Reprint from:
M.R. Pinsky, D. Payen (Eds.)
Functional Hemodynamic Monitoring
Update in Intensive Care and Emergency Medicine 42
pp 183–192

Arterial Pulse Power Analysis: The LiDCO^{TM}plus System

A. Rhodes and R. Sunderland

Springer

Arterial Pulse Power Analysis: The LiDCO^{TM}plus System

A. Rhodes and R. Sunderland

Introduction

The aims of hemodynamic monitoring are to provide a comprehensive overview of a patient's circulatory status in order to inform and direct clinicians as to diagnostic state, treatment strategies, and prognosis. The monitoring, therefore, needs to provide useful information at an appropriate time and with limited complications that could be directly attributed to the individual technique. Measurement of cardiac output or stroke volume has been regarded as a necessary facet of caring for critically ill patients, however until recently has been only possible with the use of the pulmonary artery catheter (PAC). With the current controversies regarding the use of the PAC, several new less invasive technologies have become available to provide similar information. This chapter focuses on the use of arterial pulse contour and power analysis as a technique to measure and monitor cardiac output or stroke volume and focuses on the technology introduced by the LiDCO company with their LiDCO^{TM}*plus* monitor.

Arterial Pulse Contour Analysis

Arterial pulse contour analysis is a technique of measuring and monitoring stroke volume on a beat-to-beat basis from the arterial pulse pressure waveform. This has several advantages over existing technologies, as the majority of critically ill patients already have arterial pressure traces transduced making the technique virtually non-invasive and able to monitor changes in stroke volume and cardiac output on an almost continuous basis.

History of Arterial Pulse Contour Analysis (Table 1)

The first direct measurement of arterial blood pressure was by the Reverend Stephen Hales in 1733. As early as 1899, the concept of using the blood pressure waveform to measure blood flow changes was first suggested by Otto Frank [2].

Otto Frank described the circulation in terms of a Windkessel model (Windkessel is the German word for air-chamber). The Windkessel model described the loads faced by the heart in pumping blood through the pulmonary or systemic

Table 1. History of pressure waveform analysis

1. Windkessel model of the circulation – Otto Frank, 1899 [1, 2]
2. First pulse pressure method – Erlanger and Hooker, 1904 – suggested that stroke volume is proportional to the pulse pressure (systolic – diastolic) [3]
3. Requirement for calibration of pulse pressure by an independent cardiac output measure was suggested by Wezler and Bogler in 1904 [21]
4. Pulse pressure simply corrected for arterial compliance was investigated by Liljestrand and Zander, 1927
5. Compliance of the human aorta documented first by Remington et al., 1948 [4]
6. Aortic systolic area based pulse contour method, Kouchoukos et al., 1970 [5]
7. Systolic area with correction factors (3 element Windkessel model), Wesseling and Jansen, 1993 [6, 7]
8. Compliance corrected pressure waveform 'net' pulse power approach – Band et al, 1996 [22]

circulations and the relationship between blood pressure and flow in the aorta or pulmonary arteries. This model likens the heart and systemic arterial system to a closed hydraulic circuit comprised of a water pump connected to a chamber. The circuit is filled with water except for a pocket of air in the chamber. As water is pumped into the chamber, the water both compresses the air in the pocket and pushes water back out of the chamber, back to the pump. The compressibility of air in the pocket simulates the elasticity and extensibility of the major arteries, as blood is pumped through them from the heart. This is commonly referred to as arterial compliance. The resistance that the water encounters whilst leaving the Windkessel and flowing back to the pump equates to the resistance to flow that blood encounters on its passage through the arterial tree. This is commonly referred to as peripheral resistance. This somewhat simplistic view of the circulation was referred to as the '2-element Windkessel model' and has helped us to understand the underlying physiology and, by solving the individual components of the model, to calculate flow. Frank's objective was to derive cardiac output from the aortic pressure. By measuring the pulse wave velocity over the aorta (carotid to femoral) the compliance could be estimated. Knowing the time constant from the diastolic aortic pressure decay and compliance, the peripheral resistance could then be derived. From mean pressure and resistance, using Ohm's law, mean flow could be calculated. This technique has been further refined in recent years to develop a 3 and 4 element Windkessel model. This has been used to define the systolic area under the pulse contour curve and thus help to estimate stroke volume.

