Assessment of fluid responsiveness in ICU

Akash, SR, Pulmonary medicine

PGIMER

What is fluid responsiveness?

- Fluid responsiveness is defined as an increase in cardiac output by 10-20% after a fluid bolus of at least 4 mL/Kg or 500 mL
- Depending upon the accuracy of the method used for CO monitoring this may range between 5% and 25%

Journal of Cardiothoracic and Vascular Anesthesia, Vol 28, No 3 (June), 2014: pp 745–754

What is importance of assessing fluid responsiveness?

- Decrease unnecessary use of vasopressors
- Avoid unnecessary fluid in patients who may be harmed
- Decrease health-care cost-burden

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

- 2006 study compared ARDS patients receiving liberal and restricted fluid therapy
- The target for fluid resuscitation was PAOP and CVP (>18 vs >24 and >13 vs >18 respectively)
- Primary outcome was 60-day-mortality: no significant difference
- Higher ventilator-free days, and days alive in ICU in first 28 days among those receiving conservative fluids

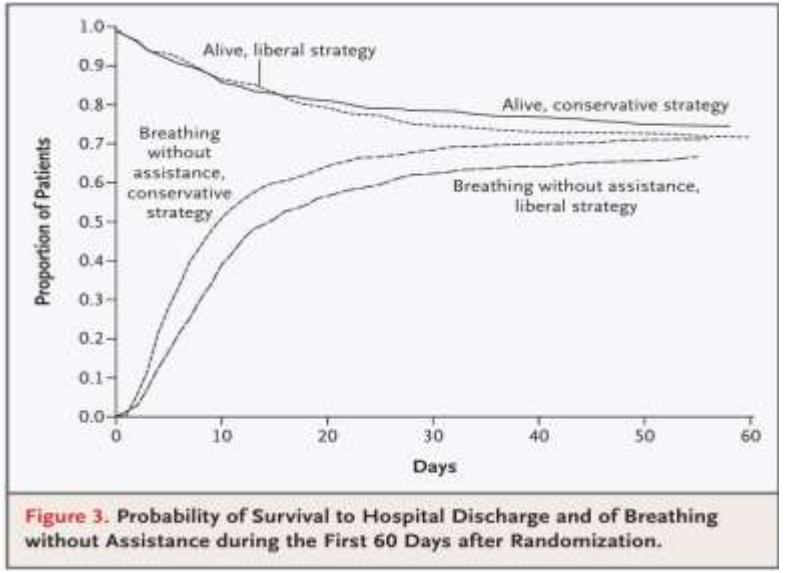

Figure 3. Probability of Survival to Hospital Discharge and of Breathing without Assistance during the First 60 Days after Randomization.

N Engl J Med 2006 Jun 15;354(24):2564-75.

Goal-directed vs usual fluid strategy

proCESS (2014, n-1351)	ARISE (2014, n-1600)	proMISE (2015, n-1260)
EGDT vs standard vs usual (1:1:1)	EGDT vs usual (1:1)	EGDT vs usual (1:1)
No significant difference in 60-day mortality, RR~1	No difference in 90-day mortality	No significant difference in 90-day mortality, RR~1

- Studied 1554 patients in septic shock and randomized 1:1 to restricted fluid group or standard group
- Intended to see a 15% change in relative risk (reflected by a 7 percentage point difference in 90 days mortality)
- Fluid administered were larger in the standard therapy group
- Failed to show any difference in 90-day-mortality, days without life support or days alive outside hospital within 90 days

Indication for fluid	
Restricted group	Standard group
Severe hypoperfusion (lactate>4mmol/Kg, MAP<50 despite vasopressor, mottling score>2 at knee, UO<0.1 mL/Kg in 2 hours following randomization)	As long as there is improvement in haemodynamic parameters (no upper limit)
Replenish documented loss	Replenish expected/observed loss
To correct electrolytes/dehydration if oral rout C/I	Maintenance fluid
Ensure total daily intake of 1L fluid	

Meyhoff TS, Hjortrup PB, Wetterslev J, Sivapalan P, Laake JH, Cronhjort M, et al. Restriction of Intravenous Fluid in ICU Patients with Septic Shock. New England Journal of Medicine. 2022 Jun 30;386(26):2459–70.

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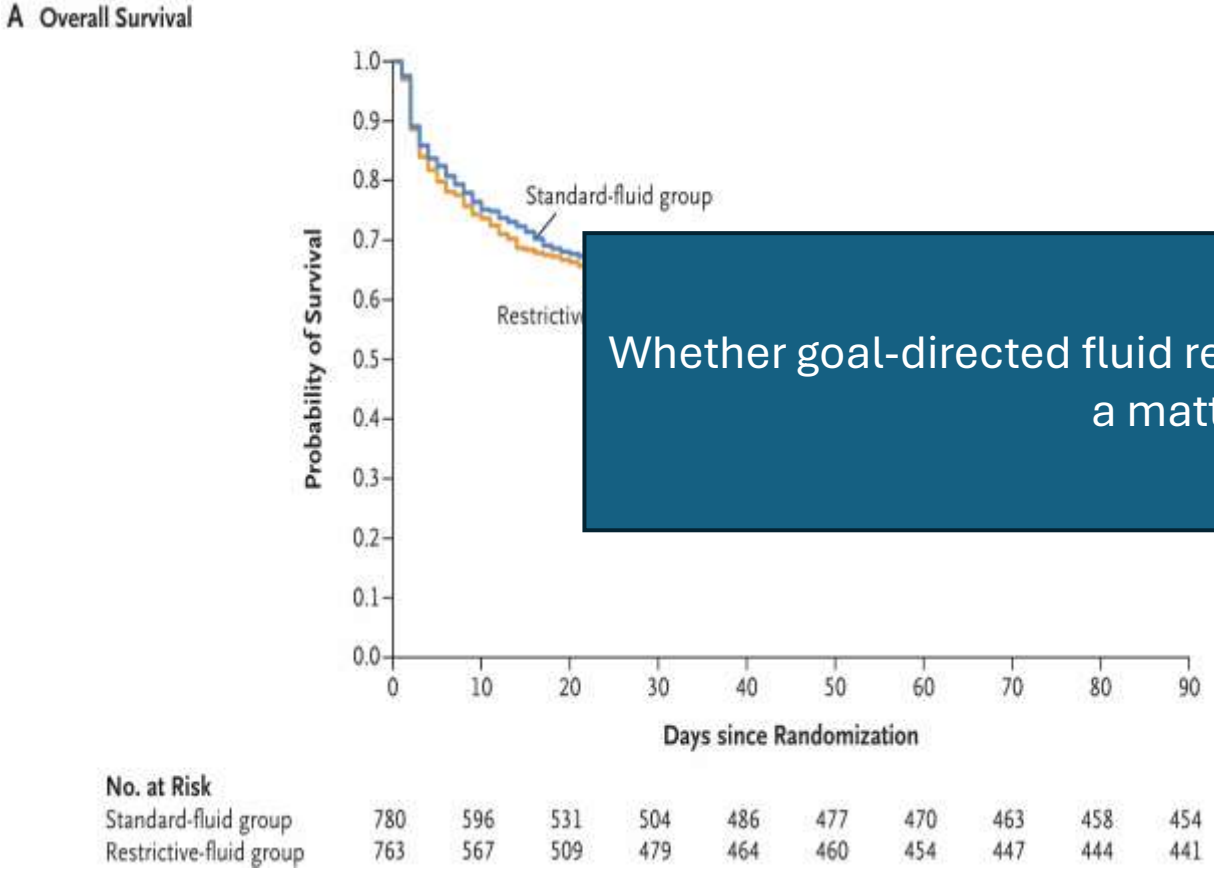
ESTABLISHED IN 1812 JUNE 30, 2022 VOL. 386 NO. 26

Restriction of Intravenous Fluid in ICU Patients with Septic Shock

T.S. Meyhoff, P.B. Hjortrup, J. Wetterslev, P. Sivapalan, J.H. Laake, M. Cronhjort, S.M. Jakob, M. Cecconi, M. Nalos, M. Ostermann, M. Malbrain, V. Pettilä, M.H. Møller, M.-B.N. Kjær, T. Lange, C. Overgaard-Steensen, B.A. Brand, M. Winther-Olesen, J.O. White, L. Quist, B. Westergaard, A.B. Jonsson, C.J.S. Hjortsø, N. Meier, T.S. Jensen, J. Engstrøm, L. Nebrich, N.C. Andersen-Ranberg, J.V. Jensen, N.A. Joseph, L.M. Poulsen, L.S. Herlov, C.G. Selling, S.K. Pedersen, K.K. Knudsen, T.S. Straarup, M.L. Vang, H. Bundgaard, B.S. Rasmussen, S.R. Aagaard, T. Hildebrandt, L. Russell, M.H. Bestle, M. Schønemann-Lund, A.C. Brochner, C.F. Elvander, S.K.L. Hoffmann, M.L. Rasmussen, Y.K. Martin, F.F. Friberg, H. Seter, T.N. Aslam, S. Ådnøy, P. Seidel, K. Strand, B. Johnstad, E. Joelsson-Alm, J. Christensen, C. Ahlstedt, C.A. Pfortmueller, M. Siegemund, M. Greco, J. Radej, M. Kitz, D.W. Gould, K.M. Rowan, P.R. Mouncey, and A. Perner, for the CLASSIC Trial Group*



Whether goal-directed fluid resuscitation improves survival is still a matter of debate

Table 3. Primary and Secondary Outcomes.

Outcome	Restrictive-Fluid Group	Standard-Fluid Group	Adjusted Absolute Difference	Adjusted Relative Risk	P Value
			percentage points		
Primary outcome*					
Death by day 90 — no./total	323/764 (42.3)	329/781 (42.1)	0.1 % CI, −4.7 to 4.9)	1.00 (95% CI, 0.89 to 1.13)	0.96
			−1.7 % CI, −7.7 to 4.3)	0.95 (99% CI, 0.77 to 1.15)	0.46
Serious adverse reaction — no./total no. (%)¶	31/755 (4.1)	32/776 (4.1)	−0.1 (99% CI, −2.8 to 2.6)	0.99 (99% CI, 0.50 to 1.93)	0.95
No. of days alive without life support‖					
Median (IQR)	77 (1 to 87)	77 (1 to 87)	0 (−11 to 11)	—	0.84
Mean	50	51			
No. of days alive and out of the hospital**					
Median (IQR)	21 (0 to 69)	33 (0 to 70)	−12 (−30 to 6)	—	0.84
Mean	33	35			

Meyhoff TS, Hjortrup PB, Wetterslev J, Sivapalan P, Laake JH, Cronhjort M, et al. Restriction of Intravenous Fluid in ICU Patients with Septic Shock. New England Journal of Medicine. 2022 Jun 30;386(26):2459–70.

When should we assess for FR?

- hypotension: MAP<65 mm Hg, SBP<90 mm Hg or fall of >40 mm Hg in hypertensive patients from their baseline

(Aetiology: septic, hypovolemic and in some situations cardiogenic)

- Tachycardia not explained by reasons other than hypovolemia
- Decreased urine output (<0.5 ml/Kg/Hr for 2 hours)
- Other signs of decreased end-organ perfusion: rising lactate in absence of another obvious explanation (>2mmol/L), CRT>3 seconds, mottling of skin

How to assess for fluid responsiveness?

Static parameters

Central venous pressure
Pulmonary artery occlusion pressure
LVEDV
LVEDAI

Dynamic parameters

Dynamic parameters that use respiratory variability

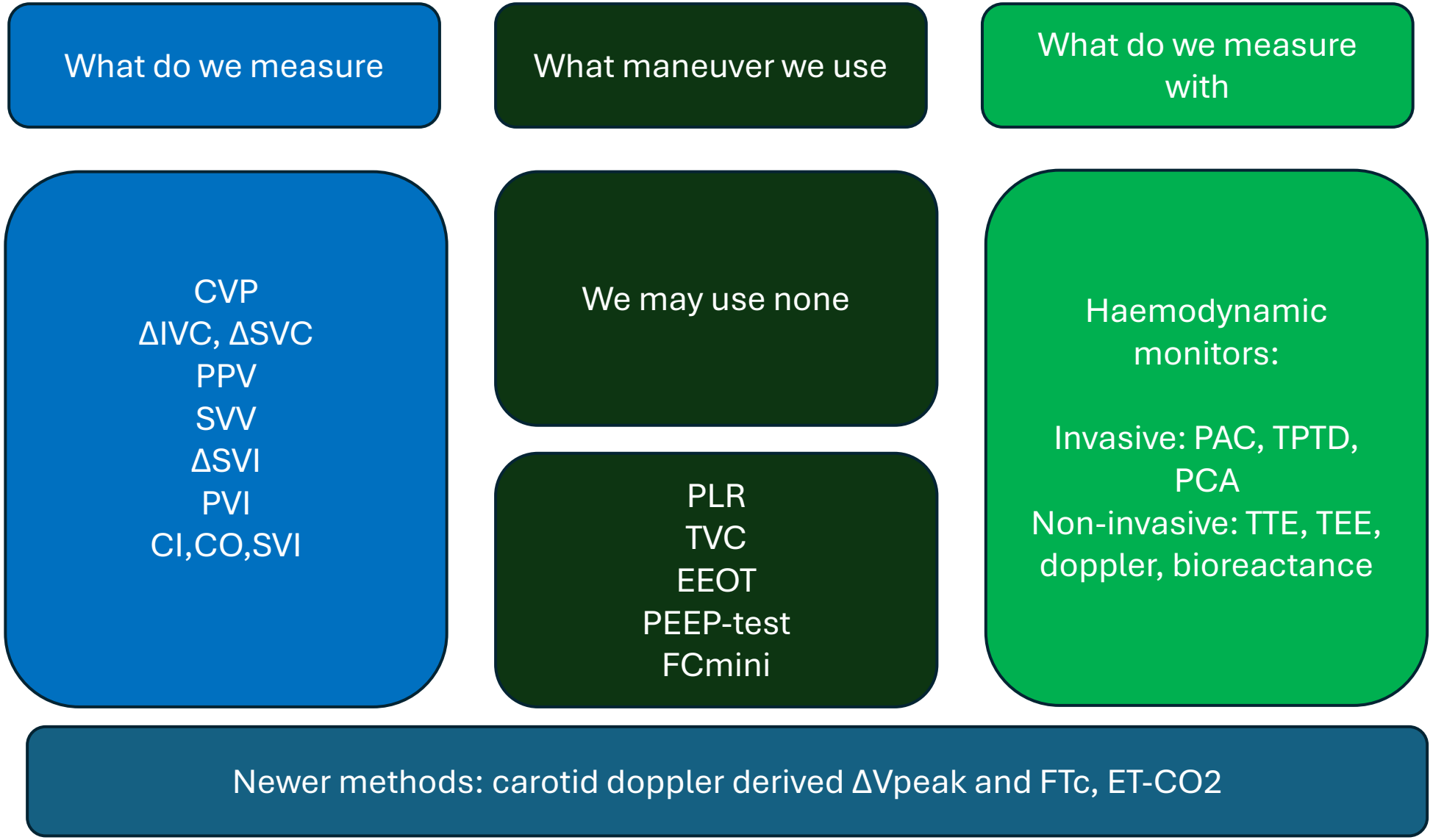
Pulse pressure variation
Stroke volume variation
Plethysmograph variability Index
Aortic blood flow variation
IVC/SVC diameter variation

Dynamic parameters that use alternative method

End-expiratory occlusion test
Tidal volume challenge
Mini-fluid challenge
Passive leg raising

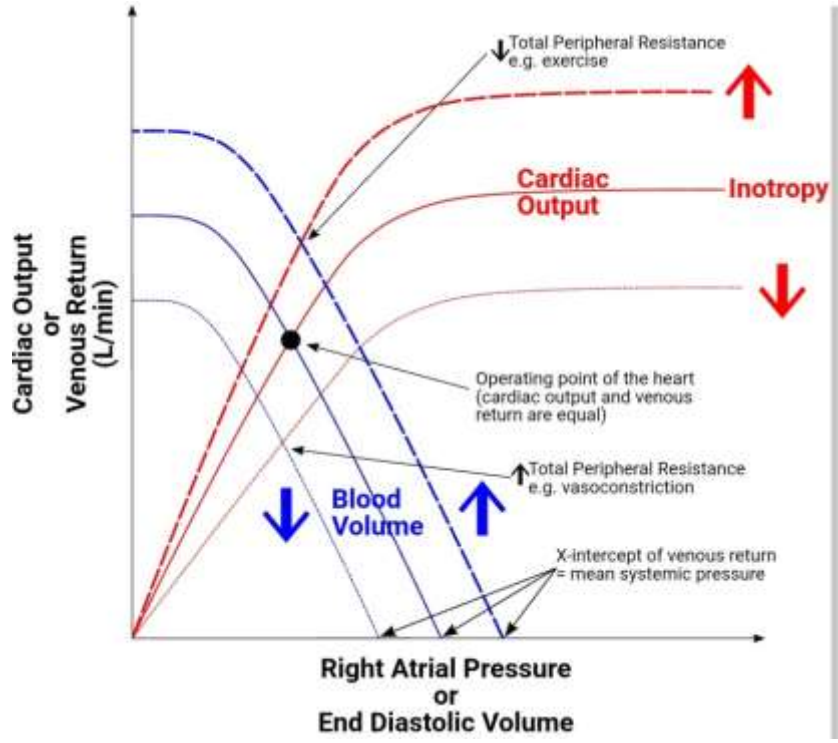
How to measure changes in CO?

Invasive	Minimally invasive	Non-invasive
Pulmonary artery catheter- dye dilution PAC-thermodilution Transpulmonary thermodilution Pulse contour analysis	Trans-oeseophageal echocardiography	Trans-thoracic echocardiography Bio-impedance Bio-reactance

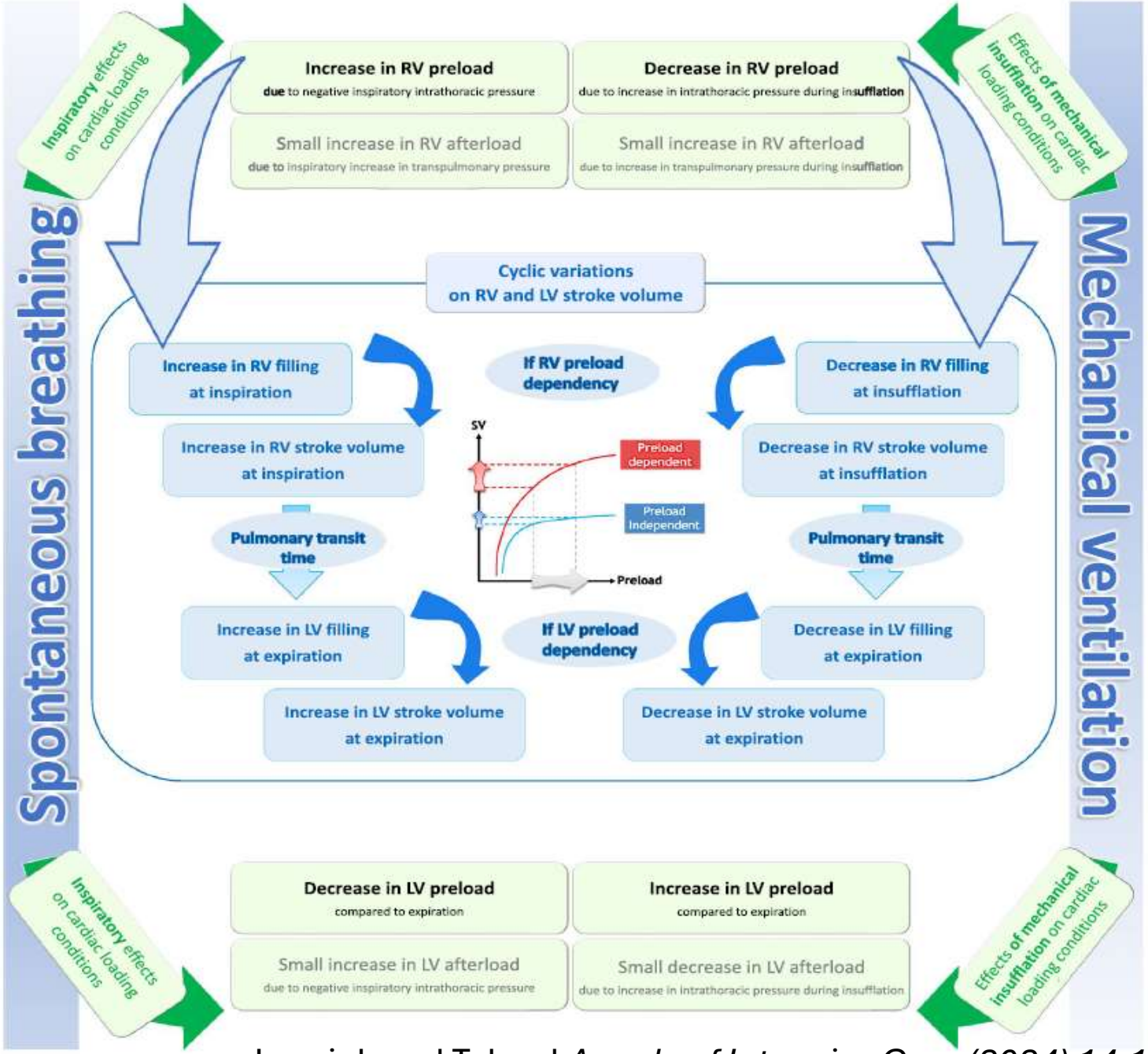

What do we measure
What maneuver we use
What do we measure with
CVP
ΔIVC, ΔSVC
PPV
SVV
ΔSVI
PVI
CI,CO,SVI
We may use none
PLR
TVC
EEOT
PEEP-test
FCmini
Haemodynamic monitors:
Invasive: PAC, TPTD, PCA
Non-invasive: TTE, TEE, doppler, bioreactance
Newer methods: carotid doppler derived ΔVpeak and FTc, ET-CO2

Basis of static parameters: Frank-Starling law

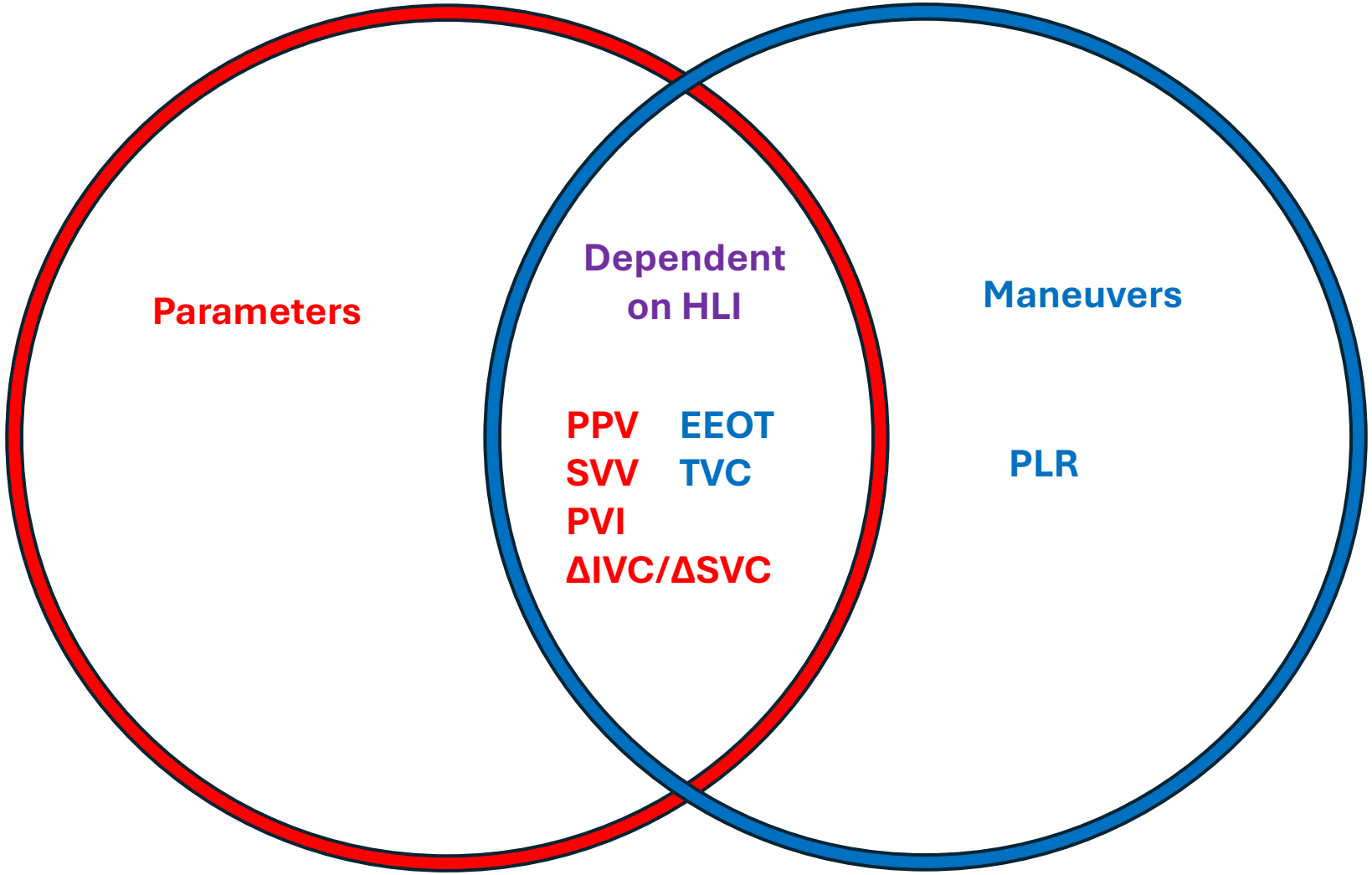
- Increase in sarcomere length by stretching of ventricle (as a result of increased venous return) shall increase contractile power of the ventricle and hence cardiac output
- Beyond the optimal length of sarcomere, the CO will fall
- Static parameters utilize surrogates of venous return but can not identify the optimal sarcomere length
- Dynamic parameters use heart-lung interaction to assess where on the Frank-Starling curve a particular patient is at a particular situation



What is heart-lung interaction

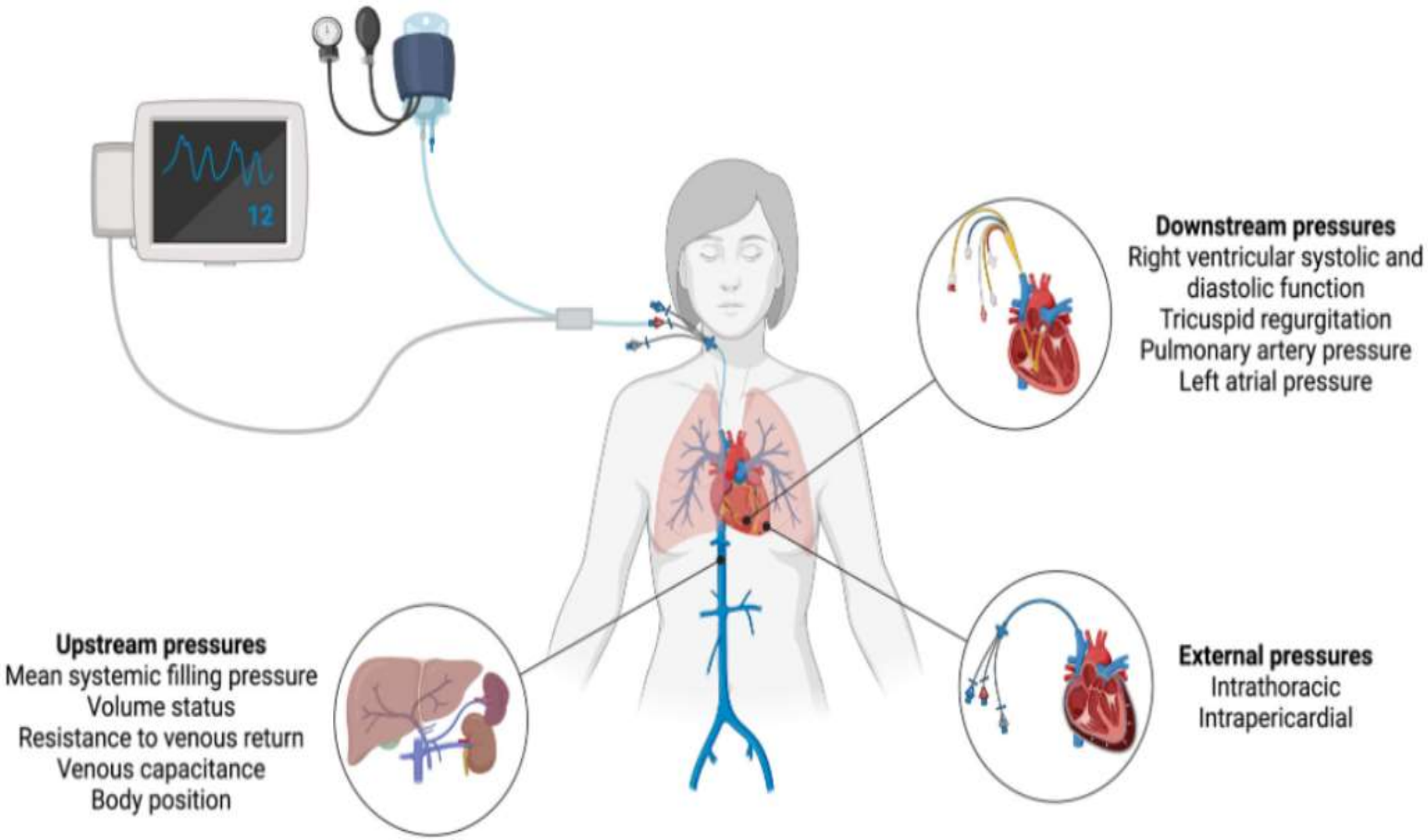


Jozwiak and Teboul *Annals of Intensive Care (2024) 14:122*


Parameters
Dependent on HLI
PPV
SVV
PVI
ΔIVC/ΔSVC
EEOT
TVC
Maneuvers
PLR

Central venous pressure:

- Ideally measured by a central venous catheter with tip at the junction of the SVC and RA
- Measured at the level of tricuspid valve (5 cm ventral to sternal angle)
- Taken as the surrogate for RA pressure and RV diastolic pressure
- A higher value is supposed to mean a greater venous return and better RV filling leading to increased CO
- Studies have failed to show any significant relationship between CVP and fluid responsiveness
- Extreme values (<8 mmHg and >12mm Hg) may still provide predictive information



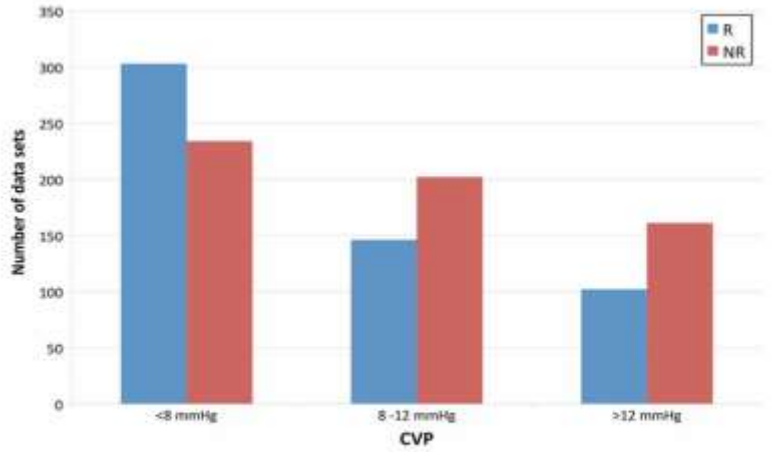


Fig. 2 Distribution of responders (*R*) and non-responders (NR) in the CVP subgroups [lower (<8 mmHg), intermediate (8–12 mmHg) and higher (>12 mmHg) baseline CVP groups] of individual patient data sets ($n = 1148$)

Eskesen TG, Wetterslev M, Perner A. Systematic review including re-analyses of 1148 individual data sets of central venous pressure as a predictor of fluid responsiveness. Intensive Care Medicine. 2016 Mar;42(3):324–32

PAOP, LVEDV, LVEDAI

- Measures the LV filling pressure or the anatomical stretching of LV at the end-diastole
- Does not use right sided pressures as surrogate
- PAOP has shown a poor predictive value for fluid responsiveness (Sensitivity-77% and specificity- 51% at the best cut off of 11mm Hg)
- Similarly, LVEDV and LVDAI also showed poor accuracy in predicting fluid responsiveness

	Responders		Nonresponders	
	Pre-infusion	Postinfusion	Pre-infusion	Postinfusion
Heart rate, beats/min	109 ± 21	103 ± 21[a]	105 ± 22	102 ± 21
Stroke volume index, mL·m^{-2}	31 ± 12	40 ± 13[a]	38 ± 11	39 ± 12
Cardiac index, mL·min^{-1}·m^{-2}	3.2 ± 1	3.9 ± 1[a]	3.7 ± 1	3.8 ± 1
Central venous pressure, mm Hg	8 ± 4	11 ± 4[a]	9 ± 4	12 ± 5[a]
PAOP, mm Hg	10 ± 4	14 ± 5[a]	11 ± 4	16 ± 5[a]
SVRI, mm Hg·L^{-1}·min^{-1}·m^{-2}	22 ± 9	19 ± 7[a]	19 ± 8	19 ± 7
MPAP, mm Hg	23 ± 6	29 ± 6[a]	25 ± 7	29 ± 7[a]
PVRI, mm Hg·L^{-1}·min^{-1}·m^{-2}	3 ± 3	3 ± 3	3 ± 3	3 ± 3

PAOP, pulmonary artery occlusion pressure; SVRI, systemic vascular resistance index; MPAP, mean pulmonary artery pressure; PVRI, pulmonary vascular resistance index.
[a] $p < .05$ pre-infusion vs. postinfusion.

Osman D, Ridel C, Ray P, Monnet X, Anguel N, Richard C, et al. Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge*. Critical Care Medicine. 2007 Jan;35(1):64–8.

Variable	ROC AUC (95% CI)
CVP	0.55 (95% CI, 0.48 – 0.62)
GEDVI	0.56 (95% CI, 0.37 – 0.67)
LVEDAI	0.64 (95% CI, 0.54 – 0.74)

ROC AUC, area under the curve of the receiver operating characteristics curve; GEDVI, global end-diastolic volume index; LVEDAI, left ventricular end-diastolic area index.

