Chapter 6

Arm occlusion pressure is a useful predictor of an increase in cardiac output after fluid loading following cardiac surgery

Bart F. Geerts[1], Jacinta J. Maas[2], Rob B.P. de Wilde[2], Leon P.H.J. Aarts[1] and Jos R.C. Jansen[2]

[1]Department of Anesthesiology, Leiden University Medical Center, The Netherlands,
[2]Department of Intensive Care Medicine, Leiden University Medical Center, The Netherlands

European Journal of Anaesthesiology 2011;28:802-806

Abstract

In pharmacological research, arm occlusion pressure is used to study hemodynamic effects of drugs. However, arm occlusion pressure might be an indicator of static filling pressure of the arm. We hypothesised that arm occlusion pressure can be used to predict fluid loading responsiveness. Twenty-four patients who underwent cardiac surgery were studied during their first 2 hours in the ICU. The lungs were ventilated mechanically and left ventricular function was supported as necessary. Arm occlusion pressure was defined as the radial artery pressure after occluding arterial flow for 35 seconds by a blood pressure inflated to 50 mmHg above systolic blood pressure. The cuff was positioned around the arm in which a radial artery catheter had been inserted. Measurements were performed before (baseline) and after fluid loading (500 ml hydroxyethyl starch 6%). Patients whose cardiac output increased by at least 10% were defined as responders. In responders (n = 17), arm occlusion pressure, mean arterial pressure and central venous pressure increased and stroke volume variation and pulse pressure variation decreased. In non-responders (n = 7), arm occlusion pressure and central venous pressure increased, and pulse pressure variation decreased. Mean arterial pressure, stroke volume variation and heart rate did not change significantly. The area under the curve to predict fluid loading responsiveness for arm occlusion pressure was 0.786 (95% confidence interval 0.567-1.000), at a cut-off of 21.9 mmHg, with sensitivity of 71% and specificity of 88% in predicting fluid loading responsiveness. Prediction of responders with baseline arm occlusion pressure was as good as baseline stroke volume variation and pulse pressure variation. In conclusion, arm occlusion pressure was a good predictor of fluid loading responsiveness in our group of cardiac surgery patients and offers clinical advantages over stroke volume variation and pulse pressure variation.

Introduction

Fluid therapy is an important tool in hemodynamic management of patients with suboptimal tissue perfusion. However, excessive fluid resuscitation can result in general and pulmonary oedema, increasing hospital stay and even mortality.[1] In mechanically ventilated patients with a regular heart rhythm, stroke volume variation (SVV) and pulse pressure variation (PPV) perform well as predictors of a clinically significant increase in cardiac output (CO) after fluid administration (i.e. fluid loading responsiveness).[2,3] In vasoplegic patients, both indicators failed.[4,5] Furthermore, SVV and PPV have never been shown to act as a measure of volume status. Therefore, the search for a measure of volume status and a predictor of fluid loading responsiveness which can be used independent of respiratory settings and heart rhythm continues.[6]

A physiological measure of effective volume status is mean systemic filling pressure: the equilibrium pressure anywhere in the circulation under circulatory arrest. The pressure gradient between static filling pressure and central venous pressure (Pcv) is the driving force for venous return and thus for CO. Consequently, increasing mean systemic filling pressure and thereby the pressure gradient for venous return by fluid expansion should improve CO, assuming a constant resistance to venous return and adequate myocardial function.

In pharmacology research, upper arm occlusion pressure (Parm) has been used to determine the effects of drugs on venous capacitance and arterial resistance.[7] We hypothesised that Parm might function as an indicator of mean filling pressure and volume status of the arm. Mean filling pressure of the arm has never been studied as a predictor of fluid responsiveness. We determined Parm by measuring radial artery pressure 30 seconds after occlusion of arterial flow induced by inflating a cuff around the upper arm. The aim of this study was to explore the value of Parm as a predictor of fluid loading responsiveness. This approach is attractive, as it would provide the clinician with a simple, readily available and robust measurement that can be made at the bedside.

Methods

Twenty-four patients undergoing elective cardiac surgery were included after approval of the institutional ethics committee (P06.149, chairman Prof. Dr. F.C. Breedveld, approval date 5 December 2006) and personal informed consent was obtained. All patients had symptomatic coronary artery or valve disease with preserved ventricular function. Patients with aortic aneurysm, extensive peripheral arterial occlusive disease, postoperative severe arrhythmia, postoperative valve insufficiency or the necessity for artificial pacing or use of a cardiac assist device were excluded.

