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ORIGINAL RESEARCH

SHoC-IVC: Does assessment of the inferior vena cava by point-of-care ultrasound independently predict fluid status in spontaneously breathing patients with undifferentiated hypotension?

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Abstract

Background Accurately determining the fluid status of a patient during resuscitation in the emergency department (ED) helps guide appropriate fluid administration in the setting of undifferentiated hypotension. Our goal was to determine the diagnostic utility of point-of-care ultrasound (PoCUS) for inferior vena cava (IVC) size and collapsibility in predicting a volume overload fluid status in spontaneously breathing hypotensive ED patients.

Methods This was a post hoc secondary analysis of the SHOC-ED data, a prospective randomized controlled trial investigating PoCUS in patients with undifferentiated hypotension. We prospectively collected data on IVC size and collapsibility for 138 patients in the PoCUS group using a standard data collection form, and independently assigned a fluid status (volume overloaded, normal, volume deplete) from a composite clinical chart review blinded to PoCUS findings. The primary outcome was the diagnostic performance of IVC characteristics on PoCUS in the detection of a volume overloaded fluid status.

Results One hundred twenty-nine patients had completed determinant IVC assessment by PoCUS, with one hundred twenty-five receiving successful final fluid status determination, of which one hundred and seven were classified as volume deplete, thirteen normal, and seven volume overloaded. A receiver operating characteristic (ROC) curve was plotted using several IVC size and collapsibility categories. The best overall performance utilized the combined parameters of a dilated IVC (> 2.5 cm) with minimal collapsibility (less than 50%) which had a sensitivity of 85.7% and specificity of 86.4% with an area under the curve (AOC) of 0.92 for predicting an volume overloaded fluid status.

Conclusion IVC PoCUS is feasible in spontaneously breathing hypotensive adult ED patients, and demonstrates potential value as a predictor of a volume overloaded fluid status in patients with undifferentiated hypotension. IVC size may be the preferred measure.

Keywords Point-of-care ultrasound · Inferior vena cava · Hypotension · Fluid status · Emergency department

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Résumé

Contexte La détermination précise de l'état du liquide d'un patient pendant la réanimation au service des urgences (SU) aide à guider l'administration appropriée du liquide dans le cadre d'une hypotension indifférenciée. Notre objectif était de déterminer l'utilité diagnostique de l'échographie au point de soins (PoCUS) pour la taille de la veine cave inférieure (IVC) et l'collapsibilité dans la prédiction d'un état de liquide de surcharge volumique chez les patients souffrant d'une hypotension respiratoire spontanée.

Méthodes Il s'agissait d'une analyse secondaire post-hoc des données SHOC-ED, un essai contrôlé randomisé prospectif examinant PoCUS chez des patients atteints d'hypotension indifférenciée. Nous avons collecté prospectivement des données sur la taille et la collapsibilité des IVC pour 138 patients du groupe PoCUS à l'aide d'un formulaire de collecte de données standard, et attribué indépendamment un état de fluide (volume surchargé, normal, épuisement du volume) à partir d'une revue de dossier clinique composite mise en aveugle aux résultats PoCUS. Le résultat principal était la performance diagnostique des caractéristiques IVC sur PoCUS dans la détection d'un état de fluide surchargé en volume.

Résultats 129 patients avaient terminé l'évaluation IVC des déterminants par PoCUS, dont 125 ont reçu une détermination finale du statut hydrique, dont 107 ont été classés comme étant une diminution du volume, 13 normaux et 7 surchargés. Une courbe des caractéristiques de fonctionnement du récepteur (ROC) a été tracée en utilisant plusieurs catégories de taille et d'affaissement IVC. La meilleure performance globale a utilisé les paramètres combinés d'une IVC dilatée (> 2,5 cm) avec une collapsibilité minimale (moins de 50%) qui avait une sensibilité de 85,7% et une spécificité de 86,4% avec une zone sous la courbe (AOC) de 0,92 pour prédire un état de fluide surchargé en volume.

Conclusion IVC PoCUS est faisable chez les patients adultes souffrant d'une hypotension respiratoire spontanée et démontre une valeur potentielle en tant que prédicteur d'un état de liquide surchargé en volume chez les patients atteints d'hypotension indifférenciée. La taille IVC peut être la mesure préférée.

