

# Pulse contour cardiac output: an evaluation of the FloTrac method

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**Background and objective** The aim of this study was to determine the agreement between pulmonary artery thermodilution (PA-TD) and a new pulse contour method (PCM), FloTrac/Vigileo version 1.0, and to assess the ability of FloTrac to track sudden changes in cardiac output.

**Methods** Cardiac output was determined twice after induction of anaesthesia, but before cardiac surgery, with both PA-TD and a PCM in order to determine the precision of both methods. The bias and agreement between the two methods were calculated using Bland–Altman analysis. Postoperatively, in patients with heart rates under 60 beats  $\text{min}^{-1}$ , atrial pacing was initiated and cardiac output was determined before and after with both methods.

**Results** Twenty-five patients were investigated. The precisions of PA-TD and the PCM were 0.35 (95% confidence interval  $\pm 0.12$ ) and 0.6  $\text{l min}^{-1}$  (95% confidence interval  $\pm 0.21\%$ ). The bias between PA-TD and the PCM was  $-0.51 \text{ l min}^{-1}$  and the limits of agreement were  $\pm 1.87 \text{ l min}^{-1}$  (95% confidence interval  $\pm 0.39$  and  $\pm 0.66$ ).

The percentage error was 48%. The changes in cardiac output with atrial pacing were in the same direction in all nine patients.

**Conclusion** In this study, agreement between PA-TD and the PCM was poor, but the PCM was able to track the direction of pace-induced changes in cardiac output. *Eur J Anaesthesiol* 26:484–489 © 2009 European Society of Anaesthesiology.

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## Introduction

Measurement of cardiac output (CO) is widely used in critically ill patients and cardiac surgical patients. Over recent decades, the main method for determination of CO has been pulmonary artery thermodilution (PA-TD) requiring insertion of a pulmonary artery catheter (PAC). More recently, new less invasive methods have been developed. Technology using pulse contour CO (PiCCO System; PULSION Medical Systems AG, Munich, Germany, and LiDCO; LiDCO Ltd, London, UK) is now used as an alternative to PA-TD and has in some clinics replaced the use of a PAC.

The theory behind the calculations of CO from the pulse wave has been known for decades, but was reintroduced by Wesseling *et al.* [1]. From analysis of the pulse wave contour, compliance and impedance of the arterial system, CO is calculated. The compliance of the arterial system varies individually and pressure/volume relations of arteries are known not to be linear. Therefore, an independent technique is required to provide initial calibration of the pulse contour CO analysis, as this technique cannot account for variables such as compliance of the vascular tree. In most cases, this is done by

calibration with thermo or lithium dilution using the Stewart–Hamilton formula (PiCCO and LiDCO). Although considered less invasive than PAC, these methods do need insertion of a central venous catheter (CVC) and/or special arterial lines.

Therefore, the development of the FloTrac monitor (FloTrac/Vigileo, Edwards Lifesciences, Irvine, California, USA), which requires only a standard arterial line and no independent calibration for measurement of continuous CO (CCO), sounds appealing.

FloTrac calculates CO with a new algorithm, which should eliminate the necessity for independent calibration and insertion of a CVC. From comprehensive analysis of the pulse waveform characteristics and dynamic changes, patient-to-patient differences estimated from demographic data, heart rate (HR), mean arterial pressure (MAP) and pulse pressure, this pulse contour method (PCM) should, according to the manufacturers, compensate for differences in arterial size and vascular tone (compliance and resistance). CO is calculated as an average of the previous 20 s measurements and uses the previous 10 min for ‘internal calibration’.

However, the exact algorithm is not available and only limited validation data for this technique have so far been published. These are showing conflicting results from acceptable [2–7] to limited [8,9] to poor agreement [10–12], just like previous validation of the PCM with calibration [13–19]. None of the studies investigating FloTrac have calculated the precision of the investigated method (FloTrac) or the reference method (PA-TD) in order to determine an unbiased estimate of acceptable limits of agreement (LOA).

Only one of these 11 studies [2] investigating FloTrac has tried to calculate the precision of the investigated method (FloTrac) and the reference method (PA-TD) in order to determine an unbiased estimate of acceptable LOA [2]; unfortunately, this was calculated in an incorrect way.

