

## Inferior Vena Cava Ultrasound for Assessing Volume Status and Fluid Responsiveness in Critically ill Patients: A Systematic Review

*Ultrassonografia da Veia Cava Inferior na Avaliação do Volume Intravascular e Fluido-Responsividade em Pacientes Críticos: Uma Revisão Sistemática*

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### Abstract

**Background:** The assessment of intravascular volume and fluid responsiveness is challenging in the management of critically ill patients. Diagnostic methods of hemodynamic monitoring must be safe, reproducible, and practical. **Objective:** To describe the applicability of ultrasound indices of the inferior vena cava in the assessment of intravascular volume and prediction of fluid responsiveness in critically ill patients. **Method:** A systematic review performed of the PubMed®, Latin American and Caribbean Health Sciences Literature, and Scientific Electronic Library Online databases for articles published in the previous five years. The descriptors used were “inferior vena cava,” “ultrasonography,” “fluid responsiveness,” and “volume status.” **Results:** The search identified 13 relevant articles. The collapsibility index of the inferior vena cava was 25%–50% as the cutoff point for defining hypovolemia and showed applicability in predicting fluid responsiveness in patients breathing spontaneously with cutoff points of 25%–57%. In mechanical ventilation scenarios, the distensibility index of the inferior vena cava was more effective at predicting fluid responsiveness than the other measurements with variation of 10.2%–20.5%. The inferior vena cava/aorta diameter index was especially useful in the pediatric population for defining intravascular volume; however, in adults, there were many divergences in its applicability. **Conclusion:** The assessment of intravascular volume and fluid responsiveness through ultrasound indices of the inferior vena cava is applicable and safe for diagnosing and monitoring hemodynamic instability. However, studies of value standardization are necessary due to divergences in the cutoff points used in each index.

### Introduction

The assessment of intravascular volume is challenging in the management of critical patients. Clinical history and

### Keywords

Hemodynamics; Inferior vena cava; Intensive care unit; Organism fluid status; . Ultrasonography.

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physical examination provide the initial information about blood volume. However, even when combined with laboratory tests, chest X-ray, central venous pressure, and cardiac afterload monitoring, these parameters are not sufficiently accurate or reliable for determining a patient’s intravascular volume, particularly in cases of hypovolemia not associated with blood loss.<sup>1</sup>

Critically ill patients with hemodynamic instability are managed according to the definition of intravascular volume and based on the improvement or worsening of hemodynamic parameters due to therapeutic test results. The diagnostic methods used for this purpose require safety, receptivity, reproducibility, and continuous monitoring since fluid replacement therapies impact a patient’s systemic perfusion and influence the risk of organ failure.<sup>2</sup>

Fluid responsiveness is generically defined as a 10%–15% increase in stroke volume after crystalloid infusion. Volume replacement improves the oxygen supply to the tissues by increasing afterload and cardiac output. However, only 50% of critically ill patients are on the ascending portion of the Frank-Starling curve, i.e., cardiac output increases in response to increased preload. Volume overload in heart failure is associated with the need for mechanical ventilation, an increased incidence of acute kidney injury, and an increased mortality rate.<sup>3,4</sup>

In recent years, due to these limitations, ultrasound of the inferior vena cava (IVC) has been widely used as a non-invasive diagnostic method for intravascular volume and predicting fluid responsiveness. Most venous return to the heart occurs through the IVC. The correct assessment of its diameter and dynamics during respiratory cycles may provide an approximate ventricular preload estimate and, consequently, demonstrate its relationship with afterload and cardiac output.<sup>5</sup>

In clinical practice, there are no direct methods of assessing preload, which is traditionally estimated through static measurements such as central venous pressure and pulmonary artery occlusion pressure or dynamic measurements such as ejection volume variation and pulse pressure. Most of these diagnostic methods are invasive and risky.<sup>6</sup>

Challenges defining blood volume and fluid management in critically ill patients justify efforts to assess the applicability of IVC ultrasonography as an alternative, safe, and non-invasive method.

This study aimed to describe the applicability of ultrasound indices for assessing intravascular volume and predicting fluid responsiveness in critically ill patients.



# Systematic Review

## Methods

This systematic review of the literature following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISM) guidelines<sup>7</sup> aimed to answer the following research question: “What is the applicability of IVC ultrasound indices for assessing intravascular volume and predicting fluid responsiveness in critically ill patients?” The PICOS strategy was used to prepare the guiding question (Table 1).

