CME

Blood Pressure Monitoring for the Anesthesiologist: A Practical Review

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Periodic, quantitative measurement of blood pressure (BP) in humans, predating the era of evidence-based medicine by over a century, is a component of the American Society of Anesthesiologists standards for basic anesthetic monitoring and is a staple of anesthetic management worldwide. Adherence to traditional BP parameters complicates the ability of investigators to determine whether particular BP ranges confer any clinical benefits. The BP waveform is a complex amalgamation of both antegrade and retrograde (reflected) pressure waves and is affected by vascular compliance, distance from the left ventricle, and the 3D structure of the vascular tree. Although oscillometry is the standard method of measuring BP semicontinuously in anesthetized patients and is the primary form of measurement in >80% of general anesthetics, major shortcomings of oscillometry are its poor performance at the extremes and its lack of information concerning BP waveform. Although arterial catheterization remains the gold standard for accurate BP measurement, 2 classes of devices have been developed to noninvasively measure the BP waveform continuously, including tonometric and volume clamp devices. Described in terms of a feedback loop, control of BP requires measurement, an algorithm (usually human), and an intervention. This narrative review article discusses the details of BP measurement and the advantages and disadvantages of both noninvasive and invasive monitoring, as well as the principles and algorithms associated with each technique. (Anesth Analg 2016;122:1866–79)

The purpose of this narrative review[1] is to discuss the details of blood pressure (BP) measurement, including its history, the advantages and disadvantages of available noninvasive and invasive monitoring, the principles and algorithms associated with each technique, the engineering theories that describe how BP can be optimally managed, as well as available clinical data on BP management.

HISTORICAL INTRODUCTION

Qualitative analysis of the systemic arterial pulse BP waveform has been in practice for millennia, having been used by the Egyptians, Greeks, and Han Chinese.[2,3] Construction of a physiologic model that matched anatomic observations with clinical experience would not occur for another 15 centuries, beginning with Harvey's demonstration that arteries and veins exist in series. This discovery was followed by independent work by both Borelli and Hales examining the concept of arterial elasticity with dampened flow in the periphery.[4]

In 1733, Hales performed the first known direct measurement of arterial BP in a white mare. He inserted a brass tube into the horse's artery, affixing it to an approximately 3.5-m glass tube with the flexible trachea of a goose. The height of the column of blood reportedly rose 2.51 m (approximately 185 mm Hg). Hales noted BP oscillations in the column, corresponding with both ventricular heart rate and respiratory rate.[2,5] Over 100 years later, J. Faivre, a French surgeon, performed the first known direct measurement of arterial BP in a human, connecting the superficial femoral artery of an amputee directly to a manometer.[2,5] Although historically significant, Faivre's technique was clinically impractical at the time.

Because it required invasive arterial cannulation, direct measurement of arterial BP was typically performed only in the context of animal research until the mid-19th century. One hundred years after Hales' experiment, Jules Herrison produced the first noninvasive BP monitor, consisting of a mercury-filled bulb attached to a glass column. Application of the bulb to the radial artery at increasing pressures would eventually produce cessation of pulsatility in the fluid column, the point at which systolic pressure is estimated.[4] In 1855, Karl Vierordt developed the first prototype for the sphygmomanometer, using a lever and weight system attached to a recording arm to obliterate the pulse.[2] In 1860, Jules Maray developed a more accurate variation of this device. Although too cumbersome for clinical use, it was a major advance for BP research because investigators could accurately measure systolic and diastolic BP.[2]

In 1901, Theodore Janeway first published the suggestion that auscultation could be used to quantify arterial BP measurements: "… *certain experiments in a number of cases concerning the pressure tone and murmur in the brachial, to be described later, show that the production of the tone always occurs at a lower pressure than the point in question (disappearance of secondary waves) …. It is to be hoped that some more satisfactory method for estimating mean arterial pressure may yet be devised.*"[4] The ausculatory technique, as used today, would be reported 4 years later by a Russian surgeon, Nicolai Korotkov.[2,5] Used for decades, the Korotkov technique eventually adapted to the oscillometric technique, which allowed for the automated, noninvasive measurement of BP.

DOES BP MATTER?

