Performance of a minimally invasive uncalibrated cardiac output monitoring system (FloTrac™/Vigileo™) in haemodynamically unstable patients†


Department of Nephrology, Charité University Medicine Berlin, Campus Benjamin Franklin, Hindenburgdamm 30, D-12200 Berlin, Germany

*Corresponding author: Charité Centrum 10, Medizinische Klinik für Nephrologie, Charité Campus Benjamin Franklin, Hindenburgdamm 30, D-12200 Berlin, Germany.
E-mail: friederike.compton@charite.de

Background. Early haemodynamic assessment is of particular importance in the evaluation of haemodynamically compromised patients, but is often precluded by the invasiveness and complexity of the established cardiac output (CO) monitoring techniques. The FloTrac™/Vigileo™ system allows minimally invasive CO determination based on the arterial pressure waveform derived from any standard arterial catheter, and the algorithm underlying CO calculation was recently modified to allow a more precise estimate of aortic compliance.

Methods. Using the new software, we studied 25 haemodynamically unstable patients who had a radial artery catheter and underwent invasive haemodynamic monitoring with the PiCCO™ system. PiCCO™-derived transpulmonary thermodilution and pulse contour CO (reference-CO) were compared with the CO values obtained with the FloTrac™/Vigileo™ system (AP-CO). Reported CO values are indexed to body surface area. Agreement between reference-CO and AP-CO recorded during routine clinical care was assessed using Bland–Altman statistics.

Results. Overall bias between the reference-CO and the AP-CO (n=324) was 0.68 litre min⁻¹ m⁻² with a high percentage error of ± 58.8% (95% limits of agreement ± 1.94 litre min⁻¹ m⁻²). There was a significant difference (P<0.001) between the radial and the femoral mean arterial pressures, and bias was significantly larger for a mean pressure difference of >5 mm Hg (0.93 vs 0.57 litre min⁻¹ m⁻², P=0.032). No connection was found between the nor-epinephrine dose and the CO agreement.

Conclusions. Despite the updated algorithm, AP-CO still showed a limited agreement with the reference-CO and systematically underestimated the CO so that the method is not suitable to replace invasive CO monitoring at present.

Br J Anaesth 2008; 100: 451–6

Keywords: arterial pressure, measurement; intensive care; measurement techniques, cardiac output

Accepted for publication: December 6, 2007

Assessment of the cardiac output (CO) is increasingly recommended during the initial evaluation of haemodynamically compromised patients, which often takes place in the emergency department or elsewhere outside the intensive care unit (ICU).¹ ² The invasiveness and complexity of the established CO monitoring devices (pulmonary artery catheter, transpulmonary thermodilution systems) usually preclude their use outside the ICU or the operating room, so that new, easier to use, and less invasive techniques to determine CO are being sought.

The recently introduced CO monitoring FloTrac™/Vigileo™ device (Edwards Lifescience LLC, Irvine,

†This work was presented in part at the annual congress of the European Society of Intensive Care Medicine (ESICM) 2007 in Berlin, Germany.
CA, USA) allows CO determination from the arterial pressure waveform of any existing peripheral arterial line without external calibration. Ease of use and minimal invasiveness render the device suitable for use outside the ICU, and its application in the emergency department was reported. \(^3\)

Initial evaluation of the device suggested that CO results are reliable and robust, \(^4\) but more recent studies performed in haemodynamically unstable patients questioned this agreement with established invasive CO monitoring systems. \(^5\)–\(^8\) The algorithm underlying the uncalibrated CO calculation has been modified and updated since, and we therefore conducted a study to re-evaluate the FloTrac\(^\text{TM}\)/Vigileo\(^\text{TM}\) system in haemodynamically unstable patients using this new software.

### Methods

Twenty-five patients treated in the medical ICU of the Charité University Medicine Campus Benjamin Franklin, Berlin, Germany, between July 2006 and May 2007 were consecutively enrolled in the prospective open study. For inclusion, patients had to fulfil the following criteria: (a) haemodynamic instability with the need for fluid resuscitation or vasopressor therapy, (b) existence of a radial artery catheter for direct blood pressure monitoring, and (c) placement of a femoral artery catheter for invasive haemodynamic monitoring using the PiCCO\(^\text{TM}\) system. All procedures and therapies were performed as part of routine patient care and at the discretion of the treating physician; none of the above interventions was initiated for study purposes. Sinus rhythm was not a prerequisite for inclusion in the study. Approval was obtained from the institutional ethics committee, who waived the need for informed consent.

