Predictors of fluid responsiveness in critically ill patients

13/3/2015 and 20/3/2015

M Valliappan
Senior resident
Department of pulmonary medicine, PGIMER

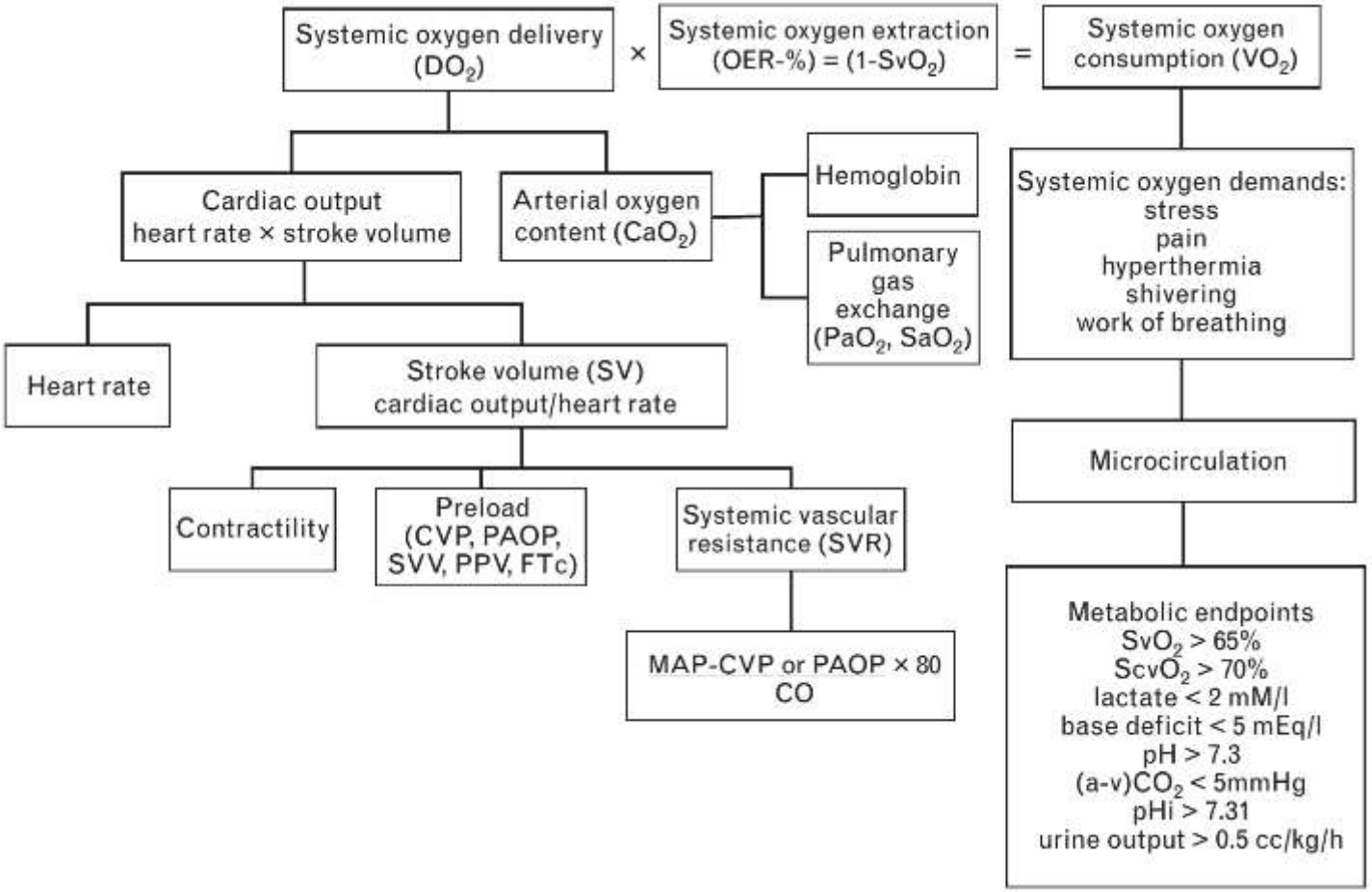
- Introduction
- Static indicators – CVP
- Dynamic indicators
  - Passive leg raising
  - IVC and SVC collapsibility
  - Plethysmography
  - Echocardiography and doppler measurements
- Arterial waveform analysis – methods and dynamic indicators
  - Stroke volume variation
  - Pulse pressure variation
- Conclusion

Goal of fluid therapy

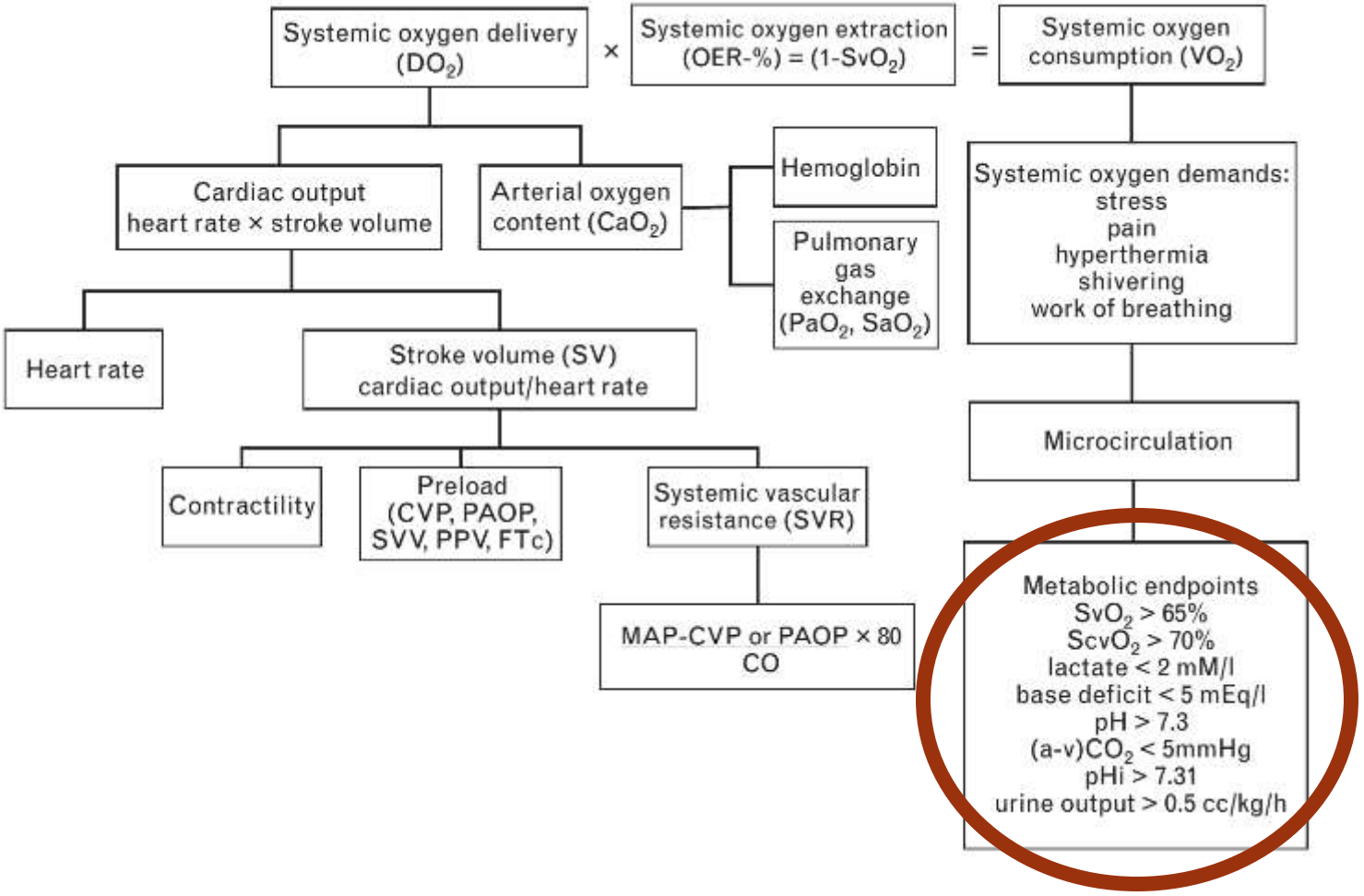
- Ensure adequate tissue perfusion (and oxygen delivery) without increasing cardiac filling pressures (may result in pulmonary edema)

Rivers et al. Curr Opin Crit Care 2010,16:297–308

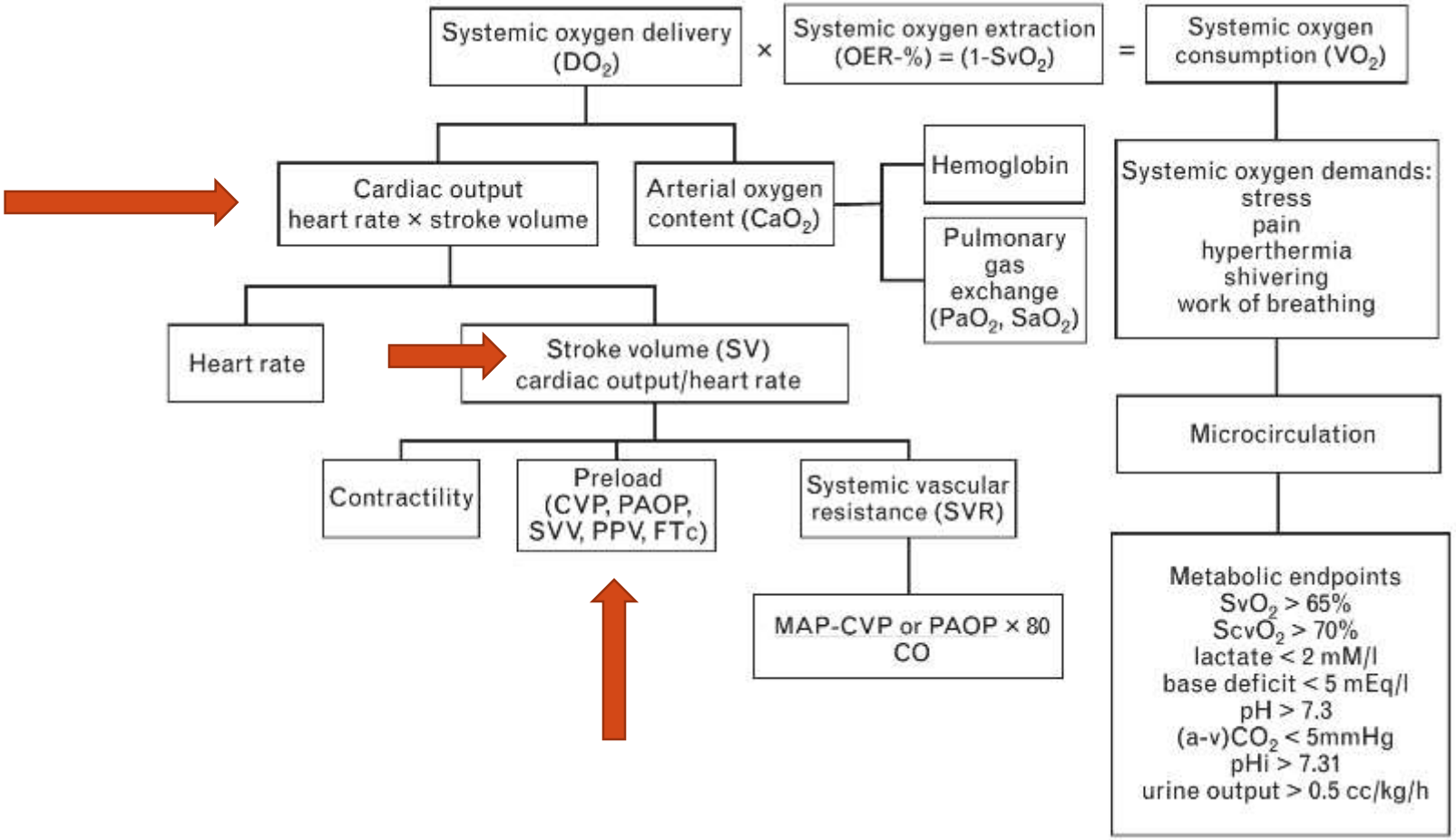
Tissue perfusion - determinants



Rivers et al. Curr Opin Crit Care 2010,16:297–308



Late indicators



Rivers et al. Curr Opin Crit Care 2010,16:297–308

Why optimize fluid therapy?

