MONITORING OF cardiac performance is important to either confirm diagnosis or guide therapy in patients undergoing major surgery and critically ill patients in the intensive care unit (ICU). The invasive technique of pulmonary artery catheterization has been used effectively to optimize hemodynamics. However, it is about to lose its role as the tool of first choice since alternative, less invasive devices to measure cardiac output (CO) have become available. Techniques such as transthoracic bioimpedance, pulse dye densitometry, and esophageal Doppler have been developed for assessing CO and have become increasingly accepted in clinical practice. The results of these techniques with regard to validity, practicability, and accuracy are not uniform, and only a few techniques are universally applicable. Transthoracic bioimpedance, for example, may not be feasible in the operating room (depending on the surgery), and esophageal Doppler is difficult to perform in awake patients. Arterial pulse-wave analysis as provided by the PiCCO (PiCCO Plus; Pulsion Medical Systems, Munich, Germany) and LiDCO (LiDCO Plus; LiDCO, Cambridge, UK) systems is already available; numerous validation studies have shown overall good correlation compared with the pulmonary artery thermodilution technique. However, manual invasive calibration by transpulmonary thermodilution (PiCCO), lithium dilution (LiDCO), or previous measurement of the aortic diameter is required to compensate for interindividual differences in arterial compliance. In addition, central venous access and the cannulation of a large arterial vessel are necessary for use of the PiCCO system.

The recently introduced FloTrac/Vigileo (Edwards Lifesciences, Irvine, CA) calculates continuous CO from arterial pressure waveform characteristics but does not require external calibration. Individual demographic data including height, weight, age and sex, and real-time arterial pressure waveform analysis are used instead. The direct proportionality between arterial pulsatility and the stroke volume in conjunction with heart rate is used to calculate CO. Sex, age, and the body surface area are used to correct for interindividual differences in arterial compliance based on the model described by Lange-wouters et al. Changes in vascular tone and the site of arterial cannulation are automatically corrected for by analyzing skewness, kurtosis, and other aspects of the arterial pressure waveform in combination with the mean arterial pressure. With the second-generation operating system (v.1.07 or later), these correction variables are updated every 60 seconds. The arterial pressure waveform itself is analyzed and averaged over a period of 20 seconds, and a beat-detection algorithm eliminates extrasystoles and other small artifacts.

In addition to CO (index), the FloTrac/Vigileo calculates stroke volume variation (SVV). If central venous pressure is available, systemic vascular resistance and the systemic vascular resistance index are calculated. With a specially designed central venous catheter (Preceep, Edwards Lifesciences), a continuous central venous oxygen saturation can be obtained and displayed as well. The FloTrac/Vigileo does not provide data about mixed venous oxygen saturation and cardiac filling pressures such as central venous pressure, pulmonary artery pressure, and pulmonary artery occlusion pressure. In contrast to the pulmonary artery catheter or the PiCCO system, which both require considerable training, the FloTrac/Vigileo device is easy to set up and use. Standard arterial access can be used to connect the Vigileo device via the FloTrac pressure transducer, and, after zeroing and entering patient data, CO is displayed after 40 seconds.

This report gives an overview of the literature about this new technique, provides a meta-analysis of the available studies comparing it with intermittent thermodilution (ITD), and discusses its potential clinical utility and limitations.

VALIDATION STUDIES

One of the first studies was published by Sander et al using a first-generation operating system. They analyzed 108 comparative measurements of CO measured by the FloTrac/Vigileo and ITD in 30 patients undergoing elective coronary artery
bypass graft (CABG) surgery and found a mean bias of 0.6 L/min and limits of agreement of −2.2 to 3.4 L/min. Sander et al found a percentage error of 54%, which is well above the 30% limit of acceptance suggested by Critchley and Critchley. The percentage error incorporates the error of both the reference method and the method to be tested and is recommended for use when comparing different methods for assessing CO. A percentage error of 30% or less between the test and the reference method indicates that the test method is no less accurate than the reference method, provided the reference method has a percentage error of 20% or less.14

Opdam et al13 investigated the performance of the FloTrac/Vigileo compared with ITD after CABG surgery in the ICU, also using an early algorithm. They reported a limited correlation of $r^2 = 0.26$ and found the femoral artery to be superior to brachial and radial insertion sites. However, it was a very small study with only 6 patients.