### Study search and selection strategy

A bibliographic survey of studies published through October 9, 2020 was conducted of the PubMed®, Latin American and Caribbean Health Sciences Literature (Lilacs), and Scientific Electronic Library Online (SciELO) databases. The search strategy comprised the search for the descriptors “inferior vena cava,” “ultrasonography,” “fluid responsiveness,” “volume status,” and “critical care,” all of which appear in the Medical Subject Headings (MeSH) list of the National Library of Medicine in addition to their respective Portuguese equivalents. The database search process is shown in Table 2.

### Eligibility criteria

Study type (original article, systematic review, and meta-analysis) and publication language (English and Portuguese) were the eligibility criteria. Critical care ultrasonography in the training of intensive care physicians is considered recent; therefore, the inclusion criteria for this review were free access articles published between 2015 and 2020, full-text availability, and the main objective of analyzing the applicability of IVC ultrasound indices alone or associated to assess intravascular volume and predict fluid responsiveness. Critical patients were those with clinical and laboratory signs of acute circulatory failure, i.e., with a systolic pressure < 90 mmHg or mean arterial pressure < 65 mmHg, decreased urinary output < 0.5 mL/kg/hour, persistent tachycardia, pH < 7.3, and lactate > 2 mEq/L.

The exclusion criteria were simple review, letters to the editor, and animal model studies. Studies in which the calculation used to obtain the assessed ultrasound index was not clear were also excluded.

## Data extraction and analysis

The titles and abstracts identified in the search strategy were initially analyzed by two independent reviewers according to the inclusion and exclusion criteria. Later, the same reviewers read the selected articles in full to independently confirm the eligibility criteria. Disagreements were resolved by consensus between the two reviewers. Methodological quality was descriptively and independently assessed. The reviewers were not blinded to the authors or institutions of the reviewed studies.

After the initial screening, a descriptive data analysis was performed using a standardized data extraction form. The following elements were extracted by the authors: IVC collapsibility index (IVCci), IVC distensibility index (IVCdi), IVC/aorta diameter index (IVC/Ao), characterization and number of patients involved, study type and period, language, main results, and conclusions.

## Results

Initially, 130 (81.8%) studies were identified in the PubMed®, 15 (9.4%) in the Lilacs, and 14 (8.8%) in the SciELO databases. Of these 159 articles, 18 (11.3%) were eliminated as duplicates. Of the 141 resulting reports, 108 (76.6%) were excluded after the title and abstract screening for not meeting the study objective. Thus, a total of 33 articles were subjected to full-text review.

After the full-text review, 21 (63.63%) were excluded, nine (27.27%) for being conducted in environments other than the intensive care unit, nine (27.27%) for being using an unclear method of calculating the evaluated ultrasound index, and three (9.09%) for using animal models. Finally, the final sample included 12 scientific articles, the selection process of which is shown in Figure 1.

The 12 analyzed articles were observational in design. Of them, three (25%) were included children and nine (75%) included adults. A total of 1,047 patients were evaluated. Five studies (41.66%) were performed of mechanically ventilated patients, one (8.33%) of spontaneously ventilated patients receiving ventilatory support, and six (50%) of spontaneously ventilated patients.

