

CLINICAL PRACTICE

**Evaluation of an uncalibrated arterial pulse contour cardiac output monitoring system in cirrhotic patients undergoing liver surgery**

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**Background.** The pulmonary artery catheter is invasive and may cause serious complications. A safe method of cardiac output (CO) measurement is needed. We have assessed the accuracy and reliability of a recently marketed self-calibrating arterial pulse contour CO monitoring system (FloTrac/Vigileo<sup>TM</sup>) in end-stage liver failure patients undergoing liver transplant. The pattern of alterations known as cirrhotic cardiomyopathy, and the transplant procedure itself, provided an evaluation under varying clinical conditions.

**Methods.** The cardiac index was measured simultaneously by thermodilution (CI<sub>TD</sub>: mean of four readings) using a pulmonary artery catheter and pulse contour analysis (CI<sub>V</sub>: mean value computed by the FloTrac/Vigileo<sup>TM</sup> over the same time period). Readings were made at 10 time-points during liver transplant surgery (T1–T5) and on the intensive care unit (T6–T10). CI<sub>V</sub> was computed using the latest Vigileo software version 01.10.

**Results.** A total of 290 paired readings from 29 patients were collected. Mean (SD) CI<sub>TD</sub> was 5.2 (1.3) and CI<sub>V</sub> was 3.9 (0.9) litre min<sup>-1</sup> m<sup>-2</sup>, with a corrected for repeated measures bias between readings of 1.3 (0.2) litre min<sup>-1</sup> m<sup>-2</sup> and 95% limits of agreement of -1.5 (0.2) to 4.1 (0.3) litre min<sup>-1</sup> m<sup>-2</sup>. The percentage error (2SD<sub>Bias</sub>/meanCI<sub>TD</sub>) was 54%, which exceeded a 30% limit of acceptance. Low peripheral resistance and increasing bias were related ( $r=0.69$ ;  $P<0.001$ ). The Vigileo system failed to reliably trend CI data, with a concordance compared with thermodilution below an acceptable level (at best 68% of sequential readings).

**Conclusions.** In cirrhotic patients with hyperdynamic circulation, the Vigileo system showed a degree of error and unreliability higher than that considered acceptable for clinical purposes.

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Patients with liver cirrhosis frequently require haemodynamic monitoring including cardiac output (CO) assessment, particularly when admitted to the intensive care or when undergoing surgery.<sup>1</sup> Cirrhosis is associated with a pattern of alterations in the cardiovascular system, known as cirrhotic cardiomyopathy, which is characterized by a hyperdynamic circulation, increased baseline CO, decreased

peripheral vascular resistance and reduced ventricular response to physiological, pharmacological and surgical stressors.<sup>2,3</sup> Furthermore, the peripheral autonomic neuropathy, which is common in these patients, may result in pronounced haemodynamic instability.<sup>3,4</sup>

The pulmonary artery catheter and thermodilution CO measurement has emerged as the gold standard for CO

**Table 1** Summary of recent publications that clinically evaluate the FloTrac/Vigileo™. \*Estimated value; †Data include the use of vasopressors; ‡Only postoperative patients; †Classical thermodilution not used

| Paper                                     | Year published | Type of cases | Number of patients | Data pairs | Percentage error (%) |
|---|----------------|---------------|--------------------|------------|----------------------|
| Costa and colleagues <sup>20</sup>        | 2006           | Cirrhosis     | 14                 | 50         | 35                   |
| Sander and colleagues <sup>21</sup>       | 2006           | Cardiac       | 30                 | 120        | 54                   |
| Breukers and colleagues <sup>22</sup>     | 2007           | Cardiac       | 20                 | 56         | 36                   |
| Button and colleagues <sup>23</sup>       | 2007           | Cardiac       | 31                 | 217        | 45*                  |
| Canesson and colleagues <sup>24</sup>     | 2007           | Cardiac       | 11                 | 166        | 38                   |
| †de Waal and colleagues <sup>25</sup>     | 2007           | Cardiac       | 22                 | 184        | <56                  |
| Manecke and Auger <sup>26</sup>           | 2007           | Cardiac       | 50                 | 290        | 33*                  |
| Mayer and colleagues <sup>27</sup>        | 2007           | Cardiac       | 40                 | 320        | 46                   |
| ‡Prasser and colleagues <sup>28</sup>     | 2007           | Cardiac       | 20                 | 158        | 26.9                 |
| †Lorsomradee and colleagues <sup>29</sup> | 2007           | Cardiac       | 52                 | 315        | 33–50                |
| Mayer and colleagues <sup>30</sup>        | 2008           | Cardiac       | 40                 | 282        | 24.6                 |
| †Sakka and colleagues <sup>31</sup>       | 2007           | Sepsis        | 24                 | 24         | 35                   |
| Compton and colleagues <sup>32</sup>      | 2008           | Cardiac       | 25                 | 324        | 58.8                 |
| Our data                                  | 2009           | Cirrhosis     | 29                 | 290        | 54                   |

