Original Article

Internal jugular vein distensibility: Rapid and reliable bedside assessment tool to predict fluid responsiveness in mechanically ventilated septic patients

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Abstract

Background and Aims: This study aims to evaluate whether respiratory changes in internal jugular vein (IJV) diameter predicts fluid responsiveness in mechanically ventilated patients with sepsis.

Methods: In this prospective observational analytic study, mechanically ventilated patients in septic shock received 7ml/kg of Normal Saline (NS) over 15 minutes. Patients were then categorized into two groups retrospectively; fluid responders (R), if there was an increment in Cardiac Index (CI) by more than or equal to 15% following fluid administration, and non-responders (NR) if the increase in CI was less than 15%. The primary outcome was respiratory changes in IJV diameter before and after fluid administration. Ultrasonographic assessment of IJV distensibility was carried out in all mechanically ventilated septic patients before and after fluid administration.

Results: In our study, 74 mechanically ventilated septic patients were enrolled. Among them, 29 (39.2%) patients were fluid responders whereas 45 (60.8%) patients were non-responders. Responders demonstrated higher IJV distensibility before volume expansion than non-responders (33.33% vs 16.9%; P <0.001). Significant reduction in this difference was observed following volume challenge in responders (33.33% to 20.18%). An IJV distensibility of >28.2% before fluid administration predicted the change in CI ≥15% with 90% sensitivity and 100% specificity with area under curve of 0.985 (CI 0.963 to 1.006).

Conclusion: Ultrasound evaluation of respiratory changes in IJV distensibility effectively predicts fluid responsiveness in mechanically ventilated septic patients.

Introduction

Predicting fluid responsiveness in a patient with circulatory failure due to sepsis is an important aspect of patient management. Rapid, reproducible and accurate prediction of intravascular volume and maintenance of cardiac output helps to improve the outcomes of patients who are critically ill.[1, 2] However, it is difficult to determine intravascular volume status of critically ill patients. Various studies show that approximately only 50% of haemodynamically unstable patients are fluid responsive.[3] Fluid loading without predicting responsiveness may not be effective or even deleterious, in subset of patients with pre-existing heart failure or on mechanical ventilation.[4,5] Similarly, injudicious use of vasopressors may lead to tissue hypoperfusion.[6] Studies have also shown relationship between positive fluid status and mortality in septic patients.[7] Therefore, number of studies have been done for determination of predictors of fluid responsiveness. Studies

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have recommended that volume responsiveness can be identified by increase in SV or CO by 15% or more after 500-ml infusion of crystalloid solution.[8-10] In addition, evidence has shown that echocardiography is very useful dynamic and non-invasive tool for identification of volume responsiveness in hemodynamically unstable patients.[11, 12]

Several static and dynamic parameters have been developed in clinical practice over time for predicting fluid responsiveness and to subsequently guide the therapy. Moreover, dynamic parameters have been considerably studied and used, including superior venacava collapsibility, inferior venacava collapsibility, and alterations in cardiac output in response to passive leg raising (PLR).[13, 14] However, IVC measurements are not always possible because of distension of abdomen, tissue edema, abdominal wounds, morbid obesity or presence of large amounts of intrathoracic air. SVC imaging, in spite of being more precise, requires transesophageal echocardiography resulting in limited application.[4, 15] It has been demonstrated that volume and pressure alterations in intrathoracic systemic venous compartment are reciprocated in extrathoracic veins, like extrathoracic IJV.[13,14] In addition, transesophageal echocardiography is not required for IJV imaging and is technically simpler to perform than visualization of IVC.

On the basis of this relationship of intrathoracic venous volume and pressure to extrathoracic venous pressure, we tested the hypothesis that respiratory variations in internal jugular vein diameter in mechanically ventilated septic patients would predict fluid responsiveness.