Implicit in the inclusion of semiautomated BP measurements as a standard in the American Society of Anesthesiologists

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monitoring guidelines are the assumptions that BP is physiologically relevant and that deviation outside a particular range has clinical consequences.[a] Systemic BP provides the energy source required to transport oxygen and nutrients to cells and tissues, and it is worth asking whether there is a relationship between BP and cardiac output and/or organ-specific blood flow. Although the physiology of the cardiovascular system is complex, especially as it relates to autoregulation and what appears to be a blood flow hierarchy at the level of individual organs,[6,7] it is worth pointing out that in human beings undergoing general anesthesia, there is almost no relationship between mean arterial BP and delivery of oxygen (DO_2), presumably because of widely varying systemic vascular resistances[8] (Fig. 1). Furthermore, in organs that autoregulate (e.g., the brain), BP and organ-specific blood flow are clearly uncorrelated over a range of pressure.[9]

To our knowledge, there are no known prospective, randomized controlled trials comparing 2 different defined ranges of BPs in patients undergoing surgery and general anesthesia. There have been such studies in the context of BP management during cardiopulmonary bypass, which have indicated fewer neurologic and cardiac complications in patients managed with higher versus lower mean arterial BP goals (80–100 mm Hg versus 50–60 mm Hg[10] and 60–70 mm Hg versus 80–90 mm Hg[11]). In the critical care literature, the Sepsis and Mean Arterial Pressure (SEPSISPAM) trial randomly assigned septic patients to mean arterial pressure (MAP) 65 to 70 mm Hg (low-target group) and MAP 80 to 85 mm Hg (high-target group) and found no difference in the primary outcome (28-day mortality).[12]

BP has also been included as a component in some perioperative and critical care hemodynamic management protocols, most notably as a component of Rivers' Early Goal-Directed Therapy sepsis protocol, where a MAP ≥ 65 mm Hg was associated with a substantial reduction in mortality.[13] This observation was subsequently refuted by 3 larger, multicenter studies.[14–16] BP targets have been sparingly used as a part of intraoperative goal-directed therapy algorithms. In 2 meta-analyses of perioperative goal-directed therapy totaling 61 studies,[17,18] only 2 studies were identified, which used BP as a hemodynamic end point—one of which was negative.[19]

This is not to say that BP holds no clinical relevance. Indeed, because of its long history and relative ease of measurement, randomly assigning patients to what most would consider to be "low" BP may be a real challenge, especially considering varying patient populations. Thus, the question of how much hypotension is acceptable may never be answered in a prospective fashion, and large, complex trials may be required to begin answering this question in a rigorous fashion. In addition, there may be clinically significant differences related to how BP is maintained within a particular range (e.g., administration of fluid versus vasoactive agents). Vasoactive agents in particular have differing physiologic effects with, in some cases, significant clinical implications. A comprehensive review of fluid management strategies and detailed comparison of available vasoactive agents are beyond the scope of this review but are available elsewhere.[6,7,20,21]

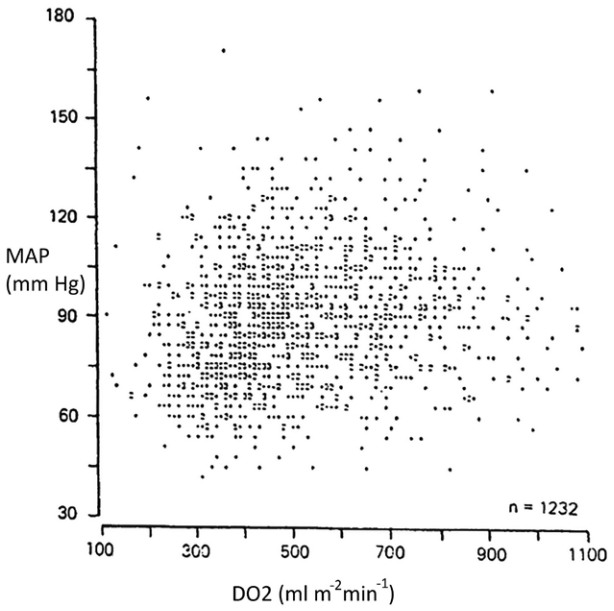

Figure 1. Correlation of O_2 delivery (DO_2) with mean arterial pressure (MAP) in the perioperative period in patients undergoing abdominal aortic surgery. Figure used with permission from Springer. Reinhart K. Zum Monitoring des Sauerstofftransportsystems. Der Anaesthesist 1988;37:1–9. © Springer - Verlag 1988.[8]