- Decreases inflammation

Prehydration (isotonic fluids given in human models of endotoxemia) decreased pro-inflammatory cytokines (TNFα, IL-1β, IL-8) and increased anti-inflammatory IL-10

Dorresteijn MJ et al. J Endotoxin Res 2005; 11:287–293

- Decreases need for vasopressor therapy

Static vs. dynamic indicators of volume status and fluid responsiveness

- Central venous pressure
- Pulmonary artery occlusion pressure
- Left ventricular end diastolic area
- RV end diastolic volume
- IVC diameter
- Global end diastolic volume index

Guerin et al. Best Practice & Research Clinical Anaesthesiology 27 (2013) 177–185

Static vs. dynamic indicators of volume status and fluid responsiveness

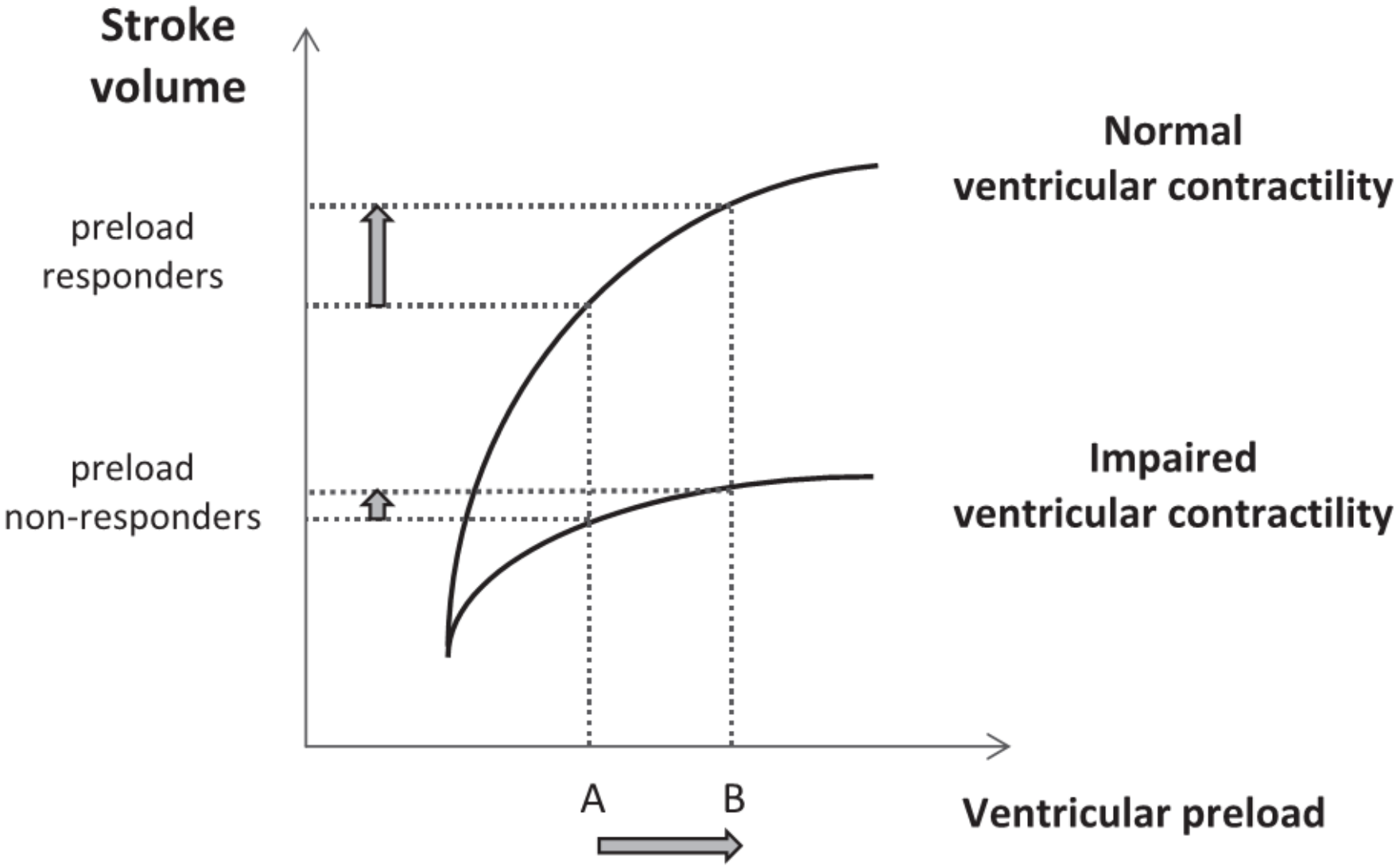
Static indicators - supposed to **reflect preload**, but are not accurate

Apart from preload, stroke volume and cardiac output also depends on cardiac contractility

But they can be used to confirm that the fluid boluses have filled the cardiac chambers (used as safety parameter to stop further infusion)

Guerin et al. Best Practice & Research Clinical Anaesthesiology 27 (2013) 177–185

Why preload alone may not predict stroke volume?



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Central venous pressure

- CVP measured at RA/IVC, thought to be reflective of intravascular volume status/blood volume
- Endorsed in Surviving sepsis and various other guidelines

- Several studies proved it to be a poor predictor of both intravascular volume and blood volume

Source	Setting	Type	Patients, No.	Methodology	AUC†	*r*, CVP/SI	*r*, ΔCVP/SI	CVP-R	CVP-NR
Calvin et al,[15] 1981	ICU	Mixed ICU	28	PAC/Scint		0.16	0.26	4.7	4.8
Reuse et al,[16] 1990	ICU	ICU	41	PAC		0.21		8.5	8.4
Godje et al,[17] 1998	ICU	CABG	30	PAC, COLD system‡			0.09		
Wagner and Leatherman,[18] 1998	ICU	ICU	25	PAC		0.44		7.4	10.1
Wiesenack et al,[19] 2001	OR	CABG	18	PAC, TPT			0.09		
Berkenstad et al,[20] 2001	OR	Neurosurgery	15	TPT	0.49	0.05	0.08	9.3	9.3
Michard et al,[21] 2000	ICU	ICU	40	PAC	0.51				
Reuter et al,[22] 2002	ICU	CABG	20	TPT	0.42				
Reuter et al,[23] 2003	ICU	CABG	26	PAC, TEE	0.71				
Barbier et al,[24] 2004	ICU	Sepsis	20	TEE	0.57			10	9
Kramer et al,[25] 2004	ICU	CABG	21	PAC	0.49	0.13		13.5	13.3
Marx et al,[24] 2004	ICU	Sepsis	10	PAC, TPT		0.41	0.28		
Preisman et al,[27] 2005	OR	CABG	18	TPT, TEE	0.61			8.7	10
Perel et al,[28] 2005	ICU	Vascular surgery	14	TEE		0.27		9.6	12.2
Hofer et al,[29] 2005	OR	CABG	40	PAC, TEE	0.54	0.02	0.2		
De Backer et al,[30] 2005	ICU	ICU	60	PAC	0.54			10	12
Kumar et al,[31] 2004	ICU	Healthy volunteers	12	PAC/Scint		0.32	0.22		
Osman et al,[32] 2007	ICU	Septic	96	PAC	0.58			8	9
Magder and Bafaqeeh,[33] 2007	ICU	CABG	66	PAC		0.36		5.9	8.7
Pooled					0.56	0.18	0.11	8.7	9.7

*PAC = pulmonary artery catheter; TEE = transesophageal echocardiography; Scint = radionuclide scintography; TPT = transpulmonary thermodilution; CVP-R = baseline CVP of responders; CVP-NR = baseline CVP of nonresponders; SI = fluid responsiveness; see Table 1 for expansion of abbreviations.

†Area under ROC curve of CVP and fluid responsiveness.

Marik PE et al. CHEST 2008; 134:172–178

Conclusion

- Poor correlation with blood volume
- Poor correlation in predicting fluid responsiveness compared to CO,SV indices
- Baseline CVP was no different among responders and non responders
- AUC 0.56 (95% CI, 0.51 to 0.6)

- A very high CVP in appropriate clinical context may prevent further fluid administration

Marik PE et al. CHEST 2008; 134:172–178

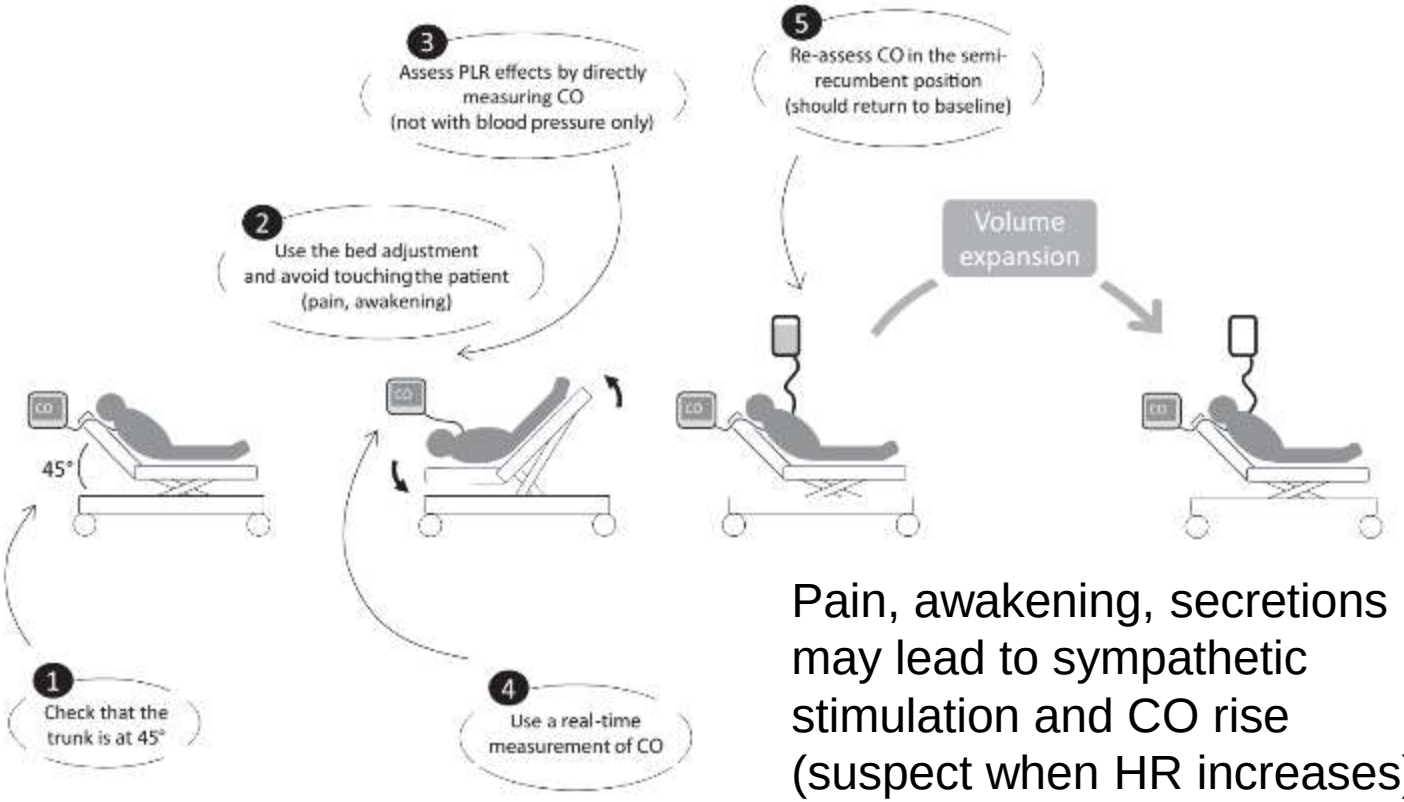
Dynamic indicators

- Induce a change in preload and assess its effects on cardiac output/stroke volume or its surrogates
- Pulse pressure variability (PPV)
- SVV
- CO, cardiac index variation
- PLR
- Plethysmographic variables
- Esophageal doppler monitoring
- Echocardiography (TTE TEE) and doppler

Passive leg raising test

- Passive leg raising adds 300 mL approximately to the circulation
- No fluid infused, rapidly reversible test
- Can be used in spontaneously breathing patients, low tidal volume, low lung compliance, in patients with arrhythmia
- Begin procedure in semi recumbent position (blood from splanchnic circulation also adds to the ‘infused’ volume)
- Measure CO and not BP

Monnet X et al. crit care. 2015 Jan 14;19(1):18



Pain, awakening, secretions may lead to sympathetic stimulation and CO rise (suspect when HR increases)

Monnet X et al. crit care. 2015 Jan 14;19(1):18

PLR - evidence

- Several studies performed: measurement of cardiac output has been done in various trials after 60s, 90s, 120s, 4 mt, 5 mt after PLR
- Responders defined as increase in CO by 12-15%
- Reference standards – CO, cardiac index, stroke volume and aortic flow measurements after fluid challenge
- PLR induced CO changes as well as pulse pressure changes (PP) have been studied
- PLR CO *[pooled AUC 0.81(0.75–0.86)]* predicts fluid responsiveness better than PLR PP *[pooled AUC is only 0.76 (0.67–0.86)]*

Cavallaro et al. Intensive Care Med (2010) 36:1475–1483

Summary of studies

Reference	Setting/ patients	Ventilation	Rhythm	Fluid challenge	Definition of responders	Index	Device
Boulain et al. [17]	ICU/shock	MV adapted		Colloids 300 ml		cPPrad	Arterial BP transducer
						cSV	PAC
Lafanechère et al. [18]	ICU/shock	MV adapted	Sinus	Crystalloids 500 ml	ΔABF > 15%	cABF%	Esophageal Doppler
Monnet et al. [19]	ICU/shock	MV adapted/trigger	Sinus/arrhythmias	Crystalloids 500 ml	ΔABF > 15%	cPP%	Arterial BP transducer
						cABF%	Esophageal Doppler
Lamia et al. [20]	ICU/shock	MV trigger/SB	Sinus/AF	Crystalloids 500 ml	ΔSVI > 15%	cVTIAo	TTE
						cCO	TTE
Maizel et al. [21]	ICU/shock	SB	Sinus	crystalloids 500 ml	ΔCO > 12%	cSV%	TTE
						cCO%	TTE
Thiel et al. [13]	ICU/shock	MV adapted/trigger/SB	Sinus/arrhythmias	Crystalloids or colloids 500 ml	ΔSV > 15%	cSV%	Transthoracic Doppler USCOM®
Monnet et al. [22]	ICU/shock	MV adapted/trigger	Sinus/arrhythmias	Crystalloids 500 ml	ΔCI > 15%	cCI%	PiCCO®
						cPP%	Arterial BP transducer
Biais et al. [23]	ICU/shock	MV trigger/SB	Sinus	Crystalloids 500 ml	ΔSV > 15%	cSV%	TTE
						cSV %	Vigileo/FloTrac®
Préau et al. [24]	ICU/shock	SB	Sinus	Colloids 500 ml	ΔSV > 15%	cSV%	TTE
						cPP%	Arterial BP transducer
						cVF	Doppler

