Preload optimisation in severe sepsis

and septic shock

Prof. Jean-Louis TEBOUL



Medical ICU Bicetre hospital University Paris South France



onstruire l'avenir

Conflicts of interest

Member of the Medical Advisory Board of Pulsion

Decision of starting fluid administration

- presence of hemodynamic instability/peripheral hypoperfusion (mottled skin, hypotension, oliguria, hyperlactatemia...)
- and presence of **preload responsiveness**
- and limited risks of fluid overload

Fluid Challenge

> Predictors of fluid responsiveness/unresponsiveness

Fluid challenge revisited

Jean-Louis Vincent, MD, PhD, FCCM; Max Harry Weil, MD, PhD, ScD (Hon), FCCM

Crit Care Med 2006; 34:1333-1337

- Rate of infusion: 500-1000 mL crystalloids or 300-500 mL colloids over 30 mins
- Goal: **reversal** of the **marker of perfusion failure** that prompted the fluid challenge (ex: hypotension, tachycardia, oliguria, etc)
- Safety limits: CVP of 15 mmHg measured every 10 mins

Fluid challenge revisited

Jean-Louis Vincent, MD, PhD, FCCM; Max Harry Weil, MD, PhD, ScD (Hon), FCCM

Crit Care Med 2006; 34:1333-1337

Limitations

• Fluid challenge cannot serve as a <u>test</u> to <u>predict</u> fluid responsiveness

>First, it is not a test but a real therapy

500-1000 mL crystalloids or **300-500 mL** colloids/30 mins **Not negligible amounts!**

>Second, by definition, it cannot predict fluid responsiveness

• Fluid challenge is successful in only 50% cases

Predicting Fluid Responsiveness in ICU Patients*

A Critical Analysis of the Evidence

Frédéric Michard, MD, PhD; and Jean-Louis Teboul, MD, PhD

CHEST 2002, 121:2000-8

| Source | Patients, No. | FC, No. | Fluid Infused | Volume Infused, mL | Speed of FC, min | Definition of Response | Re | Rate of esponse, % |
|------------------------------------|------------------|------------|------------------|-----------------------|---------------------|---------------------------|----|-----------------------|
| Calvin et al ² | 28 | 28 | 5% Alb | 250 | 20-30 | $\Delta SV > 0\%$ | | 71 |
| Schneider et al ³ | 18 | 18 | \mathbf{FFP} | 500 | 30 | $\Delta SV > 0\%$ | | 72 |
| Reuse et al ⁴ | 41 | 41 | 4.5% Alb | 300 | 30 | $\Delta \text{CO} > 0\%$ | | 63 |
| Magder et al ⁵ | 33 | 33 | 9% NaCl | 100 - 950 | | $\Delta \text{CO} > 250$ | | 52 |
| | | | | | | mL/min | | |
| Diebel et al ⁶ | 15 | 22 | R. lactate | 300-500 | | $\Delta \text{CO} > 10\%$ | | 59 |
| | | | Colloids | 500 | | | | |
| Diebel et al ⁷ | 32 | 65 | R. lactate | 300-500 | | $\Delta \text{CO} > 20\%$ | | 40 |
| Wagner and | 25 | 36 | 9% NaCl | 938 ± 480 | 7 - 120 | $\Delta SV > 10\%$ | | 56 |
| Leatherman ⁸ | | | 5% Alb, FFP | $574~\pm~187$ | | | | |
| Tavernier et al ⁹ | 15 | 35 | HES | 500 | 30 | $\Delta { m SV} > 15\%$ | | 60 |
| Magder and Lagonidis ¹⁰ | 29 | 29 | 25% Alb | 100 | 15 | $\Delta \text{CO} > 250$ | | 45 |
| | | | 9% NaCl | 150 - 400 | | mL/min | | |
| Tousignant et al ¹¹ | 40 | 40 | HES | 500 | 15 | $\Delta SV > 20\%$ | | 40 |
| Michard et al^{12} | 40 | 40 | HES | 500 | 30 | $\Delta \text{CO} > 15\%$ | | 40 |
| Feissel et al ¹³ | 19 | 19 | HES | 8 mL/kg | 30 | $\Delta \text{CO} > 15\%$ | | 53 |
| Total | 334 | 406 | | 0 | | | | 52 |

Fluid challenge revisited

Jean-Louis Vincent, MD, PhD, FCCM; Max Harry Weil, MD, PhD, ScD (Hon), FCCM

Crit Care Med 2006; 34:1333-1337

Limitations

• Fluid challenge cannot serve as a test to predict fluid responsiveness

>First, it is not a test but a real therapy

500-1000 mL crystalloids or **300-500 mL** colloids/30 mins **Not negligible amounts!**

Second, by definition, it cannot predict fluid responsiveness

- Fluid challenge is successful in only 50% cases
- Fluid challenge is potentially risky