**Table 1 - Research question components according to the PICOS anagram.**

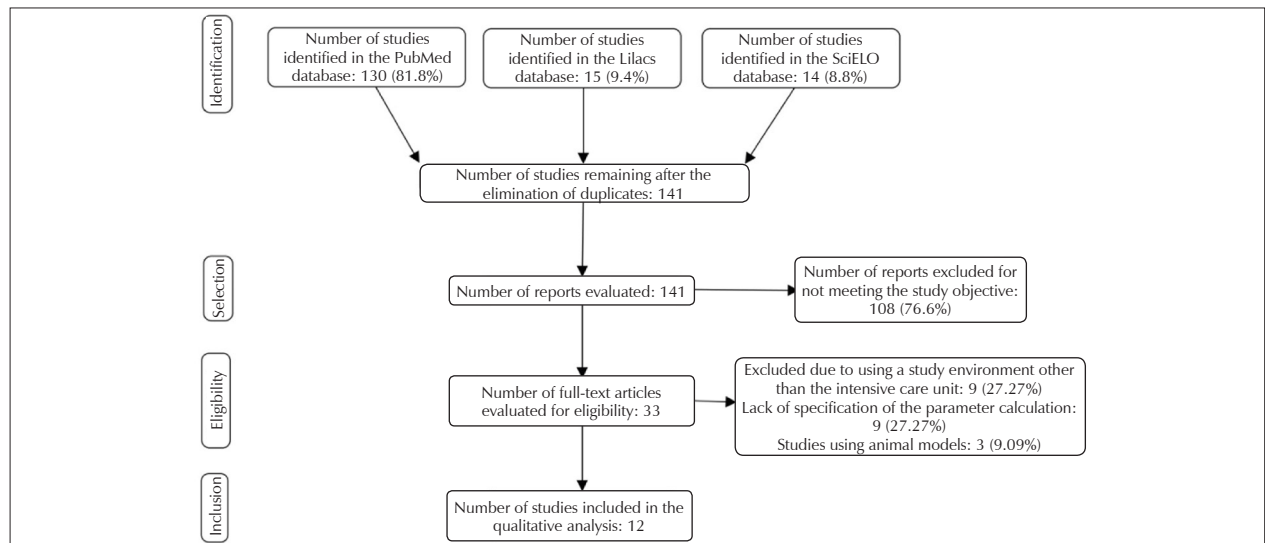
Description	Abbreviation	Question components
Population, patient, or problem	P	Patients under mechanical or spontaneous ventilation with clinical or laboratory signs of acute circulatory failure
Intervention	I	IVC diameter was analyzed on M-mode ultrasound, and diameter variability according to respiratory phase was obtained from the calculation of the following index: IVCci obtained by the IVCci function = [(end expiratory diameter – end inspiratory diameter)/(end expiratory diameter)] × 100; IVCdi was calculated as IVCdi = [(maximum diameter-minimum diameter)/(minimum diameter)] × 100. <sup>8</sup> IVC/Ao was obtained by the ratio of the measurements of the maximum diameter of the IVC and the Ao. <sup>9</sup>
Comparison, control, comparator	C	The intravascular volume assessment was compared with CVP. Pulse pressure variation, stroke volume variation, and cardiac output were used for a comparative fluid responsiveness analysis in addition to CVP
Outcomes	O	Applicability of IVCci, IVCdi, and IVC/Ao for assessing intravascular volume and predicting fluid responsiveness
Study design	S	Original articles and systematic reviews

CVP, central venous pressure; IVC, inferior vena cava; IVC/Ao, inferior vena cava/aorta diameter index; IVCci, inferior vena cava collapsibility index; IVCdi, inferior vena cava distensibility index.

**Table 2 - Search process of the PubMed®, Latin American and Caribbean Health Sciences Literature, Scientific Electronic Library Online MEDLINE® databases.**

	#1	(((Vena Cava, Inferior[MeSHTerms]) OR (Inferior Vena Cavas[MeSHTerms])) OR (Vena Cavas, Inferior[MeSHTerms]) OR (Inferior Vena Cava[MeSHTerms])) OR (Inferior Vena Cava
	#2	((((((((((((Ultrasonography[MeSH Terms]) OR (Diagnostic Ultrasound[MeSH Terms])) OR (Diagnostic Ultrasounds[MeSH Terms])) OR (Ultrasound, Diagnostic[MeSH Terms])) OR (Ultrasounds, Diagnostic[MeSH Terms])) OR (Ultrasound Imaging[MeSH Terms])) OR (Imaging, Ultrasound[MeSH Terms])) OR (Imagings, Ultrasound[MeSH Terms])) OR (Ultrasonic Imaging[MeSH Terms])) OR (Imaging, Ultrasonic[MeSH Terms])) OR (Sonography, Medical[MeSH Terms])) OR (Medical Sonography[MeSH Terms])) OR (Ultrasonographic Imaging[MeSH Terms])) OR (Imaging, Ultrasonographic[MeSH Terms])) OR (Imagings, Ultrasonographic[MeSH Terms])) OR (Ultrasonographic Imagings[MeSH Terms])) OR (Ultrasonography
MEDLINE® via PubMed®	#3	((((Critical Care[MeSH Terms]) OR (Care, Critical[MeSH Terms])) OR (Intensive Care[MeSH Terms])) OR (Care, Intensive[MeSH Terms])) OR (Surgical Intensive Care[MeSH Terms])) OR (Care, Surgical Intensive[MeSH Terms])) OR (Intensive Care, Surgical[MeSH Terms])
	#4	Fluid responsiveness
	#5	Volume status
	#6	((#1 AND #2 AND #3) AND #4)
	#7	((#1 AND #2 AND #3) AND #5)
	#8	Ultrasonografia [MeSHTerms] or Diagnóstico por Ultrassom [MeSHTerms] or Ultrasonography [MeSHTerms]
	#9	Veia Cava Inferior [MeSHTerms] or Vena Cava, Inferior [MeSHTerms] or Inferior Vena Cava [MeSHTerms]
Lilacs/SciELO	#10	Cuidado Intensivo [MeSHTerms] or Cuidados Intensivos [MeSHTerms] or Critical Care [MeSHTerms]
	#11	Fluid responsiveness
	#12	Volume status
	#13	((#8 AND #9 AND #10) AND #11)
	#14	((#8 AND #9 AND #10) AND #12)

