technical report

Technology report: ccNexfin monitor

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DISCLOSURE:
W. Wesseling is employed by BMEYE / Edwards Lifesciences

The ccNexfin monitor is a noninvasive device permitting beat-to-beat monitoring of blood pressure and flow, cardiac function and fluid dynamics. Whereas continuous or advanced hemodynamic monitoring is normally restricted to a small selection of (major) surgical procedures, this new technology offers the chance of using its advantages in our whole patient population in a beneficially fast and noninvasive fashion.
During routine anesthesia practice, blood pressure and heart rate normally are the main variables used to assess the patient's hemodynamic condition. Continuous and precise assessment of blood pressure via an arterial line is always most desirable, however this is only used in a minority of cases because of its invasive and laborious nature and costs. In addition, while blood pressure and heart rate may provide a satisfying picture of the patient's hemodynamic condition, it gives an inaccurate reflection of blood flow, tissue oxygenation and fluid balance. In particular, the use of sympathomimetic drugs often restores blood pressure at the expense of blood flow and tissue oxygenation, while hypovolemia/blood loss only induce changes in blood pressure or heart rate after major deficits due to compensatory sympathoadrenergic stimulation/centralization [1]. In both cases, blood pressure and heart rate poorly reflect tissue perfusion and oxygenation. For decades now, we have the clinical availability of advanced hemodynamic monitoring that can provide beat-to-beat information on flow- and volume related variables such as stroke volume, cardiac output, fluid responsiveness and preload status, but the invasiveness of most of these techniques restricts their use to major surgery and/or high risk patients and in addition may be the cause of important iatrogenous morbidity.
Growing evidence supports the importance of goal directed fluid therapy [2] and meticulous blood pressure management. This endorses the importance of beat-to-beat monitoring to allow fast intervention in case of swift hemodynamic changes, together with the use of dynamic preload variables to guide fluid management and preserve euvolemia [3]. While monitoring of these variables until recently required invasive methods and/or specific skills including a considerable learning curve, new technological advancements such as ccNexfin permit noninvasive beat-to-beat assessment of blood pressure, blood flow, cardiac function and fluid responsiveness in a very intuitive fashion.

Technological background

In the ccNexfin monitor, two advanced technologies work in concert to measure and calculate the variables of interest to the clinician. Using the volume clamp method the arterial pressure waveform is measured, and secondly advanced pulse-contour analysis algorithms calculate stroke volume (and thus cardiac output). These variables also allow computation of dynamic preload variables.

Volume clamp method

The principle of volume clamping was invented by the Czech physiologist Jan Peňáz and further developed by Wesseling in the 1980s resulting in the commercially available Finapres™ device [4]. Because accurate measurements strongly rely on fast and accurate sensors, micro-mechanical technology, and computer power, recently an even more reliable device has been developed that better complies with clinical requirements. The first next generation device, the Nexfin monitor is commercially available since 2007.

A disposable cuff with an integrated photo-plethysmograph is placed around one finger. When light is emitted through the finger, the infrared absorption fluctuates with the cardiac cycle, with higher absorption during systole. The resulting absorption curve (=plethysmogram) can be appreciated as a measure for arterial blood volume in the finger. The essence of the volume clamp method is to dynamically provide equal pressures on either side of the wall of the artery by clamping the artery to a certain constant volume. As a first calibration step, the cuff is automatically inflated and the device searches for the optimal cuff pressure for reliable measurement. This is the level of 'vascular unloading': within this small pressure range, there is no transmural pressure gradient over the vessel wall. This is accomplished by the 'Physiocal®' algorithm, developed by Wesseling et al.[4] At that moment, the pressure in the cuff is close to the mean arterial pressure (MAP). Then,

Figure 1 A disposable cuff with integrated photo-plethysmograph is placed around one finger. Three different dimensions of cuff exist to fit fingers from small to (very) large adults.

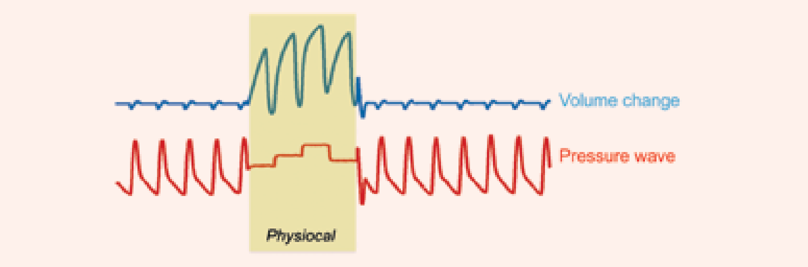

Figure 2 Continuous adaptation of the cuff pressure results in an apparent flat-line plethysmogram. The pressure in the cuff then reflects intra-arterial pressure. Periodic Physiocal recalibration allows accurate tracking of significant changes in vascular physiological states.

the diameter of the finger artery under the cuff is 'clamped' at that level, i.e. it is kept at a constant diameter in the presence of changes of arterial pressure during a cardiac cycle. To accomplish this, the light absorption is measured by the plethysmograph and the pressure in the cuff is adapted at a rate of 1000 Hertz, to apply the exact counter pressure in the cuff to prevent volume change. This in turn results in a constant infrared absorption (an apparent flat line plethysmogram, see Figure 2). When this is accomplished, the continuously varying pressure in the cuff equals the intra-arterial pressure wave.