Methods

A prospective observational analytical study was carried out at Intensive Care Unit (ICU) with 11 beds at Tribhuvan University Teaching Hospital (TUTH). After approval of the study by Institutional Review Committee, written informed consent was obtained from legal guardian prior to inclusion. This study was conducted from November 1st 2018 to June 30th 2019.

Adult patients of age, 18 years or more, diagnosed with sepsis and on mechanical ventilation, presenting in acute circulatory failure were included in our study. Sepsis, in our study, was defined as per Sepsis-3 definition which defined it as a life-threatening organ dysfunction as a result of dysregulated host response to infection. Patients with severe aortic stenosis, irregular ventricular rhythm, mechanical ventilation with high PEEP (≥10 cm H20), lung hyperinflation due to conditions like asthma/ COPD exacerbation, cardiac conditions impeding venous return, increased intra-abdominal pressure and pregnancy were excluded from our study.

Baseline demographics, diagnosis at ICU admission, SOFA score, hemodynamic parameters (CI, HR, MAP), vasopressor use, ventilator settings, and ultrasonographic measurement of the IJV were recorded in all the patients fulfilling the eligibility criteria. All enrolled patients were sedated using fentanyl (1mcg/ kg) and paralyzed using atracurium (0.5mg/kg). Absence of inspiratory efforts was ensured based on ventilator waveform and monitoring parameters. Mechanical ventilation was done in volume-controlled mode with tidal volume (TV) of 8ml/kg, plateau pressure (Pplat) < 30 cmH2O, I: E ratio: 1:2, PEEP <10 cmH2O and respiratory rate of 14 breaths/ minute during the study period. Ventilator settings were again changed back to the previousl settings after the completion of data collection.

The ultrasound examination of IJV was carried out with a 6-13 MHz linear transducer and ultrasound system. The IJV was identified at the level of cricoid cartilage and confirmed by compression, pulse wave Doppler and color Doppler. Taking into consideration, the effect of patient position on IJV, each and every measurement was done in semi-recumbent position with head elevation of 30°. Measurements were carried out on the contralateral side of central venous catheter insertion to avoid catheter infection. Examinations were performed by anesthesiologists, each of whom had expertise of greater than 100 ultrasound-guided IJV cannulations. The antero-posterior (AP) diameter of IJV was calculated by use of M-mode. At the time of ultrasonography, sufficient ultrasound gel, such that a thin film of gel was visualized between the probe and skin, was applied to avoid direct contact between skin and transducer to eliminate the effect of compression on the IJV diameter. IJV evaluation was carried out by positioning the probe perpendicular to skin with orthogonal orientation (first along long axis and then perpendicular to it) to the jugular vein short-axis diameter.

Transthoracic echocardiography (TTE) was then carried out using the multiarray probe (1-5 MHz) to measure the CO and then CI. TTE was done by a critical care resident who has performed at least 30 fully supervised TTE studies. The area of aortic valve was determined by diameter of aortic outlet which was studied at insertion of aortic cusp in parasternal long axis view during systole, as aortic valve area= $\pi \times (\text{aortic diameter}/2)^2$. The stroke volume was defined as stroke volume = aortic valve area× velocity time integral (VTI) of Left Ventricular Outflow Tract (LVOT). VTI was measured in apical five-chamber view of TTE. Cardiac output was measured as cardiac output = stroke volume (SV) × heart rate (HR). Cardiac output was then divided by body surface area to get cardiac index.

All haemodynamic and ultrasonic measurements were done before and after 7ml/kg of NS administration over 15 minutes. Infusion rates of vasoactive drugs and settings of the ventilator were kept constant during this 15-minute observation period. Measurement of change in CI was done to identify responders and non-responders and analyze hemodynamic variables including CI, MAP, and HR between the two groups. Patients were labeled as fluid responders if there was increase in CI by ≥15% following volume loading, and as non-responders if the change in cardiac index was <15%. The IJV distensibility index (%) was defined as ratio of difference in IJV maximum AP diameter during inspiration and minimal IJV diameter during expiration to minimal IJV diameter during expiration × 100. Receiver operator characteristic (ROC) curves were also constructed to calculate maximum sensitivity and specificity of IJV distensibility for predicting fluid responsiveness (i.e. ΔCI ≥15%).