In 1904, Erlanger and Hooker stated "Upon the amount of blood that is thrown out by the heart during systole then, does the magnitude of the pulse-pressure in the aorta depend" [3]. Although this is an intuitive statement, the translation of these observations into a robust system of measuring cardiac output has had to overcome a number of confounding problems that has led to the introduction of this technique only in the last few years.

Table 2. Lithium dilution cardiac output (CO) measurement validation studies

Author	Species	Validation	Mean	Range CO	Bias of CO	2 x SD	%Error of bias
Kurita [9]	Swine	PAC, EMF	1.5	0.2–2.8	0.1	0.36	24
Mason [10]	Dogs	PAC	3	1–13	0.1	0.9	30
Linton [11]	Horse	PAC	20*	12–42	–0.9	2.8	14
Corley [12]	Foals	PAC	13*	4–22	0.05	3.0	13
Garcia-Rodriguez [13]	Human	PAC	6*	3.5–9.5	–0.5	1.2	20
Linton [14]	Human	TPTD	2	0.4–6	–0.1	0.6	30
Linton [15]	Human	PAC	5 *	2.4–10.2	–0.2	0.9	18

PAC: pulmonary artery catheter; EMF: electromagnetic flow probes; TPTD: transpulmonary thermodilution; * is where the data for mean cardiac output are not readily available from the papers and have had to be estimated from the original data.

Following Otto Frank, attention turned to using the aortic /arterial pulse pressure to estimate the stroke volume. The concept centered around the theory that fluctuations in blood pressure (pulse height) around a mean value are caused by the volume of blood (the stroke volume) forced into the arterial conduit by each systole. However, a number of complicating factors were identified – first the requirement for calibration via an indicator dilution measurement. At that time this was by no means a trivial problem and remained so until the recent advent of transpulmonary indicator dilution techniques – such as the LiDCO lithium method. Second, and of equal importance is the correction of pulse pressure necessary due to the non-linear compliance of the arterial wall. Effectively this means that when stretched (through the input of a further volume of blood) at a higher blood pressure, the compliance of the aorta is less than at low blood pressures. It was not until 1948 [4], that there were accurate enough data from human aortas to attempt compliance correction of blood pressure data. So by the 1970s both compliance correction (to linearize the blood pressure data) and calibration via indicator dilution (green dye and thermal indicators) was possible. This led to the suggestion that one could move away from simplistic pulse pressure approaches to actually measuring the systolic area (to closure of the aortic valve) of the calibrated and compliance corrected waveform [5]. In essence, this approach is one based on integrating the area of the systolic part of the linear pressure/volume waveform. These approaches are generically referred to as Pulse Contour Methods [5–7].

Pulse Pressure Relationship to Stroke Volume

The fluctuations of blood pressure around a mean value are caused by the volume of blood (the stroke volume) forced into the arterial conduit by each systole. The magnitude of this change in pressure – known as the pulse pressure – is a function of the magnitude of the stroke volume. The translation of these concepts into a workable system has been complicated by a number of factors that make this relationship between pulse pressure and stroke volume more difficult:

1. The compliance of the aorta is not a linear relationship between pressure and volume. This non-linearity prevents any simple approach to estimate volumes from the pressure change. There needs to be correction for this non-linearity for any individual patient.
2. Wave reflection. The pulse pressure measured from an arterial trace is actually the combination of an incident pressure wave ejected from the heart and a reflected pressure wave from the periphery. In order to calculate the stroke volume, these two waves have to be recognized and separated. This is further complicated by the fact that the reflected waves change in size dependent on the proximity of the sampling site to the heart and also the patients age.
3. Damping. As the change in pressure around a mean value describes the stroke volume, accurate pressure measurements are imperative. Unfortunately pressure transducer systems used in routine clinical practice often suffer from either being under or over damped, leading to imperfect waveforms and measurements.
4. Aortic flow during systole. Although the filling of the aorta is on an intermittent pulsatile basis, the outflow tends to be more continuous.

