WHITE PAPER

Evidence-Based Summary: The Demonstrated Clinical Efficacy of the PulseCO™ Algorithm in Assessing and Managing Hemodynamic Status and Changes

INTRODUCTION

The PulseCO Autocorrelation Algorithm (LiDCO Ltd., London, UK) is a clinically proven in-vivo patient monitoring technology that calculates continuous beat-to-beat cardiac output (CO), stroke volume (SV), stroke volume variation (SVV), and pulse pressure variation (PPV) by analyzing an arterial blood pressure waveform. The PulseCO algorithm transforms the arterial waveform from pressure to a volume equivalent by correcting for compliance and aortic volume.[1] The algorithm, which has been used in the clinical management of critical care patients since 2001, overcomes the well-documented limitations of other pressure-based hemodynamic monitoring technologies that are caused by variations in arterial reflected wave resistance changes that can occur in peripheral arteries.

The PulseCO algorithm has been clinically proven to be the most reliable arterial pressure-based method for the hemodynamic assessment and management of critically ill patients.

Specific hemodynamic parameters measured and calculated by the PulseCO algorithm include:

- Mean Arterial Pressure
- Cardiac Output
- Cardiac Index
- Heart Rate Variability
- Stroke Volume
- Stroke Volume Index
- Stroke Volume Variation
- Pulse Pressure Variation
- Systolic Pressure Variation
- Systemic Vascular Resistance
- Systemic Vascular Resistance Index

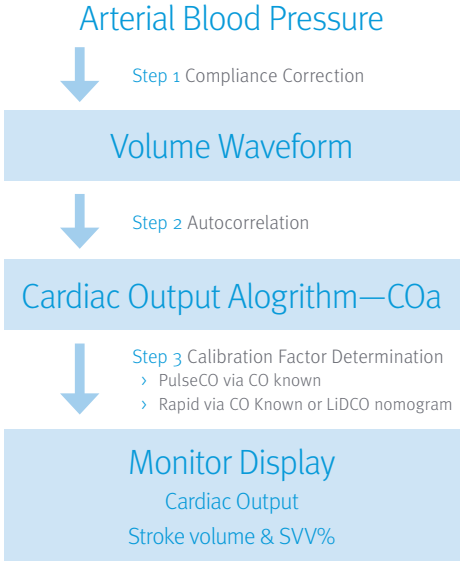
PulseCO PRESSURE WAVEFORM ANALYSIS METHODOLOGY

The PulseCO algorithm is commercially deployed in three separate patient monitoring platforms: LiDCO*plus* and LiDCO*rapid* (LiDCO Ltd., London, UK), and the Cogent™ 2-in-1 hemodynamic monitoring system (ICU Medical Inc., San Clemente, CA). These monitoring platforms use identical implementations of the algorithm and deliver equivalent measurements.

In each implementation, pre calibration cardiac output (COa) is made more accurate by scaling with a calibration factor (CF). This calibration is performed when the known cardiac output (COk) is entered into the monitor or when a nomogram is used to calculate the CF based on the patient's age, height, and weight (see Figure 1).

The PulseCO algorithm has been clinically proven to be the most reliable arterial pressure-based method for the hemodynamic assessment and management of critically ill patients. This method provides a minimally invasive alternative to the long-held gold standard for monitoring CO—thermodilution via pulmonary artery catheterization (PAC)—which is an invasive technique associated with significant risk of complications.[2-7]

FIGURE 1. PRE CALIBRATION CARDIAC OUTPUT (COa) USING THE PulseCO AUTOCORRELATION ALOGRITHM.



The core software code of the PulseCO algorithm has remained consistent since its launch, meaning that the amassed clinical evidence supporting the algorithm's efficacy—more than 100 papers and published abstracts—is comparable and applicable to all monitoring platforms commercially available today.