The primary outcome under study was respiratory changes in IJV diameter among responders and non-responders in mechanically ventilated septic patients in response to fluid administration. The secondary outcomes were hemodynamic changes including heart rate, cardiac index and mean arterial pressure (MAP) in Responders and non-responders, Receiver-Operating-Characteristic (ROC) curves of optimal IJV distensibility, and sensitivity and specificity of IJV distensibility in predicting Responders.

All data were recorded in Microsoft Excel 2010 spreadsheet and then analysed using “Statistical Package for Social Sciences” version 17. The different parameters for two groups were analysed by Student’s t-test, Wilcoxon test or Mann Whitney test, depending upon whether the data were normal or skewed.

The qualitative data were matched using Chi- Square test. The Quantitative data were presented by Mean ±SD or median/ Interquartile range test, based on normality of the data. The qualitative data were presented as percentages, rates etc. The data were also presented graphically using tables, pie charts etc. 'P' value of <0.05 was taken as statistically significant. Receiver operator characteristic (ROC) curves were constructed to calculate maximal sensitivity and specificity of IJV distensibility for predicting responsiveness to fluids (i.e., ΔCI ≥15%).

Results

In the present study, 74 mechanically ventilated septic patients were included. Among them, 29 (39.2%) patients were fluid responders whereas 45 (60.8%) patients were non-responders. Both the study groups were comparable in terms of age, BSA, BMI, SOFA score, time since admission, tidal volume, Positive End Expiratory pressure, plateau pressure, Intra- abdominal Pressure (IAP) and TAPSE (Tricuspid Annulus Plane Systolic Excursion) (Table 1)

Table 2 shows haemodynamic and ultrasonographic evaluation between responders and non-responders. Regarding hemodynamic data, there was no statistically significant discrepancy between two groups in baseline mean arterial pressure and HR. Heart rate was not found to vary between responder and non-responder groups both before and following volume challenge. However, responders displayed an increase of mean arterial blood pressure (p<0.001) following fluid challenge. No significant variations in arterial pressure were seen in non-responder group. Though cardiac index was found to increase in both the groups (R, P < 0.001; NR, P < 0.001), the change in CI was 24.91% IQR 22.75-28.735 in case of responders whereas the change was 5.63% IQR 4.055-8.55 in non- responders. The change in CI between two groups was significant statistically (p<0.001).

Similarly, the change in Left Venticular Outflow Tract -Velocity Time Integral (LVOT-VTI) before and after volume expansion was 28.21% in case of responders whereas it was only 4.74% in case of non-responders which was again statistically significant (p<0.001).

Regarding IJV distensibility, IJV distensibility was greater in responders before volume expansion compared to non-responders (33.33% vs 16.9%; P <0.001). This difference was significantly reduced after volume challenge in case of responders (33.33% to 20.18%). In case of non-responders, change was from 16.9% to 16.09%. Responders demonstrated significant reduction in IJV distensibility after volume expansion, which was not seen in NR (16.03% vs 1.35%; P< 0.001).

ROC curves were constructed to determine sensitivity and specificity of IJV distensibility to predict fluid responsiveness. An IJV distensibility of >28.2% before fluid administration prognosticated a change in cardiac index (CI) ≥15% with 90% sensitivity and 100% specificity, AUC 0.985 (CI 0.963 to 1.006) (Table 3 and Figure 1).