A retrospective analysis of 24,120 patients undergoing noncardiac anesthetics, the "Triple Low" study, investigated the impact of MAP, Bispectral Index score, and minimum alveolar concentration on 30-day mortality. It found that the relative risk of death for patients who had isolated low BP (defined as MAP < 81.7 mm Hg) was 0.729 (95% confidence interval [CI], 0.342–1.558).[22] However, in another large, single-center retrospective study of 33,330 noncardiac surgeries, a more conservative threshold to define hypotension (MAP < 55 mmHg), for even brief periods of time (1–5 minutes), was associated with increased relative risks of acute kidney injury (1.18 [95% CI, 1.06–1.31]) and myocardial injury (1.3 [95% CI, 1.06–1.5]).[23]

PHYSIOLOGIC BASIS OF SYSTEMIC ARTERIAL PRESSURE WAVEFORM

In subjects with normal body physiology, BP waveforms are produced by left ventricular contraction. Although the left ventricular pressure waveform may be relatively simple, the resultant peripheral pressure waveform is a function of distance from the aortic valve, compliance of the systemic arterial blood vessels, and geometric considerations (in particular, arterial diameter and arterial branch points).[3]

In the absence of disease, left ventricular pressure is transmitted directly to the ascending aorta during systole. Most of the ejected blood will pass through the aorta, which primarily serves as a conduit. Because the aorta is compliant, it expands as pressure rises, storing blood and ventricular energy, in the form of pressure, to be used during diastole. As systole comes to an end, ventricular pressure falls rapidly, and forward flow through the aortic valve diminishes. When the aortic valve closes and diastole begins, the left ventricle

[a]Available at: http://www.asahq.org/~/media/Sites/ASAHQ/Files/Public/Resources/standards-guidelines/standards-for-basic-anesthetic-monitoring.pdf. Accessed February 1, 2016.

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and ascending aorta are no longer hydraulically connected. Aortic pressure then becomes a function of the interaction between the compliant aorta, which expands and contracts, and the downstream arterial beds, which resist flow. This simplified model of aortic blood flow is known as the Windkessel model, developed by Otto Frank.[24–26] In what is referred to as the "two-element Windkessel model," the aorta behaves as a capacitor and the tissue beds as a resistor. Models of increasing complexity, which include inductance and aortic input impedance, have been developed.[27]

Although the Windkessel model was a major advance in our understanding of BP and hemodynamics, it is an oversimplification of reality and has shortcomings. One of the most relevant assumptions of this model is that the aorta is modeled as a single, infinitely long tube of consistent diameter and compliance. In reality, the aorta is finite, gradually branching off until becoming the left and right common iliac arteries. These major arteries lead to arterioles and the capillary bed, which, collectively, have a much larger cross-sectional area than the aorta and completely different mechanical properties.

Changes in aortic diameter (leading to changes in resistance) and compliance affect *impedance* or resistance to pulsatile flow. These impedance changes are mainly responsible for reflected pressure waves traveling backward, from the periphery toward the left ventricle.[28,29] Thus, the shape of the systemic arterial pressure waveform at any point along the arterial tree is a sum of the forward traveling (incident) wave, as well as any reflected waves (Fig. 2). Different arteries have different shapes, and these shapes change over time. As individuals age, and arterial compliance is diminished, the summation of forward and backward travelling waves leads to a gradual increase in pulse pressure in the direction of the periphery.

BP MONITORING TECHNOLOGY

Sphygmomanometry and Oscillometry

Sphygmomanometry

An understanding of the pulsatile nature of the systemic arterial blood stream, combined with previous efforts at estimating BP using primitive devices, allowed Korotkov to develop the auscultatory technique for BP measurement. Korotkov's major intellectual contribution to BP measurement was the recognition that the application of external pressure exceeding systolic BP would completely eliminate blood flow and that as this external pressure was gradually reduced, blood flow would return in a predictable manner.

