Original Contribution

Comparison of noninvasive cardiac output measurements using the Nexfin monitoring device and the esophageal Doppler

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Abstract

Study Objective: To evaluate the validity of cardiac output (CO) measurements obtained using the Nexfin device in comparison to those obtained with the esophageal Doppler in steady-state conditions and after phenylephrine administration.

Design: Prospective observational study.

Setting: Operating room of a North American academic medical center.

Patients: 25 ASA physical status 1, 2, and 3 patients referred for abdominal or orthopedic surgeries.

Interventions: After endotracheal intubation, patients who presented with a 20% or greater decrease in mean arterial pressure (MAP) received an intravenous (IV) bolus of 100 μg of phenylephrine. If MAP was still 20% lower than the patient’s baseline level at least 10 minutes after the first vasopressor treatment, a second bolus of 100 μg of phenylephrine was given.

Measurements: CO was measured simultaneously by esophageal Doppler (COED) and Nexfin (CONXF) at baseline and when blood pressure peaked after an IV 100 μg phenylephrine bolus. Comparisons were then made between the two devices to evaluate the ability of the Nexfin device to track changes in CO.

Main Results: 66 pairs of data were obtained. Mean COED and CONXF were 4.7 ± 1.8 L/min and 5.6 ± 2.0 L/min, respectively. There was a significant relationship between COED and CONXF (r² = 0.82; P < 0.001). The agreement between COED and CONXF was 0.88 ± 0.86 L/min (Bland Altman). The mean percent error (Critchley and Critchley) of CONXF versus COED was 37%. Trending analysis found a 94% concordance between changes in COED and CONXF after phenylephrine administration.

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1. Introduction

In recent years there has been increasing interest in perioperative hemodynamic management through the incorporation of cardiac output (CO) measurements [1-4]. Several technologies are now available for minimally invasive or noninvasive CO monitoring in the perioperative setting [5,6]. However, most of these are either operator-dependent (esophageal Doppler) or require the use of intra-arterial catheters (pulse contour analysis). A new CO monitoring system based on the volume-clamp method (Nexfin; BMEYE B.V, Amsterdam, The Netherlands) was recently proposed for noninvasive and continuous CO monitoring. This method uses the area under the systolic part of the blood pressure waveform as input into an algorithm incorporating patient-specific aortic vascular characteristics to calculate beat-to-beat stroke volume (SV) and CO [7,8]. This device is noninvasive, relatively simple, and nonoperator-dependent [7], and it has been tested in healthy volunteers during orthostasis and for optimization of cardiac resynchronization therapy [9,10]. It has also been compared with thermodilution CO measurements in 25 awake patients after coronary artery bypass surgery [11]. All of these previous studies suggest that Nexfin CO readings have the potential to be used for intraoperative hemodynamic optimization. Currently we lack data focusing on the accuracy and trending abilities of this device during general anesthesia. Moreover, pulse contour analysis methods may be impacted by the administration of vasopressors [12-14] such as phenylephrine [15].

The esophageal Doppler is a minimally invasive hemodynamic monitoring device that measures beat-to-beat blood flow in the descending aorta. Cardiac output is then determined by multiplying the cross-sectional area of the aorta by blood flow velocity integrated over time [16,17]. Hemodynamic optimization using Doppler-derived CO measurements leads to a decrease in perioperative morbidity and in postoperative intensive care unit (ICU) length of stay [18,19]. This device was an acceptable surrogate for an invasive CO trending monitor in studies that evaluated the accuracy of new CO monitors [20,21] and in studies focusing on fluid responsiveness [22,23].

The goals of our study were to compare the CO measuring capabilities of the Nexfin device with those of the esophageal Doppler during general anesthesia and after phenylephrine administration.