Mots clés échographie au point de service · veine cave inférieure · hypotension · état du liquide · service d'urgence

Clinician's capsule

What is known about the topic?
Determining a shocked patient's initial fluid status in the emergency department can be time-consuming and imprecise.

What did this study ask?
Does inferior vena cava point-of-care-ultrasound independently predict the volume overloaded fluid status in hypotensive, spontaneously breathing adult patients?

What did this study find?
Point-of-care-ultrasound measured IVC size and perhaps collapsibility, showed reasonable sensitivity and specificity for identifying patients who are volume overloaded, though the target population numbers were low.

Why does this study matter to clinicians?
Having a rapid and effective method of identifying fluid overloaded patients could potentially prevent harm with inadvertent excess fluid administration.

Introduction

In the initial assessment and resuscitation of a hypotensive patient, the best way to rapidly determine fluid status and calculate the volume of fluid to be administered remains a topic of continued debate. Total fluid status is generally categorized as *volume deplete*, *euvolemic (normal)*, or *volume overloaded* [1]. Fluid status assessment remains a complicated composite of vital signs, physical examination, and investigations [2], many of which remain inconvenient and difficult to administer in a timely fashion, and which can be inaccurate when applied to patients at both extremes of the fluid status spectrum [1, 3]. Avoiding inappropriate fluid administration is particularly important in volume overloaded patients where additional fluid administration can contribute to pulmonary edema, organ failure, coagulopathy, and infection [4, 5]; with approximately 50% of patients receiving fluid resuscitation for acute circulatory failure with unknown initial fluid status having worse outcomes [6].

The integration of point-of-care-ultrasound (PoCUS) for the assessment of inferior vena cava (IVC) diameter and respiratory variability, or collapsibility, has become a more feasible option for assessing a patient's intravascular fluid status, though much of the current literature includes intubated intensive care unit patients. IVC variability represents the change in IVC diameter during a respiratory cycle. Greater IVC collapsibility indices correlate with an increased likelihood of fluid responsiveness [3]; however,

there is conflicting evidence as to whether IVC parameters alone provide an accurate assessment of a patient's fluid responsiveness [3, 7–13], though PoCUS assessment does improve diagnostic certainty for initial treatment plans in hypovolemic patients (SBP < 90 mmHg)[8]. A *normal* IVC diameter is considered to be 1.7 cm ± 0.4 cm, with an average decrease in diameter by 50% during tidal respiration [7], with generally accepted pragmatic limits of IVC size being "small" at less than 1.0 cm or "dilated" at greater than 2.5 cm [1]. The literature to date is not clear on whether IVC size, collapsibility, or a combination of each is most reliable.

In this secondary analysis of the Sonography in Hypotension and Cardiac Arrest in the Emergency Department (SHoC-ED) study dataset [12], we examine whether the IVC measurement with PoCUS can accurately determine initial fluid status in spontaneously breathing adult patients who present to the ED with undifferentiated hypotension. Specifically, as a measure of harm reduction, our primary outcome was to assess if IVC ultrasound measurements of size and collapsibility could identify shocked patients who are *volume overloaded* at initial presentation, with an additional focus on whether *IVC size* or *collapsibility* is most useful.

Methods

We performed a post hoc secondary analysis of data collected on the 138 patients randomized to PoCUS during an international randomized controlled trial set in 6 high volume centers across North America and South Africa [10]. A detailed study protocol is available in the original report [10] and further outlined in Supplementary Fig. 1 in the Appendix. The study represents real-world standards for sonographer skill levels, with all physicians performing PoCUS being trained, with each site using local processes to confirm credentialing, qualifications, and skill level for ultrasound. As reported in the original study, most physicians were able to generate a complete PoCUS protocol with conclusive views. PoCUS machines were a mixture of models and brands but all were deemed to provide quality images by the study group. Table 1 provides details on the patient characteristics and baseline measures from the original study.

The study population included all patients who underwent assessment by PoCUS and who subsequently had their fluid status determined by expert clinical review, utilizing a structured chart review blinded to PoCUS findings. Spontaneously breathing adult patients were screened after triage by trained staff to identify two parameters: a sustained systolic blood pressure (SBP) < 100 mmHg or a shock index > 1.0. Shock index (SI) is defined as heart rate over SBP. Inclusion criteria for study enrollment were: 19 years of age and older; presentation with a sustained initial systolic blood pressure < 100 or a shock index > 1.0 (with systolic blood pressure < 120 mmHg).