AF atrial fibrillation, *BP* blood pressure, *ICU* intensive care unit, *MV* mechanical ventilation, *PAC* pulmonary artery catheter, *SB* spontaneous breathing, *TTE* tran echocardiography, Δ variation; *c* PLR-induced changes in…, *ABF* aortic blood flow, *CI* cardiac index, *CO* cardiac output, *PP* pulse pressure, *PPrad* radial pulse *SV* stroke volume, *SVI* stroke volume index, *VF* peak velocity in femoral artery, *VTIAo* aortic velocity–time integral

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Monnet et al. [22]	ICU/shock	MV adapted/trigger	Sinus/arrhythmias	Crystalloids 500 ml	ΔCI > 15%	cCI% cPP%	PiCCO® Arterial BP transducer
Biais et al. [23]	ICU/shock	MV trigger/SB	Sinus	Crystalloids 500 ml	ΔSV > 15%	cSV% cSV %	TTE Vigileo/FloTrac®
Préau et al. [24]	ICU/shock	SB	Sinus	Colloids 500 ml	ΔSV > 15%	cSV% cPP% cVF	TTE Arterial BP transducer Doppler

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Cavallaro et al. Intensive Care Med (2010) 36:1475–1483

PLR in predicting CO raise and surrogates

Reference	Index	No. of pts/ boluses	% Resp.	Mean (SD) resp.	Mean (SD) non-resp.	*r*	AUC (SE)	Best threshold	Sens.	Spec.	DOR
Boulain et al. [17]	cSV	15/15				0.89					
Lafanechère et al. [18]	cABF%	22/22	45			0.71	0.95 (0.040)	8.0	90	83	45
Monnet et al. [19]	cABF%	71/71	52	28.4 (20.6)	1.2 (6.1)	0.83	0.96 (0.020)	10.0	97	94	576
Lamia et al. [20]	cVTIAo	24/24	54	24.5 (9.7)	5.0 (5.5)	0.83	0.96 (0.040)	12.5	77	100	69
	cCO	24/24	54			0.79					
Maizel et al. [21]	cSV%	34/34	50	14.8 (8.8)	1.3 (8.6)	0.56	0.89 (0.059)	8.0	88	83	
	cCO%	34/34	50	12.0 (4.2)	−0.5 (10.0)	0.75	0.89 (0.060)	5.0	94	83	75
Thiel et al. [13]	cSV%	89/102	46	21.0 (12.5)	3.2 (10.4)		0.89 (0.040)	15.0	81	93	66
Monnet et al. [22]	cCI%	34/34	68	21.9 (17.9)	1.3 (0.7)		0.94 (0.050)	10.0	91	100	198
Biais et al. [23]	cSV% (TTE)	30/30	67				0.96 (0.030)	13.0	100	80	139
	cSV% (Vigileo®)	30/30	67				0.92 (0.050)	16.0	85	90	
Préau et al. [24]	cSV%	34/34	41	17.0 (7.0)	4.0 (5.0)		0.94 (0.040)	10.0	86	90	54
Overall (95% CIs)		353/366	52.9	Pooled difference in means 17.7% (13.6–21.8%)		0.81 (0.75–0.86)	0.95 (0.92–0.97)		89.4 (84.1–93.4)	91.4 (85.9–95.2)	89.0 (40.2–197.3)

AUC area under the receiver operating characteristics curve, *95% CIs* 95% confidence intervals, *DOR* diagnostic odds ratio, *pts* patients, *r* correlation coefficient, *resp.* responders, *SD* standard deviation, *SE* standard error, *Sens* sensitivity, *Spec* specificity; *c* PLR-induced changes in…, *ABF* aortic blood flow, *CI* cardiac index, *CO* cardiac output, *SV* stroke volume, *VF* peak velocity in femoral artery, *VTIAo* aortic velocity–time integral

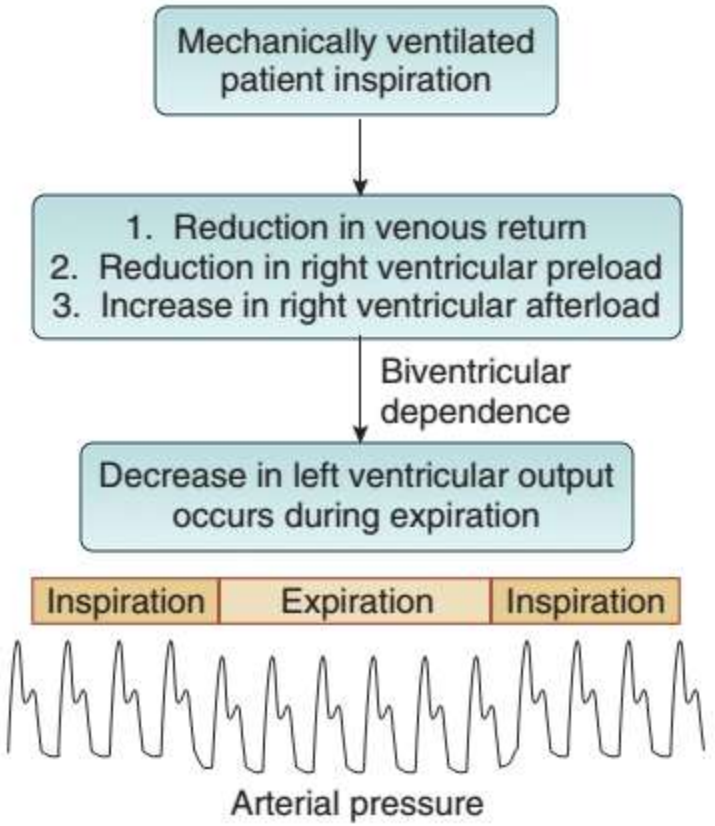
Cavallaro et al. Intensive Care Med (2010) 36:1475–1483

PLR in arrhythmias, spontaneous breaths and various postures

Subgroup	Correlation r	p*	AUC	p*
Ventilation				
Adapted	0.81 (0.53–0.93)	0.97	0.94 (0.87–1.00)	0.74
Inspiratory efforts	0.81 (0.74–0.87)		0.95 (0.91–0.99)	
Cardiac rhythm				
Sinus rhythm	0.73 (0.58–0.84)	0.15	0.96 (0.92–0.99)	0.94
Arrhythmias	0.83 (0.75–0.89)		0.96 (0.89–1.03)	
Starting position				
Supine	0.78 (0.64–0.87)	0.39	0.93 (0.87–1.00)	0.62
Semirecumbent	0.83 (0.75–0.89)		0.95 (0.92–0.97)	

Cavallaro et al. Intensive Care Med (2010) 36:1475–1483

Principle: heart-lung interaction

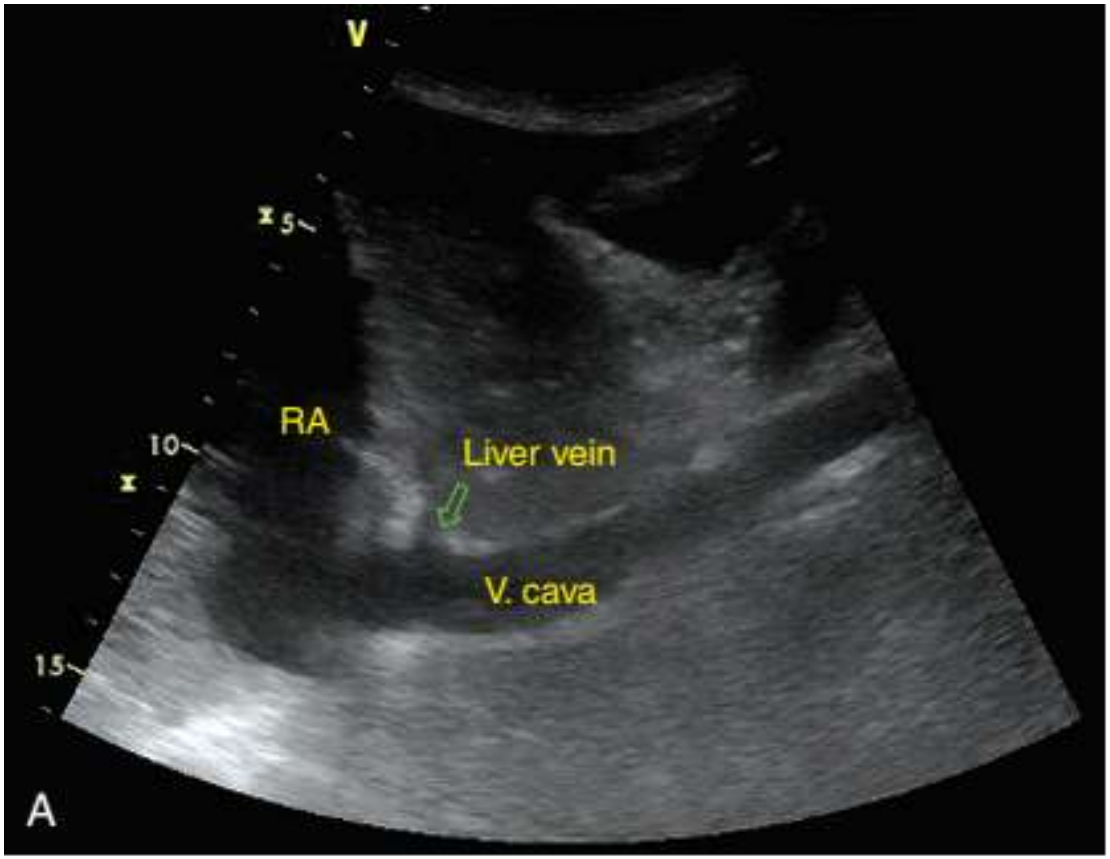


Kalantri et al. Kidney International (2013) 83, 1017–1028

IVC diameter

- Elevated right atrial pressure (indicating preload) is associated with dilated IVC
- Can be totally collapsed to 2.5 cm or more
- Inter-individual variability is significant
- Collapsibility index (CI) (percentage of maximum diameter) [max-min diameter/max diameter %]
- CI 40-50% in spontaneously breathing individuals(1,2)
- CI 12-18% in mechanically ventilated individuals (3)

Tan HL, et al. Trends in Anaesthesia and Critical Care (2015)
(1) Kircher BJ, et al.Am J Cardiol 1990;66:493e6)
(2) Nagdev AD, et al. Ann Emerg Med 2010 Mar;55(3):290e5
(3) Berbier C et al. Intensive Care Med2004 Sep;30(9):1740e6
(4) Feissel M et al. Intensive Care Med 2004 Sep;30(9):1834e7


V
5
RA
10
Liver vein
V. cava
15
A

Factors affecting IVC measurements - Luminal factors

Factor	Comments
RV compliance	LV diastolic dysfunction is usually associated with RV diastolic dysfunction ICU patients may have transient ventricular dysfunction
Tricuspid valve disease	TR and TS falsely results in raised RAP independent of fluid status
Obstructed right atrium	
Pulmonary artery hypertension	Increased RAP
Portosystemic shunting	Blood flows through veins other than IVC

Tan HL, et al. Trends in Anaesthesia and Critical Care (2015)

Extra Luminal factors affecting IVC

Factor	Comments
Tension pneumothorax	Raised intrathoracic pressure distends the IVC
Spontaneous ventilation	Increased respiratory efforts result in compression of IVC during diaphragmatic excursion Standardization therefore cannot be done for spontaneously breathing patients
Mechanical ventilation	PEEP, tidal volume mode of ventilation, paralysis all affect IVC diameter
Pericardial tamponade	Increased intra pericardial pressure
Intra abdominal pressure	Edema, ascites may all increase intra abdominal pressure and may falsely decrease IVC diameter in an already volume overloaded patient

Tan HL, et al. Trends in Anaesthesia and Critical Care (2015)

Other factors affecting IVC

Factor	Comments
Position	Smallest in left lateral, intermediate in supine, largest in right lateral position
Age and ethnicity	Decreases with age
Technical difficulty	May not be visualized in up to 18%
Inter observer variability	
Intra abdominal pressure	Edema, ascites may all increase intra abdominal pressure and may falsely decrease IVC diameter in an already volume overloaded patient

Tan HL, et al. Trends in Anaesthesia and Critical Care (2015)