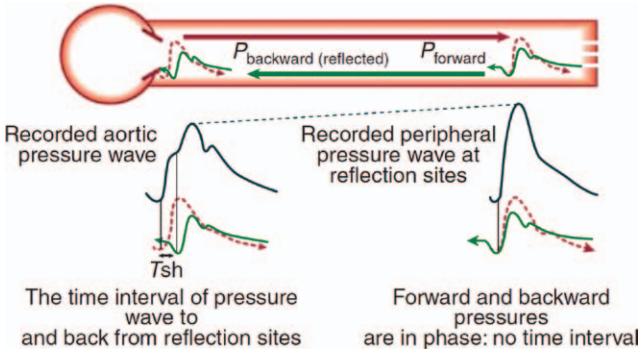

Figure 2. Representation of forward and reflected pressure wave travel and the influence of their timing and overlap on recorded aortic and peripheral pressure waves. Tsh = time to shoulder. Figure used with permission from Elsevier. Briet M, Boutouyrie P, Laurent S, London GM. Arterial stiffness and pulse pressure in CKD and ESRD. Kidney International 2012;82:388–400. © Elsevier 2012.[117]

The Korotkov technique required the use of both a sphygmomanometer (inflatable cuff with pressure gauge) and a stethoscope to link pressure changes with return of blood flow. A major disadvantage of this technique is that it requires enough blood flow to generate the turbulence needed to produce Korotkov sounds. In instances in which blood flow to an extremity may be compromised (e.g., central redistribution in the setting of shock), this technique may fail secondary to the inability to detect Korotkov sounds.[30] Furthermore, sphygmomanometry also requires that cuff inflation lead to arterial occlusion. In extremely large patients, or in those with excessively calcified (and rigid) arteries, this may not be possible. Despite these limitations, sphygmomanometry is generally accurate in relatively healthy, normal-sized patients.[31]

Unfortunately, sphygmomanometry is time consuming and labor intensive. Because it does not lend itself well to automation, semicontinuous measurement and use during anesthesia are impractical. It would not be until the development of oscillometry, a mechanical extension of sphygmomanometry, that automated, semicontinuous measurement of BP would be possible (Fig. 3).

Oscillometry

The concept of oscillometry was first developed by Marey[32] in mid-19th century. Sixteen years after first demonstrating the arterial "sphygmograph" in 1860, Marey conducted a series of experiments in which the forearm was placed in a water-filled chamber to which counterpressure was applied. This work formed the foundation for both the recognition that the magnitude of these pulsations could be used to approximate BP (oscillometric technique)[33–35] and the appreciation that a counterpressure waveform designed to perfectly eliminate the pulsatility of distal tissue bed could accurately reproduce the BP waveform (volume clamp technique).[36]

Unlike the auscultatory technique, in which the return of blood flow is detected *audibly*, the oscillometric technique measures the changes in cuff pressure that occur when blood flow returns during deflation. As demonstrated by Yelderman and Ream,[33] the amplitude of pressure changes detected in the cuff is near-maximal when the cuff is inflated at MAP. Systolic and diastolic pressures are estimated using proprietary algorithms unique to each manufacturer and should not be considered as accurate as MAP.[33,35,37]

Because the physical principles on which they are based are similar, the oscillometric technique suffers some of the same disadvantages as the auscultatory technique, including poor performance in larger patients and patients with calcified arteries, as well as in those with reduced blood flow. Because the oscillometric technique uses an inflatable cuff to both stop blood flow and detect return, proper cuff sizing is particularly important. In general, the cuff dimensions, indexed to arm circumference, should be 80% in length and 40% in width.[37] As might be expected, oscillometric measurements are site dependent.[38] Oscillometry is particularly challenging in neonates because of their small size (cuff sizing is crucially important) and artifacts associated with crying and moving. Furthermore, these devices may not be accurate in measuring BP in infants of low birth weight who are hypotensive.[39]

