Inferior vena cava distensibility from subcostal and trans-hepatic imaging using both M-mode or artificial intelligence: a prospective study on mechanically ventilated patients. Short Title: Subcostal vs transhepatic IVC evaluation

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Abstract

**Background:** Variation of inferior vena cava (IVC) is used to predict fluid-responsiveness, but the IVC visualization with standard sagittal approach (SC, subcostal) cannot be always achieved. In such cases, coronal trans-hepatic (TH) window may offer an alternative, but the interchangeability of IVC measurements in SC and TH is not fully established. Further, artificial intelligence (AI) with automated border detection may be of clinical value but it needs validation.

**Methods:** Prospective observational study in mechanically ventilated patients with pressure-controlled mode. Primary outcome was the IVC distensibility (IVCd) in SC and TH imaging, with measurements taken both in M-Mode or with AI software. We calculated mean bias, limits of agreement (LoA), and intra-class correlation (ICC) coefficient.

**Results:** Thirty-three patients were included. Feasibility rate was 87.9% and 81.8% for SC and TH visualization, respectively. Comparing imaging from the same anatomical site acquired with different modalities (M-Mode vs AI), we found the following IVCd differences: 1)SC: mean bias -3.1%, LoA [-20.1;13.9], ICC=0.65; 2)TH: mean bias -2.0%, LoA [-19.3;15.4], ICC=0.65. When comparing the results obtained from the same modality but from different sites (SC vs TH), IVCd differences were: 3)M-Mode: mean bias 1.1%, LoA [-6.9;9.1], ICC=0.54; 4)AI: mean bias 2.0%, LoA [-25.7;29.7], ICC=0.32.

**Conclusions:** In patients mechanically ventilated, AI software shows good accuracy (modest overestimation) and moderate correlation as compared to M-mode assessment of IVCd, both for SC and TH windows. However, precision seems suboptimal with wide LoA. The comparison of M-Mode or AI between different sites yields similar results but with weaker correlation.

Introduction

Evaluation of fluid responsiveness (FR) has a prominent role in the treatment of intensive care unit (ICU) patients; in fact, both fluid overload or dehydration have been demonstrated a negative impact on morbidity and mortality of critically ill patients[1]. Hypovolemia and reduced preload are responsible for a reduction in stroke volume, thus causing organ hypo-perfusion[2], while hypervolemia impairs organ perfusion by determining fluid overload, with consequent tissue edema and pulmonary and/or systemic congestion[3–5]. Therefore, ICU patients usually require the evaluation of FR several times a day[6], since loading conditions tend to be modified by different variables (vasomotor tone[7], analgo-sedation level, capillary permeability related to inflammation[8], etc).

Prediction of FR can be performed with several methods, both in spontaneously breathing and mechanically ventilated patients[9, 10]. Some are non-invasive or minimally-invasive, while others require advanced cardiac output monitoring and arterial cannulation. Among the non-invasive ones, variation of inferior vena cava (IVC) diameter within the respiratory cycle is commonly adopted, and it has been validated for both mechanically ventilated patients (IVC distensibility, IVCd = ΔIVC/IVCmin, with 18% as best cut-off)[11], and for patients with spontaneous respiratory activity (IVC collapsibility, IVCc =
ΔIVC/IVCmax, with cut-offs around 40%-48%[12–14]. Even though there are several limitations in these indexes for prediction of FR[15–17], IVC assessment is highly feasible, thus explaining the growing application in most critically-ill patients[18, 19]. However, standard subcostal (SC or sagittal) approach for the IVC assessment is not always achievable as in case of laparotomy, presence of chest drains, obesity or enlarged bowel. In these instances, the trans-hepatic (TH, coronal, or right lateral) approach for IVC visualization could be an alternative, offering a latero-lateral visualization of the vessel excursions. Available data on the interchangeability of IVC assessments with SC and TH approach are conflicting[20, 21], and a systematic review showed limited evidence to draw conclusions. Indeed, the available studies are grossly heterogeneous and used different approaches in data reporting, suggesting the need for further research[22].