Study	Population	Exclusion criteria	Sample size	Respiratory pattern	Site of IVC measurement	Index test	Reference standard	assessing fluid responsiveness	Volume expansion
Barbier et al. 2004	Ventilated; severe sepsis with circulatory failure	Morbidly obese; poor response to echo-cardiography	20	Mechanical ventilation (TV = 8.5 ± 1.5 mL/kg; PEEP = 4 ± 2 cm H_2O)	Upstream of origin of suprahepatic vein	$(D_{max} - D_{min})/D_{min}$	Cardiac index > 15%	US	7 mL/kg plasma expander
Brun et al. 2013	Severe pre-eclampsia	Cardiac or renal disorders, age <18, pre-eclampsia after delivery	23	NR	Before IVC junction into right atrium	$(D_{max} - D_{min})/[(D_{max} + D_{min})/2]$	SVI > 15%	US	500 mL normal saline
Byon HJ 2013	Mechanically ventilated children	Cardiac or pulmonary disorder, or vasoactive and/or inotropic support	33	Mechanical ventilation (pressure controlled; PEEP = 0)	2 cm from right atrium	$(D_{max} - D_{min})/[(D_{max} + D_{min})/2]$	SVI > 10%	US	10 mL/kg HES
Corl et al. 2012	Emergency department patients	Age < 18 y, pregnant, incarcerated, sustained significant trauma or unable to consent	26	Spontaneously breathing	3 cm caudad to right atrial border	$(D_{max} - D_{min})/D_{max}$	Cardiac index > 10%	US	Passive leg raise
Feissel et al. 2004	Mechanically ventilated patients in septic shock	NR	39	Mechanical ventilation (volume controlled, TV = 8–10 mL/kg)	3 cm from right atrium	$(D_{max} - D_{min})/[(D_{max} + D_{min})/2]$	Cardiac output > 15%	US	8 mL/kg 6% HES
Machare-Delgado et al. 2011	Mechanical ventilation requiring vasopressors	Escalating doses of vasopressors, hemodialysis, ascites, atrial	25	Mechanical ventilation (assist/control mode; TV = 8	2 cm from right atrium	$(D_{max} - D_{min})/D_{min}$	SVI > 10%	Vigileo monitor	500 mL normal saline
Moretti and Pizzi 2010	Sub-arachnoid hemorrhage, sedation, mechanical ventilation	Age < 18, pre-existing heart failure, cardiac arrhythmias, ARDS, inability to perform femoral artery cannulation or ultra-sonography	29	Mechanical ventilation (volume controlled, PEEP = 0, TV = 8 mL/kg)	2 cm upstream of origin of suprahepatic vein	$(D_{max} - D_{min})/D_{min}$	Cardiac index > 15%	TPTD	7 mL/kg 6% HES
Muller et al. 2012	Acute circulatory failure	Fluid challenge contra-indicated	40	Spontaneously breathing	2–3 cm from right atrium	$(D_{max} - D_{min})/D_{max}$	Sub-aortic VTI ≥ 15%	US	500 mL of 6% 130/0.4 HES in NaCl solution

Zhang et al. Ultrasound in Med. & Biol., Vol. 40, No. 5, pp. 845–853, 2014

Reference standard used

- Cardiac index improvement (3 studies)
- Stroke volume index in three studies
- Cardiac output and velocity time index in two studies

- Echocardiography and other invasive methods (thermodilution, vigileo FLoTRac) were used to measure these parameters

Zhang et al. Ultrasound in Med. & Biol., Vol. 40, No. 5, pp. 845–853, 2014

Study	Cutoff value increase in percentage)	Sensitivity (%)	Specificity (%)	AUROC (95% CI
Barbier et al. 2004	18%	90	90	0.91 (0.84, 0.98)
Brun et al. 2013	—	50	73	0.57 (0.32, 0.82)
Byon et al. 2013	—	—	—	0.604 (0.418–0.84
Corl et al. 2012	—	—	—	0.56 (0.31–0.81)
Feissel et al. 2004	12%	—	—	—
Machare-Delgado et al. 2011	12%	100	53	0.81 (0.64–0.99)
Moretti and Pizzi 2010	16%	70.95	100	0.902 (0.733–0.97
Muller et al. 2012	40%	70	84	0.77 (0.60–0.88)

Zhang et al. Ultrasound in Med. & Biol., Vol. 40, No. 5, pp. 845–853, 2014

Setting (number of studies)	Total number of patients	Sensitivity (95% CI)	Specificity (95% CI)	Diagnostic odds ratio (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Overall (6)	179	0.76 (0.61–0.86)	0.86 (0.69–0.95)	20.2 (6.1–67.1)	5.6 (2.2–14.1)	0.28 (0.16–0.47)
Mechanical ventilation (4)	116	0.81 (0.67–0.91)	0.87 (0.63–0.97)	30.8 (7.3–130.0)	6.4 (1.9–21.5)	0.21 (0.11–0.39)
Spontaneous breathing (1)	40	0.70 (0.46–0.88)	0.85 (0.62–0.97)	13.2 (2.8–62.7)	4.7 (1.6–13.8)	0.35 (0.18–0.71)
Colloids for fluid challenge (4)	131	0.76 (0.64–0.86)	0.92 (0.83–0.98)	32.1 (10.6–96.9)	7.5 (3.4–16.9)	0.29 (0.19–0.44)
Normal saline for fluid challenge (2)	48	0.70 (0.46–0.88)	0.61 (0.41–0.79)	4.9 (0.78–30.7)	2.0 (1.2–3.1)	0.36 (0.04–3.4)

Change in IVC diameter may predict fluid responsiveness better in mechanically ventilated patients and if fluid challenge is with colloids

Triggered breaths in mechanically ventilated patients may also make IVC variability less reliable

Juhl-Olsen P et al. Ultraschall Med. 2012 Apr;33(2):152-9

SVC variability

Reference	Study design and patient population	Measurements	Results
Viallard Baron A et al Intensive Care Med (2004) 30:1734–1739	66 MV patients on VCV Vt 8-10mL/kg Peep 5-7 cmH2O	TEE performed SVC in long axis, collapsibility seen Echo-doppler measurement used to calculate CO and Cardiac index 10 mL/kg 6% HES used for fluid challenge	SVC collapsibility 36% predicted responders (11% increase in cardiac index after fluid challenge) Sensitivity 90% Specificity 100%

Plethysmography

- Delta POP – (respiratory variation of pulse oximetry plethysmographic amplitude) (POP max – POP min/average POP) as percentage
- PVI is PI max- PI min/PI max as percentage
- PI is plethysmographic perfusion index in one respiratory cycle
- Delta POP has to be calculated

Plethysmography

- Delta POP and PVI can predict fluid responsiveness in mechanically ventilated patients
- Same principle of heart-lung interaction in mechanically ventilated patients is employed
- Initially used in operating rooms, Subsequently tried as a non-invasive marker of fluid responsiveness in ICUs

PVI

- A new algorithm was developed based on respiratory variation of plethysmographic waves (Massimo, Irvine, CA)

- Automatically measures PVI and displays along with pulse oximetry
- Studies on MV patients on VCV with early sepsis using 8 mL/kg, 6% HES as challenge (31 patients)
- Echocardiography (TTE) Ao VTI measured as reference standard

Feissel M et al. Journal of Critical Care (2013) 28,639

- VTI Ao 15% were considered responders
- PVI threshold 19% discriminated responders vs. non-responders with sensitivity of 94% and specificity (87%)

Feissel M et al. Journal of Critical Care (2013) 28,639

ICU studies - deltaPOP

Reference	Number of patients	% responders	Threshold	Comparator	AUC	Sensitivity	Specificity
Natalini et al.Anesth Analg 103:1478–1484	22	61	15%	CI > 15% after colloid 500 mL	0.70	0.63	0.83
Feissel et al. Intensive Care Med 33:993–9	23	64	14%	CI > 15% after colloid 8 mL/kg	0.94	0.94	0.80
Wyffels et al.	32	62.5	11.8%	CI > 15% after colloid	0.89	0.90	0.83

Summary of studies assessing plethysmography

References (first author)	Index	Setting	Type of patients/surgery	Ventilation mode	Tidal volume (ml/kg)	Fluid bolus	Definition of responders	QUADAS score [14]
Natalini [22]	ΔPOP	ICU	Shock, various etiologies	Volume control	8 ± 2	Colloids 500 ml (large)	ΔCI >15 %	13
Solus-Biguenet [23]	ΔPOP	OR	Hepatic surgery	Volume control	8–10	Colloids 250 ml (small)	ΔSVI >10 %	13
Cannesson [17]	ΔPOP	OR	Cardiac surgery	Volume control	8–10	Colloids 500 ml (large)	ΔCI >15 %	12
Feissel [19]	ΔPOP	ICU	Septic shock	Volume control	8–10	Colloids 8 ml/kg (large)	ΔCI >15 %	13
Wyffels [24]	ΔPOP	ICU	Postoperative, cardiac surgery	Volume control	8–10	Colloids 500 ml (large)	ΔCI >15 %	12
Hoiseth [20]	ΔPOP	OR	Abdominal surgery	Volume control	8	Colloids 250 ml (small)	ΔSV >15 %	13
Cannesson [11]	ΔPOP PVI	OR	Cardiac surgery	Volume control	8–10	Colloids 500 ml (large)	ΔCI >15 %	12
Zimmermann [12]	PVI	OR	Abdominal surgery	Volume control	7	Colloids 7 ml/kg (large)	ΔSVI >15 %	12
Desgranges [18]	PVI	OR	Cardiac surgery	Volume control	8	Colloids 500 ml (large)	ΔCI >15 %	12
			Low-risk colorectal surgery (pre-incision)	Volume control	8–10	Colloids 500 ml (large)	ΔSV >15 %	12
Hood [21]	PVI	OR	Low-risk colorectal surgery (intra-operative)	Volume control		Colloids 250 ml (small)		

ΔCI/ΔSV/ΔSVI Increase in cardiac index/stroke volume/stroke volume index after fluid infusion, respectively, *ΔPOP* respiratory variation in pulse oximetry plethysmographic waveform amplitude, *ICU* intensive care unit, *OR* operating room, *PVI* pleth variability index

Sandroni C et al. Intensive Care Med (2012) 38:1429–1437

Summary PVI and delta POP

- Ten studies in 233 patients
- AUC responders 0.85 [95 %CI 0.79–0.92]
- Pooled sensitivity and specificity 0.80 (95 % CI 0.74–0.85) and 0.76 (0.68–0.82), respectively
- Large boluses (500 mL) had better predictive value than small boluses (250 mL)

Sandroni C et al. Intensive Care Med (2012) 38:1429–1437

PVI at different sites

- PVI has been measured in fingers, ear lobules and forehead in anesthetized patients (28 subjects)
- Threshold value differed, but all three were able to predict fluid responsiveness
- PVI (finger)12% AUROC 0.836
- PVI (forehead)15% AUROC 0.906
- PVI (ear)16% AUROC 0.880

Desgranges FP et al. Br J anestesiol. 2011 Sep;107(3):329-35

PVI – not always reliable

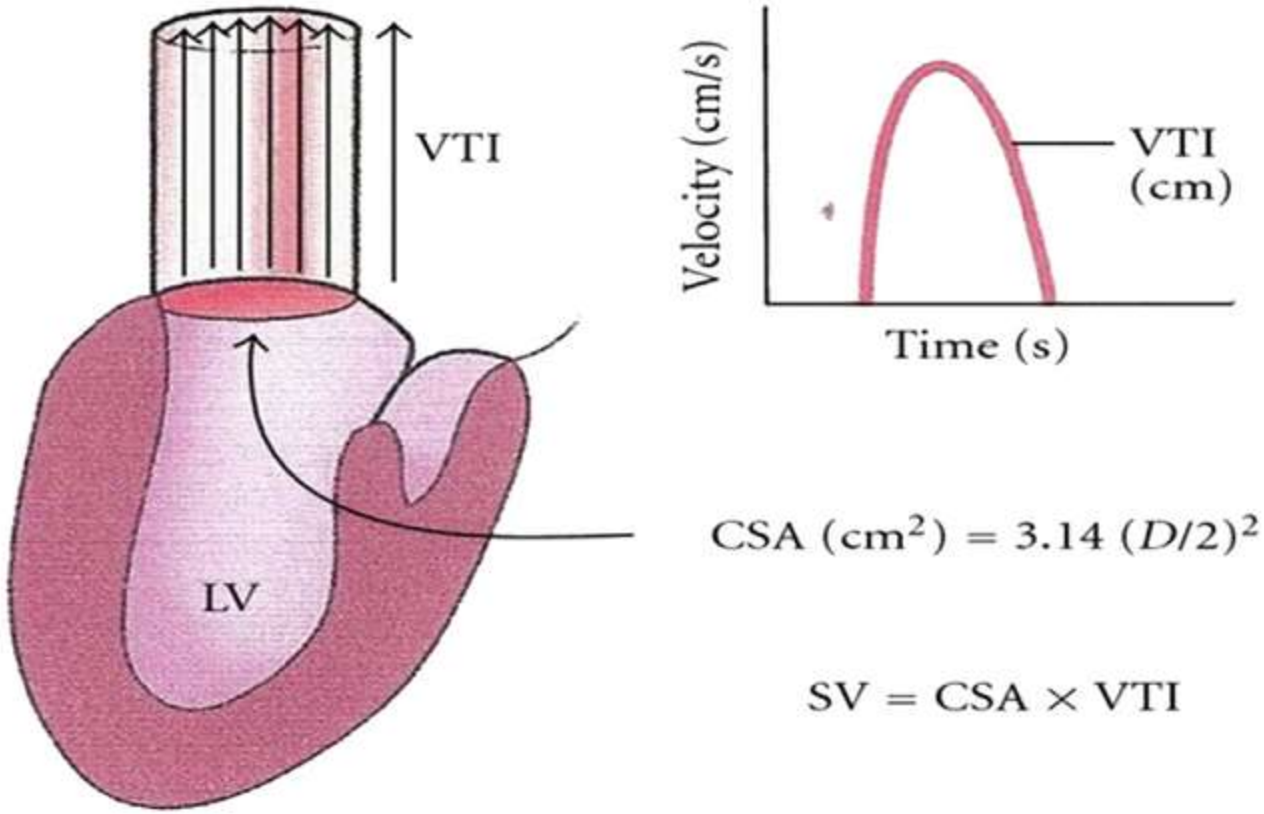
- In patients receiving norepinephrine PVI 16% or more predicted fluid responsiveness (sens 47% specificity 90%, AUROC 0.68) when compared with PPV, SVV it was poor *
- PVI had a poor predictive value for fluid responsiveness in elective cardiac surgery patients (AUROC 0.60 with 95% CI 0.48-0.71)

*Monnet X et al. Br J Anaesth. 2013 Feb; 110(2):207-13
** Fischer Mo et al. J cardio Vasc anaesth. 2013 Dec;27(6):1087-93