Discussion

The results of our study demonstrated that ultrasound evaluation of respiratory variations in IJV distensibility in mechanically ventilated septic patients is a reliable, easily acquired non-invasive parameter that can function as a substitute marker for other dynamic parameters of fluid responsiveness. Fluid resuscitation is imperative in management of septic shock. However, it can be detrimental in patients on flat portion of Frank-Starling curve. As a result, it is very important to monitor volume responsiveness in the ICU.[5,16]

Multiple results till date have shown that static parameters have reduced ability to adjudicate fluid responsiveness in patients who are critically ill.[17,18] Recent Surviving sepsis campaign guidelines suggest application of dynamic in place of static parameters to predict fluid responsiveness, where available.[19]

Various dynamic parameters include passive leg raising, stroke volume or cardiac output or VTI changes to fluid challenges, or pulse pressure variations to intrathoracic pressure changes generated by mechanical ventilation. Passive leg raising is a bed side test which is easy to perform and has shown to allow dependable recognition of fluid responsiveness even in context of arrhythmias or spontaneous breathing. However, it is important not to conduct PLR in patients of head injury and also in those sensitive to effects of raised intra-abdominal pressure. At the same time, it cannot be applied in patients having fracture or after surgery.[16,20,21] Therefore, there is an increasing need of more convenient and safe method of predicting fluid responsiveness.

Several studies have analyzed respiratory variations in extra-thoracic venous diameter during assessment of hypovolemia or cardiovascular response to fluid challenge.[1,4] Number of studies have been done on variations in venacava diameter and fluid responsiveness, and it has been found that these variations are dependable predictors of fluid responsiveness.[22,23] Broilo et al[4] substantiated the theory that respiratory changes of IJV and IVC were related. However, they did not measure differences in cardiac output and diameters of the veins before and after fluid challenge. There have been some studies on respiratory variations in IJV diameter done mainly in patients who were breathing spontaneously.[24,25] However, the studies on mechanically ventilated, critically ill patients are more scarce. Few years ago, Guarracino et al[26] demonstrated that IJV distensibility predicts volume responsiveness in mechanically ventilated critically ill patients with good precision.

Our study also intended to verify whether respiratory changes in IJV diameter is a reliable index to predict fluid responsiveness in mechanically ventilated septic patients. Our results showed that an IJV distensibility of >28.2% before fluid administration augured a change in CI ≥15% with 90% sensitivity and 100% specificity. Various studies evaluating operational parameters to augur cardiac index response to volume loading have used ROC-curve to determine optimal threshold, enabling maximum sensitivity and specificity. In our study, AUC for assessment of fluid responsiveness was 0.985 (CI 0.963 to 1.006). Guarracino et al[26] had shown the predictability of IJV distensibility on assessing fluid responsiveness of ventilated patients, with a value of over18% IJV distensibility, predicting alteration in CI ≥15% with 80% sensitivity and 95% specificity, AUC 0.915 (CI 0.801 to 0.975). They also studied IJV distensibility and PPV in combination and it was found that the combination of IJV distensibility of >9.9% and PPV of >12% predicted fluid responsiveness with 100% sensitivity and 95% specificity.

Some discrepancies between our study and that by Guarracino et al may be due to various reasons. Though the amount of fluid administered was same (7ml/kg) in both the studies, the mechanical ventilation settings were not similar. In study by Guarracino et al, the TV used was 6-8ml/kg and PEEP was 6 cm of H_2O with median RR of 16. However, in our study, we used TV of 8ml/kg with median PEEP of 8 cm of H_2O and RR of 14. Besides, the haemodynamic data were monitored using system based on PRAM (pressure recording analytical method) algorithm. However, we used TTE for measuring Cardiac Index.

On the other hand, Ma et al[13] showed the predictability of IJV variability in accessing fluid responsiveness with a value of 12.99%, having 91.43% sensitivity and 82.86% specificity in mechanically ventilated cardiac surgical patients. The areas under ROC curves for determining fluid responsiveness were 0.88 (CI 0.78–0.94) for Internal Jugular Vein Variability. The results were different from our study. It may be because this study was done on post-operative cardiac patients whereas our study was done on septic patients.