Prior to surgery, a pulmonary artery catheter (Intellicath; Edwards Lifesciences; Irvine, CA, USA) was inserted to measure thermodilution cardiac output (COtd) and Pcv, and a 20 G radial artery catheter was used to measure radial artery pressure. Anaesthesia was maintained with propofol (2.5 $mg \cdot kg^{-1} \cdot h^{-1}$) and sufentanil (0.06-0.20 $\mu g \cdot kg^{-1} \cdot h^{-1}$). The lungs were mechanically ventilated (Evita 4; Dräger, Lübeck, Germany) in a volume-control mode with standard settings (12 $breaths \cdot min^{-1}$, tidal volume 8-10 $ml \cdot kg^{-1} \cdot min^{-1}$, FiO_2 0.4, positive end-expiratory pressure 5 cmH_2O). During the observation period, the patients were kept in the supine position. The use of sedative and vascular medication remained unchanged. No fluids were administered during the observation period outside the study protocol.

Arterial occlusion in the arm was created with a rapid cuff inflator (Hokanson E20, Bellevue, Washington, USA) connected to compressed air and an upper arm cuff. The cuff was positioned around the same arm as that used to measure radial artery pressure. The cuff pressure was increased stepwise to 50 mmHg above the patients' systolic arterial pressure. The duration of arm occlusion was 35 seconds. Arm occlusion pressure (Parm) was calculated as the average value of the radial artery pressure over 1 second at 30 seconds after the start of arm occlusion.

The radial artery pressure was analysed with the "Modelflow" program (FMS, Amsterdam, the Netherlands) to provide beat-to-beat values of cardiac output (COmf) using the pulse contour CO method, calibrated using the averaged value of three COtd measurements spread equally over the ventilatory cycle.[8] From the beat-to-beat values of "Modelflow", SVV, PPV and heart rate (HR) were determined. SVV and PPV were calculated for 5 ventilatory cycles and their values were averaged. Pcv, mean arterial pressure (Pa), COmf and HR were averaged over 30 second intervals.

The study protocol started within 2 hours after arrival of the patients in the ICU and took approximately 15 minutes. Values of Parm, Pcv, Pa, COmf, SVV and PPV were collected before (baseline) and 2-5 minutes after rapid fluid loading. Volume loading was achieved by using 500 ml 6% hydroxyethyl starch solution (Voluven; Fresenius Kabi, Bad Homburg, Germany). Shortly after the end of the study protocol, sedation was stopped and weaning procedures were started. We observed no adverse events during the study protocol and all patients were discharged from the ICU on the first postoperative day.

Statistical analysis

A formal power analysis was not performed because relevant data were not available from the literature. However, study sample size is similar to those in other fluid loading responsiveness studies. We used a Kolmogorov-Smirnov test and a paired t-test. Patients were classified as responders to fluid loading when the increase in COmf was at least

10%. The 10% cut-off corresponds to more than twice the reported precision of the "Modelflow" method (i.e. twice the SD for repeated measurements).[9,10] Consequently, responders experienced a clinically significant change in CO. Prediction of fluid responsiveness for COmf, Parm, Pa, Pcv, SVV and PPV was tested by calculating the area under the receiver operating characteristic (ROC) curve (AUC) together with the 95% confidence intervals (95% CI). A p-value for the difference between the AUC and the reference value of 0.5 (i.e. prediction of responders and non-responders by chance) was calculated. All values are given as mean ± SD. A p-value of less than 0.05 was considered to be statistically significant. Statistical analysis was performed using SPSS 16.0 (SPSS Inc., Chicago, Illinois, USA) and MedCalc 9 (MedCalc Inc., Mariakerke, Belgium) software.

Results

Twenty-four patients (19 males) aged 64 ± 10 years with a body surface area of 2.0 ± 0.2 m^2 completed the study protocol. Seventeen underwent coronary artery bypass grafting, and seven also underwent repair of one or two valves. Norepinephrine (0.01-0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was used in 16 patients, dobutamine (1.0-7.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) in nine and sodium nitroprusside (0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) in one. The doses of these drugs were not changed during the observation period. Hemodynamic data were distributed normally. Pooled results of hemodynamic variables at baseline and after administration of 500 ml of fluid are shown in table 6.1. After fluid loading with 500 ml, COmf, Parm, Pa and Pcv increased. HR did not change. PPV and SVV decreased.