Manecke et al16 compared 295 measurement pairs of CO between the FloTrac/Vigileo and bolus thermodilution in postoperative cardiac surgery patients receiving little or no vasoactive treatment. They found a bias of 0.55 L/min and a precision of 0.98 L/min with the first-generation software and concluded that CO measurements using this technique produce reliable results in an ICU setting in stable patients after cardiac surgery.

Mayer et al17 used a subsequent first-generation software version (1.03) and found a disappointing overall percentage error of 46% in 244 simultaneous measurements between the FloTrac/Vigileo and ITD in patients undergoing CABG surgery. Bias and precision (2 standard deviation) were 0.46 L/min/m² and ±1.15 L/min/m² for all cardiac index (CI) data pairs (intraoperative and ICU).

The performance of the FloTrac/Vigileo was compared with transpulmonary thermodilution in patients in septic shock by Sakka et al.18 Comparative measurements were performed in 24 patients at 3 times using software version 1.07. The first CO measurement was at baseline and then a norepinephrine infusion was started and increased to achieve a mean arterial pressure of approximately 90 mmHg. Another CO measurement was obtained after returning to baseline mean arterial pressure values. A limited overall correlation of $r^2 = 0.26$ and a mean bias of 0.5 L/min with a low precision of 2.3 L/min were found. For each time, $r^2$ was 0.10, 0.30, and 0.21, respectively, with norepinephrine doses ranging between 0.05 and 0.11 µg/kg/min. The authors concluded that in patients with reduced peripheral resistance, the FloTrac/Vigileo is not as reliable as the transpulmonary thermodilution technique for measuring CO. Likewise, Biais et al19 found a percentage error of 43% between FloTrac/Vigileo and ITD (software v.1.07) in patients undergoing liver transplantation with low systemic vascular resistance.

McGee et al20 conducted a multicenter study in an intensive care setting. Eighty-six patients needing invasive hemodynamic management with a pulmonary artery catheter (PAC) for various reasons were included, and the bolus thermodilution measurements were compared with CO measurements by using the FloTrac/Vigileo. The authors judged a bias of 0.20 L/min and precision of 1.28 L/min to be acceptable. A percentage error was not stated, but, with the given data, it exceeds 30%.

The exact software version used in this study was not given, but measurements were performed most likely using an early algorithm.

Lorsomradee et al21 compared FloTrac/Vigileo with continuous thermodilution and found poor correlation, primarily during sternotomy and phenylephrine administration. This is understandable because the relatively slow reaction time of a continuous thermodilution catheter most likely causes bias when compared with the fast-responding FloTrac/Vigileo22 in an intraoperative setting or with unstable patients.23 An interesting aspect of this study was that the authors studied possible differences in patients with aortic stenosis or aortic insufficiency. According to the underlying pathology, the bias in patients with aortic insufficiency was higher than in patients with aortic stenosis and in patients without valvular lesions. In patients requiring cardiac support by an intra-aortic balloon pump (IABP), the arterial waveform is severely altered and the authors often could not obtain arterial waveform signals interpretable by the FloTrac/Vigileo.

Breukers et al24 using a second-generation operating system (v.1.07), compared 20 patients and 56 measurement sets with bolus thermodilution in ICU patients after cardiac surgery and found a reasonable agreement with a percentage error of about 30%. They hypothesized that the FloTrac/Vigileo overestimates the CO at low values and underestimates it at high values. Another study compared the Vigileo (v.1.07) with intermittent thermodilution in patients during and after cardiac surgery25 and found a lower bias in the postoperative period than in the intraoperative period, although the limits of agreement were high at both times.

De Waal et al26 using a first-generation operating system (v.1.03), found a percentage error of 33% between transpulmonary thermodilution and the Vigileo device in postbypass closed-chest conditions, although the difference was found to be increased in situations with rapidly changing cardiovascular tone.

