CME

Arterial Waveform Analysis for the Anesthesiologist: Past, Present, and Future Concepts

Robert H. Thiele, MD, and Marcel E. Durieux, MD, PhD

Qualitative arterial waveform analysis has been in existence for millennia; quantitative arterial waveform analysis techniques, which can be traced back to Euler's work in the 18th century, have not been widely used by anesthesiologists and other clinicians. This is likely attributable, in part, to the widespread use of the sphygmomanometer, which allows the practitioner to assess arterial blood pressure without having to develop a sense for the higher-order characteristics of the arterial waveform. The 20-year delay in the development of devices that measure these traits is a testament to the primitiveness of our appreciation for this information. The shape of the peripheral arterial pressure waveform may indeed contain information useful to the anesthesiologist and intensivist. The maximal slope of the peripheral arterial pressure tracing seems to be related to left ventricular contractility, although the relationship may be confounded by other hemodynamic variables. The area under the peripheral arterial pressure tracing is related to stroke volume when loading conditions are stable; this finding has been used in the development of several continuous cardiac output monitors. Pulse wave velocity may be related to vascular impedance and could potentially improve the accuracy of waveform-based stroke volume estimates. Estimates of central arterial pressures (e.g., aortic) can be produced from peripheral (e.g., brachial, radial) tracings using a Generalized Transfer Function, and are incorporated into the algorithms of several continuous cardiac output monitors. (Anesth Analg 2011;113:766–76)

HISTORICAL BACKGROUND

Evolution of Arterial Waveform Analysis

Analysis of the arterial pulse wave predates the era of modern medicine by millennia, with the first qualitative pulse wave analysis being attributed to the Egyptians.[1] Early accounts were written by the Greeks (Rufus of Ephesus was the first to use the term "dicrotic" in the first century AD[2]); Romans (Galen's *On Prognosis from the Pulse*, written before 210 AD, describes 27 types of pulses); and Han Chinese (Wang Shu-he's *Mai Jing*, circa 220 AD, describes 24 types of pulses).

Thousands of years after these initial descriptions, William Harvey (1578–1657) demonstrated that the arteries and veins exist in series. Giovanni Borelli (1608–1679) made the observation that the elasticity of arteries was responsible for dampening the flow of peripheral blood. Stephen Hales (1677–1761) also examined the impact of arterial elasticity on arterial hemodynamics, reporting its effect on blood flow velocity in animals.[3]

Quantitative analysis of the arterial system is generally first attributed to Leonhard Euler (1707–1783), who unsuccessfully attempted to apply the principles of the Conservation of Mass and Energy to a tubular model of the cardiovascular system. Jean Louis Poiseuille (1799–1869) successfully described the flow of fluids through tubes using the equation $Q = KPD^4/L$ (where K is a fluid constant, P is the pressure gradient across the tube, D is the diameter of the tube, and L is the length of the tube), a derivation of which became known as the Hagen-Poiseuille Law of Friction. Importantly, the Hagen-Poiseuille Law is valid only under certain conditions, most critically during steady, laminar flow. Although Poiseuille's Law was not designed to describe pulsatile flow, and blood flow is not always laminar,[4] it has become a standard descriptor in almost all medical and physiologic textbooks.[3]

In 1899, Otto Frank published a mathematical formulation of Hales' earlier work, which ultimately became known as the Windkessel effect. This work was notable for its successful incorporation of both Conservation of Mass and vascular stiffness into the description of hemodynamics, which was particularly accurate during diastole. In addition to conducting work that would lead to the Frank-Starling Law, Frank was likely the first physiologist to analyze both reflected pressure waves and the spectral composition of blood pressure waveforms.[3]

The next major advance in the study of arterial hemodynamics was the recognition of behavioral similarities between the cardiovascular system and an electrical analog, first attributed to Landes in 1946[3] and advanced by Taylor to include analogues for capacitance and inductance, in addition to voltage and resistance.[5] Shortly thereafter, Cooley and Tukey published their classic manuscript "An Algorithm for the Machine Calculation of Complex Fourier Series," which subsequently became known as Fast Fourier Transformation, and in doing so reduced the time required for harmonic analysis of pressure waveforms from hours to seconds.[6] This, combined with the advent of the computer, ushered in the modern era of arterial waveform analysis, in

From the Department of Anesthesiology, University of Virginia Health Sciences Center, Charlottesville, Virginia.

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Address correspondence to Robert H. Thiele, MD, Department of Anesthesiology, University of Virginia Health Sciences Center, PO Box 800710, Charlottesville, VA 22908-0710. Address e-mail to rht7w@virginia.edu.

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which previously prohibitively complex calculations requiring manipulation of vast amounts of data were suddenly possible. Major early contributions were made by Donald McDonald and John Womersley, followed by Michael Taylor, Michael O'Rourke, Wilmer Nichols, and Mustafa Karamanoglu, some of which are referenced below. (The interested reader is referred to the outstanding review by Kim H. Parker,[3] the reviews by Booth[1] and O'Rourke,[2] and the fifth edition of McDonald's text[7] for a more complete account.)

Devolution of Arterial Waveform Analysis

Development and use of the sphygmomanometer, which was first conceived by Karl Vierordt in 1855,[1] was a major advance in that it allowed for the accurate measurement of systolic and diastolic blood pressure without placement of an intraarterial catheter. An unintended consequence of this useful device was that to assess blood pressure, physicians no longer needed to develop an appreciation for the character of the arterial pulse, and, from a clinical standpoint, this "art" was essentially lost. The *British Medical Journal* published the view that when using a sphygmomanometer, "we pauperize our senses and weaken clinical acuity."[1]

If the only hemodynamic variables that mattered were systolic and diastolic blood pressure, and if the sphygmomanometer was as accurate as intraarterial readings, this loss would not be of consequence. However, the accuracy of the sphygmomanometer has been called into question.[8] Furthermore, the shape of the systemic arterial tracing provides additional information that may have clinical significance. Thus, the near simultaneous development of the computer, Fast Fourier Transform technique, and sphygmomanometer produced a unique situation in which, from a research standpoint, production of knowledge increased rapidly, while clinically, interest in this knowledge almost evaporated (as evidenced by the delay in incorporating potentially useful waveform descriptors into modern medical devices). The intent of this review is to describe some of this additional information, with an emphasis on both clinical relevance and critical questions that need to be addressed by further research.