The population was divided into responders (n = 17) and non-responders (n = 7) (table 6.1). In the responder group COmf, Pa, Pcv and Parm increased and SVV and PPV decreased after fluid loading. Parm increased from 16 to 22 mmHg. In the non-responder group, fluid loading caused Parm to increase from 24 to 30 mmHg. Pcv also increased, PPV decreased, and COmf, Pa, SVV and HR did not change significantly.

Table 6.1 Changes in hemodynamic parameters at baseline and after fluid loading with 500 ml of colloid

	All patients (n = 24)			Responders (n = 17)			Non-responders (n = 7)		
	Baseline	500 ml	p	Baseline	500 ml	p	Baseline	500 ml	p
COmf ($l \cdot min^{-1}$)	5.2 ± 1.3	6.0 ± 1.4	< 0.001	5.1 ± 1.3	6.2 ± 1.4	< 0.001	5.5 ± 1.3	5.7 ± 1.3	0.148
Parm (mmHg)	18.6 ± 7.7	24.3 ± 8.7	< 0.001	16.2 ± 6.3	22.0 ± 7.6	< 0.001	24.3 ± 8.2	29.9 ± 9.1	< 0.001
Mean Pa (mmHg)	82.3 ± 15.6	90.7 ± 16.1	< 0.001	78.9 ± 9.9	88.9 ± 11.2	< 0.001	90.4 ± 23.6	94.8 ± 25.2	0.056
Pcv (mmHg)	9.0 ± 2.6	11.5 ± 2.9	< 0.001	8.6 ± 2.6	10.9 ± 2.5	< 0.001	9.9 ± 2.5	13.0 ± 3.4	0.004
PPV (%)	13.8 ± 9.0	8.0 ± 7.5	< 0.001	14.8 ± 7.8	8.1 ± 6.6	0.001	11.1 ± 11.5	7.7 ± 10.0	0.011
SVV (%)	15.5 ± 10.5	9.3 ± 9.3	0.001	16.5 ± 10.9	8.5 ± 6.5	< 0.001	13.0 ± 9.9	11.2 ± 14.6	0.627
HR (min^{-1})	83 ± 16	83 ± 14	0.908	83 ± 18	83 ± 16	1.000	81 ± 10	82 ± 11	0.860

CO, cardiac output; Parm, arm occlusion pressure; Pcv, central venous pressure; mean Pa, mean arterial pressure; HR, heart rate.

The statistical results of the ROC curves in predicting fluid responsiveness are shown in table 6.2 and figure 6.1. AUCs for baseline COmf, Pa and Pcv were not significantly different from 0.5, or chance. In addition, the sensitivity and/or specificity were low. The results for Parm, PPV and SVV were significantly different from chance (p-values 0.012, 0.001 and 0.010 respectively) with high sensitivity and specificity for cut-off values of 21.8 mmHg or less, at least 7.2 % and at least 8.8 % respectively, indicating that these are reliable predictors of the effect on CO of fluid loading with 500 ml. There were no significant differences between the AUCs of Parm and PPV (difference = 0.0536, 95%CI -0.198 to 0.305, p = 0.676) or Parm and SVV (difference = 0.0446, 95%CI -0.227 to 0.317, p = 0.748).

Discussion

This is the first study in which Parm has been examined as a predictor of the effect of fluid loading on CO. Baseline Parm was significantly lower in the responder group than in the non-responder group. We consider that Parm is a good predictor of fluid responsiveness in our group of mechanically ventilated patients with preserved ventricular function. Simple measurements of radial artery pressure during upper arm occlusion could help to detect patients whose CO will increase after fluid loading.