Mehta et al27 using second-generation software (v.1.07), obtained a percentage error of 29% in patients undergoing off-pump CABG surgery versus bolus thermodilution. Only male patients were enrolled, and as few as 89 data pairs were analyzed. Patients with an ejection fraction of less than 35% were excluded.

The work of Compton et al27 was performed in a medical ICU with software v.1.07 and partly v.1.10 and compared the Vigileo device with the PiCCO system (pulse contour and ITD). A limited agreement was found with a high percentage error of 58.8%. This study, however, is most likely biased because of long (24 hours) recalibration intervals of the PiCCO system in hemodynamically unstable patients, requiring vasopressor and inotropic cardiac support.

An important study was performed by Hofer et al28 assessing the ability of the FloTrac/Vigileo to predict fluid responsiveness using SVV in comparison to the PiCCO. They found the second-generation software (v.1.07) to be as accurate as the PiCCO with respect to the prediction of fluid responsiveness, although the threshold value of SVV for the FloTrac/Vigileo was lower (9.6%) than for the PiCCO (12.1%).

Studies using the latest available algorithm of the FloTrac/Vigileo (software v.1.10) are scarce so far since it was released.
recently (Fall 2006). The authors’ own data29 obtained with software v.1.10 showed a significant improvement of agreement with intermittent pulmonary artery thermodilution. Using the improved algorithm in patients during and after bypass surgery, the overall percentage error decreased from 45.9% in the authors’ first study with software v.1.03 to 24.6%. In patients with low CO (cardiac index of ≤2 L/min/m²), the percentage error decreased from 56.4% to 27.9% with the new software version, indicating reliable CO measurements even in high-risk patients. Subgroup analysis of CO values obtained in the ICU confirmed the trend toward better agreement during stable conditions, which was already seen in previous studies with earlier software versions.

Prasser et al,30 using a second-generation operating system (v.1.10), confirmed these results in a comparable study setting. They found a percentage error of 26.9% between bolus thermodilution and the FloTrac/Vigileo.

An overview of all available validation studies of the FloTrac/Vigileo device is given in Table 1. When interpreting the results, the difference between CO and CI has to be kept in mind. Because the bias and precision or limits of agreement are smaller in studies giving the CI, the percentage error should be same.

META-ANALYSIS

As described earlier, clinical studies comparing CO values from the FloTrac/Vigileo with those of ITD have yielded varied results, depending on experimental design, clinical scenario, and the operating system used. Recent studies have strongly suggested improved FloTrac/Vigileo performance with the second-generation operating systems. The authors hypothesized that, by pooling the prospective data, more definitive conclusions could be made about the agreement between FloTrac/Vigileo and ITD in various clinical arenas as well as the apparent improvement associated with more recent operating systems. Accordingly, a meta-analysis of prospective studies appearing in the peer-reviewed medical literature that compared simultaneous CO values derived by the FloTrac/Vigileo with those obtained with ITD was conducted.

METHODS

A Medline search, dating back to 2005, was conducted to discover prospective studies comparing FloTrac/Vigileo with ITD (PAC or transpulmonary). Key words such as “cardiac output assessment,” “FloTrac,” “Vigileo,” “pulse contour analysis,” “minimally invasive cardiac output,” and “thermodilution cardiac output” were used. Only studies using bias and precision statistics (Bland Altman35) were included. Investigations specifically studying acute hemodynamic instability, liver surgery with cirrhosis, aortic regurgitation, and IABP counterpulsation were excluded because issues with FloTrac performance and other arterial wave–based CO assessment devices have already been documented in these situations.

Values reported for bias, precision, limits of agreement, mean CO, and percentage error were recorded. Also, the number of data points obtained in each study was recorded. When certain values were not reported, they were calculated from the other values when possible.

The resulting data were then stratified according to clinical location: intraoperative and ICU. The intraoperative data were further stratified into segments before or not requiring cardiopulmonary bypass (CPB) and after CPB. Weighted averages of bias, precision, and limits of agreement were calculated globally and for the segments using the number of data points as the relative weight. The percentage error across all data points and for each segment was calculated according to the method suggested by Critchley and Critchley34. % Error = (2 * precision)/mean CO.