Echocardiography in ICU

- LV end diastolic volume and area – assessment of preload
- Preload and fluid responsiveness assessment by IVC measurements
- Estimation of LA pressure
- Cardiac output assessment
- LV and RV cavity size, function
- Pericardial effusion identification

Cardiac output estimation



Otto CM. Textbook of clinical echocardiography. 3rd edition

Kenaan M et al. Crit Care Clin 30 (2014) 413–445

Cardiac output = stroke volume × Heart rate(HR)

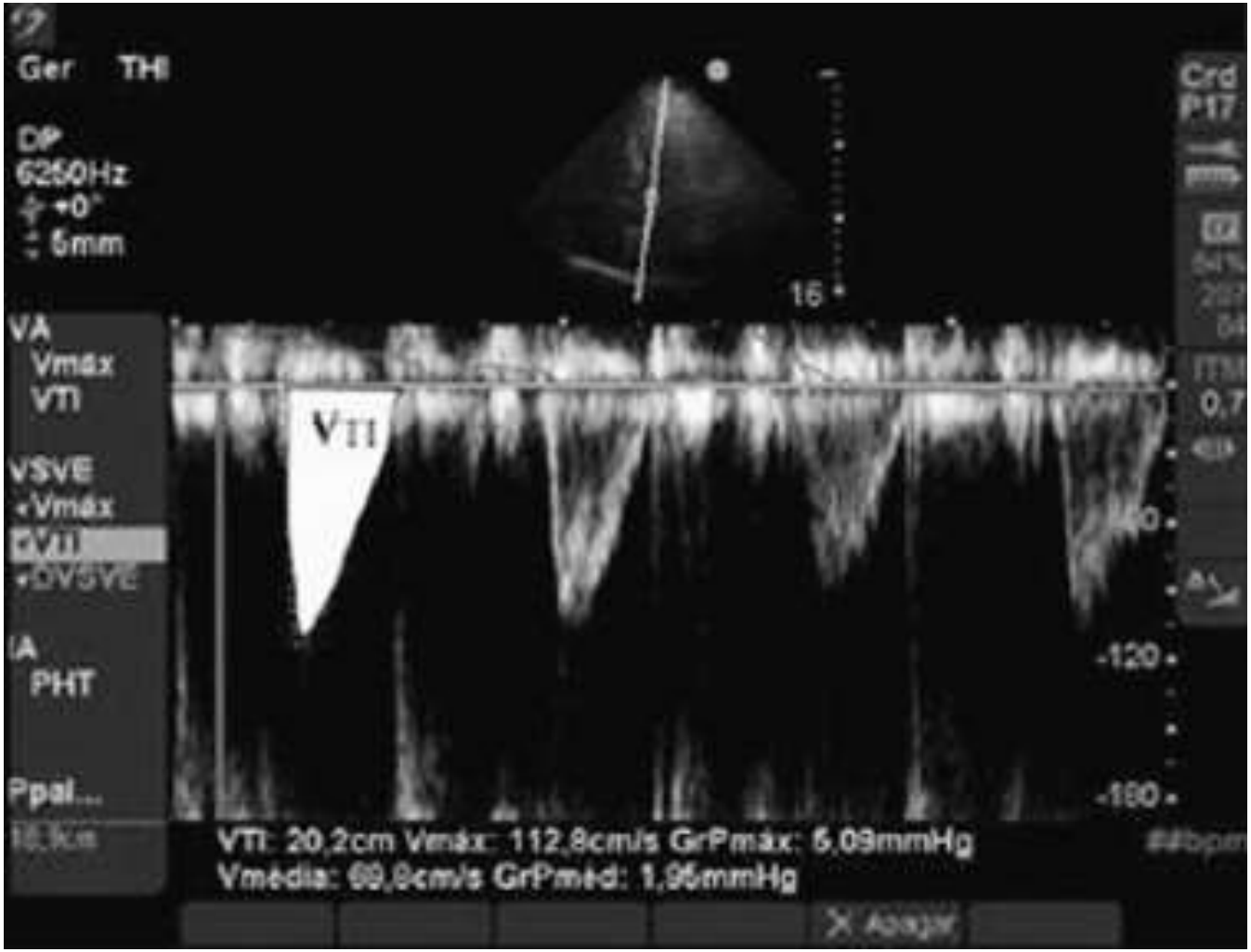
$= CSA \times VTI\ (LVOT) \times HR$

$= \pi\ d^2/4 \times VTI \times HR$

$= 0.785\ (d^2 \times VTI) \times HR$

CSA- cross sectional area of LVOT
VTI – velocity time integral measured at LVOT
LVOT – LV outflow tract
d- Diameter of aortic valve (measured in parasternal long axis view at the level of aortic leaflet insertion)

VTI at LVOT


Ger THI
DP
6250Hz
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Vmax
IA
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VTI
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P17
0,7
-120
-180
VTI: 20,2cm Vmáx: 112,8cm/s GrPmáx: 5,09mmHg
Vmédia: 69,8cm/s GrPméd: 1,95mmHg
Apagar

Cardiac output estimation – other methods

- Apart from doppler based measurements, LV volume estimation may also be used to measure cardiac output by echocardiography
- However these are not accurate, hence aortic doppler measurements are to be preferably used

(based on TEE measurements, not TTE)

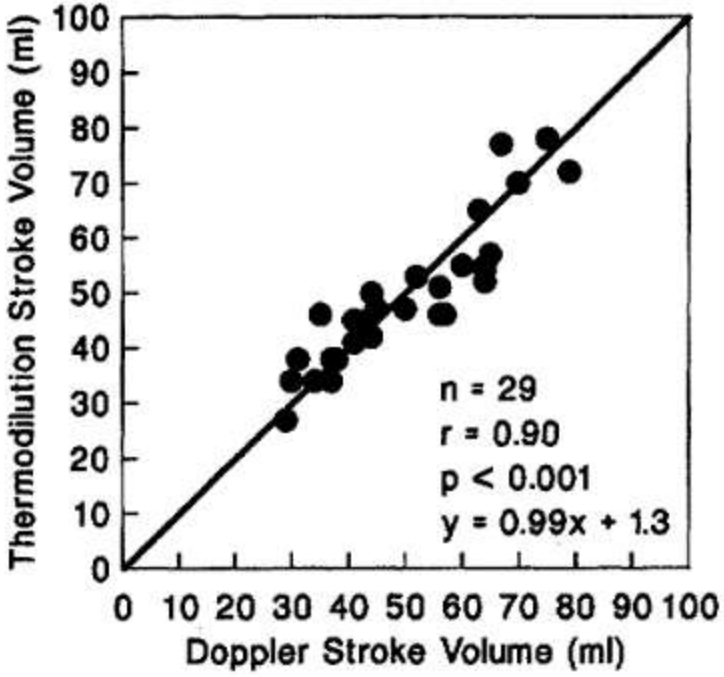
Axler O et al. Intensive care Med. 2003 Feb;29(2):208-17

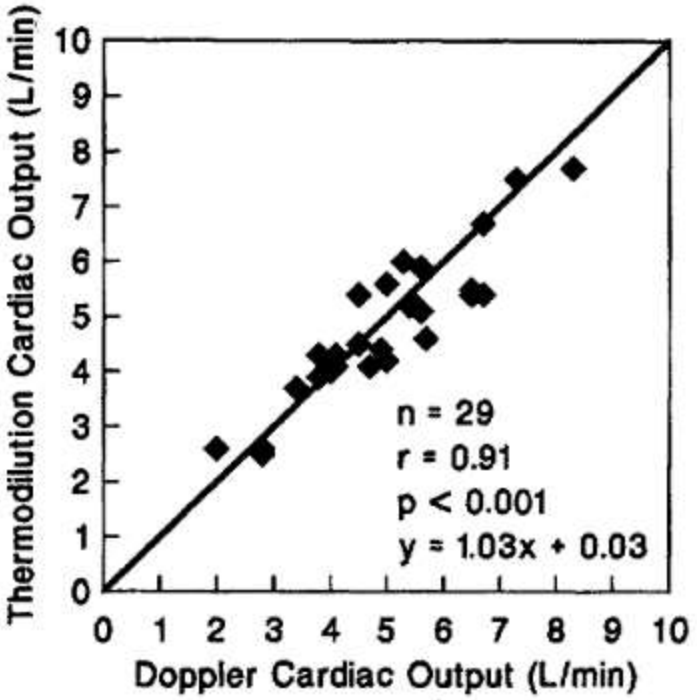
Correlation between thermodilution and doppler echocardiography in measuring CO

- 29 patients (10 had cardiac open surgeries, 9 had myocardial infarction)
- Doppler echocardiography (transesophaegeal) done proximal to the aortic valve leaflet (LVOT view)
- Measurement was possible in 88% patients
- LV stroke volume = Velocity time integral (VTI) x cross sectional area
- Thermodilution to determine CO used 10 mL iced 5% dextrose as indicator

Feinbergh MS et al. Chest 1995;107:769–73

Correlation between thermodilution and doppler echocardiography in measuring CO





Feinbergh MS et al. Chest 1995;107:769–73

- Cardiac output may also be measured across mitral and pulmonary valves
- But presence of MR in critically ill patients may pose some difficulty
- Most studies use aortic valve and LVOT as the site of doppler measurement

Aortic blood flow velocity in determining fluid responsiveness

- Echocardiographic measurement of the indexed LV end-diastolic area(EDAI) shown to reflect more accurately the LV preload compared with pulmonary artery occlusion pressure
- Able to detect changes in LV function caused by acute blood loss (Cheung AT et al. Anesthesiology 1994; 81:376 –387)
- But this had previously failed in patients with sepsis and septic shock (Tavernier B et al. Anesthesiology 1998; 89:1313–1321)

Feissel M et al. CHEST 2001; 119:867– 873

Aortic blood flow velocity in determining fluid responsiveness

- 19 mechanically ventilated septic shock patients (no arrhythmias, no contraindication for TEE, no AR, paO2/fiO2 ratio not less than 100)
- Majority were on inotropes (single inotrope at least in 13)
- VCV with tidal volume 8 to 10 mL/kg, PEEP 6 +/- 3 cmH2O, sedated, and paralysed temporarily if excessive respiratory efforts
- Measurements pre and post fluid challenge
- 8 ml/kg of 6% HES given as the bolus fluid over 30 mts
- Cardiac index increase by > 15% taken as responders

Feissel M et al. CHEST 2001; 119:867– 873

Measurements

- LV end diastolic measurements : esophageal probe transgastric, short-axis, cross-sectional view of the LV at the mid-papillary muscle level
- End diastole – echo frame showing, largest LV CSA, after the peak of R wave
- LV area/ BSA was taken as EDAI (indexed LV end-diastolic area)

Feissel M et al. CHEST 2001; 119:867– 873

Aortic blood flow velocity measurement

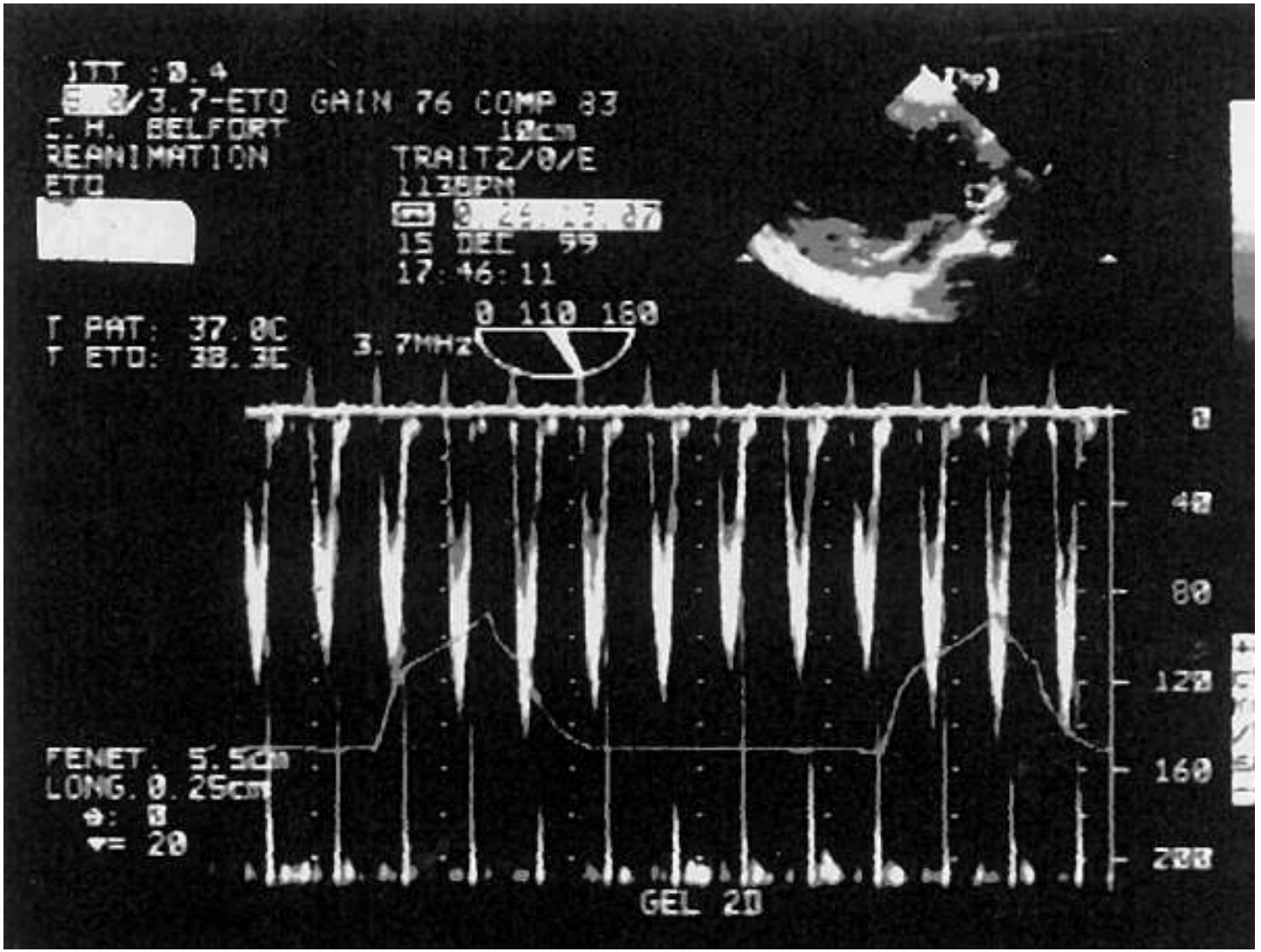
$$\Delta \mathrm{Vpeak}\,(\%) = 100 \times (\mathrm{Vpeakmax} - \mathrm{Vpeakmin})/$$
$$[\mathrm{Vpeakmax} + \mathrm{Vpeakmin})/2].$$