Similar to earlier studies, our study demonstrated that baseline HR was not adequate for determining fluid responsiveness.16 Though the MAP was increased in responders in our study population, studies suggest that Blood Pressure does not determine a patient's reaction to fluid loading with precision, as it is influenced by drugs, fever, pain, anemia, stress, and intrinsic heart disease among different factors.[26,27]

In our study, more than 60% of patients were found to be non-responders. This outcome is in line with earlier research which were carried out to examine fluid responsiveness.[4,22,23] These results highlight the need of parameters to select patients who may benefit from fluid administration, which helps to avoid detrimental volume expansion in non-responder patients.

Various previous studies have shown that response to fluids cannot be accurately predicted if tidal volume is lower than 8 ml/kg PBW.[28,29] Hence, a tidal volume equal to 8 ml/kg PBW was kept in our study. As high PEEP may show harmful consequences like overinflation, which in turn either increase or leave the IJV size unaltered introducing a bias, along with hemodynamic instability, a PEEP of < 10 cm of H_2O was used.

Our study used TTE for measurement of CO. Mercado et al[2] had conducted a study to determine the accuracy and precision of TTE compared to PAC and the reliability of transthoracic echocardiography to identify changes in cardiac output, in mechanically ventilated critically ill patients. TTE has shown few significant advantages over PAC. Firstly, TTE is a non-invasive method comparable to PAC. Secondly, this study has shown that Percentage Error is lower with TTE than other minimally invasive or non-invasive devices currently in practice. Though some studies have defined responders as an increase of >11% in cardiac index, we used 15% to be comparable with data applied in more recent literature.[22,23,29]

Our study has some limitations. First, this study was done in a single center, which limits the external validity of the study. Second, it has been done in sedated and paralyzed septic shock patients, who had no arrhythmia and were ventilated using tidal volume of 8 ml/kg. Therefore, our results cannot be directly extrapolated to spontaneously breathing patients and other clinical conditions. Third, in our study, 34 (46%) patients were on vasopressors. It is not yet known whether the use of vasoactive drugs would independently affect IJV distensibility index. This interaction and subsequent elucidation needs to be studied. Fourth, all the scans were carried out in semi-recumbent position with elevation of head end at 30°. The predictive value of IJV distensibility in other positions remains to be assessed.

Conclusion

The results of this study demonstrate that respiratory changes in IJV distensibility measured by ultrasound is an easy, non-invasive and precise tool for predicting fluid responsiveness in mechanically ventilated patients with sepsis. It can be reliably used when other dynamic indices of fluid responsiveness are difficult to obtain or are unavailable.

References

1. Halilo-lu M, Bilgili B, Kararmaz A, et al. The value of internal jugular vein collapsibility index in sepsis. Ulus Travma Acil Cerrahi Derg. 2017;23(4):294-300. [https://pubmed.ncbi.nlm.nih.gov/28762449/]

2. Mercado P, Maizel J, Beyls C, et al. Transthoracic echocardiography: an accurate and precise method for estimating cardiac output in the critically ill patient. Crit Care. 2017;21(1):136. [https://pubmed.ncbi.nlm.nih.gov/28595621/]

3. Levitov A, Marik PE. Echocardiographic assessment of preload responsiveness in critically ill patients. Cardiol Res Pract. 2012:819696. [https://pubmed.ncbi.nlm.nih.gov/21918726/]

4. Broilo F, Meregalli A, Friedman G. Right internal jugular vein distensibility appears to be a surrogate marker for inferior vena cava vein distensibility for evaluating fluid responsiveness. Rev Bras Ter Intensiva. 2015;27(3):205-11. [https://pubmed.ncbi.nlm.nih.gov/26465243/]

5. Machare-Delgado E, Decaro M, et al. Inferior vena cava variation compared to pulse contour analysis as predictors of fluid responsiveness: a prospective cohort study. J Intensive Care Med. 2011;26(2):116-24. [https://pubmed.ncbi.nlm.nih.gov/21595098/]