Operating system version 1.07 represented a significant software revision, including a more frequent calculation of the κ value (1 minute v 10 minutes). Recent studies have suggested enhanced agreement between FloTrac/Vigileo and ITD with v.1.07 or later. To confirm this, the meta-analysis data were stratified by operating system “first generation” being before v.1.07 and “second generation” being v.1.07 or later. An unpaired Student t test was performed to determine potential statistical significance of the difference in operating system performance with regard to bias and precision. A p value <0.05 was considered significant.

RESULTS

Sixteen prospective investigations, representing 3,372 data points comparing ITD and FloTrac/Vigileo, were discovered.13,15,17,20,23,26,29,30,32,36 Pulmonary artery catheterization was used in all except 2 in which transpulmonary thermodilution was used.25,34 Six of the studies were exclusively in the ICU,15,16,20,23,30,34 3 were exclusively in the operating room,26,33,35 and 7 were performed in both the ICU and the operating room.13,17,24,25,29,32,36 The results are shown in Table 2.

Comparisons between the first- and second-generation software revealed enhanced agreement between FloTrac/Vigileo and ITD in terms of bias and precision, with p < 0.0001 for both.

DISCUSSION

The introduction of operating system v.1.07 has resulted in enhanced agreement between ITD and FloTrac/Vigileo. This has likely resulted from more frequent assessment of the resistance and compliance of the vascular tree (κ value) as well as other proprietary factors in the FloTrac/Vigileo algorithm. Some authors have repeated their assessment of this technology, showing enhanced agreement in the later operating system.15,17,29 and another group has shown closer agreement in a “head-to-head” comparison of the older and newer operating systems.34 With the exception of the immediate post-CPB period, pooled data in this meta-analysis suggest that the agreement between the second-generation FloTrac/Vigileo and ITD meets the criteria suggested by Critchley and Critchley.34 In applying the Critchley “30% rule,” it is important to remember that when comparing measurement methods the percentage error depends on the precision of both technologies being compared. The “30% rule” assumes the percentage error of ITD alone to be approximately 20%. The authors of the studies included in this meta-analysis, however, rarely report the precision of the 2 technologies separately, making rigid application of this rule questionable. In the immediate post-CPB period, ITD is known to be inaccurate, most likely because of thermal issues.17 It may be that ITD is the primary “outlier” at that time. Further study should be done in the immediate postbypass period, perhaps comparing values reported by both technologies to another method such as transeosophageal echocardiography.

Concluding that the FloTrac/Vigileo agrees satisfactorily with ITD must be done with consideration of the limitations of...
Table 1. Validation Studies of the FloTrac/Vigileo Device