>Assessing fluid responsiveness is a « every day » issue

→ **Repetition** of fluid challenges could be **harmful**

Sepsis in European intensive care units: Results of the SOAP study*

Jean-Louis Vincent, MD, PhD, FCCM; Yasser Sakr, MB, BCh, MSc; Charles L. Sprung, MD; V. Marco Ranieri, MD; Konrad Reinhart, MD, PhD; Herwig Gerlach, MD, PhD; Rui Moreno, MD, PhD; Jean Carlet, MD, PhD; Jean-Roger Le Gall, MD; Didier Payen, MD; on behalf of the Sepsis Occurrence in Acutely III Patients Investigators

Crit Care Med 2006; 34:344–353

| Table 7. Multivariate, forward stepwise logistic regression analysis in sepsis patients ($n = 1177$), with intensive care unit mortality as the dependent factor | | | | | | | | |
|--|---|----------------------|--|--|--|--|--|--|
| | OR (95% CI) | p Value | | | | | | |
| SAPS II score ^a (per point increase) Cumulative fluid balance ^b (per liter increase) | 1.0 (1.0-1.1) 1 1 (1 0-1 1) | <.001 | | | | | | |
| Age (per year increase) Initial SOFA score (per point increase) | $1.0 (1.0-1.0) \\ 1.1 (1.0-1.1)$ | .001 | | | | | | |
| Blood stream infection Cirrhosis | 1.7 (1.2-2.4) 2.4 (1.3-4.5) | .004 .008 | | | | | | |
| <i>Pseudomonas</i> infection Medical admission Female gender | $1.6 (1.1-2.4) \\ 1.4 (1.0-1.8) \\ 1.4 (1.0-1.8)$ | .017 .049 .044 | | | | | | |





Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD¹; Mitchell M. Levy, MD²; Andrew Rhodes, MB BS³; Djillali Annane, MD⁴; Herwig Gerlach, MD, PhD⁵; Steven M. Opal, MD⁶; Jonathan E. Sevransky, MD⁷; Charles L. Sprung, MD⁸; Ivor S. Douglas, MD⁹; Roman Jaeschke, MD¹⁰; Tiffany M. Osborn, MD, MPH¹¹; Mark E. Nunnally, MD¹²; Sean R. Townsend, MD¹³; Konrad Reinhart, MD¹⁴; Ruth M. Kleinpell, PhD, RN-CS¹⁵; Derek C. Angus, MD, MPH¹⁶; Clifford S. Deutschman, MD, MS¹⁷; Flavia R. Machado, MD, PhD¹⁸; Gordon D. Rubenfeld, MD¹⁹; Steven A. Webb, MB BS, PhD²⁰; Richard J. Beale, MB BS²¹; Jean-Louis Vincent, MD, PhD²²; Rui Moreno, MD, PhD²³; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup^{*}

11. We recommend a conservative fluid strategy for patients with established sepsis-induced ARDS who do not have evidence of tissue hypoperfusion (grade 1C).

Fluid Challenge

>Predictors of fluid responsiveness/unresponsiveness

Can help to choose the **best** fluid **strategy**

Detecting volume responsiveness and unresponsiveness in intensive care unit patients: two different problems, only one solution

Jean-Louis Teboul^{1,2} and Xavier Monnet^{1,2}

Critical Care 2009, 13:175 (doi:10.1186/cc7979)

Fluid infusion will increase LV stroke volume only if both ventricles are preload responsive



>Fluid Challenge

>Predictors of fluid responsiveness/unresponsiveness

• Static markers of preload



Crit Care Med 2007; 35:64–68





Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD¹; Mitchell M. Levy, MD²; Andrew Rhodes, MB BS³; Djillali Annane, MD⁴; Herwig Gerlach, MD, PhD⁵; Steven M. Opal, MD⁶; Jonathan E. Sevransky, MD⁷; Charles L. Sprung, MD⁸; Ivor S. Douglas, MD⁹; Roman Jaeschke, MD¹⁰; Tiffany M. Osborn, MD, MPH¹¹; Mark E. Nunnally, MD¹²; Sean R. Townsend, MD¹³; Konrad Reinhart, MD¹⁴; Ruth M. Kleinpell, PhD, RN-CS¹⁵; Derek C. Angus, MD, MPH¹⁶; Clifford S. Deutschman, MD, MS¹⁷; Flavia R. Machado, MD, PhD¹⁸; Gordon D. Rubenfeld, MD¹⁹; Steven A. Webb, MB BS, PhD²⁰; Richard J. Beale, MB BS²¹; Jean-Louis Vincent, MD, PhD²²; Rui Moreno, MD, PhD²³; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*





>Fluid Challenge

>Predictors of fluid responsiveness/unresponsiveness

- Static markers of preload
- Dynamic markers of preload responsiveness

o heart-lung interaction tests

o variability of stroke volume and of its surrogates

MV induces cyclic changes in SV only in pts with biventricular preload responsiveness fluid responsiveness occurs only in pts with biventricular preload responsiveness

correlates with the magnitude

of the

induced by

>Fluid Challenge

> Predictors of fluid responsiveness/unresponsiveness

- Static markers of preload
- Dynamic markers of preload responsiveness

o heart-lung interaction tests

o variability of stroke volume and of its surrogates

✓ Invasive indices



FRÉDÉRIC MICHARD, SANDRINE BOUSSAT, DENIS CHEMLA, NADIA ANGUEL, ALAIN MERCAT, YVES LECARPENTIER, CHRISTIAN RICHARD, MICHAEL R. PINSKY, and JEAN-LOUIS TEBOUL