In all patients, the PiCCO\(^\text{TM}\) 5 F 20 cm arterial thermistor catheter (Pulsio cath PV2015L20, Pulsion Medical Systems, Munich, Germany) was inserted into the femoral artery, allowing CO measurement by transpulmonary thermodilution (TD-CO). TD-CO was used to calibrate the arterial pulse contour analysis derived continuous CO (PC-CO). \(^9\) TD-CO measurement was performed using 20 ml of \(<8^\circ\text{C}\) 5% dextrose solution and calculated as the average of three consecutive measurements using the Philips CCO/C.O. module (model M1012A, Philips Medical Systems, Böblingen, Germany) with the PiCCO\(^\text{TM}\) software integrated into the patient monitors (CMS monitor model M1097A, software version 17.62, Philips Medical Systems). After initial TD-CO measurement, PC-CO re-calibration was done at least every 24 h.

Radial access was obtained using a standard radial artery catheterization set (Leader Cath 115.798, Vygon GmbH & Co., KG, Aachen, Germany). The radial artery catheter was connected to the FloTrac\(^\text{TM}\) sensor (model MHD8, Edwards Lifescience LLC), which in addition to arterial pressure transduction allows CO estimation from the arterial pressure waveform (AP-CO) when linked to the Vigileo\(^\text{TM}\) monitor (model MHM1E, Edwards Lifescience LLC). AP-CO determination is based on a proprietary algorithm utilizing the relationship between pulse pressure and stroke volume and the inverse relationship with aortic compliance. A conversion factor ($\chi$) is used to account for dynamic changes in vascular tone and is calculated from certain pressure waveform characteristics along with the patient demographic data (age, gender, height, and weight) used to estimate large-vessel compliance. With the new software (version 1.10, introduced in spring 2006), $\chi$ is updated and applied to the algorithm on a rolling 60 s average now, as opposed to every 10 min with the previous software.

All pressure transducers were zeroed to the mid-chest level, and care was taken to ensure that in the individual patients, both the femoral and the radial artery transducers were zeroed to the exact same level and that the pressure waveforms were not dampened at the time of measurements.

Data collection was started with the initial calibration of the PiCCO\(^\text{TM}\) system and after a 10 min period to allow stabilization of the FloTrac\(^\text{TM}\)/Vigileo\(^\text{TM}\) system. Thereafter, data were recorded during routine clinical care with no predetermined time intervals, but not during or immediately after bolus catecholamine administration or during other periods of acute instability. Both TD-CO measurements and PC-CO determinations were used for comparison with AP-CO and are referred to as reference-CO. In addition, arterial pressure measured via the femoral and radial arterial lines was recorded with each pair of CO values and continuous catecholamine infusion doses. Certain patient characteristics were also registered, including Simplified Acute Physiology Score (SAPS2) and Sequential Organ Failure Assessment (SOFA) scores at the time of measurements.

Statistical analysis was performed using GraphPad Prism software (version 4.0c, GraphPad software Inc., San Diego, CA, USA). Data are displayed as mean (sd). CO values were indexed to body surface area and are referred to as cardiac index (CI). Statistical differences between groups and paired measurements were assessed using non-parametric Mann–Whitney U and Wilcoxon testing, respectively, and a two-sided $P$-value of $<0.05$ was considered significant. Linear regression analysis was used to determine correlation between continuous parameters. For agreement between the CO determination methods, a Bland–Altman analysis was applied calculating bias as the mean difference between both methods and limits of agreement, as the bias defining the range in which 95% of the differences between the two methods are expected to lie. Percentage error was then calculated as described by Critchley and Critchley. \(^10\) To investigate the ability to track CO changes regardless of absolute CO accuracy, delta CI ($\Delta$CI) between two consecutive measurements was calculated and the corresponding results were...
compared with a Bland–Altman analysis as well. Analyses were performed for all data pairs taken together and for subgroups (TD-CO only, first and first to third measurements per patient, high vs low arterial pressure differences between radial and femoral artery readings, and high vs low norepinephrine infusion doses).