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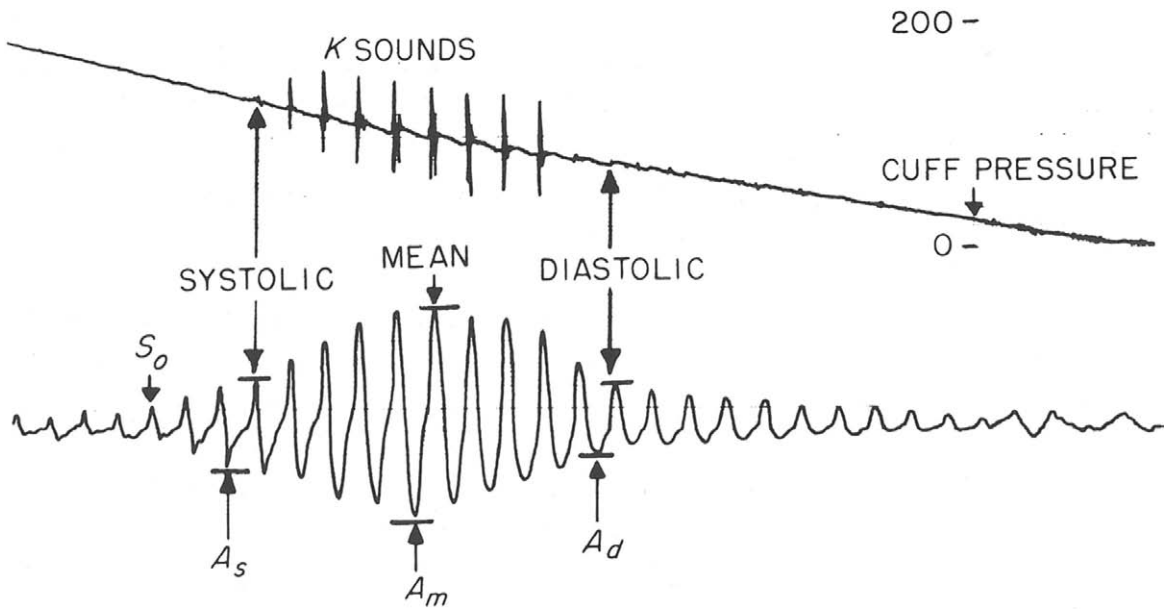

Figure 3. Cuff pressure with superimposed Korotkoff sounds and amplified cuff pressure oscillations. S_o is the point where cuff-pressure oscillations start to increase. A_s is the amplitude corresponding to auscultatory systolic pressure and A_d is the amplitude corresponding to auscultatory diastolic pressure. A_m is the maximum oscillation amplitude, which signals mean pressure. Figure used with permission from John Wiley & Sons, Inc., New York, NY. Geddes, LA. Cardiovascular Devices And Their Applications. Chapter 3, "Blood Pressure: Noninvasive Measurement", p 72. © John Wiley & Sons, Inc. 1984.[118]

Although oscillometry is typically performed in an automated fashion, it can be performed manually using a cuff and aneroid manometer—as cuff pressure drops below systolic BP, the needle will begin to oscillate with each pulsation, increasing in amplitude until MAP is approached and then diminishing toward diastole.

Accuracy

One of the largest comparisons of invasive to noninvasive BP measurements was made by Wax et al.,[40] who *retrospectively* compared BP from automated oscillometric readings with arterial BP readings derived from intravascular catheters in >15,000 noncardiac anesthetics. They found the SD of the difference between the 2 to be approximately ±12.5 mm Hg at an MAP of 75 mm Hg (which was the mode of the distribution). At the extremes (hypertension or hypotension), the SD worsened substantially, further weakening the utility of this ubiquitous (and American Society of Anesthesiologists standard) class of monitoring devices. In a meta-analysis of studies comparing commercially available noninvasive arterial BP measurements with invasive measurements, the overall random-effects pooled SD was 8.4 mm Hg for MAP for all devices. Of note, this pooled measure did not specifically isolate oscillometric devices.[41] A collection of 7 prospective studies comparing the oscillometric technique with invasive measurements of MAP is presented in Table 1.[33,42–47]

Tonometry

In search of a noninvasive mechanism by which BP waveforms (as opposed to numerical estimates) could be measured, O'Rourke et al.[48] developed the field of arterial tonometry. Tonometers "measure tone" by placing a sensor directly over an artery, just as an anesthesia provider might do when palpating the groin in search of a femoral pulse. Tonometers, such as the Sphygmocor (AtCor, Sydney, Australia), quantify and display this tactile information. The Sphygmocor device has been validated in >1600 patients (including >15,000 individual measurements), but because it requires unrestricted access to the wrist to apply a pen-like tonometric sensor, it is primarily used for research.[48]

In an effort to develop a more user-friendly and automated tonometer, Tensys Medical (Irvine, CA) affixed a tonometer to a locking clamp that stabilizes the tonometer over the radial artery in the wrist–the T-line®. Once affixed over the radial artery, it can periodically locate the ideal measuring point and adjust the tonometric pressure sensor. This feature allows the device to function with minimal operator intervention and is analogous to the development of the oscillometer (which made automated cuff-based BP measurements possible).