ESTIMATES OF CONTRACTILITY

Contractility is defined as the amount of pressure-volume work produced by the heart given a particular set of loading conditions. True measures of contractility are "load-independent" (i.e., stable in the face of changes in preload and afterload). Contractility is difficult to estimate clinically. Ejection fraction (EF), the most frequently used surrogate, is load dependent[9] and requires the use of echocardiography. Load-independent indices, such as the slope of the end-systolic pressure-volume relationship (Emax),[10–12] are clinically impractical. Thus, there has been interest in development of a contractility index that is both load-independent and easy to measure.

Early studies focused on ventricular pressure changes (dP/dt_{max}), which seemed to be related to contractility but, because they required left heart catheterization, were not clinically useful. Work on ventricular dP/dt_{max} was subsequently extended to peripheral measures of dP/dt_{max}, which are easily measured in clinical practice.

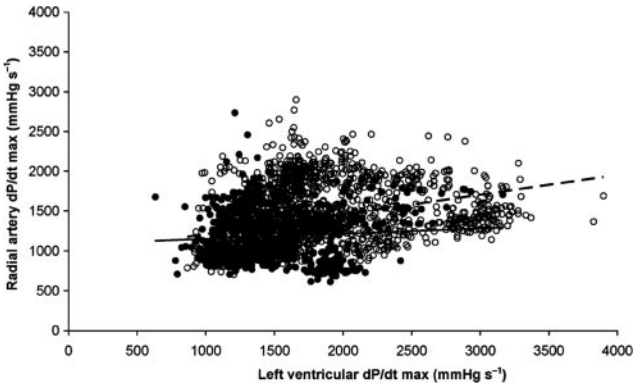

Figure 1. A comparison of noninvasive radial ventricular pressure changes (dP/dt_{max}) to left ventricular dP/dt_{max} in patients undergoing diagnostic coronary angiography or dobutamine stress echocardiography. Reproduced with permission from Sharman et al.[20]

Ventricular dP/dt_{max}

In 1914, Carl Wiggers[13] noted that as right ventricular end-diastolic pressure was increased, the "steepness" of the ventricular pressure curve increased, and later stated that "the greater systolic discharge following the injection of epinephrin, is brought about entirely by a greater velocity of discharge."[14] Reeves et al.[15] expanded on this work by comparing dP/dt_{max} and left ventricular (LV) pressure area (their chosen measure of contractility) under a variety of loading conditions, and found that by adjusting dP/dt_{max} for changes in LV end-diastolic pressure, the correlation between dP/dt_{max} and contractility over different loading conditions could be improved. Gleason and Braunwald[16] repeated these studies in humans, and found that by correcting dP/dt_{max} for heart rate (HR), a much more significant result could be obtained. Wallace et al.[17] extended the work of Reeves and Gleason in an attempt to define all of the hemodynamic variables that might influence the reliability of ventricular dP/dt_{max} as an indicator of contractility. The work of Wallace et al. confirmed that HR, preload, and aortic pressure (presumably to consider the potential for homeometric autoregulation, described in detail by Sarnoff et al.[18]) all affect ventricular dP/dt_{max}, and the authors concluded that these variables must be accounted for if ventricular dP/dt_{max} were to be used as a measure of intrinsic contractility.

Peripheral dP/dt_{max}

Ventricular dP/dt_{max} cannot be measured routinely. Investigators have therefore sought to relate peripheral dP/dt_{max} to ventricular dP/dt_{max} in the hopes of finding a more clinically useful metric for assessing ventricular function. Ventricular dP/dt_{max} occurs before aortic valve opening,[17] thus it cannot be assumed that peripherally derived indices of dP/dt_{max} are reflective of ventricular pressures. Germano et al.[19] compared noninvasively derived peripheral dP/dt_{max} from 10 normal patients with 5 patients with an EF <40%, and found a significant difference between the two. Sharman et al.[20] compared noninvasive radial

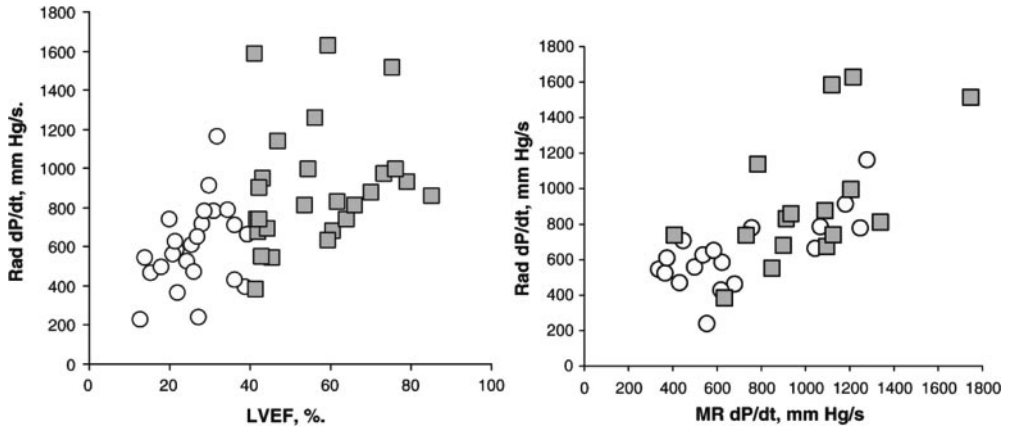

Figure 2. The relationship between noninvasively determined peripheral ventricular pressure changes (dP/dt_{max}) and ejection fraction (left) and ventricular dP/dt_{max} (based on mitral jet regurgitation, right) in stable patients with a history of acute decompensated congestive heart failure. Reproduced with permission from Tartiere et al.[21]