CLINICAL VALIDATION AND DOCUMENTED USE CASES

The PulseCO algorithm has been proven to detect changes in CO from arterial pressure in a wide range of challenging clinical settings, including general surgical patients, high cardiac outputs, hyper-dynamic liver transplantation patients, off-pump cardiac surgery, post-operative care, pre-eclampsia, congestive heart failure, general intensive care, and the cardiac catheterization lab.[8-21] The PulseCO algorithm has also demonstrated sufficient precision to follow CO changes without recalibration and is equivalent in precision to the conventional bolus thermodilution.[22] In a study comparing PulseCO-derived SV to left ventricular (LV) SV measured by an aortic flow probe, PulseCO was shown to accurately assess steady state and dynamic changes in LV SV during open chest cardiac surgery. This study also indicated that PulseCO is the only arterial-based cardiac output algorithm for which its accuracy has been quantified with a calibrated aortic flow probe.[23]

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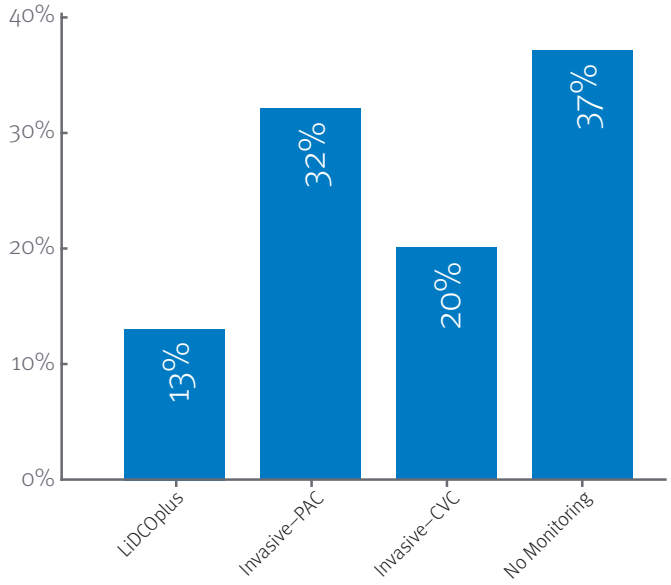
PulseCO-derived preload responsiveness parameters (SVV, PPV, and SPV) have been shown to be accurate predictors of fluid responsiveness in post operative sedated and ventilated intensive care patients. In a study of 31 fully sedated and mechanically ventilated patients, dynamic parameters, including SVV, PPV, and SPV, were compared to static parameters, including HR, MAP, and CVP.[24] Analysis showed that the PulseCO-derived dynamic parameters were better predicators of fluid responsiveness than the static parameters in this patient population.

In a study of 50 morbidly obese patients undergoing laparoscopic bariatric surgery, PulseCO-derived SVV was used as a guide to help limit excessive fluid administration.[25] This SVV-guided intraoperative fluid optimization proved to help clinicians maintain hemodynamic parameters (CO, SV, and heart rate) within 10% of the preoperative control level.

An additional study examining the accuracy of PulseCO-derived SVV in predicting fluid responsiveness in morbidly obese patients showed that sensitivity and specificity for SVV percent (100% and 75%) and PPV percent (100% and 85%) were similar and acceptable.[26] Results of the study indicate that PulseCO-derived SVV is an accurate predictor of fluid responsiveness in morbidly obese patients.