Marik PE, Cavallazzi R, Vasu T, et al. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. Crit Care Med.2009;37(9):2642–2647

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021

KEY WORDS: adults; evidence-based medicine; guidelines; sepsis; septic shock

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ISCCM Guidelines for Hemodynamic Monitoring in the Critically Ill

Atul Prabhakar Kulkarni[1], Deepak Govil[2], Srinivas Samavedam[3], Shrikanth Srinivasan[4], Suresh Ramasubban[5], Ramesh Venkataraman[6], Kishore Pichamuthu[7], Sameer Arvind Jog[8], Jigeeshu V Divatia[9], Sheila Nainan Myatra[10]

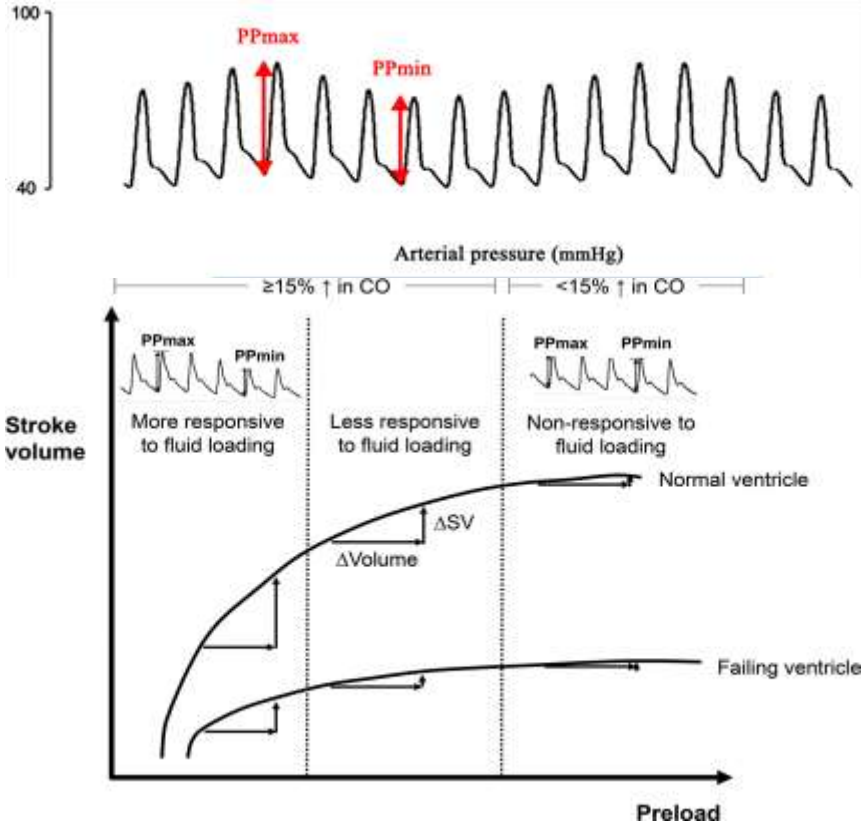
Received on: 21 July 2022; *Accepted on:* 26 September 2022; *Published on:* 29 October 2022

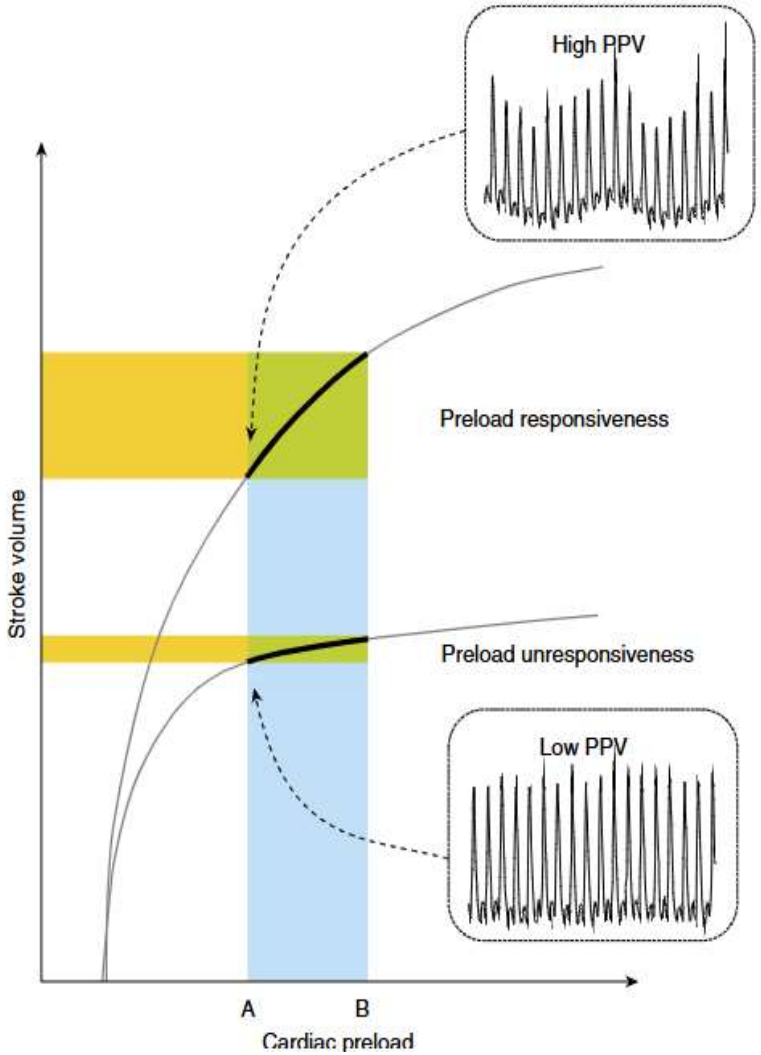
- Recommends using dynamic parameters for deciding on fluid resuscitation over static parameters
- Recommends using PPV, SVV, delta-IVC, EEOT, TVC and PLR for determining fluid responsiveness

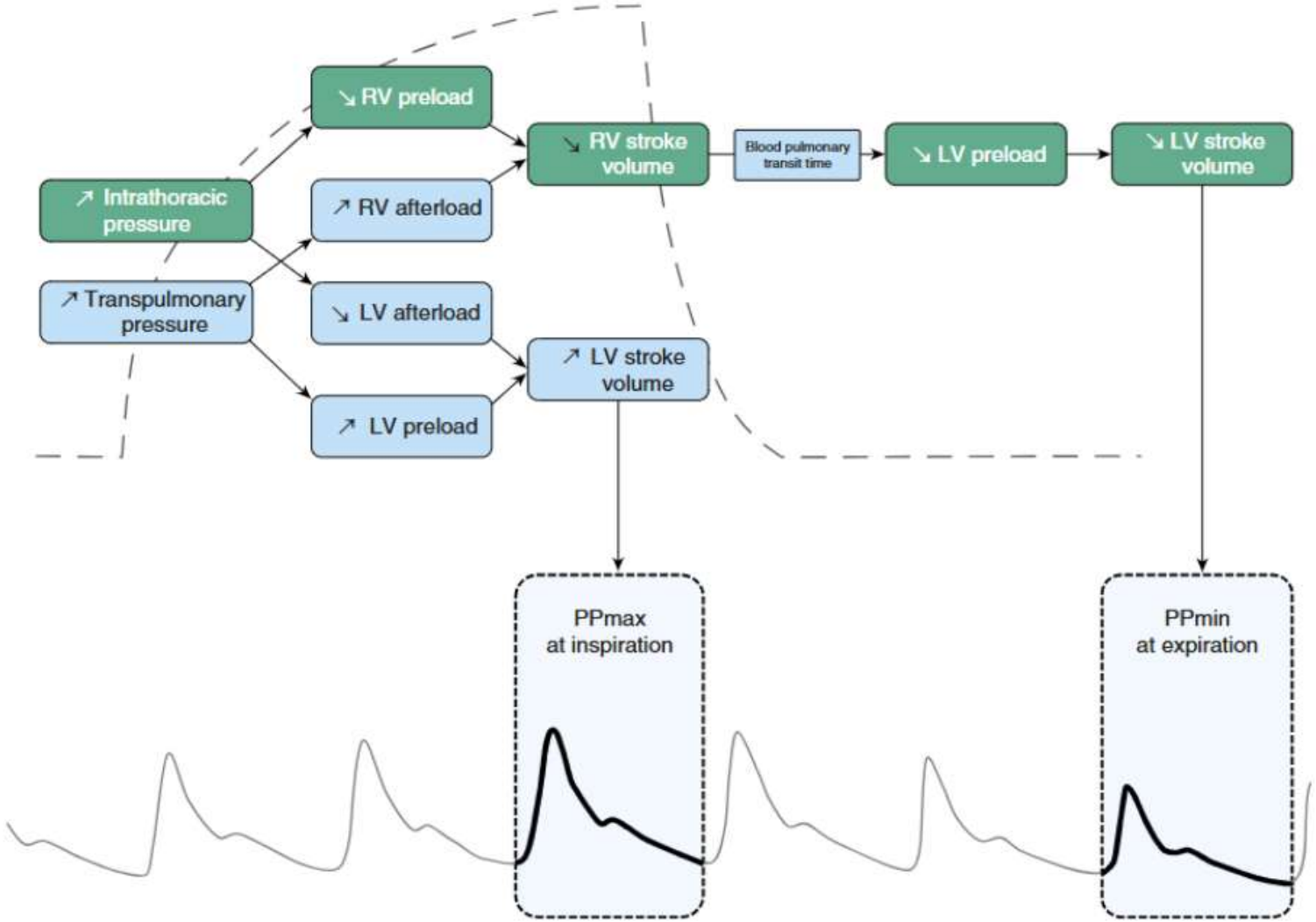
Pulse-pressure variation

- Works by the principle of heart-lung interaction
- An increase in intrathoracic pressure during mechanical insufflation decreases venous return and RV output in pre-load dependent RV
- Decreased RV output is reflected in decreased LV output during expiration
- Higher the degree of preload-dependence, higher should be the degree of variation (during respiratory cycle)

PPV= (PPmax-PPmin) X 100
PPmean







Teboul JL, Monnet X, Chemla D, Michard F. Arterial Pulse Pressure Variation with Mechanical Ventilation. American Journal of Respiratory and Critical Care Medicine. 2019 Jan;199(1):22–31.

How to measure PPV?

PPV

Invasive arterial cannula

- PAC
- LIDCO
- PICCO (TPTD+PCA)
- Flotrac (PCA)

- In a systematic review and meta-analysis that included mechanically ventilated patients, overall sensitivity and specificity of PPV were 74% and 82% respectively (for a cut off of 11.5%)
- The study included patients ventilated with high tidal volume as well as those ventilated by low tidal volume
- Patients ventilated at lower tidal volumes (<8mL/Kg) may not have a sufficiently large respiratory variation in PPV
- May contribute to decreased sensitivity of the test

Carneiro R, Silvia C, Neves V, Ary Serpa Neto, Rodrigo Octavio Deliberato, Adriano José Pereira, et al. Assessment of fluid responsiveness using pulse pressure variation, stroke volume variation, plethysmographic variability index, central venous pressure, and inferior vena cava variation in patients undergoing mechanical ventilation: a systematic review and meta-analysis. Critical Care. 2024 Aug 31;28(1).

- Poor compliance of the respiratory system (as in ARDS) may dampen the transmission of intra-thoracic pressure to the vascular compartment
- Decreased compliance may be a more important factor than low tidal volume ventilation in interfering with the accuracy of PPV
- Higher respiratory rate (a HR:RR<3.6) also decreases the sensitivity of PPV
- Additional shortcomings of PPV include its unreliability during cardiac arrhythmia

A PPV of >10-15% has been considered as an indicator of fluid responsiveness

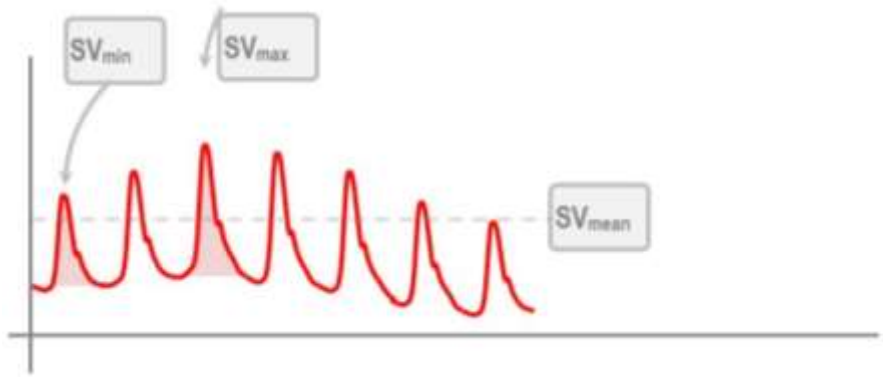
pre-requisites	Pitfalls	Solution
Arterial catheter in situ	Requires high tidal volume ventilation (>8ml/Kg)	Tidal volume challenge, PLR may be useful in low tidal volume ventilation
Haemodynamic monitoring devices	Spontaneous breathing efforts interfere with values	Deep sedation, PLR
	Right ventricular failure may give false positive value	PLR may differentiate between right ventricular afterload dependence and actual fluid responsiveness
	Cardiac arrhythmias interfere with readings	

Stroke volume variation

- Stroke volume can be estimated accurately by pulse contour analysis if an arterial line is in place
- Stroke volume variation is calculated by {(Svmax-Svmin)/Svmean}X100 (over a 20s period)
- Based on principles of heart-lung interaction, a SVV of >10% has shown to predict fluid responsiveness
- ΔSVV is the difference between SVV before and after fluid bolus

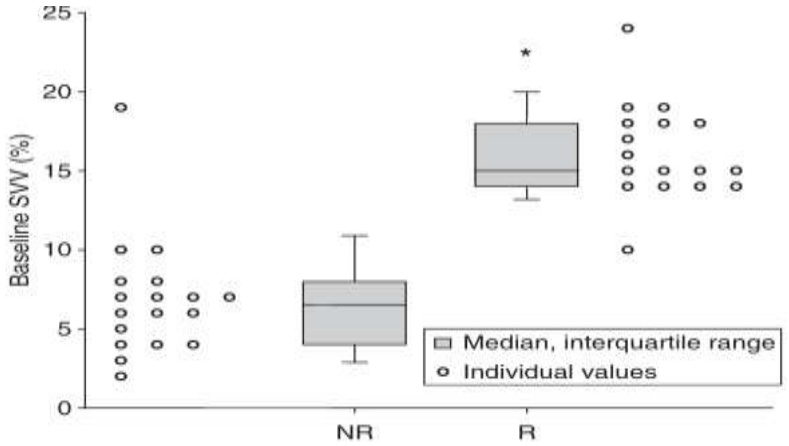
SV=k X pulsatility

Pulsatility= SD of arterial pressure over 20s
k= derivative of arterial compliance and vascular resistance



$$SVV = \frac{SV_{max} - SV_{min}}{SV_{mean}}$$

- A 2008 study examined patient of CLD post-hepatic transplant for fluid responsiveness by measuring SVV before and after giving fluid (colloid) by estimating CO on those two timepoints (with TTE, PAC and pulse contour analysis)
- The study showed that there was significant difference in baseline values of SVV between fluid responders and fluid non-responders



Biais M, Nouette-Gaulain K, Cottenceau V, Revel P, Sztark F. Uncalibrated pulse contour-derived stroke volume variation predicts fluid responsiveness in mechanically ventilated patients undergoing liver transplantation. British Journal of Anaesthesia [Internet]. 2008 Dec [cited 2020 Jan 21];101(6):761–8.

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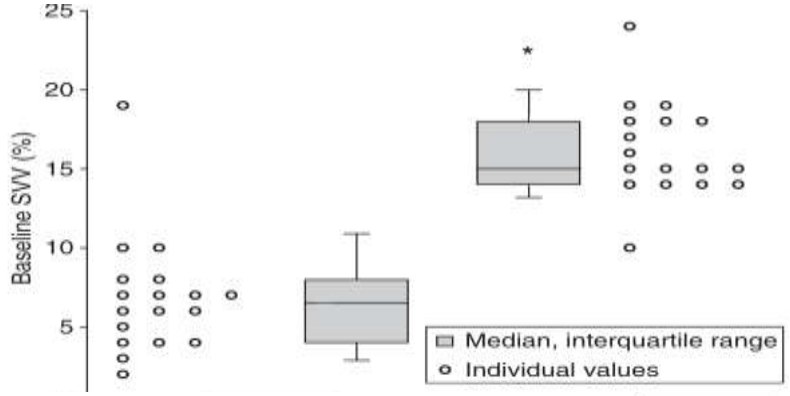
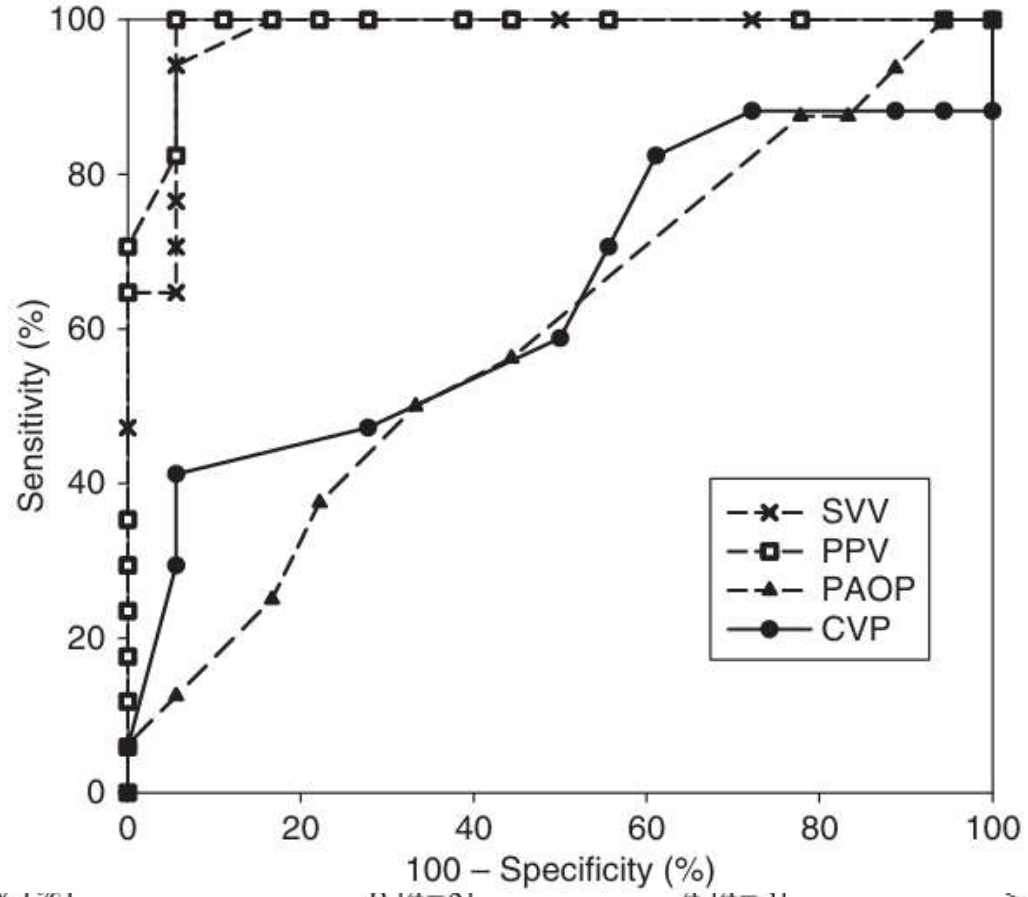
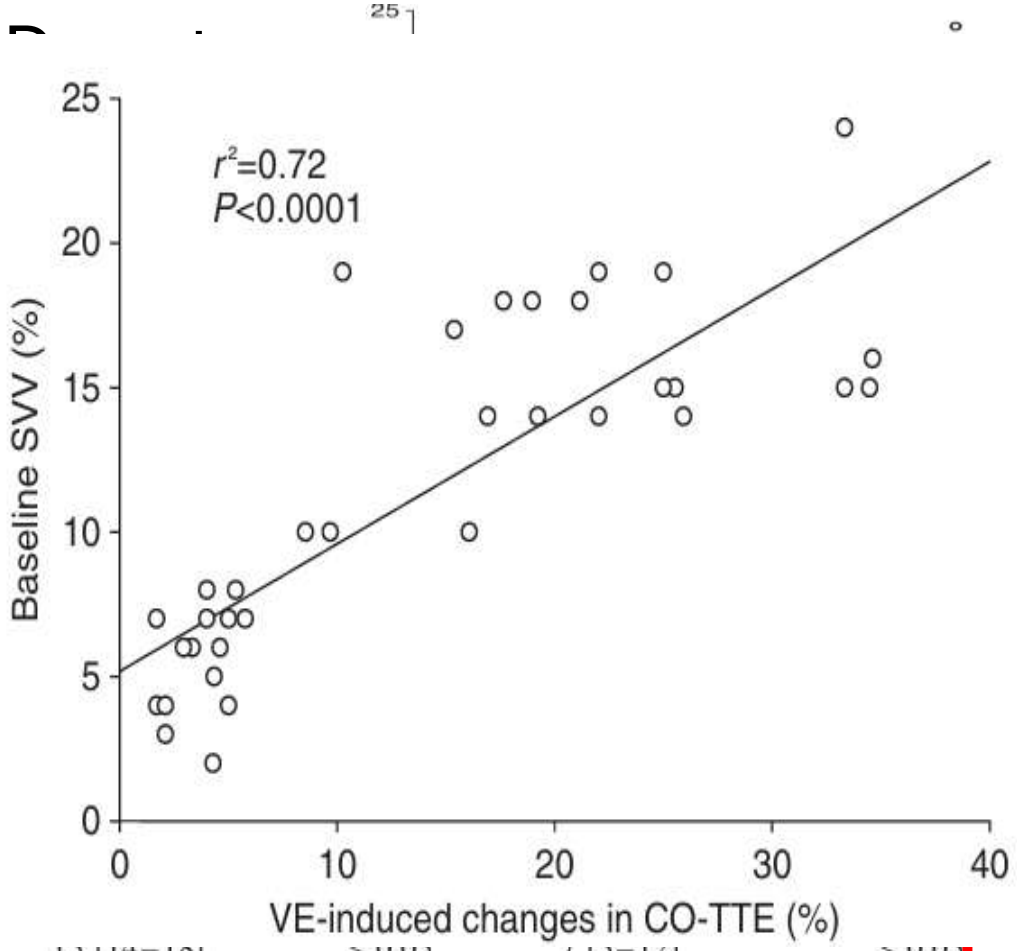


Variables	Fluid non-responders (n=18)			Fluid responders (n=17)			
	Baseline	Volume expansion	$P1$	Baseline	$P2$	Volume expansion	$P3$
HR (beats min^{-1})	62 [55–69]	58 [55–63]	<0.05	72 [75–84]	NS	65 [62–79]	<0.05
MAP (mm Hg)	90 [80–104]	91 [85–102]	NS	83 [65–94]	NS	91 [80–106]	<0.05
CO-TTE (litre min^{-1})	6.3 [5.9–7.1]	6.8 [6–7.8]	<0.05	5.8 [5.2–6.7]	<0.05	6.9 [6.4–8.1]	<0.05
SVR (dyn s^{-1} cm^{-5})	975 [821–1200]	921 [741–1177]	NS	970 [820–1238]	NS	812 [742–1025]	NS
CVP (mm Hg)	7 [5–10]	12 [8–14]	<0.05	6 [2–8]	<0.05	10 [6–11]	<0.05
MPAP (mm Hg)	18 [14–24]	22 [16–25]	<0.05	15 [11–19]	<0.05	22 [16–24]	<0.05
PAOP (mm Hg)	12 [10–12]	13 [11–14]	<0.05	10 [7–12]	<0.05	12 [10–13]	<0.05
SVV (%)	6 [4–8]	4 [4–5]	<0.05	15 [14–18]	<0.05	7 [5–12]	<0.05
PPV (%)	6 [5–9]	4 [3–5]	<0.05	16 [15–19]	<0.05	7 [3–11]	<0.05

Biais M, Nouette-Gaulain K, Cottenceau V, Revel P, Sztark F. Uncalibrated pulse contour-derived stroke volume variation predicts fluid responsiveness in mechanically ventilated patients undergoing liver transplantation. British Journal of Anaesthesia [Internet]. 2008 Dec [cited 2020 Jan 21];101(6):761–8.





- CVP and PAOP values did not have a significantly good accuracy for predicting FR
- Baseline SVV was significantly correlated with post-VE changes in CO

- Stroke volume variation also depends upon principles of heart-lung interaction and performs better in patients with Vt=8-12ml/Kg
- At the cut-off of 12.5% it has shown to predict fluid responsiveness with a sensitivity of 100% and a specificity of 57% in patients ventilated at Vt=8mL/Kg
- For patients ventilated at Vt=6mL/Kg, sensitivity and specificity were 91% and 71%
- But studies have pointed out that both PPV and SVV can be unreliable in patients with poor respiratory system compliance

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Plethysmograph variability index

- Pulse oximetry gives a value of PI or perfusion index
- PI= (AC/DC) X 100 (AC- alternative current due to pulsatile absorption of infra-red light representing amplitude of amplitude of pulsatility peripheral arterioles ; DC- direct current due to constant absorption of infra-red light by non-pulsatile tissue)
- PVI= {(PImax-PImin)/Pimax} X 100
- PVI values can range from 1 to 100
- The respiratory variability will impact PI due to heart lung interaction
- Theoretically, pre-load dependence of LV can be predicted by a high PVI

- It can be measured at forehead, index finger or ear.
- The cut-off varies according to the site used (forehead 16%, ear 15% and finger 12%)
- Forehead and ear provide better accuracy
- Combining the values of PVIforehead and PIforehead (<1.37) may improve the accuracy of prediction*
- With a cut-off value of 11% PVI can predict fluid responsiveness with sensitivity of 95.7% and specificity of 59%**
- But most of the studies examining its reliability was done in peri-operative patients not in shock

*Desgranges FP, Olivier Desebbe, A. Ghazouani, Gilbert K, Keller G, Chiari P, et al. Influence of the site of measurement on the ability of plethysmographic variability index to predict fluid responsiveness. British Journal of Anaesthesia. 2011 Sep 1;107(3):329–35.

**Eur J Anaesthesiol 2016; 33:645–652

- Only few studies evaluated patients in shock on vasopressors
- A 2012 prospective study has shown that when on norepinephrine, PVI becomes less reliable
- PVI poorly correlated with PPV and SVV in patients on norepinephrine (both PPV and SVV showed good fluid responsiveness)
- In such situations: Sensitivity 47% and specificity 90%
- In 16% patients, PVI could not be measured due to poor peripheral perfusion

Monnet X, Guérin L, Jozwiak M, Bataille A, Julien F, Richard C, et al. Pleth variability index is a weak predictor of fluid responsiveness in patients receiving norepinephrine. British Journal of Anaesthesia. 2013 Feb;110(2):207–13.

	Responders	Non-responders
Age (range, yr)	(23–82)	(35–81)
Origin of shock (no. of patients)		
Septic	15	14
Hypovolaemic	2	3
Tidal volume (ml kg^{-1} of predicted body weight)	9.0 (0.7)	9.1 (0.8)
Total PEEP (cm H_2O)	6 (3)	7 (3)
Compliance of the respiratory system (ml cm H_2O^{-1})	41 (12)	40 (11)
Left ventricular ejection fraction (%)	51 (17)	56 (10)
Time from onset of shock (h)	2.1 (1.8)	2.8 (2.0)
Lactate (mmol $litre^{-1}$)	2.3 (1.3)	2.2 (1.2)
Dose of norepinephrine (inter-quartile range, μg kg^{-1} min^{-1})	1.00 (0.62–3.4)	0.68 (0.18–3.2)

Variable	AUC	Best cut-off value (%)	Sensitivity (%)	Specificity (%)	Positive likelihood ratio	Negative likelihood ratio
PPV	0.93 (0.06)	11	93 (68–100)	95 (74–100)	17.7 (14.9–21.1)	0.1 (0.0–1.0)
SVV	0.89 (0.07)	10	93 (68–100)	90 (68–100)	9.3 (7.6–11.4)	0.1 (0.0–0.7)
PVI	0.68 (0.09)*	16	47 (21–73)	90 (68–99)	1.9 (1.2–3.0)	0.3 (0.1–1.0)

Monnet X, Guérin L, Jozwiak M, Bataille A, Julien F, Richard C, et al. Pleth variability index is a weak predictor of fluid responsiveness in patients receiving norepinephrine. British Journal of Anaesthesia. 2013 Feb;110(2):207–13.

- A 2019 meta-analysis showed that pooled sensitivity of PVI was 0.77 and specificity was 0.77 across different cohorts of patients
- The studies included had widely varying cut-offs (7-20%)
- PVI performed more poorly among patients spontaneously breathing (not on ventilator), those with poor peripheral perfusion (on vasopressors, peripheral arterial disease, cardiogenic shock)
- Among the studies that examined patients in septic shock, the cut-off used was 15.5% and it showed sensitivity of 65% and specificity and 80%*

Liu, T., Xu, C., Wang, M. *et al.* Reliability of pleth variability index in predicting preload responsiveness of mechanically ventilated patients under various conditions: a systematic review and meta-analysis. *BMC Anesthesiol* **19**, 67 (2019).

*Lu N, Xi X, Jiang L, Yang D, Yin K. Exploring the best predictors of fluid responsiveness in patients with septic shock. The American Journal of Emergency Medicine. 2017 Mar 22;35(9):1258–61.

Setting (numbers of studies)	Sensitivity(95% CI)	Specificity(95% CI)	Youden index	AUC(95% CI)-ROC	I^2(%)
PVI across all settings($n = 27$)	0.77 (0.67–0.85)	0.77 (0.71–0.82)	0.54	0.82 (0.79–0.85)	95
PVI in OR($n = 18$)	0.76 (0.67–0.84)	0.76 (0.68–0.82)	0.52	0.82 (0.79–0.85)	81
PVI in ICU($n = 4$)	0.79 (0.41–0.95)	0.88 (0.77–0.94)	0.67	0.89 (0.86–0.92)	89
PVI in adult($n = 22$)	0.77 (0.65–0.85)	0.77 (0.70–0.82)	0.54	0.82 (0.79–0.85)	95
PVI in cardiac surgery($n = 9$)	0.67 (0.40–0.87)	0.78 (0.66–0.87)	0.45	0.80 (0.77–0.84)	89
PVI in noncardiac surgery($n = 12$)	0.78 (0.64–0.88)	0.71 (0.58–0.82)	0.49	0.80 (0.76–0.83)	63
PVI without surgery($n = 6$)	0.85 (0.69–0.94)	0.80 (0.70–0.87)	0.65	0.86 (0.82–0.89)	33
PVI with colloid injection($n = 17$)	0.77 (0.67–0.85)	0.82 (0.77–0.86)	0.59	0.83 (0.80–0.86)	87
PVI with crystalloid injection($n = 4$)	0.77 (0.60–0.88)	0.69 (0.52–0.81)	0.46	0.79 (0.75–0.82)	23

Liu, T., Xu, C., Wang, M. *et al.* Reliability of pleth variability index in predicting preload responsiveness of mechanically ventilated patients under various conditions: a systematic review and meta-analysis. *BMC Anesthesiol* **19**, 67 (2019). https://doi.org/10.1186/s12871-019-0744-4

*Lu N, Xi X, Jiang L, Yang D, Yin K. Exploring the best predictors of fluid responsiveness in patients with septic shock. The American Journal of Emergency Medicine. 2017 Mar 22;35(9):1258–61.

	Responder group ($N = 27$)	Non-responder group ($N = 22$)
Age, year, mean ± SD	55.7 ± 12.6	55.0 ± 12.8
Gender, male/female, N	19/8	14/8
Body mass index, kg/m^2, mean ± SD	24.6 ± 9.3	25.3 ± 9.5
APACHE II score, mean ± SD	26.5 ± 10.0	27.2 ± 10.5
SOFA score, mean ± SD	18.3 ± 7.2	18.6 ± 7.5
Sources of infection, N (%)		
Respiratory tract	18 (66.7%)	15 (68.2%)
Urinary tract	4 (14.8%)	3 (13.6%)
Gastrointestinal	2 (7.4%)	1 (4.5%)
Hematogenous	1 (3.7%)	1 (4.5%)
Others	2 (7.4%)	2 (9.1%)

Hemodynamic parameters	AUC	95% Confidence Interval	*P* value	Threshold	Sensitivity (%)	Specificity (%)
CVP	0.675	0.506–0.844	0.058	6.5	65	70
ITBVI	0.664	0.493–0.835	0.076	871	55	65
SVV	0.848	0.726–0.969	0.000	11.5	75	85
PVI	0.816	0.686–0.946	0.001	15.5	65	80
ΔIVC	0.805	0.671–0.939	0.001	20.5	67	77
ΔCDPV	0.910	0.817–1.0	<0.001	13.0	78	90
ΔVpeak brach	0.761	0.604–0.918	0.005	11.7	70	80

Liu, T., Xu, C., Wang, M. *et al.* Reliability of pleth variability index in predicting preload responsiveness of mechanically ventilated patients under various conditions: a systematic review and meta-analysis. *BMC Anesthesiol* **19**, 67 (2019). https://doi.org/10.1186/s12871-019-0744-4

*Lu N, Xi X, Jiang L, Yang D, Yin K. Exploring the best predictors of fluid responsiveness in patients with septic shock. The American Journal of Emergency Medicine. 2017 Mar 22;35(9):1258–61.

PVI for fluid responsiveness

Advantages	Disadvantages
• Non-invasive • Requires just a pulse oximeter and compatible monitor	• Not reliable when on vasopressors • Not reliable in cardiogenic shock • Not reliable is skin in monitoring area is wounded • Not reliable in patients not on mechanical ventilator with Vt<8mL/Kg • No universally accepted cut off value (11-15.5%)

Maneuvers to predict fluid-responsiveness

- End-expiratory occlusion test (EEOT)
- Passive leg raising test (PLR)
- Tidal volume challenge test (TVC)
- Mini-fluid challenge test (FCmini)
- PEEP-test

What is EEOT?

Gavelli *et al. Critical Care* (2019) 23:274
https://doi.org/10.1186/s13054-019-2554-y

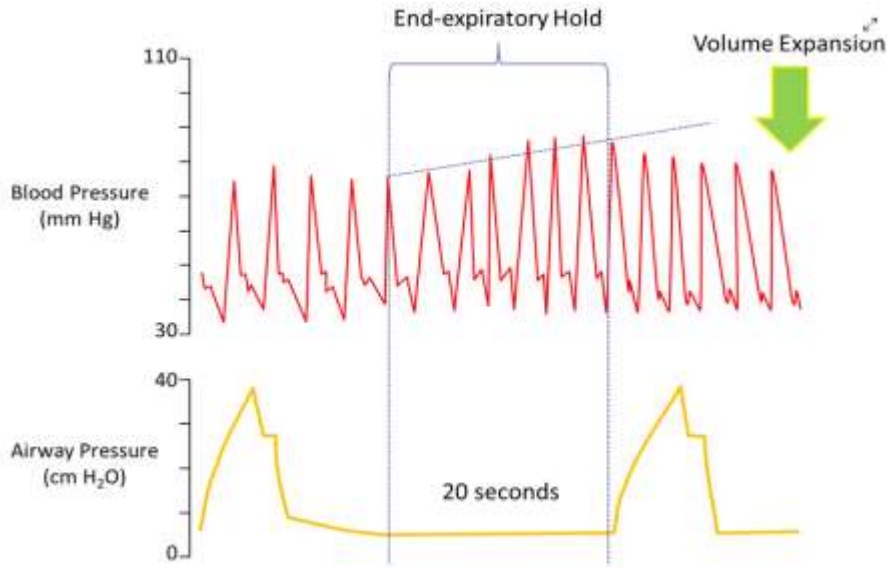
Critical Care

EDITORIAL Open Access

The end-expiratory occlusion test: please, let me hold your breath!