In the past decade the role of artificial intelligence (AI) grew rapidly in several medical fields. Among these, also echocardiography is experiencing a significant expansion of AI applications that might help daily practice. Indeed, AI has been used for the assessment of left ventricular systolic[23, 24] and diastolic[25–27] function, right ventricular function[28], but also for the evaluation of heart valve[29] and congenital heart diseases[30]. Moreover, machine learning has been developed for predicting FR at patient's bedside[31] with preliminary data on the implementation of AI for IVC assessment[32].

We conducted a prospective observational study in mechanically ventilated critically-ill patients to compare differences in IVC size and variation between measurements taken in traditional M-Mode or with AI approach, as well as to evaluate the differences between measurements taken at the two different anatomical sites (SC and TH).

**Materials And Methods**

Our prospective observational study was approved from our local Ethical Committee (Reference protocol: 53/2022/PO). We aimed at evaluating the differences between assessment of the IVC in SC and TH windows.

**Participants**

We included consecutive adult patients admitted to the General ICU of the Azienda Ospedaliera Universitaria “Policlinico-San Marco”, Catania if they were fully ventilated in pressure-controlled ventilation (PCV) without own respiratory activity and stable hemodynamic conditions. We collected data as suggested by the PRICES guidelines[33, 34], recording ICU admission diagnosis, patient’s demographics, the hemodynamic conditions and the ventilatory settings, and ICU mortality.

**Study procedure**

All patients were in semi-recumbent (35°) position. An experienced certified operator (FS) acquired IVC imaging in both standard M-mode and with the aid of AI, using the same portable ultrasound machine General Electric (GE) Venue Go R2. In particular, M-Mode imaging was stored with the calculation of IVC
diameters and IVCd index performed subsequently off-line. For the IVC analysis in M-mode, the experienced operator performing the calculations took several measures of the diameters and finally used the most appropriate ones for the calculation of the IVCd. The AI imaging were acquired with the automated border detection function (each clip lasting 6 seconds). In case of the analysis with artificial intelligence (AI), repeated measures were taken and saved in the database. The images were subsequently reviewed off-line checking for artifacts and errors.

**Study groups and outcomes**

Four groups of data were generated from the combination of the view of image acquisition (SC or TH) and the data calculation modality: 1) SC in M-mode; 2) SC in AI; 3) TH in M-mode; 4) TH in AI. Our study had a factorial 2x2 design, comparing the differences and correlations of IVC measurements according to:

1. **Different measuring modality:** the same site of acquisition but with different acquisition modality (M-mode vs AI), thus comparing:
   - SC-in M-mode vs SC in AI; and
   - TH in M-mode vs TH in AI;

2. **Different acquisition view:** the same measuring modality with different view of imaging (SC vs TH), thus comparing:
   - SC in M-mode vs TH in M-mode; and
   - SC in AI vs TH in AI.

The variable of primary interest in our study was the IVCd index. As secondary endpoints we analyzed the IVC diameters (IVCmax and IVCmin).

**Statistical analysis**

A study reported high correlation between SC and TH imaging of the IVC (Pearson coefficient $r = 0.86$), but the authors included a heterogeneous population of patients ventilated in pressure support or PCV, as well as patients on non-invasive ventilation and high-flow nasal oxygen[35]. Conversely, another study reported much lower correlation coefficients (0.14 to 0.32)[36]. The impression from a systematic review conducted on this argument[22] and including seven studies was that overall agreement between the two approaches is moderate at best. Therefore, sample size was calculated assuming a statistical power of 80% and an $\alpha$ level at 0.05, with a correlation coefficient estimated at $r = 0.55$. The resulted sample size calculation was $n = 24$.

We calculated the agreements mean bias, and limits of agreement (LOA) between IVC measurements in different areas/modalities with the Bland and Altman plots. Bland-Altman plots and statistics were adjusted for the effect of multiple measures as described by Zou only for the comparison of AI modalities[37]. The bias indicates the accuracy of measurements methods, while the LOA specifies the
precision. Their values are reported with the relative 95% confidence interval. Considering that the best cut-off for prediction of FR using the IVCd index in mechanically ventilated patients is considered 18% [12–14], we decided that a mean bias of 4% and 2% would describe acceptable and good accuracy, respectively. Regarding the precision (LOA) of the measurements, we considered a range of 16% and 8% as acceptable and good precision, respectively. The relationship among variables was evaluated calculating the intra-class correlation (ICC) coefficient in order to describe the inter-rater variability between measures acquired with the same modality (AI TH vs AI SC, or M-mode TH vs M-mode SC) or in the same approach (AI TH vs M-mode TH, or AI SC vs M-mode SC) resemble each other. Interpretation of correlation was performed according to established cut-offs[38].