Exclusion criteria for this analysis were: indication of an indeterminate (or incomplete) scan; PoCUS findings of cardiac tamponade, pulmonary hypertension, mechanical ventilation, pregnancy known at time of presentation or discovered during initial screening; the necessity of CPR or other advanced cardiac life support interventions (e.g., defibrillation, emergency pacing, insertion of ventricular

Table 1 Patient characteristic, baseline measurements, and category of shock for all patients eligible to undergo IVC PoCUS

Patient characteristics and baseline measures	
Characteristic	Variable
Total participants (*n*)	138
North America *n* (%; binomial CI)	90 (65.2%; 56.6 to 73.1%)
South Africa *n* (%; binomial CI)	48 (34.8%; 26.8 to 43.3%)
Male n (%; binomial CI)	73 (52.9%; 44.2 to 61.4%)
Age in years: median (IQR)	56 (53.4 to 59.8)
Systolic blood pressure in mmHg: median (IQR)	91.0 (88.5 to 94.2)
Heart rate in bpm: median (IQR)	106.5 (102.4 to 111.8)
Respiratory rate per minute: median (IQR)	24.3 (22.3 to 26.0)
Temperature in °C: median (IQR)	36.7 (36.5 to 36.9)
Category of shock *n* (%; binomial CI)	
Cardiogenic	15 (10.8%; 6.2 to 17.3%)
Non-cardiogenic	121 (87.6%; 81.0 to 92.6%)
Both	1 (0.7%; 0.0 to 3.9%)
Uncertain	1 (0.7%; 0.0 to 3.9%)

assist device, etc.) prior to screening or enrollment; a history of significant trauma in past 24 h; a 12 lead electrocardiogram (ECG) diagnostic of acute myocardial infarction (AMI); a clear mechanism or etiology for the hypotension or shock is evident (i.e., where an obvious cause for the shocked state, such as gastrointestinal bleeding, or ruptured aortic aneurysm, is immediately identifiable by the treating physician, and therefore the patient does not have *undifferentiated* shock), a previously known diagnosis from other hospital (for transferred patients); a vagal episode (as cause of hypotension) and low blood pressure considered to be non-pathologic (normal variant or other). Research ethics approval was obtained from all local research ethics boards.

IVC Parameters and blinded fluid status assessment

Initial IVC size, measured by PoCUS during the first hour of ED assessment, was initially categorized as *small* (diameter < 1 cm), *normal, or dilated* (> 2.5 cm)* [1]. Collapsibility (variability) was defined as; *none, less than 50%, greater than 50%, or complete*.

The criterion standard defining actual fluid status was determined by blinded chart review assessment that included records detailing clinical assessment, a composite of vital signs (heart rate, blood pressure, and orthostatic changes in blood pressure and heart rate), physical examination (mentation, capillary refill, skin turgor and dryness, skin perfusion, temperature, and urine output), and investigations (fractional excretion of sodium and urea, blood lactate, and mixed venous oxygen saturation) as well as response to treatment during the patient's hospital stay. The reviews were performed independently by two specialist clinicians who had access to all aspects of the patients' care and status other than the initial PoCUS assessment. The patient's fluid status was classified as *volume deplete, normal, or* volume overloaded using a consensus process [14]. Inter-rater reliability was not assessed.

*For the purpose of focusing on the primary objective of identifying volume overloaded patients, for the primary analysis, *volume deplete* and *normal* patients were combined into one group, separate from the high-risk *volume overloaded* patient group of interest in this analysis.

Statistical analysis

A receiver operating characteristic (ROC) curve analysis was performed to determine the optimal sensitivity, specificity, and likelihood ratios of various combinations of IVC size and collapsibility as predictors potential harm from excess intravenous fluids (patients classified as "volume overloaded"). Further details can be seen in Supplementary Fig. 3 in the appendix. We also report diagnostic performance with 95% confidence intervals. Analysis was performed using Stat v 15 software. We estimated sample size using a power analysis, which determined a sample size of 100 patients undergoing initial PoCUS provided a power of 80% with an alpha of 0.05, based upon an expected prevalence of 20% for patients not requiring IV fluid resuscitation.