Lilacs, Latin American and Caribbean Health Sciences Literature; SciELO, Scientific Electronic Library Online.



**Figure 1 – Systematic review article search flowchart.**

There was no significant variation among studies regarding the method of IVC diameter acquisition and its variation during the respiratory cycle. All measurements were performed on M-mode ultrasonography. The objectives of each study were to demonstrate, alone or comparatively, the sensitivity and specificity of the cutoff points of each index used to assess intravascular volume and predict fluid responsiveness (Table 3).

**IVC collapsibility index**

Babaie et al. reported a strong negative linear correlation between CVP and IVCci in a prospective observational study of 70 children admitted to the intensive care unit under

mechanical ventilation support. A sensitivity of 45.5% and specificity of 91.7% were identified for predicting hypovolemia with an IVCci0.5 and CVP ≤ 8 cmH<sub>2</sub>O.<sup>10</sup>

Saritas et al. reported that the IVCci significantly decreased from the hypovolemic (CVP < 8 cmH<sub>2</sub>O) to the hypervolemic (CVP > 12 cmH<sub>2</sub>O) group in spontaneously breathing adult patients receiving different positive pressure supports. The index values were lower than 0.5 in all positive pressure scenarios. Thus, the IVC cutoff point of 0.5 was considered insufficient for distinguishing between hypervolemic and hypovolemic states. No inversely proportional relationship was found between CVP and IVCci. However, an index lower than

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**Table 3 - Summary of analyzed studies.**

Author, country	Patients	N	Index	Objective	Sensitivity (%)	Specificity (%)	AUC ROC (95% CI)
Babaie et al., <sup>10</sup> Iran	Children	70	IVCci/IVC/Ao	Evaluate the predictive value of IVCci $\geq 0.5$ and IVC/Ao $\leq 0.8$ for CVP $\leq 8$ cmH <sub>2</sub> O	IVCci = 45.5 IVC/Ao = 50.8  PS = 0 mmHg PEEP = 5 mmHg  IVCci = 5.7 IVCdi = 100	IVCci = 91.7 IVC/Ao = 87.5  PS = 0 mmHg PEEP = 5 mmHg  IVCci = 100 IVCdi = 63	NE  PS = 0 mmHg PEEP = 5 mmHg  IVCci = 0.529 IVCdi = 0.816
Saritas et al., <sup>11</sup> Turkey	Adults	100	IVCci/IVCdi	To evaluate the predictive value of IVCci $< 0.25$ for CVP $< 8$ cmH <sub>2</sub> O and of IVCdi $< 0.18$ for CVP $\geq 15$ cmH <sub>2</sub> O	PS = 10 mmHg PEEP = 5 mmHg  IVCci = 5.7 IVCdi = 98  PS = 0 mmHg PEEP = 0 mmHg IVCci = 97	PS = 10 mmHg PEEP = 5 mmHg  IVCci = 100 IVCdi = 68  PS = 0 mmHg PEEP = 0 mmHg IVCci = 100	PS = 10 mmHg PEEP = 5 mmHg  IVCci = 0.529 IVCdi = 0.835  PS = 0 mmHg PEEP = 0 mmHg IVCci = 0.55
Preau et al., <sup>12</sup> France	Adults	90	IVCci	Evaluate the predictive value of IVCci $\geq 0.48$ for fluid responsiveness	84	90	0.89
Airapetian et al., <sup>13</sup> France	Adults	57	IVCci	To evaluate the predictive value of IVCci $\geq 0.42$ for fluid responsiveness	31	97	0.62
Corl et al., <sup>14</sup> USA	Adults	124	IVCci	To evaluate the predictive value of IVCci $\geq 0.25$ for fluid responsiveness	87	81	0.84
Long et al., <sup>15</sup> Australia	Children	39	IVCci	To evaluate the predictive value of IVCci $\geq 0.57$ for fluid responsiveness	44	33	0.38
Oliveira et al., <sup>16</sup> Brazil	Children	20	IVCdi	To evaluate the predictive value of the 16% IVCdi index cutoff for predicting fluid responsiveness	67	100	0.84
Vignon et al., <sup>17</sup> France	Adults	319	IVCdi	To evaluate the predictive value of the 13% IVCdi index cutoff for predicting fluid responsiveness	44	85	0.65
Lu et al., <sup>18</sup> China	Adults	49	IVCdi	To evaluate the predictive value of the 20.5% IVCdi index cutoff for predicting fluid responsiveness	67	77	0.80
Theerawit et al., <sup>19</sup> Thailand	Adults	29	IVCdi	To evaluate the predictive value of the 10.2% IVCdi index cutoff for predicting fluid responsiveness	75	76.9	0.69
Salama et al., <sup>20</sup> Egypt	Adults	100	IVC/Ao	To evaluate the predictive value of the IVC/Ao cutoff point $< 1.2$ for hypovolemic states	96  IVC/Ao of 0.8 for CVP $\leq 7$ cmH <sub>2</sub> O  93	88  IVC/Ao of 0.8 for CVP $\leq 7$ cmH <sub>2</sub> O  66	0.96
El-Baradei et al., <sup>9</sup> Egypt	Adults	50	IVC/Ao	To evaluate the predictive value of the 0.8 IVC/Ao cutoff point associated with CVP $\leq 7$ cmH <sub>2</sub> O, IVC/Ao of 1.5 for CVP 8-12 cmH <sub>2</sub> O, IVC/Ao of 1.8 for CVP $> 12$ cmH <sub>2</sub> O	IVC/Ao of 1.5 for CVP 8-12 cmH <sub>2</sub> O  96  IVC/Ao of 1.8 for CVP $> 12$ cmH <sub>2</sub> O  93	IVC/Ao of 1.5 for CVP 8-12 cmH <sub>2</sub> O  42  IVC/Ao of 1.8 for CVP $> 12$ cmH <sub>2</sub> O  58	NE