Results

Descriptive statistics of the patients participating in the study are reported in Table 1. Of the 33 patients included, one did not have any acoustic window (3%) and was excluded; further three patients did not have SC view (9.1%) and for other five (15.2%) it was not possible to obtain the TH visualization. Overall feasibility was 87.9% for SC imaging and 81.8% for TH visualization. The mean IVCd indexes were 14.8% ±7.9 and 15.1%±8.5 for SC and TH imaging, respectively.

Table 1.

<table>
<thead>
<tr>
<th>Baseline characteristics and measurements</th>
<th>Ventilatory settings and Hemodynamics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>PEEP (cmH\textsubscript{2}O)</td>
</tr>
<tr>
<td>25/32 (78%)</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>Age (years-old)</td>
<td>Pressure Control (cmH\textsubscript{2}O)</td>
</tr>
<tr>
<td>65 ± 13</td>
<td>16 ± 6</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>Tidal Volume (ml)</td>
</tr>
<tr>
<td>80 ± 21</td>
<td>517 ± 124</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>Respiratory Rate (bpm)</td>
</tr>
<tr>
<td>170 ± 7</td>
<td>16 ± 3</td>
</tr>
<tr>
<td>SaO\textsubscript{2} (%)</td>
<td>98 ± 3</td>
</tr>
<tr>
<td>IVCmin in SC (mm)</td>
<td>Heart Rate (bpm)</td>
</tr>
<tr>
<td>20.8 ± 4.4</td>
<td>83 ± 19</td>
</tr>
<tr>
<td>IVCmax in SC (mm)</td>
<td>Sinus rhythm (n=)</td>
</tr>
<tr>
<td>23.7 ± 4.3</td>
<td>29/32</td>
</tr>
<tr>
<td>IVCd in SC (%)</td>
<td>SAP (mmHg)</td>
</tr>
<tr>
<td>14.8 ± 7.9</td>
<td>106 ± 22</td>
</tr>
<tr>
<td>IVCmin in TH (mm)</td>
<td>MAP (mmHg)</td>
</tr>
<tr>
<td>19.8 ± 4.2</td>
<td>74 ± 14</td>
</tr>
<tr>
<td>IVCmax in TH (mm)</td>
<td>DAP (mmHg)</td>
</tr>
<tr>
<td>22.6 ± 4.2</td>
<td>58 ± 12</td>
</tr>
<tr>
<td>IVCd in TH (%)</td>
<td>PPV (%)</td>
</tr>
<tr>
<td>15.1 ± 8.5</td>
<td>13 ± 10</td>
</tr>
<tr>
<td>Norepinephrine (mcg/kg/min)</td>
<td>0.33 ± 0.22</td>
</tr>
<tr>
<td>Mortality</td>
<td>Vasoactive (n=)</td>
</tr>
<tr>
<td>22/32 (69%)</td>
<td>20/32 (63%)</td>
</tr>
<tr>
<td>Second vasoactive drug (n=)</td>
<td>5</td>
</tr>
</tbody>
</table>
Characteristics of the study population and average results of the inferior vena cava (IVC) distensibility, minimum and maximum diameters (IVCd, IVC-min and IVC-max, respectively) calculated in subcostal (SC) and transhepatic (TH) windows. DAP: diastolic arterial pressure; MAP; mean arterial pressure; PPV: pulse pressure variation; PEEP: positive end-expiratory pressure; SAP: systolic arterial pressure. Data are reported as mean and standard deviation.

Results of the Bland Altman plots are reported in Table 2, where the mean bias, the lower and the upper LOA with their 95%CI are shown. In the same table we report also the Spearman rho and ICC to describe how strong measurements resemble each other.