Results

Of the 138 patients included in the PoCUS arm of the SHoC-ED study, 137 had scans of their IVC recorded. Of those 137 patients, 8 had indeterminate IVC scans and were excluded. Of the 129 who had determinate scans, 4 lacked enough data (i.e., charting, laboratory investigations, equivocal imaging) for the blinded assessors make a classification of fluid status. As a result, 125 patients were included in the final analysis (see Supplementary Fig. 2 in the appendix).

From the 125 patients who were included in the final analysis, the IVC size and collapsibility frequencies as determined by PoCUS are summarized in Table 2 and Supplementary Table 3. There were no patients with an IVC that was assessed as both dilated and completely collapsible.

In terms of clinical fluid status, of the 125 patients who were included in the study, 105 (84%) were *volume deplete*, 13 (10.4%) were *euvolemic*, and 7 (5.6%) were *volume overloaded* as determined by expert clinical consensus.

Size and collapsibility

IVC size, using a binary approach with a cutoff for a large or dilated IVC set at greater than 2.5 cm, performed well for the identification of fluid overload, with a sensitivity of 100% (95% CI 59.0 to 100.0%), and a specificity of 95.4 (88.6 to 98.7%). Other parameters are shown in Table 3.

Table 2 Number of patients grouped by IVC size and collapsibility as measured by PoCUS

		IVC SIZE (n=125)		
		Dilated (n=14)	**Normal** (n=43)	**Small** (n=68)
IVC COLLAPSIBILITY (n=125)	**None** (n=18)	6	9	3
	Under 50% (n=43)	7	19	17
	Over 50% (n=46)	1	11	34
	Complete (n=18)	0	4	14

Table 3 Performance of PoCUS-measured IVC size as a predictor of fluid overload

	Overfilled status	Underfilled + normal status
Large IVC size	7	4
Small + normal IVC size	0	83
Measure	Value	95% CI
Sensitivity	100.0%	59.0 to 100.0%
Specificity	95.4%	88.6 to 98.7%
Positive likelihood ratio	21.8	8.4 to 56.7
Negative likelihood ratio	0	N/A
Disease prevalence	7.5%	3.1 to 14.7%
Positive predictive value	63.6%	40.2 to 82.0%
Negative predictive value	100.0%	N/A
Accuracy	95.7%	89.5 to 98.8%

Table 4 Performance of PoCUS-measured-IVC collapsibility as a predictor of fluid overload

	Overfilled status	Underfilled + normal status
IVC collapse under 50%	6	46
IVC collapse over 50%	1	41
Measure	Value	95% CI
Sensitivity	85.2%	42.1 to 99.6%
Specificity	47.1%	36.3 to 56.1%
Positive likelihood ratio	1.6	1.13 to 2.3
Negative likelihood ratio	0.3	0.1 to 1.9
Disease prevalence	7.5%	3.1 to 13.7%
Positive predictive value	11.5%	8.3 to 15.8%
Negative predictive value	97.6%	86.8 to 99.6%
Accuracy	50.0%	39.5 to 60.5%

IVC variability as measured by collapsibility was slightly less reliable as an independent measure for the detection of fluid overload, with a sensitivity of 85.2% (42.1 to 99.6%) and a specificity of 47.1% (36.3 to 56.1%). Other parameters are shown in Table 4.

No patients had incongruous combinations of a small IVC diameter with no or minimal collapsibility, or a dilated IVC diameter with maximal collapsibility. The four combinations that underwent analysis were limited to normal and dilated IVC sizes along with no or minimal (< 50%) collapse. The receiver operating characteristic (ROC) curve (Supplementary Fig. 3) provided a sensitivity analysis for these four IVC parameter combinations in (with an area under the curve (AOC) of 0.92) predicting a volume overloaded fluid status. The various combinations of size and collapsibility were performed along a continuum from maximal sensitivity through to maximal specificity. Sensitivity was maximized with a normal IVC size (< 2.5 cm) and minimal (< 50%) collapsibility, which was 100% sensitive and while retaining 71.2% specificity for predicting the volume overloaded status. Specificity was maximized with a normal IVC size and no collapse with 42.9% sensitivity and 94.9% specificity. The intermediate combinations of a dilated IVC with no collapsibility had a sensitivity of 71.4% and specificity of 91.53%; whereas a dilated IVC with minimal collapsibility was 85.7% sensitive and 86.4% specific. As a rule-in test, highest specificities (over 90%) were seen in the *no IVC collapse* category. Confidence intervals are presumed wide for all values due to the low numbers (see Supplementary Tables 5 and 6). No combination outperformed IVC size alone.

