.88 | 98.25±34.64 |
| FTc               | 360±64.07   | 361.73±77.41| 352.04±58.37|
| MA                | 10.04±4.15  | 9.87±3.89   | 12.4±5.73   |
| SVR               | 884.91±292.17| 779.68±276.83| 814.77±304.13|
| SVRI              | 1523.3±382.71| 1361.79±334.36| 1490.67±499.50|
| IVC variability   | 15.76±6.91  | -           | 14.18±9.25  |

Data presented as mean±SD. SD: Standard deviation; HR: Heart rate; MAP: Mean arterial pressure; SD: Stroke distance; SV: Stroke volume; SVI: Stroke Volume Index; CO: Cardiac output; CI: Cardiac index; PV: Peak velocity; MA: Mean acceleration; SVR: Systemic vascular resistance; SVRI: SVR index; FTc: Corrected flow time; IVC: Inferior vena cava

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**Figure 1:** Inferior vena cava assessment in prone position

**Figure 2:** Study inclusion design
Table 3 represents the comparative data between patients with dIVC >18% and dIVC <18% in supine position. dIVC showed significant correlation with flow time corrected (FTc: EDM-derived value) in supine position (P = 0.012).

Table 4 demonstrates the comparison between patients with dIVC >18% and dIVC <18% in prone position. After proning, dIVC was >18% in eight patients. In prone, EDM-derived FTc was found to have statistically significant correlation with dIVC (P = 0.04).

The respiratory compliance and IAP did not differ significantly [Table 5] between the dIVC groups after proning the patient.

**Discussion**

Around 10%–15% of the patients admitted in ICU suffer from ARDS. Nearly 20%–25% of them require mechanical ventilation.[27,28] Severe ARDS, defined by PaO2/FiO2 ratio <100, has an associated mortality of 46%.[29] Prone ventilation strategy may be helpful in ARDS to improve oxygenation when traditional modes of ventilation fail. There are controversial data on effect on mortality; however, early and prolonged proning is associated with significant mortality benefit.[30,31] Prolonged proning is associated with some major complications including hemodynamic perturbations. Hypotension may be due to mechanical complications or sepsis. Fluid resuscitation may be hampered by hypoxia. Further assessment of FR is required in this situation. Proning itself poses difficulty to the introduction of invasive and semi-invasive monitors which are required for the assessment of FR. IVC is a noninvasive technique used for the assessment of FR in supine. We desired to observe its role in prone position.

We compared dIVC with EDM in supine position in predicting FR and found moderate agreement between the two methods. We regarded EDM as a standard for measuring FR, as it has been shown to predict FR with good accuracy in supine as well as in prone positions.[13-16]

dIVC had significant correlation with FTc, both in supine position (after PLR) and prone position.

IVC measurement is easily available bedside, noninvasive, and can easily be done by nonradiologist trainee intensivist after a short period of training. Measurement of IVC changes is useful for fluid assessment and resuscitation in mechanically ventilated patients in septic shock.[20-22] IVC diameter is measured usually at the level of junction of IVC and right atrium or 2–3 cm beyond that at epigastrium region. During ventilation, the IVC diameter changes according to the phases of breathing. In mechanically ventilated patients, IVC diameter increases during inspiration due to rise in right atrial pressure and decreases during expiration due to release of the airway pressure. The variability in diameter has been used for the diagnosis of FR. It has been shown that the variability of 12%–18% is suggestive of FR in mechanically ventilated patients.[19,21]

**Table 3: Comparison between patients with Inferior Vena Cava Distensibility Index >18% and Inferior Vena Cava Distensibility Index <18% in supine position**

| Parameters          | dIVC >18% (n=10) | dIVC <18% (n=15) | P    |
|---------------------|------------------|------------------|------|
| T1HR                | 115.80±24.49     | 116.40±20.94     | 0.94 |
| T1norad dose        | 0.31±0.43        | 0.39±0.62        | 0.72 |
| T1SD                | 11.39±4.12       | 16.78±7.70       | 0.05 |
| T1SV                | 64.00±18.62      | 70.87±24.81      | 0.46 |
| T1SVI               | 32.53±12.32      | 34.53±8.74       | 0.63 |
| T1CO                | 6.92±1.70        | 7.18±1.31        | 0.67 |
| T1CI                | 3.59±0.95        | 3.85±0.67        | 0.42 |
| T1MA                | 9.96±4.59        | 10.57±4.43       | 0.74 |
| T1PV                | 85.00±29.75      | 99.12±32.39      | 0.28 |
| T1CVP               | 11.00±1.15       | 11.13±2.72       | 0.88 |
| T1SVR               | 929.40±270.20    | 833.33±282.19    | 0.40 |
| T1SVRI              | 1598.59±440.28   | 1468.43±301.47   | 0.38 |
| T1FTc               | 319.50±80.39     | 381.60±35.64     | 0.01 |
| T1dIVC              | 22.15±2.28       | 10.46±4.77       | 0.01 |