95% CI, 95% confidence interval; AUC ROC, area under the curve receiving operating characteristic; CVP, central venous pressure; IVC/Ao, inferior vena cava/aorta diameter index; IVCci, inferior vena cava collapsibility index; IVCdi, inferior vena cava distensibility index; NE, not evaluated; PS, positive pressure support; PEEP, positive end expiratory pressure.

0.5 was associated with hypovolemia with a CVP < 8 cmH<sub>2</sub>O, not corroborating the results of other studies in which IVCci ≥ 0.5 was associated with hypovolemic states. As for predicting fluid responsiveness, patients would be responsive to fluid at a CVP ≥ 10 cmH<sub>2</sub>O and IVCci < 25%.<sup>11</sup>

Preauet al. performed a similar analysis in spontaneous ventilation scenarios but without positive pressure support and identified IVCci ≥ 48% after volume expansion as a cutoff point for predicting fluid responsiveness in septic patients with acute circulatory failure. Sensitivity and specificity were 84% and 90%, respectively.<sup>12</sup> On the other hand, Airapetian et al. studied patients under spontaneous ventilation and reported that the IVCci had no ability to predict fluid responsiveness since it presented only 31% sensitivity and 97% specificity in patients considered fluid responsive at an IVCci > 42%. However, it is necessary to consider that the study sample was small and CVP was not measured as a comparative fluid responsiveness measurement.<sup>13</sup>

Corl et al. studied 124 spontaneously ventilated patients. The IVCci cutoff point of 25% achieved 87% sensitivity and 81% specificity. This lower cutoff value resulted in a lower rate (16.1%) of incorrect classification regarding fluid responsiveness. Compared to cutoff point values of 40% and 42%, the error rates were 34.7% and 36.3%, respectively.<sup>14</sup>

Long et al. reported a low predictive value for identifying a response to fluid therapy of an IVCci > 57% in children admitted to an intensive care unit with sepsis. Its sensitivity was 44% and specificity was 33%. However, its sample of only 33 children is a limiting factor.<sup>15</sup> Altogether, these data suggest that the IVCci cutoff point for predicting fluid responsiveness is quite heterogeneous, ranging from 25% to 57%, and factors such as the pediatric age group and the presence of sepsis contribute to the different cutoff points.