The aim of this study is to validate the CO measured with FloTrac against PA-TD CO (still regarded as the *de facto* clinical gold standard) in an unbiased fashion by calculating the precision of the two methods and the bias and LOA between the methods as recommended by Bland and Altman [20] and Critchley and Critchley [21].

The present study will present the precision of PA-TD and the PCM; agreement analysis between PA-TD and the PCM; and a comparison of the pace-induced changes in CO determined with PA-TD and the PCM.

## Methods

Following ethical committee approval and written informed consent, 27 adult patients scheduled for coronary artery bypass grafting were included in the study. Patients with heart valve disorder, intracardiac shunts and arrhythmias were excluded.

General anaesthesia was induced with fentanyl 5–10  $\mu\text{g kg}^{-1}$ , midazolam 0.05–0.1  $\text{mg kg}^{-1}$  and rocuronium 0.5–0.7  $\text{mg kg}^{-1}$ . Anaesthesia was continued with sevoflurane 1–2% inspired in oxygen. During extracorporeal circulation, anaesthesia was maintained with propofol 200–300  $\text{mg h}^{-1}$ . All patients were normothermic and normoventilated ( $P_a\text{CO}_2$  between 4.5 and 6.0 kPa) during the study period.

A 7.5F PA-TD catheter (Paceport, Edwards, Copenhagen, Denmark) was inserted via an internal jugular vein and advanced until a typical pulmonary artery pressure contour, measured from the tip of the catheter, was evident. The PA-TD CO was determined by the Phillips monitor.

A standard arterial line (BD 20G) was inserted in the radial artery and connected to the FloTrac/Vigileo monitor (version 1.0).

After the induction of anaesthesia and haemodynamic stabilization, CO was determined twice with both PA-TD and FloTrac in order to determine the precision of the two methods. The four FloTrac CO readings, matching the four thermal indicator injections for PA-TD, were averaged to determine the pulse contour CO. The thermodilution results of the PA-TD CO were calculated as the average of four thermal indicator injections of 10 ml iced isotonic saline as advocated by Nilsson *et al.* [22] and Berthelsen *et al.* [23]. The injections were done manually, all by the same physician and completed within 3 s. All injections were started as soon as the CO computer indicated that the pulmonary and peripheral artery temperatures were stable ( $\pm 0.05^\circ\text{C}$ ), without considering the relationship between the timing of the injection and the respiratory cycle. All curves of changes in temperature in the pulmonary artery were inspected for irregularities and accepted/rejected before results were displayed on the monitor. Aborted attempts were replaced by a new injection. The FloTrac CO measurements were obtained from the FloTrac/Vigileo monitor at the exact same time as the matching PA-TD CO calculation was finished. This means that CO was determined for the same  $4 \times 20$  s periods.

All these basic measurements included four measurements, performed twice simultaneously for each method, within 5 min before any surgery was commenced. It was regarded as essential that the patients were absolutely haemodynamically stable during this period.

Postoperatively, CO was again determined simultaneously using the PCM and the PA-TD method. In patients with a HR less than 60  $\text{beats min}^{-1}$ , epicardial pacing (HR 80–90  $\text{beats min}^{-1}$ ) from the right atrium was initiated and CO was again determined using PA-TD and the PCM. In the present investigation, we had defined an increase/decrease in CO as a change of more than 1 SD of the difference in replicate CO determinations with PA-TD.

Throughout the whole study, the arterial waveform was visually controlled and action was taken if signs of damping occurred. Likewise, the pressure transducer was kept throughout the whole study at the mid-axillary level. Before any measurements, the FloTrac/Vigileo monitor had for at least 10 min been able to record and analyse the actual arterial pulse wave, in order to adjust for vascular compliance (internal calibration).

## Statistics

Data are presented as medians (range). From the data on the preoperative CO measurements, the precision (2 SD of the difference between replicate measurements) of both methods was determined. PA-TD and PCM COs were compared with bias and LOA analysis according to Bland and Altman [20].

Changes in CO ( $\Delta$ CO) after the initiation of pacing are analysed using a paired *t*-test.  $\Delta$ CO values measured with the PA-TD and the PCM were compared using correlation analysis.

