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Respirophasic carotid artery peak velocity variation as a predictor of fluid responsiveness in mechanically ventilated patients with coronary artery disease

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Editor's key points

- Non-invasive indices of fluid responsiveness are critical to goal-directed therapy.
- Respiratory variation in peak carotid artery blood flow velocity was studied in anaesthetized patients before cardiac surgery and after a fluid challenge.
- This non-invasive measure reliably predicted fluid responsiveness in mechanically ventilated patients.

Background. We studied respirophasic variation in carotid artery blood flow peak velocity (ΔVpeak-CA) measured by pulsed wave Doppler ultrasound as a predictor of fluid responsiveness in mechanically ventilated patients with coronary artery disease.

Methods. Forty patients undergoing elective coronary artery bypass surgery were enrolled. Subjects were classified as responders if stroke volume index (SVI) increased ≥15% after volume expansion (6 ml kg^{-1}). The ΔVpeak-CA was calculated as the difference between the maximum and minimum values of peak velocity over a single respiratory cycle, divided by the average. Central venous pressure, pulmonary artery occlusion pressure, pulse pressure variation (PPV), and ΔVpeak-CA were recorded before and after volume expansion.

Results. PPV and ΔVpeak-CA correlated significantly with an increase in SVI after volume expansion. Area under the receiver-operator characteristic curve (AUROC) of PPV and ΔVpeak-CA were 0.75 [95% confidence interval (CI) 0.59–0.90] and 0.85 (95% CI 0.72–0.97). The optimal cut-off values for fluid responsiveness of PPV and ΔVpeak-CA were 13% (sensitivity and specificity of 0.74 and 0.71) and 11% (sensitivity and specificity of 0.85 and 0.82), respectively. In a subgroup analysis of 17 subjects having pulse pressure hypertension (≥ 60 mm Hg), PPV failed to predict fluid responsiveness (AUROC 0.70, P=0.163), whereas the predictability of ΔVpeak-CA remained unchanged (AUROC 0.90, P=0.006).

Conclusions. Doppler assessment of respirophasic ΔVpeak-CA seems to be a highly feasible and reliable method to predict fluid responsiveness in mechanically ventilated patients undergoing coronary revascularization.

Clinical trial registration. NCT 01836081.

Keywords: blood flow velocity; carotid artery; Doppler ultrasound; fluid therapy; mechanical ventilation

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In the critical care unit and operating theatre, adequate fluid resuscitation is often considered the first step to optimize cardiac output and tissue oxygen delivery before advancing to vasoactive, inotropic, or both therapies. Yet, deciding a fluid challenge based on the traditionally measured cardiac filling pressures is problematic, as they are often misleading, despite their invasive nature.[1 2] Fluid challenge should not be performed empirically, considering that only half of critically ill patients are fluid responsive.[3] As fluid excess can worsen outcome,[4 5] proper assessment of the patient's status on the Frank–Starling curve should be a prerequisite before giving fluid.

Over the last decade, dynamic indices measuring respirophasic variations in stroke volume have emerged as useful guides for fluid challenge in mechanically ventilated patients. These variations can be assessed using the echocardiography or pulse contour analysis devices, and are quantified as aortic peak velocity variation, stroke volume variation (SVV), or pulse pressure variation (PPV).[6 7] These dynamic indices are currently considered as the most accurate predictors of fluid responsiveness,[6] but the measurement of these indices requires sophisticated devices with either specific skills or invasive catheterization.

Recently, the feasibility of measuring respirophasic variations in brachial artery peak flow velocity by hand-carried ultrasound device has been addressed, with promising results showing close correlation with PPV.[8] In the same context, the common carotid artery is larger and also provides easy accessibility. Of note, preferential diversion of blood flow towards the

carotid arteries away from the peripheries has been demonstrated in shock status.[9 10] This would be of particular importance in haemodynamically unstable patients, as the most commonly accessed radial artery could yield erroneous information regarding systemic vascular resistance and respirophasic variations in stroke volume as well.[11 12]

This study aimed to validate the usefulness of respirophasic variation in carotid artery blood flow peak velocity (ΔVpeak-CA) measured by Doppler ultrasound as a predictor of fluid responsiveness in mechanically ventilated patients with coronary artery disease (CAD).