Francesco Gavelli[1,2,3*], Jean-Louis Teboul[1,2] and Xavier Monnet[1,2]

- During mechanical insufflation, the increased intrathoracic pressure decreases venous return and right-ventricular preload ultimately reducing LV output during expiration in pre-load dependent states
- An end-expiratory occlusion test impairs the cyclical impediment to venous return and improves RV output
- If EEOT is long enough, it is ultimately reflected in an increase in LV output (CO) in pre-load dependent LV indicating fluid responsiveness



Gavelli et al. Critical Care (2019) 23:274

- It is performed by instituting an end-expiratory pause for 15 seconds
- The cardiac output or its surrogate (CI) as derived by TPTD or PCA should be recorded at the last 5 seconds of the maneuver
- An increase of 5% in cardiac index can predict fluid responsiveness with sensitivity of 91% and specificity of 100%
- The accuracy is not affected by compliance of respiratory system, low-tidal volume ventilation, PEEP levels and cardiac arrhythmia
- Reliability in prone patients is not established
- It is not as reliable when the effects are measured by TTE (difficult to detect such a small change in VTE-derived CO)

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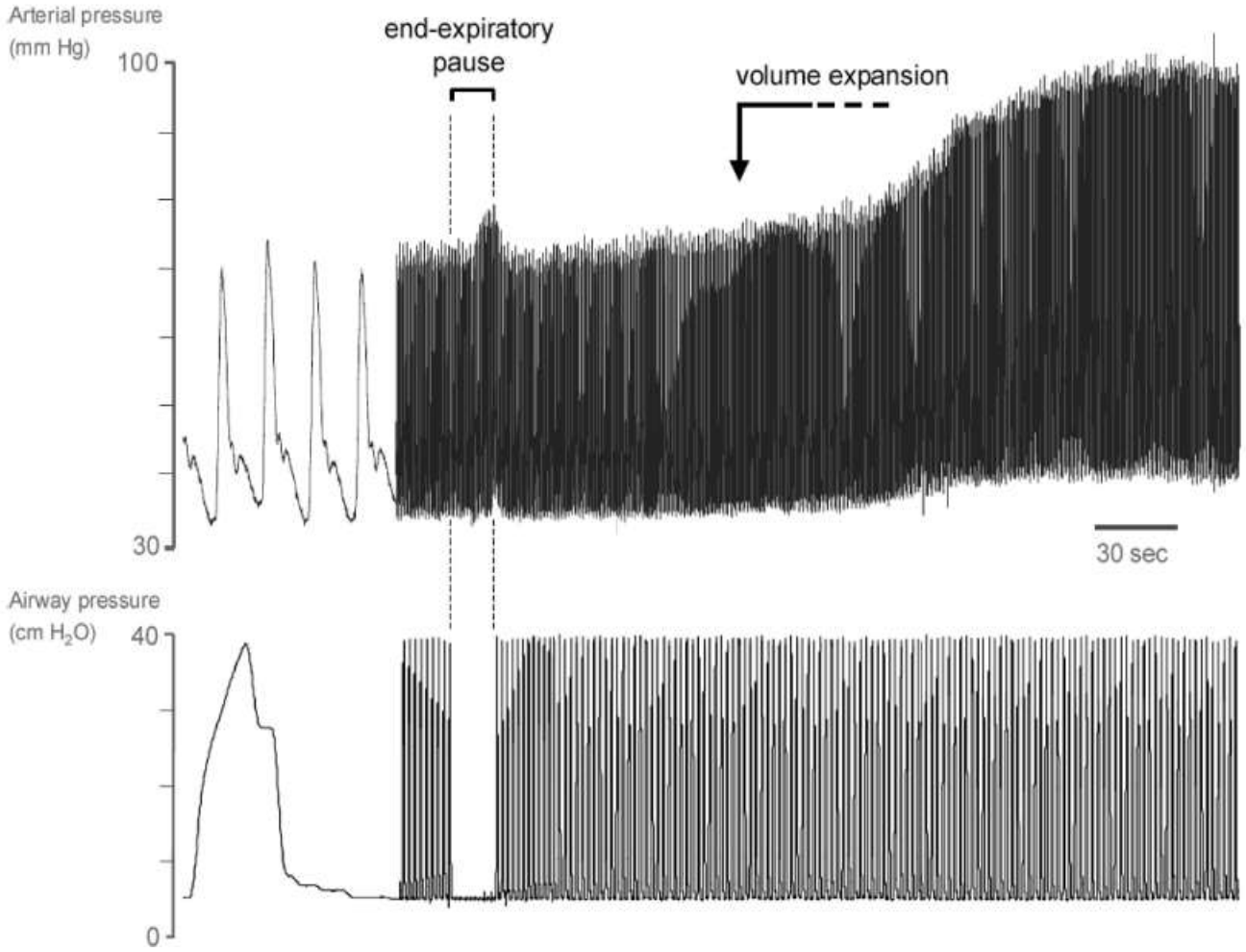
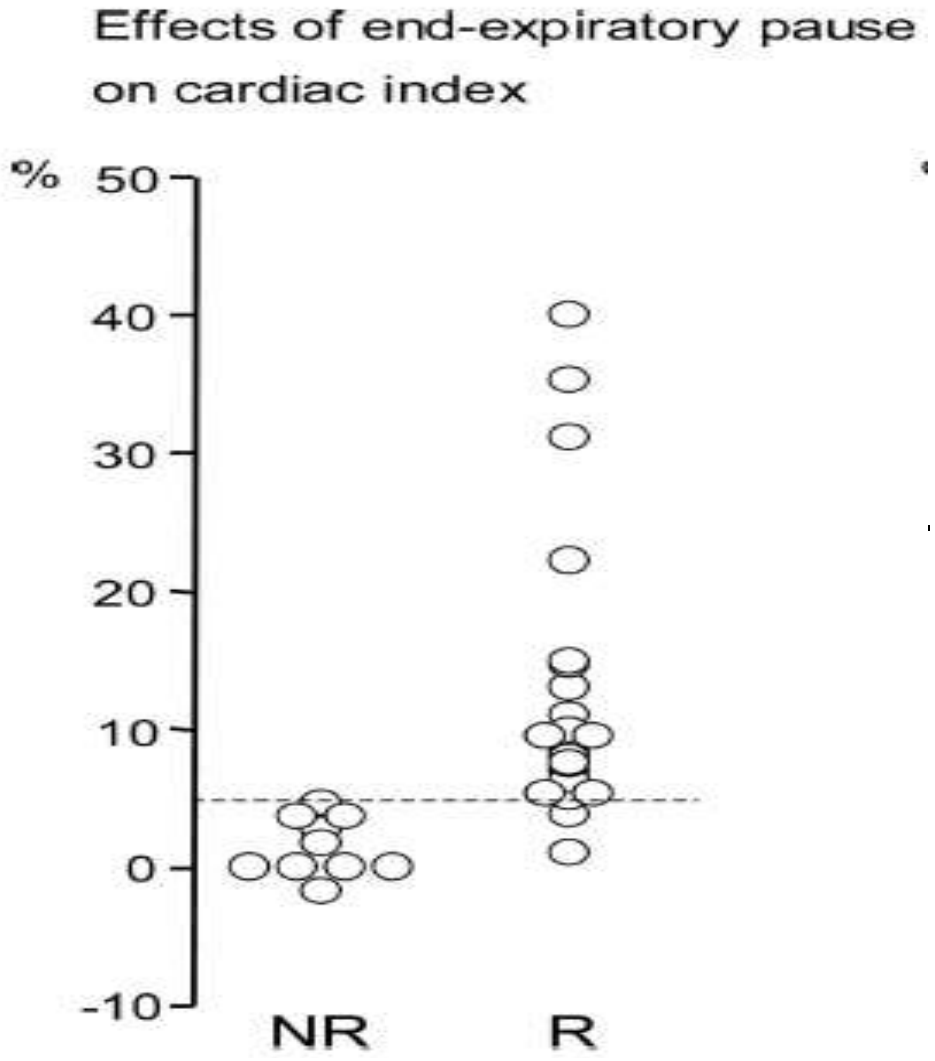
- The accuracy is not affected by compliance of respiratory system, low-tidal volume ventilation, PEEP levels and cardiac arrhythmia
- Reliability in prone patients is not established
- If EEOT and EIOT are combined the change of VTI>13% can circumvent this problem and predict fluid responsiveness accurately

Monnet X, Osman D, Ridel C, Lamia B, Richard C, Teboul JL. Predicting volume responsiveness by using the end-expiratory occlusion in mechanically ventilated intensive care unit patients. Critical Care Medicine. 2009 Mar;37(3):951–6.





Monnet X, Osman D, Ridel C, Lamia B, Richard C, Teboul JL. Predicting volume responsiveness by using the end-expiratory occlusion in mechanically ventilated intensive care unit patients. Critical Care Medicine. 2009 Mar;37(3):951–6.

- Subsequent studies with larger number of patients have shown similar accuracy of this maneuver
- However, cardiac arrhythmia has been consistently an exclusion criteria
- A recent study (2023) failed to show good accuracy for combined EEOT+EIOT to predict fluid responsiveness*
- Studies including patients with arrhythmia are required to replicate the results of original study by Monnet et al 2009

Velmurugan Selvam, Dilip Shende, Anand RK, Kashyap L, Ray BR. End-expiratory Occlusion Test and Mini-fluid Challenge Test for Predicting Fluid Responsiveness in Acute Circulatory Failure. Journal of Emergencies Trauma and Shock. 2023 Jan 1;16(3):109–15.

*Horejsek J, Balík M, Kunstýř J, Pavel Michálek, Tomáš Brožek, Petr Kopecký, et al. Prediction of Fluid Responsiveness Using Combined End-Expiratory and End-Inspiratory Occlusion Tests in Cardiac Surgical Patients. Journal of Clinical Medicine [Internet]. 2023 Mar 29;12(7):2569–9.

$SIGH_{35}$ in patients on PSV

- One of the problems of EEOT in spontaneously breathing patients- trigger by patient during the manoeuvre
- In $SIGH_{35}$ maneuverer, a 4 second increase in airway pressure to 35 cm H2O is given to patients on pressure support ventilation
- During this ventilator mode is set as SIMV-PC+PSV with SIMV rate of 1/minute set inspiratory time of 4 secs
- The Nadir PP value during the manoeuvre is taken
- A cut off value of 25% (baseline PP-nadir PP, invasively monitored) predicts fluid responsiveness with sensitivity of 0.93 and specificity of 0.91

Messina A, Calabrò L, Benedetto F, Villa A, Guia Margherita Matronola, Brunati A, et al. SIGH35 and end-expiratory occlusion test for assessing fluid responsiveness in critically ill patients undergoing pressure support ventilation. Critical Care [Internet]. 2025 May 2 [cited 2025 Aug 17];29(1).

- The Hering-Breuer reflex prolongs expiratory time and prevents inspiration in between the manoeuvre
- Patients mildly sedated at RASS =–2 provide better results
- Patients whose inspiratory pressure are less negative have better performance (P0.1<1.5)
- In these patients, $SIGH_{35}$ has better predictive value than EEOT

Messina A, Calabrò L, Benedetto F, Villa A, Guia Margherita Matronola, Brunati A, et al. SIGH35 and end-expiratory occlusion test for assessing fluid responsiveness in critically ill patients undergoing pressure support ventilation. Critical Care [Internet]. 2025 May 2 [cited 2025 Aug 17];29(1).

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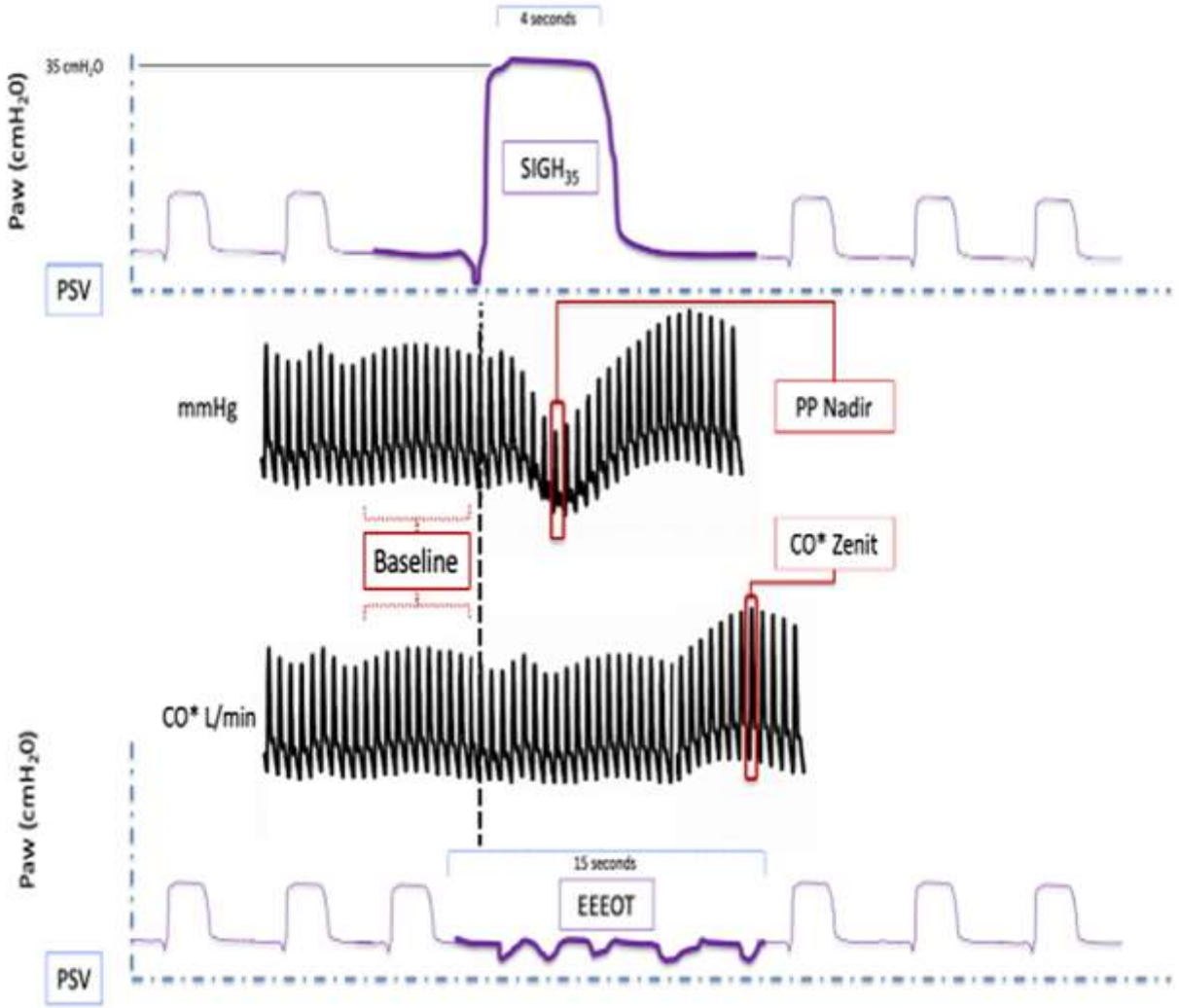

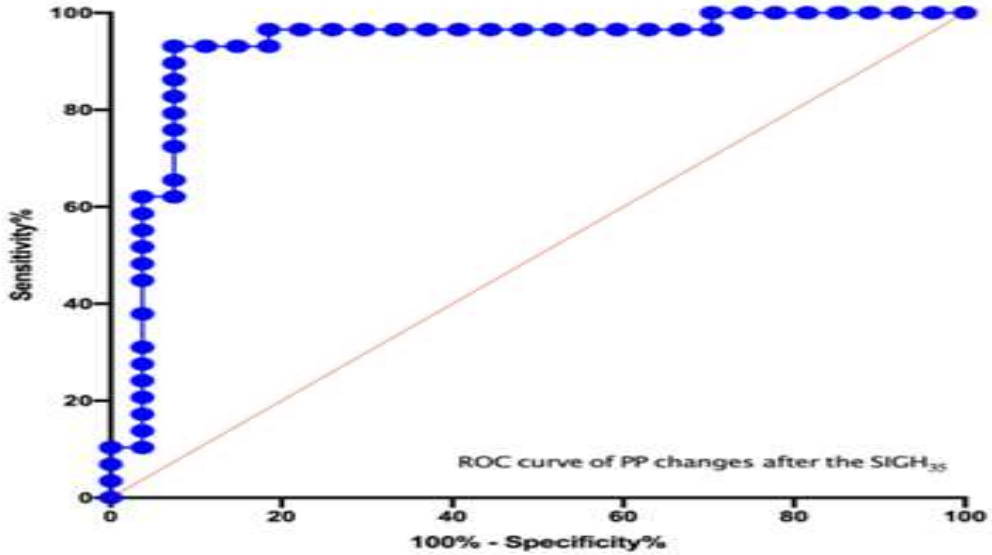

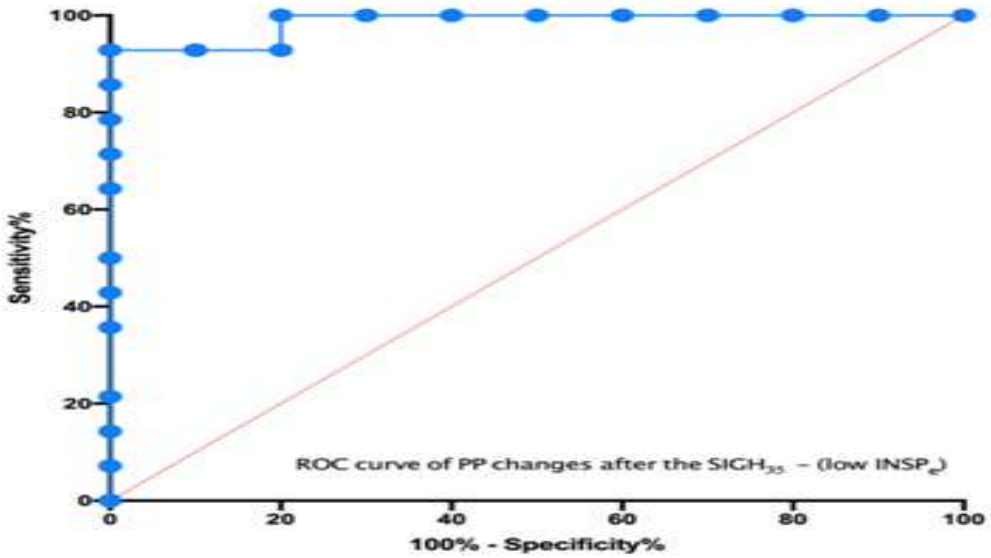

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Passive leg raising test

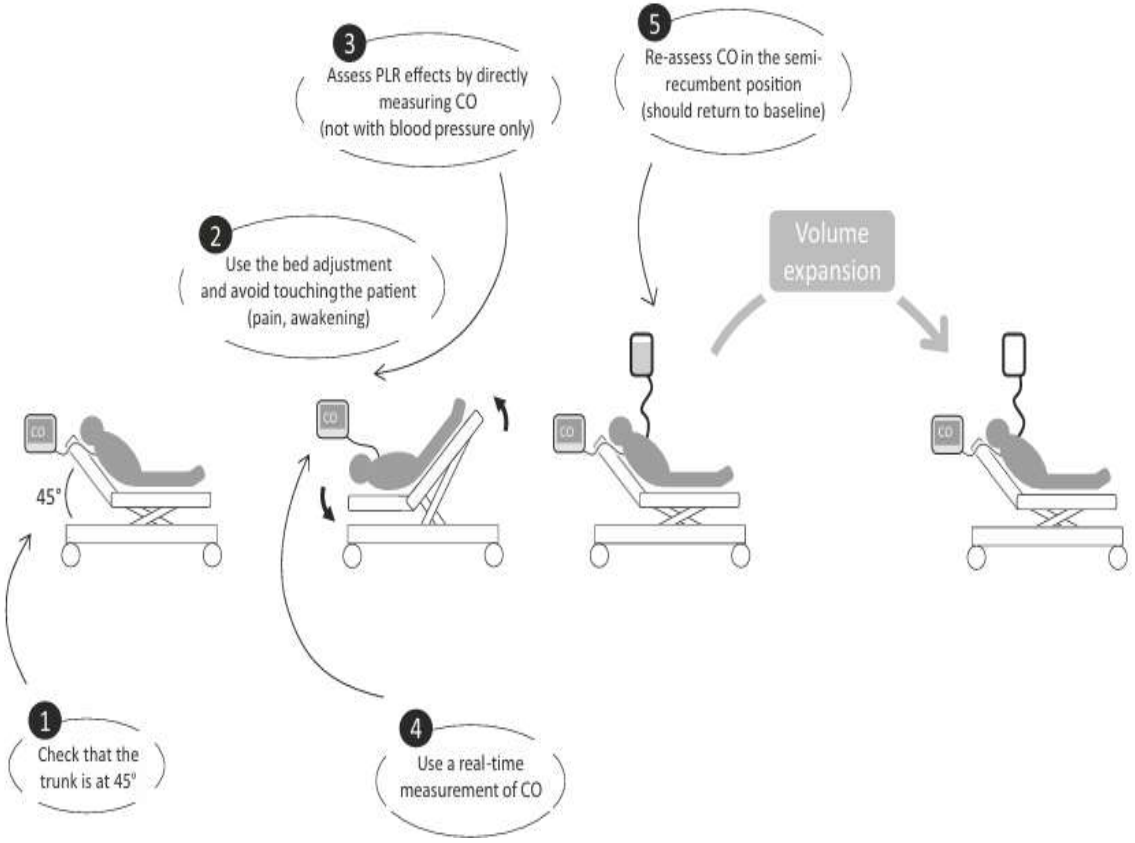
- Dubbed “internal fluid challenge”
- By raising the legs, causes displacement of blood in capacitance leg vessels to the intrathoracic veins leading into the RA
- Supposed to increase the SV in a pre-load dependent LV without the risk of volume overload in preload-independent individuals
- Dependent on the difference between mean systemic filling pressure and right atrial pressure (the driving pressure for venous return) and vascular resistance
- It is not affected by heart-lung interaction

“5 rules”

1. First to start with a semi-reclined position (45)
2. Measure the response with direct evaluation of CO
3. Continuous monitoring of CO as response is transient
4. Measure CO even after reversal to normal position, to rule out erratic CO unrelated to PLR
5. Avoid PAIN, COUGH, DISCOMFORT, AWAKENING

Monnet and Teboul Critical Care (2015) 19:18

Passive leg raising test



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Monnet and Teboul Critical Care (2015) 19:18

	PLR	Fluid challenge
Volume	Variable, 150–300 mL, less in severe hypovolaemia	Clinician defined, typically 250–500 mL
Duration including measurements (min)	1–3	10–30
Sympathetic tone	Often requires increased sedation and analgesia that must be at steady state during positional changes	No changes to sedation/analgesia
Risks	Increased intracranial pressure, reduced cerebral blood flow, decreased pulmonary compliance, decreased functional residual capacity, decreased arterial oxygenation	Fluid overload
Benefits	None per se	May improve perfusion
CO monitoring	Identify rapid and transient changes; typically using arterial pulse contour analysis or Doppler flows	Identify sustained changes; the gold standard TD PAC is applicable or devices similar to PLR
Utility	Predict fluid responsiveness related to changes in cardiac output/stroke volume	Predict fluid responsiveness related to changes in cardiac output or other indices of DO_2/VO_2 matching (e.g. arteriovenous O_2, CO_2 gradients, lactate, S_vO_2, $S_{cv}O_2$)
Position	45° hip flexion	No change from patient's most optimal
Ventilation mode	Spontaneous or PPV—still valid with spontaneous breathing efforts	Any
Cardiac rhythm	Any, provided no major changes over 30–90 s	Any
Concurrency	May need interruption of other interventions	Other interventions ongoing

Intensive Care Med (2016) 42:1493–1495


Passive leg raising
CO
SVI
PPV
PVI
ET CO2

Method used to measure response to PLR	Cut off	Accuracy	Comments
CO or CI (by PICCO)	ΔCI>9%	Sn-0.84 and Sp-0.97	
ΔPPV	Relative: >18.2% Absolute: >2%	Relative: Sn-0.90, Sp-0.88 Absolute: Sn-0.89, Sp-0.85	Irrespective of presence or absence of spontaneous breathing
ΔSV	>16%	Sn-0.85 and Sp-0.90	Measured by flotrac
CI/SVI (NICCOM)	>10%	Unacceptably low accuracy (both ~60-70%)	Unreliable in septic shock patients
Carotid doppler flow	ΔVpeak-Not reliable ΔFTc>7.58 ms ΔVTI>11%	ΔFTc- Sn- 0.71 and Sp-0.75 ΔVTI- Sn-0.77, Sp-0.78	Compared against gold standard of LVOT-VTI change of >15%
ΔET CO2	>5%	Sn-0.75, Sp-0.99	
TTE	ΔSV>13%	Sn-1, Sp-0.80	Compared with 500 mL infusion of crystalloid
Overall		Sn-0.85, Sp-0.91	Used varied cut-off of varied parameters

NICCOM-PLR used in RICU to assess fluid-responsiveness

- PLR should be avoided in patients who have had recent abdominal, thoracic, orthopedic or vascular surgeries, or with intracranial hypertension
- Affected by changes in levels of sedation and vasopressor infusion: keep a steady-state through-out
- Keep in mind: high dose of vasopressor, cardiogenic shock and severe hypovolemia decreases the volume of internal fluid bolus—interpret carefully (remove lower extremity compression stockings)
- The changes in CO should be monitored fast- within minutes of the maneuver
- Uncalibrated pulse contour analysis may give spurious results if there is change in arterial compliance/wave reflection in between

Intensive Care Med (2016) 42:1493–1495

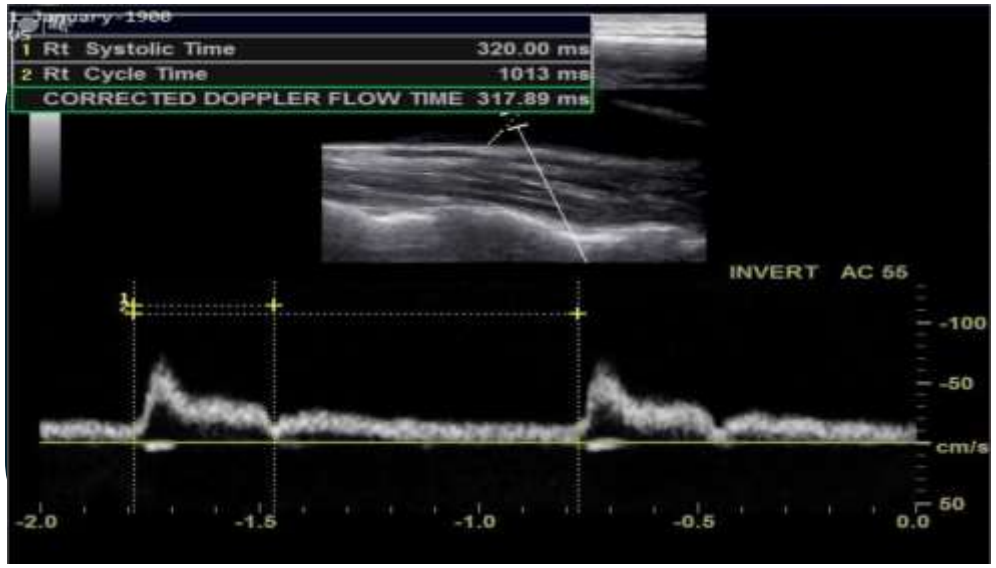
Few points regarding the maneuver:

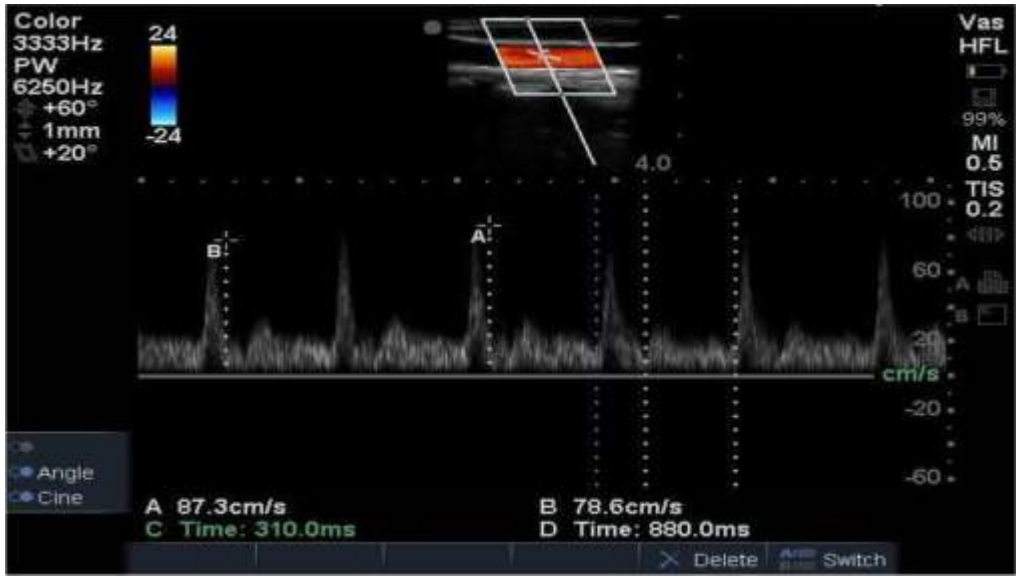
- Best results when legs are raised for 2-3 minutes
- Measure the changes in haemodynamic parameters within 1 minute (transient effect)
- A higher pretest probability improves accuracy- if in doubt, repeat or use another method additionally
- Always remember to remove pillows from under the patient, and switch off compressive-stockings

Passive leg raising test	
Advantages	Disadvantages
• Non-invasive • Easy to perform maneuver • Rapid assessment • Reliable even in spontaneously breathing patients and those with arrhythmia	• Best measured with invasive methods • Requires special beds (ideally) • Changes in vasopressor, sedation levels mid-maneuver can interfere with results • Sudden movements give unstable results

Carotid corrected flow time and reciprophasic variation in blood flow peak velocity

Measured by keeping the linear probe along the common carotid with indicator towards patients head 2 cm proximal to the carotid bifurcation;





Shortened in fluid depleted patients

Larger in fluid depleted patients

Kim DH ., Shin S, Kim N, Choi T, Choi SH, Choi YS. Carotid ultrasound measurements for assessing fluid responsiveness in spontaneously breathing patients: corrected flow time and respirophasic variation in blood flow peak velocity. British Journal of Anaesthesia. 2018 Sep;121(3):541–9.

Carotid corrected flow time and reciprophasic variation in blood flow peak velocity

Measured by keeping the linear probe along the common carotid with indicator towards patients head 2 cm proximal to the carotid bifurcation;

- ΔVpeak at a cut off of 9.1% has shown a sensitivity of 0.83 and specificity of 0.81 for predicting FR
- FTc at a cut off of 350 ms shows sensitivity of 0.72 and specificity of 0.83 for predicting FR
- Advantage- more easily measured than TTE, can be measured in prone patients and spontaneously breathing patients
- Disadvantage- requires skilled operator, inter-observer and intra-observer variability exist

Shortened in fluid depleted patients

Larger in fluid depleted patients

Singla D, Gupta B, Varshney P, Mangla M, Walikar BN, Jamir T. Role of carotid corrected flow time and peak velocity variation in predicting fluid responsiveness: a systematic review and meta-analysis. Korean journal of anesthesiology [Internet]. 2023 Jun;76(3):183–93.

Pros and cons of FTc and ΔVpeak

ADVANTAGES

- Non-invasive
- Inexpensive
- Not affected by mode of respiration

DISADVANTAGES

- CUT OFF not standardized
- Requires skilled sonologist
- Can not use in arrythmia, valvular disease and carotid artery stenosis

ETCO2 for fluid responsiveness:

- ET CO2 is the amount of the exhaled (partial pressure) CO2 measured by an infrared sensor (mainstream/sidestream)
- ET CO2 is dependent on the volume of blood in the pulmonary circulation (taking part in gas exchange) and by extension, on the cardiac output
- It can be hypothesized that a change in ET CO2 can be interpreted as a change in CO
- But for that to be true, it must be assumed that other factors influencing ETCO2 levels are constant

Factors affecting ET CO2 levels	
Elevated ET CO2	Decreased ET CO2
Metabolic- pain, hyperthermia, shivering	Metabolism- hypothermia, metabolic acidosis
Respiratory- Hypoventilation (COPD, sedation)	Respiratory system- hyperventilation, increased dead-space ventilation
Circulatory- increased CO	Circulatory- decreased CO, pulmonary embolism
Drugs- bicarbonate	

ETCO2 for fluid responsiveness:

- A 2019 systematic review and meta-analysis examined 7 studies evaluating predictive ability of ET-CO2 for diagnosing fluid-responsiveness
- 2 studies in cardiac OR after anaesthesia induction, 5 studies in critically ill patients in ICU
- Only one sided used blinded investigator, Bias was high for other studies
- The cut-off offering best sensitivity and specificity was ΔETCO2 of 2 mm Hg
- Median AUROC 0.82, median sensitivity 0.75 and median specificity 0.94

Reference	Type of investigation	Sample size, n: calculation	Fluid responders, n (%)	PLR or fluid infusion	Reference method	Precision/LSC	ET-CO_2 method	Precision/LSC	Blinded outcome assessors
Lakhal et al, 2017 [3]	Prospective observational ICU	86: –	33 (38)	500 ml crystalloid/ colloid	Transthoracic echocardiography Vivid S6/i (GE Healthcare)	9%/–	Mainstream infrared Servo I (Marquet) or Evita 4 (Dräeger Medical)	–/–	No
Jacquet-Lagrèze et al, 2016 [4]	Prospective observational OR	40: +	15 (38)	500 ml HAES	Oesophageal Doppler HemoSonic 100 (Arrow International)	–/–	Sidestream infrared Infinity $EtCO_2$ Microstream SmartPod (Dräeger)	2.2%/3.2%	No
Toupin et al, 2016 [5]	Prospective observational OR	90: +	28 (31)	PLR	Pulmonary artery thermodilution Swan Ganz catheter	–/–	Mainstream infrared (Philips)	–/–	Yes
Xiao-ting et al, 2015 [6]	Prospective observational ICU	48: –	34 (71)	PLR	Transpulmonary thermodiluton PICCO (Pulsion Medical Systems)	–/–	Mainstream infrared CO_2 sensor M2741A (Philips)	–/–	No
Monnet et al, 2013 [7]	Prospective observational ICU	40: –	21 (53)	PLR	Transpulmonary thermodiluton PICCO (Pulsion Medical Systems)	12%/–	Mainstream infrared CO_2 sensor M2741A (Philips)	1.3%/1.8%	No
Young et al, 2013 [8]	Retrospective chart review ICU	34: –	24 (55)	PLR and/or 500 ml crystalloid/ colloid	Bioreactance NICOM (Cheetah Medical)	–/–	Mainstream infrared Respironics NM3 (Philips)	–/–	No
García et al, 2012 [9]	Prospective observational ICU	37: –	21 (57)	500 ml crystalloid/ colloid	Oesophageal Doppler Cardio0 (Deltex Medical)	2.3%/3.2%	Sidestream infrared M-COVX (Datex-Ohmeda)	1.3%/1.85%	No

ET = end-tidal; HAES = health at every size; ICU = intensive care unit; LSC = least significant change; OR = operating room before surgery; PLR = passive leg raising.