## Results

### Patients' characteristics

Twenty-seven patients were included in the study. One was excluded due to malfunction of the FloTrac pressure transducer and the other was excluded due to haemodynamic instability at the time of preoperative basic measurements.

Twenty-five patients (22 men) completed the study. The median age was 65 (44–76) years, weight 81 (43–128) kg and height 175 (158–186) cm.

### Baseline measurements

The median left ventricle ejection fraction was 0.40 (0.20–0.60), HR 55 (50–71) beats  $\text{min}^{-1}$ , median arterial blood pressure 66 (55–90) mmHg, median pulmonary artery pressure 16 (12–23) mmHg, central venous pressure 6 (2–12) mmHg, body temperature 35.7 (35.2–36.4) $^{\circ}\text{C}$ , cardiopulmonary bypass time 68 (39–193) min, aortic clamp time 52 (23–142) min and total surgery time 180 (140–285) min. Three basic thermodilution measurements were aborted and replaced due to irregularities of the thermodilution curves as described in the Methods.

### Precision of cardiac output measurements: pulmonary artery thermodilution

The mean difference (bias) between replicate measurements of CO was  $0.031 \text{ min}^{-1}$ , the precision (2 SD of the difference between repeated measurements) was  $0.351 \text{ min}^{-1}$  [95% confidence interval (CI)  $\pm 0.12$ ] and percentage error, 9%. The difference between two determinations of CO did not change throughout the range of the measurements (Fig. 1). Median CO was  $3.81 \text{ min}^{-1}$  ( $2.1\text{--}7.11 \text{ min}^{-1}$ ) and the coefficient of variation was 5%.

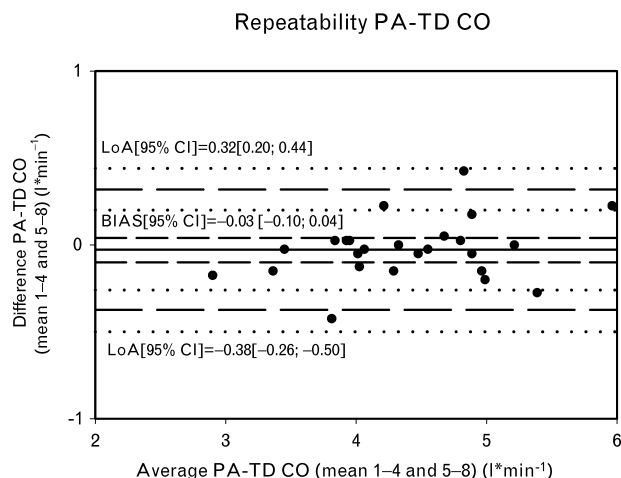
### Precision of cardiac output measurements: pulse contour method

The bias between replicate measurements of CO was  $0.11 \text{ min}^{-1}$ , the precision was  $0.61 \text{ min}^{-1}$  (95% CI  $\pm 0.21$ ) and percentage error, 16%. The difference between two determinations of CO did not change throughout the range of the measurements (Fig. 2). Median CO was  $4.41 \text{ min}^{-1}$  ( $2.9\text{--}6.01 \text{ min}^{-1}$ ) and the coefficient of variation was 5%.

### Agreement between pulmonary artery thermodilution cardiac output and pulse contour method cardiac output

The bias between PA-TD CO and PCM CO was  $-0.511 \text{ min}^{-1}$  (95% CI  $\pm 0.39$ ) with LOA of  $\pm 1.871 \text{ min}^{-1}$  (95% CI  $\pm 0.66$ ). The CO was  $4.21 \text{ min}^{-1}$  ( $2.7\text{--}6.211 \text{ min}^{-1}$ ) and the percentage error was 48% (Fig. 3).

Fig. 1



Limits of precision with 95% confidence intervals (CI) depicted according to Bland and Altman [20]. Results from replicate determinations of cardiac output (CO) with pulmonary artery thermodilution (PA-TD) in 25 patients. LOA, limits of agreement.