Methods

After approval of the research protocol by the institutional review board at the Yonsei University Health System, written informed consent was obtained from 45 patients undergoing elective multi-vessel coronary artery bypass graft surgery. Exclusion criteria included cardiac rhythm other than sinus, congestive heart failure, left ventricular ejection fraction (LVEF) $<45\%$, pre-existing cerebrovascular disease, peripheral arterial occlusive disease, or the presence of carotid artery stenosis $>50\%$ (either by angiography or by ultrasound assessment).

Anaesthetic management

All subjects received standardized anaesthetic care, as follows: upon arriving at the operating theatre, standard monitoring was applied including radial artery catheter and pulmonary artery catheter. Anaesthesia was induced with midazolam (0.05 mg kg^{-1}), sufentanil (1.5–2.0 μg kg^{-1}), and rocuronium bromide (0.9 mg kg^{-1}). The patients' lungs were ventilated with a tidal volume of 8 ml kg^{-1} of ideal body weight, *I*:*E* ratio of 1:2, and PEEP of 5 cm H_2O in 40% oxygen with air at a respiratory rate of 8–12 bpm to maintain normocarbia. Anaesthesia was maintained with sevoflurane and continuous infusion of sufentanil to maintain the bispectral index score between 40 and 60. Vecuronium was also continuously infused to prevent abdominal guarding or spontaneous breathing efforts. The mean arterial pressure was maintained between 60 and 80 mm Hg using norepinephrine as necessary.

Study protocol

In each subject, the mean arterial pressure, heart rate, central venous pressure (CVP), pulmonary arterial occlusion pressure (PAOP), PPV, and ΔVpeak-CA were recorded 15 min after anaesthetic induction and 10 min after a fluid challenge of 6 ml kg^{-1} of 6% hydroxyethyl starch 130/0.4. PPV (average of four cycles of 8 s) was acquired from the radial artery pressure waveform, using a Philips Intellivue MP70 monitor (Philips Medical Systems, Suresnes, France). Cardiac index was obtained through the pulmonary artery catheter, which was connected to the Vigilance monitor (Edwards Lifesciences LLC, Irvine, CA, USA), and the average of three consecutive STAT mode measurements was recorded. Stroke volume index (SVI) was calculated as cardiac index/heart rate. To eliminate any personal bias, all of the above parameters were recorded by anaesthesia nurses who were not aware of this study. Carotid artery peak velocity was measured by two independent examiners who were blinded to each other's Doppler results and haemodynamic variables of the subjects, using an 8 MHz linear probe (Sequoia C512; Siemens Medical Solutions USA, Inc.) at the left common carotid artery (Fig. 1). On the two-dimensional image, the optimal image of the long-axis view was obtained at the left common carotid artery. The sample volume was placed on the centre of the lumen, 2 cm proximal to the bulb,