The unloaded volume of an artery is not constant, however, and changes with arterial wall smooth muscle stress and tone. Therefore the Physiocal® analysis (see Figure 2) is automatically performed recurrently, to follow changing physiological states of the vasculature and keep the artery at its 'unloaded' volume.

At this stage, the device has acquired the arterial pressure waveform at the finger. A reliable waveform transformation is then applied to reconstruct the arterial pressure wave at the brachial level [6] (see Figure 3), since that is the clinical standard for noninvasive blood pressure measurement, which is usually performed with a cuff around the upper arm. When the hand is not at the heart level, an additional small 'heart reference system' is located at the level of the finger and the heart to compensate for the hydrostatic pressure difference.

Cardiac output modeling

In order to determine beat-to-beat stroke volume from the arterial pressure waveform, a pulse contour analysis is performed. The fundamental principle of this calculation is based on determination of the area below the systolic part of the arterial pressure curve and a three-element Windkessel model to determine cardiac afterload.
The physiologically three distinct elements that govern the relationship between pressure and flow can succinctly be explained as:

1. The inertia of the blood (Z). It takes energy to accelerate the blood during systole, and the accumulated kinetic energy keeps the blood flowing during diastole.
2. The compliance of aorta and large arteries (C). During systole, the stroke volume is ejected in the elastic arterial system, which expands and "accepts" part of the blood volume, reducing the systolic pressure peak. This 'stored energy and volume' is released during diastole, sustaining diastolic pressure and flow.
3. Peripheral vascular resistance (R), representing the resistance to outflow of blood to all vascular beds.

During ejection into the blood-filled proximal aorta, the left heart encounters the combined effects of the proximal aortic compliance and its blood mass, or inertance. This combined effect is called the characteristic impedance. Inertance increases the resistance to ejection while compliance facilitates ejection.
For easy comprehension, these three elements can be depicted by their electronic equivalents (see Figure 4). While Z and C can vary moderately for a given patient, R varies greatly with changing physiological states.

Wesseling et al. [7] developed a working algorithm to derive cardiac output from the arterial pressure curve using the three-element Windkessel model. The characteristic impedance (Z) and total arterial compliance (C) are given as nonlinear functions of pressure based on gender, age, body length and weight. An initial value for peripheral resistance is calculated based on these characteristics. Stroke volume (SV) is then calculated from the arterial pressure curve (see Figure 5) and the estimated afterload. Cardiac output (CO) is derived as SV x HR and total peripheral resistance (TPR) is calculated as MAP/CO. This resistance value

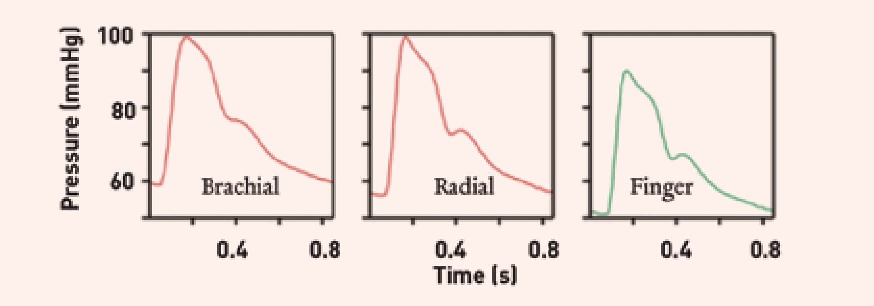

Figure 3 Pressure waves along arterial tree.

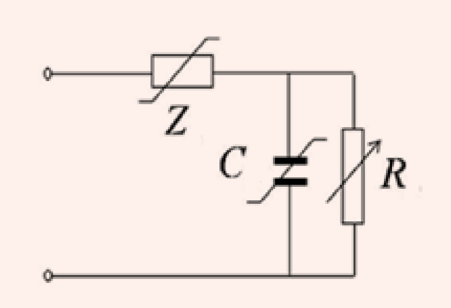

Figure 4 Electronic equivalence of the three-element windkessel model.

is inserted again in the three-element windkessel and SV for the next beat is calculated based on this new TPR. After a few beats, convergence is obtained and the true resistance is found: MAP/TPR = CO. The non-linear behavior of the compliance and characteristic impedance combined with the adaptive peripheral resistance assure excellent tracking afterload and therefore of cardiac output [8, 9].