Table 6.2 Receiver operating characteristics from baseline values as predictors of increase of cardiac output by more than 10% after fluid loading

	AUC	95% CI Lower	Upper	p	Sensitivity	Specificity	Cut-off
COmf (l•min^{-1})	0.588	0.371	0.783	0.507	35	100	≤ 4.0
Mean Pa (mmHg)	0.588	0.371	0.783	0.507	100	29	≤ 91.0
Pcv (mmHg)	0.687	0.427	0.829	0.259	71	57	≤ 9.0
Parm (mmHg)	0.786	0.572	0.924	0.012	88	71	≤ 21.8
PPV (%)	0.844	0.649	0.962	0.001	77	71	≥ 7.2
SVV (%)	0.746	0.544	0.908	0.010	82	86	≥ 8.8

AUC, area under receiver operating curve; 95% CI, 95% confidence interval; p-value, comparison of AUC with AUC = 0.5; COmf, cardiac output; mean Pa, mean arterial pressure; Pcv, central venous pressure; Parm, stop-flow pressure of the arm; PPV, pulse pressure variation; SVV, stroke volume variation.

In our study, the results from ROC analysis indicate that prediction of fluid loading on CO was identified equally using baseline Parm, PPV and SVV, but that prediction was not possible using baseline COmf, Pa or Pcv. Both SVV and PPV have been reported to perform better as predictors of fluid responsiveness than static pressures (Pa, Pcv and pulmonary artery occlusion pressure).[3,11-14] However, SVV or PPV are influenced by ventilator settings as tidal volume[11,15], respiratory rate[16] and also by cardiac function. In patients with reduced cardiac function, SVV is expected to be smaller because stroke volume is obviously limited and consequently ventilator-induced changes in stroke volume will be reduced.[3,12] Reuter *et al.*[15] showed that SVV could still perform as a predictor of fluid loading responsiveness in patients with reduced cardiac function.

In addition, determination of SVV and PPV is possible only if the patient is fully dependent on mechanical ventilation and has a regular cardiac rhythm. SVV and PPV failed to predict the effects of fluid loading on CO accurately in spontaneously breathing patients[4,5] and in mechanically ventilated patients with tidal volumes less than 8 ml·kg^{-1} body weight.[11] In our study, the lungs were ventilated mechanically with tidal volumes ranging from 7 to 12 ml·kg^{-1} predicted body weight. Thus, for some of our patients SVV and PPV may have been less reliable.

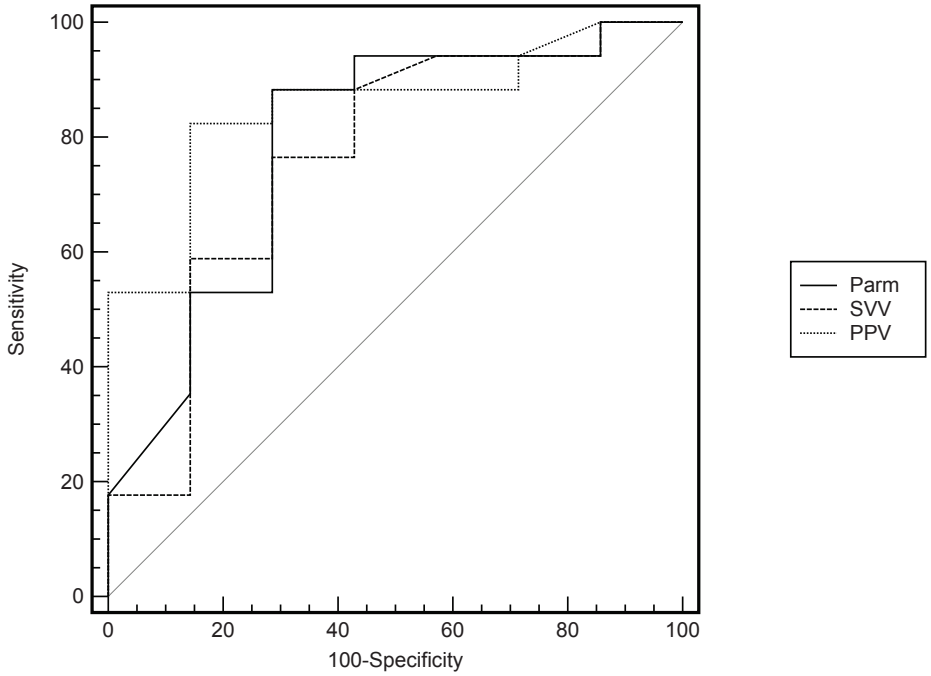

Figure 6.1 Prediction of cardiac output response
Receiver operating characteristic curves comparing the ability of baseline arm occlusion pressure (Parm), pulse pressure variation (PPV) and stroke volume variation (SVV) to discriminate between responders and non-responders. Patients were characterized as responders when cardiac output increased by at least 10% after fluid loading with 500 ml colloid.