2. Materials and methods

2.1. Patients

After Institutional Review Board approval from the University of California, Irvine Medical Center and written, informed consent, 25 patients undergoing abdominal or orthopedic surgery in the supine position were enrolled. Six patients were classified as ASA physical status 1, 16 were ASA physical status 2, and three patients were ASA physical status 3. Eleven patients underwent lower leg surgery, 5 had urologic surgery, 6 patients had rectal surgery, and three had a hip replacement. Exclusion criteria were advanced dysfunction of peripheral perfusion (ie, Raynaud’s syndrome), arteriovenous shunts for hemodialysis, patients having vascular surgery of the upper extremities, poorly controlled hypertension [systolic blood pressure (SBP) ≥ 160 mmHg], history of congestive heart failure, diabetes, and peripheral arterial disease. Both devices may be affected by patient-specific disease states; thus only patients with relatively healthy cardiovascular systems were recruited to the study.

A right radial intra-arterial catheter (Becton Dickinson Co., Franklin Lakes, NJ, USA) was placed before anesthesia induction. After being zeroed to atmospheric pressure, the arterial pressure transducer (Transpac IV Monitoring Kit, No. 42584-05; ICU Medical, Inc., San Clemente, CA, USA) was secured at the midaxillary level. Anesthesia was induced with fentanyl (1.5-2.0 μg/kg) and propofol (2-3 mg/kg). All patients were intubated and maintained with total intravenous (IV) anesthesia (propofol 100-150 μg/kg/min and remifentanil 0.3 - 0.5 μg/kg/min). All patients were mechanically ventilated with a tidal volume of 8 to 10 mL/kg of body weight at a frequency of 10-12 breaths per minute to maintain end-tidal carbon dioxide (ETCO2) between 35 and 40 mmHg. The anesthesia regimen and ventilation settings were kept constant throughout the study.

After invasive arterial pressure was obtained, an appropriate size Nexfin finger cuff was applied to the midphalanx of the left middle finger according to guidelines provided by the manufacturer. If initial placement was inadequate, the finger cuff was repositioned until a good finger arterial curve appeared on the screen. An acceptable Nexfin waveform was characterized by a high-quality shape, amplitude, velocity, area, and visible dicrotic notch. The arm and finger were then positioned alongside the body at midtorax level to prevent any hydrostatic level errors. Attention was paid to avoid cold fingers during initiation of the measurement by placing the hand under a warm blanket. The hand and fingers were checked regularly for signs of tissue hypoxia (cyanosis, temperature relative to proximal tissues).

After anesthetic induction and subsequent endotracheal intubation, an esophageal Doppler probe [6-mm diameter unidirectional continuous wave Doppler transducer (4 MHz)] was lubricated and inserted into the oropharynx. The probe was inserted to the proper depth using probe depth markers and waveform monitoring. Optimizing the Doppler beam was critical to assure the best data acquisition. Optimizing...
the waveform was verified by 1) a crisp aortic sound, 2) heart rate (HR) obtained from the Doppler device that matched the HR from the electrocardiography monitor, and 3) correct identification of the base and top of the waveform. The probe was secured after an adequate waveform was obtained.

2.2. Cardiac output determination using Nexfin HD

The methodology of the Nexfin HD (BMEYE B.V., Amsterdam, Netherlands) is based on the development of pulsatile unloading of the finger arterial walls using an inflatable finger cuff with a built-in photoelectric plethysmograph that uses pressure to maintain a constant blood volume in the finger. This technology was first introduced by Peñaz in 1973 and has achieved significant development in the past 40 years [24]. Nexfin calculates beat-to-beat SV by dividing the area under the SBP curve (measured at 200 Hz) by the aortic input impedance, $Z_{in}$, similar to the method described by Wesseling et al and Westerhof et al [25,26]. The value of $Z_{in}$ is determined from a three-element Windkessel model [27] in which the nonlinear effect of mean arterial pressure (MAP) and the influence of the patient’s age, height, weight, and gender on aortic mechanical properties are incorporated. Because the waveform at the finger shows a more undulatory appearance than the radial pressure waveform, Nexfin transforms the (noninvasive) finger waveform into a brachial waveform with a specific filter. Nexfin uses the integrated area under the pulsatile systolic waveform from the brachial pressure wave as an input to the model, which directly yields SV and produces CO by multiplying beat-to-beat SV by instantaneous heart rate (HR).