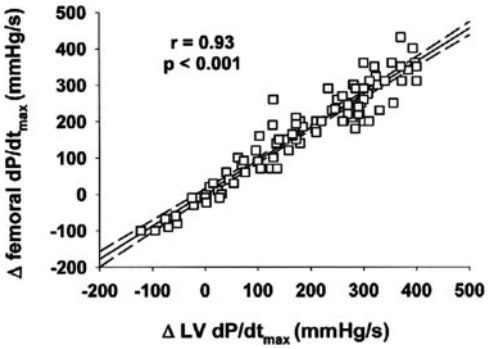

Figure 3. A comparison of changes in femoral ventricular pressure (dP/dt_{max}) with changes in left ventricular dP/dt_{max} in patients undergoing coronary artery bypass grafting. Reproduced with permission from de Hert et al.[23]

dP/dt_{max} with direct measurements of LV dP/dt_{max} and found no relationship ($r^2 = 0.006$, 681 data points; Fig. 1), but did find a trend toward higher radial dP/dt_{max} in patients with an EF >54% (994 mm Hg/s) as compared with those with an EF <55% (852 mm Hg/s, $P = 0.10$). Tartiere et al.[21] examined the relationship between noninvasively determined peripheral dP/dt_{max} and a variety of echocardiographic markers of LV function and found statistically significant correlations between peripheral dP/dt_{max} and both ventricular dP/dt_{max} (based on quantification of mitral jet regurgitation) and EF (Fig. 2). In a subsequent study of radial dP/dt_{max} in 310 patients with heart failure, Tartiere et al.[22] found that a cutoff value of 440 mm Hg/s was highly predictive of mortality or need for transplantation (odds ratio, 2.88 [confidence interval, 1.33–3.58]; $P = 0.009$). Furthermore, radial dP/dt_{max} was significantly related to LV EF on both univariate ($P < 0.001$) and multivariate analyses ($P < 0.05$).

De Hert et al.[23] used the PiCCO monitor (Pulsion Medical Systems, Munich, Germany) to compare femoral dP/dt_{max} with direct measurements of LV dP/dt_{max} and found a significant correlation between the two ($r^2 = 0.67$), although femoral dP/dt_{max} underestimated LV dP/dt_{max} by an average of 361 mm Hg/s. The correlation between changes in femoral dP/dt_{max} and changes in LV dP/dt_{max} was stronger ($r^2 = 0.86$) than the correlation between absolute values (Fig. 3).

Clinical Relevance

Ventricular dP/dt_{max} is clearly related to ventricular function. The usefulness of peripherally derived dP/dt_{max} is still a matter of controversy,[24,25] although data from the PiCCO suggest that peripheral dP/dt_{max} may trend with ventricular dP/dt_{max}.[23] Unpublished data from the study by Sharman et al.[20] suggest that there is no linear relationship between changes in ventricular dP/dt_{max} and changes in noninvasive radial dP/dt_{max} (James E. Sharman, University of Queensland, October 10, 2010, personal communication). More studies are needed.

dP/dt_{max} has 3 major advantages: the intuitiveness of the measurement, the ability to at least partially "correct" it for physiologic changes that may affect its meaning, and the rapidity with which it changes. Although dP/dt_{max} is undoubtedly load dependent, common echocardiographic measures of ventricular function (e.g., EF) are as well.[26] Furthermore, the load dependence of dP/dt_{max} does not necessarily minimize its clinical utility. When the impact of acute interventions on myocardial contractility over time periods in which loading conditions are stable is desired, load dependence becomes irrelevant and changes in dP/dt_{max}, which can be measured on a beat-to-beat basis, might be particularly useful. Furthermore, whereas dP/dt_{max} is clearly preload sensitive, it seems to be relatively insensitive to changes in afterload.[27]

In addition to the PiCCO monitor, 2 technological developments may be of interest to the anesthesiologist. First, using transthoracic echocardiography in combination with an arterial blood pressure cuff, Rhodes et al.[28] showed that it is possible to estimate LV dP/dt_{max} noninvasively. This approach could potentially be adapted for the operating room using transesophageal echocardiography in place of transthoracic echocardiography. Second, the SphygmoCor™ tonometric (external pressure measurements) device (AtCor Medical, Sydney, Australia), which reliably estimates aortic blood pressure and reports radial dP/dt_{max}, has been validated using >15,000 data points from >1600 patients (see Estimates of Central Arterial Pressure), although it has not been studied intraoperatively.[29] The ability to estimate ventricular dP/dt_{max} from a transformed peripheral waveform would represent an exciting advance in intraoperative monitoring.

ESTIMATES OF STROKE VOLUME

> "The discovery of a technically simple and nontraumatic way of estimating the output of the heart per beat is something of an El Dorado."[30]
>
> —Donald A. McDonald, 1960

Derivation of stroke volume (SV) from the arterial pressure tracing would allow for cardiac output monitoring on a near-instantaneous basis, which is a significant improvement over current thermodilution techniques (which require either significant operator intervention [intermittent bolus technique] or substantial lag time [thermistor-based continuous cardiac output catheters[31]]) and themselves have questionable accuracy as compared with the true "gold standard," the Fick method.[32–35]

Pulse Pressure

Initial attempts at estimating SV used pulse pressure (or some variation) to make their determinations.[36–38] These techniques, some of which obtained extraordinary accuracy in animal models,[37] were found to be less accurate in humans.[39] Thus, pulse pressure–derived estimates of SV were abandoned for more sophisticated techniques, such as the area under the curve (AUC) approach.

Area Under the Curve: The Windkessel Approach

Most early attempts at estimating SV from analysis of the arterial waveform were based on Frank's Windkessel model of blood flow.[30,39,40] Although these methods all have subtle differences, they incorporate the same assumptions (and are thus susceptible to the same shortcomings).