Results

Patient characteristics are displayed in Table 1. Nineteen patients were admitted to the ICU primarily for acute respiratory failure, one patient was admitted after successful cardiopulmonary resuscitation and was therefore also on ventilator support at admission. In the five remaining patients, reasons for ICU admission were septic shock (n=2), acute renal failure (n=2), and cardiac failure (n=1). Radial artery access was obtained on the day of admission in 18 patients [mean 0.5 (sd 0.9) days after admission], femoral arterial line placement to initiate invasive haemodynamic monitoring was performed with an average of 1.5 days later [mean 2.0 (2.0) days after admission].

A total of 324 measurements were recorded in the 25 patients with a mean of 13 (9.9) measurements per patient over a mean of 3 (2) days. In one patient, only one measurement was available because he died shortly after initiation of haemodynamic monitoring. The maximum number of measurements was 40, performed in one patient over a period of 8 days.

All patients but one received continuous catecholamine infusions at the time of study entry and during 315 of the 324 recorded measurements. Continuous catecholamine infusion doses at the time of measurements are displayed in Table 2. In 19 cases, dopamine was used in a dose of <5 μg kg⁻¹ min⁻¹, at all other times norepinephrine, epinephrine, or higher dose dopamine was given with the intention of a vasopressor effect (n=296). None of the patients received inotropic support with dobutamine alone.

When arterial pressures derived from the radial and femoral arterial lines, respectively, were compared, the radial artery pressures were significantly lower than the femoral artery pressures (Table 3). Agreement between the mean radial and femoral artery pressures is shown in Figure 1. Bias was 3 mm Hg with limits of agreement of ±14 mm Hg, yielding a percentage error of ±17.6%. There was no linear correlation between the mean arterial pressure difference and the norepinephrine infusion dose (r=0.04, P=0.416). When CO measurements were compared, AP-CI values obtained with the radial artery derived FloTrac™/Vigileo™ were also significantly lower than the reference-CI measured with the PiCCO™ system using the femoral arterial line (P<0.001). For all 324 data pairs taken together, bias was at 0.68 litre min⁻¹ m⁻² with limits of agreement of ±1.94 litre min⁻¹ m⁻² and a percentage error of ±58.8% (Fig. 2A). Comparing only TD-CI values (n=90) with the respective AP-CI results yielded a slightly larger bias of 0.76 litre min⁻¹ m⁻² with limits of agreement of ±1.75 litre min⁻¹ m⁻² and a slightly smaller percentage error of ±51.7% (Fig. 2B). To avoid statistical bias, CO values were also compared for subgroups with equal numbers of measurements per patient. Comparing only the first TD-CI measurement recorded with the simultaneously obtained AP-CI results (n=25), bias and agreement were 0.95 (2.13) litre min⁻¹ m⁻². When the first three measurements per patient were used and the one patient in whom only one measurement was available was

Table 3 Comparison of radial and femoral arterial pressures (mm Hg). *Wilcoxon matched pairs test

<table>
<thead>
<tr>
<th></th>
<th>Femoral artery [mean (sd)]</th>
<th>Radial artery [mean (sd)]</th>
<th>P-value*</th>
</tr>
</thead>
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<tr>
<td>Systolic pressure</td>
<td>119 (21)</td>
<td>116 (25)</td>
<td>0.252</td>
</tr>
<tr>
<td>Diastolic pressure</td>
<td>61 (11)</td>
<td>59 (11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>79 (13)</td>
<td>76 (13)</td>
<td>&lt;0.001</td>
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</table>

![Fig 1](image-url) Agreement between mean radial (MAP_rad) and femoral (MAP_fem) artery pressures (bias 3 mm Hg, limits of agreement –11 to 17 mm Hg).
excluded from the analysis (n=72, patient number=24), bias and agreement were 0.61 (1.98) litre min\(^{-1}\) m\(^{-2}\), limits of agreement -1.26 to 2.62 litre min\(^{-1}\) m\(^{-2}\); n: thermodilution CI (TD-CI) values alone, bias 0.76 litre min\(^{-1}\) m\(^{-2}\), limits of agreement -0.99 to 2.51 litre min\(^{-1}\) m\(^{-2}\).