Delta V peak is the respiratory changes in V peak:

V peakmax and V peakmin are the maximum and minimum respectively velocities in a given respiratory cycle

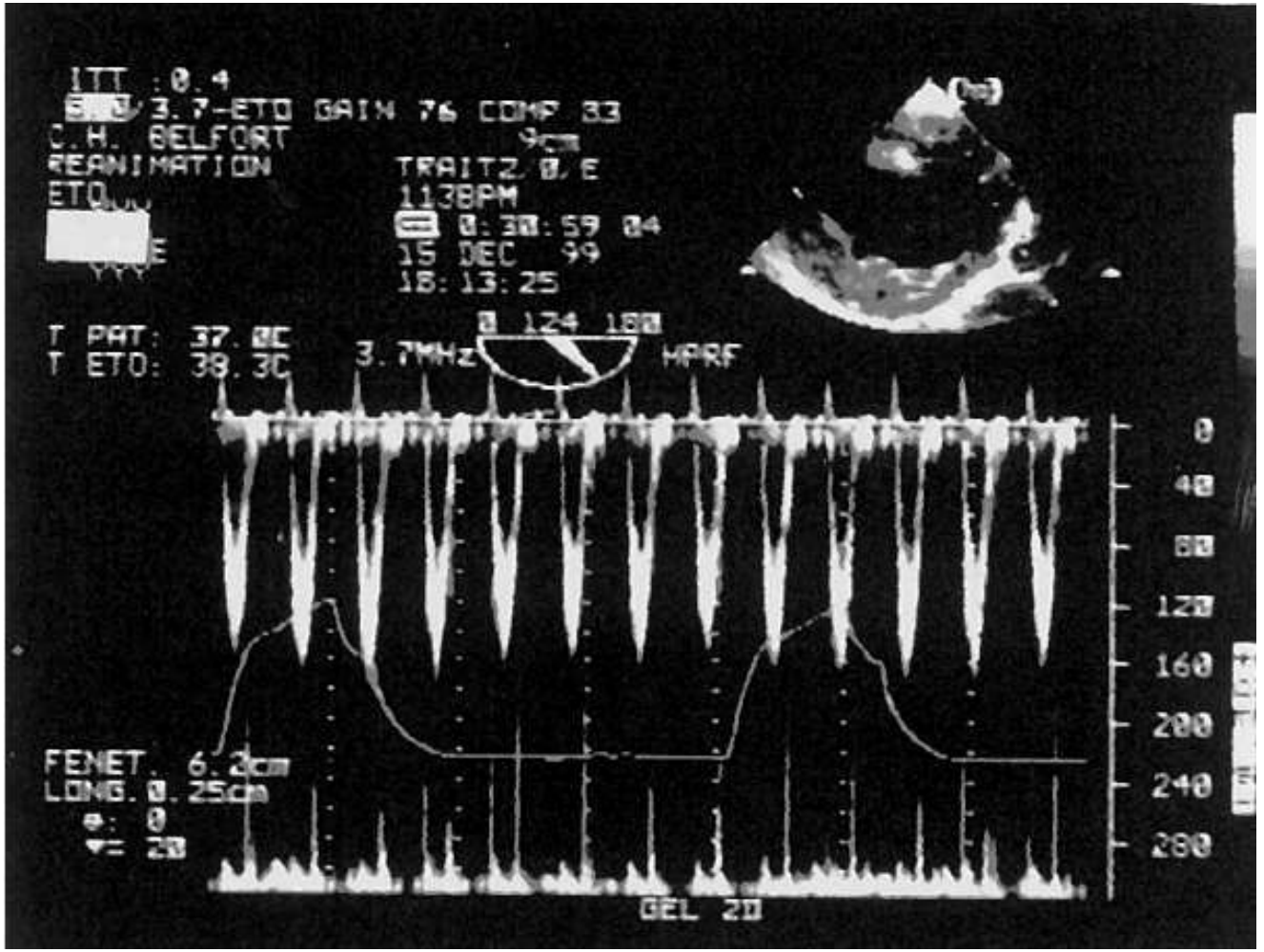
Feissel M et al. CHEST 2001; 119:867– 873

Before fluids



Feissel M et al. CHEST 2001; 119:867– 873

After fluids



Feissel M et al. CHEST 2001; 119:867– 873

Results

- Baseline EDAI as well as pre and post fluid EDAI were not able to differentiate fluid responders and non-responders
- Delta V peak was a better indicator (12% cut off 100% sensitive and 89% specificity)
- > 12% had PPV of 91% to predict fluid responsiveness
- ≤ 12% had NPV 100% for being a non-responder

Feissel M et al. CHEST 2001; 119:867– 873

Reference	Dynamic parameter assessed	Study design	Result	Conclusion
Monge garcia et al. Crit care.2009;13(5):R142	**Brachial artery peak velocity variation**	38 MV patients 500 ML colloid for volume expansion Responders had SV increase by 15% or more after volume expansion Radial artery pressure variation (delta PPrad) and SV variation measured by FloTrac/Vigileo	19 responders All three parameters were significantly different at baseline among responders vs. non-responders	**Delta Vpeakbrach >10%** had 74% sensitivity And 95% specificity to predict responders **DeltaPPrad > 10%** 95% sensitivity and 95% specificity **Delta SVVigileo > 11%** 79% sensitivity 89% specificity

Reference	Dynamic parameter assessed	Study design	Result	Conclusion
	Radial Artery Pulse Pressure Variation Correlation with Brachial Artery Peak Velocity Variation	30 VCV patients, Vt 9+-2 mL/kg, PEEP 7+-3cmH2O Responders had deltaPP cutoff 13% after volume expansion Radial artery catheter was used for arterial wave tracing. Delta PP calculated from maximum PP and minimum PP over 30s	CVP Delta PP And Brachial artery velocity variation measured by IM residents with hand held doppler (30 minute training)	Delta Vpeak-BA correlated well with Delta PP (r 0.84) **Delta Vpeak-BA > 16%** 91% sensitivity and 95% specificity for 13% deltaPP variation in responders **Poor correlaton of CVP and delta Vpeak BA as well as delta PP**

Reference	Dynamic parameter assessed	Study design	Result	Conclusion
Luzi et al. Journal of Critical Care 28 (2013) 902–907	**Femoral artery blood flow Doppler**	52 MV patients 500 ML 0.9% NS for volume expansion Responders had SV increase by 15% or more after volume expansion Cardiac output estimation pre and post fluid performed by measuring peak aortic flow velocity by TTE	26 responders and 26 non responders Velocity time integral (VTIf) And maximal systolic velocity (Vfmax) measured pre and post fluid challenge	**VTIf increase >10%** had 80% sensitivity And 85% specificity to predict responders (PPV 84% and NPV 81%) **Vfmax > 7%** 84% sensitivity and 73% specificity PPV 74% and NPV 86%

Pulse pressure variability (PPV)

- Systolic pressure variation (SPV) and pulse pressure variation (PPV) during mechanical ventilation, shown to predict the hemodynamic effects of volume expansion in patients with septic shock
- Mean percentage of PPV (%PPV) and percentage of SPV(%SPV) calculated as:

$$\%SPV = (SBPmax - SBPmin)/[(SBPmax + SBPmin)/2] \times 100\%$$

$$\%PPV = (PPmax - PPmin)/[(PPmax + PPmin)/2] \times 100\%$$

where SBPmax is maximum SBP, SBPmin is minimum SBP, PPmax is maximum pulse pressure, and PPmin is minimum pulse pressure.

Does pulse pressure variation predict fluid responsiveness in critically ill patients? A systematic review and meta-analysis

Xiaobo Yang and Bin Du*

- 22 studies, 807 MV patients (Vt 8-10 mL/kg), no spontaneous breathing or arrhythmia
- Majority of studies used colloids , HES for fluid challenge
- Six used crystalloids
- CO measured by PiCCO (n-7), PAC (n-6) and TEE/TTE echo-doppler measurements
- PPV measured by waveform analysis with software (n-12), direct arterial analysis in two, LiDCO in 1 and PiCCO (n-7)

Yang and Du. Critical Care2014,18:650

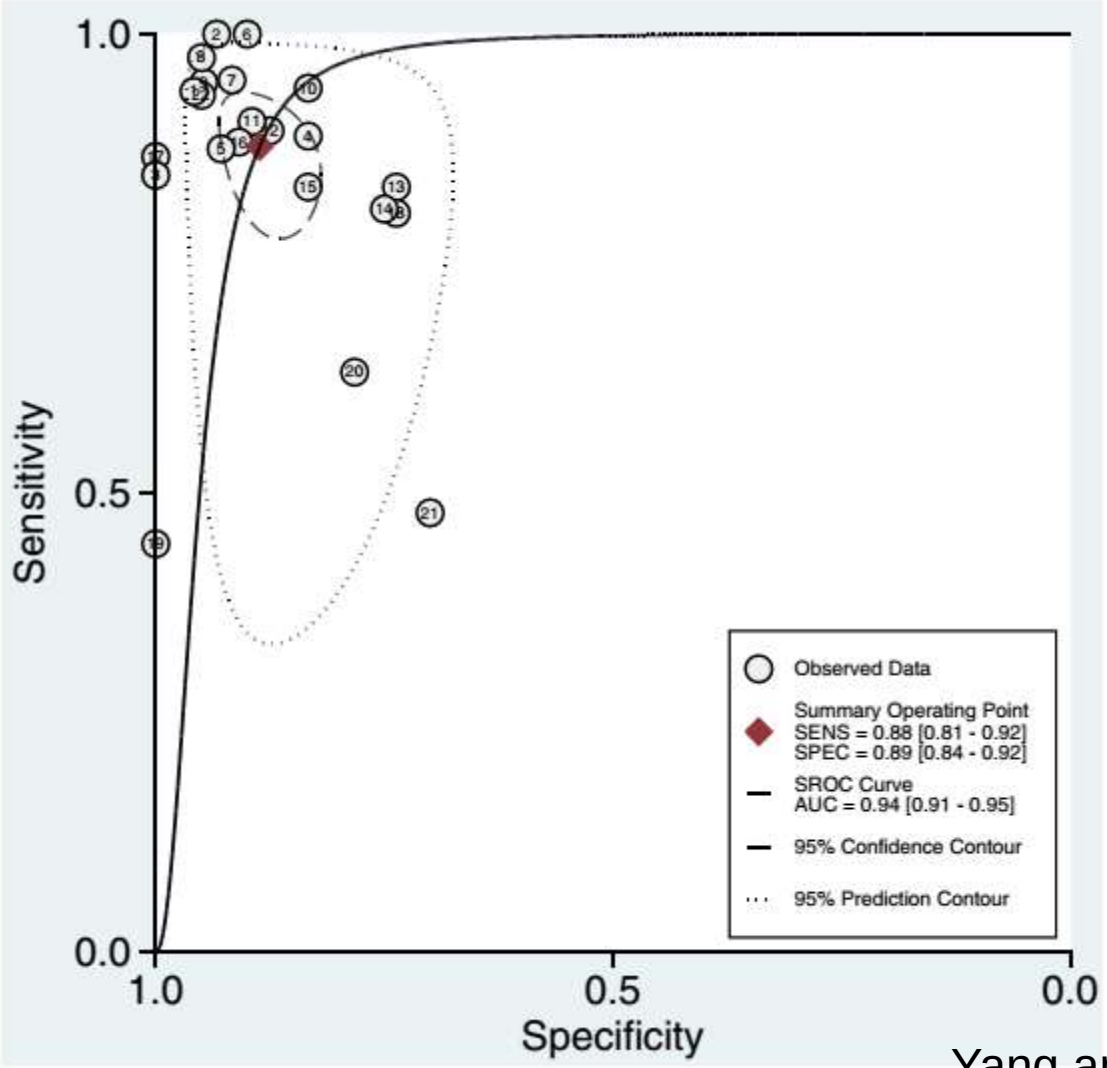
Order	Authors	Year	Vt (ml/kg)	Body weight	Spontaneous breathing	Respiratory rate (times/minute)	Cardiac arrhythmia	Infusion fluid	Infusion volume	Infusion time (minutes)	Indices	Method for indices	Cutoff value (%)
1	Michard and colleagues [23]	2000	8 to 12	NA	No	NA	No	6% HES	500 ml	30	CI	PAC	15
2	Kramer and colleagues [24]	2004	8 to 10	NA	No	NA	No	Blood	500 ml	10 to 15	CO	PAC	12
3	Feissel and colleagues [25]	2005	8 to 10	NA	No	NA	No	6% HES	7 ml/kg	30	CI	Echo	15
4	Charron and colleagues [26]	2006	6 to 10	NA	No	14 to 20	No	6% HES	100 ml	1	SV	Echo	15
5	Monnet and colleagues [27]	2006	NA	NA	No	23 ± 5	No	Saline	500 ml	10	Aortic blood flow	Esophageal Doppler	15
6	Feissel and colleagues [28]	2007	8 to 10	NA	No	NA	No	6% HES	8 ml/kg	30	CI	Echo	15
7	Wyffels and colleagues [29]	2007	8 to 10	NA	No	NA	No	6% HES	500 ml	20	CO	PAC	15
8	Auler and colleagues [30]	2008	8	NA	No	NA	No	LR	20 ml/kg	20	CI	PAC	15
9	Monge Garcia and colleagues [31]	2009	9	Ideal	No	18 to 20	No	6% HES	500 ml	30	SV	FloTrac	15
10	Vistisen and colleagues [32]	2009	8.1[a]	Predicted	NA	14	No	6% HES	500 ml	45	CI	PAC	15
11	Loupec and colleagues [33]	2011	8 to 10	Predicted	No	NA	No	6% HES[b]	500 ml	10	CO	Echo	15
12	Biais and colleagues [34]	2012	8 to 10	Predicted	No	16 ± 3[c]	No	Saline	500 ml	15	SV	Echo	15
13	Cecconi and colleagues [35]	2012	8	Ideal	No	14	No	Colloid	250 ml	5	CO	LiDCO plus	15
14	Fellahi and colleagues [36]	2012	NA	NA	NA	12 ± 2	No	6% HES	500 ml	15	CI	PiCCO2	15
15	Khwannimit and colleagues [37]	2012	≥ 8	NA	No	NA	No	6% HES	500 ml	30	SV	FloTrac	15
16	Monnet and colleagues [38]	2012	8.8[d]	Predicted	No	NA	No	Saline	500 ml	20	CI	PiCCO2	15
17	Monnet and colleagues [39]	2012	8.5[e]	Predicted	No	NA	No	Saline	500 ml	30	CI	PiCCO2	15
18	Yazigi and colleagues [40]	2012	8	NA	No	12	No	6% HES	7 ml/kg	20	SV	PAC	15
19	Fischer and colleagues [41]	2013	8.6	NA	NA	NA[f]	No	6% HES	500 ml	15	CI	PiCCO2	15
20	Fischer and colleagues [42]	2013	8.2	NA	No	NA[c]	No	6% HES	500 ml	15	CI	PiCCO2	15
21	Ishihara and colleagues [43]	2013	≥ 8	Ideal	No	12 to 15	No	10% dextran	250 ml	20	CI	PiCCO	15
22	Monnet and colleagues [44]	2013	9	Predicted	No	NA	No	Saline	500 ml	30	CI	PiCCO2	15