Ideal Algorithm for Arterial Pulse Contour Analysis

Taking these problems discussed above into account, the ideal algorithm for arterial pulse contour analysis would contain the following features:

1. The algorithm would work independent of the artery the blood pressure is monitored from – despite the fact that the arterial pressure waveform shape and pressure is changed by its transmission through the arterial tree to the periphery.
2. It would correct for aortic non linearity and may be calibrated to take account of individual variations in aortic characteristics and therefore give absolute stroke volume.
3. It would be minimally or even not affected by changes in systemic vascular resistance causing changes in reflected wave augmentation of the arterial pressure.
4. It would not rely on identifying details of wave morphology.
5. It would be only minimally affected by the damping often seen in arterial lines.

The LiDCO^{TM}plus Method of Pulse Power Analysis

The algorithm utilized for the LiDCO^{TM}*plus* technique of arterial pulse power analysis has a number of features that gets around the problems discussed above. This approach is non morphology based, i.e., is not a pulse contour method. Rather it is based on the assumption that the net power change in a heartbeat is the balance between the input of a mass (stroke volume) of blood minus the blood mass lost to the periphery during the beat. It is based on simple physics, i.e., conservation of mass/power and an assumption that following correction for compliance and calibration there is a linear relationship between net power and net flow. Autocorrelation is used to both define the beat period and the net power change across the whole beat. In taking the whole beat, and not a portion of the beat, the method is independent of the position of the reflected wave. Autocorrelation is a time based method and thereby avoids using a frequency approach to measuring power (such as Fourier transforms) and thus the effects of arterial damping (which change frequency response) are limited.

These can be summarized as follows:

1. The algorithm compliance corrects any arterial pressure signal to a standardized volume waveform (volume in arbitrary units) through the equation

   $$\Delta V/\Delta bp = \text{calibration} \times 250 \times e^{-k.bp}$$

   where V is volume, bp is blood pressure and k is the curve coefficient. The number 250 represents the saturation value in mls, i.e., maximum additional volume above the starting volume at atmospheric pressure that the aorta/arterial tree can fill to.
2. Autocorrelation of the now standardized volume waveform – derives both the period of the beat plus a net effective beat 'power factor (R.M.S – root mean square) which is proportional to the 'nominal stroke volume ejected into the aorta.
3. This 'nominal' stroke volume can be scaled to an actual stroke volume by an independent indicator dilution measurement, e.g., lithium dilution cardiac output from the LiDCO^{TM} system.
4. The scaling/calibration factor corrects for the arterial tree compliance for a given blood pressure and corrects for variations between individuals.
5. The scaling/calibration factor changes the saturation value (maximum volume of the aorta/arterial tree) used for the compliance correcting equation – rather than the curve coefficient (k). Thus any potential drift/change in the calibration factor is limited to the extent that the aortic/arterial tree maximum volume can change over the short term (hours).

Theoretical benefits of the Pulse Power Approach to Pulse Contour Analysis

In theory, the features of the pulse power algorithm enable the LiDCO^{TM}*plus* to have several advantages over the pulse contour/systolic area analysis approach. These advantages include:

1. Any arterial site can be used for blood pressure measurement, not just a central artery. As the algorithm looks at the power of the whole pulse contour and not just the systolic area, morphology is not as important. The net power from the input of stroke volume – outflow during the beat is calculated, thus negating the effect of reflected waves.
2. The effect of damping on the transducer system will be similarly reduced. Within reasonable limits the power of the waveform will remain the same, whether the system is over or under damped and thus the changes in stroke volume will remain accurate [15].
3. This system can be calibrated with any form of measurement of cardiac output, so long as the error coefficient of the calibrating technique is less than the error of the LiDCO^{TM}*plus* system. The lithium dilution cardiac output system that is incorporated in this technology (see later) enables a relatively non-invasive and highly accurate mechanism of calibration.