2.3. Cardiac output determination using the esophageal Doppler

The esophageal Doppler (CardioQ; Deltex Medical Ltd., Chichester, Sussex, UK) engineering principle is based on the concept that sound transmitted from the Doppler probe reflects off of moving objects (such as red blood cells) and returns at an altered frequency. With each heartbeat, the Doppler beam traverses the esophagus and detects the velocity and distance travelled of blood flow in the descending aorta. The Doppler probe is attached to a monitor to display the blood flow velocity profile from the reflected signal. The result is an aortic waveform, with velocity on the y-axis and time on the x-axis. The distance that the blood travels down the descending thoracic aorta with each contraction is called the stroke distance and is determined by integrating the flow velocity over time. The device calculates the aortic cross-sectional area (independent of real-time measurements) using a proprietary algorithm that uses the patient’s age, height, and weight. The monitor then converts the linear measurement of stroke distance into a volumetric measurement of SV by multiplying the stroke distance by the aortic cross-sectional area. Finally, CO is obtained by multiplying SV by HR.

2.4. Protocol

After anesthesia induction, patients who presented with a 20% or greater decrease in MAP received an IV bolus of 100 μg of phenylephrine. This dose was selected and standardized as a result of clinical opinion and patient safety (previous studies have typically used more than this amount) [28]. If MAP was still 20% lower than the patient’s baseline level at least 10 minutes after the first pressor treatment, a second bolus of 100 μg of phenylephrine was administered. Both CO values using Nexfin ($CO_{NXF}$) and esophageal Doppler ($CO_{ED}$) were recorded immediately before phenylephrine injection and when blood pressure (BP) peaked after the IV 100 μg phenylephrine bolus. Three successive CO values were recorded simultaneously using the Nexfin and esophageal Doppler.
(CONXF) and the esophageal Doppler (COED). The mean value of each triplet of consecutive measurements was used for statistical analysis. The observer who recorded the Nexfin data (GC) was blinded to data from the esophageal Doppler data; the observer of the esophageal Doppler data similarly was blinded to Nexfin data.

2.5. Statistical analysis

Data are expressed as means ± SD. The Kolmogorov-Smirnov test was used to test the normality of the distributions. Correlation between CONXF and COED was determined by linear regression. Changes in CO induced by phenylephrine were analyzed using a paired Student’s t-test. Bland Altman analysis [29] was used to assess the bias (mean difference) and precision (SD of the bias) between CO_NXF and CO_ED. The mean percent error between CO_NXF and CO_ED was assessed using the Critchley and Critchley method [30]. Finally, we used the 4-quadrant concordance plots recently described by Critchley et al to analyze the trending abilities of CO_NXF against CO_ED [21]. For this analysis, we selected an exclusion zone of 15% representing the expected intrinsic error of the devices. For all statistical analyses, P-values < 0.05 were considered statistically significant.

3. Results

Twenty-five patients (15 men and 10 women, age 41 ± 12 yrs, weight 92 ± 17 kg, and height 172 ± 18 cm) were enrolled in our study. Seventeen patients received one bolus of 100 μg of phenylephrine, while 8 patients received two phenylephrine boluses. Consequently, 66 pairs of CO data were obtained, including 33 pairs before the IV phenylephrine bolus and 33 pairs after the phenylephrine bolus. The quality of the arterial waveform from the Nexfin device was classified as good or excellent in all 25 patients.

3.1. Comparison of CO_ED and CO_NXF measurements

3.1.1. Overall population

When analysis was conducted for the total 66 pairs of data, the mean ± SD CO_NXF was 5.6 ± 2.0 L/min and the mean ± SD CO_ED was 4.7 ± 1.8 L/min (P < 0.001). There was a significant relationship between CO_ED and CO_NXF (n = 66; r² = 0.82; P < 0.001) (Fig. 1A). The agreement between CO_ED and CO_NXF was 0.88 ± 0.86 L/min (Bland Altman) (Fig. 1B). The mean percent error of CO_NXF compared with CO_ED was 36.6%. The effect of systemic vascular resistance (SVR) on the bias between CO_ED and CO_NXF was also plotted; a significant relationship was observed (P < 0.0001) (Fig. 2).