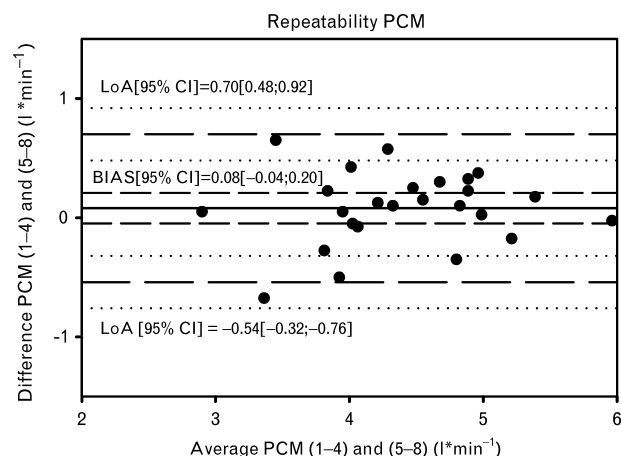
### Changes in cardiac output after atrial pacing

Of the 25 patients included in the study, nine needed atrial pacing to fulfil prespecified haemodynamic criteria.

PA-TD CO increased significantly from a value of  $4.3$  ( $3.5\text{--}5.41 \text{ min}^{-1}$ ) to  $5.61 \text{ min}^{-1}$  ( $3.9\text{--}7.41 \text{ min}^{-1}$ ) with pacing, a mean  $\Delta$ CO of  $1.11 \text{ min}^{-1}$ . PCM CO likewise increased significantly from  $3.7$  ( $2.2\text{--}5.81 \text{ min}^{-1}$ ) to  $5.81 \text{ min}^{-1}$  ( $4.9\text{--}7.81 \text{ min}^{-1}$ ), a mean  $\Delta$ CO of  $2.11 \text{ min}^{-1}$ .

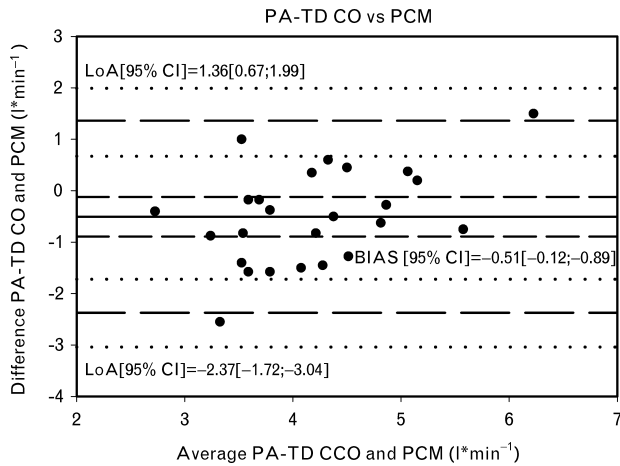
All nine patients who needed atrial pacing increased their CO (more than 1 SD of the difference in replicate CO

Fig. 2



Limits of precision with 95% confidence intervals (CI) depicted according to Bland and Altman [20]. Results from replicate determinations of cardiac output (CO) with pulse contour method (PCM) in 25 patients. LOA, limits of agreement.

Fig. 3



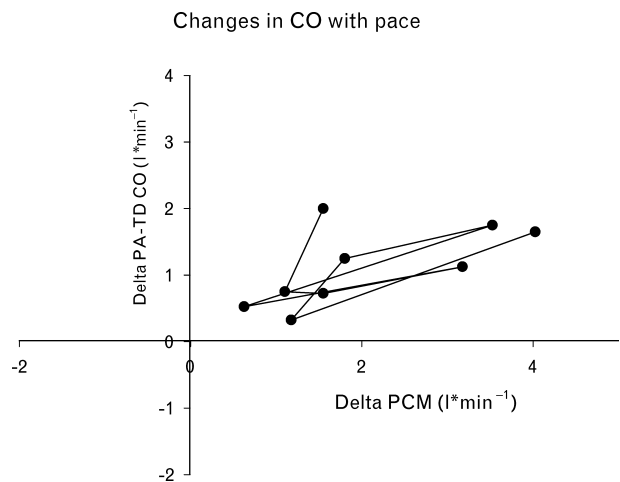
Agreement between cardiac output (CO) determined with pulmonary artery thermodilution (PA-TD) and the pulse contour method (PCM). CI, confidence interval; LOA, limits of agreement.

determinations with PA-TD) according to both methods and all but one by more than 700 ml (2 SD) (Fig. 4).