6. Michard F. Changes in arterial pressure during mechanical ventilation. Anesthesiology. 2005;103(2):419-28. [https://pubmed.ncbi.nlm.nih.gov/16052125/]

7. Acheampong A, Vincent JL. A positive fluid balance is an independent prognostic factor in patients with sepsis. Crit Care. 2015;19(1):251. [https://pubmed.ncbi.nlm.nih.gov/26073560/]

8. Critchley LA, Lee A, Ho AMH. A critical review of the ability of continuous cardiac output monitors to measure trends in cardiac output. Anesth Analg. 2010;111(5):1180-92. [https://pubmed.ncbi.nlm.nih.gov/20736431/]

9. Thiel SW, Kollef MH, Isakow W. Non-invasive stroke volume measurement and passive leg raising predict volume responsiveness in medical ICU patients: an observational cohort study. Crit Care. 2009;13(4):R111. [https://pubmed.ncbi.nlm.nih.gov/19586543/]

10. Guinot PG, Zogheib E, Detave M, et al. Passive leg raising can predict fluid responsiveness in patients placed on venovenous extracorporeal membrane oxygenation. Crit Care. 2011;15(5):R216. [https://pubmed.ncbi.nlm.nih.gov/21923944/]

11. Brun C, Zieleskiewicz L, Textoris J, et al. Prediction of fluid responsiveness in severe preeclamptic patients with oliguria. Intensive Care Med. 2013;39(4):593-600. [https://pubmed.ncbi.nlm.nih.gov/23223774/]

12. Mandeville JC, Colebourn CL. Can transthoracic echocardiography be used to predict fluid responsiveness in the critically ill patient? A systematic review. Crit Care Res Pract. 2012;513480. [https://pubmed.ncbi.nlm.nih.gov/22400109/]

13. Ma GG, Hao GW, Yang XM, et al. Internal jugular vein variability predicts fluid responsiveness in cardiac surgical patients with mechanical ventilation. Ann Intensive Care. 2018;8(1):6. [https://pubmed.ncbi.nlm.nih.gov/29340792/]

14. Charbonneau H, Riu B, Faron M, et al. Predicting preload responsiveness using simultaneous recordings of inferior and superior vena cavae diameters. Crit Care. 2014;18(5):473. [https://pubmed.ncbi.nlm.nih.gov/25189403/]

15. Nagdev AD, Merchant RC, Tirado-Gonzalez A, et al. Emergency department bedside ultrasonographic measurement of the caval index for noninvasive determination of low central venous pressure. Ann Emerg Med. 2010;55(3):290-5. [https://pubmed.ncbi.nlm.nih.gov/19556029/]

16. Wu Y, Zhou S, Zhou Z, et al. A 10-second fluid challenge guided by transthoracic echocardiography can predict fluid responsiveness. Crit Care. 2014;18(3):R108. [https://pubmed.ncbi.nlm.nih.gov/24886990/]

17. Guarracino F, Ferro B, Forfori F, et al. Jugular vein distensibility predicts fluid responsiveness in septic patients. Crit Care. 2014;18(6):647. [https://pubmed.ncbi.nlm.nih.gov/25475099/]

18. Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? : A systematic review of the literature and the tale of seven mares. Chest. 2008;134(1):172-8. [https://pubmed.ncbi.nlm.nih.gov/18628220/]

19. Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med. 2017;43(3):304-77. [https://pubmed.ncbi.nlm.nih.gov/28101605/]

20. Mahjoub Y, Touzeau J, Airapetian N, et al. The passive leg- raising maneuver cannot accurately predict fluid responsiveness in patients with intra- abdominal hypertension. Crit Care Med. 2010;38(9):1824-9. [https://pubmed.ncbi.nlm.nih.gov/20639753/]

21. Monnet X, Teboul JL. Passive leg raising. Intensive Care Med 2008;34(4):659–63. [https://pubmed.ncbi.nlm.nih.gov/18214429/]