monitoring and, over the past 25 yr, has become part of the routine care for critically ill patients in both intensive care units (ICUs) and during major surgery.<sup>5</sup> However, questions have recently been raised about its invasive nature and potential for serious complications,<sup>6, 7</sup> and its use is now declining in favour of less invasive alternatives.<sup>5</sup> CO can be measured less invasively by arterial pulse wave analysis, which has the advantage of providing continuous CO readings. Until recently commercially available pulse wave methods have required calibration by a more invasive technique, such as lithium or thermodilution. A pulse-wave technique, has recently been marketed that self-calibrates, using the patient's blood pressure and patient characteristics data. This is the FloTrac/Vigileo™ system (Edwards Lifescience, Irvine, CA, USA). Its reliability and role in the clinical practice has yet to be determined.<sup>8</sup> The aim of this study was to assess the accuracy and reliability of the Vigileo in end-stage liver failure patients undergoing liver transplant. At the time of this study the Vigileo had only been tested clinically in cardiac surgery patients and septic patients being ventilated on intensive care and some of these studies involved older and less reliable software (Table 1). We considered that monitoring in cirrhosis and liver transplantation would provide a vigorous examination of the Vigileo's potential due to the presence of a wide range of circulatory changes. Comparisons were made against intermittent thermodilution, the current gold standard in CO monitoring.

## Methods

### *Patients and anaesthesia*

After review board approval, 31 cirrhotic patients scheduled for liver transplantation were enrolled in the study between October and December of 2007. Anaesthesia was the same in all cases. Anaesthesia was induced with i.v. sodium thiopentone and fentanyl and the trachea intubated. Muscle relaxation was provided by cisatracurium bolus followed by an infusion  $3 \mu\text{g kg}^{-1} \text{min}^{-1}$ . The patient's lungs were ventilated using a low-flow circuit with 50% oxygen in air. The ventilator was set to provide a tidal volume of  $8\text{--}10 \text{ ml kg}^{-1}$  using pressure support mode without PEEP. The end tidal capnograph was maintained between 4.5 and 5.3 kPa. Anaesthesia was maintained with inhaled sevoflurane and a remifentanyl infusion  $0.2\text{--}0.3 \mu\text{g kg}^{-1} \text{min}^{-1}$  titrated to patient response. Monitoring included invasive radial artery blood pressure measurement and the use of a pulmonary artery catheter with continuous CO (CCO) and  $Sv_{O_2}$  measurement capacity (Edwards Life Sciences LLC, Irvine, CA, USA). Radial access was obtained using a radial artery catheterization set (Radial Artery Catheterization Set, Arrow International, Reading, PA, USA) that was connected to the FloTrac sensor which in addition to arterial pressure transduction allowed CO estimation from the arterial pressure waveform when connected to the Vigileo monitor. The most recent Vigileo software version 01.10 was used. All intravascular pressure measurements were zeroed to the mid-axillary line. In all cases an extracorporeal veno-venous bypass shunt from the portal vein and the inferior vena cava via a pump to the axillary vein was used during the anhepatic stage. Circulatory management of patient during surgery and on the ICU was guided by CO readings obtained by the thermodilution technique. All cases were treated according to our fast-track liver transplant protocol and patients were admitted to the ICU following the procedure.<sup>9</sup> Patients were allowed to breath spontaneously once on the ICU. The measured CO values were indexed by dividing the CO by the body surface area. The severity of the liver disease making the transplant necessary was assessed by the United Network for Organ Sharing (UNOS) status<sup>10</sup> and the Mayo End Stage Liver Disease (MELD) score (range 0–40), UNOS modification, as calculated through a website calculator.<sup>11</sup>

### *Data collection*

All measurements and recordings were performed by a senior staff anaesthesiologist (G.B., L.B., M.B., M.E.). Data were recorded at the following times: T1—on abdominal incision; T2—immediately before the start of the bypass; T3—30 min later; T4—5 min after graft reperfusion; T5—on abdominal closure, and T6—1 h; T7—6 h;

T8—12 h; T9—18 h, and T10—24 h after intensive care admission.