Fundamental to Frank's Windkessel theory are 2 concepts. First, at steady state, the amount of blood entering a vessel must equal the amount of blood leaving a vessel over the course of the cardiac cycle (Conservation of Mass). Second, the compliance of a vessel affects the flow through it in a very predictable way. During systole, as pressure inside the vessel is increasing, the vessel will expand, absorbing some of the blood that would otherwise pass through it. Conversely, during diastole, as the pressure inside the vessel is decreasing, the vessel will contract, expelling additional blood that was stored during systole (Fig. 4). This simplified version of the cardiovascular system is known as the 2-element (resistor and capacitor) Windkessel model. Models of up to 4 elements, which include aortic input impedance and inductance, have been developed (Fig. 5).[41]

Next, proponents of the Windkessel-based AUC approach (such as Warner et al.[39]) divide SV into 2 components: systolic outflow and diastolic outflow (Q_S and Q_D).

Q_D is proportionate to "the increment in mean pressure over the whole arterial bed at the end of systole" (referred to as end-systolic mean distending pressure, abbreviated P_{md} by Warner et al.[39], or some variation of P_{md}. For graphical representations, see Figure 6) and a constant k that must, by definition, incorporate estimates of vascular resistance, vessel compliance, and in some cases, aortic input impedance (Equation 1).

$$Q_D = k \times P_{md} \quad (1)$$

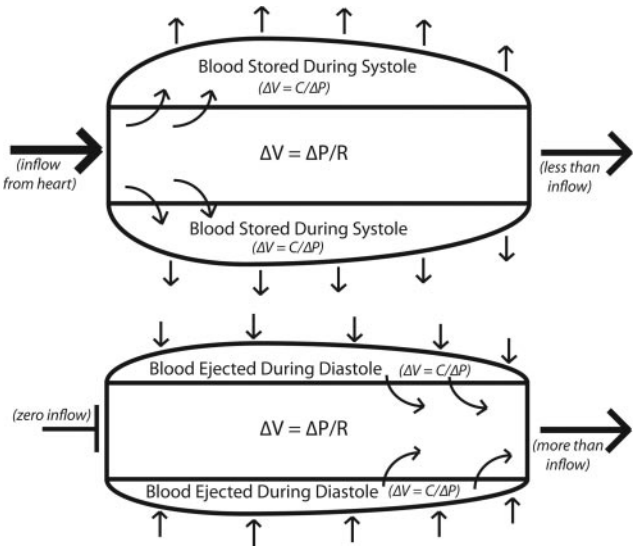

Figure 4. Depiction of blood flow into and out of a prototypical "Windkessel artery." Several points are to be noted: first, during systole, inflow into the artery is less than outflow, because some of the blood is stored in the expanding, compliant vessel. Second, during diastole, inflow into the artery is zero and outflow is enhanced by the contracting vessel.

SV is the sum of systolic flow and diastolic flow ($SV = Q_S + Q_D$). Because peripheral vascular resistance is assumed to be constant over the course of 1 cardiac cycle, it is assumed that Q_S and Q_D are proportionate to their respective areas under the pressure curve (A_S = AUC for systole, A_D = AUC for diastole), i.e., that $Q_S/A_S = Q_D/A_D$. Therefore:

$$Q_S = Q_D \times (A_S/A_D) \quad (2)$$

Because $SV = Q_S + Q_D$, and $Q_S = Q_D \times (A_S/A_D)$, and $Q_D = k \times P_{md}$ (as noted above) it follows that:

$$SV = Q_D \times (A_S/A_D) + Q_D \quad (3)$$

$$\text{or } SV = Q_D\,(A_S/A_D + 1) \quad (4)$$

and that:

$$SV = k \times P_{md}\,(1 + A_S/A_D) \quad (5)$$

To use Equation 5, or some variation of it, SV had to be measured by invasive means (i.e., the model requires calibration). This would allow the user to solve for k (because $P_{systole}$, A_S, and A_D could be calculated from the blood pressure tracing). Once k was known, SV could be followed on a beat-to-beat basis.

The exact equations used by the original proponents of this method vary slightly, mostly in the means by which they calculate P_{md},[30,39,42,43] but also in their use of A_S and A_D (which, as the definition of P_{md} is changed, must be adjusted accordingly). For unclear reasons, some authors chose to use T_S and T_D, the time spent in systole and diastole, respectively. The technique described above is based on a 2-element Windkessel model, the major components of which are peripheral resistance and Windkessel compliance.

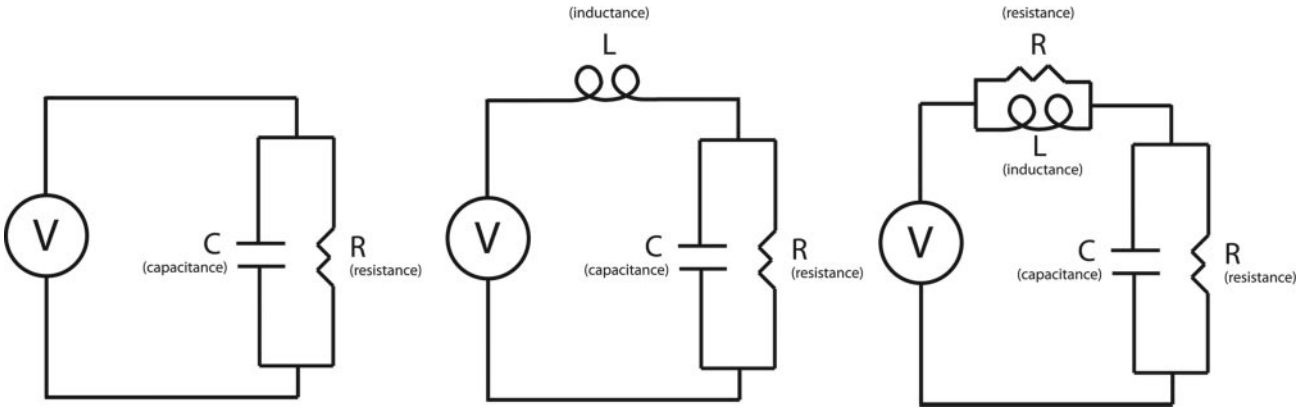

Figure 5. An electrical analog of 2 (right), 3 (center), and 4 (right) component Windkessel systems. Voltage (V) can be replaced by pressure to make the analogy complete.