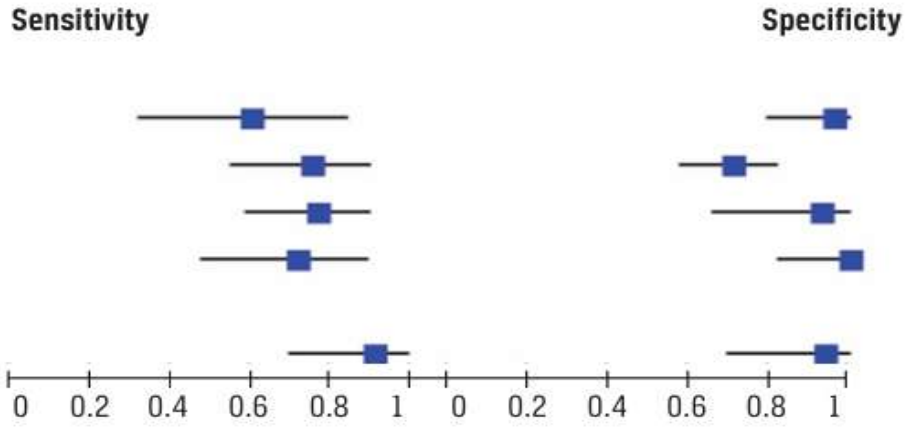
End-tidal CO2 in the diagnosis of fluid responsiveness – a systematic review [Internet]. Ugeskriftet.dk. 2019.

ETCO2 for fluid responsiveness:

If the minute ventilation is kept constant and rate of aerobic respiration is assumed to be fixed, a change in ET CO2 with PLR or fluid challenge may predict fluid responsiveness with fair sensitivity and good specificity;

induction, 6 studies in critically ill patients

Study	Ref methods	Sensitivity	Specificity
Lakhal et al, 2017 [3]	0 0 0 0	Not estimable	Not estimable
Jacquet-Lagrèze et al, 2016 [4]	Oesophag. Doppler	0.60 (0.32-0.84)	0.96 (0.80-1.00)
Toupin et al, 2016 [5]	PAC TPTD	0.75 (0.55-0.89)	0.71 (0.58-0.82)
Xiao-ting et al, 2015 [6]	PiCCO TPTD	0.76 (0.59-0,89)	0.93 (0.66-1.00)
Monnet et al, 2013 [7]	PiCCO TPTD	0.71 (0.48-0.89)	1.00 (0.82-1.00)
Young et al, 2013 [8]	NICCOM	Not estimable	Not estimable
Garcia et al, 2012 [9]	Oesophag. Doppler	0.90 (0.70-0.99)	0.94 (0.70-1.00)



End-tidal CO2 in the diagnosis of fluid responsiveness – a systematic review [Internet]. Ugeskriftet.dk. 2019.

- A 2024 prospective observational study evaluated the predictive ability of ET CO2 after PLR
- 107 patients evaluated
- All ventilated with 8mL/Kg IBW, PEEP-6 (variation in MV/RR>10% were excluded) and sedated
- PLR performed for 2 minutes after keeping patients semi-reclined at 45° for 2 minutes
- Arterial cannula used to record PPV, SVV; ETCO2 recorded through mainstream infrared sensor
- Reference method: CO measured by TTE with subaortic VTI technique (Api 5C view)
- 15% change in cardiac output defined fluid responsiveness

Table 1. Demographic data and first day laboratory data

	Non-Responder	Responder	p-value
Age[1]	55 (26)	65 (21)	0.112
Sex[1] (F/M; n)	31/24	26/27	0.447
APACHE-2[1]	19 (10)	22 (11)	0.145
ICU Admission Diagnosis (n) %			0.568
Pneumonia	13 (21.8%)	13 (24.5%)	
Neurological Disease	12 (23.6%)	9 (17%)	
Urological Disease	5 (9.1%)	5 (9.4%)	
Intra-Abdominal Disease	14 (25.5%)	11 (20.8%)	
Cardiological Diseases	5 (9.1%)	6 (11.3%)	
Trauma	6 (10.9%)	8 (15.1%)	
Hematologic Diseases	0	1 (1.9%)	

Özkarakaş H, Uçar O, Tekgül ZT, Ozmuk O, Öztürk MC, Bilgin MU, Samsa M, Şahinkaya HH, Yesilnacar Ç. Easy method to determine fluid responsiveness in septic shock patients: end-tidal CO2 – a prospective observational study. Ulus Travma Acil Cerrahi Derg 2024;30:90-96.

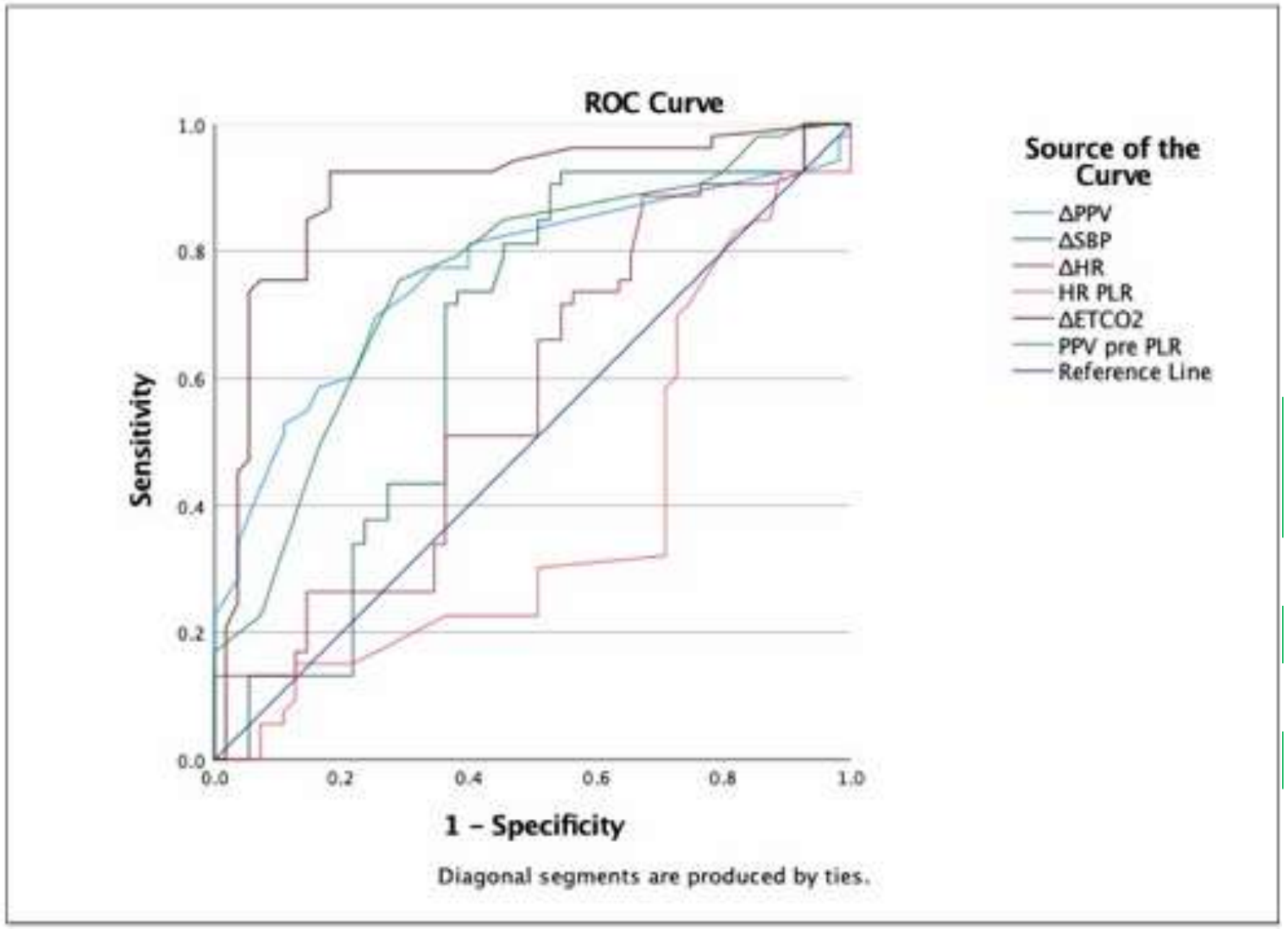
Table 2. Hemodynamic parameters at baseline and after passive leg raising

	Non-Responder	Responder	p-value
HR[1]	102 (20)	94 (18)	0.062
HR PLR[1]	105 (24)	93 (16)	0.035
ΔHR[1]	1.01 (3.62)	1.03 (3.7)	0.182
SBP[1]	115 (22)	118 (25)	0.768
SBP PLR[1]	115 (20)	122 (22.5)	0.500
ΔSBP[1]	-0.67 (7.03)	1.70 (4.17)	0.007
CVP[1]	9 (4)	8 (4)	0.309
PPV[1] pre PLR	9 (4)	13 (2.5)	<0.001
PPV PLR[1]	10 (4)	11 (2)	<0.001
ΔPPV[1]	0 (8.3)	13.3 (9.5)	<0.001
$ETCO_2$[1]	39 (8)	37 (10)	0.963
$ETCO_2$ PLR[1]	40 (7)	39 (11)	0.387
Δ$ETCO_2$[1]	2.57 (0.81)	5.71 (2.83)	<0.001
CO[1]	5.25 (1.38)	5.06 (0.63)	0.213
CO PLR[1]	5.35 (1.97)	6.03 (0.74)	0.018
ΔCO[1]	4.35 (7.71)	20 (4.72)	<0.001

[1]: Median (Interquartile Range). CVP: Central Venous Pressure; ETCO2: End-Tidal CO_2; HR: Heart Rate; PPV: Pulse Pressure Variation; SBP: Systolic Blood Pressure; SV: Stroke Volume.

ΔET CO2 was significantly different between responders and non-responders

Baseline PPV, PPV post-procedure and ΔPPV were significantly different between responders and non-responders



a cut off of ΔET CO2 >4% had sensitivity of 85% and specificity of 86%

A cut off of ΔET CO2>5% had sensitivity of 75.5% and specificity of 99.3% (AUC-0.89)

ΔPPV also had good predictive ability but not as good as ΔET CO2

ET CO_2 may be a good predictor of fluid responsiveness in conjunction with PLR

Advantages	Disadvantages
• Does not need invasive arterial or central venous cannulae • Not dependent on operators' skill (like TTE) • Inexpensive (in comparison to other methods of haemodynamic monitoring)	• Requires endotracheal intubation • Used in conjunction with PLR, so can not be used where PLR is contraindicated • Requires sedation • Not reliable in metabolic acidosis, increased dead-space ventilation, hypo or hyperthermia, cardiac dysfunction/arrhythmia

Tidal volume challenge

- In patients ventilated at Vt<8mL/Kg dynamic parameters perform poorly
- A transient increase in Vt to >8mL/Kg for 2 minutes improves the accuracy of dynamic parameters for FR
- ΔPPV, ΔSVV, ΔPVI and ΔSVI (the difference between these parameters at Vt-6mL/Kg and that at 8mL/Kg) are the parameters measured
- Has good accuracy in prone patients as well
- Disadvantages include- unreliable in low lung compliance, high respiratory rate (HR:RR<3.6), cardiac arrhythmia, RV dysfunction, open thoracic surgery, abdominal hypertension

Griva P, Talliou C, Soulioti E, Milionis O, Sidiropoulou T. The role of the tidal volume challenge test in volume responsiveness assessment: a narrative review. Journal of anesthesia, analgesia and critical care [Internet]. 2025 Jan;5(1):37.

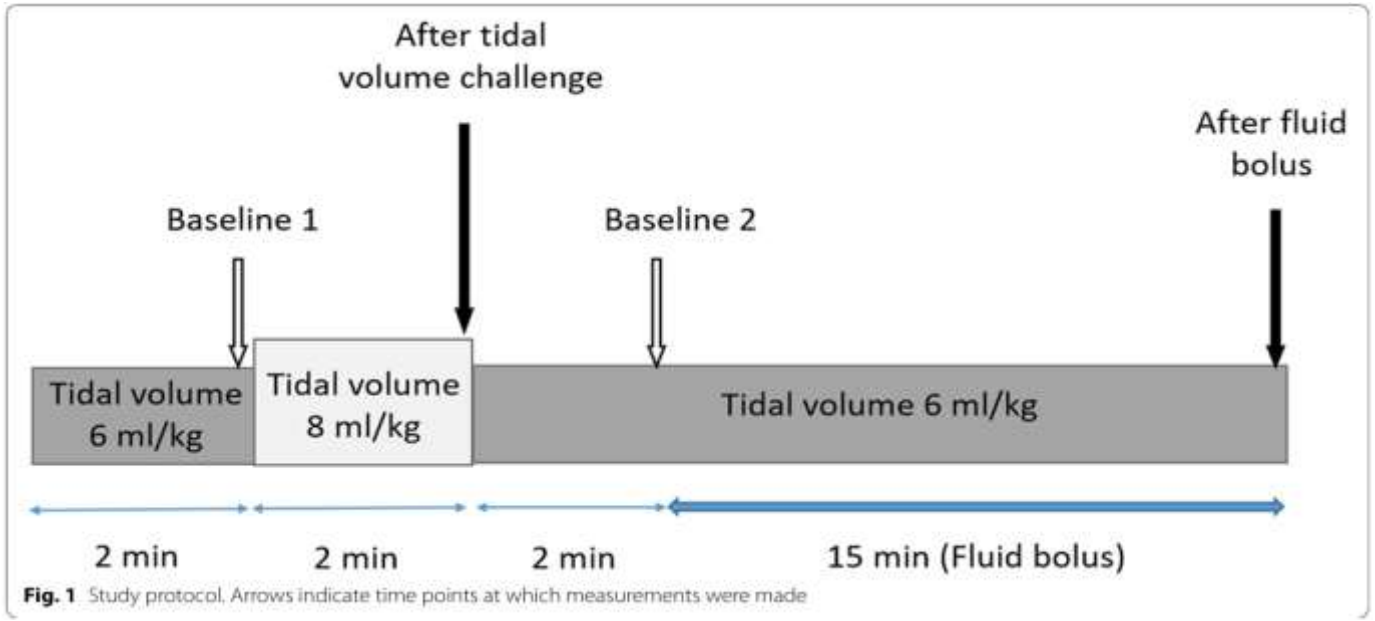
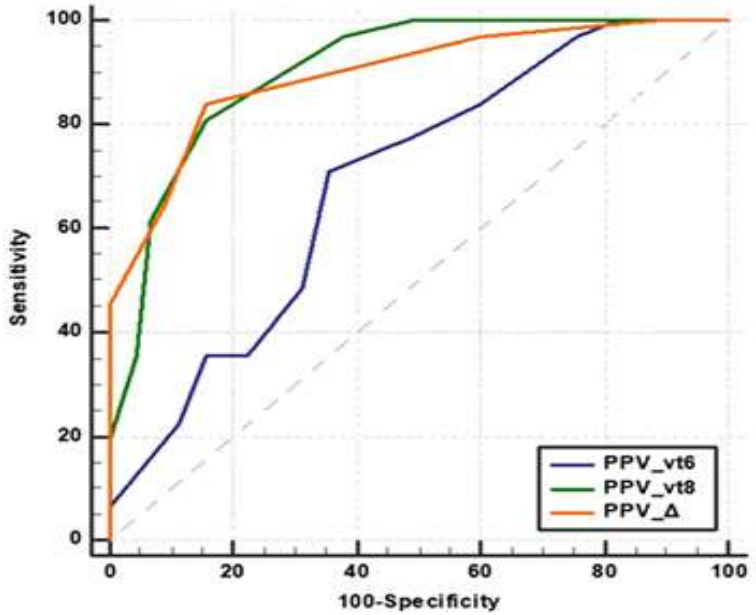


Fig. 1 Study protocol. Arrows indicate time points at which measurements were made



	AUC(95%CI)	*p*	cut off value	Youden index	Sensitivity (%)	Specifficity (%)
MAP	0.55(0.43–0.66)	0.466	72	.198	71	49
Heart rate	0.61(0.48–0.71)	0.102	99	.203	87	33
CCI	0.67(0.55–0.72)	0.007	2.96	0.342	74	60
PPV_6	0.69(0.57–0.79)	0.002	7	.354	71	64
PPV_8	0.90(0.81–0.96)	< 0.001	11	.651	80	84
ΔPPV_{6-8}	0.90(0.80–0.95)	< 0.001	2	.683	84	84
CVP_6	0.67(0.55–0.77)	0.007	10	.216	84	38
CVP_8	0.68(0.56–0.78)	0.008	9	.284	48	80
ΔCVP_{6-8}	0.52(0.40–0.63)	0.81	1	.079	61	47

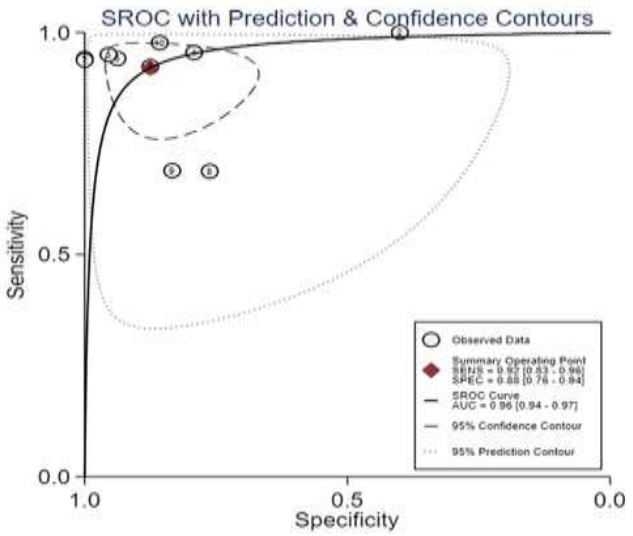
Xu Y, Guo J, Wu Q, Chen J. Efficacy of using tidal volume challenge to improve the reliability of pulse pressure variation reduced in low tidal volume ventilated critically ill patients with decreased respiratory system compliance. BMC Anesthesiology. 2022 May 4;22(1).

Table 2 Predictive performance of PPV change after TVC in low tidal mechanically ventilated patients

	Study/year	predictor	Subjective numbers could be calculated				Threshold (%)	Sensitivity	Specificity	AUROC of PPV change	AUROC of PPV
			TP	FP	FN	TN					
	Myatra2017 [14]*	ΔPPV	16	0	1	14	3.5	0.94	1.00	0.99 (0.98, 1.00)	0.69
		ΔPPV%	16	0	1	14	48	0.94	1.00	0.97 (0.92, 1.00)	
prone	Yonis 2017 [15]	ΔPPV%	9	15	0	10	29	1.00 (0.66, 1.00)	0.40 (0.1, 0.7)	0.59 (0.31, 0.88)	0.49 (0.21, 0.77)
	Jun2019 [16]*	ΔPPV	24	2	2	14	1	0.92 (0.73, 0.99)	0.86 (0.57, 0.98)	0.95 (0.83, 0.99)	0.69 (0.52, 0.83)
		ΔPPV%	24	4	5	14	25	0.83 ((0.63, 0.95)	0.79 (0.49, 0.95)	0.87 (0.72, 0.96)	
prone	Messina2019 [17]	ΔPPV%	21	5	1	19	13.3	0.95 (0.74, 1.00)	0.76 (0.53, 0.92)	0.94 (0.82, 0.99)	0.68 (0.50, 0.85)
	Messina2020 [18]	ΔPPV%	19	1	1	21	12.2	0.95	0.95	0.96 (0.87, 1.00)	0.69
	Elsayed2021 [19]	ΔPPV	16	2	1	30	3.5	0.94	0.94	0.96	0.85
	Taccheri2021 [20]*	ΔPPV	15	0	1	15	1	0.93 (0.68, 1.00)	1.00 (0.78, 1.00)	0.98 ± 0.02	0.66
		ΔPPV%	15	2	1	15	20	0.93 (0.68, 1)	0.87 (0.59, 0.98)	0.94 ± 0.04	
Spont breath	Hamzaoui2021 [21]	ΔPPV	22	10	10	32	2	0.69	0.76	0.73 (0.60, 0.84)	0.61 (0.48, 0.75)
prone	Shi2022 [22]	ΔPPV	42	7	1	42	3.5	0.98 (0.89, 0.99)	0.86 (0.75, 0.79)	0.94 (0.88, 0.99)	0.85 (0.77, 0.92)
	Xu2022 [23]	ΔPPV	31	9	14	45	2	0.84	0.84	0.90 (0.81, 0.96)	0.69 (0.57, 0.79)

Wang X, Liu S, Gao J, Zhang Y, Huang T. Does tidal volume challenge improve the feasibility of pulse pressure variation in patients mechanically ventilated at low tidal volumes? A systematic review and meta-analysis. Critical Care. 2023 Feb 2;27(1).

Subgroups	Samples	AUROC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	DOR (95% CI)	I^2 (%) (95% CI)	Q	*P* value	Spearman correlation coefficient	Statistical heterogeneity	Heterogeneity source
Patients in ICU group	7	0.95 (0.93, 0.97)	0.91 (0.77, 0.97)	0.88 (0.69, 0.96)	72 (13, 396)	77 (74, 100)	8.53	< 0.01	0.22	Significant	Others
Supine or semi-recumbent	6	0.95 (0.92, 0.96)	0.88 (0.73, 0.95)	0.89 (0.79, 0.95)	62 (13, 297)	0 (0, 100)	0.42	0.41	1	Very low	Totally threshold effect
Low lung compliance < 30 cm H_2O	4	0.96 (0.94, 0.97)	0.89 (0.72, 0.96)	0.91 (0.81, 0.96)	87 (15, 506)	0 (0, 100)	0.51	0.39	1	Very low	Totally threshold effect
PEEP ≥ 5 cm H_2O and ≤ 15 cm H_2O group	9	0.95 (0.93—0.97)	0.92 (0.82, 0.97)	0.86 (0.73, 0.94)	72 (19, 270)	77 (51, 100)	8.87	< 0.01	0.19	Significant	Others
Measure tools except TPTD	5	0.94 (0.92, 0.96)	0.91 (0.78, 0.97)	0.87 (0.78, 0.93)	70 (16, 308)	0 (0, 100)	0.86	0.33	1	Very low	Totally threshold effect
Overall data except Yonis 2017	9	0.94 (0.92, 0.96)	0.92 (0.82,0.96)	0.88 (0.82,0 .92)	83 (26, 260)	42 (0, 100)	3.5	0.09	1	Low	Totally threshold effect
Overall date	10	0.96 (0.94, 0.97)	0.92 (0.83, 0.96)	0.88 (0.76, 0.94)	81 (23, 284)	76 (47, 100)	8.3,	< 0.01	0.06	Significant	Others

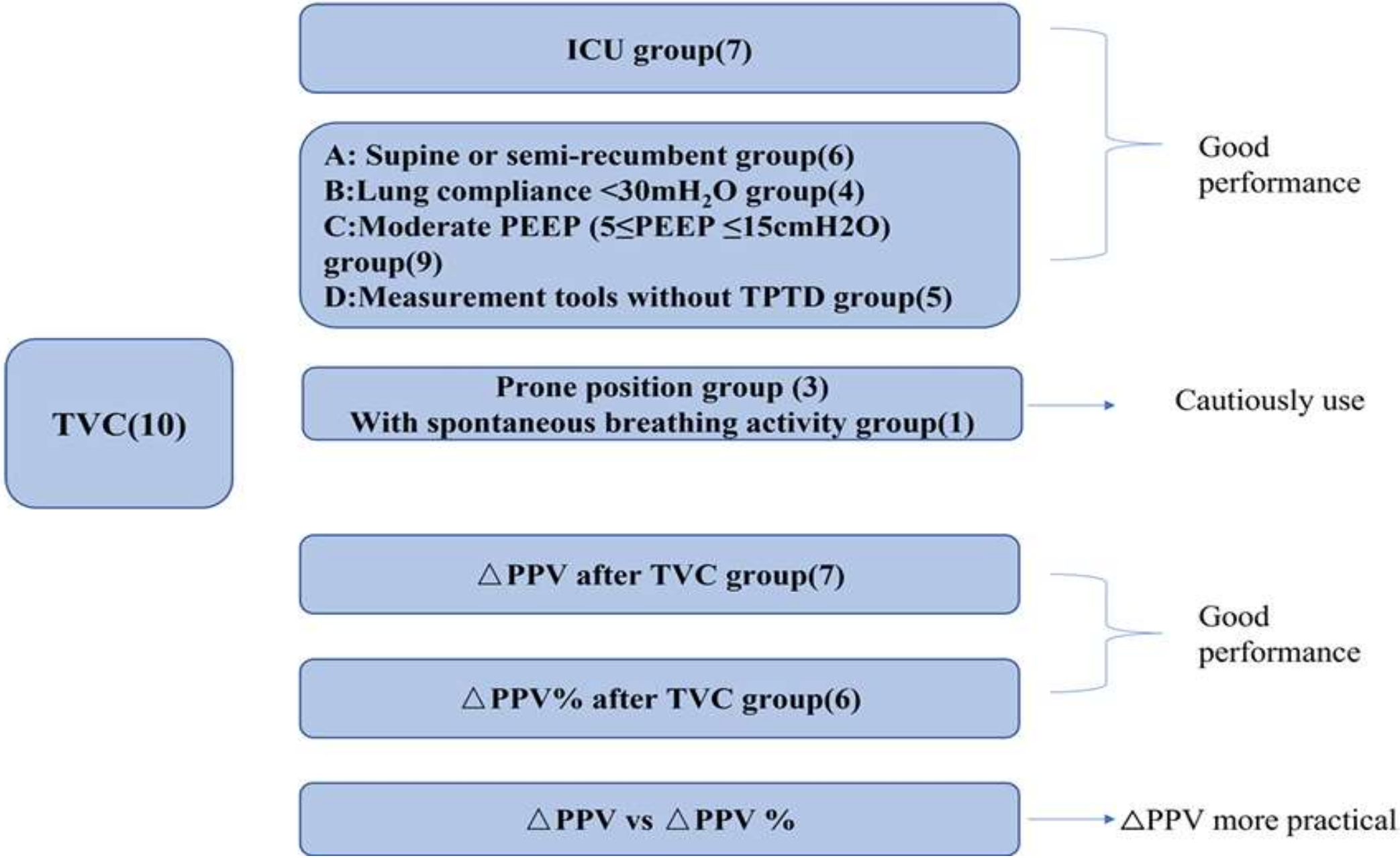


- SROC of ΔPPV showed an AUC of 0.96 , Sensitivity-0.92, specificity 0.88
- Overall, the position, method of CI measurement (TPTD or others), PEEP levels, lung compliance did not decrease the predictive ability of ΔPPV

Wang X, Liu S, Gao J, Zhang Y, Huang T. Does tidal volume challenge improve the feasibility of pulse pressure variation in patients mechanically ventilated at low tidal volumes? A systematic review and meta-analysis. Critical Care. 2023 Feb 2;27(1).

Different parameters used to measure effects of TVC

Parameter used	Cut-off	Sensitivity	Specificity	Comments
ΔPPV	3.5	0.94	1	Some studies showed comparable accuracy with thresholds 1-2
ΔPPV%	48%	0.94	1	Highest cut-off in any study; others used 12-29%)
ΔSVI%	7.5%	0.90	0.96	Varies widely (16%, 23%) among studies
ΔPVI	2.5	0.95	0.68	Patients of pancreatic sx, not septic shock/ards
ΔPVI%	29%	0.82	0.75	


TVC(10)
ICU group(7)
A: Supine or semi-recumbent group(6)
B:Lung compliance <30mH2O group(4)
C:Moderate PEEP (5≤PEEP ≤15cmH2O) group(9)
D:Measurement tools without TPTD group(5)
Good performance
Prone position group (3)
With spontaneous breathing activity group(1)
Cautiously use
△PPV after TVC group(7)
△PPV% after TVC group(6)
Good performance
△PPV vs △PPV %
△PPV more practical

No cut-off is absolute

- A higher threshold may improve specificity at the cost of sensitivity
- In patients with high pre-test probability (of being fluid responsive) a lower threshold can be used (or else they may be erroneously overlooked)
- In patients with higher risk of fluid overload/harm, a higher threshold (with more specificity) can be used
- Using a single threshold value runs the risk of both missing out patients who may benefit or unnecessary infusions to patients who would not benefit/be harmed by it

Mini-fluid challenge

- A large amount of fluid in a patient who may or may actually benefit from it, may cause deleterious effect
- If a smaller bolus can predict responsiveness would be preferrable
- 100 mL bolus given over 2 minutes may predict fluid responsiveness
- When using a ΔSVI of >7% as cut off, it can predict fluid responsiveness with sensitivity of 0.93 and specificity of 0.85

Biais M, de Courson H, Lanchon R, Pereira B, Bardonneau G, Griton M, et al. Mini-fluid Challenge of 100 ml of Crystalloid Predicts Fluid Responsiveness in the Operating Room. Anesthesiology [Internet]. 2017 Sep 1;127(3):450–6.

Mini-fluid challenge

Index	Best Threshold, %	Gray Zone, range, %	Patients Whose Measurements Were in the Gray Zone, %	AUROC (95% CI)	Sensitivity (95% CI), %	Specificity (95% CI), %	Youden Index J
ΔSVI 50	> 2	0–7	47	0.83 (0.75–0.92)	89 (72–98)	67 (53–78)	0.56
ΔSVI 100	> 6	4–7	19	0.95 (0.90–0.99)	93 (77–99)	85 (73–93)	0.78
PPV	> 10	6–14	75	0.65 (0.53–0.78)	54 (34–73)	68 (55–80)	0.22

- In the situations of LTV (Vt<7mL/Kg) mini-fluid challenge performs better than PPV

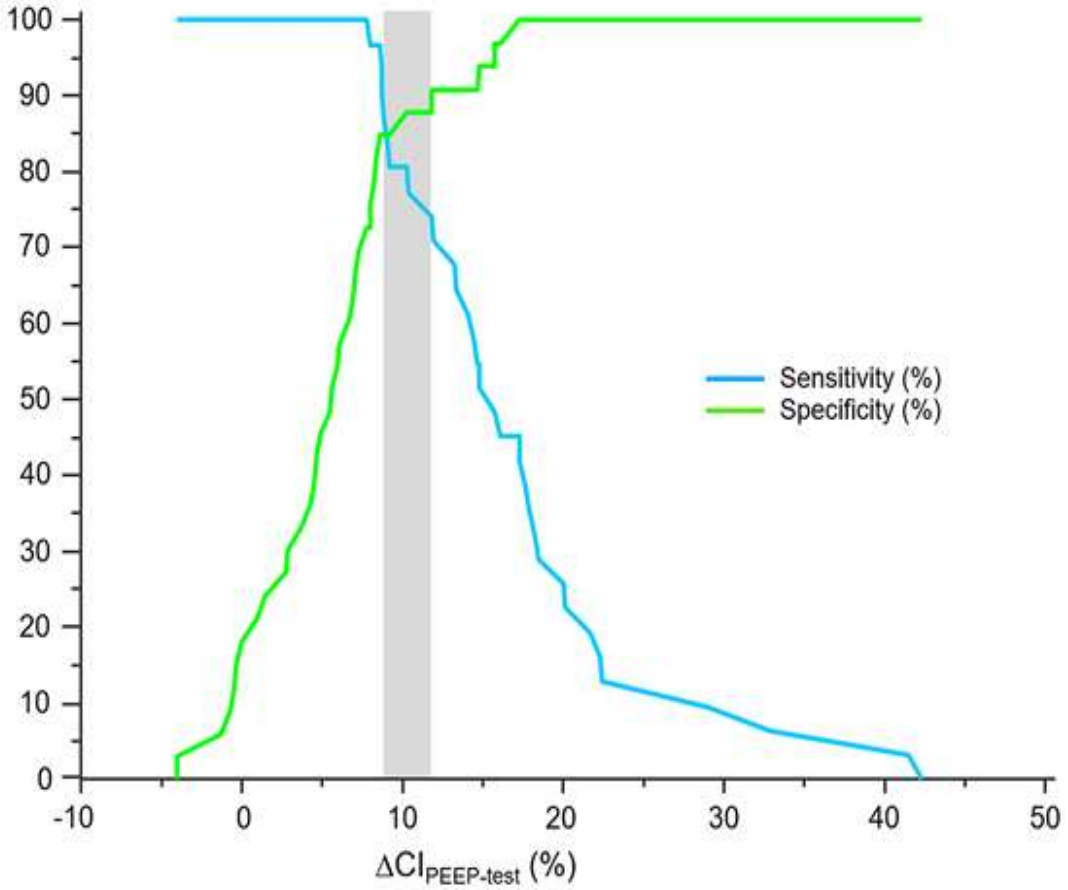
Biais M, de Courson H, Lanchon R, Pereira B, Bardonneau G, Griton M, et al. Mini-fluid Challenge of 100 ml of Crystalloid Predicts Fluid Responsiveness in the Operating Room. Anesthesiology [Internet]. 2017 Sep 1;127(3):450–6.