**Discussion**

The present study presents a comparison of CO measurements between the FloTrac/Vigileo monitor (PCM) and PA-TD, showing an unacceptable agreement. However, it seems that the FloTrac/Vigileo monitor is able to detect the same direction of sudden changes in CO due to epicardial pacing as PA-TD.

Fig. 4



Correlation between changes in cardiac output (CO) measured with pulmonary artery thermodilution (PA-TD) and the pulse contour method (PCM).

**Pulmonary artery thermodilution vs. pulse contour method**

Introducing new CO monitors requires comprehensive validation with estimation of precision of both the new monitor and the reference method. In this case, the reference method is the *de facto* gold standard, PA-TD. PA-TD is shown to have a high precision, when averaged from four replicates, and most clinical guidelines and haemodynamic algorithms are based on CO measured with PA-TD [22]. Because of this, PA-TD must still be regarded as the reference method of choice.

Comparing two methods, the use of bias and LOA according to Bland and Altman [20], is essential and, before introducing or replacing the old gold standard, the new method needs to be proven reliable and precise.

In the present study, the precision of the two methods is found acceptable. The precision of PA-CO is comparable with previous studies [13,22]. From these precisions, it is possible to calculate the level of the LOA, which we, according to Critchley and Critchley [21], at least have to accept. This is calculated to be 1.31 min<sup>-1</sup> or 18% using the equation  $SDa + b = \sqrt{(\Sigma \Delta \alpha \alpha) + \Sigma \Delta \beta \beta}$ .

Comparing the two methods, we found a bias indicating that FloTrac is overestimating CO by 0.51 min<sup>-1</sup> compared with PA-TD, and a very wide LOA ( $\pm 1.871$  min<sup>-1</sup> or 48%), clearly above the calculated, acceptable level of 1.31 min<sup>-1</sup>.

Previous studies, comparing FloTrac with PA-TD [2–12], have shown similar results with bias between 0 and 0.91 min<sup>-1</sup> and the LOA around  $\pm 2$ –2.61 min<sup>-1</sup> and with conclusions ranging from acceptable [2–7] to limited [8,9] to poor agreement [10–12]. Three of the studies have used cardiac index (rather than CO), which will give a CO of more or less double that found in adults [5,8,12]. In all studies, calculations of bias and LOA are carried out on many repeated measurements for each patient without statistical correction. As this could falsely increase the agreement, interpretation should be cautious [20]. Only one of these studies [2] has (unfortunately in an incorrect way) calculated the precision of the reference and the investigated methods. This is essential in order to determine the acceptability of the LOA in an unbiased fashion.

Interpreting the LOA of previous studies, [2–4,6–12] we believe, contrary to the editorial of Manecke [24], that none of them seem to be clinically acceptable and, therefore, in our view, PCM and PA-TD cannot be regarded as interchangeable methods for measuring CO in the patient groups studied.

The present study is performed with version 1.0 of the FloTrac/Vigileo system like most of the other studies. Only two studies [5,7] have investigated the new version

(version 1.07). Button *et al.* [7] found LOA around  $1.81 \text{ min}^{-1}$  between the PCM and TD-CO, interpreted from their figures. Also using the new version, Mayer *et al.* [5] found LOA of  $0.61 \text{ min}^{-1}$  for the cardiac index, which could be potentially acceptable, depending on the CO behind the calculations and the precision of the methods. Moreover, Mayer *et al.* conducted 282 CO calculations on 40 patients without statistical correction for repeated measurements.

#### Pacing-induced changes in cardiac output measured with pulmonary artery thermodilution and the pulse contour method

$\Delta\text{CO}$ , induced by pacing, was tracked in the same direction by the two methods. The magnitude of  $\Delta\text{CO}$  found in our study was not of the same size. Owing to the small number of patients studied (nine out of 25), it is not possible to conclude more than that the two methods track changes of CO in the same direction.

This finding is concurrent with the finding of Mayer *et al.* [12], who found a good ability of FloTrac to track haemodynamic changes compared with PA-TD.