Dynamic preload variables

At this stage, beat-to-beat systolic, mean and diastolic blood pressures are determined, as well as stroke volume, cardiac output and total peripheral resistance. These variables yet have a poor ability to predict fluid responsiveness as a prerequisite for guiding fluid therapy. Since central venous pressure, blood pressure or heart rate have failed to predict fluid responsiveness, the availability of a simple variable that can fairly well predict how a patient will respond to fluid administration is profoundly appealing. The Frank-Starling law of the heart (see Figure 6) describes the relation between stroke volume and filling and can be used to maximize stroke volume of an individual by achieving an 'optimal cardiac preload'. Although this 'optimal preload' corresponds with a certain central venous pressure (or PCWP for the left heart) for a given patient, its numerical value depends on several unpredictable variables (such as diastolic function) and therefore lacks any predictive value [10].

Importantly, however, intrathoracic pressure variations induced by positive pressure ventilation affect the end-diastolic volume in a predictable manner. Figure 6 illustrates that the changes in stroke volume associated with ventilation-induced changes in preload are predictably determined by the position of the heart on the Frank-Starling relationship. As a consequence, the degree of variation in stroke volume throughout the ventilatory cycle can reliably determine the position of the heart on its particular Frank-Starling relationship and can therefore predict fluid responsiveness of the individual patient. Although some limitations exist on the use of this principle (such as positive pressure ventilation in a volume-controlled matter and with sufficient tidal volume, regular heart rhythm, and acceptable lung compliance), the use of a dynamic preload variable can be very advantageous to optimise fluid management in most ventilated patients. The ccNexfin monitor calculates stroke volume variation (SVV) and pulse pressure variation (PPV) continuously as the relative variation over a 15 second period: $SVV = (SV_{max} - SV_{min}) / SV_{average}$; $PPV = (PP_{max} - PP_{min}) / PP_{average}$. This averaging window is moved every 5 seconds and the values displayed on the monitor represent a 1-minute average. Depending on the specific comorbidity and nature of the surgical procedure, the anesthetist will have to decide what position on the Frank-Starling relationship is most beneficial for this specific patient – in most cases between 5 and 15% PPV or SVV. After this clinical decision is made, SVV or PPV can facilitate optimal fluid administration to reach this goal.

Reliability of the Nexfin monitor

Both ccNexfin blood pressure and cardiac output have been validated against various reference methods. Recent studies comparing Nexfin against auscultatory blood pressure measurement [11] or invasive radial artery measurement [12] demonstrated excellent correlations and good within-subject precision over wide ranges of pressures. In addition, bias and precision were within AAMI criteria [13] in a variety of hemodynamic states. The main limitation of the Nexfin is that adequate flow in the finger is imperative. In general however, relative changes in blood pressure had been considered reliable even in the earlier devices [14]. A validation study of the Nexfin CO in septic shock patients showed poor results, most likely because of compromised peripheral flow [15]. In non-septic patients, the accuracy of cardiac output measurement by ccNexfin was compared to a thermodilution reference and shown to be a "reliable method of measuring cardiac output during and after cardiac surgery" [16]. Other studies comparing Nexfin CO measurements with those obtained by echo Doppler [17] or by inert gas-rebreathing [18] showed good correlations. Correspondingly, assessment of cardiac output with Nexfin is not considered completely accurate, particularly in critically ill patients, and therefore more invasive techniques may be more appropriate in these cases. A recent study [19] comparing Nexfin CO with transesophageal doppler showed a strong correlation and excellent tracking of changes in CO after phenylephrine administration. Others concluded that Nexfin is a reliable method to measure CO during cardiac surgery [16]. In a recent study [20], we evaluated the ability of SVV to predict effective changes in cardiac output and blood pressure after administration of a fluid load of 500 ml, and demonstrated that the Nexfin can reliably predict to what degree there will be an increase of these variables in a heterogeneous patient population.

Use of the Nexfin monitor in daily practice

The Nexfin monitor permits completely noninvasive continuous monitoring of hemodynamics in a large patient population, which is comparatively poorly monitored as of yet. In addition, in some patients conventional NIBP may be impossible (burns, dialysis patients with shunts, fractures, ...). While in obese patients measurement of conventional noninvasive blood pressure by arm cuff may be difficult or unreliable, the Nexfin may be a good alternative since fingers usually do not fatten up so that the finger cuff still fits.