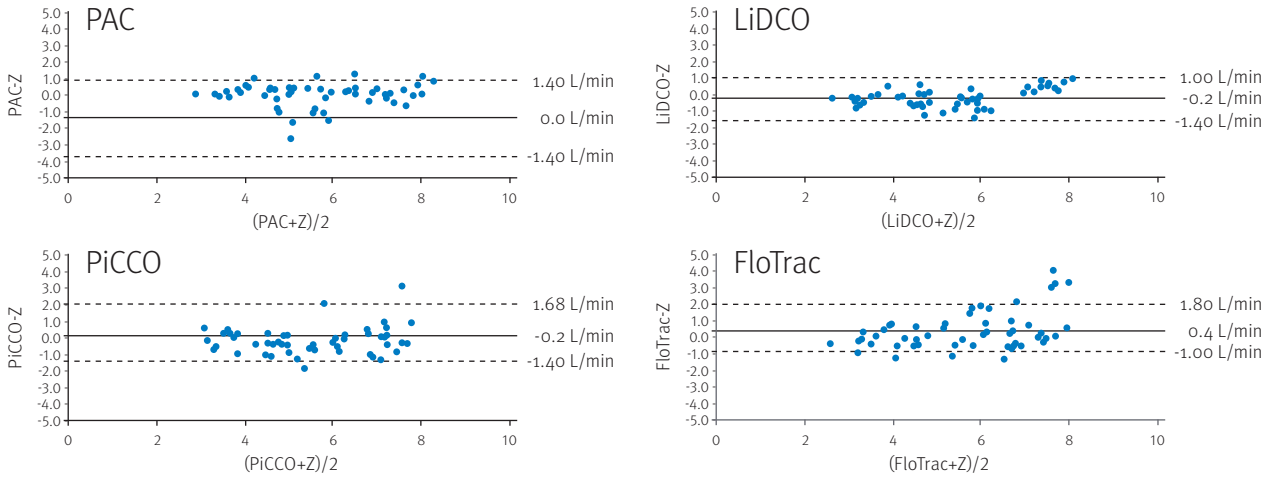
Another study comparing the effectiveness of LiDCO*plus* PulseCO minimally invasive hemodynamic monitoring to both invasive monitoring (CVC or PAC) and no hemodynamic monitoring at all showed that monitoring patients with LiDCO*plus* significantly reduces the mortality rate in patients treated for shock (see Figure 2).[27] In this evaluation of 237 shock patients, the mortality rate of the LiDCO*plus*-monitored group was observed to be 13%, compared to 32% and 20% in the invasively monitored group, and 37% in the unmonitored group. Results of this study confirm the effectiveness of arterial waveform CO assessment compared to conventional patient-management techniques.

FIGURE 2. COMPARISON OF OBSERVED MORTALITY RATES ASSOCIATED WITH MULTIPLE MONITORING METHODS.[27]



One analysis of the effects of phenylephrine administration on changes in vascular tone compared CO measurements from a bioimpedance system to CO measurements from LiDCO*plus*. Data from the study showed that dynamic trending CO values from LiDCO*plus* are of greater use than absolute bioimpedance values when managing patients with rapid changes in vascular tone, specifically in obstetric anesthesia and critically ill obstetric patients.[28]

FIGURE 3. SIDE-BY-SIDE COMPARISONS WITH OTHER TECHNOLOGIES.[22]



Bland-Altman analysis of each device against the mean of all devices across all patients, wherein pulmonary arterial catheter (PAC) thermodilution CO (COtd) and continuous CO (CCO) are pooled to be one variable (Z-statistic). The results show that LiDCO and PAC have greater agreement with pooled CO data (Z-statistic) than do either PiCCO *plus* or FloTrac.

SIDE-BY-SIDE COMPARISON WITH OTHER TECHNOLOGIES

One study comparing the accuracy, bias, and trending ability of LiDCO, PiCCO *plus*® (Pulsion Ltd, Munich, Germany), and FloTrac™ (Edwards Lifesciences Corporation, Irvine, CA) found that CO values derived from LiDCO*plus* have a greater agreement with PAC-derived CO than do either PiCCO *plus* or FloTrac with PAC.[22] The limits of agreements between LiDCO*plus* and PAC also fell within the boundaries of the Critchley-Critchley criteria, or generally accepted limits for cardiac output validation.[29] In contrast, agreement between PiCCO or FloTrac and PAC exceeded the Critchley-Critchley criteria.