Discussion

Interpretation of findings

Most importantly, this study confirms that obtaining IVC measurement by PoCUS is feasible in the ED in spontaneously breathing patients with undifferentiated hypotension. The vast majority of patients (94.1%) had successful (determinate) IVC scans, adequately measuring IVC size and collapsibility. Although patients with a volume overloaded fluid status were quite infrequent in this patient population, our analysis indicates that IVC size alone as determined by PoCUS, along with various combinations of IVC size and collapsibility could possibly be helpful in identifying these patients, and potentially avoiding harmful fluid administration. Again, being cautious due to the low number of patients in question, with subsequently poor confidence intervals, our data show that a dilated IVC over 2.5 cm in diameter performs well as a predictor of fluid overload with very high sensitivity and specificity; while a lack of IVC collapse is highly specific in *ruling in* the volume overloaded status, and that combinations of IVC size and collapse can perform well overall in predicting the volume overloaded fluid status with dilated IVC and no or minimal collapsibility being the most

reliable combinations, with collapsibility in isolation being 21.8 shown to be a somewhat unreliable measure.

Comparison to previous studies

Whereas most previous studies assessing PoCUS of the IVC aim to predict fluid responsiveness, our study focused on determining fluid status, specifically for the identification of volume overloaded patients to prevent additional harm from inappropriate administration of intravenous fluids during initial resuscitation. In contrast to a meta-analyses on IVC ultrasound in assessing fluid responsiveness [6, 10], our results showed a higher area under the curve (0.92), with improved sensitivity, specificity, and positive likelihood ratios in identifying patients who are fluid overloaded. We found no previous studies that focused on identifying fluid overloaded patients based on these categories of IVC measurement.

Strengths and limitations

Our study had high levels of follow up to 7 days or hospital discharge, and was able to demonstrate real-world feasibility, with scans being performed by practicing emergency physicians who obtained a high percentage of successful IVC measurements using PoCUS. Other strengths further include the blinded nature of the final fluid status assessment. There are, however, several significant limitations to the current study. The first and most significant limitation is the small number of patients who were classified with the target fluid status of being overloaded. In addition, by sub-dividing the diagnostic categories by both IVC size and collapsibility, the remaining numbers of patients included in each category are extremely small, impacting the strength of the recommendations that can be made. With the retrospective nature of the final clinical fluid status assessment performed by two blinded clinicians, but with no inter-rater reliability assessment, it is not possible to verify the validity of the gold standard composite fluid status chart review; we recognize that this can make replication and generalizability difficult. Furthermore, there is some debate around the consistency of IVC measurement among clinicians, particularly variability in IVC measurement with intrathoracic pressure changes (such as with spontaneous tidal respiration) and other causes such as chronic RV dysfunction, chronic tricuspid regurgitation, cardiac tamponade, and increased intra-abdominal pressure [4]. Additionally, obesity, abdominal distension, wound dressings, monitor wiring, and intra-abdominal hypertension are all potential barriers to obtaining accurate IVC measurements [7]. These findings are further limited to a certain population of patients, specifically those who are breathing spontaneously and have undifferentiated hypotension, and these results are not applicable to pediatric patients. No data abstraction tool was used by clinical experts when performing the chart review and this could impact the reproducibility of this study.

Research implications

Further studies should prospectively investigate these specific IVC characteristics as measured by PoCUS as predictors of fluid status and responsiveness in the spontaneously breathing hypotensive or shocked patient, with larger numbers of patients in general, and specifically the target group, but also with improved criterion standards.