Simultaneous CI measurements were made by intermittent thermodilution and the Vigileo system according to a set protocol. For each thermodilution reading ( $CI_{TD}$ ) four consecutive measurements were made using the pulmonary artery catheter by injecting 10 ml of ice-cold saline at random times during the respiratory cycle. The consistency of the washout curve was judged visually on the Vigilance monitor. If readings differed by more than 10% the measurements were repeated. The average of these readings was used. Pulse contour readings (mean CI value over the same period) were computed by the Vigileo monitor ( $CI_V$ ), which uses a proprietary algorithm based on the analysis of the relationship between pulse pressure and stroke volume and the inverse relationship with aortic compliance. A conversion factor accounts for dynamic changes in vascular tone and is calculated from pressure waveform characteristics and the patient's age, gender, height, and weight. In the software release that we used (version 1.10), the conversion factor is updated and applied to the algorithm on a rolling 60 s average as opposed to every 10 min with the previous software version.

Mean arterial blood pressure (MAP), mean pulmonary artery pressure (PAP), and central venous pressure (CVP) measurements were also recorded. Systemic vascular resistance index (SVRI) was calculated using the equation:

$$SVRI = (MAP - CVP) \times 80 / CI_{TD}$$

where  $CI_{TD}$  was our best estimate of CO.

### Data analysis and statistics

Results are presented as mean (SD) unless otherwise stated.  $P < 0.05$  was considered significant. Statistical analysis was performed using the software programs GraphPad PRISM version 4.0 (San Diego, CA, USA) and Stata version 10 (StataCorp, College Station, TX, USA). Data were analysed using Student's *t*-test, analysis of variance with the Bonferroni test for post-test comparisons, Pearson's correlation coefficient, and linear regression.

The method of Bland and Altman was used to estimate the bias, 95% (or 2SD) limits of agreement and the percentage error between the two methods of measuring cardiac index.<sup>12</sup> The percentage error was calculated from two times the SD of the bias over the mean  $CI_{TD}$  for the analysis.  $CI_{TD}$  was preferred over the mean CI because it was a better estimate of true CO. Changes in haemodynamic variables were also analysed at different stages during the procedure (T1–T10).

We adjusted for the effects of repeated measurements in our Bland and Altman analysis using the methods suggested by Myles and Cui.<sup>13</sup> A random effects model for repeated measures data was analysed using the 'xtmixed' function in Stata version 10. The random effects model adjusted for the baseline measurement for each

subject, mean measurement for each subject over time, mean measurement between two methods, and mean measurement for each method over time.<sup>14</sup> Repeatability was calculated based on the SD of the measurement attributable to measurement error and SD of the common random effect of each pair of linked replicate measurements.<sup>14</sup> A plot of within subject standard deviation against the mean of each subject by each method was used to check the underlying assumption of the Bland and Altman plot; that the variance of the repeated measurements for each subject by each method is independent of the mean of the repeated measures. For  $CI_{TD}$  this held true, but for  $CI_V$  there appeared to be a trend towards increasing SD with increasing mean CI. However, the plot of difference in method vs average of CI suggested that it was reasonable to assume that the assumption held. We were unable to apply Myles and Cui correct to our trend data because the model did not converge. We are unsure of the specific reason for the non-convergence, but it may be that of a boundary problem when one of the random effects being estimated was close to zero.

The ability of the Flo Trac/Vigileo to follow changes or trends in CO with reliability was assessed by (i) determining the correlation coefficient between  $CI_V$  and  $CI_{TD}$  for serial data in each patient and (ii) plotting  $\Delta CI_V$  against  $\Delta CI_{TD}$  on a four-quadrant plot of serial changes in CO<sup>15</sup> and a modified Bland and Altman plot, where  $\Delta CI$  was the change in CI between sequential readings [i.e. ( $T1_{CI}$ )–( $T2_{CI}$ ), etc.].

Trending was further assessed by the direction of change analysis. The concordance, or agreement, of the direction of change between consecutive readings from the thermodilution and the Vigileo was scored as a percentage of the data pairs that agreed. For example, if  $\Delta CI_{TD}$  was +1.0 and  $\Delta CI_V$  was +1.2 their directions of change agreed and they were in concordance, whereas if  $\Delta CI_{TD}$  was –0.5 and  $\Delta CI_V$  was +0.7 their directions of change did not agree and they were not in concordance. For small changes in CO and values of  $\Delta CI$ , the concordance between pairs,  $\Delta CI_{TD}$  and  $\Delta CI_V$ , will tend to be 50:50 or 50%, because random effects dominate the statistics. As the size of  $\Delta CO$  increases the direction of change of pairs of readings is more likely to agree and the concordance rate will increase towards 100%. Therefore, if data sets where only small changes in CO have occurred were excluded, the validity of the statistical analysis is improved. Thus, some authors when using concordance have excluded  $\Delta CO$ s of  $< 0.5$ – $1.0$  litre  $\text{min}^{-1}$  or less than 15% for their concordance analysis.<sup>15–17</sup> In the present study, we measured the concordance with no data exclusions and data excluded when  $\Delta CI_{TD} < 0.5$  litre  $\text{min}^{-1} \text{m}^{-2}$  and  $\Delta CI_{TD} < 1.0$  litre  $\text{min}^{-1} \text{m}^{-2}$ . Thermodilution measurements were used as they were more likely to reflect the true value of CO. Based on previous reports, the concordance should be  $> 90$ – $95\%$  when exclusion criteria of  $0.5$ – $1.0$  litre  $\text{min}^{-1} \text{m}^{-2}$  are applied.<sup>15–17</sup>