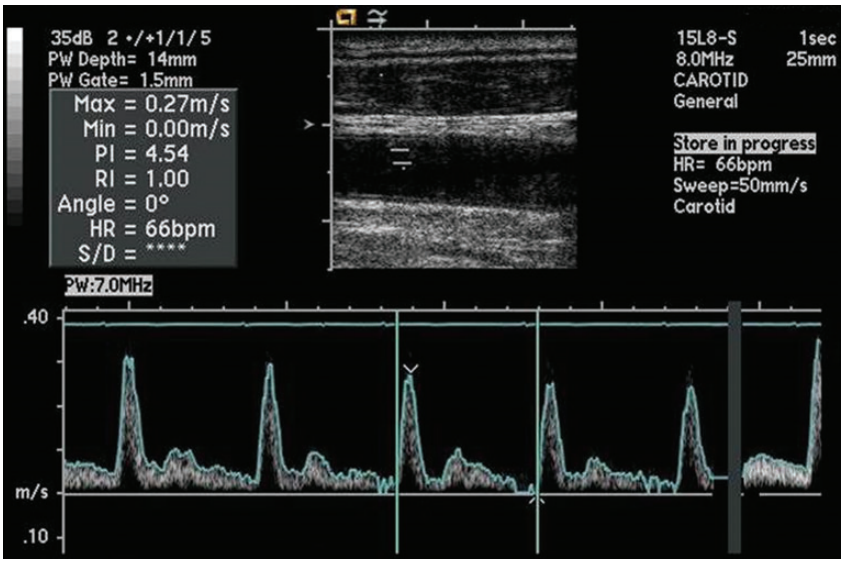

Fig 1 Recording of carotid arterial blood flow in a representative subject. Beat-to-beat measurement of carotid blood peak velocity allowed the determination of maximum and minimum values over a single respiratory cycle.

and a pulsed wave Doppler examination was performed. The Doppler beams were adjusted to ensure $<60^{\circ}$ of angle for the best signal. The peak velocity was measured automatically and the maximum and minimum values during one respiratory cycle were recorded. ΔVpeak-CA was calculated as follows: 100×(maximum peak velocity−minimum peak velocity)/[(maximum peak velocity+minimum peak velocity)/2], and the average value of the three consecutive measurements was recorded. The mean of the two examiners was used in the analysis.

Study endpoints

The primary endpoint was to determine the predictive value of ΔVpeak-CA for fluid responsiveness (≥15% increases in SVI after fluid challenge)[13 14] in mechanically ventilated patients with CAD.

Statistical analysis

Sample size calculation was performed using Power Analysis and Sample Size 2008 software (NCSS, Statistical Software, Kaysville, UT, USA). Considering the result of a previous meta-analysis,[6] we determined that 40 subjects would be required to detect differences of 0.20 between the areas under the receiver operating characteristic (AUROC) curve of CVP (0.50) and ΔVpeak-CA (0.75) with an 80% power and type I error of 5%, assuming 50% incidence of fluid responsiveness.

The inter-observer reproducibility for ΔVpeak-CA measurement was determined by the Bland–Altman plot and correlation analysis using Medcalc 12.1.3 (Mariakerke, Belgium), and described as the mean bias with limit of agreement and correlation coefficient.

Statistical analysis was performed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Because the data were not normally distributed, non-parametric tests were applied for continuous variables. Subject characteristics and baseline indices of preload were compared in responders and non-responders with the Mann–Whitney test. The effects of intravascular volume expansion on indices of preload were assessed using the Wilcoxon rank-sum test. Categorical variables were compared by the Fisher exact test or χ^2 test as appropriate. Results are expressed as median (inter-quartile range) or number of subjects (%). The relationships between the indices of preload before volume expansion (and, per cent change with volume expansion) and per cent change of SVI after volume expansion were evaluated using the Spearman rank test. Receiver-operating characteristic curves were generated for indices of preload to assess the ability to predict fluid responsiveness. The corresponding optimal cut-off values providing the greatest sum of sensitivity and specificity were calculated for PPV and ΔVpeak-CA. A *P*-value of <0.05 was considered to be statistically significant.

Results

Forty-five subjects were initially enrolled. Five subjects were excluded for repeated occurrence of arrhythmia (two) and carotid stenosis >50% (three), which were newly detected during the study. Inter-observer agreement was good (mean bias of 0.57% with 95% limit of agreement between −0.25 and 1.39, correlation coefficient of 0.91).

The main characteristics of the 40 included subjects are shown in Table 1. Patient characteristic and echocardiographic data were comparable except for LVEF, which was higher in responders than in non-responders. Cardiac index and SVI before volume expansion were significantly lower in responders than in non-responders.

Tested indices of preload before and after volume expansion are shown in Table 2. Before volume expansion, all parameters were significantly lower in responders than in non-responders, except for CVP. After volume expansion, CVP, PAOP, and PPV showed significant changes from the baseline in non-responders and responders. Only ΔVpeak-CA was not changed in non-responders with volume expansion, whereas responders demonstrated a significant decrease.

Baseline PPV and ΔVpeak-CA correlated positively with volume expansion-induced change in SVI (Table 3). Volume expansion-induced changes in PPV and ΔVpeak-CA correlated positively with volume expansion-induced change in SVI. CVP and PAOP did not correlate with volume expansion-associated changes in SVI.