3.1.2. Before phenylephrine injection

When analysis was conducted for the 33 pairs of data obtained before the phenylephrine injection, the mean CO_NXF was 6.2 ± 2.2 L/min and the mean CO_ED was 5.4 ± 1.7 L/min (P < 0.001). There was a significant relationship between CO_ED and CO_NXF (n = 33; r² = 0.87; P < 0.001) (Fig. 3A). The agreement between CO_NXF and CO_ED was 0.75 ± 0.90 L/min before phenylephrine (Fig. 3B), and the mean percent error of CO_NXF versus CO_ED was 33.0%.

![Fig. 2](image-url) The effect of systemic vascular resistance (SVR) on the bias between cardiac output (CO) measured by Nexfin and by esophageal Doppler. CO_ED = cardiac output as assessed by esophageal Doppler; CO_NXF = cardiac output as assessed by Nexfin.
3.1.3. After phenylephrine injection

When the 33 pairs of data obtained after phenylephrine injection were analyzed, mean \( \text{CONXF} \) was 5.0 ± 1.7 L/min and mean \( \text{COED} \) was 3.9 ± 1.3 L/min \((P < 0.001)\). There was a significant relationship between \( \text{COED} \) and \( \text{CONXF} \) \((n = 33; r^2 = 0.80; P = 0.0002)\) (Fig. 4A). The agreement between \( \text{CONXF} \) and \( \text{COED} \) was 1.05 ± 0.88 L/min after phenylephrine (Fig. 4B), and the mean percent error of \( \text{CONXF} \) versus \( \text{COED} \) was 42.5% after phenylephrine.

3.2. Impact of phenylephrine on \( \text{COED} \) and \( \text{CONXF} \)

Hemodynamic parameters are reported in Table 1. Phenylephrine induced a significant decrease in both \( \text{CONXF} \) and \( \text{COED} \) (from 6.2 ± 2.2 to 5.0 ± 1.7 L/min; \( P < 0.001 \); and from 5.4 ± 1.7 to 3.9 ± 1.3 L/min; \( P < 0.001 \); respectively). The changes in \( \text{CONXF} \) and \( \text{COED} \) were -1.2 ± 0.8 L/min and -1.5 ± 0.7 L/min \((P = 0.004)\) after phenylephrine injection, respectively (Table 2). The difference between changes in \( \text{CONXF} \) and \( \text{COED} \) was -0.3 ± -0.1 L/min. The changes in \( \text{CONXF} \) correlated well with those of \( \text{COED} \) \((r^2 = 0.55; P < 0.001)\).

A 93.8% concordance was found between changes in \( \text{COED} \) and \( \text{CONXF} \) after phenylephrine administration in 33 pairs, while a 100% concordance was observed in 26 pairs when the exclusion zone was 15% (Fig. 5). We also created a polar plot, as described by Critchley et al [21], which more accurately describes trending ability (Fig. 6). This approach also showed strong agreement between the two devices.

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**Fig. 3** Cardiac outputs (COs) measured by esophageal Doppler and Nexfin before intravenous bolus phenylephrine. A. Regression analysis. B. Agreement between COs measured by esophageal Doppler and Nexfin based on Bland Altman analysis [mean (2SD)]. \( \text{COED} \) = cardiac output as assessed by esophageal Doppler; \( \text{CONXF} \) = cardiac output as assessed by Nexfin.

**Fig. 4** Cardiac outputs (COs) measured by esophageal Doppler and Nexfin after intravenous bolus phenylephrine. A. Regression analysis. B. Agreement between COs measured by esophageal Doppler and Nexfin based on Bland Altman analysis [mean (2SD)]. \( \text{COED} \) = cardiac output as assessed by esophageal Doppler; \( \text{CONXF} \) = cardiac output as assessed by Nexfin.
We observed no side effects related to use of the device (ie, discolored or cold fingers) during application of the finger cuff, indicating that the Nexfin system was safe to use.