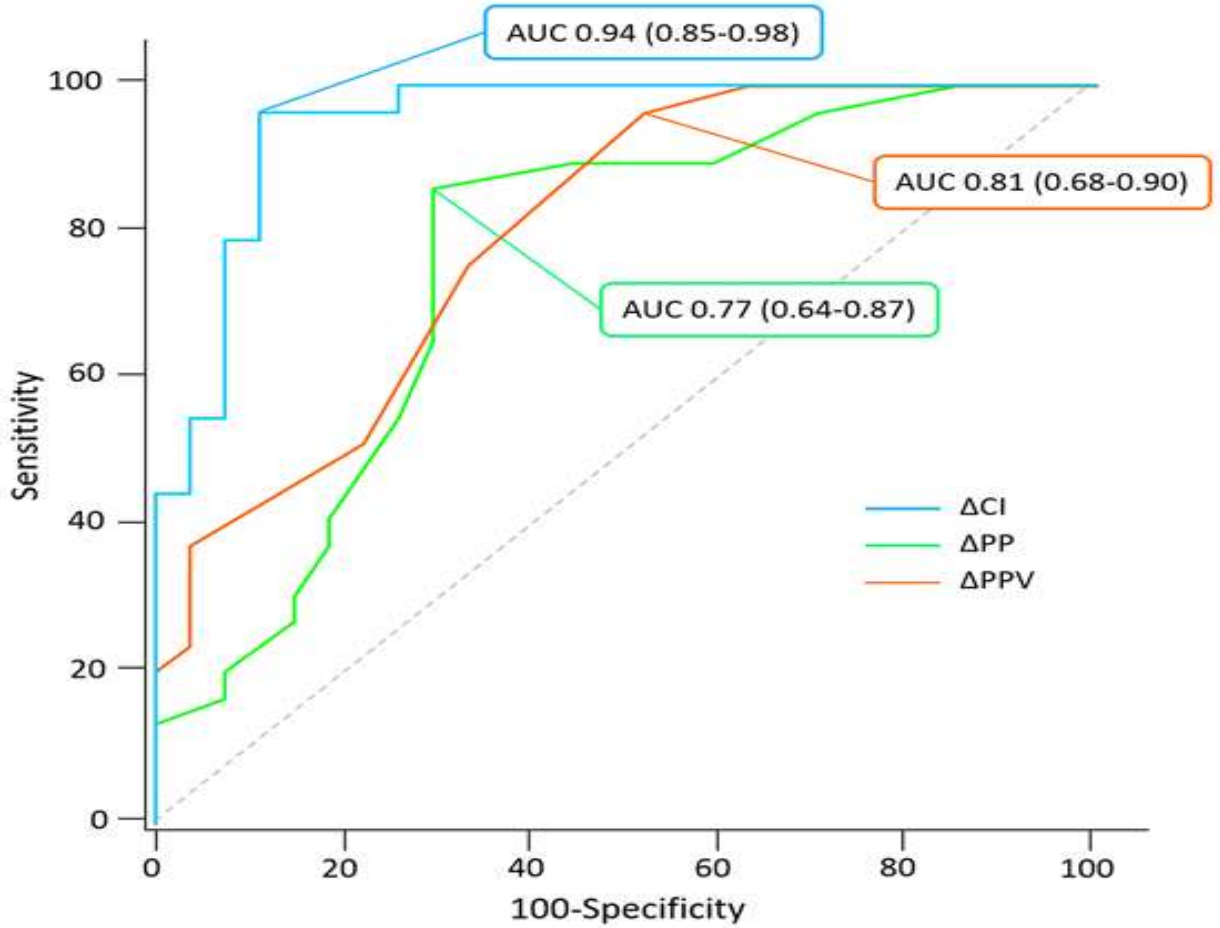
PEEP-test for fluid responsiveness

- Higher PEEP causes increase in intrathoracic pressure, leading to decreased venous return, as well as increased RV afterload, and subsequent fall in LV output during expiration
- A transient drop in PEEP hinders this mechanism leading to improvement in LV output
- To do PEEP-test, PEEP is reduced from its pre-test value to 5 cm H20 for 1 minute and CI measured immediately (highest change in CI seen about 50 seconds following setting the new PEEP)
- A CI cut-off of 8.7% predicts fluid responsiveness with sensitivity of 0.97 and specificity of 0.85

Lai C, Shi R, Beurton A, Moretto F, Soufia Ayed, Fage N, et al. The increase in cardiac output induced by a decrease in positive end-expiratory pressure reliably detects volume responsiveness: the PEEP-test study. Critical Care. 2023 Apr 9;27(1).

PEEP-test for fluid responsiveness





Lai C, Shi R, Beurton A, Moretto F, Soufia Ayed, Fage N, et al. The increase in cardiac output induced by a decrease in positive end-expiratory pressure reliably detects volume responsiveness: the PEEP-test study. Critical Care. 2023 Apr 9;27(1).

- Alternatively, ΔSVV can also be measured (similar AUC)
- ΔPPV and ΔPP have poor specificity with PEEP-test (50-60%)
- It was not affected by LTV or recruitability (although a significant number of ARDS patients included in the study had good recruitability)
- Drop of PEEP causes transient hypoxia and Sp02 recovers quickly

Pit-falls in the theory

- PEEP also causes increase in RV afterload and decrease in RV output
- This dose not depend upon preload-dependence
- Hence, fall in PEEP may increase CO in patients who are not preload-dependent (fluid-non-responsive) as well
- For the same reason, it will increase CO in patients with RV failure without fluid-responsiveness
- Decrease in PEEP may cause lung de-recruitment and resultant pulmonary vasoconstriction may increase RV afterload
- This may cause false negative results
- However, pulmonary vasoconstriction takes several minutes to take effect, and the results of PEEP-test is measured before that

Dynamic Inferior Vena Cava parameters

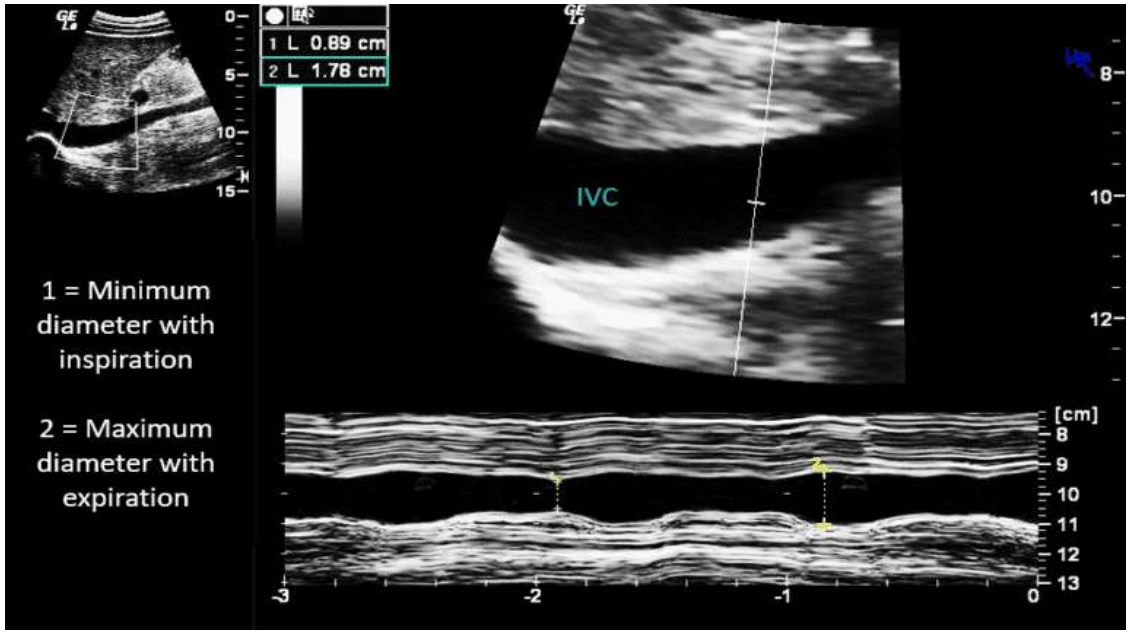
- During invasive mechanical ventilation, insufflation causes increase in itrathoracic pressure and impedes venous return, distending IVC
- During expiration, the IVC collapses due to draining of blood into RA
- It is hypothesized that the degree of these variability may predict fluid responsiveness

IVC collapsibility index=$\frac{IVCDmax-IVCDmin}{IVCDmax}$ X 100

IVC distensibility index=$\frac{IVCDmax-IVCDmin}{IVCDmin}$ X 100

IVC respiratory variation=$\frac{IVCDmax-IVCDmin}{(IVCDmax+IVCDmin)/2}$ X 100

- IVC diameters are assessed 2 cm from its drainage into the RA in the subxiphoid view
- Assessed throughout a full respiratory cycle
- Maximum and minimum value on M-mode are noted



- In mechanically ventilated patients with Vt>8mL/Kg and PEEP<5cmH2O, IVC distensibility index cut-off of 17.5% predicts fluid responsiveness with sensitivity of 65% and specificity of 85%
- IVC respiratory variation index cut-off of 16.5% predicts fluid responsiveness with similar sensitivity and specificity
- Predictive value falls when used in LTV and higher PEEP (ARDS patients)

Parameter	$\Delta_{RH}IVC_1$	$\Delta_{RH}IVC_2$
Response group (n = 54)		
before the VL test	19.1 ± 3.4	17.4 ± 3.4
after the VL test	16.0 ± 4.0	15.0 ± 3.1
t	5.109	7.568
p-value	**<0.001**	**<0.001**
Non-response group (n = 48)		
before the VL test	14.4 ± 2.6*	13.6 ± 2.2*
after the VL test	14.2 ± 2.6	13.2 ± 1.8
t	0.998	1.789
p-value	0.328	0.089

He H, Pan N, Zhou X. Application value of bedside ultrasound for assessing volume responsiveness in patients with septic shock. Vojnosanitetski pregled [Internet]. 2022 Jul 14 [cited 2025 Aug 18];80(5):439–45.

- In spontaneously breathing critically ill patients (not on NIV) ‘caval index’ (cIVC) or the collapsibility index- (IVCDe-IVCDi)/IVCDe can be used as a predictor of fluid responsiveness
- At a cut off value of 25% it predicts fluid responsiveness with sensitivity of 0.87 and specificity of 0.81
- If a standardized breathing technique is employed, with an inspiration of <5 secs with buccal pressure between –5 and –10 cm H2O, cIVC (collapsibility) at a cut-off of 48% predicts fluid responsiveness with sensitivity of 0.84 and specificity of 0.90
- Measurement should take place during the period of standardized breathing maneuver

Corl KA, George NR, Romanoff J, Levinson AT, Chheng DB, Merchant RC, et al. Inferior vena cava collapsibility detects fluid responsiveness among spontaneously breathing critically-ill patients. Journal of Critical Care. 2017 Oct;41:130–7

Preau S, Bortolotti P, Colling D, Dewavrin F, Colas V, Voisin B, et al. Diagnostic Accuracy of the Inferior Vena Cava Collapsibility to Predict Fluid Responsiveness in Spontaneously Breathing Patients With Sepsis and Acute Circulatory Failure. Critical Care Medicine. 2017 Mar;45(3):e290–7..

- A 2025 meta-analysis that included both ventilated (majority ventilated with 8-10mL/Kg Vt) and spontaneously breathing patients found the sensitivity and specificity of dynamic IVC parameters to be about 0.82 each
- Wide variation in cut-off has been used (10-30%) and patients having intra-abdominal hypertension, LV systolic failure and RV systolic failure were not included
- A 2021 meta-analysis that included only spontaneously breathing patients found the sensitivity of cIVC to be 0.63 and specificity to be 0.83
- Cut-off values between 20-40% were chosen among various studies

Wenwen Y, Ping X, Yue D, Xuan L. Accuracy of indices of inferior vena cava in predicting fluid responsiveness in patients with shock: A systematic review and meta-analysis. Intensive and Critical Care Nursing [Internet]. 2025 Apr 8;89:104015.
Cardozo Júnior LCM, Lemos GSD, Besen BAMP. Fluid responsiveness assessment using inferior vena cava collapsibility among spontaneously breathing patients: Systematic review and meta-analysis. Medicina Intensiva (English Edition) [Internet]. 2022 Oct 19;47(2):90–8.

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First author	Country	Sample size	Type of shock	IVC indices	Mechanical ventilation	Tidal volume	Fluid infusion ingredient	Fluid infusion volume	Reference standards and thresholds	Invasive or not
Zheng, X [33]	China	140	Septic shock	IVCD, dIVC	Yes	/	/	/	PICCO △SV ≥ 15 %	Yes
Zhao, J [34]	China	42	Septic shock	IVCCI	Yes	/	6 % hydroxyethyl starch	500 ml	PICCO △CI ≥ 15 %	Yes
Yao, X [35]	China	70	Septic shock	RVI	Yes	10 mL/kg	6 % hydroxyethyl starch	500 ml	PICCO △CI ≥ 15 %	Yes
Wu, J [36]	China	28	Septic shock	dIVC	Yes	8 — 10 ml/kg	6 % hydroxyethyl starch	500 ml	PICCO △SV ≥ 10 %	Yes
Li, Z [37]	China	59	Septic shock	IVCD, RVI	Yes	8 ml/kg	0.9 %sodium chloride	250 ml	Vigileo-FloTrac system △CI ≥ 15 %	Yes
Charbonneau, H [51]	France	44	Septic shock	△SVC, △IVC	Yes	8 — 10 ml/kg	6 % hydroxyethyl starch	7 ml/kg	TEE △IVC ≥ 18 %	No
Benoit Bataille [52]	France	100	Septic shock	c-IVC and velocitye time interval	Yes	/	Passive leg raising	/	TEE △SV > 15 %	No
Wang junsheng [38]	China	40	Septic shock	IVCD, RVI	Yes	5 ~ 8ml/Kg	Compound sodium chloride solution	500 ml	PICCO △CI ≥ 15%	Yes
Ling wei [39]	China	120	Septic shock	IVC-RVI	/	/	Lactated Ringer's solution	500 mL	TEE △SV ≥ 15 %	No
Peng zhang [40]	China	40	Shock	IVC	Yes	6 — 8 ml/kg	6 % hydroxyethyl starch	7 ml/kg	TEE △CO ≥ 15 %	No
Li raowei [41]	China	56	Septic shock	IVC-RVI	Yes	/	Lactated Ringer's solution	30 mL/Kg	△CO ≥ 15 %	No
Li ting [42]	China	47	Septic shock	ΔIVC_1, ΔIVC_2	Yes	8 — 12 ml/kg	Compound sodium chloride solution	500 mL	PICCO △SV ≥ 15%	Yes
Hu bin [43]	China	92	Septic shock	IVC-RVI	Yes	/	Electrolyte balances salt solution	500 mL	TEE △SV ≥ 15 %	No
Gao shan [44]	China	27	Septic shock	d-IVC, c-IVC	Yes	6 — 10 ml/kg	Lactated Ringer's solution	7 mL/kg	PICCO △CI ≥ 15 %	Yes
Chen fanfan [50]	China	88	Traumatic shock	RVI	No	/	/	/	Shock or not	No
Piskin [57]	Turkey	72	Shock	△IVC	Yes	8 ml/kg	Passive leg raising	/	TEE △CI ≥ 15 %	No
Oliveira [61]	Brail	20	Shock	△IVC	Yes	8 ml/kg	0.9 %sodium chloride	500 ml	TTE △VTI > 10 %	No
Preau [53]	France	90	Shock	△IVC	No	/	4 %succinylated gelatin	500 ml	TTE △STI > 10 %	No
Airapetian [54]	France	59	Shock	△IVC	No	/	Passive leg raising	/	Agilent △CO > 10 %	Yes
Corl [58]	American	124	Shock	△IVC	No	/	0.9 %sodium chloride	500 ml	NICOM △CI > 10 %	No
Theerawit [59]	Thailand	29	Septic shock	△IVC	Yes	8 ml/kg	6 % hydroxyethyl starch	500 ml	ViGILEO △CO > 10 %	Yes
Aboelnile [60]	Egypt	88	Shock	△IVC	Yes	8 ml/kg	Passive leg raising	/	TTE △CI ≥ 15 %	No
Barbier [55]	France	20	Septic shock	△IVC	Yes	8 ml/kg	4 % succinylated gelatin	7 ml/kg	TTE △CI ≥ 15 %	No
Muller [56]	France	40	Shock	△IVC	No	/	6 % hydroxyethyl starch	500 ml	TTE △VTI ≥ 15 %	No
Bo Yao [45]	China	67	Shock	△IVC	Yes	< 8ml/kg	Passive leg raising	/	CNAP △CI ≥ 10 %	No
Wang huijuan [46]	China	40	Septic shock	△IVC	Yes	10 ml/kg	6 % hydroxyethyl starch	500 ml	PICCO △CI ≥ 10 %	Yes
Xing yanbin [47]	China	86	Septic shock	△IVC	Yes	10 ml/kg	Compound sodium chloride solution	500 mL	PICCO △CI ≥ 10 %	Yes
Zhu weihua [48]	China	58	Septic shock	△IVC	Yes	/	6 % hydroxyethyl starch	500 ml	PICCO △CI ≥ 10 %	Yes
Tang hailian [49]	China	47	Septic shock	△IVC	Yes	8–12 ml/kg	0.9 %sodium chloride	200 ml	PICCO △SVV ≥ 15 %	Yes

Wer

C

: A systematic
r 8;89:104015.
spontaneously
19;47(2):90–8.

- A 2025 meta-analysis that included both ventilated (majority ventilated with 8-10mL/Kg Vt) and spontaneously breathing patients found the sensitivity and specificity of dynamic IVC parameters to be about 0.82 each

Table 2 Data extracted from included studies assessing accuracy of IVCc as a predictor of fluid responsiveness.

Author and year	*N*	Fluid responders	IVCc cut-off	IVCc – responders	IVCc – non responders	Sensitivity	Specificity	AUC (95% CI)
Mcgregor, 2020	30	63.3%	>40%	NA	NA	47%	63%	0.46 (0.26–0.67)
Corl, 2019	85	52%	>25%	38.2%	12.9%	86%	78%	0.82 (0.74–0.88)
Bortolotti, 2018	55	53%	>37%	49%	11%	66%	85%	0.82 (0.70–0.93)
Corl, 2017	124	49.2%	>25%	NA	NA	87%	81%	0.84 (0.76–0.81)
Preau, 2017	90	55%	>31%	47%	14%	76%	88%	0.82 (0.73–0.91)
Airapetian, 2015	59	49%	>42%	35%	27%	31%	97%	0.62 (0.49–0.74)
Lanspa, 2013	14	35%	>15%	52%	11%	100%	66%	0.83 (0.58–1.00)
Muller, 2012	40	50%	>40%	64%	19%	70%	80%	0.77 (0.60–0.88)

Legend – IVCc: inferior vena cava collapsibility; AUC: *area under curve*; 95% CI: 95% confidence interval; NA: not available.

Wenwen Y, Ping X, Yue D, Xuan L. Accuracy of indices of inferior vena cava in predicting fluid responsiveness in patients with shock: A systematic review and meta-analysis. Intensive and Critical Care Nursing [Internet]. 2025 Apr 8;89:104015.
Cardozo Júnior LCM, Lemos GSD, Besen BAMP. Fluid responsiveness assessment using inferior vena cava collapsibility among spontaneously breathing patients: Systematic review and meta-analysis. Medicina Intensiva (English Edition) [Internet]. 2022 Oct 19;47(2):90–8.

SVCCI for fluid responsiveness

- SVC collapsibility index is defined as {(SVCmax-SVCmin)/SVCmax} X 100
- Usually measured through TEE which requires expertise and has higher rate of complications
- Measured with patient at semi-recumbent posture, at the parasternal region, between 2nd and 4th ICS
- At a cut off value of 19%, sensitivity 0.93 and specificity 0.75
- 15% patients was found to be in the “grey zone”

Ma Q, Ji J, Shi X, Lu Z, Xu L, Hao J, et al. Clinical validation of superior vena cava respiratory variation in predicting fluid responsiveness using transthoracic echocardiography technique: a pilot study. Archives of Medical Science. 2022 Jun 23;18(4):1118–22.

SVCCI for fluid responsiveness

- Useful in patient of abdominal distension not allowing good view of IVC, or post-op patients of abdominal surgery
- Requires skilled operator
- All shortcomings of assessing TTE remain (obesity, emphysema, poor window)

Ma Q, Ji J, Shi X, Lu Z, Xu L, Hao J, et al. Clinical validation of superior vena cava respiratory variation in predicting fluid responsiveness using transthoracic echocardiography technique: a pilot study. Archives of Medical Science. 2022 Jun 23;18(4):1118–22.

Assessment in special situations

- Prone position
- Pregnancy
- Obese patients
- Cardiac arrhythmia

Insufficient data exist for this patient group: for most studies, these patients are excluded

Assessment in prone position:

- COVID-19 pandemic posed the question of fluid assessment in prone position
- Prone positioning was required in those with severe ARDS (another challenge in fluid assessment)
- H-phenotype had lower compliance and required LTV and high PEEP- dynamic parameters became unreliable
- About 30% patients of COVID19 pneumonia developed circulatory shock
- About 12% had cardiogenic shock
- a group of patients also had right ventricular dysfunction- making dynamic assessment more difficult

Journal of Anesthesia (2020) 34:758–764

Prone position- what are reliable?

- In patients who are ventilated by high tidal volume PPV and SVV are good predictors of fluid responsiveness
- another pre-requisite: good respiratory system compliance
- In this group a PPV cut-off of 15% has a sensitivity of 1 and specificity of 0.80 for predicting fluid responsiveness
- SVV at a cut-off of 14% predicted fluid responsiveness with sensitivity of 94% and specificity of 80%

Biais M, Bernard O, Ha JC, Degryse C, Sztark F. Abilities of pulse pressure variations and stroke volume variations to predict fluid responsiveness in prone position during scoliosis surgery. British Journal of Anaesthesia. 2010 Apr;104(4):407–13.

Prone position- what are reliable?

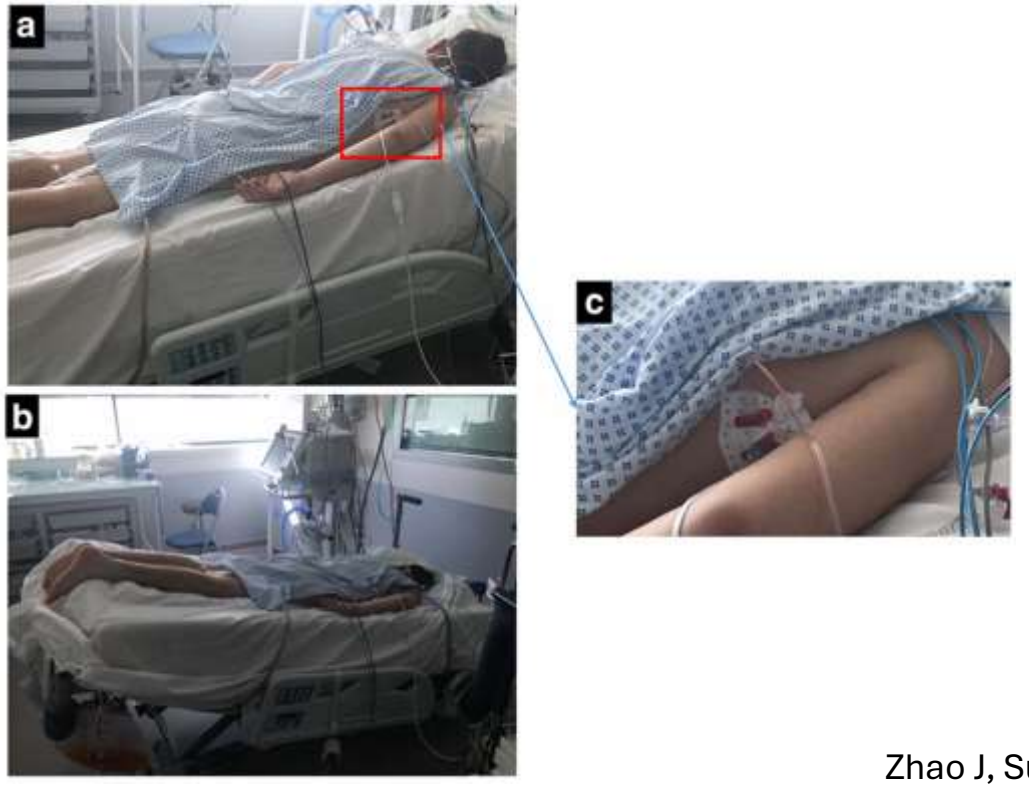
- During prone position with low tidal volume ventilation the predictive value of PPV falls
- An alternative can be Trendelenberg position
- Initially the patient is kept in a 13° head end-elevated position
- Then a 13° head-end depression is performed for 1 minute
- ΔCCI measured during this period with a cut-off of 8% can predict fluid responsiveness with sensitivity of 0.87 and specificity of 0.89
- Tidal volume challenge and EEOT are also not reliable in this patients

Yonis H, Bitker L, Aublanc M, Perinel Ragey S, Riad Z, Lissonde F, et al. Change in cardiac output during Trendelenburg maneuver is a reliable predictor of fluid responsiveness in patients with acute respiratory distress syndrome in the prone position under protective ventilation. Critical Care. 2017 Dec;21(1).

Prone position- what are reliable?

- During prone position with low tidal volume ventilation the predictive value of PPV falls
- Considering the difficulty in doing TTE in prone patients, and in cases where invasive monitoring is not possible, FTc and ΔVpeak derived from carotid doppler can be considered alternatively
- In patients ventilated with Vt <8mL/Kg they show predictive values comparable to ΔSVI
- FTc has sensitivity of 0.84 and specificity of 0.83 at cut-off of 331.5 ms
- ΔVpeak has sensitivity of 0.81 and specificity of 0.77 at 10.1% cut-off

Zhao J, Sun Y, Tang J, Guo K, Jiancheng Zhuge, Fang H. Predictive value of trendelenburg position and carotid ultrasound for fluid responsiveness in patients on VV-ECMO with acute respiratory distress syndrome in the prone position. Scientific Reports. 2024 Dec 30;14(1).



Variables	FTc	ΔV_{peak}
AUROC [95% CI]	0.866[0.755-0.977]	0.833[0.716-0.949]
P-value	<0.05	<0.05
Optimal cut-off value	<331.5ms	>10.1%
Grey zone	317.5-335ms	8.95-13.20%
Patients in grey zone (%)	15(29%)	23(45%)
Sensitivity (%) (95% CI)	84.85[0.691-0.934]	81.82[0.656-0.914]
Specificity (%)(95% CI)	83.33[0.608-0.942]	77.78[0.548-0.910]
PPV (%) (95%CI)	0.90[0.731-0.975]	0.82[0.639-0.924]
NPV (%) (95%CI)	0.75[0.506-0.904]	0.78[0.519-0.926]
Youden index	0.681	0.590

Zhao J, Sun Y, Tang J, Guo K, Jiancheng Zhuge, Fang H. Predictive value of trendelenburg position and carotid ultrasound for fluid responsiveness in patients on VV-ECMO with acute respiratory distress syndrome in the prone position. Scientific Reports. 2024 Dec 30;14(1).

Tests	Number of patients analyzed	AUC ($CI_{95\%}$)	Optimal threshold	Gray zone of optimal threshold	Patients in gray zone, (number (%))	Sensitivity ($CI_{95\%}$)	Specificity ($CI_{95\%}$)	PLR	NLR
ΔCCI_{TREND}	33	0.90* (0.80–1.00)	8%	(5–12%)	10 (30%)	87% (67–100%)	89% (72–100%)	7.90	0.15
$PPV_{BASELINE-1}$	19	0.49 (0.21–0.77)	10%	(–Inf to Inf)	19 (100%)	33% (0–67%)	80% (50–100%)	1.65	0.84
PPV_{VT8}	19	0.52 (0.24–0.80)	9%	(–Inf to Inf)	19 (100%)	78% (44–100%)	40% (10–70%)	1.30	0.56
ΔPPV_{6-8}	19	0.59 (0.31–0.88)	29%	(17%–Inf)	16 (84%)	100% (100–100%)	40% (10–70%)	1.67	0
ΔCCI_{EEO}	33	0.65 (0.46–0.84)	10%	(–4% to 11%)	26 (79%)	33% (13–60%)	100 (100–100%)	Inf	0.67

Yonis H, Bitker L, Aublanc M, Perinel Ragey S, Riad Z, Lissonde F, et al. Change in cardiac output during Trendelenburg maneuver is a reliable predictor of fluid responsiveness in patients with acute respiratory distress syndrome in the prone position under protective ventilation. Critical Care. 2017 Dec;21(1).

Cardiac power index

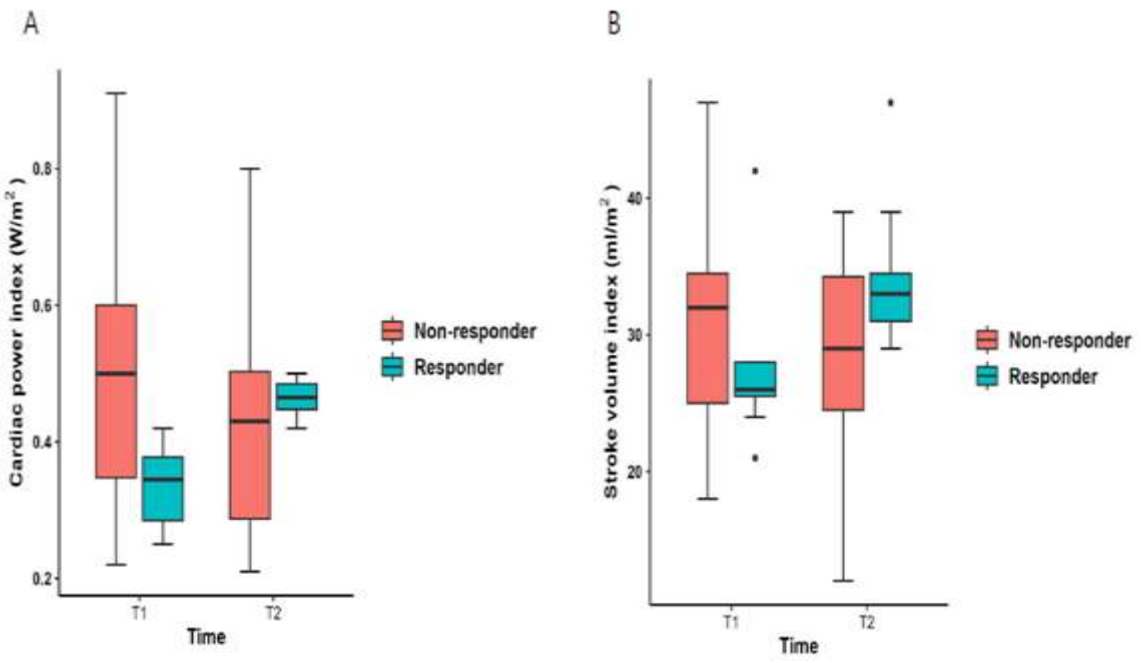
- Cardiac power index is a measure of work performed by heart
- Studies have shown that a lower value is associated with increased risk of mortality in heart failure patients

Cardiac power index= $\frac{cardiac\ power\ output}{BSA}$

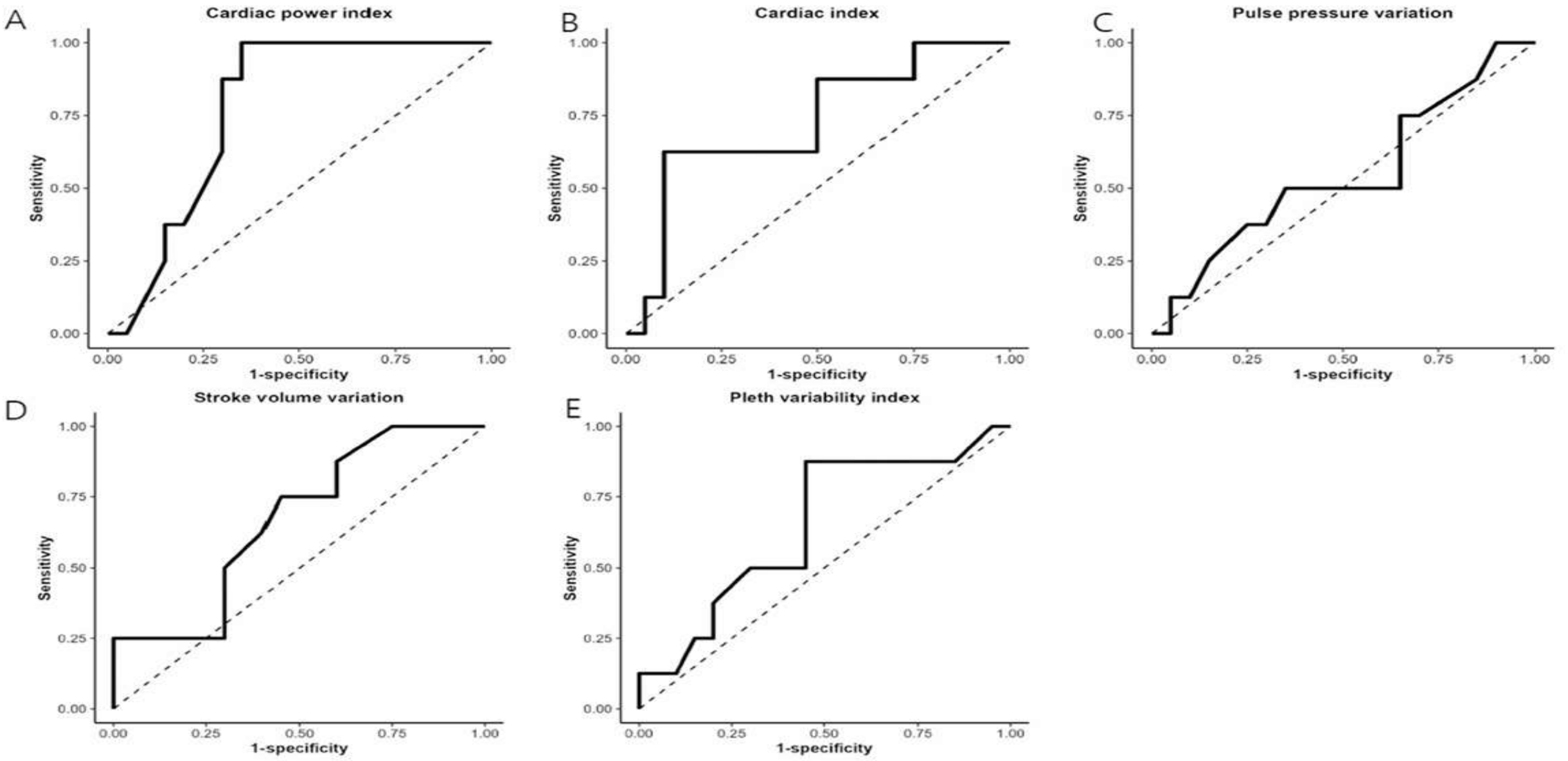
Cardiac power output=CO X MAP X 0.0022

*Eur J Heart Fail. 2015 Apr 28;17(7):689–696.

- A 2024 study hypothesized that changes in CPI may predict fluid responsiveness in prone patients when calculated through arterial pulse contour analysis
- The patients were ventilated with Vt-8mL/Kg
- With the cut-off value of ≤0.42 W/m^2, AUROC for CPI predicting fluid responsiveness was 0.78, with Sn-1 and Sp-0.65
- Only SVI and CPI were significantly correlated with fluid responsiveness while PPV and SVV correlated poorly



Min JY, Jeon JP, Chung MY, Kim CJ. Use of the cardiac power index to predict fluid responsiveness in the prone position: a proof-of-concept study. Brazilian Journal of Anesthesiology (English Edition) [Internet]. 2024 Aug 6;74(6):844545.