Table 4 shows the AUROCs of preload indices that predicted an increase in SVI ≥15%. The AUROC of PPV and ΔVpeak-CA were 0.75 [*P*=0.008, 95% confidence interval (CI) 0.59–0.91]

Table 1 Subject characteristics and haemodynamic parameters before volume expansion. Values are expressed as median (inter-quartile range) or number of subjects (%). R, responders; NR, non-responders

	R (*n*=23)	NR (*n*=17)	*P*-value
Age (yr)	66 (61–69)	67 (53–71)	0.701
Female	10 (40)	3 (20)	0.298
BMI (kg m^{-2})	25 (24–28)	24 (23–27)	0.352
Hypertension	18 (72)	10 (67)	0.736
Diabetes mellitus	10 (40)	8 (53)	0.412
Number of diseased vessel (2/3)	4 (17)/19 (83)	7 (64)/10 (59)	0.153
Left ventricular ejection fraction (%)	67 (59–72)	59 (47–66)	0.012
Mean arterial pressure (mm Hg)	67 (59–76)	69 (59–75)	0.945
Heart rate (beats min^{-1})	63 (54–71)	64 (55–72)	1.000
Cardiac index (litre min^{-1} m^{-2})	2.3 (2.1–2.5)	2.7 (2.5–2.9)	0.001
Stroke volume index (ml m^{-2})	37 (31–41)	41 (39–50)	0.007
Requiring norepinephrine	14 (61)	9 (56)	0.773
Respiratory rate (cycles min^{-1})	10 (9–11)	11 (10–12)	0.197
Plateau inspiratory pressure (mm Hg)	16 (15–17)	17 (14–19)	0.423

Table 2 Static and dynamic indices of preload before and after volume expansion. Values are expressed as median (inter-quartile range). R, responders; NR, non-responders; P1, statistical significance of the difference before and after volume expansion; P2, statistical significance of the difference between baseline values for responders and non-responders; CVP, central venous pressure; PAOP, pulmonary artery occlusion pressure; PPV, radial arterial pulse pressure variation; ΔVpeak-carotid artery, respiratory variations of carotid peak velocity

Indices of preload	Before volume expansion	After volume expansion	P1
CVP (mm Hg)			
R	8 (5–8)	10 (8–13)	<0.001
NR	8 (7–10)	11 (10–12)	<0.001
P2	0.057	0.340	
PAOP (mm Hg)			
R	10 (9–12)	13 (11–15)	<0.001
NR	12 (10–14)	16 (13–17)	0.001
P2	0.030	0.110	
PPV (%)			
R	14 (11–19)	6 (5–8)	<0.001
NR	10 (8–13)	5 (4–6)	0.001
P2	0.008	0.172	
ΔVpeak-carotid artery (%)			
R	13 (11–16)	6 (5–8)	<0.001
NR	8 (7–10)	8 (5–8)	0.334
P2	<0.001	0.297	

Table 3 Relationships between indices of preload and per cent change in SVI with volume expansion. *r*, Correlation coefficient; CVP, central venous pressure; PAOP, pulmonary artery occlusion pressure; PPV, radial arterial pulse pressure variation; ΔVpeak-carotid artery, respiratory variations of carotid peak velocity

	r	*P*-value
Indices before volume expansion		
CVP	−0.223	0.166
PAOP	−0.290	0.069
PPV	0.559	<0.001
ΔVpeak-carotid artery	0.636	<0.001
% change in indices after volume expansion		
CVP	0.172	0.287
PAOP	0.127	0.436
PPV	0.320	0.047
ΔVpeak-carotid artery	0.477	0.003

and 0.85 ($P<0.001$, 95% CI 0.72–0.97), respectively. Threshold values discriminating between responders and non-responders to fluid administration were 13% (sensitivity and specificity of 0.74 and 0.71) for PPV and 11% (sensitivity and specificity of 0.83 and 0.82) for ΔVpeak-CA.