## Results

Due to incomplete data collection in two cases, data from 29 of the original 31 patients were analysed (23 males, 6 females). Mean age was 47.3 (SD 11.8, range 19–64) yr and mean (SD) BMI was 24.7 (2.2)  $\text{kg m}^{-2}$ . The underlying diseases necessitating liver transplantation were 22 cases of liver cirrhosis (16 viral and 6 alcoholic), three of primary hepatocarcinoma, three of primary biliary cirrhosis, and one of haemochromatosis. The mean MELD score of the study population was 21 (6). According to the UNOS classification, one patient was status 1, one was status 2a, 16 were status 2b, and 11 were status 3. Two patients needed postoperative ventilation on the ICU, one for 12 h and one for 26 h. Seven patients needed cardiovascular drug support postoperatively, four received noradrenaline ( $0.5\text{--}1.5 \mu\text{g kg}^{-1} \text{min}^{-1}$ ) and three received dopamine ( $4\text{--}8 \mu\text{g kg}^{-1} \text{min}^{-1}$ ).

A total of 290 paired readings were collected. Data were collected from each patient at the 10 sample times during the surgery and intensive care admission. The overall median (range)  $\text{CI}_{\text{TD}}$  was 5.2 (2.1–10.8)  $\text{litre min}^{-1} \text{m}^{-2}$ , which was significantly higher than the overall median  $\text{CI}_{\text{V}}$  which was 3.9 (2.1–6.9)  $\text{litre min}^{-1} \text{m}^{-2}$  ( $P<0.001$ ). The scatter and Bland and Altman plots of these paired readings are presented in Figure 1. The regression line was  $\text{CI}_{\text{V}}=(0.28)\times\text{CI}_{\text{TD}}+2.6$  and correlation coefficient was  $r=0.39$  ( $P<0.001$ ). The mean bias ( $\text{CI}_{\text{TD}}-\text{CI}_{\text{V}}$ ) corrected for repeated measures using random effects modelling<sup>13 14</sup> was 1.3  $\text{litre min}^{-1} \text{m}^{-2}$  (95% Confidence Interval: 1.1–1.4  $\text{litre min}^{-1} \text{m}^{-2}$ ) with 95% limits of agreement of  $-1.5$  (95% Confidence Interval:  $-1.8$  to  $-1.3$ ) to 4.1 (95% Confidence Interval: 3.8–4.3)  $\text{litre min}^{-1} \text{m}^{-2}$ . The adjusted percentage error was 54% (Fig. 1) using  $\text{CI}_{\text{TD}}$  as the best measure of mean CO.

Mean (95% Confidence Interval) MAP, PAP, CVP, CIs, and SVRI measurements for each stage of the procedure

were plotted (Fig. 2). The variation in the mean bias (separation between  $\text{CI}_{\text{TD}}$  and  $\text{CI}_{\text{V}}$ : middle plot) is shown over the course of the study. There was a relationship between this separation and SVRI (lower plot). This relationship is more clearly demonstrated in Figure 3 where a log-linear plot ( $r=0.69$ ;  $P<0.001$ ) is used to show that as peripheral resistance decreased the discrepancy or bias between CI measurements increased.