Min JY, Jeon JP, Chung MY, Kim CJ. Use of the cardiac power index to predict fluid responsiveness in the prone position: a proof-of-concept study. Brazilian Journal of Anesthesiology (English Edition) [Internet]. 2024 Aug 6;74(6):844545.

Assessment in pregnant patients

- Assessment of fluid responsiveness is difficult in pregnant patients
- Assessment of IVC may be erroneous due to the pressure of the uterus
- Assessment by PLR may not yield accurate results due to physiologically increased abdominal pressure
- Carotid artery blood flow distinguishes between fluid responders and non-responders with sensitivity-0.74 and specificity-0.78
- For CA-VTI , Sn-67%, Sp-90%

Assessment in pregnant patients

Table 3 Prediction of fluid responsiveness by receiver operating characteristic curves of the baseline VTI and CABF

	AUROC curve (95% CI)	*P*-value	Optimal cut-off value	Grey zone	Patients in grey zone (%)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	Youden index	PPV (%) (95%CI)	NPV (%) (95%CI)
VTI	0.821 (0.720–0.922)	0.0003	8.7 cm/s	6.8–8.7 cm/s	13(18%)	67.0(50.1–86.0)	90.0 (80.0-100.0)	0.577	0.84 (0.68-1.00)	0.79 (0.66–0.91)
CABF	0.803 (0.701–0.905)	0.0001	175.9 ml/min	114.2-175.9 ml/min	29(40%)	74.0(57.0–91.0)	78.0 (64.0–92.0)	0.520	0.72 (0.55–0.89)	0.67 (0.67–0.93)

Table 2 Hemodynamic variables before and after fluid challenge

	Responders group ($n=31$)		Non-responders group ($n=41$)		*P* value	*P* value
	Before	After	Before	After	Before	After
CABF (ml/min)	161.2 ± 50.4	317.3 ± 105.1*	236.4 ± 72.9#	321.7 ± 79.4*	0.0002	0.843
VTI (cm/s)	9.0 ± 2.9	15.8 ± 4.8*	13.1 ± 3.9#	16.4 ± 3.7*	0.0003	0.587
SVI (ml m^{-2})	61.7 ± 11.2	84.5 ± 16.0*	68.3 ± 13.2#	79.5 ± 16.4*	0.018	0.196
HR (beat min-1)	87.5 ± 14.3	88.2 ± 13.5	84.4 ± 11.7	83.2 ± 11.6	0.318	0.096
MAP (mmHg)	83.7 ± 7.5	89.3 ± 8.6	85.3 ± 14.9	90.8 ± 8.4	0.573	0.473

*$p < 0.05$ compared with before fluid challenge. #$p < 0.05$ compared with Responders group

Cardiogenic shock and fluid responsiveness:

- Cardiogenic shock has the highest mortality rates (42%) followed by septic shock (38%)
- Administration of fluid must be extremely judicious
- Pathophysiologically, those with RV dysfunction (RVMI) with IWMI should benefit from fluid due to preload dependence of LV

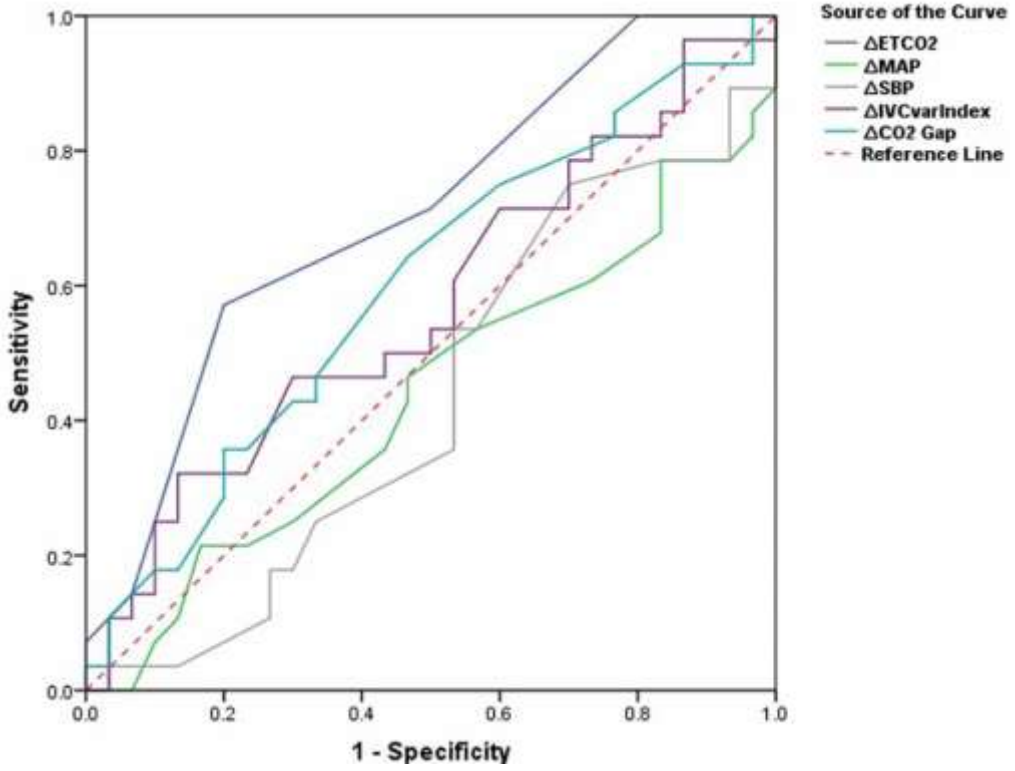
Current Problems in Cardiology 49 (2024) 102123

- A 2021 study evaluated 60 patients with cardiogenic shock for fluid responsiveness to compare predictive value of ΔETCO2, P(v-a)CO2 gap and IVCI against LVOT-VTI by TTE (>10% change- responder)
- PLR or 300 mL crystalloid bolus was the intervention (fluid bolus was given to those in whom PLR was contra-indicated)

	Fluid Responsiveness after PLR		P-value
	Non responders (ΔVTI≤10%)	Responders (ΔVTI>10%)	
Total (N)	31	29	-
Ejection fraction (EF)			
≤ 25%	58.1% (18)	51.7% (15)	0.622
> 25%	41.9% (13)	48.3% (14)	
Myocardial infarction			
STEMI	54.8% (17)	65.5% (19)	0.399
Anterior Wall MI	70.6% (12)	36.8% (7)	0.041*
Inferior Wall MI	0% (0)	36.8% (7)	
Inferior Posterior Wall MI	11.8% (2)	10.5% (2)	
Antero Inferior Wall MI	5.9% (1)	10.5% (2)	
High Lateral Wall MI	11.8% (2)	0% (0)	
Infero-Lateral Wall MI	0% (0)	5.3% (1)	
NSTEMI	41.9% (13)	31% (9)	0.381
Non-ICMP	3.2% (1)	3.4% (1)	0.962

Baloch K, Rehman Memon A, Ikhlaq U, et al. (February 05, 2021) Assessing the Utility of End-Tidal Carbon Dioxide as a Marker for Fluid Responsiveness in Cardiogenic Shock. Cureus 13(2): e13164. DOI 10.7759/cureus.13164

- About 50% of total patients were fluid responsive
- Among non-responders there was 0 IWMI and IWMI+LWMI patients: all of these patients were fluid-responders (as per PLR/fluid bolus)
- They found ΔETCO2≥2 can identify fluid responders with an accuracy of 70%, Sn-58.6% and Sp-80.7% (against LVOT-VTI)
- Did not comment on outcome of these patients



- A 2021 observational study evaluated elderly 71 patients (60 were analyzed) in cardiogenic shock in terms of conventional management Vs management directed by PiCCO-derived parameters
- The control group received PCI or thrombolysis, along with fluid guided by CVP, vasopressors and/or inotrops based on TTE-derived VTI, vasodilators and diuretics based on clinical features
- The intervention group received fluid, vasopressors, diuretics and vasodilators depending upon the values of CI, GEDVI and EVLWI derived from PiCCO (TPTD)

Zhang YB, Zhang ZZ, Li JX, Wang YH, Zhang WL, Tian XL, Han YF, Yang M, Liu Y. Application of pulse index continuous cardiac output system in elderly patients with acute myocardial infarction complicated by cardiogenic shock: A prospective randomized study. World J Clin Cases 2019; 7(11): 1291-1301

CI (L/min/m2)	GEDVI (mL/m2)	EVLWI (mL/kg)	Intervention
<3	<680	<3	Fluid
<3	680-800	<3	Vasoactive drugs
<3	>800	>3	Vasoactive drug+diuretics
>3	>800	>3	Diuretics
>3	680-800	<3	Clinical monitoring

Target: CI-3-5 L/min/m2, GEDVI- 680-800 mL/m2, EVLWI <3 mL/kg

- The study showed that PiCCO-guided management caused significantly larger drop in values of APACHEII score, SOFA score, hs-TNI and NT-proBNP values
- Oxygentaion index and lactate levels showed significant difference after 7 days of treatment
- PiCCO group showed significantly higher ADL scores and significantly shorter time on vasoactive drugs, shorter ICU length of stay and lesser days on mechanical ventilation
- Incidence of pulmonary oedema was similar among two groups

Group	No.	Treatment time	APACHE II score	SOFA score	Hs-TnI (ng/mL)	NT-proBNP (pg/ml)	PaO_2/FiO_2 (mmHg)	Lac (mmol/L)
Control group	30	1 d	25.03 ± 7.35	11.31 ± 3.57	0.54 ± 0.33	13781.31 ± 9508.70	260.32 ± 111.50	2.41 ± 1.17
		3 d	22.00 ± 5.61	9.00 ± 3.39	0.40 ± 0.35	11537.69 ± 9701.62	294.94 ± 102.80	2.30 ± 1.03
		7 d	17.57 ± 4.89	7.09 ± 3.34	0.33 ± 0.28	9083.04 ± 7702.01	341.10 ± 98.05	1.99 ± 0.70
PiCCO Group	30	1 d	21.10 ± 5.95[a]	8.37 ± 3.44[b]	0.34 ± 0.25[a]	8947.00 ± 5739.86[a]	284.05 ± 127.06	2.15 ± 1.13
		3 d	17.52 ± 4.88[b]	6.38 ± 3.05[b]	0.17 ± 0.24[b]	7294.83 ± 3638.23[a]	346.96 ± 108.39	1.80 ± 0.95
		7 d	11.89 ± 3.38[b]	4.07 ± 2.02[b]	0.11 ± 0.14[b]	5939.14 ± 2396.84[a]	395.36 ± 88.20[a]	1.52 ± 0.74[a]

Group	No.	Time frame	Infusion volume in mL	Urine volume in mL
Control group	30	0-1 d	2673.52 ± 945.22	1895.28 ± 717.58
		1-2 d	2806.61 ± 724.07	2111.75 ± 684.02
		2-3 d	2643.42 ± 674.59	2199.85 ± 666.83
PiCCO group	30	0-24 h	3201.07 ± 967.64[a]	2492.67 ± 868.05[b]
		24-48 h	3162.48 ± 770.95	2363.10 ± 755.36
		48-72 h	2842.76 ± 765.30	2502.76 ± 728.34

	PiCCO group, $n = 30$	Control group, $n = 30$	P value
Primary outcome			
ADL score	66.83 ± 14.65	11.33 ± 5.71	0.000
Secondary outcomes			
Days on vasoactive agents	10.04 ± 2.52	12.09 ± 3.16	0.013
Duration of mechanical ventilation in d	8.13 ± 1.51	10.81 ± 2.10	0.000
Days on MV	9.21 ± 4.40	12.39 ± 4.14	0.011
EICU/CCU length of stay	12.57 ± 2.78	14.83 ± 2.59	0.005
Pulmonary edema	18 (60%)	21 (70%)	0.589

- Mortality benefit from fluid administration in cardiogenic shock still unfounded
- Individualised approach is preferred
- Patients in cardiogenic shock are fluid-responsive in almost half the cases
- A subgroup of these patients may benefit from fluid resuscitation

Haemodynamic monitor tools in use

Method	Type	Requirements	Advantages	Disadvantages
Pulmonary artery catheter (Fick's dye dilution method)	Invasive	Pulmonary artery catheter	Accurate (gold standard) Continuous monitoring	Complication rates high
PAC with thermodilution	Invasive	Pulmonary artery catheter	Accurate	Complications of catheter tip in RV
Li-indicator (LidCo) dilution method (pulse power analysis)	Minimally invasive	Central venous access, arterial cannula	Good correlation with PAC	Needs calibration 8 hourly, can not be used in patients on Li, and on NMB
Pulse contour analysis-PICCO (PCA+TPTD)	Minimally invasive	Central venous access, arterial cannula	Good correlation with PAC; Additionally gives PPV, SVV, EVLW, GEDV, ITBV	Needs calibration 8 hourly/during haemodynamic instability
Pulse contour analysis-Flotrac	Minimally invasive	Arterial cannula	Same Does not require external calibration	Not reliable in arrhythmia
Volume view (PCA+TPTD)	Minimally invasive	Arterial cannula and central venous access	Same	Same

Mehta Y et al. Cardiac output monitoring (2014)

Method	Type	Requirements	Advantages	Disadvantages
Oesophageal doppler (measure flow in descending thoracic aorta)	Minimally invasive	Oesophageal catheter with transducer tip in mid-oesopagus	Measures CO/CI/VTI without any vascular puncture	Measures only 70% of flow, requires correction factor; aortic coarctation causes error in measurement;
TEE	Minimally invasive	Transoesophageal echo probe	Accurate measurement	Requires skilled personnel, can not monitor continuously
TTE	Non-invasive	2d echo machine	Accurate measurement	Requires skilled operator, can not be continuous, difficult if echo window is poor
Partial gas rebreathing (NICO)	Non-invasive	Endotracheal intubation, steady state of ventilation, infrared CO2 sensor	Non-invasive	Not accurate in comparative studies with PAC
Thoracic bioimpedance	Non-invasive	electrodes (6)/sensors	Non-invasive Good accuracy in intra-op patients	Not validated in critically ill; affected by arrhythmia, small mistakes in lead placement
Thoracic bioreactance (Baxter, Cheetah medical)	Non-invasive	Electrodes, monitor	Good accuracy in patients with minimal movement	Patient movement interferes with measurement

Mehta Y et al. Cardiac output monitoring (2014)

Haemodynamic monitor tools in RICU

- **PICCO** (uses Stewert-Hamilton equation, requires external calibration)
- **Flotrac** (beat to beat analysis of pulse contour)
- **Philips** intellivue monitor (uses integration of systolic waveform, but uses demographic data to correct for aortic compliance)
- **VolumeView** (uses downslope time for CO estimation)
- Non-invasive- volume clamp, applanation tonometry
- NICCOM (bioreactance, Baxter-Starling, Cheetah medical)
- Transthoracic echocardiography

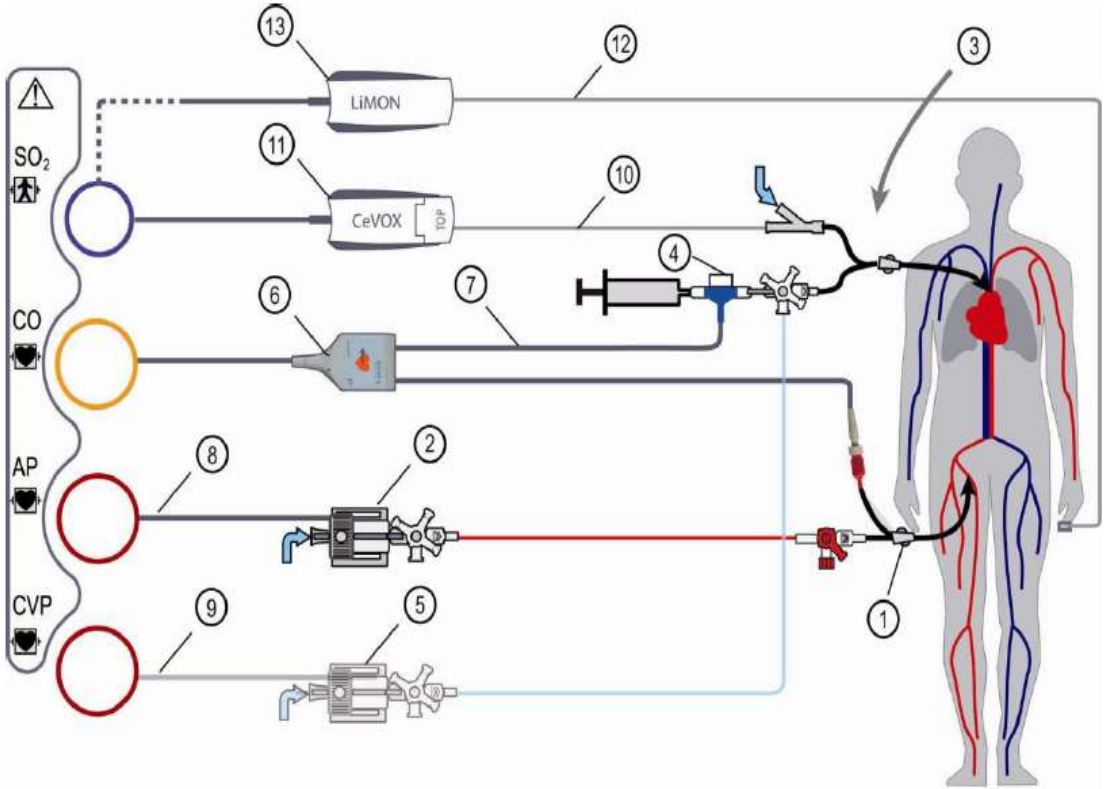
- Gold standard for measurement of cardiac output has been dye-dilution/thermodilution by pulmonary artery catheter
- Catheter-related complications high restricting use of pulmonary artery catheter
- CO measured by transpulmonary thermodilution as measured by PiCCO system correlate significantly with CO measured by PAC
- Flotrac uses pulse contour analysis for determining CO and has poor reliability for measuring absolute CO (in septic shock patients) in comparison to PiCCO, but it can track changes in CO reliably (after change in vasopressor dose and fluid bolus)

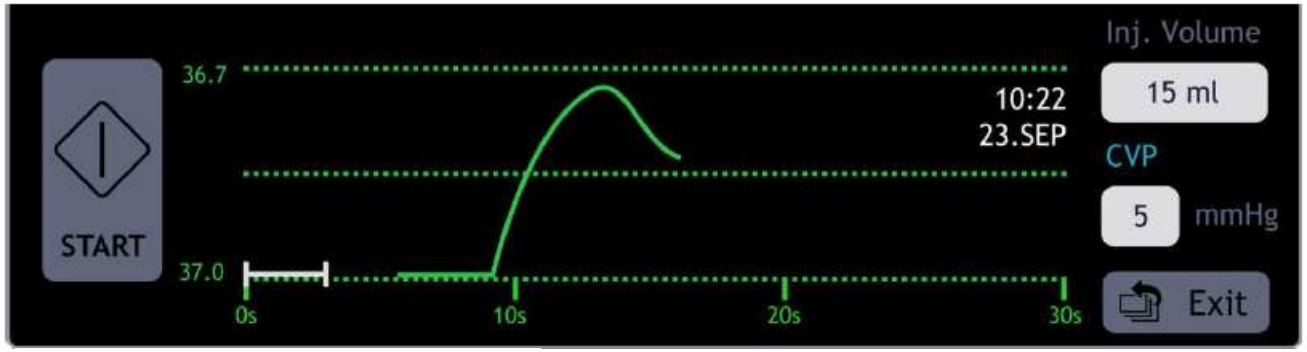
KHWANNIMIT B, JOMSURIYA R. Comparison the accuracy and trending ability of cardiac index measured by the fourth-generation of FloTrac with the PiCCO device in septic shock patients. TURKISH JOURNAL OF MEDICAL SCIENCES. 2020 Jun 23;50(4):860–9.

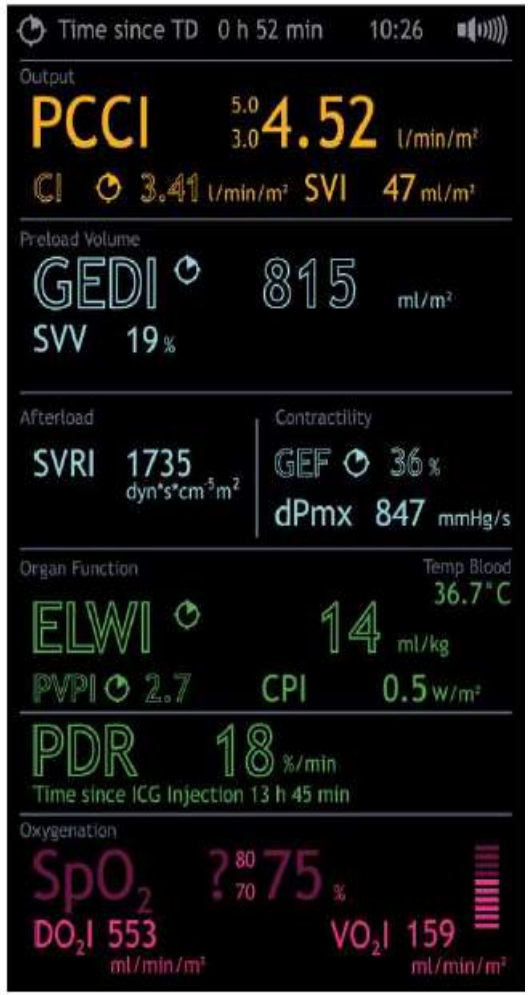
PiCCO

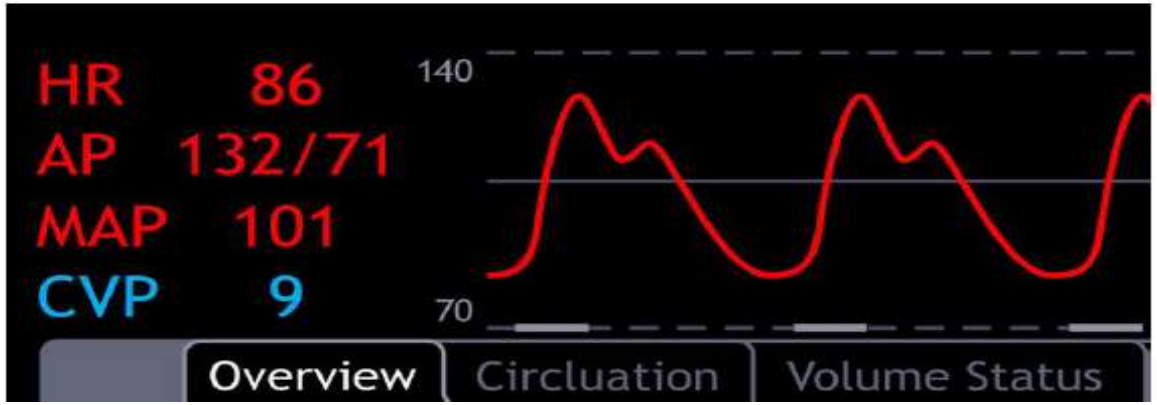
- Requires insertion of a central venous catheter and a thermistor-tipped arterial cannula in a large artery (preferably in femoral artery)
- Uses both thermodilution and pulse contour analysis to determine CO
- In a patient with stable haemodynamics, 8 hourly thermodilution is needed for external calibration (5 measurements over a 10-minute span)- more frequently if haemodynamic state changes
- A 10-15 ml of 0.9 NS at room temperature (or 8°C) is used for generating a thermodilution curve which is used for determination of CO
- Continuous CO, CI, MAP, SV, PPV, SVV are displayed
- Additional parameters displayed- GEDV, GEDVI,GEF, EVLWI, PVPI

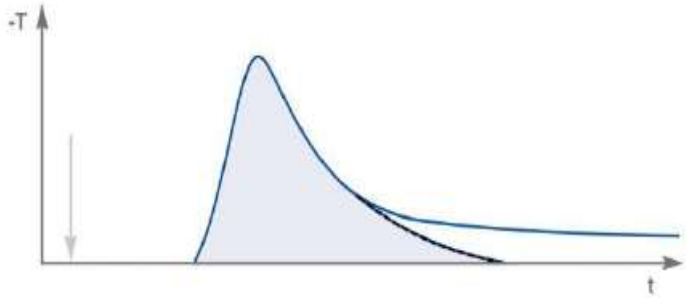
PiCCO











Thermodilution curve

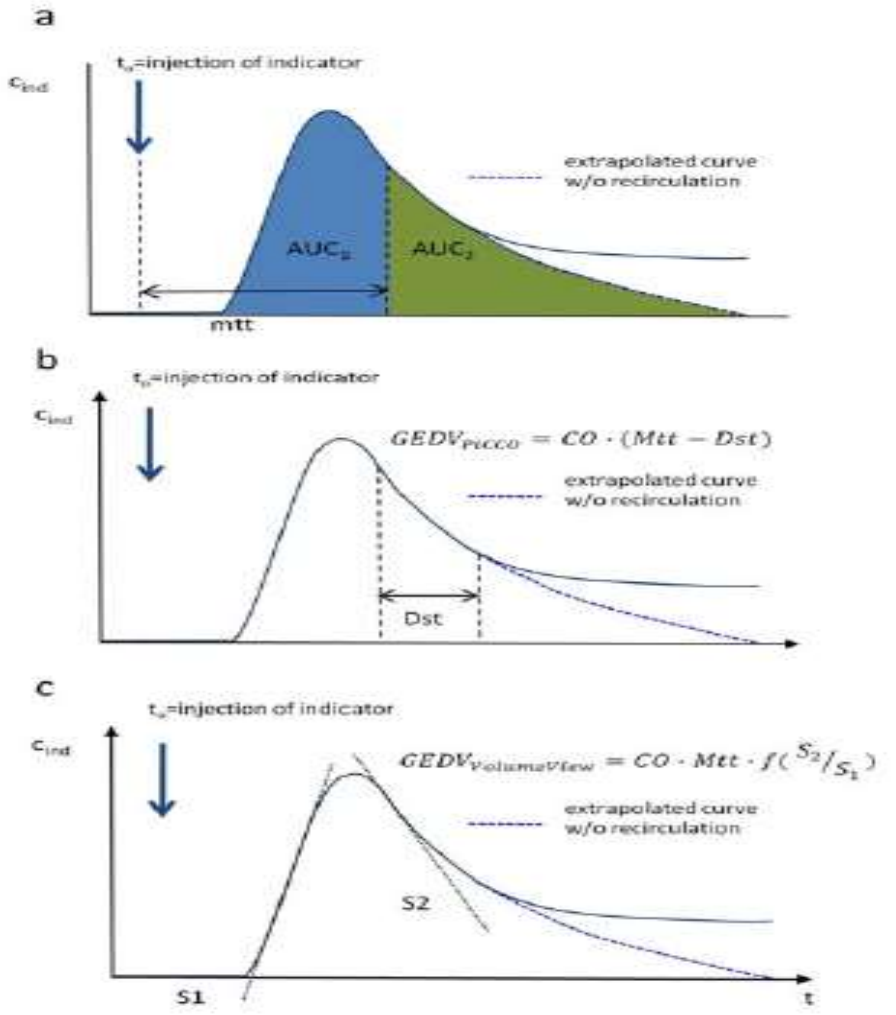


Figure 1 Mathematical analysis of the thermodilution curve. Panel **a**) Both algorithms rely on mean transit time (Mtt), the time required for half of the indicator to pass the thermistor in the femoral artery. Mtt divides the area under the curve (AUC) into two areas of the same size (AUC_1 and AUC_2). Panel **b**) Downslope time (Dst) is part of the PiCCO™ GEDV algorithm. It is the time of the temperature decay between two set points in the thermodilution curve, for example, 80% to 40%. Theoretically, the decay is mono-exponential, so it can be measured at any time point after the peak and be adjusted by a constant factor. Panel **c**) The VolumeView™ algorithm relies on maximum up-slope (S_1) and maximum down-slope (S_2) of the dilution curve. This approach may be less sensitive to early recirculation and thermal noise.

$$CO_{TD} = \frac{V_i \cdot (T_{blood} - T_{injectate}) \cdot k}{\int \Delta T_{blood} \cdot dt}$$

Stewert-Hamilton equation

k= constant proportional to the specific heat and density of blood and injectate

$$GEDV_{PiCCO} = CO \cdot (Mtt - Dst)$$

$$GEDV_{VolumeView} = CO \cdot Mtt \cdot f(S_1/S_2)$$

f= proprietary function

$$EVLW_{PiCCO} = CO \cdot Dst - (0.25 \cdot GEDV_{PiCCO})$$

$$EVLW_{VolumeView} = CO \cdot Dst - (0.25 \cdot GEDV_{VolumeView})$$

The methods used by PiCCO and VolumeView have shown to produce CO values that are in good agreement

Kiefer et al. Critical Care 2012, 16:R98

Pulse contour analysis

Flotrac

Cardiac output (CO)= PR X $(\sigma * \chi)$

σ = SD of arterial pulse pressure (proportional to PP) (measured 100 times/sec, for 20 secs)

X= a **multivariate polynomial equation** which assesses the impact of the patient's ever-changing **vascular tone on pulse pressure**.

- X is calculated by analyzing the patient's **PR**, **MAP**, **SD** of MAP, large-vessel **compliance** as estimated by patient demographics, and **skewness** and **kurtosis** of the arterial waveform.
- Updated and applied to the FloTrac algorithm on a rolling 60-second average

- Measurement of kurtosis and skewness allows compensation for changes in variables **at different locations** (radial, femoral, brachial) so that pressure won't vary at different sites
- χ is calculated every **60** seconds
- Flotrac 4.0 incorporates new physiological factors to account for change in **SVR** due to vasopressors, septic shock, vasodilatation in liver failure

$$C(P)=L \bullet \frac{\frac{A_{max}}{\pi \bullet P_1}}{1+\left(\frac{P-P_0}{P_1}\right)^2}$$

Edwards

L = estimated aortic length

Amax = aortic root cross sectional area maximum

P = arterial pressure

P_0 = pressure at which compliance reaches its maximum

P_1 = the width of compliance curve at half of maximum compliance; additional measures of weight and height (BSA) were also found to correlate with vascular tone and were added to enhance the calculation of aortic compliance

Pulse contour analysis by Flotrac

Remember when setting up

- Set pressure at pressure-infusion-bag at 300 mm Hg
- Make the PM line air-free
- Use square-wave test (fast-flush)
- Level the sensors to Phlebostatic axis (intersection of 4th ICS and mid-point of AP diameter)
- Zero with atmospheric pressure

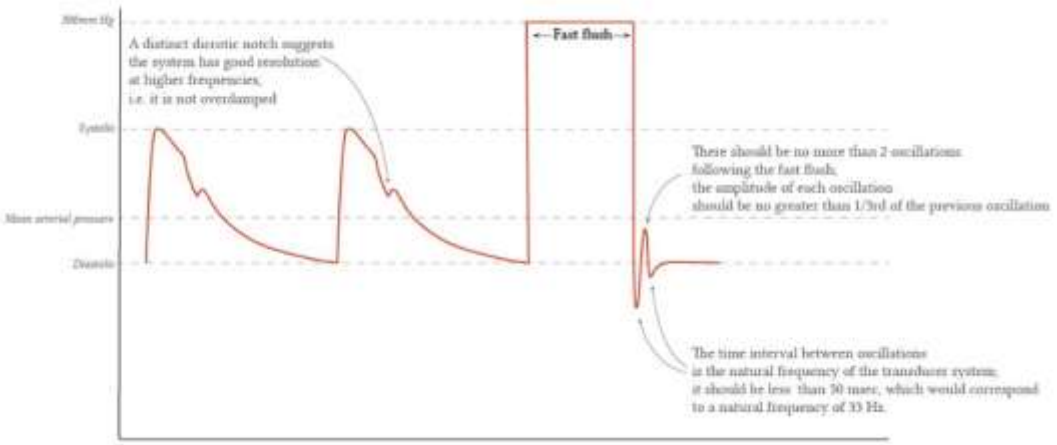
Advantages

- No external calibration
- No central venous catheter mandatorily needed
- Good agreement with PAC-CO
- Good for CO-trending

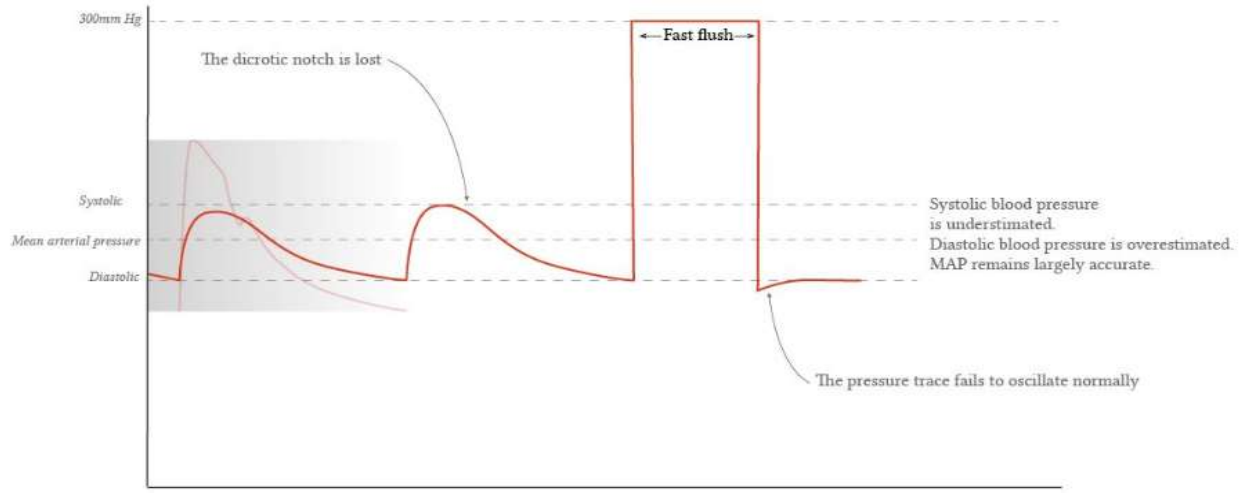
Disadvantages

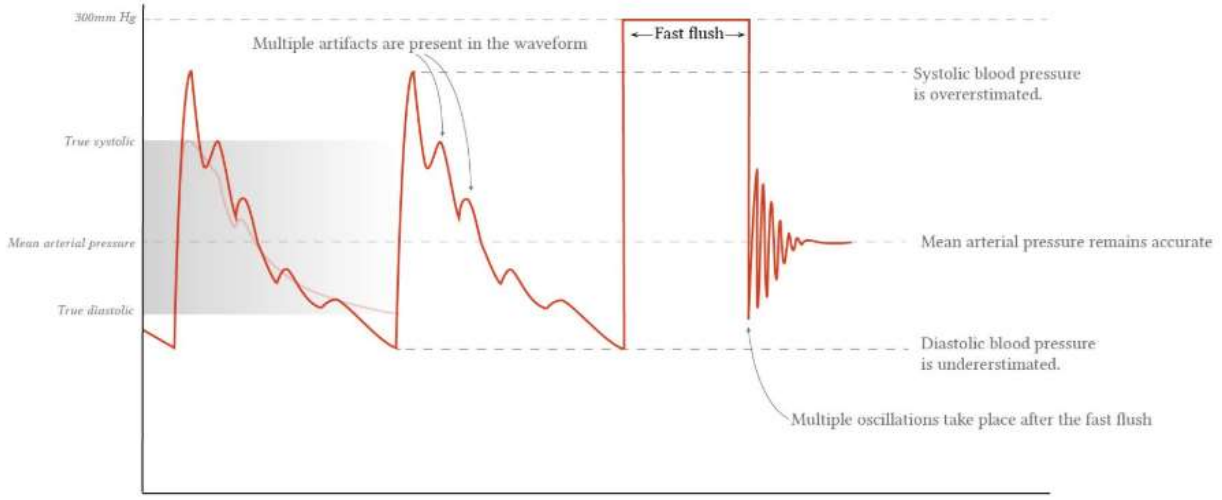
- Not reliable in severe septic shock, liver failure (wide changes in SVR)
- Only counts perfused beats (unreliable during AF, IABP)