Lithium Dilution Cardiac Output Measurement: The LiDCO^{TM} system

The technique of lithium dilution cardiac output measurement was described by Linton in 1993. A bolus of isotonic lithium chloride (0.002–0.004 mmol/kg) is injected using either central or peripheral venous access. The subsequent concentration of lithium in the circulation is then measured by a lithium ion-selective electrode situated in an appropriate arterial line. This information is used to generate a concentration time curve and the cardiac output can then be calculated from the known amount of lithium and the area under the curve after the first peak, representing the cardiac output before recirculation. Lithium, long established in psychiatric practice as a treatment for mania, has several advantages when used as the indicator in a dilution technique; it does not naturally occur in plasma and therefore can generate a high signal to noise ratio when using an ion selective electrode to measure changes in plasma concentration thus allowing small doses of lithium to be used. At these levels lithium is pharmacologically inert and safe, toxic levels would only be achieved if the maximum recommended dose were greatly exceeded. Rapid redistribution and no significant first pass loss from the circulation add to the suitability of lithium for this technique [8].

The lithium ion selective electrode is central to the LiDCO system and is housed in a flow-through cell attached to the manometer tubing of an arterial cannula. A peristaltic pump is used to control the rate of blood flow through the sensor at 4 ml/min and the eccentric inlet insures mixing of the sample as it passes the membrane selectively permeable to lithium. The Nernst equation relates the plasma lithium concentration to the voltage across the membrane, after the appli-

cation of a correction for plasma sodium, the main determinant of baseline voltage in the absence of lithium. An isolated amplifier is used to measure the voltage that is then digitalized prior to analysis online. The sensor must be primed before use with heparinized saline in order to make an electrical connection between the reference electrode and the blood sample at the electrode tip.

Validation Studies – LiDCO calibration

Calibration precision is very important for arterial pressure waveform analysis systems – the minimum specification is that calibration has to be at least as accurate as green dye or averaged triplicate bolus pulmonary artery thermodilution. Inaccuracy beyond these standards will result in confusion between changes in patient hemodynamic status and scatter in the measurement itself. Lithium dilution has been validated against several methods including electromagnetic flow probes and pulmonary artery thermodilution and has proven to be a very robust and accurate mechanism for measuring cardiac output in both adults, children and animals (Table 2) [9–15].

Linton et al. [15] demonstrated good overall agreement between thermodilution and the LiDCO in 40 patients from a high dependency post operative unit and intensive care unit (ICU). Thirty-four had undergone cardiac surgery requiring cardiopulmonary bypass (CPB) within the previous two days, the other diagnoses were two recent myocardial infarcts, two septicemias, one acute respiratory distress syndrome (ARDS), and one pericardectomy. Cardiac output was measured five times in each patient using lithium dilution (single measurement) and bolus thermodilution (series of three to six measurements according to standard clinical practice and taking the average of the closest three). Linear regression analysis ($r^2 = 0.94$) for lithium dilution vs. thermodilution demonstrated that lithium dilution was at least as accurate as bolus thermodilution.

Kurita et al. [9] compared cardiac output measurements in their sample group of ten pigs undergoing general anesthesia; they used LiDCO, thermodilution, and electromagnetic flowmetry. This necessitated a PAC, femoral artery catheter and an electromagnetic flowmeter placed around the ascending aorta. Baseline measurements for all three techniques were compared to hyper- and hypodynamic states induced by dobutamine and propranolol, respectively. Over a range of cardiac outputs from 0.2 to 2.8 l/min, the correlation between LiDCO and electromagnetic flowmetry ($r^2 = 0.95$) was higher than that between thermodilution and electromagnetic flowmetry ($r^2 = 0.87$) suggesting that the LiDCO was more reliable than conventional thermodilution.