4. Discussion

This study is the first to evaluate the accuracy and tracking abilities of CONXF during surgery and to show clinically acceptable agreement and strong tracking abilities for CO measurements between the Nexfin and esophageal Doppler after phenylephrine administration. These data suggest that the Nexfin device was not impacted by changes in vasomotor tone (direct result of phenylephrine administration).

Cardiac output monitoring is of major importance during surgery; recent studies suggest that CO optimization improves patient outcome [1,2]. However, CO monitoring is challenging from a technological standpoint and several different techniques have been proposed during the last decade [5,6]. Apart from the difficulty in reliably measuring flow, evaluation of new CO monitors still remains controversial [21,30-33]. The methodology used to evaluate the accuracy and trending abilities of a new monitor is still not standardized and the questions of an accepted gold standard and statistics are still debated [21,30].

In the present study, we used the esophageal Doppler for comparison to evaluate the effectiveness of the Nexfin device. We were not the first to choose this device as an acceptable surrogate for invasive measurements of CO trending. Several authors have already used the esophageal Doppler in studies evaluating the accuracy of a new CO monitor [20,21] and in evaluating fluid responsiveness [22,34]. The main advantage of this device is that it is a

### Table 1  Hemodynamic changes after intravenous phenylephrine bolus administration

<table>
<thead>
<tr>
<th>Phenylephrine</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre (n = 33)</td>
<td>Post (n = 33)</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>70 (12)</td>
</tr>
<tr>
<td>SAPART (mmHg)</td>
<td>79 (12)</td>
</tr>
<tr>
<td>SAPNXF (mmHg)</td>
<td>82 (10)*</td>
</tr>
<tr>
<td>DAPART (mmHg)</td>
<td>55 (13)</td>
</tr>
<tr>
<td>DAPNXF (mmHg)</td>
<td>61 (12)*</td>
</tr>
<tr>
<td>MAPART (mmHg)</td>
<td>63 (10)</td>
</tr>
<tr>
<td>MAPNXF (mmHg)</td>
<td>67 (11)*</td>
</tr>
<tr>
<td>SpO2 (%)</td>
<td>99 (1)</td>
</tr>
</tbody>
</table>

Data are means (SD).

HR = heart rate, SAPART = systolic arterial pressure from invasive arterial pressure, DAPART = diastolic arterial pressure from invasive arterial pressure, MAPART = mean arterial pressure from invasive arterial pressure, SAPNXF = systolic arterial pressure from Nexfin, DAPNXF = diastolic arterial pressure from Nexfin, MAPNXF = mean arterial pressure from Nexfin.

* P < 0.05 vs. invasive arterial pressure.

### Table 2  Cardiac output (CO) measurement comparison of the Nexfin and esophageal Doppler

<table>
<thead>
<tr>
<th>CO (L/min)</th>
<th>P-value</th>
<th>SV (mL)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ED</td>
<td>NXF</td>
<td></td>
</tr>
<tr>
<td>Pre&amp;post-phenylephrine (n = 66)</td>
<td>4.7 (1.8)</td>
<td>5.6 (2.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Pre-phenylephrine (n = 33)</td>
<td>5.4 (1.7)</td>
<td>6.2 (2.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Post-phenylephrine (n = 33)</td>
<td>3.9 (1.3)</td>
<td>5.0 (1.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Difference (Post-Pro) (n = 33)</td>
<td>-1.5 (0.7)</td>
<td>-1.2 (0.8)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Data are means (SD).