**Table 2.**
<table>
<thead>
<tr>
<th>Comparison</th>
<th>Variable</th>
<th>ICC 95% CI</th>
<th>Mean Bias 95% CI</th>
<th>Upper LOA 95% CI</th>
<th>Lower LOA 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>M-SC</strong></td>
<td>IVC Min (mm)</td>
<td>0.79; -0.01 to 0.93</td>
<td>3.0; 2.0 to 4.0</td>
<td>8.1; 6.3 to 9.8</td>
<td>-2.1; -3.8 to -0.3</td>
</tr>
<tr>
<td><strong>AI-SC</strong></td>
<td>IVC Max (mm)</td>
<td>0.78; 0.02 to 0.93</td>
<td>2.9; 1.9 to 3.9</td>
<td>8.1; 6.4 to 9.9</td>
<td>-2.3; -4.1 to -0.5</td>
</tr>
<tr>
<td><strong>IVC DI (%)</strong></td>
<td>0.65; 0.27 to 0.83</td>
<td>-3.1; -6.4 to 0.3</td>
<td>13.9; 8.1 to 19.7</td>
<td>-20.1; -25.9 to -14.3</td>
<td></td>
</tr>
<tr>
<td><strong>M-SC</strong></td>
<td>IVC Min (mm)</td>
<td>0.88; -0.06 to 0.96</td>
<td>2.4; 1.8 to 3.1</td>
<td>5.6; 4.5 to 6.7</td>
<td>-0.7; -1.8 to 0.4</td>
</tr>
<tr>
<td><strong>AI-TH</strong></td>
<td>IVC Max (mm)</td>
<td>0.85; -0.08 to 0.96</td>
<td>2.5; 1.9 to 3.2</td>
<td>5.9; 4.7 to 7.1</td>
<td>-0.8; -2.0 to 0.3</td>
</tr>
<tr>
<td><strong>IVC DI (%)</strong></td>
<td>0.65; 0.25 to 0.84</td>
<td>-2.0; -5.5 to 1.5</td>
<td>15.4; 9.3 to 21.5</td>
<td>-19.3; -25.4 to 13.3</td>
<td></td>
</tr>
<tr>
<td><strong>M-SC</strong></td>
<td>IVC Min (mm)</td>
<td>0.74; 0.41 to 0.88</td>
<td>1.1; -0.7 to 2.8</td>
<td>9.1; 6.1 to 12.0</td>
<td>-6.9; -9.9 to -4.0</td>
</tr>
<tr>
<td><strong>M-TH</strong></td>
<td>IVC Max (mm)</td>
<td>0.69; 0.30 to 0.86</td>
<td>1.2; -0.5 to 3.0</td>
<td>9.5; 6.4 to 12.5</td>
<td>-7.0; -10.0 to -3.9</td>
</tr>
<tr>
<td><strong>IVC DI (%)</strong></td>
<td>0.54; -0.09 to 0.80</td>
<td>0.1; -4.0 to 4.2</td>
<td>19.3; 12.1 to 26.4</td>
<td>-19.0; -26.2 to -11.9</td>
<td></td>
</tr>
<tr>
<td><strong>AI-SC</strong></td>
<td>IVC Min (mm)</td>
<td>0.77; 0.46 to 0.90</td>
<td>0.4;</td>
<td>7.8; 5.75 to 10.82</td>
<td>-6.9; -9.9 to -4.9</td>
</tr>
<tr>
<td><strong>AI-TH</strong></td>
<td>IVC Max (mm)</td>
<td>0.76; 0.45 to 0.90</td>
<td>0.9;</td>
<td>7.8; 5.9 to 10.7</td>
<td>-6.0; -8.92 to -4.1</td>
</tr>
<tr>
<td><strong>IVC DI (%)</strong></td>
<td>0.32; -0.63 to 0.72</td>
<td>2.0</td>
<td>29.7; 23.3 to 39.4</td>
<td>-25.7; -35.4 to -19.3</td>
<td></td>
</tr>
</tbody>
</table>