Detecting blood loss and preventing hypovolemia is an essential element of critical patient care and an important consideration for minimizing postoperative complications. One study comparing the ability of four minimally invasive CO monitoring devices to detect significant changes in blood volume showed that LiDCO*rapid* was the most effective at identifying early signs of blood loss. This study compared the Vigileo® FloTrac, LiDCO*rapid*, USCOM 1A, and the CardioQ™ (Deltex Medical, Chichester, West Sussex, UK) esophageal Doppler and found that LiDCO*rapid* detected a statistically significant difference in blood volume after only 2.5% of blood loss, compared to 7.5% with USCOM, and 12.5% with both CardioQ and FloTrac.[30]

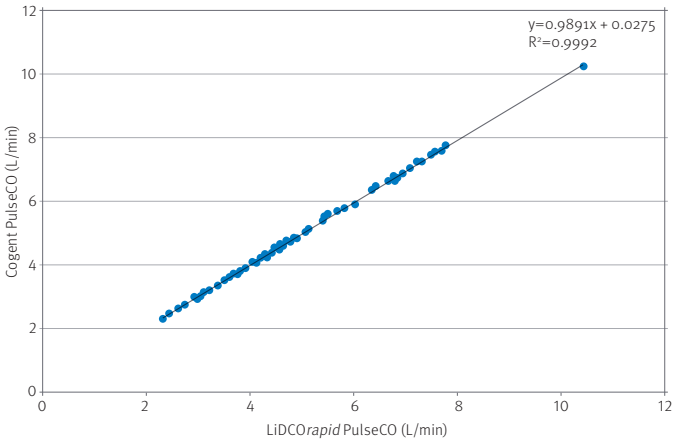
> Data from validation testing shows that the Cogent system, which integrates the proven LiDCO PulseCO algorithm, provides accuracy that meets or exceeds LiDCO's published performance specifications.[31]

TESTED ACCURACY OF THE COGENT HEMODYNAMIC MONITORING SYSTEM

Data from validation testing shows that the Cogent system, which integrates LiDCO's proven PulseCO algorithm, provides accuracy that meets or exceeds LiDCO's published performance specifications.[31] This validation testing consisted of bench testing performed with three Cogent units and one LiDCO*rapid* unit using both simulated pressure waveforms and previously recorded human clinical pressure waveforms. The accuracy and repeatability of CCO values between the Cogent systems and the LiDCO*rapid* system were then compared and analyzed.

The Cogent PulseCO algorithm implementation met a repeatability acceptance criterion of a coefficient of variation (CV) of less than or equal to 6% or 0.1 L/min. A linear regression of the Cogent PulseCO CCO values against the LiDCO*rapid* PulseCO CCO values from testing with human clinical pressure waveforms exhibited a correlation coefficient close to 0.9992, indicating an excellent agreement between the Cogent and LiDCO*rapid* PulseCO CCO outputs (see Figure 4).[31] The results of this validation testing demonstrate that the Cogent system's integration of the PulseCO algorithm performs equivalently to the PulseCO algorithm in the LiDCO*rapid* predicate device.

FIGURE 4. COGENT VS. LIDCO*rapid* PulseCO VALUES: HUMAN CLINICAL PRESSURE DATA.[31]



CONCLUSION

Unchanged since its release in 2001, the PulseCO Autocorrelation Algorithm is the most extensively tested pressure-based method for minimally invasive CO, SV, SVV, and PPV monitoring. PulseCO has also been shown in extensive clinical studies to be more accurate than competing pressure-based technologies across a variety of dynamic, rapidly changing patient conditions. Available in LiDCO's own LiDCO*plus* and LiDCO*rapid* monitors, as well as ICU Medical's Cogent system, in which application of the algorithm has proven to be as accurate as the original LiDCO systems, PulseCO will continue to be a viable, less invasive alternative for accurate cardiac output monitoring.

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