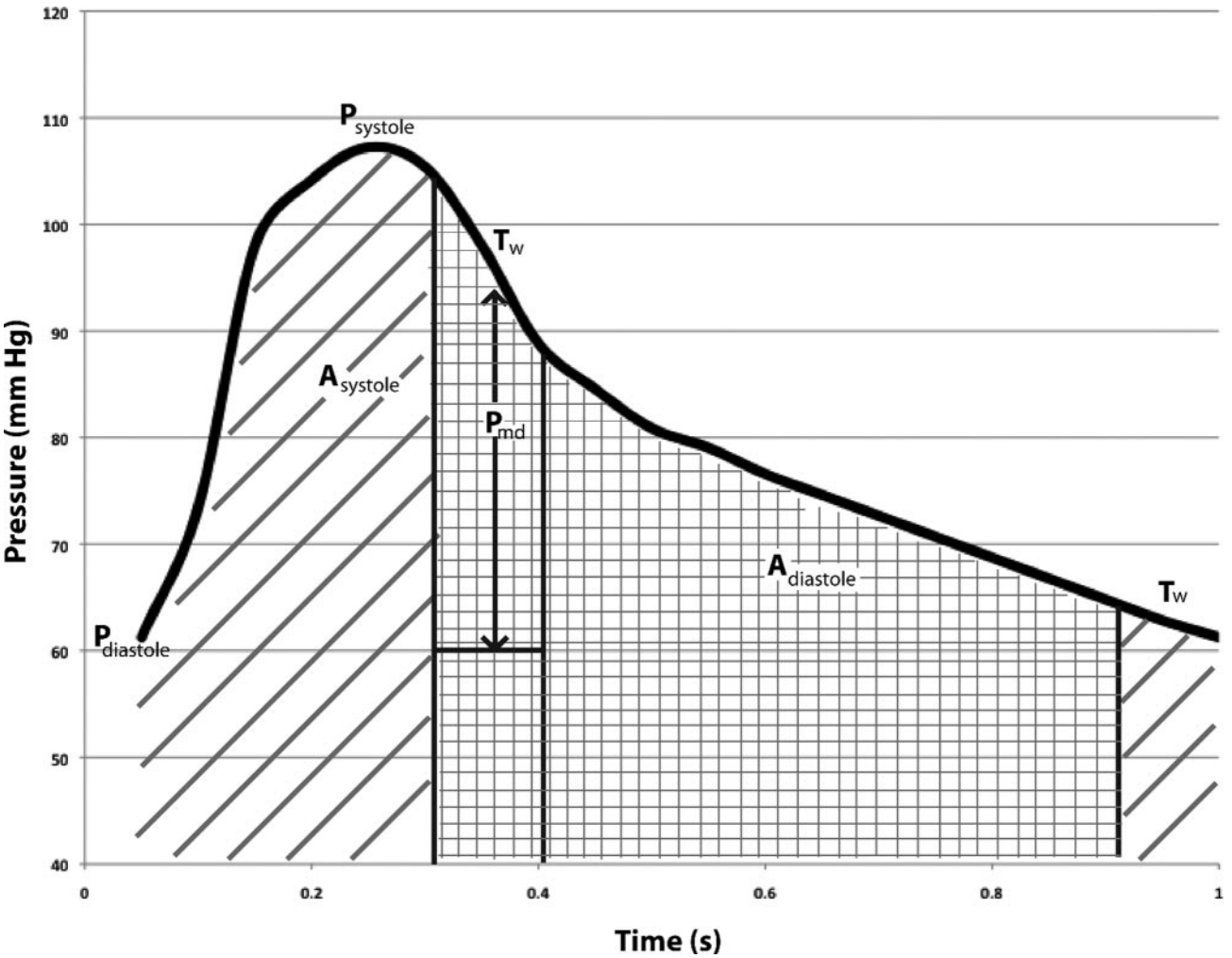

Figure 6. A graphical depiction of the components of the arterial waveform used by the Windkessel-based area under the curve method. Note that P_{md} represents the increment in mean pressure over the whole arterial bed at the end of systole[39] and that T_w represents the transmission time (from the aorta to the periphery).

Several investigators have attempted to develop an AUC method based generally on the outline presented above.[30,39,44] When tested in an uncontrolled clinical environment, all of these early methods failed,[45,46] prompting subsequent investigators to refine the Windkessel-based methodology.[40,43]

This approach entails several assumptions. First, it assumes no backward flow during any part of the cardiac cycle, thus should not be considered reliable in the setting of aortic insufficiency. Second, it neglects the effects of wave reflections on the pressure waveform (Frank's Windkessel model

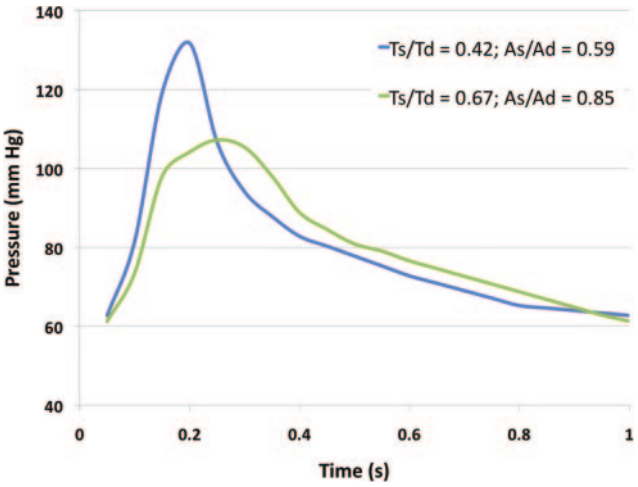

Figure 7. Two pressure waveforms with identical areas under the curve (AUC) (mean arterial blood pressure = 80 mm Hg for both), but for whom AUC-based estimates result in different estimates of stroke volume.

assumed that the vessel had infinite length, i.e., that reflected pressure waves were negligible). Of note, Mukkamala and Xu[47] have attempted to correct for this assumption using "long time interval analysis techniques," the preliminary data for which look promising. Third, it assumes that vascular resistance is constant over the cardiac cycle. Fourth, it assumes that vascular resistance can be accounted for by the changing shape of the pressure waveform.