In contrast, the Parm technique does not require a specific tidal volume or respiratory rate. To measure Parm with the arm occlusion method, only a peripheral arterial catheter is required. These requirements allow measurement in almost any environment in the operating theatre and ICU. Its application is not limited to sedated and mechanically ventilated patients with a regular heart rhythm. In our study, Parm was a good predictor of fluid loading responsiveness, equal to SVV or PPV in predicting value. However, our study patients were a relatively homogeneous group.

Definition of fluid loading responsiveness

There is no consensus on the amount of fluid or use of measurements to assess fluid loading responsiveness. Fluid amounts between 250 and 1000 ml have been reported.[3-5,17,18] Outcome measures used include CO[4,5,18], stroke volume[17] and stroke volume index.[3] Positive responses have been defined as a change in outcome measure of more than 10%-25%.[3,4,18] We chose a 10% change in pulse contour CO as cut-off

level after fluid loading with 500 ml. The 10% increase in CO was chosen because this increase can be measured accurately with the modified "Modelflow" pulse contour method.[9,10,19,20] This value corresponds with the boundaries used in other studies in which a 10% cut-off was used for 500 ml fluid loading responsiveness.[4,21-23]

Considerations and limitations

The number of patients (n = 24) included in our study is relatively small and the distribution of responders and non-responders is unequal. However, despite this small number of patients, we were able to find highly significant results. Prediction of fluid loading responsiveness by baseline Parm had high sensitivity (71%) and specificity (88%). We theorise that these results can be explained by the similarity between Parm and mean systemic filling pressure. Mean systemic filling pressure is the equilibrium pressure anywhere in the circulation under circulatory arrest, whereas Parm might be seen as the equilibrium pressure of the arm. We hypothesise that mean systemic filling pressure may be largely equal for different vascular compartments of the body because their venous outflow pressures and arterial input pressures are relatively similar. Mean systemic filling pressure is a physiological measure of effective volume status.[24,25] The pressure gradient between mean systemic filling pressure and Pcv is the driving force for venous return and thus for CO. Increasing mean systemic filling pressure and thereby the pressure gradient for venous return by fluid expansion should improve CO, assuming a constant resistance to venous return. If there is hypervolemia or limitation of cardiac function (i.e. the heart operates on the flat part of the Frank-Starling curve) fluid loading will increase Pcv along with mean systemic filling pressure, and venous return will not increase. It is important to stress that we excluded patients with previous myocardial infarction and patients with congestive heart failure (New York Heart Association class 4). Unfortunately, we could not classify our patients because no ejection fraction data were available. Therefore, we must be careful not to extrapolate our results to patients with heart failure. In our patients, a low Parm (< 22 mmHg) predicted fluid loading responsiveness. In the case of cardiac failure or tamponade, Pcv will rise along with Parm during volume administration. This will result in an unchanged pressure gradient for venous return and thus, will fail to induce an improvement in CO. Therefore, we anticipate that our results will be applicable to patients with compromised cardiac function. Rapid increments of Pcv can be seen as a warning of right ventricular limitation.

Conclusions

Arm occlusion pressure can be measured at the bedside. Unlike SVV and PPV, the measurement of Parm is relatively independent of heart rhythm, mechanical or spontaneous breathing, or sedation. Parm is a good predictor of fluid loading responsiveness in cardiac surgery patients with normal ventricular function.

References

1 Chappell D, Jacob M, Hofmann-Kiefer K, Conzen P, Rehm M: A rational approach to perioperative fluid management. *Anesthesiology* 2008; 109**:**723-740.

2 Michard F, Reuter DA: Assessing cardiac preload or fluid responsiveness? It depends on the question we want to answer. *Intensive Care Med* 2003; 29**:**1396.

3 Hofer CK, Muller SM, Furrer L, Klaghofer R, Genoni M, Zollinger A: Stroke volume and pulse pressure variation for prediction of fluid responsiveness in patients undergoing off-pump coronary artery bypass grafting. *Chest* 2005; 128**:**848-854.

4 Perner A, Faber T: Stroke volume variation does not predict fluid responsiveness in patients with septic shock on pressure support ventilation. *Acta Anaesthesiol Scand* 2006; 50**:**1068-1073.

5 Heenen S, De Backer D, Vincent JL: How can the response to volume expansion in patients with spontaneous respiratory movements be predicted? *Crit Care* 2006; 10**:**R102.