Pulse contour analysis by Flotrac: fast-flush test



Normal: only two oscillations after fast-flush with dicrotic notch and appropriate distance





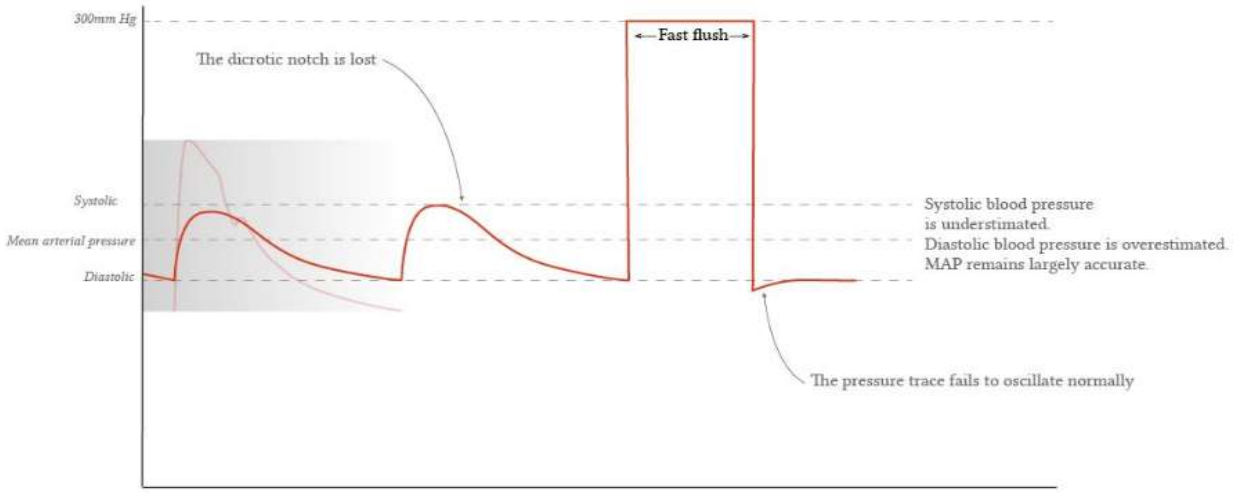
Pulse contour analysis by Flotrac

The time between oscillations will be short. the natural frequency of the system: <20-30 msec

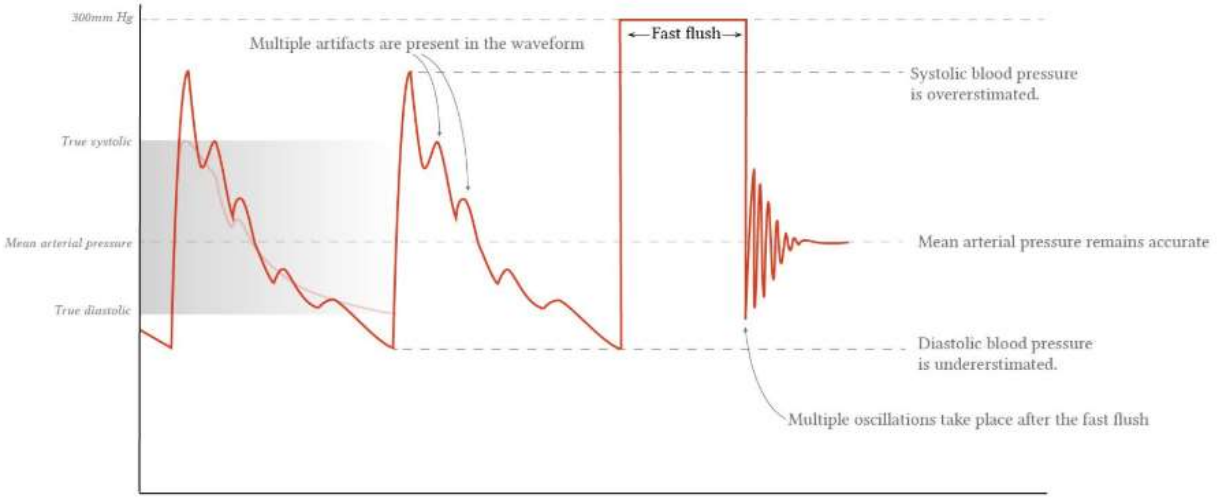
There should be at least one "bounce" oscillation. (If no oscillation, there is too much damping.)

There should be no more than two oscillations. (too much oscillation=under-damping)

There should be a distinct dicrotic notch.
(If the arterial line is progressively becoming more and more damped, the dicrotic notch is the first feature to disappear.)

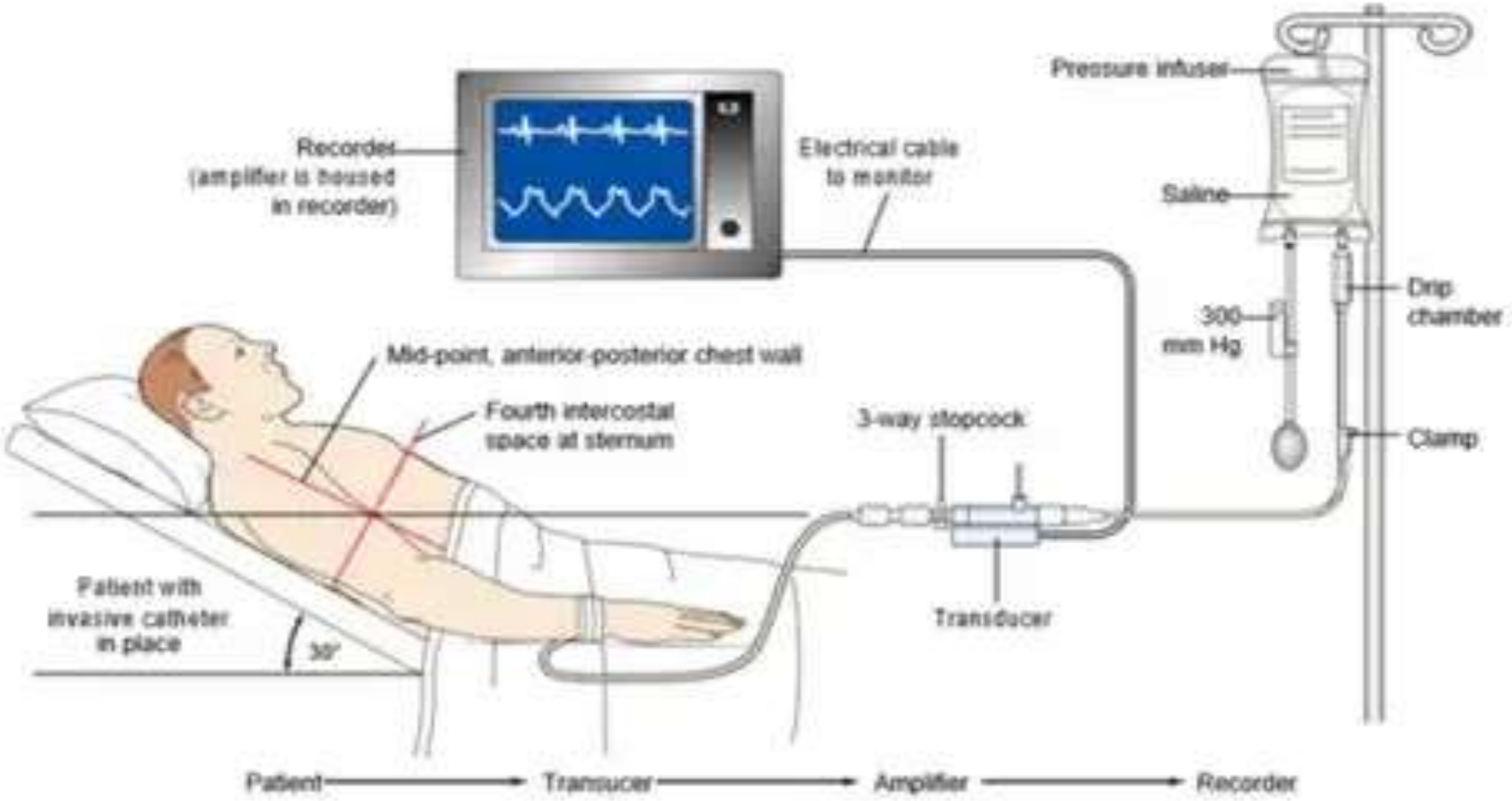


Over-damping: rule out clot at cath tip/bubble



Under-damping

Pulse contour analysis by Flotrac: phlebostatic axis



Pulse contour analysis by Philips monitor (model M10212A)

$$\mathrm{CIp} = \mathrm{cal} \times \mathrm{HR} \times \times \mathrm{dt} \int systole \left(\frac{\mathrm{P(t)}}{\mathrm{SVR}} + \mathrm{C(p)} \times \frac{\mathrm{dP}}{\mathrm{dt}} \right)$$

Ideally requires thermodilution to determine the patient-specific calibration factor

Advantage: uses the whole systolic waveform, less prone to changes in vascular compliance (septic shock, vasoplegia)
Disadvantage: in absence of TPTD, uses demographic data to correct for aortic compliance

CIp= cardiac output measured by the monitor

Cal= patient specific calibration factor

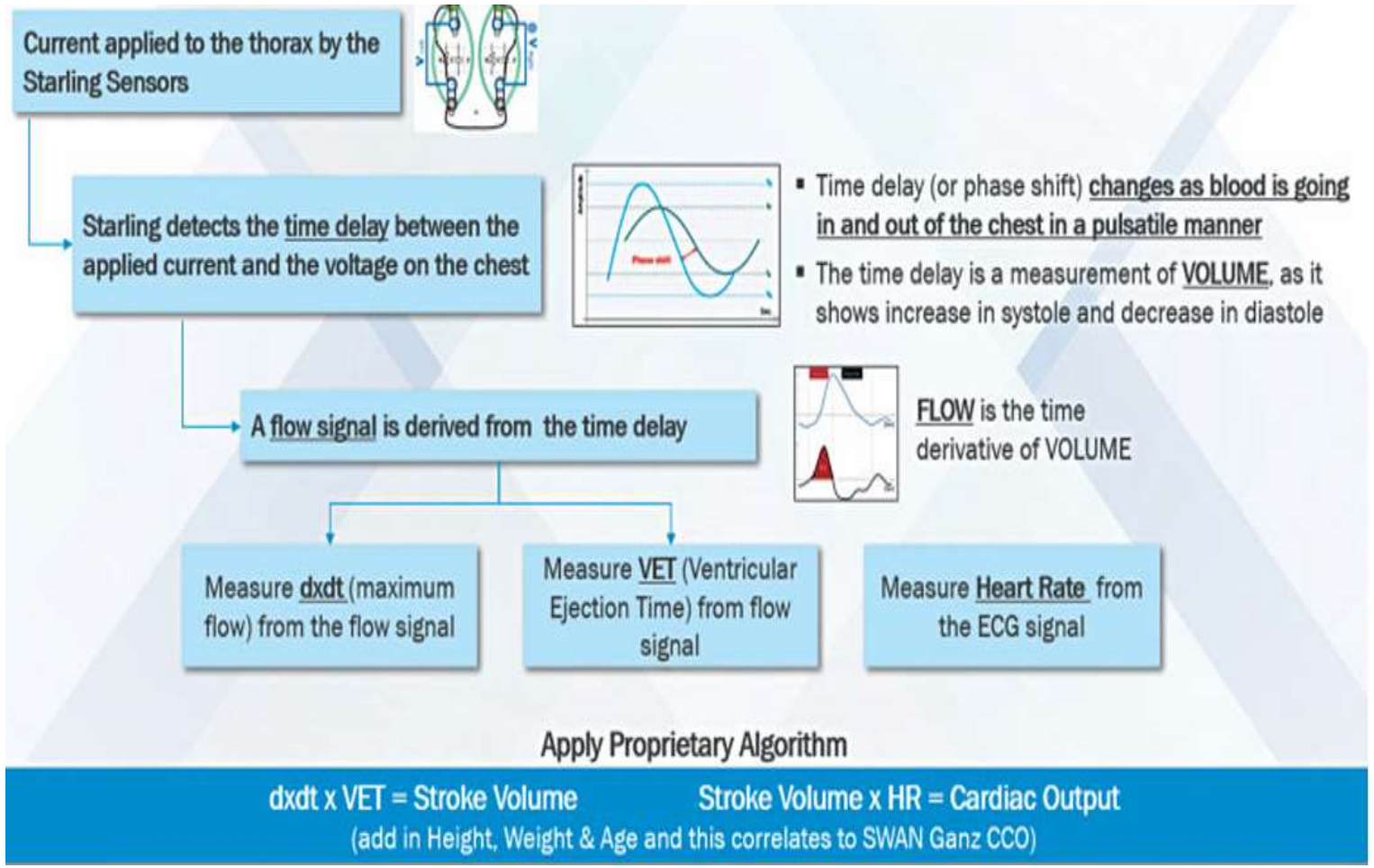
$\frac{P(t)}{SVR} =$ Area under pressure curve

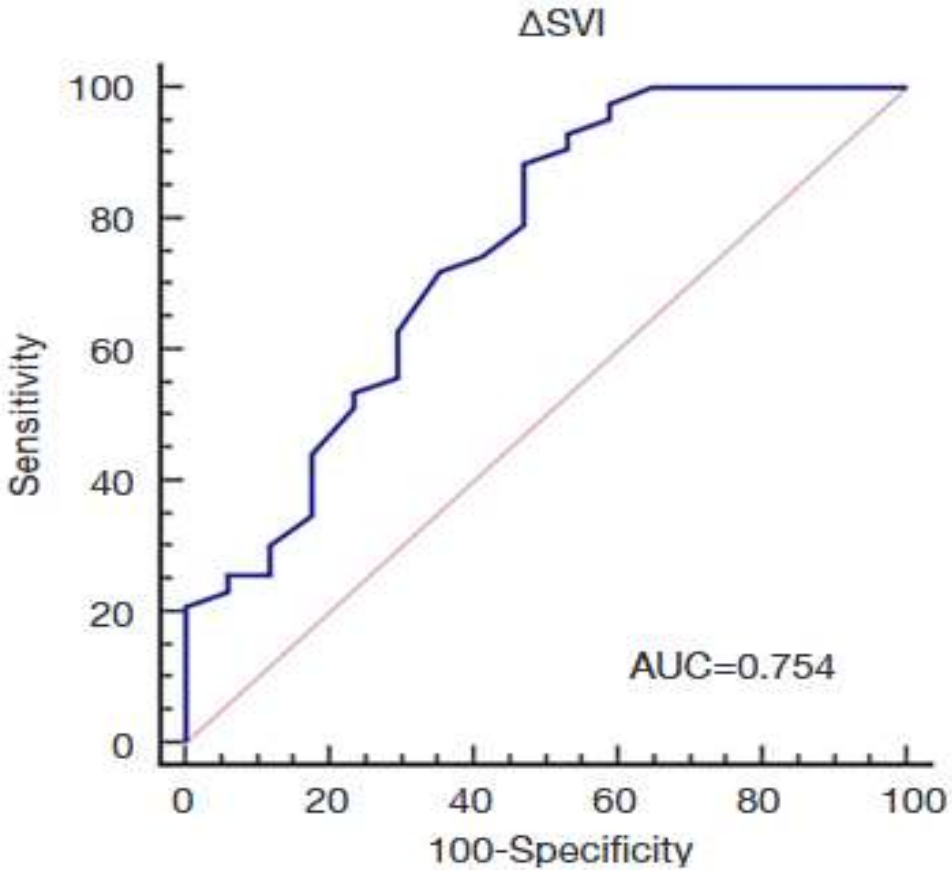
C(p)= Compliance

$\frac{dP}{dt} =$ Shape of pressure curve

- NICCOM uses the principles of bioreactance to determine CO, CI, SVI and incorporates a built-in PLR (or fluid bolus) maneuver
- 4 sensors are placed over thorax (each side, one above the heart and the other below it) and each sensor is equipped with transmitter and receiver
- The receivers detect the rhythmic phase shift (time delay) of delivered current in comparison to received current which is proportional to blood moving in or out of the thorax
- It is not affected by fluid in thorax (pulmonary oedema, pneumonia) (advantage over bio-impedance)
- In septic shock patients, at a cut-off of ΔSVI>18% it has a sensitivity of 0.88 and specificity of 0.52 for detecting fluid responsiveness (when measured after in-built PLR maneuver)

Zhu G, Zhang K, Fu Y, Hu Z. Accuracy assessment of noninvasive cardiac output monitoring in the hemodynamic monitoring in critically ill patients. Annals of Palliative Medicine. 2020 Sep;9(5):3506–12.



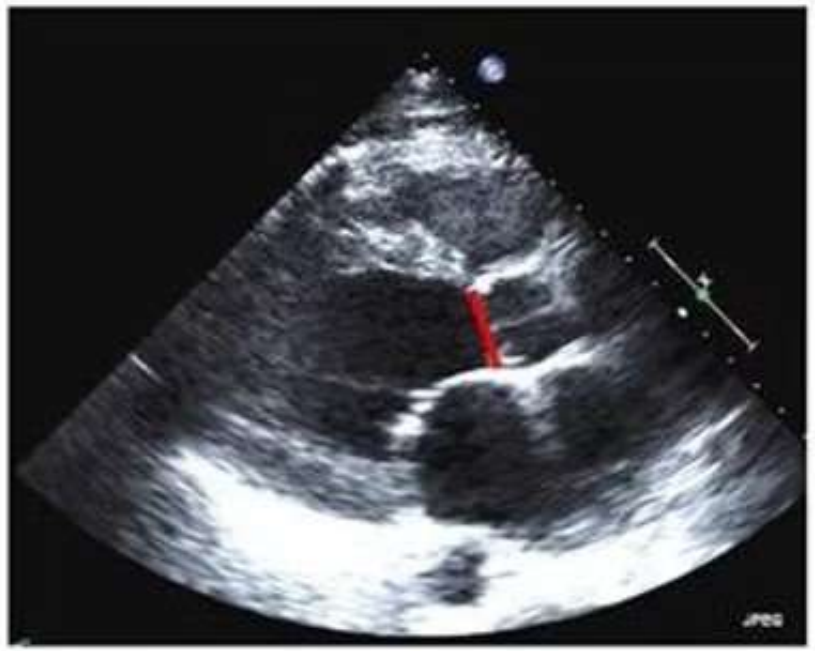


Zhu G, Zhang K, Fu Y, Hu Z. Accuracy assessment of noninvasive cardiac output monitoring in the hemodynamic monitoring in critically ill patients. Annals of Palliative Medicine. 2020 Sep;9(5):3506–12.

Cardiac output by LVOT-VTI

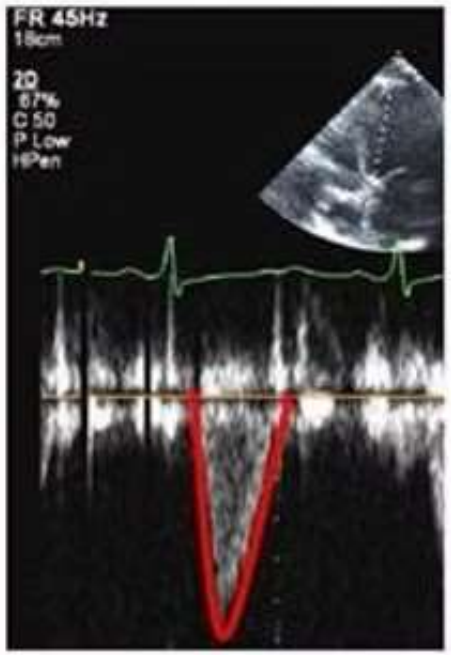
- Obtain Parasternal long axis view- calculate aortic diameter
- Obtain apical 5 chamber view
- Identify the flow from LV into aorta
- Use doppler to measure the velocity-time-integral through aorta
- CO= SV X HR
- SV=VTI X area of aortic opening (area= 3.14 X square of diameter/4)

PLAX Systole



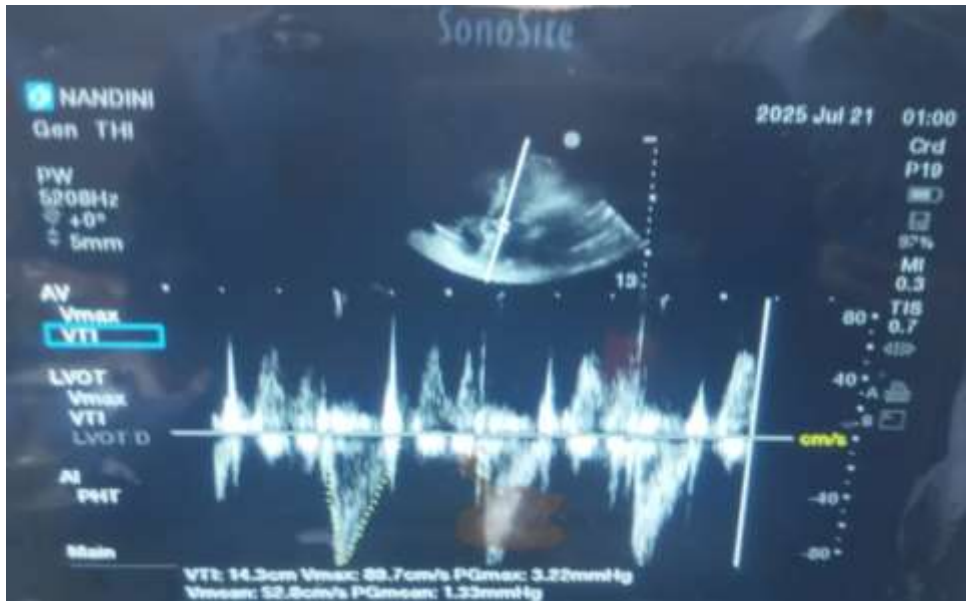
LVOT diameter = 2.0 cm

5 chamber LVOT PW



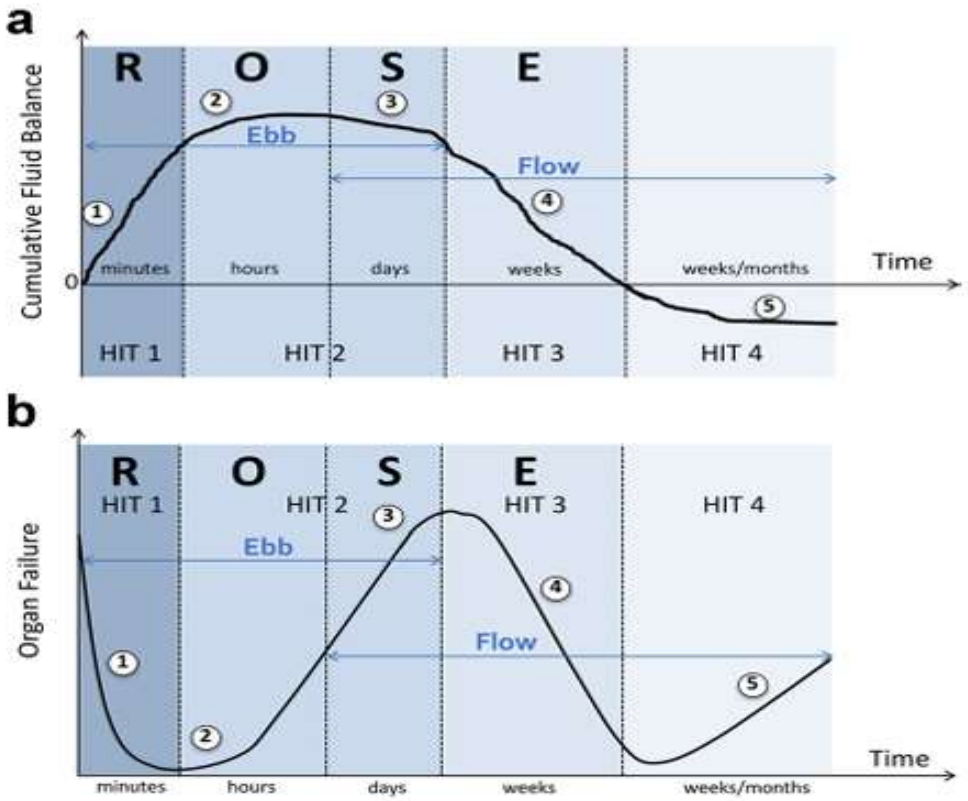
LVOT VTI = 19 cm

VTI being measured in RICU



- Keep in mind limitation of pulse wave doppler- Aliasing
- Proper echo window and good apical view is necessary with correct probe position
- Difficult in severe emphysema, obesity

When to stop?



RESUSCITATION

OPTIMISATION

STABILISATION

EVACUATION

Malbrain et al. Ann. Intensive Care (2018) 8:66

When to stop?

When the fluid deficit has been corrected

Assess success of resuscitation at regular interval

PLR

CRT

Lactate

Complications (fluid overload) apparent/imminent

Assess for fluid overload at regular interval

LUS

EVLWI

?IAP

ANDROMEDA-SHOCK trial

Group A

1. Initial fluid resuscitation+norepinephrine
2. Check fluid responsiveness
3. If responsive, give fluid
4. If not, vasopressor and/or inodilator
5. Target: CRT<3 sec

Group B

1. Initial fluid resuscitation+norepinephrine
2. Check fluid responsiveness
3. If responsive, give fluid
4. If not, vasopressor and/or inodilator
5. Target: lactate reduction at a rate of 20%/2 hours

Incluusion:
>18 years
Septic shock- sign of infection+lactate> 2 and requiring vasopressor after at least 20mL/Kg fluid bolus over 1 hour

Exclusion:
Bleeding
Severe ARDS
DNR

Primary outcome: 28-day mortality

CRT measured every 30 minutes, lactate every 2 hours

ANDROMEDA-SHOCK trial

How was CRT tested?

1. Press the pulp of the index finger
2. With a glass slide
3. Press for 10 seconds after skin is blanched
4. Measure with chronometer how long it takes for skin to regain its baseline colour

Incluusion:
>18 years
Septic shock- sign of infection+lactate> 2 and requiring vasopressor after at least 20mL/Kg fluid bolus over 1 hour

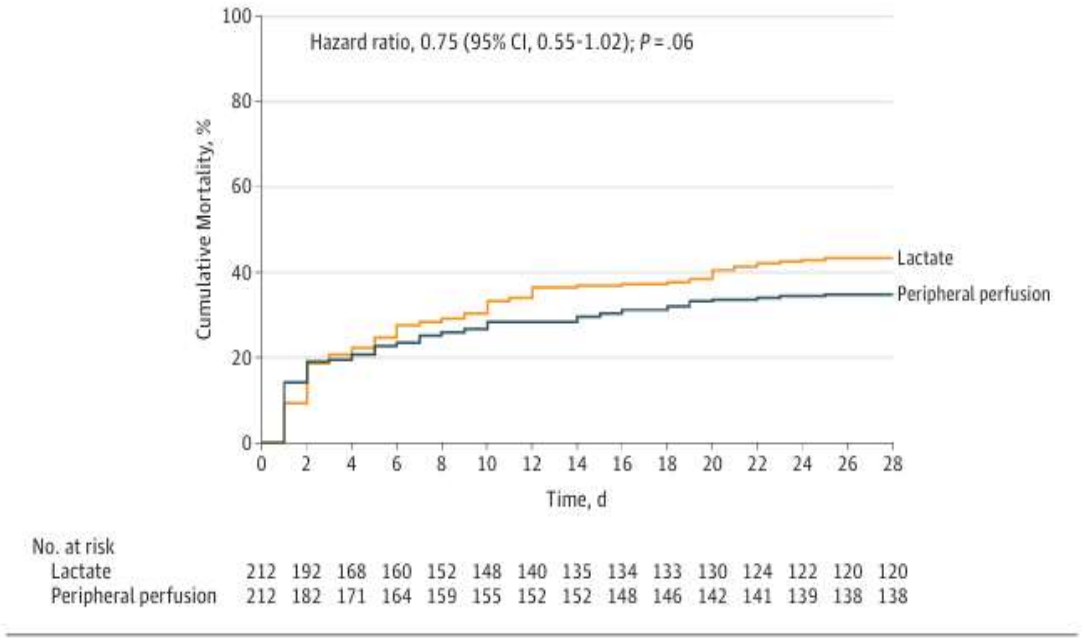
Exclusion:
Bleeding
Severe ARDS
DNR

Primary outcome: 28-day mortality

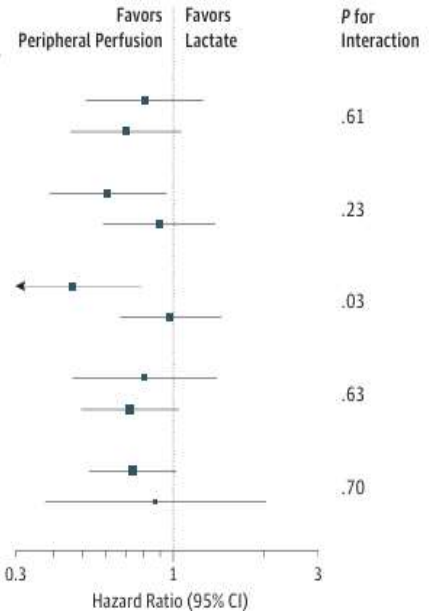
CRT measured every 30 minutes, lactate every 2 hours

Outcome	Peripheral Perfusion–Targeted Resuscitation (n = 212)	Lactate Level–Targeted Resuscitation (n = 212)	Unadjusted Absolute Difference (95% CI)	Adjusted Relative Measure (95% CI)	*P* Value
Primary Outcome					
Death within 28 d, No. (%)	74 (34.9)	92 (43.4)	−8.5 (−18.2 to 1.2)[b]	HR, 0.75 (0.55 to 1.02)[a]	.06[a]
Secondary Outcomes					
Death within 90 d, No. (%)	87 (41.0)	99 (46.7)	−5.7 (−15.6 to 4.2)[b]	HR, 0.82 (0.61 to 1.09)[a]	.17[a]
Mechanical ventilation–free days within 28 d, mean (SD)[c]	14.6 (12.1)	12.7 (12.2)	1.9 (−0.6 to 4.3)		.14
Renal replacement therapy–free days within 28 d, mean (SD)[c]	18.5 (12.1)	16.9 (12.1)	1.7 (−1.5 to 4.8)		.31
Vasopressor-free days within 28 d, mean (SD)[c]	16.7 (12.0)	15.1 (12.3)	1.6 (−0.7 to 3.9)		.18
SOFA at 72 h, No.[d]	165	166			.045
Mean (SD)	5.6 (4.3)	6.6 (4.7)	−1.00 (−1.97 to −0.02)		
ICU length of stay, mean (SD), d[e]	9.1 (9.8)	9.0 (9.6)	0.1 (−1.7 to 2.0)		.91
Hospital length of stay, mean (SD), d[f]	22.9 (28.8)	18.3 (19.0)	4.6 (0.0 to 9.1)		.05
Exploratory Outcomes					
Amount of resuscitation fluids within the first 8 h, No.	206	209			
Mean (SD), mL	2359 (1344)	2767 (1749)	−408 (−705 to −110)		.01
Total fluid balance, mL[g]					
Within 8 h, No.	198	205			
Mean (SD)	1587 (1388)	1874 (1756)	−288 (−598 to 22.0)		.07
Within 24 h, No.	176	185			
Mean (SD)	2025 (2181)	2343 (2336)	−318 (−785 to 149)		.18
Within 48 h, No.	153	160			
Mean (SD)	992 (1810)	1224 (3336)	−233 (−831 to 366)		.45
Within 72 h, No.	157	162			
Mean (SD)	1389 (2809)	1601 (3069)	−212 (−858 to 434)		.52
Intra-abdominal hypertension, No. of events/total (%)[h]	75/119 (63.0)	68/120 (56.7)	6.4 (−6.9 to 19.6)	RR, 1.11 (0.90 to 1.37)	.36[i]
Use of renal replacement therapy, No. (%)	30 (14.2)	42 (19.8)	−5.7 (−13.3 to 1.9)	RR, 0.71 (0.47 to 1.10)	.15[i]
In-hospital mortality, No. (%)	84 (39.6)	97 (45.8)	−6.1 (−16.0 to 3.7)	RR, 0.87 (0.69 to 1.08)	.20[i]

- There was no significant difference between 28-day-mortality between the CRT group and the Lactate group
  - The SOFA score was significantly lower at 72 hours in CRT group
    - The CRT group received significantly less resuscitation fluid
  - No difference in any prespecified subgroups (except lower baseline SOFA and APACHEII)



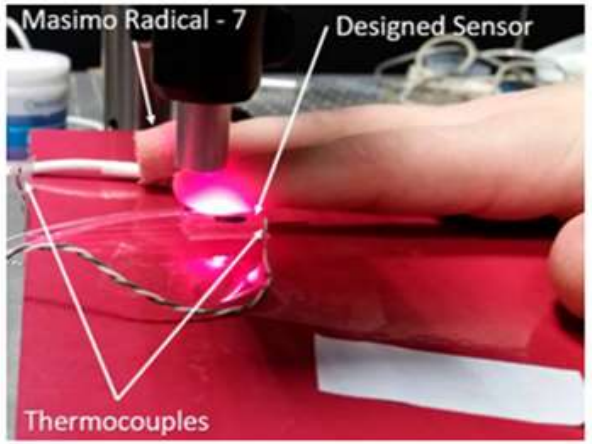
Subgroup	No. of Events/Total (%) Peripheral Perfusion-Targeted Resuscitation	Lactate Level-Targeted Resuscitation	Hazard Ratio (95% CI)	P for Interaction
Baseline lactate, mmol/L				
>4	37/85 (43.5)	41/88 (46.6)	0.82 (0.52-1.28)	.61
≤4	37/127 (29.1)	51/124 (41.1)	0.70 (0.46-1.07)	
APACHE II				
<25	32/130 (24.6)	49/135 (36.3)	0.61 (0.39-0.96)	.23
≥25	42/82 (51.2)	43/77 (55.8)	0.90 (0.59-1.38)	
SOFA				
<10	21/103 (20.4)	42/107 (39.3)	0.46 (0.27-0.78)	.03
≥10	53/109 (48.6)	50/105 (47.6)	0.98 (0.67-1.45)	
Confirmed source of infection				
No	25/61 (41)	26/59 (44.1)	0.84 (0.48-1.45)	.63
Yes	49/151 (32.5)	66/153 (43.1)	0.71 (0.49-1.03)	
Lactate decrease from admission to baseline measurement, %				
≤10	64/181 (35.4)	80/171 (46.8)	0.73 (0.53-1.02)	.70
>10	10/31 (32.3)	12/41 (29.3)	0.87 (0.38-2.04)	