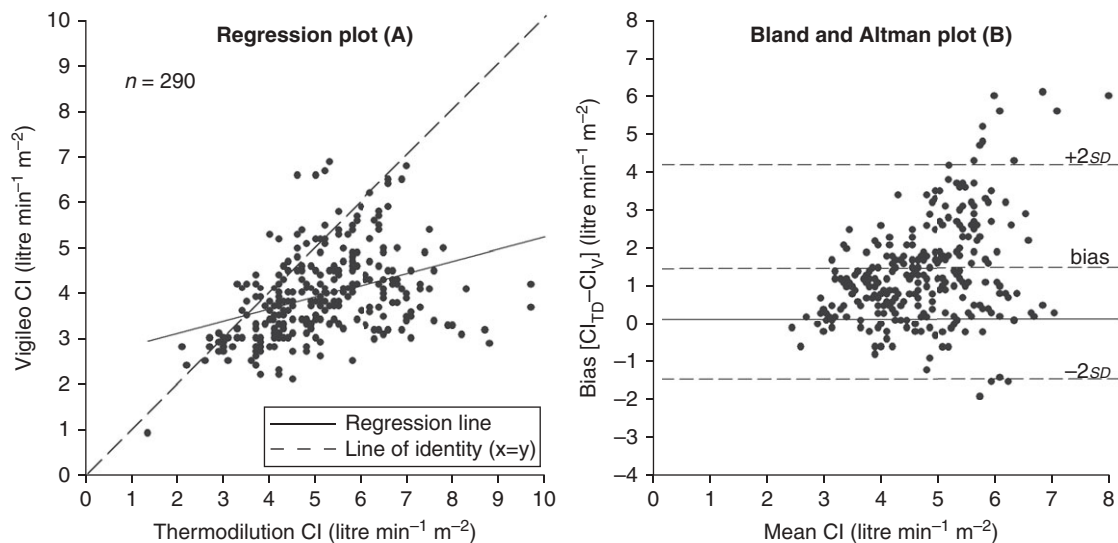
### Results of trend analysis

Significant correlation between the data pairs over the course of surgery and first 24 h on ICU (i.e. T1–10) could be shown in six out of the 29 patients ( $P$ -value for test  $<0.05$ ). The mean  $r$ -value for the correlation was  $r=0.41$  (inter-quartile range 0.22–0.64). Therefore, the Vigileo failed to track changes in CO in most patients over the course of surgery and ICU admission.

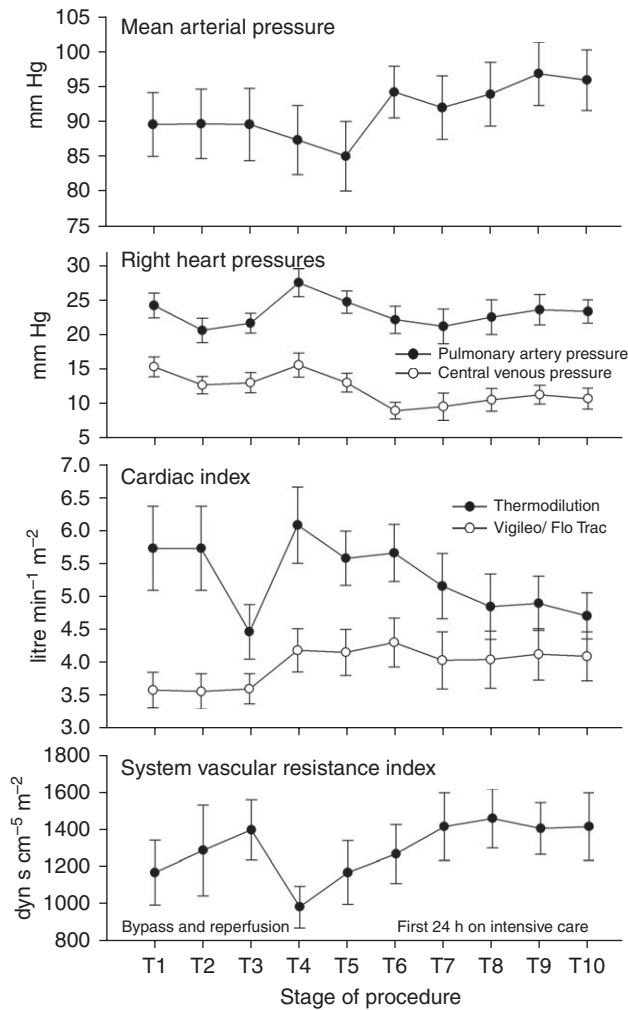
The four-quadrants plot of  $\Delta\text{CI}$  values for FloTrac/Vigileo against thermodilution are shown in Figure 4. No significant trending effect could be shown, with an  $r$ -value of  $r=0.25$ . The Bland and Altman plot had a bias of  $-0.2$   $\text{litre min}^{-1} \text{m}^{-2}$  and limits of agreement of  $-3.1$  to 2.9  $\text{litre min}^{-1} \text{m}^{-2}$ . There was an obvious sloping relationship between the two methods in plot B (Fig. 4).