Table 4 Receiver-operator characteristics curves of static and dynamic indices of preload for predicting fluid responsiveness. AUROC, area under the receiver operator curve; CVP, central venous pressure; PAOP, pulmonary artery occlusion pressure; PPV, radial arterial pulse pressure variation; ΔVpeak-carotid artery, respiratory variations of carotid peak velocity

	AUROC	95% confidence interval	*P*-value
CVP	0.675	0.507–0.843	0.061
PAOP	0.701	0.535–0.866	0.032
PPV	0.747	0.588–0.905	0.008
ΔVpeak-carotid artery	0.849	0.724–0.974	<0.001

Discussion

Our results suggest that a measure of respirophasic variation of carotid artery peak flow velocity is a simple and reliable method for determining fluid responsiveness in mechanically ventilated subjects. The predictive power of ΔVpeak-CA was greater than that of radial arterial PPV and also those of traditional static indices.

Knowing whether a fluid challenge would augment cardiac output is of great importance as it would avoid unnecessary fluid administration and facilitate pharmacological therapy for an improvement of tissue oxygenation in a timely manner. Cardiac filling pressures are less appealing to guide fluid therapy in the surgical theatre and intensive care unit due to their lack of predictability.[1–3] Dynamic indices have emerged based on the observation that respirophasic variations in stroke volume closely correlates with position on the Frank–Starling curve in mechanically ventilated patients.[7] Among the dynamic indices, SVV and PPV derived from arterial waveform analysis are the two representative indices, and are currently being widely used as preload indices in mechanically ventilated patients.[15 16] Assessments of respirophasic changes in flow velocity (ΔVpeak) at the aorta using the transoesophageal echocardiography, transthoracic echocardiography, or oesophageal Doppler probe have gained interest as alternatives.[13 17 18]

Despite their well-validated predictive power for fluid responsiveness, acquiring these indices requires invasive arterial catheterization, sophisticated monitoring devices, oesophageal probe placement, or echocardiographic expertise, which is not readily available in every institution. Moreover, depending on the clinical scenario or type of surgery, the application of these indices might not be feasible. Based on the premise that non-invasive and readily available measures are undoubtedly favourable, ΔVpeak of brachial artery has been suggested as a simple predictor of fluid responsiveness.[8 19] Measuring ΔVpeak of the carotid artery might be advantageous to measuring ΔVpeak of the brachial artery for the several following reasons. First, the carotid artery is larger and provides easy accessibility to Doppler flow acquisition due to its superficial location. During some surgical settings, it might be the only

accessible artery when unexpected haemodynamic instability occurs. Secondly, a recent study demonstrated a preferential distribution of blood flow towards the carotid circulation away from the brachial artery in haemodynamically unstable patients.[20] In conjunction, inconsistent results have been reported regarding the diagnostic values of SVV and PPV in cases of circulatory failure.[21 22] Thirdly, in conditions accompanied by systemic inflammatory response such as post-cardiopulmonary bypass or septic shock, clinicians are often confronted with erroneously low radial arterial pressure compared with arterial pressures near the central aorta, which might mislead subsequent therapeutic interventions.[11 12]

Based on these theoretical advantages, we investigated the feasibility and predictive power of Doppler-acquired respirophasic carotid flow dynamics on fluid responsiveness in mechanically ventilated patients. As our results indicate, the predictability of ΔVpeak-CA was superior to that of PPV with excellent inter-observer agreement. Moreover, ΔVpeak-CA yielded a cut-off value with the highest sensitivity and specificity. In addition, ΔVpeak-CA was the only variable that showed no significant changes in non-responders after the fluid challenge, suggesting its strong association with preload, while PPV showed a significant decrease after fluid challenge even in non-responders. In contrast, the traditionally used invasive static indices of preload, CVP and PAOP, were not able to predict fluid responsiveness in the current study.