Compared to invasive blood pressure measurement, the Nexfin monitor has obviously less accuracy, so that in critical patients it should not be considered a sound alternative until more research has been done. In our own evaluation [21] we demonstrated an accuracy of ±10 mmHg in 90% of the patients. This accuracy moreover was significantly better than conventional non-invasive blood pressure measurement by arm cuff so that, in addition to the obvious advantage of continuous measurement, the Nexfin could serve a superior alternative for noninvasive blood pressure recording. This is in agreement with a recent study showing that continuous blood pressure monitoring obtained by Nexfin allows for shorter delay in response to perioperative hypotension in comparison to conventional intermittent NIBP measurements [22].

Therefore Nexfin provides superior blood pressure monitoring compared to conventional NIBP, even if the more advanced hemodynamic information is not considered. Whether this will positively impact patient outcome is yet to be proven, but this may be expected.

Likewise, in our experience the accuracy of stroke volume and systemic vascular resistance is definitely appropriate to assist decision-making and optimise hemodynamic and fluid management. More importantly, while absolute values of these variables may sometimes deviate significantly from actual numbers, the high reliability of relative changes in response to interventions or events provides essential information to refine hemodynamic and fluid management.

There are some limitations for the use of the Nexfin monitor. Most importantly, any circumstances that severely reduce the blood flow in the fingers decreases the reliability of Nexfin, as in septic patients or patients receiving very high doses of vasoconstricting agents. But also low temperature of the hands is in our experience a common reason for unreliable measurements.

The proprietary algorithms however can detect unreliable signal quality, and will try to recalibrate the system in such events. Generally, an interval between Physiocal calibrations of more than 30 beats is an accepted indicator for reliable measurement [4].

After initiation of measurements, frequent recalibration is necessary until stable values are found. Pressure and flow values are typically available within approximately 1 min after starting the measurement, and SVV and PPV 1 minute thereafter. In patients with rather cold hands, the Nexfin often fails to obtain measurements while awake, but a few minutes after induction of anesthesia and subsequent arterial vasodilation, reliable data become available. Keeping patients warm in the preoperative stage can prevent this difficulty, although this may not always be possible.

Nevertheless, in a very large majority of patients, reliable values are available within a mere seconds, which is even faster than conventional NIBP. Just like any anesthetist intuitively feels with other variables such as SpO_2 or end-tidal CO_2 where some clinical experience must be gained to visually appreciate the waveforms and assess the reliability of the numerical values, this is also true for the Nexfin monitor, where the waveform representation permits a straightforward approach to evaluate sensor reliability.

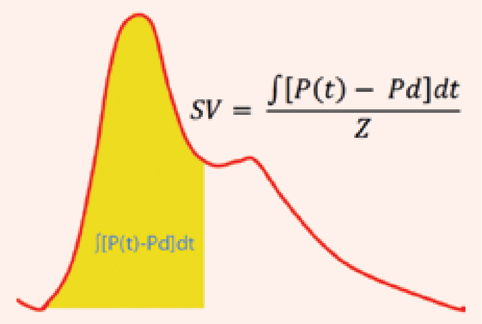

Figure 5 The parameters of the three-element windkessel model are calculated from demographic data and the reconstructed arterial pressure waveform: SV is a function of Z and the pressure-time integral of the systolic pressure wave (yellow area).

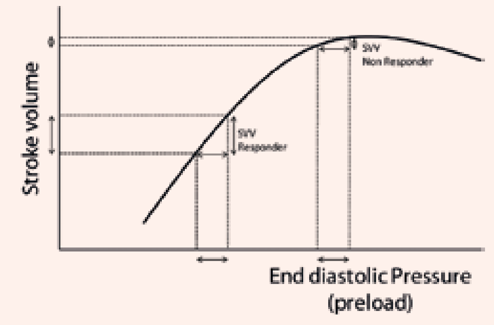

Figure 6 Ventilation-induced oscillation in preload result in a variable oscillation of stroke volume. These stroke volume variations (SVV) reliably reflect the position of the heart on the Frank-Starling relationship (A).

History and future

The Nexfin monitor is based on Dutch technology, first developed within a TNO (Nederlandse Organisatie voor toegepast natuurwetenschappelijk onderzoek) project to monitor astronauts, then further commercialized by BMEYE (Amsterdam). In 2012, Edwards Lifesciences acquired BMEYE and the technology will be further developed and commercialized by Edwards. The design of the ccNexfin monitor will remain unchanged for the time being, while probably in 2014 a Nexfin-module will become available for the EV1000 monitor platform of Edwards. In addition to reusable finger cuffs, disposable cuffs will become available soon. Besides, we believe that any additional electronic device in an already overcrowded operating theatre restricts its convenient use, hence a modular device to fit in the existing anesthesia monitors would be of significant practical advantage and even essential to establish universal implementation.

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