To analyse if the magnitude of arterial pressure differences between the radial and the femoral arterial lines had an influence on CI agreements, subgroup analysis was performed including only cases with mean arterial pressure differences of up to 5 mm Hg (n=228) and with larger arterial pressure differences (n=96), respectively. Bias [0.93 (2.09) litre min\(^{-1}\) m\(^{-2}\), percentage error ±62.6%] was significantly larger for those measurements where arterial pressure differences were above 5 mm Hg than for those cases where there was an arterial pressure difference of up to 5 mm Hg [0.57 (1.83) litre min\(^{-1}\) m\(^{-2}\), percentage error 55.7%] (P=0.032). Data are displayed in Figure 3.

Subgroup analysis was also performed with respect to norepinephrine dose. For those cases where the steady-state norepinephrine infusion dose was below 0.1 μg kg\(^{-1}\) min\(^{-1}\) (n=70) at the time of measurement, CI bias and agreement were 0.68 (1.79) litre min\(^{-1}\) m\(^{-2}\) (percentage error 55.9%), for measurements at which the norepinephrine infusion dose was higher (n=254), bias was unchanged, but limits of agreement were somewhat larger [0.68 (2.04) litre min\(^{-1}\) m\(^{-2}\), percentage error 60.4%].

To analyse the ability of the FloTrac\textsuperscript{TM}/Vigileo\textsuperscript{TM} system to track intra-individual CO changes regardless of absolute accuracy, \(\Delta\text{CI}\) between consecutive AP-CI and reference-CI values was calculated and compared as well. Bias between respective AP-\(\Delta\text{CI}\) and reference-\(\Delta\text{CI}\) values was small at \(-0.03\) litre min\(^{-1}\) m\(^{-2}\), but limits of agreement were large at \(\pm1.60\) litre min\(^{-1}\) m\(^{-2}\) with a correspondingly high percentage error of 159.6%.

**Discussion**

The aim of our study was to investigate the performance of the updated uncalibrated arterial pressure-based CO (AP-CO) monitoring device (FloTrac\textsuperscript{TM}/Vigileo\textsuperscript{TM}) in haemodynamically unstable patients, after the algorithm underlying the AP-CO calculation had been modified by the manufacturer in 2006 to allow a better compensation for ongoing changes in the vascular tone. Our data show that despite the software update, the AP-CO still
underestimates the reference-CO determined either by transpulmonary thermodilution (TD-CO) or by TD-CO calibrated pulse contour analysis (PC-CO). As described by Sakka and colleagues\(^8\) for the previous software version, we also found only moderate agreement between the reference-CO and the AP-CO. Critchley and Critchley\(^9\) proposed that the acceptance of any new CO determination method (AP-CO) should be judged against the accuracy of the reference method. Since the measurement of physiological variables generally lacks precision, errors of ±10–20% are not uncommon even for the reference method. Applying the same error limit to the new method results in a combined percentage error of ±28.3% (calculated using a Pythagorean approach) so that the authors recommend that limits of agreement between the new and the reference technique of up to ±30% should be accepted. The percentage errors obtained when comparing the AP-CO with the reference-CO ranged from ±51.7% to ±62.6% and thus clearly exceeded this margin for acceptance.

Potential sources of error include both device-related as unrelated reasons. Limitations of the FloTrac\(^{TM}/\)Vigileo\(^{TM}\) algorithm result from the estimation of the aortic compliance using demographic data instead of an external calibration, as discussed by Mayer and colleagues.\(^6\) Although the algorithm was established using data collected from a wide variety of clinical situations involving patients and healthy volunteers as reported by the manufacturer, the situation might still be different for the individual patient. Another limitation of the system especially when used in critically ill patients seems to be the heart rhythm at the time of measurement. Opdam and colleagues\(^7\) reported that the correlation between the FloTrac\(^{TM}/\)Vigileo\(^{TM}\) and the pulmonary artery catheter determined CO was better for patients being paced or in sinus rhythm and poor for patients in atrial fibrillation. Sinus rhythm was not a prerequisite for inclusion in our study, and atrial fibrillation is not uncommon in critically ill patients. Since heart rhythm was not documented as part of the study protocol, no data can be provided on the potential influence of atrial fibrillation on the results we obtained.

On the other hand, limitations of the PC-CO method have to be considered as well, especially since TD-CO calibration was performed less frequently than recommended for haemodynamically unstable patients in our study.\(^11\) We thus expected to find better agreement when we compared TD-CO results only with the respective AP-CO results, but the percentage error was only slightly smaller than with TD-CO and PC-CO values taken together (±51.7% vs ±58.8%).