AM J RESPIR CRIT CARE MED 1999;159:935-939

Am J Respir Crit Care Med 2000; 162:134-8



FRÉDÉRIC MICHARD, SANDRINE BOUSSAT, DENIS CHEMLA, NADIA ANGUEL, ALAIN MERCAT, YVES LECARPENTIER, CHRISTIAN RICHARD, MICHAEL R. PINSKY, and JEAN-LOUIS TEBOUL

Am J Respir Crit Care Med 2000,162 134–138



FRÉDÉRIC MICHARD, SANDRINE BOUSSAT, DENIS CHEMLA, NADIA ANGUEL, ALAIN MERCAT, YVES LECARPENTIER, CHRISTIAN RICHARD, MICHAEL R. PINSKY, and JEAN-LOUIS TEBOUL

Am J Respir Crit Care Med 2000,162 134-138



Intensive Care Med (2004) 30:1734–1739 DOI 10.1007/s00134-004-2361-y

ORIGINAL

| FRI Ch | édéric Mic Ristian Ri | CHARD, SANDRING CHARD, MICHAEL | E BOUSSAT, DENIS CHEMI R. PINSKY, and JEAN-L | Alidation of p | British Journal | of Anaesthesia 95 (6): 746- | ss (2005) and correct(| ed flow | Super of vol | ion and stroke | Volume : | and Pulse Press | ure lict fluid |
|-----------|--|---|---|--|---|---|---|---|---|---|--|--|-------------------------------|
| | Pu | Pulse p | ressure val | ime as predict n the prone po Y. Yang ¹ , JK. Shim ² , Y | tors of fluid res osition Y. Song ² , SJ. Seo ² and Y. | ponsiven | ess in patie | nts | s in mo | echanically v ertension | entilate | d patients expe | riencing |
| | Ard Andre Beul | responsi volumes | IVENESS IN P | Prediction o | of fluid responsi | British Journal of A | naesthesia 110 (5): 7 0011, 112,522 9 a continuo | 13-20 (2013) US NON- | r u, weid | iong wir , rieman | <i>BioScie</i> ess in tl | ence Trends. 2013; 7(| 2):101-108. |
| L | Critica Predict | al Care 2006, 1 | Efficacy of f in predict | n C. Richard ^{1,2} and J1 | sessment of art mparison with t es ^{1,2} , A. Ferré ^{1,2} , G. Le Teuff ⁴ L. Teboul ^{1,2} Britich | erial press four other , M. Jozwiak ^{1,2} , A. | sure in critic dynamic in Bleibtreu ^{1,2} , MC. Lo | cally ill ndices e Deley ⁴ , D. Cher | * 1 mla ^{1,3} , ^{cl} | Fadia Haddad, MD,* <i>ular Anesthesia,</i> 2011 | Pressure iveness | e raphic Variat | ions Predict ative Cardiac |
| | stroke The Fluid | area by tran Influence o I Responsiv | powe M. cecconi †, g. M. l. tuccillo | MONTI ² , M. A. HAM ^{1, 3} , G. DELLA ROCC | Predictive va responsivene ventilation s | lue of puess in sep trategies | ilse pressu itic patient | re variat s using l | tion fo | or fluid protective | | -41 | 52 |
| | Cyril C Jean-Xa Alain I | ^{avier} Arteri R. Ed Respo | al Versus Plet onsiveness for | to predict fluid | F. G. R. Freitas*, A. T. | Bafi, A. P. M. No | ascente, M. Assun BJA / | ção, B. Mazza, Advance Acce | , L. C. P. A ess publi | Azevedo and F. R. M shed November 4 | Machado 15, 2012 | BJA fluid ephrine | 99;108:513-7 |
| | Comparison of an automated respiratory systolic variation test with dynamic preload indicators to predict fluid responsiveness after major surgery C. J. C. Trepte ^{†*} , V. Eichhorn [†] , S. A. Haas, K. Stahl, F. Schmid, R. Nitzschke, A. E. Goetz and D. A. Reuter British Journal of Anaesthesia | | | | | | L. Guerin ^{1,2} , M. J | ozwiak ^{1,2} , A. E aicts Fiuia | Bataille ^{1,2} Kespor | ² , F. Julien ^{1,2} , C. Ri | chard ^{1,2} , J-I ng Heart | L. Teboul ^{1,2} | to Guide |
| [| | | | | | | nt for Off-Pu D,* Yunseok Jeon MD, PhD,§ Deok I | Comparis waveform responsiv | son of o m-base veness | n of arterial pressure and plethysmographic -based dynamic preload variables in assessing fluid eness and dynamic arterial tone in patients | | | |
| | recor Matthieu Stéphan | ding anal J Biais, MD; Vin ie Roullet, MD; | ytic method* cent Cottenceau, MD; L Alice Quinart, MD; Fran | aurent Stecken, MD; Ma çois Sztark, MD, PhD | aylis Jean; Laetitia Ottoler | rdio du nghi, MD; | thoracic and Vascul radia A. Derichard | undergoi J. J. Vos*, A. F. | i ng ma j . Kalmar, M. | jor hepatic re . M. R. F. Struys, J. K. G | Section . Wietasch, H. British Journal | G. D. Hendriks and T. W. L. I of Anaesthesia 110 (6): 94 | Scheeren -0-6 (2013) |
| | | . , | | Crit . | Care Med 2012;40:11 | 86–1191 ¹ , F 7. vanct | | | J] | P. Chambon ² and British Journa | l B. Vallet¹ al of Anae | esthesia 103 (5): 678 | 3–84 (2009) |