### IVC distensibility index

The IVCdi is considered a good predictor of a patient's response to volume expansion. A study of 20 mechanically ventilated patients by Oliveira et al. showed the predictive value of fluid responsiveness of an IVCdi cutoff point of 16%. Its sensitivity and specificity were 67% and 100%, respectively.<sup>16</sup>

A different result was reported by Vignon et al. of a sample of 319 patients with acute circulatory failure. The 13% IVCdi cutoff point showed a sensitivity of 44% and specificity of 85%. Compared to other predictive fluid responsiveness indices such as pulse pressure variations and respiratory variations in superior vena cava diameter, the IVCdi showed a lower predictive value than the others.<sup>17</sup>

Lu et al. studied 49 patients diagnosed with septic shock and reported a 20.5% IVCdi cutoff point for predicting fluid responsiveness with 67% sensitivity and 77% specificity. The IVCdi was considered useful for predicting the response to fluid replacement during continuous and non-invasive monitoring of hemodynamic status in mechanically ventilated patients.<sup>18</sup> In contrast, Theerawit et al. demonstrated that a lower cutoff point (10.2%) was associated with a sensitivity of 75% and specificity of 76.9% in a study of 29 patients with septic shock under mechanical ventilation.<sup>19</sup> Although the IVCdi cutoff point was 10.2%–20.5%, patients in septic shock have

better sensitivity and specificity results for predicting fluid responsiveness.

Saritas et al. compared the ability of IVC ultrasound indices (IVCdi and IVCci) to predict the volumetric status of patients under positive pressure support. The percentages of the indexes varied significantly among ventilatory pressures. IVCdi was the most effective at estimating intravascular volume. A sensitivity of 100% and specificity of 63% were identified for the group of patients under 0 mmHg pressure support and 5 mmHg positive end expiratory pressure (PEEP). The group with 10 mmHg ventilatory support and 5 mmHg PEEP presented 98% sensitivity and 68% specificity. Finally, an inversely proportional relationship was found between CVP and IVCdi; thus, an IVCdi < 18% was associated with a CVP > 15 cmH<sub>2</sub>O, which is present, for example, in hypervolemic states.<sup>11</sup>

### IVC/aorta diameter index

Salama et al. reported good applicability of IVC/Ao for predicting the occurrence of hypotension after the induction of spinal anesthesia (IVC/Ao cutoff point, < 1.2) and had a sensitivity of 96% and specificity of 88%. IVC/Ao showed greater ability to predict hypotension than IVCci (IVCci cutoff point, > 44.7%) at 88% sensitivity, 77% specificity, and 84% accuracy.<sup>20</sup>

Babaie et al. reported a sensitivity of 50.8% and specificity of 87.5% for predicting hypovolemic states (CVP < 8 cmH<sub>2</sub>O) with an IVC/Ao ≤ 0.8.<sup>10</sup> El-Baradei et al. evaluated the value of VCI/Ao for predicting pre- and intraoperative intravascular volume and reported CVP values ≤ 7 cmH<sub>2</sub>O associated with a VCI/Ao of 0.8 (93% sensitivity, 66% specificity); a PVC of 8–12 cmH<sub>2</sub>O correlated with a VCI/Ao of 1.5 (96% sensitivity, 42% specificity); and a PVC > 12 cmH<sub>2</sub>O related to a VCI/Ao of 1.8 (93% sensitivity, 58% specificity).<sup>9</sup>

## Discussion

Estimating right ventricular preload is important for defining intravascular volume and predicting fluid responsiveness since the relationship between diastolic filling volume and stroke volume is mainly influenced by the Frank-Starling mechanism. An increased or decreased preload in the right ventricle translates to a change in the left ventricular systolic volume.<sup>3</sup> Accordingly, the ultrasonographic evaluation of the IVC is a non-invasive instantaneous method that strongly correlates with ventricular preload and circulating blood volume. Hypovolemic patients are expected to present the image of a depleted or collapsed vessel. However, in conditions that course with hypovolemia, the IVC is dilated or lacks respiratory collapse.<sup>5</sup> This is because the IVC reaches its maximum and minimum diameters due to interactions between the heart and lung during the respiratory cycle, i.e., in spontaneous breathing, inspiration induces an increased intra-abdominal pressure due to the diaphragmatic movement toward this cavity. Thus, the IVC diameter decreases. On the other hand, a decreased abdominal pressure results in an increased vessel diameter.<sup>21</sup>