Summary of comparisons between measurement of the inferior vena cava (IVC) in adult patients mechanically ventilated in pressure control mode. In case of the IVC size analysis in M-mode (M), we analyzed a single measure which was the most reliable measure as decided by the experienced operator performing the calculations. In case of the analysis with artificial intelligence (AI), repeated measures...
were taken and saved in the database. Results of IVC distensibility, minimum and maximum diameters (IVCd, IVC-min and IVC-max, respectively) are provided in term of mean Bias and limits of agreement (LoA) with their relative 95% confidence interval (CI), where appropriate. We also provide intraclass correlation coefficient (ICC) to describe how strong the measurements resemble each other.

**Different acquisition modality**

Comparing M-mode and AI strategy for IVC assessment, measurements where similar both for SC IVCd index (bias -3.1%, LoA [-20.1; 13.9], Figure 1) and diameters (IVCmax: bias 2.9mm, LoA [-2.3; 8.1]; IVCmin: bias 3.0 mm, LoA [-2.1; 8.1]), as well as for the TH IVCd (bias -2.0%, LoA [-19.3; 15.4]; Figure 2) and diameters (IVCmax: bias 2.5 mm, LoA [-0.8; 5.9]; IVCmin: bias 2.4 mm, LoA [-0.7, 5.6]). As shown by the violet dotted line in the Bland-Altman plots of Figure 1, there was a clear trend in the bias for the IVCd index when calculated in SC imaging: precisely, a lower bias between M-Mode and AI was seen when the IVCd index was approaching 5%. Conversely, a trend in the bias between modalities of IVCd calculation was not present in the case of TH imaging.

Overall, the ICC coefficients showed moderate to good reliability; in particular, the ICC of the IVCd was 0.65 [0.25, 0.84] for SC imaging, and 0.65 [0.27, 0.83] for the TH window.

**Different acquisition site**

When the assessments of the IVC were compared between anatomical sites (SC vs TH) we found that comparing the SC and TH M-mode assessment, IVCd had a mean bias 0.1% with LoA [-19.0; 19.3] (Figure 3); also, the IVC diameters showed differences between anatomical sites (IVCmax: bias 1.2 mm, LoA [-7.0; 9.5]; IVCmin: bias 1.1 mm, LoA [-6.9; 9.1]). When the evaluation was performed with the aid of AI, the differences between SC and TH seemed slightly higher for the IVCd (bias 2.0%, LoA [-25.7; 29.7]; Figure 4) and the diameters (IVCmax: bias 0.9 mm, LoA [-6.0; 7.8]; IVCmin: bias 0.4 mm, LoA [-6.9, 7.8]). The correlation of IVCd index seemed slightly weaker when comparing the SC and the TH windows, with ICC ranging between 0.32 and 0.54 (Table 2).

**Discussion**

Our study evaluated the assessment of the IVCd index (and of the IVC diameters) at two different anatomical regions, comparing results obtained from a standard sagittal view (SC approach) with those gathered with coronal approach (TH). Of note, our study not only evaluated the accuracy of the standard method (M-Mode), but also introduced the evaluation of the IVCd and diameters results acquired with an automated modality (AI). Thus, the present investigation has features of a 2x2 factorial study, linking evaluations of the IVC from different technical and anatomical standpoints.