Comparing FloTrac with other commercially available PCMs, such as PiCCO or LIDCO, raises several questions. The PiCCO monitor has been extensively validated in several studies and is implemented in many intensive care and semi-intensive care units. Comparisons between PiCCO and PA-TD have shown LOA of the same magnitude as comparisons between FloTrac and PA-TD, though with some studies concluding good agreement [14–17] and others poor [13,18].

However, contrary to the FloTrac system, PiCCO has an inherent transpulmonary thermodilution CO monitor, used for calibration and found to have good agreement with PA-TD [13]. In clinical situations, this feature allows us to measure reliable values of CO. In addition to this advantage, PiCCO has shown a reliable ability to track CO changes [13,19].

The obvious advantage of FloTrac is the less invasive approach and the easy access to CO monitoring. On the other hand, monitoring and treatment of critically ill patients normally require insertion of a CVC for infusion of drugs, monitoring central venous pressure or central venous blood samples [25]. Initiating therapeutic attempts guided by an unreliable CO monitor is hazardous and could cause detrimental results. Hence, before more accurate low invasive monitors are available, it seems wise to postpone CO monitoring until a PiCCO or PAC has been inserted.

#### Limitations of the study

Only patients in sinus rhythm with normal heart valves and left ventricular function were included in the study. All the

patients were haemodynamically stable, normovolaemic and normothermic, and none received vasoactive agents. Haemodynamically unstable patients due to sepsis, arrhythmia and cardiac failure were not investigated. The patients in this study are, therefore, very different from the critically ill patients who might benefit from a reliable CCO monitor. In the investigation of the ability of FloTrac to monitor trends in CO during epicardial pacing, only nine of 25 patients fulfilled the protocol.

The present study is not able to conclude which method of the two is the best; only the agreement can be assessed.

Aborting and replacing thermodilution measurements due to irregularities of the thermodilution curves could be interpreted as favouring PA-TD. But according to Bland and Altman [20], it is of crucial importance that the precisions of both methods are as good as possible. Increasing the precision of PA-TD provides the best possibility for a qualified comparison with any other method. Being able to visually detect irregularities of the thermodilution curves and potentially abort and replace these is an inherited strength of thermodilution.

All efforts to optimize the FloTrac were made by always having a good and undammed pulse curve and giving the system at least 10 min for 'internal calibration'.

#### Conclusion

The agreement between FloTrac (version 1.0) and PA-TD is not satisfactory, but the FloTrac system seems to be able to track pacing-induced sudden haemodynamic changes. Before FloTrac/Vigileo (Edwards Lifesciences) can replace PA-TD, the new modifications of the system (version 1.07) need to be further investigated in an unbiased and statistically comprehensive manner.

#### References

- 1 Wesseling KH, de Wit B, Weber JAP, *et al.* A simple device for the continuous measurement of cardiac output. *Adv Cardiovasc Physiol* 1983; **5**:16–52.
- 2 McGee WT, Horswell JL, Calderon J, *et al.* Validation of a continuous, arterial pressure-based cardiac output measurement: a multicenter, prospective clinical trial. *Crit Care* 2007; **11**:R105.
- 3 Manecke GR Jr, Auger WR. Cardiac output determination from the arterial pressure wave: clinical testing of a novel algorithm that does not require calibration. *J Cardiothorac Vasc Anesth* 2007; **21**:3–7.
- 4 Breukers RM, Sepelkhouy S, Spiegelenberg SR, Groeneveld AB. Cardiac output measured by a new arterial pressure waveform analysis method without calibration compared with thermodilution after cardiac surgery. *J Cardiothorac Vasc Anesth* 2007; **21**:632–635.
- 5 Mayer J, Boldt J, Wolf MW, *et al.* Cardiac output derived from arterial pressure waveform analysis in patients undergoing cardiac surgery: validity of a second generation device. *Anesth Analg* 2008; **106**:867–872; table of contents.
- 6 Cannesson M, Attof Y, Rosamel P, *et al.* Comparison of FloTrac cardiac output monitoring system in patients undergoing coronary artery bypass grafting with pulmonary artery cardiac output measurements. *Eur J Anaesthesiol* 2007; **24**:832–839.
- 7 Button D, Weibel L, Reuthebuch O, *et al.* Clinical evaluation of the FloTrac/Vigileo™ system and two established continuous cardiac output monitoring devices in patients undergoing cardiac surgery. *Br J Anaesth* 2007; **99**:329–336.

