A comparison of the Nexfin® and transcardiopulmonary thermodilution to estimate cardiac output during coronary artery surgery

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Summary
The newly introduced Nexfin® device allows analysis of the blood pressure trace produced by a non-invasive finger cuff. We compared the cardiac output derived from the Nexfin and PiCCO, using transcardiopulmonary thermodilution, during cardiac surgery. Forty patients with preserved left ventricular function undergoing elective coronary artery bypass graft surgery were studied after induction of general anaesthesia and until discharge to the intensive care unit. There was a significant correlation between Nexfin and PiCCO before ($r^2 = 0.81, p < 0.001$) and after ($r^2 = 0.56, p < 0.001$) cardiopulmonary bypass. Bland–Altman analysis demonstrated the mean bias of Nexfin to be $0.1 (95\%$ limits of agreement $-0.6$ to $+0.5$, percentage error 23%) and $0.1 (-0.8$ to $+0.6$, 26%) l.min$^{-1}.m^{-2}$, before and after cardiopulmonary bypass, respectively. After a passive leg-raise was performed, there was also good correlation between the two methods, both before ($r^2 = 0.72, p < 0.001$) and after ($r^2 = 0.76, p < 0.001$) cardiopulmonary bypass. We conclude that the Nexfin is a reliable method of measuring cardiac output during and after cardiac surgery.

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Monitoring of haemodynamic variables, such as cardiac output and left ventricular stroke volume, is of increasing interest, as it allows treatment to be tailored to the individual patient. Recent studies have shown that optimisation of left ventricular stroke volume or cardiac output is associated with beneficial effects on both morbidity and length of stay on the intensive care unit (ICU) [1–3]. The gold standard is the pulmonary artery catheter; however, this is associated with a number of complications and clinical limitations [4–6]. Therefore, investigators have examined the utility of less invasive techniques such as transcardiopulmonary thermodilution or continuous arterial waveform analysis [7–9].

The Nexfin® (BMEYE, Amsterdam, The Netherlands) has recently been introduced into clinical practice. It consists of a model-based method that provides beat-to-beat measurement of cardiac output by analysis of the non-invasive finger arterial blood pressure trace, which is measured continuously by the use of an inflatable finger cuff. Stroke volume is determined by dividing the pulsatile systolic area of each beat by impedance, which is estimated by the device based on patient characteristics.
We designed a study to compare the Nexfin with transcardiopulmonary thermodilution using the PiCCO (Pulsion Medical Systems, Munich, Germany), looking at the accuracy of cardiac output estimation and the ability to track haemodynamic changes and trends.

**Methods**

After approval from our institutional ethics committee, patients with preserved left ventricular function undergoing elective coronary artery bypass surgery were approached and consent for participation in the study was sought. Exclusion criteria included age < 18 years, left ventricular ejection fraction ≤ 0.5, emergency surgery, haemodynamic instability, intracardiac shunt, severe aortic, tricuspid or mitral stenosis or insufficiency, and mechanical circulatory support.

Patients were prescribed midazolam 0.1 mg.kg\(^{-1}\) orally, 30 min before induction of anaesthesia. Routine monitoring was established including peripheral oxygen saturation and heart rate (S\(/5\) monitor; GE Healthcare, Helsinki, Finland).

The Nexfin monitoring system was set up by entering patient-specific data followed by attaching the pneumatic finger cuff to the middle phalanx of the third finger (on the opposite hand to the arterial line), as recommended by the manufacturer. Finger arterial pressure measurement is based on the volume clamp method [10–12] in combination with Physiocal calibration [13]. Continuous finger pressure is reconstructed to brachial artery levels using a generalised waveform filter and a level correction formula, correcting for differences in wave shape and pressure values between these sites. Once the brachial artery waveform has been developed, the pulsatile systolic area (determined by the time integral of the pressure curve above the diastolic pressure and between the upstroke and the dicrotic notch) is calculated for each beat. Stroke volume is then calculated using the estimated arterial impedance. To that end, a patient-specific three-element Windkessel model is produced using patient characteristics (age, sex, height and weight). Moreover, for each beat, mean arterial pressure is used to correct the elements that are pressure-dependent in a non-linear way [14]. Dividing the pulsatile systolic area by the impedance gives beat-to-beat stroke volume. Heart rate was calculated from the pulse interval, followed by cardiac output (stroke volume multiplied by heart rate); variables were automatically indexed to body surface area.

After administration of sufentanil (0.5 μg.kg\(^{-1}\)), propofol (1.5 mg.kg\(^{-1}\)) and rocuronium (0.6 mg.kg\(^{-1}\)), the trachea was intubated. Anaesthesia was maintained by administering a continuous infusion of both sufentanil (1 μg.kg\(^{-1}\).h\(^{-1}\)) and propofol (3 mg.kg\(^{-1}\).h\(^{-1}\)). The patient’s lungs were ventilated with an oxygen/air mixture using a tidal volume of 8 ml.kg\(^{-1}\) ideal body weight, and positive end–expiratory pressure was set at 5 cmH\(_2\)O. Subsequently, a central venous catheter and a transpulmonary thermodilution PiCCO catheter were inserted into the right internal jugular vein and the femoral artery, respectively. The thermodilution catheter was connected to the PiCCO monitor (Software version 1.3.0.8).