Pre&post-phenylephrine = sum of before and after intravenous (IV) bolus of 100 μg of phenylephrine; Pre-phenylephrine = before IV bolus of 100 μg of phenylephrine; Post-phenylephrine = after IV bolus of 100 μg of phenylephrine; Difference (Post-Pro) = changes after IV bolus of 100 μg of phenylephrine; SV = stroke volume; ED = esophageal Doppler, NXF = Nexfin.
beat-to-beat monitor and is useful for conducting goal-directed therapy in patients undergoing surgery [18,19]. We acknowledge that intermittent thermodilution is still considered one of the reference methods but, as suggested in a recently published study by Critchley et al, esophageal Doppler “can be used as trend monitors and rapidly detect changes in CO, making it useful for monitoring therapeutic interventions.” [21].

We used a classical analysis including Bland-Altman analysis [29] and the Critchley and Critchley method (mean percent error) [30] for assessing the accuracy of the Nexfin. Our results were in accordance with previously published studies on this topic. We observed a lower mean percent error (37% vs 58%) than a previous study comparing another invasive and uncalibrated pulse contour analysis device with the esophageal Doppler [20]. Peyton et al recently published a metaanalysis assessing the accuracy of several CO monitors compared with thermodilution and found that most clinically accepted CO monitors present with a mean percent error of between 41% and 45% [35]. This analysis questioned the relevance of the 30% threshold described by Critchley and Critchley [30]. For evaluating the trending ability, we used the 4-quadrant plot recently described by Critchley et al [21]. One of the most interesting findings of our study was that phenylephrine (a pure $\alpha_1$ vasoressor) induced similar decreases in $CO_{NXX}$ and $CO_{ED}$, as shown by the very strong concordance between both devices. It has become increasingly evident that phenylephrine administration induces an afterload dependent decrease in CO [36]. By increasing left ventricular afterload, phenylephrine, a pure vasoconstrictor, decreases left ventricular SV. On the other hand, in some cases phenylephrine may increase venous return by inducing a constraint on venous pool. In the present study, phenylephrine induced a decrease in SV in most cases. However, this decrease was not identical in all patients. The information observed here is of importance since such vaspressors strongly impact the accuracy of several calibrated and uncalibrated pulse contour analysis devices [12-14,37]. This observation may be explained by technological differences between pulse contour analysis from the arterial pressure waveform (which relies on a pure pressure signal) and Nexfin technology (which relies in part on light absorption and thus on a volume signal) [38]. This has been shown and discussed in an extensive review article by Reisner et al, focusing on the potential applications of the plethysmograph for arterial pressure and CO monitoring [38].

Phenylephrine induces vasoconstriction and thus decreases the volume of blood in the periphery. As the Nexfin device relies on light absorption, it interprets this increase in resistance (inducing a decrease in blood volume) as a decrease in CO. This would suggest that this device is more accurate than pulse contour analysis devices based on arterial pressure in this setting. However, further studies are required to answer this question and to assess the accuracy of the Nexfin device in more challenging situations such as in high-risk surgery, ICU, or vasculopathic patients.

Finally, recent work has determined that assessing the trending ability of a CO monitor may be clinically more relevant than assessing the accuracy itself. This is especially true if these monitors are meant to be used for CO optimization and goal-directed fluid management [35].

### 4.1. Study limitations

We did not compare the Nexfin with thermodilution using the pulmonary artery catheter. One of our goals was to assess acute changes in CO induced by phenylephrine boluses, and thermodilution cannot assess beat-to-beat changes (the technology requires averaging over several cycles); we chose to use the esophageal Doppler as a reference. This method was used previously to assess the accuracy of CO monitoring devices [20], and it improves patient outcome when it is used for goal-directed hemodynamic optimization [1,39]. The esophageal Doppler does not allow for aortic diameter measurement. The inability to measure aortic diameter may theoretically impair the esophageal Doppler’s ability to accurately track CO changes induced by volume expansion [40] or vasopressor administration. Finally, vasoconstriction may potentially affect the accuracy of the esophageal Doppler due to its impact on aortic diameter. Future studies are warranted to address these concerns.

### 4.2. Conclusion

Cardiac output measurement by the Nexfin device appears promising during general anesthesia. This device
has potential clinical applications for CO monitoring during surgery.

Acknowledgment

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References