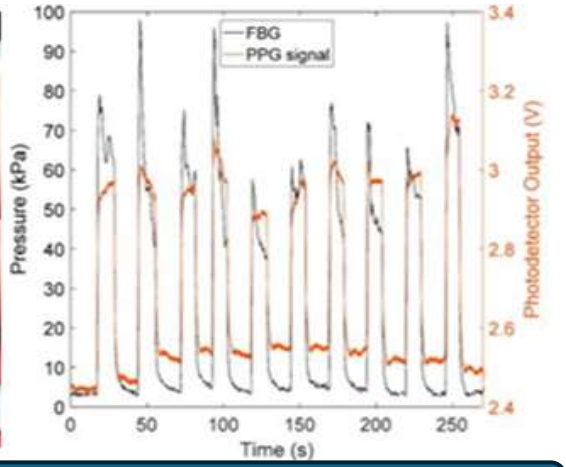


Methods to measure capillary refill time

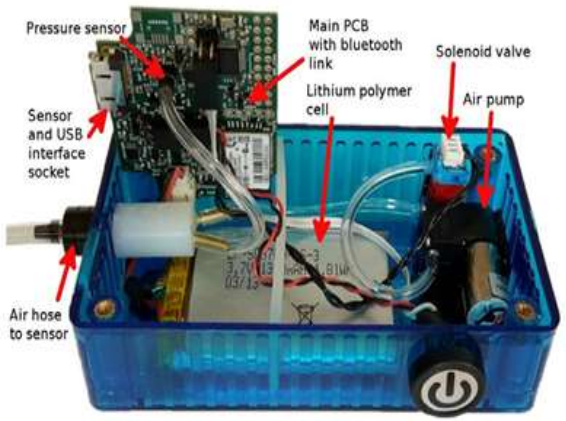
Manual method
(<2 seconds pressure is unreliable, 3-7N pressure is optimal)

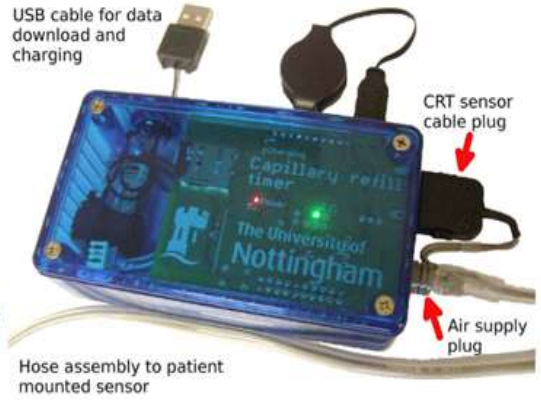
Semi-automatic (visual feedback)





Semi-automatic (POF-LED) (pulse oximeter tech)

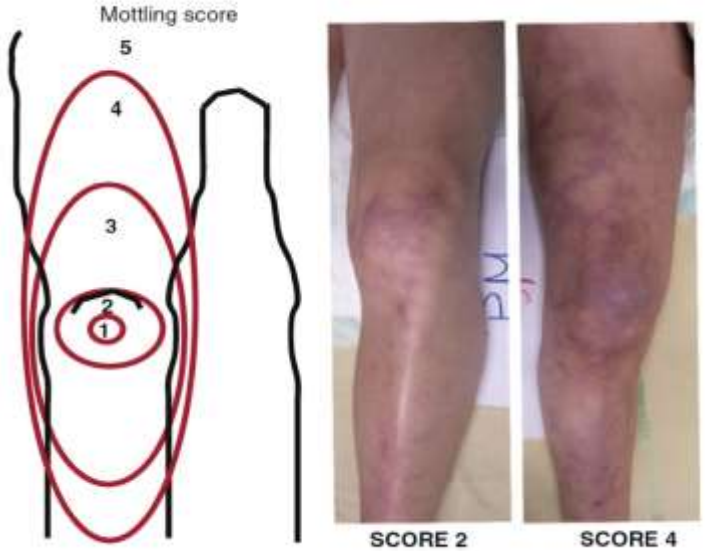




Fully automatic (pneumatic device+pressure and light sensor)

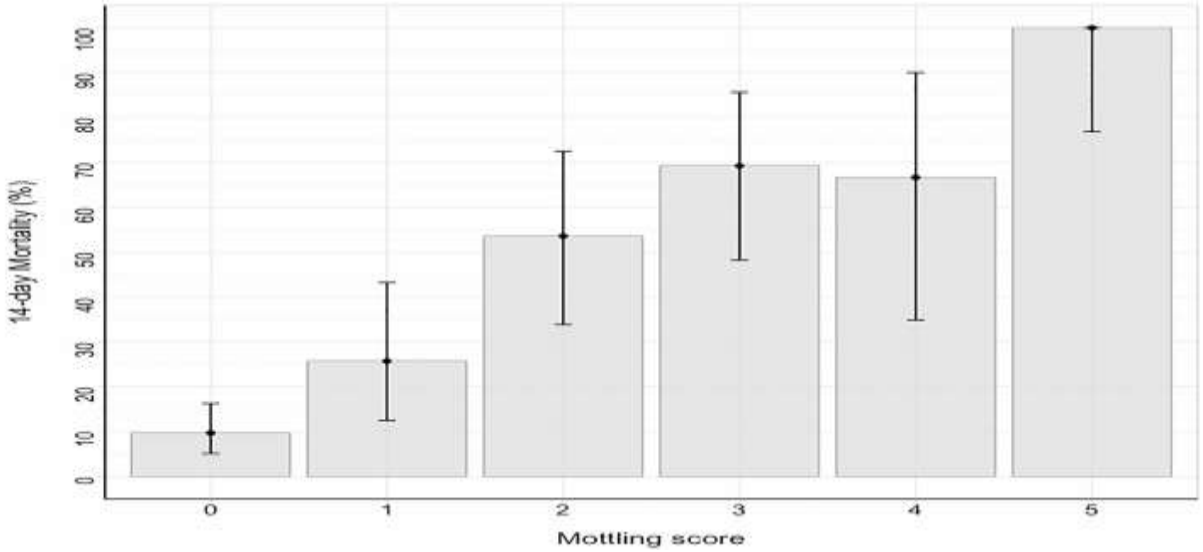
Xia Y, Guo Z, Wang X, Wang Z, Wang X, Wang Z. Research Progress on the Measurement Methods and Clinical Significance of Capillary Refill Time. Sensors. 2024 Dec 12;24(24):7941–1.

Mottling score:



0 – No mottling
1 – Coin sized mottling area on the knee.
2 – To the superior area of the knee cap.
3 – Mottling up to the middle thigh
4 – Mottling up to the fold of the groin
5 – Severe mottling that extends beyond the the groin.

Quelle: Ait-Oufella et al., Intensive Care Med 2011



- Mottling score is assessed at knee
- It is a good indicator of microcirculatory perfusion
- Measured at 6 hours following initiation of resuscitation, a higher mottling score is associated significantly (and independently) with higher 14-day and 28-day mortality (along with serum lactate and urine output <0.5mL/Kg/hour) (surrogate for success of resuscitation)
- Independent of vasopressor dose

Dumas et al. Critical Care (2019) 23:211

Measures of peripheral perfusion

- Assessing peripheral perfusion (microcirculatory) is better marker than central haemodynamics
- Correlates better with ICU mortality and morbidity
- CRT has been widely used
- Objective measurement methods for CRT are also available
- Normalisation of Lactate levels is a good indicator, but can not be sole indicator
- Other parameters assessed- skin mottling, standard base excess, SV02 and SCVO2
- Early re-assessment necessary- 0 and 6 hours (after resuscitation starts)

Gutiérrez-Zárate D, Rosas-Sánchez K, Zaragoza JJ. Clinical evaluation of peripheral tissue perfusion as a predictor of mortality in sepsis and septic shock in the intensive care unit: Systematic review and meta-analysis. Medicina Intensiva (English Edition) [Internet]. 2023 Jul 5 [cited 2023 Nov 19]

Measures of peripheral perfusion

Table 2 Analysis of diagnostic accuracy grouped by the total and by subgroups.

Analysis	Sensibility, % (95% CI)	Specificity, % (95% CI)	DOR (95% CI)	PLR (95% CI)	NLR (95% CI)
Overall	70.0 (61.0–77.7)	75.9 (61.6–86.2)	7.41 (3.91–14.04)	2.91 (1.80–4.72)	0.39 (0.30–0.51)
Capillary refill time	71.2 (62.2–78.8)	73.1 (46.1–89.6)	6.75 (2.31–19.74)	2.65 (1.18–5.97)	0.39 (0.28–0.54)
Skin mottling	65.4 (48.0–79.5)	79.5 (57.4–91.7)	7.37 (2.68–20.29)	3.20 (1.47–6.94)	0.43 (0.28–0.66)
14-day mortality	77.8 (67.9–85.3)	82.4 (74.3–88.3)	16.5 (8.70–31.31)	4.43 (2.98–6.57)	0.26 (0.18–0.39)
28-day mortality	63.1 (49.6–74.8)	69.8 (41.8–88.2)	3.97 (1.64–9.60)	2.09 (1.04–4.19)	0.52 (0.40–0.69)
ISDC	73.7 (56.7–85.7)	83.2 (74.3–89.5)	14.0 (7.66–25.54)	4.41 (3.06–6.34)	0.31 (0.18–0.52)
Sepsis-3 definition	68.7 (58.2–76.9)	71.0 (44.6–88.2)	5.40 (2.02–14.44)	2.37 (1.13–4.97)	0.44 (0.32–0.60)
Septic shock	73.0 (62.4–81.5)	71.3 (52.6–84.8)	6.75 (30.8–14.79)	2.55 (1.47–4.40)	0.37 (0.26–0.53)

Gutiérrez-Zárate D, Rosas-Sánchez K, Zaragoza JJ. Clinical evaluation of peripheral tissue perfusion as a predictor of mortality in sepsis and septic shock in the intensive care unit: Systematic review and meta-analysis. Medicina Intensiva (English Edition) [Internet]. 2023 Jul 5

Extra-vascular lung water index

- Total amount of fluid in lung outside vascular compartment
- Includes- interstitial fluid+intra-cellular fluid+lymphatic+alveolar fluid
- Can not differentiate between hydrostatic pulmonary oedema and ARDS
- Can be measured by Gravimetry, Trans-pulmonary dye-dilution and TPTD
- TPTD has shown good correlation with Gravimetry (gold standard)

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- A physiological observation study has shown normal EVLWI to be <10mL/Kg IBW
- PVPI may help differentiate between change in EVLWI due to pulmonary oedema and capillary leakage (PVPI higher in ARDS/ALI)
- Useful in detecting an end-point for fluid resuscitation

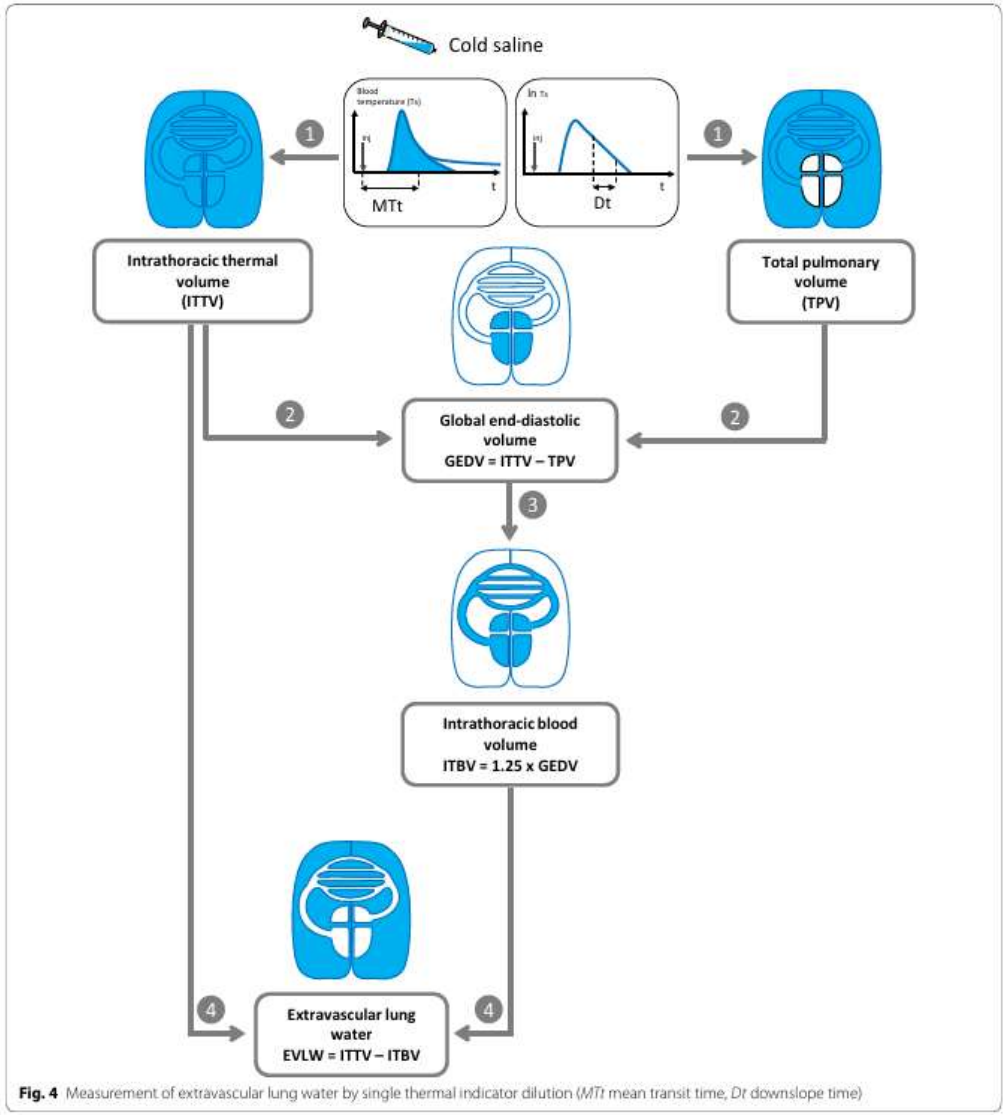


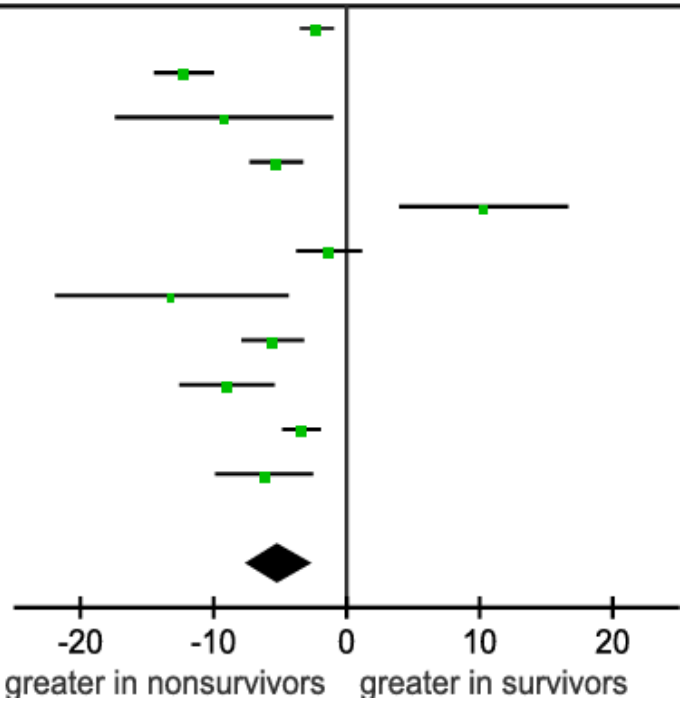
Fig. 4 Measurement of extravascular lung water by single thermal indicator dilution (*MTt* mean transit time, *Dt* downslope time)

Jozwiak et al. Ann. Intensive Care (2015) 5:38

Study or Subgroup	survivors Mean	SD	Total	nonsurvivors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Bognar Z 2010	6.56	1.36	9	8.79	2.04	19	11.3%	-2.23 [-3.51, -0.95]
Chung FT 2008	8.77	1.63	16	21	4.4	17	10.6%	-12.23 [-14.47, -9.99]
Chung FT 2010	12.8	5.7	14	22	10.3	7	5.1%	-9.20 [-17.39, -1.01]
Craig TR 2010	11.07	1.59	32	16.35	3.42	12	10.8%	-5.28 [-7.29, -3.27]
Davey-Quinn A 1999	31	5.98	4	20.7	3.32	7	6.6%	10.30 [3.94, 16.66]
Kuzkov VV 2006	8.3	2.7	16	9.6	5	22	10.4%	-1.30 [-3.77, 1.17]
Lubrano R 2011	17.08	7.84	21	30.2	10.13	6	4.7%	-13.12 [-21.89, -4.35]
Martin GS 2005	8.29	1.56	17	13.84	3.92	12	10.5%	-5.55 [-7.89, -3.21]
Phillips CR 2008	11.6	1.9	12	20.6	4.6	7	9.4%	-9.00 [-12.57, -5.43]
Sakka SG 2002	12.2	6.4	187	15.6	7.8	186	11.2%	-3.40 [-4.85, -1.95]
Yang CS 2006	8.1	2.7	26	14.3	8.8	24	9.3%	-6.20 [-9.87, -2.53]
Total (95% CI)			**354**			**319**	**100.0%**	**-5.06 [-7.53, -2.58]**

Heterogeneity: Tau² = 13.74; Chi² = 100.56, df = 10 (*P* < .00001); I² = 90%

Test for overall effect: Z = 4.00 (*P* < .0001)

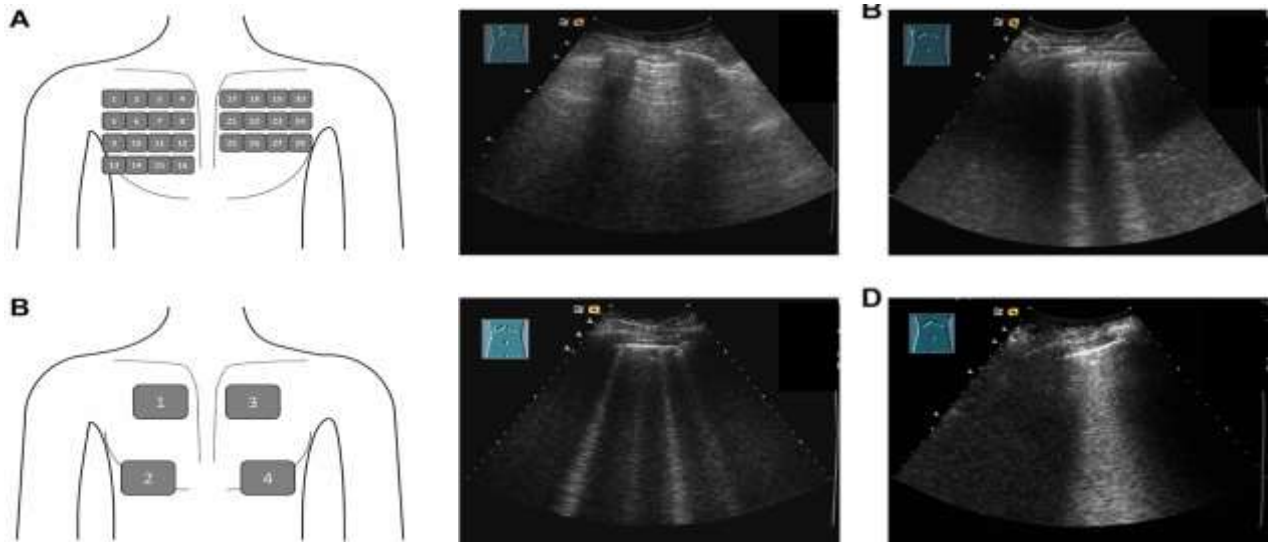


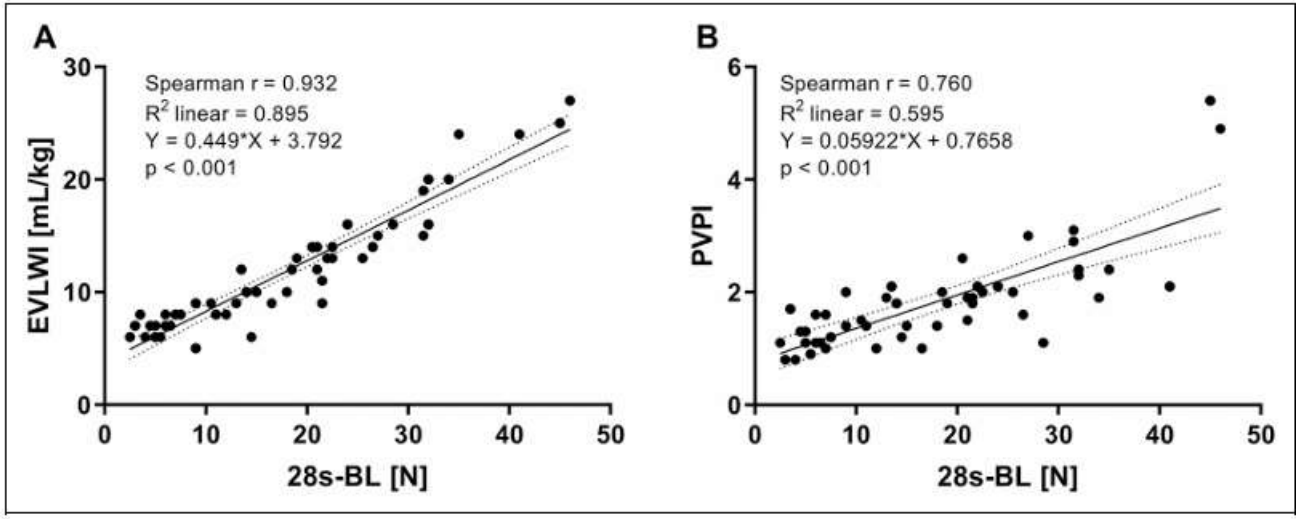
Lower Extravascular lung water index has been shown to be associated with better survival in critical illness

Zhang Z, Lu B, Ni H. Prognostic value of extravascular lung water index in critically ill patients: A systematic review of the literature. Journal of Critical Care. 2012 Aug;27(4):420.e1–8.

Lung ultrasound

- Can be extensive 28-sector or simplified 4-sector
- Quantifies B-lines in each sector scanned and assigns a score
- Both 28-sector and 4-sector scores have shown significant correlation with EVLWI as well as PVPI in observational studies
- The difference between fluid therapy guided by LUS and liberal fluid therapy (their effect of LOS and VFD) are being examined in the ongoing HEAL trial



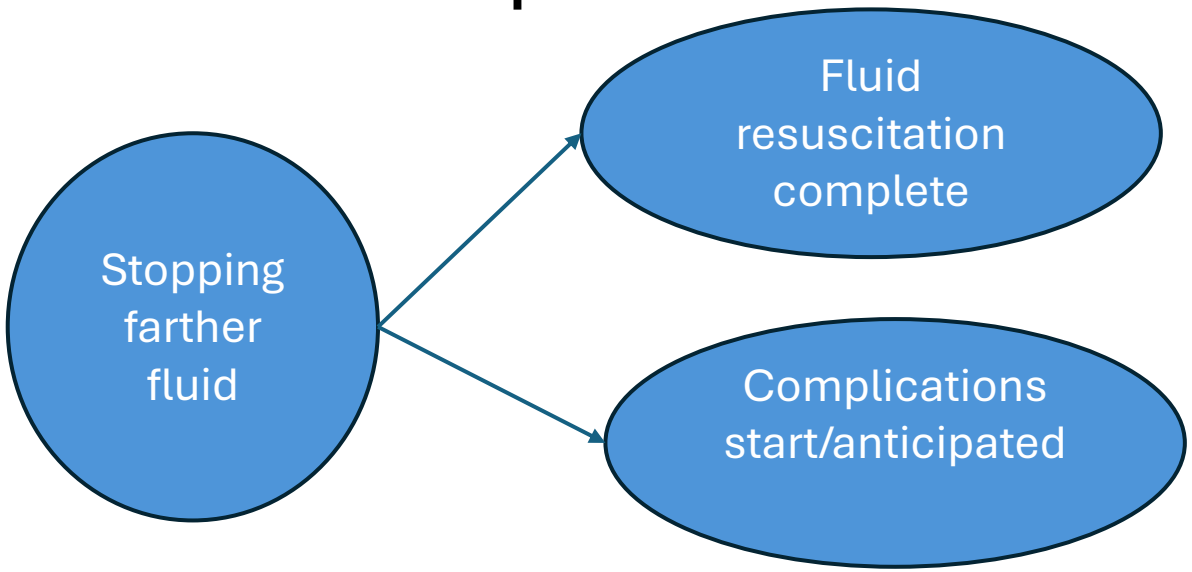


Ultrasound findings	*Score*
No B-line/ICS	0
One B-line/ICS	1
Two B-lines/ICS	2
Three B-lines/ICS	3
Four B-lines/ICS	4
Five B-lines/ICS	5
Confluent B-lines >50% ICS	6
Confluent B-lines >75% ICS	7
Confluent B-lines 100% ICS	8

- Low (1–10)
- Moderate (11–20) and
- High (21–32)

1. Rajpal M, Talwar V, Krishna B, Mustafi SM. Assessment of Extravascular Lung Water Using Lung Ultrasound in Critically Ill Patients Admitted to Intensive Care Unit. Indian J Crit Care Med 2024;28(2):165–169.
2. Journal of Intensive Care Medicine 37(1)

When to stop?



Individualize for patients with different clinical scenario- septic shock vs heart failure (to monitor patients more closely when there is LV dysfunction)

Repeated PLR- when ΔSVI<10%

ΔPPV and ΔSVV <10% or ΔPVI<10% (remember the limitations)

PiCCO- to keep EVLWI <10 ml/Kg (not useful if ARDS/pleural effusion/consolidation present already)

Clinical examination

- Assess for fluid overload – crepitations in lung (non-specific, late marker of overload)
- Clinical improvement in MAP and end-organ perfusion status (monitor mottling of skin, urine output, CRT, normalization of lactate)
- CI/VTI/CO

Kulkarni AP, Govil D, Samavedam S, Srinivasan S, Ramasubban S, Venkataraman R, et al. ISCCM Guidelines for Hemo dynamic Monitoring in the Critically Ill. Indian J Crit Care Med 2022;26(S2):S66–S76.

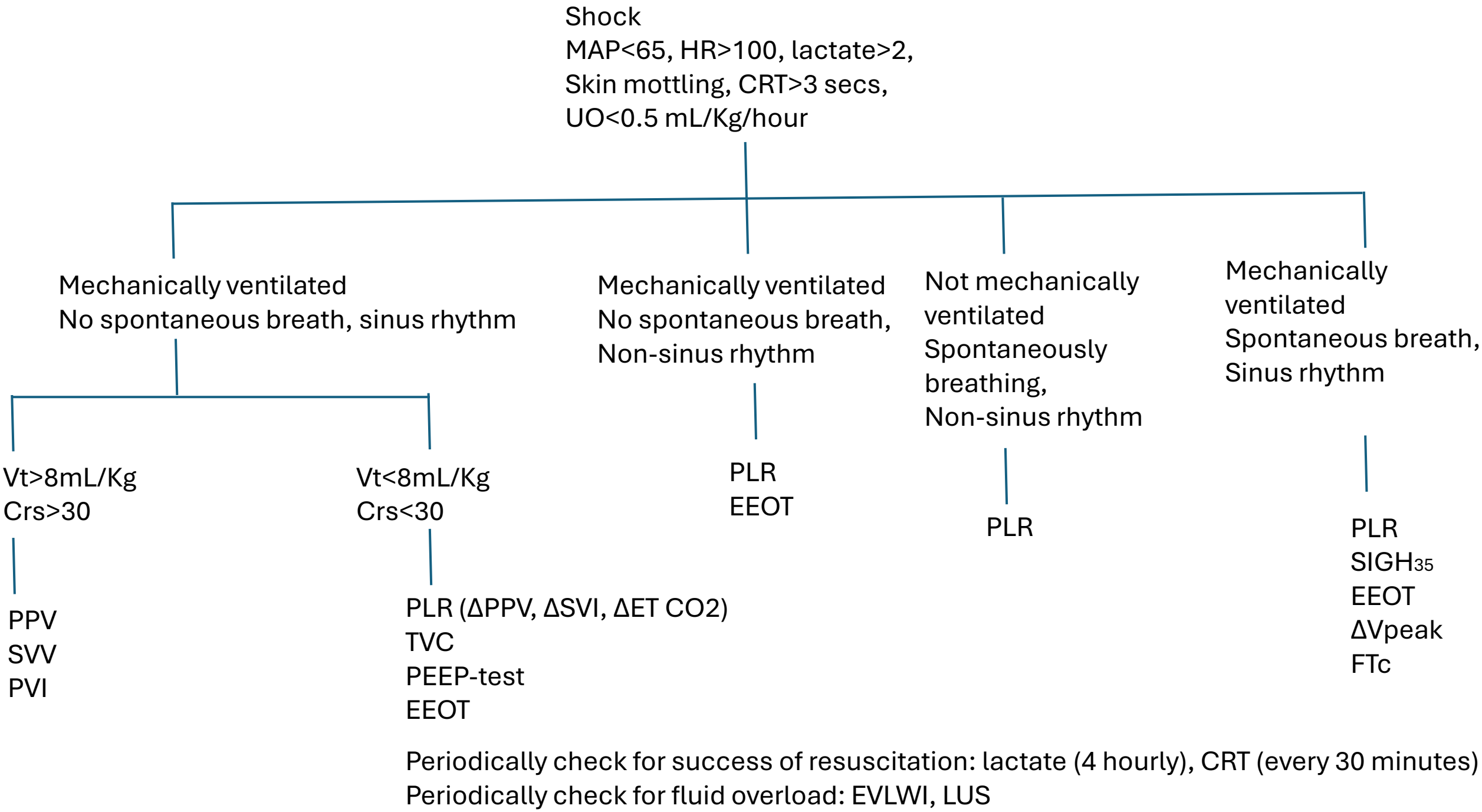
Current methods used in RICU

Parameters	Maneuver	Invasive monitoring	Non-invasive monitoring	Situations
ΔSVI (cut off 10%), **ΔPPV** (abs: cut off 2.5, rel: cut off 18%, Sn 90%, Sp 88%)	PLR	-	Bio-reactance (Baxter, Cheetah medical)	No abdominal hypertension, no intracranial injury or raised ICP, no IABP
PPV (cut off-11.5-12%, Sn 74%, Sp 82%), **SVV (**cut off 12%, Sn 76%, Sp 78%)	EEOT, TVC, also used w/o any maneuver	Pulse contour analysis through arterial line- Flotrac (Edwards EV1000)	-	No arrythmia, no right ventricular dysfunction, no low tidal volume ventilation, patient sedated without spontaneous breathing
PVI (cut off 14%, Sn 79%, Sp 78%)	-	-	Massimo continuous digital pulse oximeter	No or minimal vasopressor requirement, good peripheral perfusion, no ambient light or nail colouring that can interfere with reading
rcIVC or **ΔIVC** (cut off 15%, Sn 66%, Sp 81%)	-	-	Ultrasound, bedside 2D echo	Always in conjunction with other methods
CVP (cut off 9 mm Hg, Sn 61%, Sp 69%)	-	Central venous catheter, Flotrac	-	In conjunction with arterial pulse contour analysis

Parameters	Maneuver	Requirement	Advantages	Disadvantage
PPV, SVV	None	Arterial cannula, Flotrac Vt>8mL/Kg, PEEP<10, Crs>30, no arrythmia, RR not very high and irregular -	Accuracy very high in selected situations	Becomes unreliable in absence of aforesaid conditions; Requires invasive arterial cannulation
PPV, SVV	EEOT, TVC, PEEP decrease	Ideally requires arterial cannulation	Accuracy acceptable; Can be used in LTV, high PEEP, low Crs	Invasive method Unreliable in arrhythmia
PVI		Pulse oximeter and compatible monitor Vt>8mL/Kg, PEEP<10, Crs>30, no arrythmia, RR not very high and irregular	Non-invasive	Unreliable in absence of mentioned requirements Unreliable in low perfusion states
rcIVC or ΔIVC or ΔSVC	-	Absence of spontaneous breathing , Portable ultrasound	Non-invasive	Requires skill Not as accurate as PPV, SVV Can not be the sole parameter
CVP	-	Central venous catheter	Easy to measure -	Invasive
PPV, SVV, ΔSVI	PLR/Trendelenberg	Compatible monitor, special bed	Accurate Can be used in any Vt and Crs	Unreliable in IAH, contraindications to head lowering

What we may use

Parameters	Maneuver	Requirement	Advantages	Disadvantage
FTc		Ultrasound doppler (5-16 Hz liner array probe, PW) Skill-set	Non-invasive Can be used in PP	More validating studies required Cut-off not standardized
ΔVpeak				
ΔET CO2	PLR	ET CO2 sensor and monitor (Philips monitor/Hamilton ventilator)	Non-invasive Can be used in PP Reliable in LTV	Requires intubation Affected by multiple variables


Shock
MAP<65, HR>100, lactate>2,
Skin mottling, CRT>3 secs,
UO<0.5 mL/Kg/hour
Mechanically ventilated
No spontaneous breath, sinus rhythm
Vt>8mL/Kg
Crs>30
PPV
SVV
PVI
Vt<8mL/Kg
Crs<30
PLR (ΔPPV, ΔSVI, ΔET CO2)
TVC
PEEP-test
EEOT
Mechanically ventilated
No spontaneous breath,
Non-sinus rhythm
PLR
EEOT
Not mechanically ventilated
Spontaneously breathing,
Non-sinus rhythm
PLR
Mechanically ventilated
Spontaneous breath,
Sinus rhythm
PLR
SIGH35
EEOT
ΔVpeak
FTc
Periodically check for success of resuscitation: lactate (4 hourly), CRT (every 30 minutes)
Periodically check for fluid overload: EVLWI, LUS