After induction of anaesthesia, Nexfin and PiCCO measurements as well as other haemodynamic values were recorded every 10 min, both before and after cardiopulmonary bypass (CPB). These were only measured when the following conditions were met: stable haemodynamics; an undamped arterial pressure trace; and (with respect to the Nexfin) a frequency of physiological autocalibration > 30 heartbeats. Thermodilution measurements were made by injecting 15 ml cold saline (≤ 8°C) through the central venous line at least three times, at random points in the respiratory cycle. If a difference of ≥ 15% was detected between the PiCCO measurements, they were repeated. At the same time, Nexfin measurements were performed by collecting five numerical values over a period of 3 min and determining the mean value.

A passive leg-raising manoeuvre was performed after induction of anaesthesia and after surgery (before transfer to the ICU); this involved elevating the legs to 45° while the patient was in the horizontal position. This manoeuvre causes blood to be shifted from the lower part of the body to the intrathoracic compartment, generating an increase in right and left ventricular preload, and leads to well recognised haemodynamic effects. All measurements were repeated before, during, and after raising the legs.

Statistical comparisons were performed using commercially available statistics software (GraphPad Prism 5; GraphPad Software Inc., San Diego, CA, USA and...
To demonstrate the relationship between sample size and the width of the confidence interval of the estimated variable, we calculated the width of the 95% confidence interval of the limits of agreement as recommended by Bland and Altman (as $\pm 1.96 \sqrt{\frac{s^2}{n}}$, where $s$ is the standard deviation of the bias). To describe the agreement between PiCCO and Nexfin, Bland–Altman plots for repeated measures were calculated for each time period (before and after CPB). Percentage error was calculated as described by Critchley et al. [15], using the limits of agreement (2 SD) of the bias divided by the mean values of the two methods. Bland–Altman plots for haemodynamic trends and paired t-tests followed by Bonferroni correction for multiple comparisons were also performed.

Results

We enrolled 40 patients, 29 (73%) of whom were men; mean (SD) age was 64 (4) years, body mass index was 28 (3) kg.m$^{-2}$ and left ventricular ejection fraction was 0.6 (0.1). A total of 404 data pairs (213 before and 191 after CPB) were obtained. There was a significant difference ($p < 0.05$) between mean arterial pressure, systemic vascular resistance index, heart rate and cardiac index using both measurement devices before and after CPB. There was a significant correlation between Nexfin and thermodilution before and after CPB (Fig. 1). The bias, limits of agreement and percentage error were within the acceptable range (Table 1).

The passive leg-raise manoeuvre was performed in 37/40 patients before and 32/40 patients after CPB (Table 2). Patients who increased their stroke volume index by $>15\%$ were defined as responders. We observed 19 responders both before (51%) and after (59%) CPB. Again, the measurements obtained by the Nexfin and PiCCO were correlated, with acceptable bias and limits of agreement.

Changes in values displayed by both devices are illustrated in Fig. 2. Again, they were well correlated, with limits of agreement from $-31\%$ to $+23\%$; after CPB, limits of agreement ranged from $-12\%$ to $+13\%$.

There was no significant correlation between mean arterial pressure and Nexfin before ($r^2 = 0.01$, $p = 0.08$) and after ($r^2 = 0.009$, $p = 0.72$) CPB; however, there was

![Figure 1](image-url)
some correlation between the Nexfin and systemic vascular resistance index before ($r^2 = 0.31$, $p < 0.0001$) and after ($r^2 = 0.16$, $p < 0.0001$) CPB.

Table 1 Comparison of Nexfin and PiCCO in 40 patients undergoing coronary artery surgery. Values are mean (SD) or percentage.

<table>
<thead>
<tr>
<th></th>
<th>Before CPB (213 measurements)</th>
<th>After CPB (191 measurements)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac index; l.min$^{-1}$.m$^{-2}$</td>
<td>2.4 (0.6)</td>
<td>2.8 (0.6)</td>
</tr>
<tr>
<td>Bias; l.min$^{-1}$.m$^{-2}$</td>
<td>0.06 (0.27)</td>
<td>0.09 (0.37)</td>
</tr>
<tr>
<td>95% limits of agreement; l.min$^{-1}$.m$^{-2}$</td>
<td>$-0.60$ to $+0.49$</td>
<td>$-0.81$ to $+0.63$</td>
</tr>
<tr>
<td>Percentage error</td>
<td>23%</td>
<td>26%</td>
</tr>
</tbody>
</table>

CPB, cardiopulmonary bypass.