Assessing the Diagnostic Accuracy of Pulse Pressure Variations for the Prediction of Fluid Responsiveness



Maxime Cannesson, M.D., Ph.D.,* Yannick Le Manach, M.D., Ph.D.,† Christoph K. Hofer, M.D.,‡ Jean Pierre Goarin, M.D.,§ Jean-Jacques Lehot, M.D., Ph.D.,|| Benoît Vallet, M.D., Ph.D.,# Benoît Tavernier, M.D., Ph.D.,#

Anesthesiology 2011; 115:231-41

Conclusion: Despite a strong predictive value, PPV may be inconclusive (between 9% and 13%) in approximately 25% of patients during general anesthesia.

The **larger** the Δ **PP** *before* fluid infusion, the **larger** the **increase** in **CO** *after* fluid infusion



The **smaller** the **PPV** *before* fluid infusion, the **smaller** the **increase** in **CO** *after* fluid infusion

Pulse Pressure Variation

Calculated automatically and displayed in real-time by usual hemodynamic monitors

All these monitors are suitable

to display PPV in real-time











Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: A systematic review of the literature*

Paul E. Marik, MD, FCCM; Rodrigo Cavallazzi, MD; Tajender Vasu, MD; Amyn Hirani, MD

Crit Care Med 2009; 37:2642-2647

| Author | Year | n | Patient | | PPV | SVV | Fluid Challenge | TV (mL/kg) | Device | Cardiac End Point |
|--------------------------|------|-----------------|------------------------|----|-----|-----|---|------------|-----------------------------|----------------------|
| Tovernier (31) | 1008 | 15 | ICII consis | v | N | N | 500 mL HFS | 8 11 | PAC | SVI |
| Michard (32) | 1000 | 13 | ICU-ARDS | N | V | N | 10 PFFP^c | 7_{-12} | PAC | CI |
| Michard (32) | 2000 | 40 | ICU-sensis | V | V | N | 500 mL HFS | 8_12 | PAC | CI |
| Berkenstadt (34) | 2000 | 15 | Neurosuro ^a | N | N | V | 100 mL HES^{b} | 10 | Picco ^e | SV |
| Reuter (35) | 2001 | 20 | Post C Surg | V | N | V | $20 \text{ mL} \times \text{BML}$ delatin | 10 | PiCCO | SVI |
| Reuter (36) | 2002 | $\frac{20}{20}$ | Post C Surg | N | N | v | $20 \text{ mL} \times \text{BMI gelatin}$ | 13_15 | PiCCO | CI |
| Reuter (37) | 2002 | 12 | Post C Surg-2 | N | N | v | $10 \text{ mL} \times \text{BMI HFS}^{b}$ | 10-10 | PiCCO | SVI |
| Redter (51) | 2000 | 14 | Post C Surg-h | 14 | 1 | 1 | $10 \text{ mL} \times \text{BMI HES}^{b}$ | 10 | PiCCO | SVI |
| Rendielid (38) | 2004 | 16 | Post C.Surg | V | V | N | 10 PFP^{c} | 8-10 | PAC | SVI |
| $\operatorname{Rex}(39)$ | 2004 | 14 | Post C.Surg | N | N | v | Trendelenhurg | 8 | PiCCO | SVI |
| Kramer (40) | 2004 | 21 | Post C.Surg | Y | Y | N | 500 mL blood | 8-10 | PAC | CO |
| Marx (41) | 2004 | 10 | ICU-sensis | N | N | Y | 500 mL HES | 8-10 | Picco | |
| Hofer (42) | 2005 | 35 | Post C Surg | N | Y | Ŷ | 10 mL/kg LIES | 10 | PiCCO | SVI |
| Preisman (43) | 2005 | 18 | Post C.Surg | Ŷ | Ŷ | Ŷ | | PCV | PiCCO | SVI |
| De Backer $(44)^d$ | 2005 | 27 | ICU-mixed | N | Ŷ | Ň | 625 ntc | 8-10 | PAC | CI |
| Wiesenack (45) | 2005 | 20 | C.Surg ^a | N | Ŷ | Y | | 7 | PiCCO/PAC | SVI |
| Feissel (46) | 2005 | 20 | ICU-sepsis | N | Ŷ | N | • | 8-10 | TTE | CI |
| Solus-Biguenet (47) | 2006 | 8 | Hepatic surgery | Ν | Y | Ν | 250 mL gelatin ^{b} | 8-10 | PAC | SVI |
| Charron (48) | 2006 | 21 | ICU-mixed | Ν | Y | Ν | 100 mL HES | 8-10 | TEE | SV |
| Natalini (49) | 2006 | 22 | ICU-mixed | Y | Ŷ | N | 500 mL HES | 8 | PAC | CI |
| Wyffels (50) | 2007 | 32 | Post C.Surg | Ν | Y | Ν | 500 mL HES | 8-10 | PAC | CI |
| Feissel (51) | 2007 | 23 | ICU-sepsis | Ν | Y | Ν | 8 mL/kg HES | 8-10 | TEE | CI |
| Lee (52) | 2007 | 20 | Neurosurg ^a | Ν | Y | Ν | 7 mL/kg HES | 10 | Eso Doppler | SVI |
| Cannesson (53) | 2007 | 25 | $C.Surg^a$ | Ν | Y | Ν | 500 mL HES | 8-10 | PAC | CI |
| Cannesson (54) | 2008 | 25 | $C.Surg^a$ | Ν | Y | Ν | 500 mL HES | 8-10 | PAC | CI |
| Auler (55) | 2008 | 59 | Post C.Surg | Ν | Y | Ν | 20 mL/kg LR | 8 | PAC | CO |
| Belloni (56) | 2008 | 19 | C.Surg ^a | Y | Y | Y | 7 mL/kg HES | 8 | LiDCO ^f /PAC | CI |
| Cannesson (57) | 2008 | 25 | C.Surg ^a | Ν | Y | Ν | 500 mL HES | 8-10 | PAC | CI |
| Hofer (58) | 2008 | 40 | Post CABG | Ν | Y | Y | Trendelenburg | 8-10 | FloTrac ^g /PiCCO | SV |
| Biasis (59) | 2008 | 35 | Liver transplant | Ν | Y | Y | Albumin 20 mL \times BMI | 8-10 | FloTrac/TEE | CO |

Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: A systematic review of the literature*

Paul E. Marik, MD, FCCM; Rodrigo Cavallazzi, MD; Tajender Vasu, MD; Amyn Hirani, MD

Crit Care Med 2009; 37:2642-2647



>Fluid Challenge

> Predictors of fluid responsiveness/unresponsiveness

- Static markers of preload
- Dynamic markers of preload responsiveness

o heart-lung interaction tests

o variability of stroke volume and of its surrogates

✓ Invasive indices

✓ Non invasive indices

Prediction of fluid responsiveness by a continuous noninvasive assessment of arterial pressure in critically ill patients: comparison with four other dynamic indices

X. Monnet^{1,2*}, M. Dres^{1,2}, A. Ferré^{1,2}, G. Le Teuff⁴, M. Jozwiak^{1,2}, A. Bleibtreu^{1,2}, M.-C. Le Deley⁴, D. Chemla^{1,3}, C. Richard^{1,2} and J.-L. Teboul^{1,2}

British Journal of Anaesthesia **109** (3): 330–8 (2012)



Non-invasive

finger blood pressure monitoring **device**






Respiratory Changes in Aortic Blood Velocity as an Indicator of Fluid Responsiveness in Ventilated Patients With Septic Shock*

Marc Feissel, MD; Frédéric Michard, MD; Isabelle Mangin, MD; Olivier Ruyer, MD; Jean-Pierre Faller, MD; and Jean-Louis Teboul, MD, PhD

CHEST 2001; 119:867-873



Doppler-echo







Pulse oximeter

British Journal of Anaesthesia 101 (2): 200–6 (2008) doi:10.1093/bja/aen133 Advance Access publication June 2, 2008



Pleth variability index to monitor the respiratory variations in the pulse oximeter plethysmographic waveform amplitude and predict fluid responsiveness in the operating theatre

M. Cannesson^{1*†}, O. Desebbe¹, P. Rosamel¹, B. Delannoy¹, J. Robin², O. Bastien¹ and J.-J. Lehot¹

| Area under | r the curve | Cutoff | | |
|--------------|-------------|------------|--|--|
| ΔPP | 0.938 | 12.5% | | |
| ΔPOP | 0.944 | 12% | | |
| PPV | 0.941 | 10.5% | | |
| PVI | 0.927 | 14% | | |
| CVP | 0.417 | 12.5 mm Hg | | |
| PCWP | 0.396 | 14.5 mm Hg | | |

| Intensive Care Med (2012) 38:1429–1437 | REVIEW |
|--|---|
| Claudio Sandroni Fabio Cavallaro Cristina Marano Chiara Falcone Paolo De Santis Massimo Antonelli | Accuracy of plethysmographic indices as predictors of fluid responsiveness in mechanically ventilated adults: a systematic review and meta-analysis |