Consider the following 2 waveforms (Fig. 7), the mean arterial blood pressures (MAPs) of which are identical. Based on the traditional approach to blood flow (output = driving force/resistance), without knowledge of systemic vascular resistance (SVR), the relative SV of both curves would appear to be identical. Application of the generic Windkessel-based AUC method to these curves suggests that the SV associated with these 2 curves is vastly different, despite the identical MAPs − $P_{md} \times (1 + A_S/A_D)$ is equal to 47.5 for the first curve (blue), whereas $P_{systole} \times (1 + A_S/A_D)$ is equal to 68.2 for the second curve (green).

The generic Windkessel-based AUC method, which assumes that k is constant, must therefore assume that the SV of the green curve is 43% higher than the SV of the blue curve. Because MAP is identical, SVR in the green curve must therefore be 30.4% less than in the blue curve. Intuitively, one might look at the above waveforms and guess that SVR is lower in the green curve, as the upstroke is less steep. However, this may reflect decreased contractility, and not a difference in SVR, which would imply reduced SV.

Whether SVR can be reliably calculated from the shape of an arterial waveform is not known. Awad et al.[48] attempted to correlate SVR to the width of plethysmographic waveform and achieved a statistically significant relationship; however, the correlation was too weak (standard deviation was 587.3 dynes/s/cm^5) to be useful on a beat-to-beat basis.

One variation of the Windkessel-based approach is the characteristic impedance (cZ) method developed by Wesseling et al.[42] The major difference between the cZ method and other 2-element techniques is that the cZ method attempts to use the concept of impedance (which represents resistance to pulsatile flow), rather than the static concept of resistance. The forces that oppose blood flow at any point are dependent on both blood pressure (which affects aortic cross-sectional area as well as compliance) and HR (which affects the influence of peripherally reflected pressure waves).[49] It is important to note that cZ is actually an HR- and pressure-corrected variant of resistance and not identical to actual impedance. Wesseling et al.[42] thus described cZ as a function of both MAP and HR (in Hz, f_H, Equation 7).

$$cZ = 20/(163 - 0.48MAP + f_H) \quad (7)$$

In the most basic form of the cZ method, SV is equal to area under the pressure curve during systole [$_{\text{end-diastole}}\int^{\text{end-systole}}$ P(t)] divided by cZ (Equation 8).[50]

$$SV = {}_{\text{end-diastole}}\int^{\text{end-systole}} P(t)/cZ \quad (8)$$

The Modelflow technique, also developed by Wesseling et al.,[51] attempts to incorporate both peripheral resistance (R) and Windkessel compliance (C), as well as characteristic impedance (cZ), into a 3-element Windkessel model. This model assumes that aortic compliance and impedance can be estimated based on patient data, and that resistance can be subsequently determined by fitting blood pressure data to the 3-element model. Empiric estimates of aortic area can be off by as much as 30%, thus the Modelflow technique still requires an initial calibration against known cardiac output.[49] A variation of the Modelflow technique, which uses more accurate estimates of the pressure/aortic cross-sectional area relationship, called the Hemac technique, was recently developed.[49]

As with the cZ method, the PulseCO system (LiDCO Group, London, UK) also incorporates characteristic impedance into its model. However, the PulseCO system modifies Wesseling's original approach by considering the difference between peripheral and central pressures using a transfer function (see Estimates of Central Arterial Pressure).[52] Additionally, the LiDCO device, which relies on the PulseCO algorithm to analyze the arterial waveform, also uses a lithium dilution curve to self-calibrate.

The PiCCO system adds an estimate of aortic compliance (derived from analysis of the pressure waveform distal to the dicrotic notch) to the cZ approach, and incorporates both aortic compliance [C(p), a function of pressure] and instantaneous pressure changes (dP/dt) into the calculation, which is integrated over the time period of systole (Equation 9).[50]

$$SV = k \times {}_{\text{end-diastole}}\int^{\text{end-systole}} [P(t)/SVR + C(p) \times dP/dt]dt \quad (9)$$

The PiCCO equation is notable for its treatment of compliance as a dynamic variable that changes with time (and is thus appropriately, and uniquely, included in the integral portion of the cardiac output equation). These modifications are intended to account for the fact that a nontrivial fraction of ventricular output is stored in capacitance

vessels and subsequently ejected into the peripheral vasculature during diastole. Despite these modifications, the PiCCO requires an initial calibration to determine *k*.

Empiric Approach

A major paradigm shift in the AUC method came with the development of the FloTrac (Edwards Life Sciences, Irvine, CA).[53] Rather than be burdened by the assumptions inherent in the Windkessel-based AUC approach, the FloTrac assumes only that SV is related to 2 empiric numbers, σ_{AP}, which represents the relationship between pulse pressure and SV, and χ, which represents the effect of vascular tone on waveform morphology (Equation 10). Thus:

$$SV = \sigma_{AP} \times \chi \quad (10)$$

In addition to being an empiric (as opposed to theoretical) approach, the FloTrac does not require calibration. σ_{AP} and χ are determined based on correlations developed from a proprietary hemodynamic database. σ_{AP} is related to the standard deviation of the arterial blood pressures recorded over a 20-second epoch (Equation 11):

$$\sigma_{AP} = \{\Sigma[P(k) - P_{avg}]^2/[n-1]\}^{1/2} \quad (11)$$

χ is related to a several variables, including HR, body surface area (BSA), compliance, as well as several numerical descriptors of the waveform, abbreviated μ_n (μ_1, μ_2, μ_3, and μ_4 represent MAP, the standard deviation of a 60-second data sample, the skewness of a 60-second data sample, and the kurtosis over a 60-second data sample, respectively). Additional parameters [μ_n] are also included, although their exact description is not available (Equation 12).

$$\chi = f[HR, BSA, C(p), \mu_1, \mu_2, \mu_3, \mu_4, \ldots \mu_n] \quad (12)$$

Compliance is a function of instantaneous pressure and is related to both maximal aortic root cross-sectional area (estimated based on patient demographics) and the shape of the compliance curve (empirically derived).