In all the studies validating the LiDCO to date, acceptable levels of bias and precision have been found (Table 2). This suggests that the LiDCO system is at least as accurate and effective as standard thermodilution. Several other studies have also assessed the necessity for the lithium injection to be made via the central venous route [13,16–17]. All of these studies concluded that a peripheral venous injection was just as accurate.

Table 3. Validation studies of the pulse power algorithm in the Lidco^{tm}*plus* System

Author	Species	Validation	Mean CO	Range of CO	Bias	2 x SD of bias	%Error
Hamilton [18]	Post cardiac surgery (8hrs)	LiDCO	5.5*	3.3–8.5	0.1	1.2	22
Jonas [20]	ICU	LiDCO	8.2	5.3–17.1	0.3	1.7	21
Pittman [19]	ICU for 24 hours	LiDCO	6	3.5–10.5	0.15	1.3	22
Heller [23]	Intra op. 2.5–8.5 hours	LiDCO	5*	2.7–21.3	0	1.0	20

* is where the data for mean cardiac output (CO) are not readily available from the papers and have had to be estimated from the original data.

Validation Studies – Pulse Power Analysis with LiDCO^{TM}plus System (Table 3)

The pulse power approach has been validated in a number of clinical settings [18–20]. A number of these studies have now been published and a number presented at International meetings and are awaiting publication. Although the evidence is accumulating to demonstrate the accuracy of this technique, the validation set is not yet complete and future studies are awaited.

The accuracy of the pulse power technique has been assessed in comparison to lithium dilution as well as PAC techniques. The validation has been performed in surgical as well as ICU settings for up to eight hours between calibration intervals. The data suggest that the pulse power approach remains accurate for long time periods with minimal drift. The data remain accurate despite changes in peripheral resistance although users would be advised to make a recalibration prior to a major therapeutic shift if a calibration had not been made in the recent past. The data also remains accurate despite suboptimal arterial line damping characteristics [19].

Limitations

The main limitations to this technology revolve around the use of the lithium. As the technique requires a large difference between the signal and background noise to get a reliable indicator dilution curve, it can be difficult to get reliable readings in patients already on therapeutic lithium. Other drugs that can cross react with the lithium sensor are high peak doses of muscle relaxants and these can cause the sensor to drift. If this system is to be used intra-operatively, then the lithium

calibration needs to be performed either prior to the use of muscle relaxation or after the initial peak has had time to subside.

Conclusion

The LiDCO™*plus* system of cardiac output measurement and monitoring appears to be a safe and effective method of tracking flow. It is minimally invasive and easy to use under the majority of clinical conditions likely to be encountered.