**Comments on results from different acquisition modality**
Therefore, we separate the discussion of our results in two parts. First, we discuss results focused on the validation of AI measurements for IVC assessment, and thereafter debate the differences between imaging in SC (sagittal) or TH (coronal) approach. As other studies evaluated the differences between SC and TH imaging in mechanically ventilated patients\[20, 35, 39\], we focus first on the differences between M-Mode and AI measurements, with particular emphasis on the results on the IVCd index, which is the one used by clinicians for decision-making at the bed-space. Our results suggest that introduction of AI could have some clinical value; indeed, we found that accuracy of AI calculation was between acceptable and good according to predefined interpretation cut-offs. In particular, AI overestimate the IVCd index both for TH and SC approach (mean bias – 2% for TH and of -3.1% for SC). However, in both cases we found suboptimal precision comparing the M-Mode and the AI measurements as demonstrated by relatively wide upper and lower LoA, with roughly a 17% difference from the mean bias. In this context, it must be considered that estimating the diameters when the IVC is almost fully collapsible (i.e. IVCmin below 0.5 mm) is technically challenging. In such cases, the evaluation in M-Mode using the touch screen (as for the ultrasound machine in our study) may be prone to smaller mistakes that could affect precision of the measurements, finally influencing the LOA. Although the accuracy of TH imaging (-2%) may seem greater than SC (-3.1%), it is important to note from a clinical perspective that the Bland-Altman plot of the SC imaging (Fig. 1) showed a clear trend bias for the IVCd index (violet dotted line). In particular, as compared to AI calculation, the M-Mode seems underestimating the IVCd index, with greater differences between modalities seen for the higher values of IVCd index (i.e. fluid responders). Indeed, we noted that mean bias approaches the “zero” value (excellent accuracy between methods) when the IVC has limited excursion with minor changes in its diameter during respiration (IVCd close to 5%). Summarizing, it seems that AI offers an accurate reproduction of M-Mode calculations for the IVCd index; thus, AI introduction for automated border detection may be great assistance for clinicians in daily practice, with potentialities of saving time for bedside assessment of volume status. Moreover, the use of AI may allow a larger number of IVCd index calculations that could be averaged, with possible advantages in cases of borderline IVCd results. From practical perspectives, instead of freezing the ultrasound image, to measure the IVC diameters and to apply the IVCd index formula, with the help of AI the sonographer/physician can just hold the probe focused on the IVC whilst the ultrasound machine calculates values of IVCd (or eventually IVC collapsibility index according to the type of ventilation selected). The use of AI has been applied to the whole echocardiography setting (i.e. left ventricular systolic[23, 24] and diastolic[25–27] function, to right ventricular function[28], assessment of heart valve diseases[29], diagnosis of congenital heart diseases[30]) and also to predict of FR, with encouraging results. For instance, Bataille et al.[31] showed that machine learning models predicted FR with comparable accuracy to the hemodynamic response to passive leg raising, and evaluation of the IVC was among the key variables identified by the model, together with other Doppler derived parameters. Blaivas et al. used a deep learning algorithm capable of video classification for the estimation of FR using IVC imaging, and demonstrated that the trained algorithm had moderate performances with an area under the curve of 0.70 (95%CI: 0.43-1.00) [32]. Further, the same group verified that the performances of this algorithm were dependent on the quality of the IVC image with significantly worse performances on images of lower quality[40]. The findings of our study pooled together with the other few studies available suggests that introducing AI for
the calculation of the IVC indexes of FR may be valuable for the daily clinical practice, with good accuracy of the AI as compared to the M-Mode although the precision of the method may be suboptimal.

**Comments on results from different acquisition site**

Our study investigated also the interchangeability of IVCd index recorded in SC and in TH approaches. A recent systematic review included seven studies, suggested that results of SC and TH imaging for IVCd may be not fully interchangeable. However, the evidence comes from a very heterogeneous cohorts of participants, being present studies on both volunteers, spontaneously breathing and/or mechanically ventilated patients[22]. We observed small mean biases of IVCd index between SC and TH imaging obtained both in case of M-Mode or AI measurements (0.1% and 2%, respectively), and this finding is not novel, as similar ones have been reported for M-Mode measurements by two studies (IVCd index mean bias of 0.5%[20] and −0.5%[35]), while to the best of our knowledge, no study has compared SC and TH with the aid of AI. Despite the small mean biases, we confirmed wide LoA for both M-Mode and AI methods (roughly 19% and 28%, respectively), suggesting suboptimal precision and partially discouraging the interchangeability of measurements between sites. Interestingly, the use of AI did not improve the accuracy or precision as compared to the M-Mode calculations.

Nonetheless, regardless the interchangeability of SC and TH imaging, we believe that TH window is easy even in novice hands and can be clinically useful, especially when the sagittal (SC) imaging cannot be achieved (i.e. obesity, for the presence of laparotomy wound, mediastinal drains, etc). Thus, research should be encouraged for the investigation of cut-offs for predicting FR using the IVC in coronal view (TH). In this context, the feasibility of TH imaging in our study was 82%, very similar to the one reported by Valette et al (81%)[35].