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Software</th>
<th>Setting</th>
<th>Reference Method</th>
<th>CI/CO</th>
<th>Data Points</th>
<th>Bias ± 2 SD or (LOA)</th>
<th>Correlation</th>
<th>Percentage Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Waal et al</td>
<td>2007</td>
<td>1.01</td>
<td>Cardiac (OP/ICU)</td>
<td>PAC (ITD); PiCCO CO</td>
<td>PAC 185 PiCCO 140</td>
<td>PAC (ITD)</td>
<td>0.00 (−1.74, +1.74)</td>
<td>r² = 0.75</td>
<td>PAC 33 PiCCO 40</td>
</tr>
<tr>
<td>McGee et al</td>
<td>2007</td>
<td>1.01*</td>
<td>Various (ICU)</td>
<td>PAC (bolus) CO</td>
<td>561</td>
<td>0.20 (−2.36, +2.75)</td>
<td>r² = 0.31</td>
<td>NA</td>
<td>43*</td>
</tr>
<tr>
<td>Zimmermann et al</td>
<td>2008</td>
<td>1.01</td>
<td>Cardiac (OP/ICU)</td>
<td>PAC (bolus) CO</td>
<td>192</td>
<td>−0.10 (−3.00, +2.80)</td>
<td>r² = 0.60</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Opdam et al</td>
<td>2006</td>
<td>1.03</td>
<td>Cardiac (ICU)</td>
<td>PAC (ITD, cont) CO</td>
<td>218</td>
<td>PAC (bolus) 0.00 (−1.20, +1.19)</td>
<td>r² = 0.06</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Sander et al</td>
<td>2006</td>
<td>1.03*</td>
<td>Cardiac (OP/ICU)</td>
<td>PAC (ITD) CO</td>
<td>108</td>
<td>0.6 (−2.2, +3.4)</td>
<td>r² = 0.53</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Breukers et al</td>
<td>2006</td>
<td>1.03</td>
<td>Cardiac (ICU)</td>
<td>PAC (ITD) CO</td>
<td>56</td>
<td>−0.14 (−2.14, +1.87)</td>
<td>r² = 0.55</td>
<td>31*</td>
<td></td>
</tr>
<tr>
<td>Manecke et al</td>
<td>2007</td>
<td>1.03</td>
<td>Cardiac (ICU)</td>
<td>PAC (ITD, cont) CO</td>
<td>295</td>
<td>PAC (bolus) 0.55 (−1.96)</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Mayer et al</td>
<td>2007</td>
<td>1.03</td>
<td>Cardiac (OP/ICU)</td>
<td>PAC (ITD) CI</td>
<td>244</td>
<td>0.46 ± 1.15</td>
<td>r² = 0.53</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>Button et al</td>
<td>2007</td>
<td>1.07</td>
<td>Cardiac (OP/ICU)</td>
<td>PAC (ITD) CO</td>
<td>150</td>
<td>0.25 ± 2.27*</td>
<td>NA</td>
<td>54*</td>
<td></td>
</tr>
<tr>
<td>Cannesson et al</td>
<td>2007</td>
<td>1.07</td>
<td>Cardiac (OP/ICU)</td>
<td>PAC (ITD) CO</td>
<td>166</td>
<td>−0.26 ± 1.74</td>
<td>r² = 0.66</td>
<td>38*</td>
<td></td>
</tr>
<tr>
<td>Sakka et al</td>
<td>2007</td>
<td>1.07</td>
<td>Sepsis (ICU)</td>
<td>PiCCO CO</td>
<td>72</td>
<td>0.5 ± 4.6</td>
<td>r² = 0.26</td>
<td>68*</td>
<td></td>
</tr>
<tr>
<td>Lorsomradesee et al</td>
<td>2007</td>
<td>1.07</td>
<td>Cardiac (OP)</td>
<td>PAC (cont) CO (CCO)</td>
<td>550</td>
<td>pre-CPB −3% (−59%, +53%)</td>
<td>r² = 0.19</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Mehta et al</td>
<td>2008</td>
<td>1.07</td>
<td>Cardiac (OP)</td>
<td>PAC (ITD) CO</td>
<td>96</td>
<td>−0.27 (−0.71, +0.17)</td>
<td>NA</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Staier et al</td>
<td>2008</td>
<td>1.07†</td>
<td>Cardiac (OP)†</td>
<td>PAC (ITD) CO</td>
<td>120</td>
<td>−0.06 ± 0.91 to −0.26 ± 1.43‡</td>
<td>NA</td>
<td>36-56‡</td>
<td></td>
</tr>
<tr>
<td>Compton et al</td>
<td>2008</td>
<td>1.07/1.10</td>
<td>Medical ICU</td>
<td>PiCCO CI</td>
<td>324</td>
<td>0.68 ± 1.74</td>
<td>NA</td>
<td>58.8</td>
<td></td>
</tr>
<tr>
<td>Chakravarthy et al</td>
<td>2007</td>
<td>NA</td>
<td>Cardiac (OP)</td>
<td>PiCCO CO</td>
<td>438</td>
<td>0.15 ± 0.66</td>
<td>r² = 0.49</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Prasser et al</td>
<td>2007</td>
<td>1.10</td>
<td>Cardiac (ICU)</td>
<td>PAC (ITD) CO</td>
<td>158</td>
<td>0.01 ± 1.63</td>
<td>NA</td>
<td>26.9</td>
<td></td>
</tr>
<tr>
<td>Mayer et al</td>
<td>2008</td>
<td>1.10</td>
<td>Cardiac (OP/ICU)</td>
<td>PAC (ITD) CI</td>
<td>282</td>
<td>0.19 ± 0.6</td>
<td>NA</td>
<td>24.6</td>
<td></td>
</tr>
<tr>
<td>Senn et al</td>
<td>2009</td>
<td>1.10</td>
<td>Cardiac (ICU)</td>
<td>PiCCO (ITD) CO</td>
<td>200</td>
<td>−0.15 ± 1.6</td>
<td>NA</td>
<td>29</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: NA, not available; PAC, pulmonary artery catheter; OP, operating room.
*Estimated from given data.
†In patients with aortic stenosis.
‡Not given for the entire study population.
FloTrac/Vigileo as well as the limitations of previous studies and this meta-analysis. FloTrac/Vigileo has been shown to overestimate CO in the setting of significant aortic regurgitation, will not function during IABP counterpulsation, and appears to underestimate the CO in high-output, vasodilatory states. Studies specifically including these factors were excluded from this analysis, although they were discussed earlier. In cases of rapidly changing hemodynamics, the Vigileo and thermodilution may not simultaneously show changes. In particular, when continuous thermodilution is used, the FloTrac/Vigileo changes precede changes in thermodilution CO values. For the purpose of this investigation, studies involving rapid, sudden changes in hemodynamics were thus excluded, as were those involving continuous thermodilution.