6 Magder S: Clinical usefulness of respiratory variations in arterial pressure. *Am J Respir Crit Care Med* 2004; 169**:**151-155.

7 Pang CC: Measurement of body venous tone. *J Pharmacol Toxicol Methods* 2000; 44**:**341-360.

8 Jansen JR, Versprille A: Improvement of cardiac output estimation by the thermodilution method during mechanical ventilation. *Intensive Care Med* 1986; 12**:**71-79.

9 Jansen JR, Schreuder JJ, Mulier JP, Smith NT, Settels JJ, Wesseling KH: A comparison of cardiac output derived from the arterial pressure wave against thermodilution in cardiac surgery patients. *Br J Anaesth* 2001; 87**:**212-222.

10 Critchley LA, Critchley JA: A meta-analysis of studies using bias and precision statistics to compare cardiac output measurement techniques. *J Clin Monit Comput* 1999; 15**:**85-91.

11 De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent JL: Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. *Intensive Care Med* 2005; 31**:**517-523.

12 Huang CC, Fu JY, Hu HC, Kao KC, Chen NH, Hsieh MJ, Tsai YH: Prediction of fluid responsiveness in acute respiratory distress syndrome patients ventilated with low tidal volume and high positive end-expiratory pressure. *Crit Care Med* 2008; 36**:**2810-2816.

13 Michard F, Teboul JL: Using heart-lung interactions to assess fluid responsiveness during mechanical ventilation. *Crit Care* 2000; 4**:**282-289.

14 Michard F, Teboul JL: Predicting fluid responsiveness in ICU patients: a critical analysis of the evidence. *Chest* 2002; 121**:**2000-2008.

15 Reuter DA, Kirchner A, Felbinger TW, Weis FC, Kilger E, Lamm P, Goetz AE: Usefulness of left ventricular stroke volume variation to assess fluid responsiveness in patients with reduced cardiac function. *Crit Care Med* 2003; 31**:**1399-1404.

16 De Backer D, Taccone FS, Holsten R, Ibrahimi F, Vincent JL: Influence of respiratory rate on stroke volume variation in mechanically ventilated patients. *Anesthesiology* 2009; 110**:**1092-1097.

17 Preisman S, Kogan S, Berkenstadt H, Perel A: Predicting fluid responsiveness in patients undergoing

cardiac surgery: functional haemodynamic parameters including the Respiratory Systolic Variation Test and static preload indicators. *Br J Anaesth* 2005; 95**:**746-755.

18 Osman D, Ridel C, Ray P, Monnet X, Anguel N, Richard C, Teboul JL: Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge. *Crit Care Med* 2007; 35**:**64-68.

19 de Wilde RB, Geerts BF, Cui J, van den Berg PC, Jansen JR: Performance of three minimally invasive cardiac output monitoring systems. *Anaesthesia* 2009; 64**:**762-769.

20 de Wilde RB, Schreuder JJ, van den Berg PC, Jansen JR: An evaluation of cardiac output by five arterial pulse contour techniques during cardiac surgery. *Anaesthesia* 2007; 62**:**760-768.

21 Lee JH, Kim JT, Yoon SZ, Lim YJ, Jeon Y, Bahk JH, Kim CS: Evaluation of corrected flow time in oesophageal Doppler as a predictor of fluid responsiveness. *Br J Anaesth* 2007; 99**:**343-348.

22 Wagner JG, Leatherman JW: Right ventricular end-diastolic volume as a predictor of the hemodynamic response to a fluid challenge. *Chest* 1998; 113**:**1048-1054.

23 Solus-Biguenet H, Fleyfel M, Tavernier B, Kipnis E, Onimus J, Robin E, Lebuffe G, Decoene C, Pruvot FR, Vallet B: Non-invasive prediction of fluid responsiveness during major hepatic surgery. *Br J Anaesth* 2006; 97**:**808-816.

24 Guyton AC, Polizo D, Armstrong GG: Mean circulatory filling pressure measured immediately after cessation of heart pumping. *Am J Physiol* 1954; 179**:**261-267.

25 Maas JJ, Geerts BF, van den Berg PC, Pinsky MR, Jansen JR: Assessment of venous return curve and mean systemic filling pressure in postoperative cardiac surgery patients. *Crit Care Med* 2009; 37**:**912-918.