References

1. Frank O (1930) Schätzung des Schlagvolumens des menschlichen Herzens auf Grund der Wellen- und Windkesseltheorie. Zeitschrift für Biologie 90:405–409
2. Frank O (1899) Die Grundform des arteriellen Pulses. Erste Abhandlung. Mathematische Analyse. Zeitschrift für Biologie 37:485–526
3. Erlanger J, Hooker DR (1904) An experimental study of blood pressure and of pulse pressure in man. John Hopkins Hospital Records 12:145–378
4. Remington JW, Nobach CB, Hamilton WF, Gold JJ (1948) Volume elasticity characteristics of the human aorta and the prediction of stroke volume from the pressure pulse. Am J Physiol 153:198–308
5. Kouchoukos NT, Sheppard LC, McDonald DA (1970) Estimation of stroke volume in the dog by a pulse contour method. Circ Res 26:611–623
6. Wesseling KH, de Wit B, Weber JAP, Smith NT (1983) A simple device for the continuous measurement of cardiac output. Adv Cardiovasc Phys 5:16–52
7. Jansen JRC, Wesseling KH, Settels JJ, Schreuder JJ (1990) Continuous cardiac output monitoring by pulse contour during cardiac surgery. Eur Heart J 11:26–32.
8. Jonas MM, Linton RAF, OBrien TK, et al (2001) The pharmokinetics of intravenous lithium chloride in patients and normal volunteers. Journal of Trace and Microprobe Techniques 19:313–320
9. Kurita T, Morita K, Kato S, et al (1997) Comparison of the accuracy of the lithium dilution technique with the thermodilution technique for measurement of cardiac output. Br J Anaesthesiol 79:770–775
10. Mason DJ, OGrady M, Woods P, McDonell W (2001) Assessment of lithium dilution cardiac output as a technique for measurement of cardiac output in dogs. Am J Vet Res 62:1255–1261
11. Linton RA, Young LE, Marlin DJ, et al (2000) Cardiac output measured by lithium dilution, thermodilution and transoesophageal Doppler echocardiography in anaesthetised horses. Am J Vet Res 61:731–737
12. Corley KTT, Donaldson LL, Furr M (2002) Comparison of lithium dilution and thermodilution cardiac output measurements in anaesthetised neonatal foals. Equine Vet J 34:598–601
13. Garcia-Rodriguez C, Pittman J, Cassell CH, et al (2002) Cardiac output measurement without pulmonary artery or central venous cathetrization: a clinical assessment of the lithium indicator dilution method. Crit Care Med 30:2199–2204
14. Linton RA, Jonas MM, Tibby SM, et al (2000) Cardiac output measured by lithium dilution and transpulmonary thermodilution in patients in a paediatric intensive care unit. Intensive Care Med 26:1507–1511
15. Linton R, Band D, OBrien T, et al (1997) Lithium dilution cardiac output measurement: a comparison with thermodilution. Crit Care Med 25:1796–1800

16. Mason DJ, O'Grady M, Woods JP, McDonell W (2002) Comparison of a central and a peripheral (cephalic vein) injection site for the measurement of cardiac output using the lithium-dilution cardiac output technique in anesthetized dogs. Can J Vet Res 66:207–210
17. Jonas MM, Kelly FE, Linton RA, Band DM, O'Brien TK, Linton NW (1999) A comparison of lithium dilution cardiac output measurements made using central and antecubital venous injection of lithium chloride. J Clin Monit Comput 15:525–528
18. Hamilton TT, Huber LM, Jessen ME (2002) PulseCO: a less invasive method to monitor cardiac output from arterial pressure after cardiac surgery. Ann Thorac Surg 74:S1408–1412
19. Pittman JA, Sum Ping JS, Sherwood MW, El-Moalem H, Mark JB (2004) Continuous cardiac output monitoring by arterial pressure waveform analysis: a 24 hour comparison with the lithium dilution indicator technique. Crit Care Med (in press)
20. Jonas MM, Tanser SJ (2002) Lithium dilution measurement of cardiac output and arterial pulse waveform analysis: an indicator dilution calibrated beat-by-beat system for continuous estimation of cardiac output. Curr Opin Crit Care 8:257–261
21. Wezler K, Boger A (1939) Die Dynamik des arteriellen Systems. Der arterielle Blutdruck und seine Komponenten. Ergebn Physiol 41:292–306
22. Band D, O'Brien T, Linton N, Jonas M, Linton R (1996) Point-of-care sensor technology for critical care applications. Presentation at Colloquium on New Measurements and Techniques in Intensive Care, London, December.
23. Heller LB, Fisher M, Pfanzelter N, Jayakar D, Jeevanandam V, Aronson S (2002) Continuous intra-operative cardiac output determination with arterial pulse wave analysis (PulseCO TM) is valid and precise. Anesth Analg 93:SCA7 (abst)