**Strengths and Limitations of the study**

The main strengths of this study regard the use of AI for both validating this method as compared to the reference method (M-Mode) and for investigating the differences between SC and TH imaging. We conducted a study in a homogeneous population of mechanically ventilated patients with PCV mode with an average of 8 ml/kg of tidal volume and a low positive end expiratory pressure (5.9 cmH$_2$O). Most of the patients recruited was on vasopressor support (average norepinephrine 0.32 mcg/kg/min) and with a pulse pressure variation on the edge of FR (13%), resembling a typical population where assessment of FR may be clinically needed. Overall, our study seemed adequately powered as we recruited 24 patients with both SC and TH imaging as per sample size estimation, where we assumed a correlation coefficient of 0.55. Of note, as compared to this assumed value, we found a higher ICC in the comparison between methods (M-Mode vs AI) in the same anatomical area ($r = 0.65$ for both the SC and the TH areas), and a similar ICC when comparing different areas with M-Mode approach ($r = 0.54$). Only the ICC evaluating different areas with AI approach resulted much lower ($r = 0.32$), and therefore only the data on AI may be underpowered.

Our study has also several limitations. First, this cohort was smaller than the other three studies on ventilated patients, although it is the largest study enrolling a hybrid population with full range of
ventilatory support, from full mechanical ventilation to self-breathing patients without support. Second, a single experienced operator collected the images and performed M-mode calculations, and results may be different in less experienced hands. Third, we did not perform fluid challenge in our population so that we cannot calculate cut-offs and area under the curve for the prediction of FR. Fourth, the image acquisition followed a schematic pattern starting from SC imaging and moving to TH approach after to avoid human mistakes in data collection, but an ideal methodological design would have provided randomization of the order of image recording. Nonetheless, we believe this is unlikely to influence results but it remains fair to acknowledge such item.

Conclusions

The use of artificial intelligence for the evaluation of the inferior vena cava distensibility index seem to have good accuracy when compared with standard M-mode assessment, both in case of subcostal or transhepatic imaging. However, the precision of the method is suboptimal. Artificial intelligence does not seem to reduce the differences in inferior vena cava distensibility between SC and TH imaging, and results from these two anatomical sites yield low precision.

Abbreviations

Fluid responsiveness (FR), intensive care unit (ICU), inferior vena cava (IVC), IVC distensibility (IVCd), IVC collapsibility (IVCc), subcostal (SC), trans-hepatic (TH), artificial intelligence (AI), limits of agreement (LOA), intra-class correlation (ICC).

Declarations

Ethics approval and consent to participate: Our prospective observational study was approved from our local Ethical Committee (Ethical Committee Catania 1 - Reference protocol: 53/2022/PO).

Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors contributions: Study design by FS, LLV, VD, AN. Data extraction performed by FS, LLV, PA, VD. Data double-check performed by AM, CR, GG, AN. Discordances were resolved by agreement between FS, LLV, CR and AN. Analysis and Figures FS, LLV, GG, AN. Data interpretation FS, LLV, AM, CR, AN. Drafted the manuscript FS, LLV, VD. Critical revision AM, PA, CR, GG, AN. All authors agree on the final version of the manuscript.

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**References**


Figures
Figure 1
Bland-Altman plot for the inferior vena cava distensibility index (IVCd) measured in subcostal (SC) site with standard M-Mode or artificial intelligence (AI). SD: standard deviation.

Figure 2
Bland-Altman plot for the inferior vena cava distensibility index (IVCd) measured in Transhepatic (TH) site with standard M-Mode or artificial intelligence (AI). SD: standard deviation.
Figure 3

Bland-Altman plot for the inferior vena cava distensibility index (IVCd) measured with standard M-Mode in two different sites: subcostal (SC) and transhepatic (TH). SD: standard deviation
Figure 4

Bland-Altman plot for the inferior vena cava distensibility index (IVCd) measured with artificial intelligence (AI) mode in two different sites: subcostal (SC) and transhepatic (TH). SD: standard deviation