22. Barbier C, Loubières Y, Schmit C, et al. Respiratory changes in inferior vena cava diameter are helpful in predicting fluid responsiveness in ventilated septic patients. Intensive Care Med. 2004;30(9):1740-6. [https://pubmed.ncbi.nlm.nih.gov/15034650/]

23. Feissel M, Michard F, Faller JP, et al. The respiratory variation in inferior vena cava diameter as a guide to fluid therapy. Intensive Care Med 2004;30(9):1834-7. [https://pubmed.ncbi.nlm.nih.gov/15045170/]

24. Akilli NB, Cander B, Dundar ZD, et al. A new parameter for the diagnosis of hemorrhagic shock: jugular index. J Crit Care. 2012;27(5):530. e13-8. [https://pubmed.ncbi.nlm.nih.gov/22386226/]

25. Unluer EE, Kara PH. Ultrasonography of jugular vein as a marker of hypovolemia in healthy volunteers. Am J Emerg Med. 2013;31(1):173-7. [https://pubmed.ncbi.nlm.nih.gov/22980368/]

26. Guarracino F, Ferro B, Forfori F, et al. Jugular vein distensibility predicts fluid responsiveness in septic patients. Crit Care. 2014;18(6):647. [https://pubmed.ncbi.nlm.nih.gov/25475099/]

27. Vincent JL, Weil MH. Fluid challenge revisited. Crit Care Med. 2006;34(5):1333-7. [https://pubmed.ncbi.nlm.nih.gov/16557164/]

28. De Backer D, Heenen S, Piagnerelli M, et al. Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. Intensive Care Med. 2005;31(4):517–23. [https://pubmed.ncbi.nlm.nih.gov/15754196/]

29. Michard F, Teboul JL, Richard C. Influence of tidal volume on stroke volume variation. Does it really matter? Intensive Care Med. 2003;29(9):1613. [https://pubmed.ncbi.nlm.nih.gov/12904854/]

Tables:

Table 1: Comparison of baseline characteristics between responders and non-responders

Baseline characteristics	Non-responder (NR)			Responder (R)				
	Median	Q1	Q3	Median	Q1	Q3	Z	P
Age (yr)	54	39	66.5	45	24	64	-1.297	0.195
BSA (m^2)	1.61	1.44	1.715	1.66	1.46	1.755	-0.992	0.321
BMI (kg/m^2)	22.4	20.165	23.31	21.97	20.675	22.995	-0.382	0.702
SOFA Score	9	8	10	8	7	9	-1.904	0.057
Time since admission (days)	2	0	4.5	2	1	4.5	-0.411	0.681
TV (ml)	470	390	520	480	400	520	-0.628	0.53
Pplat (cm of H_2O)	25	22	27	26	24	27.5	-1.223	0.222
PEEP(cm of H_2O)	8	8	8	8	8	8	-0.659	0.51
IAP (mm of Hg)	9	9	10	9	8	10	-1.32	0.187
TAPSE (cm)	2	1.9	2.2	2	1.9	2.2	-0.98	0.327