We hypothesized that difficulties in the peripheral radial artery blood pressure registration might be an additional factor accounting for the limited agreement between the AP-CO and the femoral artery-derived reference-CO. Several studies have found significant differences between radial and femoral arterial pressures during cardiopulmonary bypass and also with vasopressor therapy in critically ill patients.\(^12\)\(^13\) In our haemodynamically unstable patients, most of whom were on continuous vasopressor support during the study, we confirmed that the peripherally derived radial artery pressure significantly underestimated the central arterial pressure. Subgroup analysis with regard to the magnitude of the radial and femoral pressure differences revealed that bias between the AP-CO and the reference-CO and the percentage error were significantly increased with a mean arterial pressure difference exceeding 5 mm Hg.

Circulatory impairment itself might provide enough explanation for the arterial pressure differences found, but since vasopressor-induced vasoconstriction could also have influenced the peripheral arterial pressure registration, we correlated the arterial pressure differences with the nor-epinephrine infusion dose using linear regression analysis, but found no association. Subgroup analysis of patients with high vs low norepinephrine doses did not reveal any differences in CO bias, but the percentage error was larger in the high norepinephrine dose subgroup.

In addition to the potential problems related to our observational study design discussed above, several other limitations of our data need to be mentioned. As opposed to the previous studies, our study population was rather heterogeneous with haemodynamic instability being the only prerequisite for inclusion. We intended to evaluate the FloTrac\(^{TM}/\)Vigileo\(^{TM}\) system during routine patient care under different haemodynamic conditions, and recording times were not predetermined. This approach resulted in different numbers of measurements for each patient. To account for the ensuing statistical bias, we performed subgroup analyses using the same number of measurements in all patients. Because the percentage error was equally high (±60.2%) and the number of measurements was considerably smaller, we decided to primarily report the data obtained using all available measurement pairs.

Despite all limitations, our results are in agreement with previous studies performed comparing AP-CO with either transpulmonary thermodilution or pulmonary artery thermodilution CO using the previous software version (Table 4). Four out of the five studies published to date involved intra- and postoperative measurements in cardiac surgery patients.\(^4\)\(^–\)\(^7\) and only one was performed on haemodynamically unstable septic patients in the ICU.\(^8\) Patient numbers in those studies ranged from 6 to 50, and the maximum number of data pairs was 295. Where CI was reported, bias ranged from 0.21 to 0.46 litre min\(^{-1}\) m\(^{-2}\), for CO a bias of 0.5–0.6 litre min\(^{-1}\) was found. Limits of agreement were also comparable with our data; percentage error was only calculated in two studies, ranging from 46% to 54%.\(^5\)\(^6\)

In addition to testing accuracy, Mayer and colleagues\(^6\) also investigated the ability of the FloTrac\(^{TM}/\)Vigileo\(^{TM}\) system to track individual CO changes and found a bias of only −0.04 litre min\(^{-1}\) m\(^{-2}\) (limits of agreement ±1.50 litre min\(^{-1}\) m\(^{-2}\)) comparing differences between
of agreement (±2 litre min⁻¹ in the diagram) meaning that the ability of the FloTrac™/Vigileo™ system to accurately track CO changes over time varies highly between individual patients. Considering the general limitations of our data discussed above, we believe that further studies need to be performed to address this question.

In conclusion, the updated FloTrac™/Vigileo™ uncalibrated minimally invasive CO determination system still cannot be recommended to replace more invasive CO monitoring systems in the ICU. Limited accuracy might be acceptable, though, in situations where invasive CO monitoring is not an option and tracking of individual CO changes is more important than absolute CO values, such as the evaluation of a haemodynamically unstable patient in the emergency department. Studies specifically addressing the ability of the FloTrac™/Vigileo™ system to correctly reflect CO changes over time are therefore needed.

Funding
This study was supported by an unrestricted research grant from Edwards Lifesciences LLC, Irvine, CA, USA.

References
3 Reid RD, Jayamaha J. The use of a cardiac output monitor to guide the initial fluid resuscitation in a patient with burns. Emerg Med J 2007; 24: e32

Table 4 Previous studies evaluating the FloTrac™/Vigileo™ system. PAC, pulmonary artery catheter; ICU, intensive care unit

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patients</th>
<th>Comparison with</th>
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<th>Bias± limits of agreement</th>
<th>Percentage error</th>
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<td>Manecke</td>
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<td>295</td>
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