### Concordance

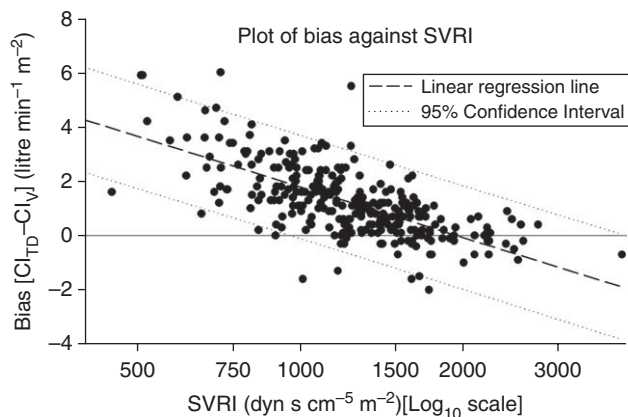
The direction of change in CI reading of the 261 data sets agreed in 145 pairs with a concordance rate of 62%. Twenty-seven pairs were excluded from the analysis as at least one of the  $\Delta\text{CI}$  values was zero. When data sets, where  $\Delta\text{CI}_{\text{TD}}$  was  $<0.5$  and  $<1.0$   $\text{litre min}^{-1} \text{m}^{-2}$ , were excluded from the analysis the concordance increased to 68% (98/145 sets) and 67% (67/100), respectively, which was below the 90–95% threshold for assuming good trending ability.<sup>15–17</sup>



**Fig 1** Regression (A) and Bland and Altman (B) plots for all 290 data comparisons.  $\text{CI}_{\text{TD}}$ , thermodilution cardiac index;  $\text{CI}_{\text{V}}$ , Vigileo cardiac index. Limits of agreement ( $\pm 2\text{SD}$ ) are shown in plot B.



**Fig 2** Haemodynamic variables (mean, 95% Confidence Interval) at different stages of the procedure (T1–T10). Start of the hepatic bypass, graft's reperfusion (T2–T4) and admission to intensive care (T6–T10) indicated. Systemic vascular resistance index estimated using thermodilution reading.



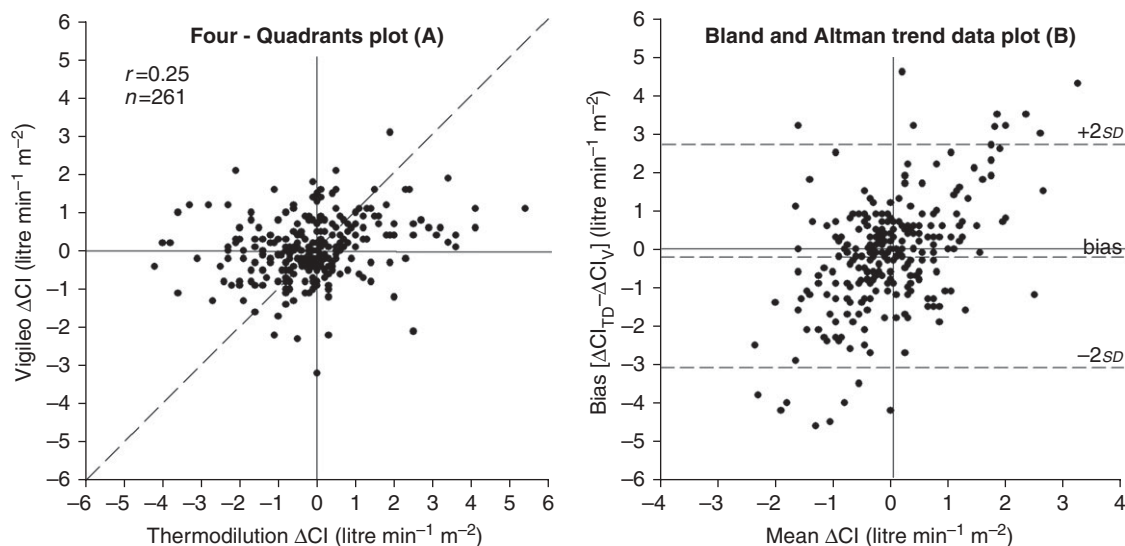
**Fig 3** Bias plotted against SVRI, shown as log scale. A log-linear plot was used to show that as peripheral resistance decreased the discrepancy or bias between CI measurements increased.  $CI_{TD}$ , thermodilution cardiac index;  $CI_V$ , Vigileo cardiac index. Data from all 10 time points used ( $n=290$ ).