| References (first author) | Index | Number of patients/boluses | % Responders | Best threshold | AUC (SE) | Sensitivity | Specificity |
|------------------------------|------------------|----------------------------|-----------------|-------------------|--------------|-------------|-------------|
| Natalini | ΔΡΟΡ | 22/31 | 61.0 | 15.0 | 0.70 (0.094) | 0.63 | 0.83 |
| Solus-Biguenet | ΔΡΟΡ | 8/54 | 42.0 | 9.5 | 0.68 (0.071) | 0.64 | 0.68 |
| Cannesson | ΔΡΟΡ | 25/25 | 60.0 | 13.0 | 0.85 (0.081) | 0.93 | 0.90 |
| Feissel | ΔΡΟΡ | 23/28 | 64.0 | 14.0 | 0.94 (0.050) | 0.94 | 0.80 |
| Wyffels | ΔΡΟΡ | 32/32 | 62.5 | 11.8 | 0.89 (0.061) | 0.90 | 0.83 |
| Hoiseth | ΔΡΟΡ | 25/34 | 64.7 | 11.4 | 0.72 (0.082) | 0.86 | 0.67 |
| Cannesson | ΔPOP^{b} | 25/25 | 64.0 | 12.0 | 0.94 (0.043) | 0.87 | 0.89 |
| | PVI | 25/25 | 64.0 | 14.0 | 0.93 (0.051) | 0.81 | 1.00 |
| Zimmermann | PVI | 20/20 | 75.0 | 9.5 | 0.97 (0.033) | 0.93 | 1.00 |
| Desgranges | PVI | 28/28 | 68.0 | 12.0 | 0.84 (0.077) | 0.74 | 0.67 |
| Hood | PVI | 25/25 | 88.0 | 10.0 | 0.96 (0.031) | 0.86 | 1.00 |
| (large bolus) | | | | | | | |
| Hood | PVI | 25/63 | 36.5 | 10.0 | 0.71 (0.071) | 0.65 | 0.67 |
| (small bolus) | | | | | | | |
| Overall ^a | | 233/365 | 62.3 ± 14.0 | 9.5-15.0 | 0.85 | 0.80 | 0.76 |
| | | | | | [0.79-0.92] | [0.74–0.85] | [0.68–0.82] |

BJA

Pleth variability index is a weak predictor of fluid responsiveness in patients receiving norepinephrine

X. Monnet^{1,2*}, L. Guérin^{1,2}, M. Jozwiak^{1,2}, A. Bataille^{1,2}, F. Julien^{1,2}, C. Richard^{1,2} and J.-L. Teboul^{1,2}



Impact of norepinephrine on the relationship between pleth variability index and pulse pressure variations in ICU adult patients

Matthieu Biais^{1,2*}, Vincent Cottenceau³, Laurent Petit³, Françoise Masson³, Jean-François Cochard³ and François Sztark^{2,3}

Sensitivity (%)

100 - Specificity (%)

Critical Care 2011, **15**:R168

>Fluid Challenge

>Predictors of fluid responsiveness/unresponsiveness

- Static markers of preload
- Dynamic markers of preload responsiveness
 - o heart-lung interaction tests
 - o variability of stroke volume and of its surrogates
 - o variability of (inferior or superior) vena cava diameter

| Intensive Care Med (2004) 30:1834–1837 | BRIEF REPORT |
|---|--|
| Marc Feissel Frédéric Michard Jean-Pierre Faller Jean-Louis Teboul | The respiratory variation in inferior vena cava diameter as a guide to fluid therapy |







 $\Delta dIVC \% =$

dIVCmax - dIVCmin

(dIVCmax + dIVCmin)/2

| Intensive | Care | Med | (2004) | 30:1 | 734-1739 | |
|-----------|------|-----|--------|------|----------|--|
| | | | | | | |

Antoine Vieillard-Baron Karim Chergui Anne Rabiller Olivier Peyrouset Bernard Page Alain Beauchet François Jardin

ORIGINAL

Superior vena caval collapsibility as a gauge of volume status in ventilated septic patients

66 pts with MV Systematic fluid loading with 10 mL/kg HES



SVC collabsibility index : 68% Cardiac Index : 3.11 L/min/m²



SVC collabsibility index : 12% Cardiac Index : 4.38 L/min/m²



• impossible to interpret in pts with **spontaneous breathing activity**

Passive leg raising predicts fluid responsiveness in the critically ill*

Xavier Monnet, MD, PhD; Mario Rienzo, MD; David Osman, MD; Nadia Anguel, MD; Christian Richard, MD; Michael R. Pinsky, MD, Dr hc; Jean-Louis Teboul, MD, PhD

Crit Care Med 2006; 34:1402–1407



- impossible to interpret in pts with **spontaneous breathing activity**
- impossible to interpret in patients with arrhythmias



- impossible to interpret in pts with **spontaneous breathing activity**
- impossible to interpret in patients with arrhythmias
- difficult to interpret if **tidal volume** is **too low**