Table 2: Haemodynamic and US evaluation between responders and non-responders

	Non-responder			Responder				
	Median	**Q1**	**Q3**	**Median**	**Q1**	**Q3**	**Z**	**P**
Max IJV AP diameter at T0(mm)	9.8	8.4	11.25	10	9.3	12.4	-1.309	0.19
Max IJV AP diameter at T1(mm)	10	8.5	11.4	10.1	9.25	12.7	-1.058	0.29
Minimum IJV diameter at T0(mm)	8.2	7.35	9.9	7.8	7.1	8.75	-1.546	0.122
Minimum IJV diameter at T1 (mm)	8.2	7.5	9.9	8.4	8	9.8	-0.698	0.485
Aortic diameter at T0 (cm)	1.88	1.84	1.96	1.96	1.86	2.02	-1.918	0.055
Aortic diameter at T1(cm)	1.88	1.84	1.96	1.96	1.86	2.02	-1.918	0.055
Aortic valve area at T0 (cm^2)	2.77	2.66	3.02	3.02	2.715	3.2	-1.928	0.054
Aortic valve area at T1(cm^2)	2.77	2.66	3.02	3.02	2.715	3.2	-1.928	0.054
HR at T0 (beats/min)	94	87.5	103	98	90	107.5	-1.187	0.235
HR at T1 (beats/min)	96	88	104	97	88.5	107	-0.216	0.829
MAP at T0 (mm of Hg)	62	60.5	63	62	61	63	-1.392	0.164
MAP at T1(mm of Hg)	61	60	62.5	65	64	66	-6.218	<0.001
LVOT_VTI at T0 (cm)	23.8	22.6	25.15	16.8	15.95	18.7	-6.868	<0.001

LVOT_VTI at T1(cm)	25.1	23.7	26.8	22.2	20.8	23.5	-4.63	<0.001
CI at T0 (L/min/m^2)	4.19	3.565	4.63	3.01	2.615	3.88	-4.507	<0.001
CI at T1(L/min/m^2)	4.42	3.885	4.955	3.81	3.41	4.795	-1.927	0.054
Cardiac Index change (%)	5.63	4.055	8.55	24.91	22.75	28.735	-7.225	<0.001
IJVdistensibility at T0 (%)	16.9	14.115	21.87	33.33	31.035	39.205	-7.004	<0.001
IJVdistensibility at T1 (%)	16.09	12.35	20.27	20.18	17.58	22.4	-3.045	0.002
IJV distensibility change (%)	1.35	-0.965	3.105	16.03	11.315	17.595	-6.904	<0.001

Table 3: Best Criterion values and coordinates of ROC curve for distensibility of IJV

		95% CI			**95% CI**	
IJV T0	**Sensitivity**	**Lower**	**Upper**	**Specificity**	**Lower**	**Upper**
>9.81	1	1	1	0.02	-0.01	0.06
>12.1	1	1	1	0.11	0.04	0.18
>15.3	1	1	1	0.33	0.23	0.44
>18.5	1	1	1	0.56	0.44	0.67
>25.6	0.93	0.87	0.99	0.96	0.93	0.99
>28.2	0.90	0.83	0.97	1	1	1
>30.6	0.86	0.80	0.92	1	1	1
>32.3	0.62	0.48	0.75	1	1	1

Figures:

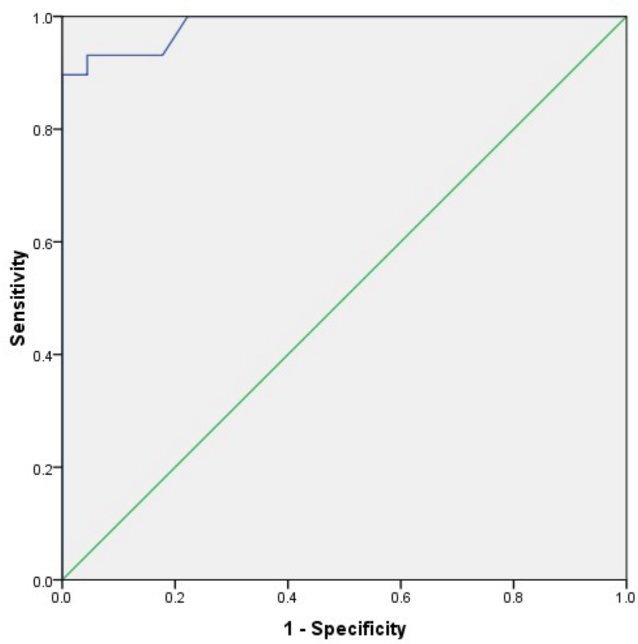

Figure 1: ROC curve of internal jugular vein distensibility for predicting fluid responsiveness with AUC of 0.985