## Discussion

The current study shows that in a cirrhotic patient population undergoing liver transplantation the measurement of CO by the Vigileo system underestimated and showed poor agreements with standard thermodilution CO measurements. The bias<sup>12</sup> was 1.3 litre  $\text{min}^{-1} \text{m}^{-2}$  and the 95% limits of agreement were  $-1.5$  to 4.1 litre  $\text{min}^{-1} \text{m}^{-2}$ . The percentage error was 54%, which exceeded a 30% limit of acceptance.<sup>18</sup> There was a clear relationship between low peripheral resistance measurements and increasing bias ( $r=0.69$ ;  $P<0.001$ ). Furthermore, the Vigileo system failed to reliably trend CO data, with a concordance compared with thermodilution CO of at best 68% of sequential readings, which was below an acceptable level of 90–95%.<sup>15–17</sup>

Inspection of our scatter plot of Vigileo against thermodilution CI (Fig. 1A) would have been expected to show the majority of data points scattered along the line of identity  $X=Y$  (slope approximately unity) with a correlation coefficient of the order of  $r=0.8$  if  $CI_V$  truly reflected  $CI_{TD}$  and taking into account the inherent imprecision of thermodilution measurements. However, this pattern was not seen and a significant number of data points fell far below the line of identity, thus indicating that the Vigileo frequently under-reads CO. This under-reading was also present in the Bland and Altman plot (Fig. 1B) where the bias ( $CI_{TD}-CI_V$ ) was 1.3 litre  $\text{min}^{-1} \text{m}^{-2}$ . There was an obvious sloping relationship between the two methods.

The ability of the Vigileo to trend CO data was analysed in the study by looking at the sequential changes in CI as measured by the two monitors. Once again one would have hoped to see the majority of data points lying close to the line of identity of the four-quadrants plot of serial changes in CI (Fig. 4A) if true trending ability existed. Again the Vigileo ( $CI_V$ ) failed to show any reliability, with poor correlation to  $CI_{TD}$  ( $r=0.25$ ). In the accompanying Bland and Altman trend plot (Fig. 4B) there was an obvious sloping relationship between the two methods with a negative bias when CI decreased and a positive bias when CI increased, indicating that  $CI_V$  was failing to track changes in the  $CI_{TD}$  measurement. This was further backed up by the analysis of data from individual patients where serial CI readings were correlated in only six out of 29 cases. Furthermore, we examined the concordance and in only 68% of readings did the direction of change agree, despite excluding data sets where  $\Delta CI$  was small and  $<1.0$  litre  $\text{min}^{-1} \text{m}^{-2}$ . Previous authors when evaluating different cardiac monitors have reported a concordance of over 80% when all data sets were included and over 95% when small values of  $\Delta CO$  were excluded.<sup>16, 17</sup> Up to the late 1980s correlation and regression was used to justify the results of comparative CO measurement device evaluation studies. In 1986 Bland and Altman proposed that correlation and  $r$ -values was inappropriate for deciding whether a new method can replace old, and they introduced their now well accepted bias and



**Fig 4** Four-quadrants trend plot (A) and modified Bland and Altman trend plot (B) for all 261 data comparisons assessing the ability of the Vigileo to trend CO data.  $\Delta CI_{TD}$ , change in thermodilution cardiac index;  $\Delta CI_V$ , change in Vigileo cardiac index. Line of identity ( $X=Y$ ) shown in plot A. Limits of agreement ( $\pm 2SD$ ) shown in plot B.

precision method.<sup>12</sup> However, we still believe that correlation and regression still has an important role in this type of statistical analysis (a) for showing the relationship between paired measurements (Fig. 1) and also (b) comparing data and results from different studies.

Based on these findings one has to conclude that current Vigileo technology does not measure or track changes in CO with any clinically acceptable reliability, at least in cirrhotic patients.

In 1999, Critchley and Critchley performed a meta-analysis of studies comparing different CO monitoring techniques and demonstrated that errors of both the test and reference methods should be combined when assessing reliability of CO measurement devices. They concluded that the combined agreement error should be  $<30\%$  for a new CO device to be accepted for clinical purposes,<sup>18</sup> which is now widely accepted. The criteria are based on a precision for standard thermodilution measurements of less than  $\pm 20\%$ .<sup>18, 19</sup> When applied to the Vigileo literature only two out of 13 published studies fulfilled the criteria (Table 1).<sup>28, 30</sup>

The Vigileo system has received mixed reviews since its introduction into clinical practice in early 2000<sup>20–32</sup> (the outcomes of these and other papers are summarized in Table 1). With the exception of Sakka's paper involving septic intensive care patients<sup>31</sup> and Costa's abstract involving cirrhotic patients,<sup>20</sup> these studies have used cohorts of exclusively 11–52 cardiac surgery patients with up to 315 data pairs. Overall the agreement errors with thermodilution have ranged from 25 to 59%, implying that the Vigileo is no better and probably a lot worse than thermodilution using the current benchmark of 30%.<sup>18</sup>

Prasser and colleagues (2007) in 20 postoperative cardiac surgery patients found an acceptable percentage

error of 27% and Mayer and colleagues (2008) in 40 coronary bypass surgery patients found an acceptable percentage error of 25% when using the new version of the Vigileo.<sup>28, 30</sup> Good as these results may seem, no correction was made for repeated measurements,<sup>13</sup> eight serial time points in both studies, and conditions may have been very similar between readings, unlike our patient cohort. It is interesting to note that in Mayer and colleagues study the percentage error varied between 28.3 and 20.3%, depending on whether comparisons were intraoperative or on the ICU, respectively.<sup>28</sup> Therefore, one has to question whether these two studies provided a vigorous enough examination of the Vigileo's monitoring potential.