Clinical implications

The main clinical implication of this study's findings is that PoCUS is a feasible and accurate additional tool to assist in the initial assessment of fluid status in spontaneously breathing adult patients with undifferentiated hypotension. Such measurements may be useful in identifying patients who are fluid overloaded at initial presentation. These patients are often unstable and require timely care, and therefore having a test that is rapid and reliable, and helps reduce barriers to care and could potentially prevent complications from administering unnecessary and potentially harmful intravenous fluids. Due to the noted study limitations, clinicians should exercise caution and should incorporate these findings into their clinical assessment rather than relying on IVC PoCUS independently for the identification of patients with volume overload.

Conclusion

IVC measurement by PoCUS is feasible in spontaneously breathing, hypotensive, adult emergency department patients, and demonstrates potential value as a predictor of a volume overloaded fluid status in this population. IVC size may be the preferred measure.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s43678-023-00584-1.

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Author contributions The study was designed by PA, RD, and JF. All authors participated in data collection and analysis, and contributed to the final manuscript. The authors have no conflicts of interest to declare.

Data availability Original data is available on request.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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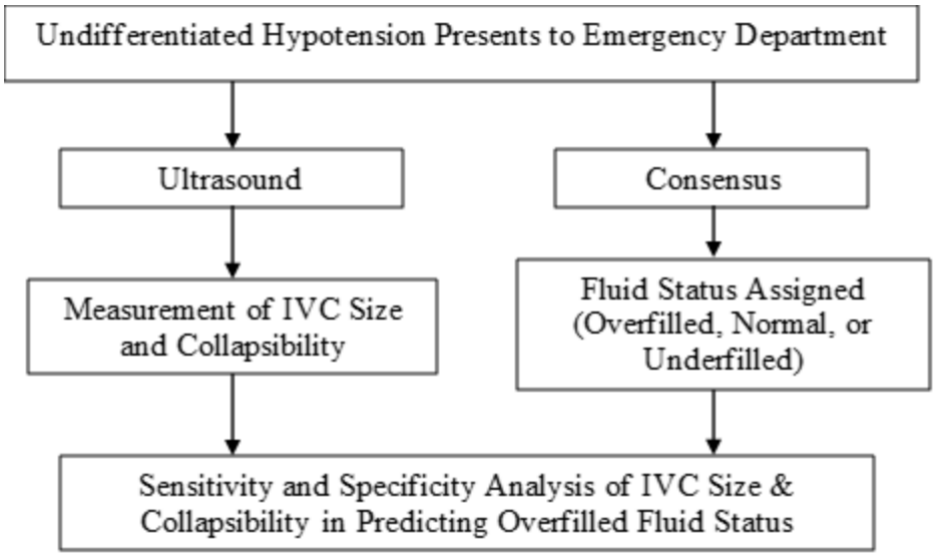
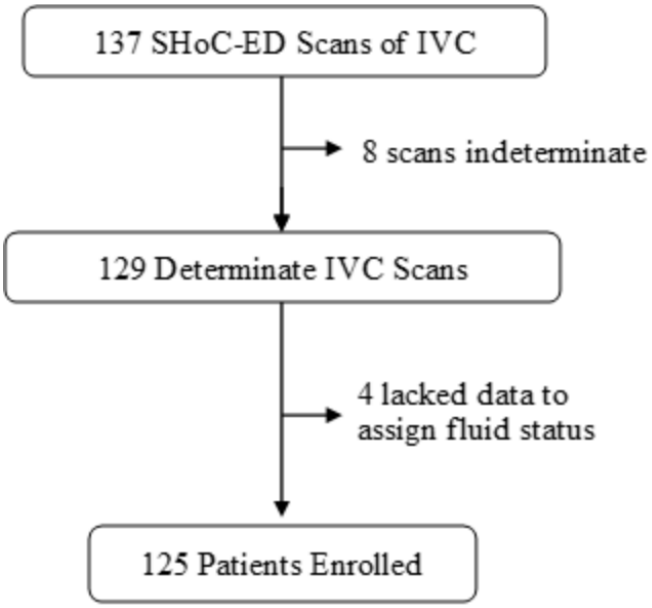
Appendix