Thus, unlike prior techniques, which tried to force empirical data into elegant constructs that were thought to accurately depict reality, the FloTrac approach tries to find meaningful correlations regardless of whether the results can be explained by a physiologic theory. Early results in postsurgical patients were promising, with mean biases of 0.20 and 0.55 L/min reported (as compared with intermittent thermodilution).[54,55]

Studies of the PulseCO,[56] PiCCO,[57,58] and FloTrac[59–61] suggest that the accuracy of AUC methods is degraded in the setting of hemodynamic instability. A recent meta-analysis that included 714 subjects in 24 studies suggested that the mean-weighted bias of AUC methods was 1.22 L/min, which was worse than esophageal Doppler (1.07 L/min), partial CO_2 rebreathing (1.12 L/min), and thoracic bioimpedance (1.14 L/min) techniques.[62]

In a simultaneous comparison of the FloTrac, LiDCO, and PiCCO monitors with intermittent thermodilution in 20 patients after cardiac surgery, the bias and limits of agreement, as compared with the pulmonary artery (PA) catheter, were −0.18, 1.38, −1.74 L/min for the LiDCO, 0.24, 2.3, and −1.98 L/min for the PiCCO, and −0.43, −2.94, and 3.80 L/min for the FloTrac.[63] The substantial difference in the limits of agreement between uncalibrated and calibrated devices was also reported by a similar comparison of the LiDCO and FloTrac with intermittent thermodilution.[64]

Improving the AUC Method: Pulse Wave Velocity

The velocity (V) of a pulse wave through an elastic tube can be described in terms of the elasticity (E, Young modulus of elasticity, defined as stress/strain), wall thickness (h), and diameter of the tube (D), as well as the density of the fluid (ρ), which is known as the Moens-Korteweg equation (Equation 13).[65,66]

$$V = k(Eh/\rho D)^{1/2} \quad (13)$$

Because the human cardiovascular system behaves as a complex series of elastic tubes, changes in pulse wave velocity (PWV) or pulse wave transit time may imply changes in elasticity, vessel diameter, or fluid (blood) density. The utility of PWV analysis is based on the assumption that changes in vascular impedance (ultimately mediated by changes in vascular tone, which lead to changes in both vessel compliance and cross-sectional diameter[67]) will result in changes in the speed at which a pressure wave, originating in the LV, travels to the periphery.[66]

Animal studies have revealed various relationships between PWV and diastolic blood pressure,[65] ventricular dP/dt_{max},[68] and SVR.[66] This latter relationship was used by Ishihara et al.[69] to improve the accuracy of noninvasive cardiac output monitors; incorporation of pulse wave transit time into a plethysmographic contour-based CCO monitor eliminated the need for recalibration after significant changes in vascular resistance. A similar strategy applied to arterial contour-based CCO techniques might mark a significant advancement in achieving clinical applicability across a wide range of hemodynamic conditions. Indeed, the PulseCO algorithm incorporates an estimate of aortic PWV (based on patient age, gender, and MAP) into its calculation of characteristic impedance,[52] a potential source of error (and improvement).

Clinical Relevance

The "gold standard" for the measurement of cardiac output is the Fick method, which is clinically impractical. Thermodilution, which requires placement of a PA catheter, is considered the clinical gold standard, and is generally used to validate new devices. The PA catheter is not as accurate as the Fick method.[32–35] To truly assess the utility of CCO monitors, a well-validated standard means of estimating cardiac output on a beat-to-beat basis is required. Currently, there is no such device, although a recently reported PA catheter incorporating orthogonally placed Doppler probes is promising.[70]

Practitioners are therefore left with the knowledge that AUC-based techniques deviate from thermodilution-based techniques in the setting of hemodynamic instability (it is impossible to know which is more "correct"), for the most part have not been tested against the Fick method, and are much more responsive than their more invasive counterpart, the PA catheter. The empiric approach used by the FloTrac, although convenient, may decrease the

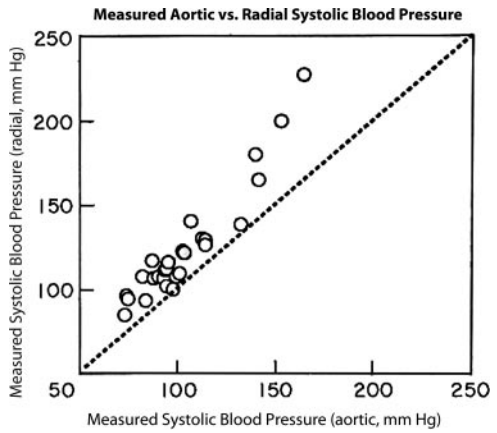

Figure 8. Comparison of aortic systolic pressure with brachial artery systolic pressure in patients undergoing diagnostic cardiac catheterization (12 of 14 patients had significant [>70% reduction in at least 1 vessel] atherosclerotic coronary artery disease). Reproduced with permission from Karamanoglu et al.[79]

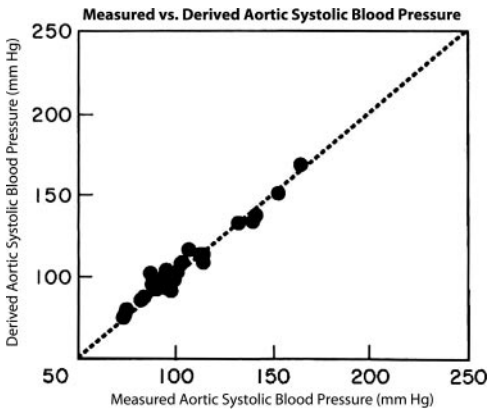

Figure 9. Comparison of actual with derived central systolic pressures using the frequency domain–based generalized transfer function of Karamanoglu et al. Reproduced with permission from Karamanoglu et al.[79]

accuracy of the device in the setting of rapidly changing hemodynamics.[63,64]

Assuming that AUC-based techniques are less accurate than the true gold standard(s), they still may be of use, for several reasons. First, they are less invasive. Second, the response time of arterial waveform analysis methods, which can estimate SV on a beat-to-beat basis, is significantly faster than intermittent thermodilution and continuous thermistor-based techniques.[31] Lastly, even if arterial waveform analysis cannot predict absolute values of cardiac output, predicting changes in cardiac output may be important. Sacrificing the ability to measure absolute values for an increased ability to track changes[71] may actually improve the utility of these devices, depending on the clinician's needs.