- 8 Opdam HI, Opdam HI, Wan L, Bellomo R. A pilot assessment of the FloTrac™ cardiac output monitoring system. *Intensive Care Med* 2007; **3**:344–349.
- 9 Manecke GR. Edwards FloTrac sensor and Vigileo monitor: Easy, accurate and reliable cardiac output assessment using the arterial pulse wave. *Expert Rev Med Devices* 2005; **2**:523–527.
- 10 Biais M, Nouette-Gaulain K, Cottenceau V, *et al.* Cardiac output measurement in patients undergoing liver transplantation: pulmonary artery catheter versus uncalibrated arterial pressure waveform analysis. *Anesth Analg* 2008; **106**:1480–1486; table of contents.
- 11 Compton FD, Zukunft B, Hoffmann C, *et al.* Performance of a minimally invasive uncalibrated cardiac output monitoring system (FloTrac/Vigileo) in haemodynamically unstable patients [review]. *Br J Anaesth* 2008; **100**:451–456.
- 12 Mayer J, Boldt J, Schöllhorn T, *et al.* Semi invasive monitoring of cardiac output by a new device using arterial pressure waveform analysis: a comparison with intermittent pulmonary artery thermodilution in patients undergoing cardiac surgery. *Br J Anaesth* 2007; **98**:176–182.
- 13 Østergaard M, Nielsen J, Rasmussen JP. Berthelsen cardiac output contour analysis vs. pulmonary artery thermodilution. *Acta Anaesthesiol Scand* 2006; **50**:1044–1049.
- 14 Zöllner C, Haller M, Weis M, *et al.* Beat-to-beat measurement of cardiac output by intravascular pulse contour analysis: a prospective criterion standard study in patients after cardiac surgery. *J Cardiothorac Vasc Anesth* 2000; **14**:125–129.
- 15 Gödje O, Höke K, Lamm P, *et al.* Continuous, less invasive hemodynamic monitoring in intensive care after cardiac surgery. *Thorac Cardiovasc Surg* 1998; **46**:242–249.
- 16 Buhre W, Weyland A, Kazmaier S, *et al.* Comparison of cardiac output assessed by pulse-contour analysis and thermodilution in patients undergoing minimally invasive direct coronary bypass grafting. *J Cardiothorac Vasc Anesth* 1999; **13**:437–440.
- 17 Mielck F, Buhre W, Hanekop G, *et al.* Comparison of continuous cardiac output measurements in patients after cardiac surgery. *J Cardiothorac Vasc Anesth* 2003; **17**:211–216.
- 18 Rauch H, Müller M, Fleischer F, *et al.* Pulse contour analysis versus thermodilution in cardiac surgery patients. *Acta Anaesthesiol Scand* 2002; **46**:424–429.
- 19 Felbinger TW, Reuter DA, Eltzschig HK, *et al.* Cardiac index measurements during rapid preload changes: a comparison of pulmonary artery thermodilution with arterial pulse contour analysis. *J Clin Anesth* 2005; **17**:241–248.
- 20 Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1**:307–310.
- 21 Critchley LAH, Critchley JAJH. A meta-analysis of studies using bias and precision statistics to compare cardiac output measurement techniques. *J Clin Monit* 1999; **15**:85–91.
- 22 Nilsson LB, Nilsson JC, Skovgaard LT, Berthelsen PG. Thermodilution cardiac output – are three injections enough? *Acta Anaesthesiol Scand* 2004; **48**:1322–1327.
- 23 Berthelsen PG, Eldrup N, Nilsson LB, Rasmussen JP. Thermodilution cardiac output. Cold vs. room temperature injectate and the importance of measuring the injectate temperature in the right atrium. *Acta Anaesthesiol Scand* 2002; **46**:1103–1110.
- 24 Manecke GR. Cardiac output from the arterial catheter: deceptively simple [editorial]. *J Cardiothorac Vasc Anesth* 2007; **21**:629–631.
- 25 Rivers E, Nguyen B, Havstad S, *et al.* Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; **19**:1368–1377.