Two studies using transpulmonary thermodilution were included in this analysis. This was done because, being similar technology, transpulmonary and PAC ITD have been shown to achieve close agreement. If these studies were to be excluded, however, the findings and conclusions of this analysis would be unchanged.

This analysis is limited by the same factors that often limit meta-analyses including differences in experimental design and quality of the investigations and assumption and calculations necessary to determine and properly format the necessary data. In addition, this meta-analysis does not specifically address agreement of directional changes in CO between the 2 technologies, although this has been reported to be good.

The results of this meta-analysis indicate that the CO values provided by FloTrac/Vigileo operating systems v. 1.07 or later show acceptable agreement with ITD, both clinically and statistically. Agreement immediately after CPB is poor, however, perhaps because of thermal issues in ITD measurements at that time. The FloTrac/Vigileo algorithm, at the time of this writing, is of questionable value in cases of rapid, extreme changes in hemodynamics, although it may still be useful as a trend monitor in cases in which use of ITD is not feasible. Likewise, extreme vasodilatation with hyperdynamic circulation, hepatic cirrhosis, aortic regurgitation, and IABP counterpulsation are circumstances in which the clinical use of FloTrac/Vigileo should be questioned. Its potential use for “early goal-directed therapy” defines its niche, perhaps as a device that can assist in preventing situations of gross hemodynamic instability. Once that instability occurs, however, more invasive technology (ITD) is usually indicated. Newer operating systems addressing the previously described issues should be studied rigorously as they are introduced.

REFERENCES


Table 2. Weighted Averages of Results From 16 Studies

<table>
<thead>
<tr>
<th>Clinical Site</th>
<th>Bias</th>
<th>Precision</th>
<th>LOA</th>
<th>% Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generation</td>
<td>1st</td>
<td>2nd</td>
<td>1st</td>
<td>2nd</td>
</tr>
<tr>
<td>OP (total)</td>
<td>0.35</td>
<td>0.18</td>
<td>1.16</td>
<td>0.62</td>
</tr>
<tr>
<td>OP Without CPB</td>
<td>0.64</td>
<td>0.16</td>
<td>1.26</td>
<td>0.48</td>
</tr>
<tr>
<td>OP after CPB</td>
<td>0.25</td>
<td>0.08</td>
<td>1.30</td>
<td>1.07</td>
</tr>
<tr>
<td>ICU</td>
<td>0.27</td>
<td>0.09</td>
<td>1.16</td>
<td>0.78</td>
</tr>
<tr>
<td>Global</td>
<td>0.32</td>
<td>0.15</td>
<td>1.16</td>
<td>0.67</td>
</tr>
</tbody>
</table>

Abbreviations: Bias, mean difference (FloTrac – ITD); LOA, limits of agreement; 1st generation, operating systems before v.1.07; 2nd generation, operating systems v.1.07 and later; OP, operating room; CPB, cardiopulmonary bypass; ICU, intensive care unit.