Intensive Care Med (2005) 31:517–523 DOI 10.1007/s00134-005-2586-4

Daniel De Backer Sarah Heenen Michael Piagnerelli Marc Koch Jean-Louis Vincent

ORIGINAL

Pulse pressure variations to predict fluid responsiveness: influence of tidal volume

Normal TV

Low TV



- impossible to interpret in pts with **spontaneous breathing activity**
- impossible to interpret in patients with **arrhythmias**
- difficult to interpret if **tidal volume** is **too low**
- difficult to interpret if **lung compliance** is **too low**

Passive leg-raising and end-expiratory occlusion tests perform better than pulse pressure variation in patients with low respiratory system compliance

Xavier Monnet, MD, PhD; Alexandre Bleibtreu, MD; Alexis Ferre, MD; Martin Dres, MD; Rim Gharbi, MD; Christian Richard, MD; Jean-Louis Teboul, MD, PhD

Crit Care Med 2012; 40:152–157

Ability of PPV to predict fluid responsiveness in function of lung compliance



- impossible to interpret in pts with **spontaneous breathing activity**
- impossible to interpret in patients with arrhythmias
- difficult to interpret if **tidal volume** is **too low**
- difficult to interpret if **lung compliance** is **too low**
- difficult to interpret in case of high frequency ventilation
 PPV can be not reliable when the heart rate/respiratory rate is > 3.6

De Backer et al Anesthesiology 2009

- impossible to interpret in pts with **spontaneous breathing activity**
- impossible to interpret in patients with **arrhythmias**
- difficult to interpret if **tidal volume** is **too low**
- difficult to interpret if **lung compliance** is **too low**
- difficult to interpret in case of **high frequency ventilation**
- difficult to interpret under **open-chest conditions**
- difficult to interpret in case of **severe RV failure**

Mahjoub et al Crit Care Med 2009, Wyler von Ballmoos et al Crit Care 2010

- impossible to interpret in pts with **spontaneous breathing activity**
- impossible to interpret in patients with arrhythmias
- difficult to interpret if **tidal volume** is **too low**
- difficult to interpret if **lung compliance** is **too low**
- difficult to interpret in case of **high frequency ventilation**

In all these situations and in case of any doubt about interpretation other reliable dynamic tests are required ... and are now available

>Fluid Challenge

>Predictors of fluid responsiveness/unresponsiveness

- Static markers of preload
- Dynamic markers of preload responsiveness

o heart-lung interaction tests

- o variability of stroke volume and of its surrogates
- o variability of (inferior or superior) vena cava diameter
- o end-expiratory occlusion test

End-expiratory occlusion test



Predicting volume responsiveness by using the end-expiratory occlusion in mechanically ventilated intensive care unit patients Xavier Monnet, MD, PhD; David Osman, MD; Christophe Ridel, MD; Bouchra Lamia. MD: Christian Richard, MD; Jean-Louis Teboul, MD, PhD Crit Care Med 2009; 37:951-956 effects of end-expiratory occlusion on Pulse contour CO % 50-40· Any real-time CO monitor A simple arterial catheter could be suitable could be suitable TU 0 -10 R NR

Passive leg-raising and end-expiratory occlusion tests perform better than pulse pressure variation in patients with low respiratory system compliance

Xavier Monnet, MD, PhD; Alexandre Bleibtreu, MD; Alexis Ferre, MD; Martin Dres, MD; Rim Gharbi, MD; Christian Richard, MD; Jean-Louis Teboul, MD, PhD

Crit Care Med 2012; 40:152–157

End-Expiratory Occlusion Test Predicts Preload Responsiveness Independently of Positive End-Expiratory Pressure During Acute Respiratory Distress Syndrome

Serena Silva, MD^{1,2}; Mathieu Jozwiak, MD^{1,2}; Jean-Louis Teboul, MD, PhD^{1,2}; Romain Persichini, MD^{1,2}; Christian Richard, MD^{1,2}; Xavier Monnet, MD, PhD^{1,2}

Crit Care Med 2013; 41:1692-1701

>Fluid Challenge

>Predictors of fluid responsiveness/unresponsiveness

- Static markers of preload
- Dynamic markers of preload responsiveness
 - o heart-lung interaction tests
 - o variability of stroke volume and of its surrogates
 - o variability of (inferior or superior) vena cava diameter
 - o end-expiratory occlusion test
 - o passive leg raising test





Passive Leg Raising: the advantages

- PLR provides a good prediction of fluid responsiveness
- Unlike fluid challenge, effects of PLR are rapidly reversible
- PLR may well assess fluid responsiveness ... in situations where PPV fails to do it

| Intensive Care Med (2008) 34:659–66 |
|-------------------------------------|
|-------------------------------------|

CLINICAL COMMENTARY

Xavier Monnet Jean-Louis Teboul **Passive leg raising**





Changes in BP Induced by Passive Leg Raising Predict Response to Fluid Loading in Critically III Patients*

Thierry Boulain, MD; Jean-Michel Achard, MD; Jean-Louis Teboul, MD; Christian Richard, MD; Dominique Perrotin, MD; and Guy Ginies, MD