Table 2 Comparison of Nexfin and PiCCO in patients undergoing coronary artery surgery in whom a passive leg-raise manoeuvre was performed. Values are mean (SD) or percentage. CPB, cardiopulmonary bypass.

<table>
<thead>
<tr>
<th></th>
<th>Before CPB (n = 37)</th>
<th>After CPB (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$r^2$</td>
<td>$r^2 = 0.72$ (p &lt; 0.0001)</td>
<td>$r^2 = 0.76$ (p &lt; 0.0001)</td>
</tr>
<tr>
<td>Bias; l.min$^{-1}$.m$^{-2}$</td>
<td>0.14 (0.43)</td>
<td>0.07 (0.26)</td>
</tr>
<tr>
<td>95% limits of agreement; l.min$^{-1}$.m$^{-2}$</td>
<td>$-0.98$ to $+0.70$</td>
<td>$-0.59$ to $+0.44$</td>
</tr>
<tr>
<td>Percentage error</td>
<td>39%</td>
<td>18%</td>
</tr>
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Discussion

We have shown that the haemodynamic values and indices measured by the Nexfin and the PiCCO in patients with preserved left ventricular function who do not require inotropic support are well correlated. Such a comparison has not been described before. The Nexfin was able to track haemodynamic changes and trends before and after CPB however values were influenced by systemic vascular resistance.

The recently introduced Nexfin monitoring system is completely non-invasive in that it requires only the use of a pneumatic finger cuff, without the insertion of any intravascular lines. We have shown that the values of cardiac output that it displays are well correlated with the more invasive PiCCO system that requires the insertion of both a central venous line and a femoral
arterial line. The PiCCO is, however, in our opinion, less invasive again than the pulmonary artery catheter, to which many more complications are attributed [16].

As we have demonstrated, the Nexfin does not appear to need calibration before use. Its accuracy depends on correct estimation of impedance, compliance and resistance [17], which are calculated using the patient-specific data entered before connecting to the patient. Aortic diameter and arterial pressure are then estimated [18–20], before cardiac output/index is calculated.

Apart from the non-invasive nature and good correlation of the device, we have shown that it is easy and rapid to set up and use, meaning that we can recommend use in similar settings. However, we have not yet shown that its accuracy can be relied on during haemodynamic instability or when inotropic or vasoactive drugs are in use, meaning that further studies in these areas must be carried out before more widespread use can be recommended.

Other studies have also shown non-invasive measurement of finger arterial pressure to be quite accurate [10, 21]. However, up to now, studies looking at their use to estimate stroke volume and cardiac index have been limited, with equivocal results [11, 22–25]. Although in the study applying the Modelflow algorithm to the finger-derived arterial pressure curve, the device showed less accuracy compared with pulmonary thermodilution, other investigations using the Nexfin found good correlation with pulmonary thermodilution and echocardiography-derived cardiac output, respectively.

As recommended by Critchley et al. [26], we used 30% as our cut-off for limits of agreement, and we have shown that the Nexfin and PiCCO are adequately correlated at varying times during coronary surgery, and also before and after rapid intravascular volume expansion, as estimated using the passive leg-raise manoeuvre. However, at the time of the passive leg-raise the Nexfin results did differ from the PiCCO by a small amount; this finding has also been shown in a previous similar study carried out in the ICU [27]. A number of previous studies have also shown that other devices that rely on pulse contour analysis are also not as accurate during marked intravascular volume changes [28–31].

Of interest, the mean arterial pressure was not correlated with the cardiac output measured by the Nexfin during the study period, but it was related to the systemic vascular resistance. This has also been shown in a number of other studies using pulse contour analysis with other devices [7, 32–35]. It must be emphasised, however, that the relationship that we have shown is based on only a few data points from a small number of patients. However, from a physiological standpoint, cardiac index will be higher for a given mean arterial pressure if systemic vascular resistance index is low, which may explain some of our findings.

As suggested by a recent study [36], we have shown that the Nexfin and PiCCO are precise during stable haemodynamic conditions, with no rapid changes during data collection. This was also demonstrated during the passive leg-raise test. This means both systems are able to track such haemodynamic changes and trends with acceptable accuracy.

Some limitations of our study should be noted. Our data were derived from patients with preserved left ventricular function undergoing elective coronary surgery under stable haemodynamic conditions and without ongoing pharmacologic support. Therefore, our results cannot automatically be transferred to other patient groups. Furthermore, we used PiCCO instead of a pulmonary artery catheter as our ‘gold standard’. We feel that this was justified because the PiCCO has been shown to be interchangeable with the pulmonary artery catheter in a number of other studies [7, 8, 37, 38]. However, the PiCCO has some limitations, particularly after weaning from CPB, with transient thermal changes leading to increased bias [35].

From the point of view of clinical relevance, individualised intra-operative goal directed therapy has been shown to lead to reduced morbidity [2]. Non-invasive and continuous estimation of stroke volume and cardiac output is required for this to be carried out, and we have demonstrated that the Nexfin is a good candidate for such a monitor.

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