Mechanical ventilation with positive pressure substantially increases intrathoracic pressure, which reduces cardiac preload and stroke volume. Consequently, the IVC diameter will maximize during inspiration and minimize during

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expiration.<sup>22,23</sup> Thus, ultrasound assesses IVC diameter variability ( $\Delta$ IVC) during a spontaneous or mechanical respiratory cycle to establish intravascular volume and predict fluid responsiveness.<sup>21,24</sup>

Spontaneously breathing patients have  $\Delta$ VCI represented by the IVCci.<sup>8</sup> The collapsibility index in healthy people during the respiratory cycle varies with a mean of 38%. Values above or below this value were considered abnormal and required further investigation.<sup>25</sup> In the studies analyzed in this review, the IVCci cutoff points were 0.25–0.5 to determine hypovolemic states. However, it is important to emphasize that the higher the IVC cutoff point, the lower the ability to distinguish hypovolemic from hypovolemic states.

CVP is one of the best established methods in clinical practice for assessing intravascular volume. A study of 100 patients admitted to an intensive care unit aimed to identify the relationship between CVP and IVC ultrasound measurements. An inversely proportional relationship was found between CVP and IVCci, i.e., the higher the IVCci, the lower the CVP, indicating hypovolemia.<sup>2</sup> These data corroborate those of the study by Babaie et al. of children aged 1 month to 12 years under mechanical ventilation. On the other hand, Saritas et al. found no negative linear correlation between CVP and IVC in the evaluated scenarios of spontaneous ventilation under ventilatory support.

The  $\Delta$ IVC in mechanically ventilated patients is represented by IVCdi and IVC distensibility variability (IVCdv).<sup>8</sup> The use of  $\Delta$ IVC in mechanically ventilated patients is recommended by the consensus on shock and hemodynamic monitoring of the European Society of Intensive Care Medicine as a dynamic measurement index of fluid responsiveness.<sup>26</sup>

However, the evaluated studies diverged in the IVCdi cutoff points used for predicting fluid responsiveness. The values were 10.2%–20.5%, with a predominance of cutoff points below 17%. Only Lu et al. reported a higher IVCdi value of (20.5%).<sup>18</sup> A systematic review and meta-analysis of the accuracy of IVCdi for defining intravascular volume in patients under mechanical ventilation reported that in scenarios of a PEEP  $\leq$  5 cmH<sub>2</sub>O at a tidal volume  $\geq$  8 mL/kg, an IVCdi of 16% accurately predicted fluid responsiveness with 80% sensitivity and 94% specificity. On the other hand, in a patient with a PEEP  $>$  5 cmH<sub>2</sub>O and a tidal volume  $<$  8 mL/kg, an IVCdi of 14% had diagnostic limitations with only 66% sensitivity and 68% specificity. Therefore, IVCdi should be cautiously used in certain mechanical ventilation scenarios.<sup>21</sup>

There are significant correlations between IVC diameter and body surface area (BSA). Estimating BSA can be challenging and time-consuming in the emergency and critical care settings. Thus, it is necessary to compare the IVC diameter using an index that does not significantly change with intravascular volume but has a similar relationship with body growth and BSA.<sup>27</sup> In turn, use of the aortic diameter (AoD) as a comparative index is justified because it is a vessel whose fetal development occurs simultaneous to that of the IVC. Thus, there is a correlation between age, sex, and BSA with AoD. Due to the anatomical characteristic of this artery, the volumetric status does not significantly change its diameter. As a consequence, the IVC/Ao was proposed to facilitate and accelerate the ultrasonographic diagnosis of intravascular volume.<sup>28</sup>

The IVC/Ao plays a relevant role in the identification of hypovolemic and hypervolemic states, especially in the pediatric population. The assessment of the impact of individual characteristics with the IVC/Ao in healthy children aged 1–13 years found significant variations in maximum IVC and aorta diameters with individual characteristics. However, they presented no significant variation versus the IVC/Ao. This analysis found that the use of the IVC/Ao with a reference value of 0.68–1.4 was useful for defining pediatric volumetric status.<sup>29</sup> In one of the analyzed studies, Babaie et al. reported a sensitivity of only 50.8% and specificity of 87.5% for predicting pediatric hypovolemic states. Furthermore, the IVC/Ao had superior ability to IVCci for predicting hypovolemia in children under spontaneous ventilation.<sup>10</sup>