Several studies have compared invasive arterial measurements of mean arterial BP with estimates from a tonometer during general anesthesia and surgery. The median SD of the difference between the 2 is 6.3 mm Hg (range 4.8–12.6 mm Hg).[49–53] Assuming no bias, the limits of agreement are approximately ±12.4 mm Hg (range ±9.4 to ±24.7 mm Hg). In a meta-analysis of studies comparing commercially available noninvasive arterial BP measurements with invasive measurements, the overall random-effects pooled SD was 5.7 mm Hg for MAP using the T-line, slightly better than the 8.4 mm Hg reported for all noninvasive devices overall, suggesting that tonometric devices outperform oscillometric techniques.[41]

Pulse Wave Velocity

Pulse wave velocity (V) in an elastic tube is a function of elasticity (E), diameter (D), wall thickness (h), and fluid density (ρ).[54,55] Mathematically this is known as the Moens-Korteweg equation[4]:

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

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Table 1. Mean Arterial Blood Pressure Measured by Intraarterial Versus Oscillometric Technique

Study	Population	Device	Bias, mm Hg	SD (95% CI), mm Hg
Heard et al. (2000)[42]	Intensive care unit patients requiring intraarterial monitoring (n = 28)	Dinamap, Critikon, Tampa Bay, FL	−1.3	6.3 (−17.7 to 13.7)
Yelderman and Ream (1979)[33]	Patients undergoing open heart surgery (n = 19)	12 or 13-cm cuff applied above brachial artery and calibrated using mercury manometer	1.4	6.22 (−4.1 to 11.7)
Borow and Newburger (1982)[43]	Patients undergoing cardiac catheterization (n = 30)	Dinamap	−3.5	4.9 (−13.1 to 6.1)
Loubser (1986)[44]	Hypertensive post-carotid endarterectomy patients (n = 30)	Dinamap	0.26	Not reported
Gravlee and Brockschmidt (1990)[45]	Adults undergoing cardiac surgery (n = 38)	Dinamap	6	8 (−9.68 to 21.7)
Gorback et al. (1991)[46]	Patients requiring intraarterial monitoring (n = 32)	Dinamap	−1.8	9.7 (−20.8 to 17.2)
Manolio et al. (1988)[47]	Patients undergoing vascular or other major surgery (n = 14)	Dinamap	2.9	1.7 (−0.4 to 6.2)

Comparison studies of intraarterial blood pressure versus blood pressure measured using oscillometric technology. If either 95% CI or SD were not reported, the missing values were calculated using the formula CI = Bias ± 1.96 × SD. Bias was recalculated from the published data as necessary to standardize: Bias = $MAP_{oscillometric} - MAP_{intraarterial}$ for all studies reported.
CI = confidence interval; MAP = mean arterial blood pressure.

In theory, changes in vascular tone should lead to changes in pulse wave velocity, calculated as the time between an R wave on the electrocardiogram and the appearance of a peripheral pulse waveform (detected by a photoplethysmogram [PPG] or an invasive arterial pressure tracing) divided by the distance between the heart and the site of measurement. In situations in which cardiac output is relatively constant, changes in vascular tone will lead to changes in BP. Thus, in theory, pulse wave velocity (or pulse transit time [PTT]) may give some indication of BP.

In one early study, PPG-based PTT was successfully used to estimate BP in patients undergoing general anesthesia[56]; however, a larger, multicenter study conducted 5 years later refuted these findings.[57] There are several reasons why PTT alone will not likely lead the clinician to absolute measures of BP. First, several of the individual components of the Moens-Korteweg equation (E, h, D) are not typically known for individuals. Second, the Moens-Korteweg equation neglects the viscous properties of blood-filled arteries, whose behavior can best be described as viscoelastic.[58] Third, cardiac output is not stable in individuals and is widely variant between them. For these reasons, PTT is more likely to achieve success as a trend monitor valid over short time periods.

Indeed, PPG-PTT was recently used to detect changes in BP during induction of both general and neuraxial anesthesia.[59,60] Although more studies are needed, the rapid response of these noninvasive monitors is encouraging and suggests they may be useful for alerting the clinician to probable hemodynamic changes before they might be detected using automated oscillometric techniques.

Volume Clamp Technique

As described earlier, Marey's work applying counterpressure to a submerged forearm formed the foundation for the volume clamp technique, which was formally developed by Peñáz,[36] a Czech physiologist.[61] Peñáz' major advance was to connect a pressure cuff (on the finger) to a distally placed PPG recorder using a feedback loop, which produced ultrafast adjustments in bladder pressure in response to changes in the PPG signal. To maintain a perfectly flat PPG waveform, increasing cuff pressure is applied in response to increasing peripheral artery pressure. