Ultrasound-guided inferior vena cava collapsibility index as a predictor of fluid responsiveness in septic cancer patients


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ABSTRACT

Background & objective: Intravenous fluid therapy is a critical step in the resuscitation of patients suffering from sepsis and septic shock. Meticulous hemodynamic monitoring is necessary before as well as during the fluid therapy to avoid under- as well as over-loading the patient. An evaluation of fluid status has been suggested to be done non-invasively using the inferior vena cava collapsibility index (IVC-CI). We assessed the effectiveness of IVC-CI in evaluating septic patients' responses to fluid therapy at our institution.

Methodology: Forty cancer patients with spontaneous breathing, who met sepsis criteria and were admitted to the intensive care unit, were included in this cross-sectional study. Over the course of three hours, the patients received crystalloids intravenously at a rate of 30 ml/kg, while CVP, ultrasonography guided IVC-CI measurement, and the vital sign monitoring was done every 30 min. Patients were divided into a responder group and a non-responder group based on a 10% change in cardiac output (CO) one hour later. IVC-CI variations in the volume responsiveness prediction served as the main outcome measure.

Results: According to the change in CO one hour after starting fluid treatment, 29 patients (72.5%) were classified as fluid responsive and the remaining 11 (27.5%) as fluid non-responsive. In the two groups, HR and IVC-CI decreased significantly; whereas MAP, CVP, and CO increased significantly. ROC-curve analysis showed a percent change ≥ 3.4% of IVC-CI predicted positive responsiveness with a sensitivity of 72.4% and a specificity of 63.6%. These values were 79.3% and 72.7%, respectively, for a change ≥ 6.3% after one hour. The baseline value of IVC-CI was not predictive of responsiveness.

Conclusion: In cancer patients with sepsis or septic shock, the change in inferior vena cava collapsibility index during the first hour of fluid therapy can predict fluid responsiveness with a moderate degree of accuracy.

Abbreviations: CO - Cardiac output; CVP - central venous pressure; IVC- inferior vena cava; IVC-CI - inferior vena cava collapsibility index; MAP - Mean arterial pressure; SV - Stroke volume

Keywords: Cancer; ICU; Critically sick; Inferior vena cava; IVC collapsibility index; Non-invasive cardiometry; Sepsis

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1. INTRODUCTION

Sepsis and septic shock are characterized by insufficient tissue oxygen delivery due to peripheral hypoperfusion. Intravenous fluid infusion is widely thought to enhance organ perfusion and reverse cellular dysxia, especially in the early stages of sepsis and septic shock. Fluid delivery expands intravascular volume and increases left ventricular end-diastolic volume, or preload, which raises stroke volume (SV). However, the process is not that simple, as sepsis and septic shock have a complicated pathophysiology with both cardiogenic and distributive elements. The patients have already compromised cardiac function and thus may experience worsening of their condition due to increasing cardiac preload. The inflammatory process linked to sepsis at the peripheral level increases capillary permeability and impairs endothelial function. Organ edema, fluid leakage into the interstitial compartment, and a decline in peripheral perfusion consequently take place.

Thus, volume excess may exacerbate central and peripheral circulation problems. Organ dysfunction, extended hospitalizations in the intensive care unit (ICU), prolonged mechanical breathing, and increased mortality rates have all been related to it. Only half of septic patients are thought to respond to fluid therapy.

Fluid infusion, therefore, requires continuous hemodynamic monitoring, since it is the most important stage in the resuscitation of patients suffering from sepsis. Fluid management has traditionally been adjusted based on the assessment of vital signs, laboratory testing (serum lactate level, mixed venous oxygen saturation), physical examination, and static evaluation of cardiac preload, such as central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP).

The IVC collapsibility index (IVC-CI) is one of the recent non-invasive techniques for evaluating fluid status and has demonstrated promising outcomes when used as a reference for fluid therapy. Many studies evaluated the effectiveness of IVC-CI to ascertain whether there is a relationship between CVP and fluid responsiveness in patients with sepsis and septic shock.

We evaluated the IVC-CI as an indicator for assessing the response of septic patients to the fluid therapy according to the guidelines of The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) within the first three hours of ICU admission.

2. METHODOLOGY

This cross-sectional study comprised forty cancer patients who met the criteria for sepsis when they arrived at the ICU. The study was carried out at National Cancer Institute of Cairo University from January to October of 2022. The diagnosis of sepsis was made using the following criteria: an immediate rise of two or more SOFA points; suspected or confirmed infection; and life-threatening organ failure brought on by a dysregulated host response to infection. The National Cancer Institute’s ethical committee approved the project. After a thorough description of the study design and the possible advantages and disadvantages of the study methodology, a first-degree relative of the enrolled patients gave written informed consent.

The inclusion criteria were spontaneously breathing patients, aged 18-60 y, ASA class II and fulfilling the criteria of sepsis. Exclusion criteria included active bleeding, anticipated surgery or dialysis in the next 8 hours, aortic regurgitation, arrhythmias, cardiac tamponade, hepatic or end-stage kidney dysfunction, massive pleural effusion, mechanical ventilation, New York Heart Association (NYHA) III and IV patients, severe acute respiratory distress syndrome, tense ascites, or using a vasopressor infusion.

2.1. Interventions

Intravenous blood samples were withdrawn to measure lactate and pro-calcitonin levels on admission to the ICU. A central venous line (CVL) was inserted and the CVP was measured, then an ultrasound-guided IVC-CI was determined as a baseline reading. During ICU admission, the patients were given crystalloids at a rate of 30 ml/kg over the first 3 h of ICU admission while monitoring vital signs, CVP, and IVC-CI every 30 min. Laboratory samples were withdrawn at the end of the three hours to calculate the changes in lactate and procalcitonin levels. Cardiac output was measured using the OSYPKA Medical ICON™ Noninvasive Cardiometer™ Model C3 (Serial Number: 1817403).

Patients were divided into 2 groups depending on the change in CO one hour after volume expansion compared with baseline: a responder group (CO increased ≥ 10%) and a non-responder group (CO increased < 10%). This was based on previous studies defining volume responsiveness as a 10%-15% increase in cardiac output or stroke volume.

2.2. Inferior Vena Cava Collapsibility Index (IVC-CI)

The device utilized was a Fujifilm Sonosite M-Turbo C Ultrasound System (SN: Q58M5D; REF: P17000-25). The inferior vena cava (IVC), which is located in the retroperitoneum to the right of the aorta, was evaluated using a low-frequency phased array transducer (2–5 MHz; REF: P20402-11; SN: 04MK49). The IVC diameter was assessed at or close to the point where it

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connected to the hepatic veins. The probe was placed in the subxiphoid 4-chamber position with the probe marker positioned vertically to locate the right ventricle and atrium to correctly observe the IVC. As the probe gradually moved in the direction of the spine, the convergence of the IVC with the right atrium was observed. To find the point where the IVC meets the hepatic veins, it was followed inferiorly. The M-mode The IVC's Doppler ultrasound was utilized to visually record the vessel's absolute dimensions as well as its dynamic caliber changes during inspiration and expiration. Following the IVC viewing, the US screen was frozen, and the maximum and minimum IVC diameters were recorded using the US machine's caliper function.

The IVC-CI is calculated using the following equation:

\[
\text{IVC-CI} = \frac{\text{IVCmax} - \text{IVCmin}}{\text{IVCmax} \times 100}\%
\]

The primary outcome measure was the value of IVC-CI changes in the prediction of volume responsiveness. The secondary outcome measures were correlating the IVC-CI with the HR, CVP, MAP, lactate clearance, and procalcitonin.

### 2.3. Statistical analysis

Statistical analysis was done using IBM© SPSS© Statistics version 23 (IBM© Corp., Armonk, NY, USA). Numerical data are summarized as mean and standard deviation or median and range. For quantitative data, comparison between the two groups was done using independent sample t-tests. Pearson product-moment was used to estimate the correlation between numerical variables. The Receiver Operating Characteristic (ROC) curve was used for the prediction of cut-off values. A p-value less than or equal to 0.05 will be considered statistically significant.

### 3. RESULTS

Table 1 shows the baseline demographic and clinical characteristics of the studied group. According to the change in CO one hour after starting fluid treatment, 29 patients (72.5%) were classified as fluid responsive and the remaining 11 (27.5%) as fluid non-responsive.

Table 2 shows the vital signs, CVP, CO, and IVC-CI, at 0 hours and after the end of treatment in fluid-responsive and fluid-non-responsive groups. In the two groups, HR and IVC-CI decreased significantly, whereas MAP, CVP, and CO increased significantly.

There was no significant difference between the fluid-responsive and non-responsive groups regarding the percentage change in lactate clearance and procalcitonin (Table 3).

Table 1: Baseline characteristics of the study group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>49.5 ± 8.4</td>
</tr>
<tr>
<td>Male/Female</td>
<td>20/20</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.5 ± 12.4</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.64 ± 0.05</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29.5 ± 4.5</td>
</tr>
<tr>
<td>Sequential Organ Failure Assessment (SOFA) Score</td>
<td>5.5 ± 1.6</td>
</tr>
<tr>
<td>Heart Rate (beats/min.)</td>
<td>109 ± 11</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>63 ± 5</td>
</tr>
<tr>
<td>Central venous pressure (mmHg)</td>
<td>2.0 (0.0-12.0)</td>
</tr>
<tr>
<td>Inferior vena cava collapsibility index</td>
<td>60.6 ± 4.4</td>
</tr>
<tr>
<td>Cardiac output (L/min.)</td>
<td>3.8 ± 0.6</td>
</tr>
<tr>
<td>Urine output (ml)</td>
<td>0.0 (0.0-100.0)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or median (range)