Data presented as mean±SD, P<0.05 taken as statistically significant value. SD: Standard deviation; HR: Heart rate; SD: Stroke distance; SV: Stroke volume; SVI: Stroke Volume Index; CO: Cardiac output; CI: Cardiac index; PV: Peak velocity; MA: Mean acceleration; SVR: Systemic vascular resistance; SVRI: SVR index; FTc: Corrected flow time; CVP: Central venous pressure; dIVC: Inferior Vena Cava Distensibility Index

**Table 4: Comparison between patients with Inferior Vena Cava Distensibility Index >18% and Inferior Vena Cava Distensibility Index <18% in prone position**

| Parameters          | dIVC >18% (n=8) | dIVC <18% (n=17) | P    |
|---------------------|-----------------|------------------|------|
| T3HR                | 118.25±26.152   | 117.00±22.285    | 0.90 |
| T3norad dose        | 0.3788±0.4739   | 0.3529±0.59      | 0.91 |
| T3SD                | 12.512500±6.0059124 | 14.235294±5.350346 | 0.47 |
| T3SV                | 63.75±16.926    | 64.41±21.027     | 0.93 |
| T3SVI               | 34.982894±9.37  | 34.901585±12.54  | 0.98 |
| T3CO                | 7.537500±2.60   | 7.629412±2.48    | 0.93 |
| T3CI                | 4.1125±1.46     | 3.9806±1.24      | 0.81 |
| T3MA                | 12.656250±6.6517150 | 12.870588±5.2016265 | 0.93 |
| T3PV                | 93.55±30.77     | 106.77±37.04     | 0.39 |
| T3CVP               | 13.50±1.3       | 14.18±4.01       | 0.65 |
| T3SVR               | 870.88±3.1881   | 855.82±287.57    | 0.90 |
| T3SVRI              | 1588.85±588.01  | 1416.47±462.84   | 0.43 |
| T3FTc               | 318.13±58.852   | 355.18±31.297    | 0.04 |
| T3dIVC              | 20.37±1.18      | 10.24±5.09       | 0.01 |

Data presented as mean±SD, P<0.05 taken as statistically significant value. SD: Standard deviation; HR: Heart rate; SD: Stroke distance; SV: Stroke volume; SVI: Stroke Volume Index; CO: Cardiac output; CI: Cardiac index; PV: Peak velocity; MA: Mean acceleration; SVR: Systemic vascular resistance; SVRI: SVR index; FTc: Corrected flow time; CVP: Central venous pressure; dIVC: Inferior Vena Cava Distensibility Index

In this study, we observed IVC changes in prone position and correlated with EDM-derived parameters. However, measuring IVC in the usual site is often not feasible in prone position. Hence, we chose the midaxillary line for IVC measurement usually at the level of junction of IVC and right atrium or 2–3 cm beyond that at epigastrium region. During ventilation, the IVC diameter changes according to the phases of breathing. In mechanically ventilated patients, IVC diameter increases during inspiration due to rise in right atrial pressure and decreases during expiration due to release of the airway pressure. The variability in diameter has been used for the diagnosis of FR. It has been shown that the variability of 12%–18% is suggestive of FR in mechanically ventilated patients.[19,21]
Table 5: Respiratory parameters and intra-abdominal pressure compared between patients with Inferior Vena Cava Distensibility Index >18% and Inferior Vena Cava Distensibility Index <18%

| dIVC | Preprone | Postprone |
|------|----------|-----------|
| >18% | <18%     | >18%      | <18%     |
| Plateau pressure | 29.20±1.39 | 30.00±0.65 | 29.63±1.30 | 29.82±0.52 |
| Compliance | 22.32±6.48 | 20.07±6.66 | 21.15±4.14 | 19.58±4.96 |
| IAP | 8.20±2.40 | 9.00±3.04 | 9.63±2.20 | 10.53±3.46 |

Data presented as mean±SD, P<0.05 taken as statistically significant value. IAP: Intra-abdominal pressure; dIVC: Inferior Vena Cava Distensibility Index; SD: Standard deviation.

Visualization. In spite of that, we had to exclude 14 patients due to nonvisualization of IVC at that site.

There is a lot of research regarding the utility of EDM in predicting FR with good correlation with the PAC. It has even been studied in prone position. The change of SV in response to fluid bolus or PLR is used to predict FR. Corrected flow time, though a static parameter, is a good indicator of preload. It has been previously studied to identify fluid responders successfully.\(^\text{16}\) We found statistically significant correlation for dIVC with the FTc value in supine and even after prone positioning. To our knowledge, this is the first study which tried to observe dIVC in prone patients.

Our study has some limitations. The use of lateral approach for IVC measurement is not widespread, and one may face difficulty especially in obese or edematous patients. Another limitation of our study was small sample size. We did not give fluid challenge in prone position which could have better predicted the role of dIVC since it was not the aim of this study. dIVC was correlated with FTc which itself is a static variable. We had to increase tidal volume to 8 ml/kg during the study period, which may not be possible in all patients.

**Conclusion**

Inferior Vena Cava Distensibility can be observed in prone patients. However, we need further insight and larger trials on its utility in prone position and to use it as a guide for fluid resuscitation.

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**Conflicts of interest**

There are no conflicts of interest.

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