Critical Review Form
Meta-analysis

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

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Objective: **"To evaluate the accuracy of SPV[*], PPV[†], and SVV[§] in predicting fluid responsiveness and to compare these variables to the static hemodynamic variables, which have been used to assess intravascular volume". (p. 2643).**

[*]SPV – systolic pressure variation
[†]PPV – pulse pressure variation
[§]SVV – stroke volume variation

Methods: **Four authors independently conducted a literature search of MEDLINE from 1966 to Nov 2008 using the search terms pulse contour analysis, or systolic pressure variation, OR SVV, OR PPV AND fluid therapy OR fluid responsiveness. Additionally investigators searched EMBASE, the Cochrane Database of Systematic Reviews and selected bibliographies. Only human adult studies of ventilated patients with TV > 7 mL/kg were included.**

Using a standardize form, all authors independently abstracted data from all studies included in the meta-analysis. Extracted data included study design, size and setting, patient population, tidal volumes used, correlation coefficients, AUC ROC, percentage of patients responding to fluid challenge and baseline PPV/SVV for fluid responders and non-responders.

Meta-analysis was conducted according to QUOROM guidelines using a fixed effects model to determine pooled AUC and correlation coefficients. The Cochrane Q statistic was used to assessed heterogeneity (significance = p <0.1). When data was available to construct 2x2 tables, pooled sensitivity, specificity, positive/negative likelihood ratios, and diagnostic odds ratios were computed using a bivariate mixed model.

Guide	Question	Comments
I	***Are the results valid?***	
1.	Did the review explicitly address a sensible question?	Yes: **How well do dynamic changes in arterial waveform-derived variables (SPV, SVV, PPV) or static indices (CVP, global end-diastolic volume index, left ventricular end-diastolic area index) predict fluid responsiveness?** Since only 50% of unstable critically ill patients respond to a fluid challenge (Michard 2002) and patient outcomes are impacted by cumulative fluid balance and the strategy used to guide fluid management (Rivers 2006), prompt means to identify fluid responders (and dynamically monitor their subsequent response to fluid challenges) are desperately needed. Unfortunately, IVC diameter, PA catheter measured RV and diastolic volume index , LV end-diastolic area index (LVEDAI) and the global and diastolic volume index (GEDVI) (via transpulmonary thermodilution "have been uniformly disappointing". (p. 2642)
2.	Was the search for relevant studies details and exhaustive?	No. Investigators used a limited number of search terms for MEDLINE and did not conduct a hand-search of the literature for scientific abstracts. They also did not assess the gray literature (industry theses).
3.	Were the primary studies of high methodological quality?	No quality assessment was reported.
4.	Were the assessments of the included studies reproducible?	Probably since standardized data abstraction forms were used. However, the authors do not report discrepancies or discrepancy resolution.
II.	***What are the results?***	

1.	What are the overall results of the study? r= correlation coefficient (>0.8 strong, <0.5 weak) AUC= 0.9-1 Ideal 0.8-0.9 Adequate 0.7-0.8 Fair 0.6-0.7 Poor <0.6 Failure	• Electronic search yielded 68 citations and 4 more were identified by bibliography search. After 43 were excluded (38 due to study design, 5 because they failed to report an outcome of interest), 29 studies were included in this meta-analysis including a total of 685 intubated patients. • 8 studies reported the SPV, 22 the PPV, 12 the SVV, 18 the CVP, 3 the GEDVI, and 5 the LVEDAI. • 20 studies were O.R. or post-op and 9 studies were in the ICU. • Most studies defined responder as SVI or CI increase ≥ 15% after a fluid or PEEP challenge. • Overall, 56% of patients responded to a fluid challenge. • There was no significant heterogeneity reported (Q-statistic and p-value not reported). • The baseline PPV was 16.6 ± 2.9% in responders vs. 7.1 ± 1.5% in non-responders (p <0.001). • The baseline SVV was 15.3 ± 3.4% in responders vs. 8.4 ± 1.9% in non-responders. (p <.001). Parameter / Pooled Correlation Coefficient* / AUC PPV: 0.78 (0.74-0.82) / 0.94†(0.93-0.95) SVV: 0.72 (0.66-0.78) / 0.84 (0.78-0.88) SPV: 0.72 (0.65-0.77) / 0.86 (0.82-0.9) CVP: 0.13(-0.1-0.28) / 0.55 (0.48-0.62) GEDVI: N/A / 0.56 (0.37-0.67) LVEDAI: N/A / 0.64 (0.53-0.74) *Correlation between hemodynamic parameter and a change in the stroke volume index of cardiac index following a fluid challenge. † p <0.001 c/w SVV or SPV • Sensitivity, specificity and LR's were reported for PPV and SVV based upon data from 14 and 5 studies, respectively (Table 3, p. 2645) (Sen / Spec / LR+ / LR-) PPV: 89(82-94) / 88(81-92) / 7.3(4.5-11.5) / 0.12(0.07-0.21) SVV: 82(75-98) / 86(77-92) / 5.8(3.4-9.7) / 0.21(0.15-0.30)
2.	How precise are the results?	See 95% CI reported above.

3.	Were the results similar from study to study?	No significant heterogeneity reported, but Cochrane Q not detailed, I^2 not computed and individual study results not detailed in order for reader to qualitatively judge study-to-study differences.
III.	***Will the results help me in caring for my patients?***	
1.	How can I best interpret the results to apply them to the care of my patients?	"Currently the SPV, PPV, and SVV are the most accurate predictors of volume responsiveness in critically ill patients". (p. 2645) Furthermore, "the PPV/SVV can be used to guide decisions regarding volume resuscitation, monitor the effects of fluid therapy, and at the same time gauge the "degree of fullness" of the intravascular compartment." (p.2645) However, "arrhythmias and spontaneous breathing activity will lead to misinterpretations of the respiratory variations in systolic pressure, SV, and pulse pressure".(p. 2645) Also, "PPV was a reliable predictor of fluid responsiveness only when the tidal volume was at least 8 mL/kg." (p. 2646)
2.	Were all patient important outcomes considered?	No patient-important outcomes were reported. Such measures would include mortality, morbidity, and length of stay.
3.	Are the benefits worth the costs and potential risks?	"By virtue of its simplicity, accuracy, and availability as a continuous monitoring tool, dynamic monitoring of pulse pressure/SV would seem to be the ideal method for the titration of fluid resuscitation in mechanically ventilated critically ill patients". (p. 2646)

Limitations

1) **Did not use guidelines for diagnostic meta-analysis (QUADAS) nor did they follow all the QUOROM recommendations.**
2) **No search of scientific abstracts or gray literature.**
3) **No assessment for publication bias.**
4) **Limited assessment for heterogeneity (I^2 neglected)**
5) **No flow diagram or references for excluded studies.**
6) **No quality assessment of the included studies.**

7) No assessment of interval LR's
8) No report of optimal cut-point for PPV from the ROC (Fig 1, p.2645)
9) Limited external validity for EM. No ED-based studies and all mechanically ventilated non-pressure control mode.

Bottom Line

Pulse pressure variation (PPV), usually measured directly from arterial pressure tracings using advanced digital software in mechanically ventilated (not pressure-support modes) with tidal volumes at least 8 mL/kg is the superior metric for the titration of fluid resuscitation. SVV and SPV are also both superior to traditional measures like CVP and LVEDAI. None of these measures (PPV, SVV, SPV) will provide information about systolic function, so optimal fluid management may also include bedside transthoracic echocardiography in hemodynamically unstable ICU patients. Future studies should assess the pragmatic application of PPV in heterogeneous ED settings among intubated patients with hemodynamic instability or shock.