Table 2: Vital signs, CVP, CO, and IVC-CI at 0 h and 3 h in the responsive and non-responsive groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Responsive (n = 29)</th>
<th>P-value</th>
<th>Non-responsive (n = 11)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 hour</td>
<td>3 hours</td>
<td>0 hour</td>
<td>3 hours</td>
</tr>
<tr>
<td>HR (beats/min.)</td>
<td>108 ± 11</td>
<td>82 ± 11</td>
<td>111 ± 7</td>
<td>84 ± 8</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>63 ± 6</td>
<td>82 ± 9</td>
<td>63 ± 2</td>
<td>81 ± 6</td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td>2.6 ± 2.7</td>
<td>8.6 ± 1.6</td>
<td>2.3 ± 2.1</td>
<td>8.2 ± 1.1</td>
</tr>
<tr>
<td>CO (L/min.)</td>
<td>3.7 ± 0.6</td>
<td>5.6 ± 0.9</td>
<td>3.9 ± 0.4</td>
<td>5.5 ± 0.6</td>
</tr>
<tr>
<td>IVC-CI (%)</td>
<td>60.5 ± 4.5</td>
<td>47.4 ± 3.3</td>
<td>60.7 ± 4.3</td>
<td>50.5 ± 2.8</td>
</tr>
</tbody>
</table>

HR: Heart Rate, MAP: Mean arterial pressure, CVP: Central venous pressure, CO: Cardiac output, IVC-CI: Inferior vena cava collapsibility index
ROC-curve analysis showed that the changes in IVC-CI after 30 min and 1 hour of starting fluid overload were predictive of responsiveness after 1 hour (Table 4). A percentage change in IVC-CI of 3.4% or more predicted positive responsiveness with a sensitivity of 72.4% and a specificity of 63.6%. These values were 79.3% and 72.7%, respectively, for a change of 6.3% or more after 1 hour of fluid therapy. However, the baseline value of IVC-CI was not predictive of responsiveness (area under the curve = 0.591). Starting from 1.5 hours until the end of the study period at 3 hours, all patients showed a change in CO of more than 10%, i.e., all cases were considered fluid responsive. There was no correlation between IVC-CI and HR, MAP, CO, and CVP at baseline and after treatment (Tables 5 and 6). Also, IVC-CI was not correlated with percent changes in lactate clearance and procalcitonin (Table 6).

4. DISCUSSION

In critically ill patients, especially those with sepsis and septic shock, hypovolemia may lead to decreased tissue perfusion, whereas fluid overload may cause organ congestion and related morbidity and mortality. Evaluation of volume status is crucial for the treating medical professionals throughout therapy and may have prognostic implications. The cornerstone for evaluating the intravascular volume is the right atrial pressure, which is an equivalent term to the CVP. Unfortunately, the standard assessment of CVP is through an invasive central venous catheter, which might be associated with introduction of infection and thrombosis. As an alternative to invasive CVP testing,
In a number of non-invasive echocardiographic measurements have been suggested. One of these techniques is concerned with IVC ultrasonography. Blood volume, right heart performance, and breathing all affect the IVC diameter. As such, it serves as a reservoir and represents volume status.

The IVC boasts the largest diameter in the venous system. It is a thin-walled, valveless vessel located in the retroperitoneal space. Its main function is to transport significant amounts of deoxygenated blood from the lower extremities and abdomen back to the right atrium. The IVC is an important blood storage space because it holds 85% of all the plasma volume in the venous circulation. Changes in circulating volume cause changes in IVC caliber.

Previous studies have demonstrated the predictive capability of IVC-CI for volume expansion in spontaneously ventilating patients with septic shock. In a group of 14 patients, IVC-CI ≥ 50% had a fair positive (75%) and good negative (80%) predictive value. In a larger study of 90 patients with septic circulatory failure, a value of IVC-CI >31% had positive and negative predictive values of 88% and 74%, respectively. In another study, a lower threshold of 20.5% of IVC-CI predicted fluid responsiveness with sensitivity and specificity of 67% and 77%, respectively.

This substantial variation in predictive thresholds for IVC-CI reflects the possible heterogeneity of measurement techniques used in different studies. This variability was demonstrated in a systematic review of 26 studies of the role of the IVC diameter of collapsibility in predicting fluid responsiveness in critically ill patients, whether ventilated or not. The meta-analysis involved 20 studies and revealed a pooled sensitivity and specificity of 71% and 75%, respectively. However, the authors concluded that IVC and its respiratory variations do not seem to be a reliable method to predict fluid responsiveness. Like other ultrasound techniques, operator experience is claimed to affect the accuracy of evaluating IVC parameters. However, it has previously been demonstrated that clinicians’ identification of vascular overload can be greatly improved by a 4-hour training on ultrasound study of the IVC. Yet, bedside ultrasound of the IVC appears to be a useful, quick, and noninvasive hemodynamic monitoring technique for the ICU.

5. CONCLUSION

The novel finding of the current study is the predictive role of the change in inferior vena cava collapsibility index rather than the pretreatment value. This measure can be used to test fluid responsiveness through a fluid overload for half an hour or even one hour to predict future responses in the ICU setting. Thus, we can conclude that the change in inferior vena cava collapsibility index during the first hour of fluid therapy can predict fluid responsiveness with moderate accuracy in cancer patients with sepsis or septic shock.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

9. Authors’ contribution

All authors took part in the conduct of the study and preparation of the manuscript. All authors approve the final draft of the manuscript for publishing.

10. REFERENCES


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