We observed a lower predictability of PPV in the present study compared with other studies.[6 7] This can be partly explained by altered arterial compliance by atherosclerosis, which is a major determinant of pulse pressure amplification influencing arterial pulse wave-based PPV or SVV.[23 24] This result is consistent with the finding of our previous study comparing the predictability of SVV determined by radial FloTrac sensor in CAD patients with or without pulse pressure hypertension, in which we observed an overall AUROC of 0.70.[25] Clinically, pulse pressure hypertension is considered as an extreme form of increased arterial stiffness and a well-known risk factor of adverse outcome.[26] Indeed, in a subgroup analysis of 17 subjects having pulse pressure hypertension ($\geq$60 mm Hg) in the current study, PPV failed to predict fluid responsiveness (AUROC 0.70, P=0.163, 95% CI 0.43–0.98), whereas the predictability of ΔVpeak-CA remained unchanged (AUROC 0.90, P=0.006, 95% CI 0.75–1.0). These findings suggest that measurement of respirophasic variations in stroke volume in patients with altered vascular compliance might be influenced by the distance from the aorta. Thus, apart from being non-invasive and practical, there might be a role for ΔVpeak-CA as a predictor of fluid responsiveness in certain clinical situations when (i) arterial cannulation is not readily feasible or (ii) the PPV (or SVV) obtained from the radial artery would yield inconclusive or inaccurate information. Thus, it remains to be proven through further studies.

The limitations of this trial are as follows. Like other dynamic indices based on heart–lung interactions, ΔVpeak-CA shares their limitations of not being applicable in patients with arrhythmia, significant valvular heart diseases, or spontaneous breathing. Also, our results cannot be extrapolated to patients with heart failure or significant carotid artery stenosis, as we had excluded those patients. Decreased ventricular contractility has the potential to shift the Frank–Starling curve and alter the operative point irrespective of the volume status. In the same context, the finding that LVEF was statistically different between the responders and non-responders might also be a limitation. As we had excluded patients with LVEF $<$45%, the confounding effect of LVEF should be negligible. Lastly, our interpretation that ΔVpeak-CA might be a better predictor of fluid responsiveness than PPV was based on the higher AUROC and retained predictability in patients with pulse pressure hypertension. Yet, defining fluid responsiveness based on a dichotomous cut-off might not be appropriate as it excludes possible responders, despite a $<$15% increase. As PPV was indeed decreased even in non-responders in contrast to ΔVpeak-CA, PPV might be more suitable as a continuous predictor. In conclusion, a measure of respirophasic variation of peak blood velocity in the carotid artery assessed by Doppler ultrasound seems to be a highly feasible and reliable method to predict fluid responsiveness in patients with CAD. The current study also suggests that ΔVpeak-CA might be valuable in patients with reduced arterial compliance, when the predictive power of PPV on fluid responsiveness is reduced. Further studies are needed to test its performance in haemodynamically unstable patients with low perfusion status.

Authors' contributions

Y.S.: acquisition and interpretation of data, drafting of manuscript, and statistical analysis. Y.L.K.: critical revision of the manuscript and study supervision. J.W.S.: acquisition of data and statistical analysis. Y.J.K.: acquisition of data. J.K.S.: study concept and design, interpretation of data, critical revision of the manuscript, and study supervision.

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Declaration of interest

None declared.

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References

1 Osman D, Ridel C, Ray P, *et al.* Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge. *Crit Care Med* 2007; **35**: 64–8

2 Kumar A, Anel R, Bunnell E, *et al.* Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. *Crit Care Med* 2004; **32**: 691–9

3 Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. *Chest* 2008; **134**: 172–8

4 Boyd JH, Forbes J, Nakada TA, Walley KR, Russell JA. Fluid resuscitation in septic shock: a positive fluid balance and elevated central venous pressure are associated with increased mortality. *Crit Care Med* 2011; **39**: 259–65

5 Rosenberg AL, Dechert RE, Park PK, Bartlett RH, Network NNA. Review of a large clinical series: association of cumulative fluid balance on outcome in acute lung injury: a retrospective review of the ARDSnet tidal volume study cohort. *J Intensive Care Med* 2009; **24**: 35–46

6 Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med* 2009; **37**: 2642–7

7 Michard F. Changes in arterial pressure during mechanical ventilation. *Anesthesiology* 2005; **103**: 419–28

8 Brennan JM, Blair JEA, Hampole C, *et al.* Radial artery pulse pressure variation correlates with brachial artery peak velocity variation in ventilated subjects when measured by internal medicine residents using hand-carried ultrasound devices. *Chest* 2007; **131**: 1301–7