An analysis of the IVC/Ao index variation by individual characteristics in healthy adults showed a significant change since the aorta was observed as the component most susceptible to the influence of individual characteristics in adults. Therefore, the IVC/Ao did not perform better than the other IVC indices at predicting volumetric status and fluid responsiveness.<sup>30</sup> However, the studies analyzed here showed the applicability of the IVC/Ao for assessing intravascular volume in adult patients with signs of hemodynamic instability with sensitivity and specificity rates higher than 93% and 42%, respectively. Thus, a mean IVC/Ao of 1.14 was established to identify the initial phase of hypovolemic shock in adults with a standard deviation of 0.18 as a cutoff point and no significant correlation with individual characteristics.<sup>31</sup>

### Limitations of IVC ultrasonography

Restrictions for the ultrasonographic assessment of the IVC are related to multiple factors such as pulmonary hyperinflation, pneumothorax, presence of intestinal gas, and obesity. Such conditions cause inappropriate sonographic windows that can cause diagnostic errors.<sup>3</sup> Thus, it is reasonable to consider these factors before using IVC ultrasonography in critically ill patients.

The evaluation of fluid responsiveness using IVC diameter assumes its correlation with right atrial pressure and preload. However, these relationships have limitations since absolute IVC diameter measurements reflect their interactions with atrial pressure but not intravascular volume per se. IVC ultrasonography considers a positive linear relationship between pressure and volume as well as the diagnosis of intravascular volume through the static measurement of CVP. Variations in vascular tone, intrathoracic pressure, or cardiac function directly change the right atrial pressure without preload variations.<sup>32</sup> This can be easily verified in clinical practice. There are cases of high filling pressures and normal IVC and others of possible fluid responsiveness but with a dilated IVC diameter. Cases such as acute right ventricular infarction, cardiac tamponade, pulmonary embolism, intra-abdominal hypertension, asthma, chronic obstructive pulmonary disease, and positive pressure ventilation are conditions in which the absolute diameter measurement may fail to diagnose intravascular volume and fluid responsiveness.<sup>5</sup> Some studies indicated higher dynamic measurement values (IVCci, IVCdi, and IVCdv) compared with static measurements in the diagnosis of fluid responsiveness under these borderline conditions.<sup>3,32</sup>

Another important limitation refers to the performance of ultrasonography with the patient in the supine position for image acquisition. This position is not recommended in the intensive care setting since it carries the risk of worsening respiratory mechanisms, increased intracranial pressure, and aspiration. The analysis of the influence of elevating the headboard for IVC diameter measurements showed that an elevation of 30° did not significantly change the maximum and minimum diameter measurements or IVCCi compared to the supine position. However, a 45° elevation caused significant maximum and minimum diameter changes but not IVCCi measurements.<sup>33</sup> Finally, it is important to consider that IVC assessments must be integrated with a comprehensive ultrasound approach to multiple organs (heart, lung, other vessels), reducing the effects of these limiting agents and resulting in a more reliable diagnosis of intravascular volume and fluid responsiveness.<sup>5</sup>

### Study limitations

One of the intrinsic limitations of this study is the limited number of patients since only two of the 13 retrieved studies presented a sample greater than or equal to 100 patients. Furthermore, few original studies were published within the proposed time interval. Finally, as for the standardization of ultrasonographic indices to define their applicability, a variety of clinical indications placed these patients in the intensive care environment. In most studies, etiological diagnoses were not listed; only acute circulatory failure was reported as a critical indication of clinical status.

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### Conclusion

The assessment of intravascular volume and the prediction of fluid responsiveness is a major challenge in the intensive care environment. Traditional diagnostic methods lead to potential complications that worsen hemodynamic instability. Although the results showed significant variations in sensitivity and specificity in critically ill patients, the use of ultrasound in the analysis of IVC indices (IVCCi, IVCdi, and IVCdv) is essential for rapid non-invasive diagnosis with good applicability in patient management, especially when integrated with a systemic ultrasound approach. However, value standardization studies are needed due to divergence in the cutoff points for each index.

### Authors' contributions

Research conception and design: DG Xavier Filho, APO Tenório; data collection: DG Xavier Filho, ALN Coutinho; data analysis and interpretation: DG Xavier Filho, ALN Coutinho, MRLopes; manuscript writing: DG Xavier Filho; critical review of the manuscript for important intellectual content: RHA Barbosa, MR Lopes, APO Tenório.

### Conflict of interest

The authors have declared that they have no conflict of interest.

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