In the present study we were able to show that the poor agreement of the Vigileo with thermodilution was in part due to a failure of its software to properly compensate for low SVRI states (Figs 2 and 3). At low SVRI measurements in cirrhotic patients there was a significant offset or bias between CI readings, which was related to the degree of peripheral vasodilation. We demonstrated a log-linear relationship between SVRI and the bias between two monitors (Fig. 3).

Costa and colleagues<sup>20</sup> evaluated the Vigileo in cirrhotic patients. They published preliminary findings from 14 liver transplant patients as a conference abstract and reported a bias between the Vigileo and thermodilution of 0.48 litre  $\text{min}^{-1} \text{m}^{-2}$ , and we estimate their percentage error to be 35%. In comparison, we found a greater bias of 1.3 litre  $\text{min}^{-1} \text{m}^{-2}$  and a percentage error of 54% in cirrhotic patients. However, Costa's patient cohort had a lower range of CO, 2–5 litre  $\text{min}^{-1} \text{m}^{-2}$  compared with 2–8 litre  $\text{min}^{-1} \text{m}^{-2}$  (Fig. 1A and B) in our study, suggesting that severe cirrhotic myopathy was more prevalent in our patients, and this could explain the difference between results.

Patients with septicaemia may also present with a low peripheral resistance and hyperdynamic circulation. Thus, it is interesting to note that the Vigileo method also significantly underestimates transpulmonary thermodilution CO in septic patients.<sup>31</sup> It has been shown that vasoactive drugs, acting on systemic vascular tension, can adversely affect the arterial waveform analysis method.<sup>25–29</sup> The above-mentioned publications and our data support the conclusion that the Vigileo system does not provide reliable CO measurements when changes in the compliance and peripheral resistance of the circulation occur.

One possible explanation for the Vigileo system's unreliability may lie with the algorithm used to derive CO. The algorithm uses an estimate of the aortic compliance based on a normogram and patient characteristics data, rather than a direct measurement. According to the manufacturers, this normogram is based on data from a wide variety of clinical situations involving patients and healthy volunteers. However, it may be inappropriate to use the Vigileo in cirrhotic patients and other patient groups who have a relatively high CO and low peripheral resistance despite a normal blood pressure<sup>1–3</sup> because the algorithm may be incorrectly set up for such patients. In contrast, cardiac surgery patients may have more normal circulatory parameters and this may explain the better results found in other recent Vigileo validation studies.<sup>28–30</sup>

Our study had some limitations. Most significant was the use of an imprecise reference standard, thermodilution. Stetz and colleagues<sup>19</sup> have quoted it to have a precision error of 13–22%. Ideally, one should have used a highly reliable reference standard to make comparisons, such as an aortic flow probe applied directly to the aorta. Unfortunately, this type of study can only be performed in the laboratory on anaesthetized animals<sup>33</sup> and it is also important to collect data from the clinical setting. However, we did optimize our thermodilution measurements by using the average of four readings with 10% variation and using intermittent measurements rather than continuous or transpulmonary thermodilution measurements. Our statistical methods were based on the most recent recommendations by Myles and Cui.<sup>13</sup> However, in respect to assessing trending ability no current consensus exists in the literature on how this should be done. Our use of the four-quadrants plot of serial changes in CO and concordance analysis were based on what we considered the most useful and sound methods currently available in the evaluation of new methods of CO measurement literature.<sup>15–17</sup>

In conclusion, as the mortality of cirrhotic patients undergoing surgery still ranges, according to severity of liver disease, between 10 and 80%,<sup>34–36</sup> careful intra and postoperative management, including haemodynamic monitoring, is necessary. In cirrhotic patients with hyperdynamic circulations, comparing the Vigileo system with thermodilution CO showed a degree of error and unreliability higher than that considered acceptable for clinical

purposes. Furthermore, we were unable to show any useful trending ability, considering the continuous nature of Vigileo measurements. In particular, our study highlights a problem that the Vigileo has with low peripheral resistance states. Further refinement of the Vigileo's algorithm and calibration method may possibly improve its accuracy in cirrhotic patients in the future. Therefore, in this class of patients the pulmonary artery catheter and thermodilution CO measurement still has its indication and should not yet be considered outdated when an evaluation of haemodynamic status is needed.

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