9 Forsyth RP, Hoffbrand BI, Melmon KL. Redistribution of cardiac output during hemorrhage in the unanesthetized monkey. *Circ Res* 1970; **27**: 311–20

10 Kaihara S, Rutherford RB, Schwentker EP, Wagner HN Jr. Distribution of cardiac output in experimental hemorrhagic shock in dogs. *J Appl Physiol* 1969; **27**: 218–22

11 Hong SW, Shim JK, Choi YS, *et al.* Predictors of ineffectual radial arterial pressure monitoring in valvular heart surgery. *J Heart Valve Dis* 2009; **18**: 546–53

12 Dorman T, Breslow MJ, Lipsett PA, *et al.* Radial artery pressure monitoring underestimates central arterial pressure during vasopressor therapy in critically ill surgical patients. *Crit Care Med* 1998; **26**: 1646–9

13 Feissel M, Michard F, Mangin I, Ruyer O, Faller JP, Teboul JL. Respiratory changes in aortic blood velocity as an indicator of fluid responsiveness in ventilated patients with septic shock. *Chest* 2001; **119**: 867–73

14 Muller L, Louart G, Bengler C, *et al.* The intrathoracic blood volume index as an indicator of fluid responsiveness in critically ill patients with acute circulatory failure: a comparison with central venous pressure. *Anesth Analg* 2008; **107**: 607–13

15 Monnet X, Dres M, Ferre A, *et al.* Prediction of fluid responsiveness by a continuous non-invasive assessment of arterial pressure in critically ill patients: comparison with four other dynamic indices. *Br J Anaesth* 2012; **109**: 330–8

16 De Backer D, Marx G, Tan A, *et al.* Arterial pressure-based cardiac output monitoring: a multicenter validation of the third-generation software in septic patients. *Intensive Care Med* 2011; **37**: 233–40

17 Slama M, Masson H, Teboul JL, *et al.* Monitoring of respiratory variations of aortic blood flow velocity using esophageal Doppler. *Intensive Care Med* 2004; **30**: 1182–7

18 Durand P, Chevret L, Essouri S, Haas V, Devictor D. Respiratory variations in aortic blood flow predict fluid responsiveness in ventilated children. *Intensive Care Med* 2008; **34**: 888–94

19 Monge Garcia MI, Gil Cano A, Diaz Monrove JC. Brachial artery peak velocity variation to predict fluid responsiveness in mechanically ventilated patients. *Crit Care* 2009; **13**: R142

20 Marik PE, Levitov A, Young A, Andrews L. The use of bioreactance and carotid Doppler to determine volume responsiveness and blood flow redistribution following passive leg raising in hemodynamically unstable patients. *Chest* 2013; **143**: 364–70

21 Mesquida J, Kim HK, Pinsky MR. Effect of tidal volume, intrathoracic pressure, and cardiac contractility on variations in pulse pressure, stroke volume, and intrathoracic blood volume. *Intensive Care Med* 2011; **37**: 1672–9

22 Gruenewald M, Meybohm P, Koerner S, *et al.* Dynamic and volumetric variables of fluid responsiveness fail during immediate postresuscitation period. *Crit Care Med* 2011; **39**: 1953–9

23 Segers P, Mahieu D, Kips J, *et al.* Amplification of the pressure pulse in the upper limb in healthy, middle-aged men and women. *Hypertension* 2009; **54**: 414–20

24 Chemla D, Hebert JL, Coirault C, *et al.* Total arterial compliance estimated by stroke volume-to-aortic pulse pressure ratio in humans. *Am J Physiol* 1998; **274**: H500–5

25 Kim SY, Song Y, Shim JK, Kwak YL. Effect of pulse pressure on the predictability of stroke volume variation for fluid responsiveness in patients with coronary disease. *J Crit Care* 2013; **28**: 318.e1–7

26 Mitchell GF, Moye LA, Braunwald E, *et al.* Sphygmomanometrically determined pulse pressure is a powerful independent predictor of recurrent events after myocardial infarction in patients with impaired left ventricular function. *Circulation* 1997; **96**: 4254–60

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