Yang and Du. Critical Care2014,18:650

Order	Authors	Year	Threshold[a] (%)	tp	fp	fn	tn	Sens. (%)	Spec. (%)	Method used to measure PPV
1	Michard and colleagues [23]	2000	13	15	1	1	23	94	96	Waveform analysis with computer software
2	Kramer and colleagues [24]	2004	11	6	1	0	14	100	93	Waveform analysis with computer software
3	Feissel and colleagues [25]	2005	17	11	0	2	9	85	100	Waveform analysis with computer software
4	Charron and colleagues [26]	2006	10	8	2	1	10	89	83	Waveform analysis with computer software
5	Monnet and colleagues [27]	2006	12	14	1	2	13	88	93	Waveform analysis with computer software
6	Feissel and colleagues [28]	2007	12	18	1	0	9	100	94	Waveform analysis with computer software
7	Wyffels and colleagues [29]	2007	11.3	19	1	1	11	95	92	Analysis of printout curves
8	Auler and colleagues [30]	2008	12	38	1	1	19	97	95	Waveform analysis with computer software
9	Monge Garcia and colleagues [31]	2009	10	18	1	1	18	95	95	Waveform analysis with computer software
10	Vistisen and colleagues [32]	2009	6.5	16	1	1	5	94	83	Waveform analysis with computer software
11	Loupec and colleagues [33]	2011	13	19	2	2	17	90	89	Waveform analysis with computer software
12	Biais and colleagues [34]	2012	10	17	2	2	14	89	88	Waveform analysis with computer software
13	Cecconi and colleagues [35]	2012	13	10	5	2	14	83	74	Waveform analysis with LiDCO
14	Fellahi and colleagues [36]	2012	10	17	1	4	3	81	75	Waveform analysis with PiCCO
15	Khwannimit and colleagues [37]	2012	12	20	3	4	15	83	83	Direct analysis of monitored arterial tracing
16	Monnet and colleagues [38]	2012	12	13	0	2	11	85	100	Waveform analysis with PiCCO
17	Monnet and colleagues [39]	2012	10	15	2	2	20	88	91	Waveform analysis with PiCCO
18	Yazigi and colleagues [40]	2012	11.5	33	5	8	14	80	74	Direct analysis of monitored arterial tracing
19	Fischer and colleagues [41]	2013	16	12	0	15	10	44	100	Waveform analysis with PiCCO
20	Fischer and colleagues [42]	2013	14	36	5	21	18	64	78	Waveform analysis with PiCCO
21	Ishihara and colleagues [43]	2013	8.5	11	6	12	14	50	71	Waveform analysis with PiCCO
22	Monnet and colleagues [44]	2013	15	14	1	1	19	93	95	Waveform analysis with PiCCO

Yang and Du. Critical Care2014,18:650

Summary



Median threshold to predict fluid responsiveness 12% (IQR 10-13%)

Sensitivity 0.88

Specificity 0.99

Yang and Du. Critical Care2014,18:650

Arterial waveform analysis (AWA)

- An alternative to more invasive methods of determining cardiac output
- CO and stroke volume estimated from arterial lines
- Fluctuations in stroke volume variation with mechanical ventilation helps predict fluid responsiveness
- Stroke volume pumped by heart reaches peripheral arteries and its strength is dependent on vessel compliance, systemic vascular resistance apart from SV

Principle: heart lung interaction

Positive pressure in MV

Decreases RV filling in inspiration and RV stroke volume

Decreased RV stroke volume reduces LV preload during expiration

These cyclic changes in LV stroke volume are more marked when operating on the steep part of frank starling curve

LV SV respiratory variation therefore indicates biventricular preload dependence and may reflect fluid responsiveness

Principle: heart-lung interaction

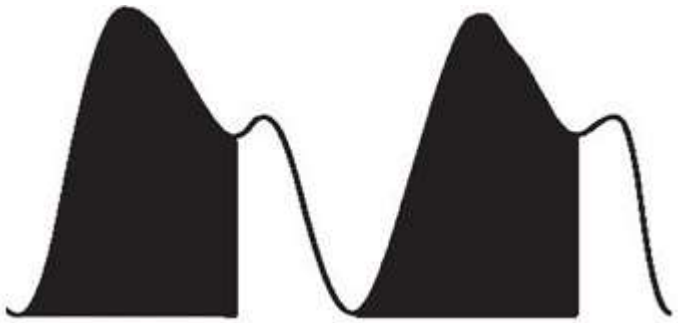
- Hypovolemic patients are more sensitive to these respirophasic changes in SV and pulse pressure

$$SVV = \frac{(SV_{max} - SV_{min})}{SV_{mean} \times 100}$$

and:

$$PPV = \frac{(PP_{max} - PP_{min})}{PP_{mean} \times 100}$$

Arterial waveform analysis - principle



PiCCO (pulse contour CO):

Arterial waveform based CO analysis as well as thermodilution based CO measurement done

(1)Area under the systolic portion of the curve
(2)Vascular compliance'
(3)SVR
(4)A patient-specific calibration factor are all needed

External measurement of CO and calibration are required (transpulmonary thermodilution method is used)

Montenij et al. Curr Opin Anesthesiol 24:651–656

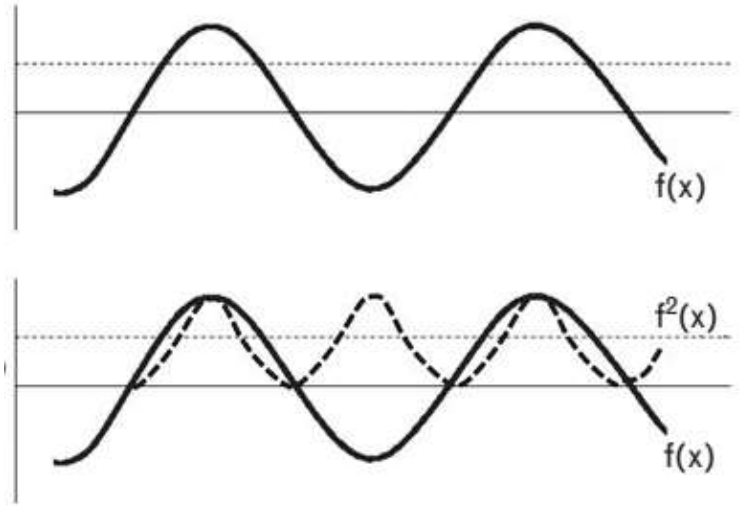
Extravascular lung volume can be estimated

Possible measurements with PiCCO

- ***via continuous pulse contour analysis***
  - Continuous pulse contour cardiac analysis (PCCO)
  - Arterial blood pressure (AP)
  - Heart rate (HR)
  - Stroke volume (SV) and Stroke volume variation (SVV)
  - Systemic vascular resistance (SVR)
- ***via intermittent transpulmonary thermodilution***
  - Transpulmonary cardiac output (C.O.)
  - Intrathoracic blood volume (ITBV)
  - Extravascular lung water (EVLW)
  - Cardiac function index (CFI)

http://www.healthcare.philips.com/main/products/patient_monitoring/products/picco/

Arterial waveform analysis - principle



LiDCO:

CO derived from lithium indicator dilution curve

Arterial waveform based analysis along with lithium indicator dilution for continuous SV and SVV monitoring

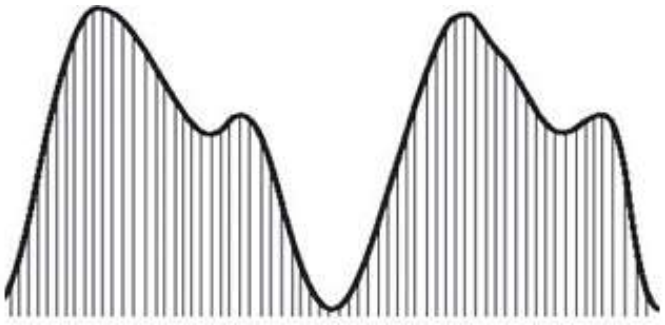
In LiDCO system arterial pressure waveform converted into standardized volume waveform
Using a ‘root mean square’ method

Montenij et al. Curr Opin Anesthesiol 24:651–656

LiDCO

- A small dose of lithium injected (central or peripheral line)
- Lithium concentration measured by lithium sensitive electrode in arterial line
- From the concentration-time curve cardiac output is calculated
- This measurement is then used to calibrate pulse contour analysis software. And now from this continuous cardiac output monitoring is possible by analyzing arterial pressure waveform
- Initial calibration and recalibration required (as in PiCCO)

Arterial waveform analysis - principle



FloTrac sensor and Vigileo monitoring system:

Arterial waveform sampled every 20 s at 100 Hz, resulting in 2000 data points

Stroke volume = Standard deviation of these data points × conversion factor

Conversion factor is the factor required to derive volume parameter from pressure parameter (depends on arterial compliance and waveform characteristics)

Montenij et al. Curr Opin Anesthesiol 24:651–656

Vigileo-FloTrac™ system

- Introduced in 2005
- Useful in
  - Cardiac output measurement (compared with PAC in >50 studies)
  - Tracking cardiac output changes, goal directed therapies in perioperative patients (not evaluated in sepsis/critically ill)
  - Predicting fluid responsiveness (SVV and dynamic preload indices)

Barash PG et al. Journal of Cardiothoracic and Vascular Anesthesia, Vol 28, No 5 (October), 2014: pp 1361–1374

Vigileo-FloTrac™ system

- First and second generation devices had problem in measuring cardiac output and were unreliable at high and low SVR states

- Third generation devices, have improved thereby ensuring better evaluation of vasomotor tone and SVR (but even these fail at extreme SVR as in septic shock patients)

Barash PG et al. Journal of Cardiothoracic and Vascular Anesthesia, Vol 28, No 5 (October), 2014: pp 1361–1374

Stroke volume variation by FloTrac

- SVV > 15% good predictive value for fluid responsiveness, AUC 0.94
- But this prediction was better at 8 ml/kg tidal volume than 6 mL/kg (0.776 vs. 0.648)
- With low tidal volume, pleural and transpulmonary pressures may be low to produce significant respirophasic variation

Suehiro et al. J Anesth 25:777-780, 2011
Barash PG et al. Journal of Cardiothoracic and Vascular Anesthesia, Vol 28, No 5 (October), 2014: pp 1361–1374

Characteristics		FloTRac system	PiCCO	LiDCO
Principle		SD of 2000 wave points	Area under systolic portion of arterial waveform analysis	Root mean square method applied to arterial pressure signal
Calibration		Not required	Thermal dilution	Li indicator dilution
Require ment	Arterial	Peripheral or central	Central only **(femoral/axillary)**	Peripheral or central
	CV line	-	required	-
SVV		yes	yes	yes
PPV		No	yes	yes
Advantages		Minimally invasive Operator independent Easy to use	More robust in hemodynamic instability Broad hemodynamic monitoring	Minimally invasive, easy usage Better in hemodynamically unstable patients
Disadvantages		Less reliable in vasoplegic patients and in hemodynamic instability	More invasive Requires calibration	Overestimation in lithium treated patients NMBAs may affect sensor