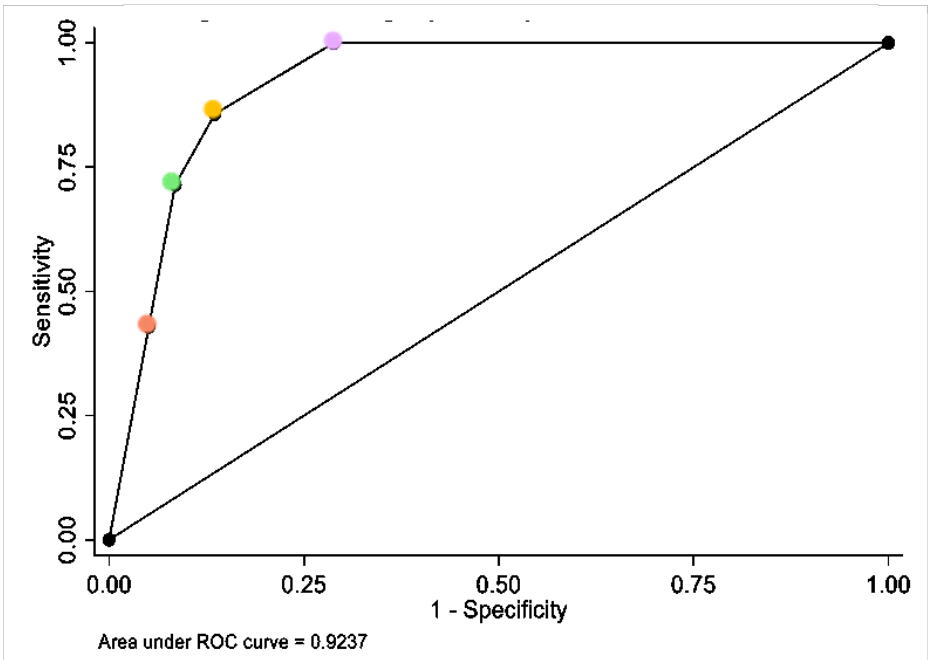
Supplementary Figure 1a: SHoC-IVC Study Protocol



Supplementary Figure 2: CONSORT Diagram


137 SHoC-ED Scans of IVC
8 scans indeterminate
129 Determinate IVC Scans
4 lacked data to assign fluid status
125 Patients Enrolled

Supplementary Figure 3: Receiver Operating Characteristic (ROC) Curve, IVC Parameters as Predictors of Volume Overloaded Status



Normal Size, No Collapse
Dilated, No Collapse
Dilated, Collapse >50%
Normal Size, Collapse <50%

Supplementary Table 5: Frequency of Clinically Volume Overloaded Patients by IVC Size and Collapsibility.

		IVC SIZE		
		Dilated	**Normal**	**Small**
IVC COLLAPSIBILITY	**None**	**2/6** = 33.3% (95% CI 9.7% to 70%)	**3/9** = 33.3% (95% CI 12.1 to 64.6%)	**0/3** = 0% (95% CI 0 to 56.2%)
	Under 50%	**1/7** = 14.3% (95% CI 2.6 to 51.3 %)	**1/19** = 5.3% (95% CI 0.9 to 24.6%)	**0/17** = 0% (95% CI 0 to 18.4%)
	Over 50%	**0/1** = 0% (95% CI 0 to 79.4%)	**0/11** = 0% (95% CI 0 to 25.9%)	**0/34** = 0% (95% CI 0 to 10.1%)
	Complete	**0/0** = 0%	**0/4** = 0% (95% CI 0 to 49.0%)	**0/14** =0% (95% CI 0 to 21.5%)

Supplementary Table 6: Performance of various combinations of IVC size and collapsibility as predictors of the Volume Overloaded Status in undifferentiated hypotensive adult patients.

IVC PARAMETER / COMBINATION	Sensitivity	Specificity	% Correctly Classified	Positive Likelihood Ratio	Negative Likelihood Ratio
Size (Max. Diameter >2.5cm)	100.0%	95.4%	95.78%	21.8	0.0
Collapse < 50%	82.5%	47.1%	50.0%	1.6	0.3
Normal Size, No Collapse	42.9%	94.9%	92.0%	8.4	0.6
Dilated, No Collapse	71.4%	91.5%	90.4%	8.4	0.3
Dilated, Collapse <50%	85.7%	86.4%	86.4%	6.3	0.2
Normal Size, Collapse <50%	100.0%	71.2%	72.8%	3.5	0.0000