ESTIMATES OF CENTRAL ARTERIAL PRESSURE

When arterial pressure is monitored invasively, it is almost always accomplished using a radial artery catheter. Because few clinicians care about blood flow to the hand specifically, the use of the radial artery implies that radial pressures provide other, more meaningful information. Unfortunately, myocardial delivery of oxygen is related to aortic (not radial) systolic pressure,[72] and LV afterload is well represented by aortic input impedance.[73–75] Central pressures are superior to peripheral pressures for the measurement of LV afterload, for estimation of carotid and coronary artery pressures,[76] and for estimating changes in SV.[47] The inability of peripheral (e.g., radial, brachial) arteries to represent aortic pressure (particularly systolic pressure)[72,77–79] (Fig. 8) may be one of the reasons that most investigations have failed to find a meaningful relationship between peripheral arterial blood pressure and clinical outcomes during anesthesia.

Most techniques used to estimate central pressure are based on the concept of the transfer function; blood pressure tracings are acquired for both central and peripheral arteries, and compared. A mathematical function that relates the central to peripheral pressure tracing is developed for each individual, which is called an individual transfer function (ITF). ITFs are developed for a population, and then combined (usually averaged) to produce a generalized transfer function (GTF) that best fits the population as a whole.

Karamanoglu et al.[79] measured ascending aortic, brachial, and radial artery pressures in 14 patients in the cardiac catheterization laboratory. Blood pressures at each site were decomposed into a series of sine waves, each of which had an amplitude and phase shift component. The amplitude and phase shifts of each pressure tracing (aortic, brachial, radial) were then compared and related. ITFs were developed for all 14 patients, then pooled to develop a single GTF. Application of the developed GTF reduced the difference between peripheral and central systolic pressures from 20 to 2.4 mm Hg (Fig. 9).[79] This frequency domain approach has been validated by >15,000 readings from >1600 patients (r^2 = 0.94 between estimated and measured aortic systolic pressure).[29]

Chen et al.[80] examined blood pressure waveforms in the time domain. ITFs were developed for 20 patients using a linear mathematical model in which aortic and radial pressures were related by the previous 10 measurements. A GTF was then produced by averaging the ITFs, and the model was tested in the setting of hemodynamic instability (created by transient occlusion of the inferior vena cava). Pauca et al. showed that in elderly, hypertensive adults, the second systolic peak of the radial artery waveform was highly correlated with aortic systolic pressure.[72,81]

In an additional attempt to estimate central pressures without the use of a tonometer, Wassertheurer et al.[82] modified a conventional blood pressure cuff by adding a high-fidelity pressure sensor (Freescale MPX5050, Tempe, AZ). The increased accuracy of this modified cuff allowed Wassertheurer et al. to transform the brachial artery pressures to aortic pressures, using a frequency-based general transfer function similar to that developed by Karamanoglu et al. Indeed, the mean bias between the ARCSolver method, as it is known, and the technique of Karamanoglu et al. was 0.1 mm Hg (SD 3.1 mm Hg).[82]

Clinical Relevance

Transfer functions are currently used in at least 3 commercially available devices. The SphygmoCor device estimates

aortic blood pressures based on tonometric readings from the radial artery.[29] Clinical use of central pressure estimates has been almost exclusively the domain of the cardiologist[29,76]; however, a modification of the original SphygmoCor device (the SphygmoCor CPM) accepts input from a radial artery catheter and could potentially be used intraoperatively. The LiDCO monitor uses a transfer function to convert radial to aortic pressure (for which the cZ model is used to estimate SV). The NexFin HD (BMEYE, Amsterdam, The Netherlands) estimates SV based on transformed finger pressure readings (and the Modelflow technique, described above).[83] Advances in blood pressure cuff technology[82] may soon allow for an additional means by which central pressures can be estimated completely noninvasively.

The ability to accurately estimate central pressures in the intraoperative setting will allow anesthesiologists to determine whether monitoring central pressures (which more accurately estimate LV afterload and perfusion pressure to major organs) can improve clinical outcomes. In the meantime, it is worth noting that data from the SphygmoCor validation studies suggest that, for the purposes of assessing central systolic blood pressure, a standard sphygmomanometer cuff seems to be more accurate than a radial artery catheter.[29] Thus, the clinician interested in monitoring LV afterload may be well advised to continue taking periodic sphygmomanometric measurements even after placing a more invasive, peripheral monitor such as a radial artery catheter.

CONCLUSIONS

Peripheral dP/dt_{max} seems to be related to LV contractility, although the relationship may be confounded by other hemodynamic variables. SV estimates based on the AUC method have a significantly shorter response time than thermodilution-based techniques, but are burdened by relatively wide limits of agreement compared with thermodilution-based techniques, particularly when loading conditions change. Direct comparisons suggest that calibrated devices may better account for these changes than uncalibrated devices. Central pressures may provide more insight into LV afterload and into the perfusion pressure of vital organs than peripheral blood pressures. Central systolic pressure may be estimated using a sphygmomanometer. The mathematical techniques used to transform peripheral pressures into central pressures (and the accompanying limitations) are an essential component to several commercial devices designed to measure SV.

Arterial waveform analysis has provided the anesthesia community with a relatively noninvasive means of estimating ventricular contractility and SV on a beat-to-beat basis. Knowledge of the mathematical assumptions that are inherent in these approaches allows the anesthesia provider to more fully understand the advantages and limitations of this technology, and thus use it appropriately to improve patient care.

RECUSE NOTE

Marcel E. Durieux is Section Editor of Anesthetic Pre-Clinical Pharmacology for the Journal. This manuscript was handled by Dwayne R. Westenskow, Section Editor of Technology, Computing, and Simulation, and Dr. Durieux was not involved in any way with the editorial process or decision.

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