Montenij et al. Curr Opin Anesthesiol 24:651–656

Drawbacks

- AWA may not be reliable in arrhythmias, peripheral arterial disease, AR, Valvular heart disease, cardiac shunts
- Trials were done on mechanically ventilated paralysed patients with Vt 8-10 mL/kg
- Role in ARDS patients requires evaluation

Pulmonary artery catheters

- Invasive hemodynamic monitoring device
- Several parameters can be obtained
- Cardiac output estimation by PAC used as one of the reference standards (thermodilution technique)
- Not indicated routinely
- Especially after non-invasive (echo) and minimally invasive options for measuring CO are present (PiCCO, LiDCO)

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Derived parameters for cardiovascular and oxygen dynamics

Cardiovascular Dynamics	
Cardiac index (L/min/m^2) = $\frac{\text{CO}\left(\frac{\text{L}}{\text{min}}\right)}{\text{BSA (m}^2\text{)}}$	2.5–4 L/min/m^2
Stroke volume (L/beat) = $\frac{\text{CO}\left(\frac{\text{L}}{\text{min}}\right)}{\text{HR}\left(\frac{\text{beats}}{\text{min}}\right)}$	0.06–0.1 L/beat
Stroke volume index (L/beat/m^2) = $\frac{\text{SV}\left(\frac{\text{L}}{\text{beat}}\right)}{\text{BSA (m}^2\text{)}}$	0.033–0.047 L/beat/m^2
MAP (mm Hg) = $\frac{2\text{Diastolic} + \text{Systolic}}{3}$	70–110 mm Hg
SVR (dyne-sec-cm^{-5}) = $\frac{\text{MAP (mm Hg)} - \text{MRAP (mm Hg)}}{\text{CO}\left(\frac{\text{L}}{\text{min}}\right)} \times 80$	800–1200 dyne-sec-cm^{-5}
SVRI ([dyne-sec-cm^{-5}]/m^2) = $\frac{\text{MAP (mm Hg)} - \text{MRAP (mm Hg)}}{\text{CI}\left(\frac{\text{L}}{\text{min}}\right)} \times 80$	1970–2390 [dyne-sec-cm^{-5}]/m^2
PVR (dyne-sec-cm^{-5}) = $\frac{\text{mPAP (mm Hg)} - \text{PCWP (mm Hg)}}{\text{CO}\left(\frac{\text{L}}{\text{min}}\right)} \times 80$	<250 dyne-sec-cm^{-5}
PVRI ([dyne/sec/cm^{-5}]/m^2) = $\frac{\text{mPAP (mm Hg)} - \text{PCWP}}{\text{CI}} \times 80$	255–285 [dyne-sec-cm^{-5}]/m^2
LVSWI (g-m/m^2/beat) = 0.0136[SVI × (MAP − PCWP)]	50–62 g-m/m^2/beat
RVSWI (g-m/m^2/beat) = 0.0136[SVI × (mPAP − RAP)]	5–10 g-m/m^2/beat
Oxygen Dynamics	
DO_2 (mL/min/m^2) = CO $\left(\frac{\text{mL}}{\text{min}}\right) \times CaO_2$ = CO [(Hb × SaO_2 × 1.34) + (PaO_2 × 0.0031)]	500–600 mL/min
VO_2 (mL/min) = 13.4[CO × Hb × (SaO_2 − SvO_2)]	200–250 mL/min
O_2ER (%) = O_2 ER = $100\left(\frac{VO_2}{DO_2}\right)$	25%–30%

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The NEW ENGLAND JOURNAL of MEDICINE

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Pulmonary-Artery versus Central Venous Catheter to Guide Treatment of Acute Lung Injury

- No improved survival or organ function
- More complications than CVC-guided therapy

N Engl J Med 2006;354:2213-24

- Cochrane review (2013), 13 studies with 5686 ICU patients
- High quality evidence that use of PAC did not alter mortality or length of ICU stay

Rajaram S et al. Cochrane Database Syst Rev 2013;(2):CD003408

PiCCO vs. CVP

- A recent study from China, assessed usefulness of PiCCO based monitoring
- Critically ill patients with septic shock and or ARDS included in a recent study
- Planned 715 as sample size, but stopped after 350 due to futility

Zhang Z et al. Intensive Care Med (2015) 41:444–451

Baseline characteristics

Characteristics	PiCCO group ($n = 168$)	Control group ($n = 182$)	P value
Male (n, %)	121 (72.0)	137 (75.3)	0.490
Age (years)	62.1 ± 15.7	64.7 ± 15.2	0.109
APACHE II (median IQR)	29 (21–35)	24 (17–31)	0.0027
SOFA (median IQR)	10 (8–12)	9 (7–12)	0.041
Site of infection (n, %)			0.251
Lung	71 (42.3)	71 (39.0)	
Urinary tract	9 (5.4)	3 (1.7)	
Abdomen	33 (19.6)	35 (19.2)	
Intestine	5 (3.0)	8 (4.4)	
Bloodstream	8 (4.8)	8 (4.4)	
Central nervous system	8 (4.8)	12 (6.6)	
Skin	5 (3.0)	15 (8.2)	
Others	29 (17.3)	30 (16.5)	
Type of patient (n, %)			0.790
ARDS	39 (23.2)	37 (20.3)	
Septic shock	79 (47.0)	87 (47.8)	
Both	50 (30.0)	58 (31.9)	
Sources (n, %)			<0.001
Emergency room	80 (47.6)	85 (46.7)	
Post-operation	31 (18.5)	63 (34.6)	
Floor ward	57 (33.9)	34 (18.7)	
Time from acute onset to ICU admission (h, median IQR)	13 (6–39)	11.5 (5–29)	0.256
Use of vasopressors (n, %)	119 (73.0)	127 (69.8)	0.508
Oxygenation index (mmHg)	180 (125–240)	206 (133–297)	0.041
Platelet count ($\times 10^9$)	133 (84–191)	136 (77.5–196)	0.845
Total bilirubin (mmol/l)	16.1 (9.4–30.5)	16.7 (9.8–31)	0.981
Glasgow coma scale	10 (6–15)	12 (8–15)	0.031
Serum creatinine (mmol/l)	156 (89.5–241.5)	133.5 (85.5–202.5)	0.148

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Outcomes

Outcome variables	PiCCO group ($n = 168$)	Control group ($n = 182$)	P value
Primary outcome			
28-day mortality	83 (49.4)	90 (49.5)	0.993
Secondary outcomes			
Maximum SOFA	13 (10–15)	12 (9–14)	0.023
14-day mortality	68 (40.5)	75 (41.2)	0.889
Days on vasopressor	4 (2–6)	3 (2–6.5)	0.852
Days on MV	6 (3–12)	5.5 (3–12)	0.897
Days on CRRT	4 (3–7)	4.5 (3–7)	0.586
Length of stay in ICU	9 (5–13)	7.5 (4–15)	0.598
Days free of vasopressor in 14 days	10 (0–12)	9 (0–12)	0.562
Days free of MV in 14 days	1 (0–10)	4 (0–12)	0.127
Days free of CRRT in 14 days	11 (3–14)	14 (4–14)	0.0038
Days free of vasopressor in 28 days	14.5 (0–25)	19 (0–26)	0.676
Days free of MV in 28 days	3 (0–24)	6 (0–25)	0.168
Days free of CRRT in 28 days	15.5 (3–28)	21 (4–28)	0.048

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Bioimpedance vector analysis (BIVA)

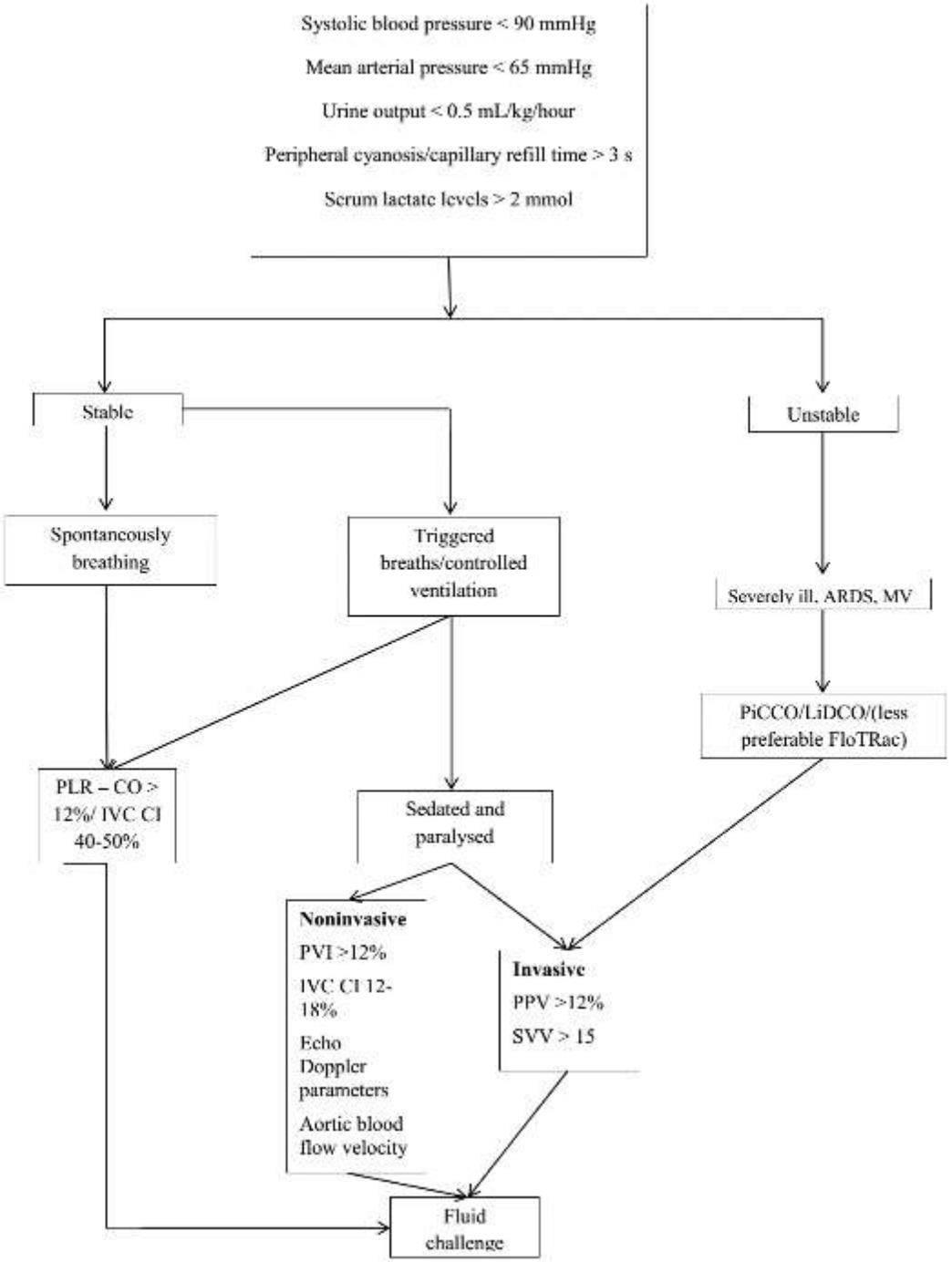
- Non-invasive real time assessment of static volume status
- Principle is similar to ohm's law (V=IR)
- Voltage drop (E) = current (I) * impedance (Z)
- Impedance is related to volume, Z = resistivity * (length^2/ volume)
- High frequency current applied across thorax and impedance measured with electrodes
- Average thoracic impedance considered as an estimate of the static volume of the thorax and dynamic changes in impedance, (correlated with ECG-derived timing measurements) used to calculate hemodynamic parameters

Kalantri et al. Kidney International (2013) 83, 1017–1028

Summary

Method	Invasive or noninvasive	Static or dynamic	Assess fluid responsiveness	Comments
Historical findings	Noninvasive	Static	No	Of limited value with poor correlation with invasive pressure measurements
Physical exam	Noninvasive	Static and dynamic	Yes	Of limited value but serial examinations may detect changes in organ perfusion
Chest radiograph	Noninvasive	Static	No	Requires use of standardized measures of vascular pedicle width and cardiothoracic ratio. Serial chest X-ray may be helpful in determining effects of fluid therapy
Central venous pressure	Invasive	Static	No	Poor correlation with fluid responsiveness
Pulmonary capillary wedge pressure	Invasive	Static	No	Poor correlation with fluid responsiveness
Echocardiogram	Noninvasive	Static	No	Single measures of cardiac chamber volume hard to assess. Serial measures may be helpful
Stroke volume or pulse pressure variation	Invasive (pulse oximeter method in noninvasive)	Dynamic	Yes	Requires sedated, mechanically ventilated patient
Esophageal doppler	Invasive	Dynamic	Yes	Not useful for continuous measurements
Vena cava diameter	Noninvasive	Dynamic	Yes	Body habitus dependent
Passive leg raising	Noninvasive (bioreactance, end-tidal CO_2) Invasive (FloTrac or PiCCO or LiDOO)	Dynamic	Yes	Unreliable with intra-abdominal hypertension
End-expiratory occlusion	Passive leg raising	Dynamic	Yes	Requires 15-s end-expiratory occlusion
Bioimpedance	Noninvasive	Static	No	Not able to assess intravascular volume

Kalantri et al. Kidney International (2013) 83, 1017–1028



Less reliable in the presence of valvular heart disease, arrhythmias