CHEST 2002; 121:1245-1252





The hemodynamic response to PLR

can predict the **hemodynamic response** to **fluid infusion**

Real-time CO response to PLR



Intensive Care Med (2007) 33:1125–1132

Bouchra Lamia Ana Ochagavia Xavier Monnet Denis Chemla Christian Richard Jean-Louis Teboul

ORIGINAL

Echocardiographic prediction of volume responsiveness in critically ill patients with spontaneously breathing activity







| Intensive Care Med (2013) 39:93–100 | ORIGINAL |
|---|--|
| Xavier Monnet Aurélien Bataille Eric Magalhaes Jérôme Barrois Marine Le Corre Clément Gosset Laurent Guerin Christian Richard Jean-Louis Teboul | End-tidal carbon dioxide is better than arterial pressure for predicting volume responsiveness by the passive leg raising test |



Intensive Care Med (2013) 39:93–100 ORIGINAL

Xavier Monnet Aurélien Bataille Eric Magalhaes Jérôme Barrois Marine Le Corre Clément Gosset Laurent Guerin Christian Richard Jean-Louis Teboul

End-tidal carbon dioxide is better than arterial pressure for predicting volume responsiveness by the passive leg raising test



Passive Leg Raising: the advantages

- PLR provides a good prediction of fluid responsiveness
- Unlike fluid challenge, effects of PLR are rapidly reversible
- PLR may well assess fluid responsiveness ... in situations where PPV fails to do it
reversible hemodynamic effects



No risk of pulmonary edema

Passive Leg Raising: the advantages

- PLR provides a good prediction of fluid responsiveness
- Unlike fluid challenge, effects of PLR are rapidly reversible
- PLR may well assess fluid responsiveness
 ... in situations where PPV fails to do it
 - Spontaneous Breathing activity



Passive Leg Raising: The advantages

- PLR provides a good prediction of fluid responsiveness
- Unlike fluid challenge, effects of PLR are rapidly reversible
- PLR may well assess fluid responsiveness
 ... in situations where PPV fails to do it
 - Spontaneous Breathing activity
 - Low lung compliance

Passive leg-raising and end-expiratory occlusion tests perform better than pulse pressure variation in patients with low respiratory system compliance

Xavier Monnet, MD, PhD; Alexandre Bleibtreu, MD; Alexis Ferre, MD; Martin Dres, MD; Rim Gharbi, MD; Christian Richard, MD; Jean-Louis Teboul, MD, PhD

Crit Care Med 2012; 40:152–157



Passive Leg Raising: the "limits"

• **PLR** should **not** start from a **horizontal** patient's position but from a **semi-recumbent** position





| Intensive Care Med (2009) 35:85–90 | ORIGINAL |
|---|--|
| Julien Jabot Jean-Louis Teboul Christian Richard Xavier Monnet | Passive leg raising for predicting fluid responsiveness: importance of the postural change |







(all responders to fluid administration)







Passive Leg Raising: the "limits"

- PLR should not start from a horizontal patient's position but from a semi-recumbent position
- The hemodynamic **response** to **PLR should not** be monitored with **arterial pressure** but **with CO** measurements

| Intensive Care Med (2010) 36:1475–1483 | REVIEW |
|--|---|
| Fabio Cavallaro Claudio Sandroni Cristina Marano Giuseppe La Torre Alice Mannocci Chiara De Waure Giuseppe Bello Riccardo Maviglia Massimo Antonelli | Diagnostic accuracy of passive leg raising for prediction of fluid responsiveness in adults: systematic review and meta-analysis of clinical studies |

PLR-induced changes in CO

| Study name | sample size | AUC |
|---------------------|-------------|------|
| Monnet CCM 2006 | 71 | 0.96 |
| Lafanéchère CC 2006 | 22 | 0.95 |
| Lamia ICM 2007 | 24 | 0.96 |
| Maizel ICM 2007 | 34 | 0.89 |
| Monnet CCM 2009 | 34 | 0.94 |
| Thiel CC 2009 | 102 | 0.89 |
| Biais CC 2009 | 30 | 0.96 |
| Preau CCM 2010 | 34 | 0.94 |
| | 351 | 0.95 |



Following the changes in arterial pressure during PLR is not suitable

(false negative cases)

A real-time CO monitor is necessary

Decision of starting fluid administration

- presence of hemodynamic instability/peripheral hypoperfusion (mottled skin, hypotension, oliguria, hyperlactatemia...)
- and presence of **preload responsiveness**
- and limited risks of fluid overload

Decision of stopping fluid administration

- disappearance of hemodynamic instability/peripheral hypoperfusion
- or presence of preload unresponsiveness
- or high risks of fluid overload or severe hypoxemic lung injury



Conclusion

Predictors of fluid responsiveness/unresponsiveness

- Pulse pressure variation or stroke volume variation
- PLR or end-expiratory occlusion tests

Can help to choose the **best** fluid **strategy** by identifying patients **eligible** for fluid infusion and by **avoiding** to fluid **overload** patients who would be fluid **unresponsive**

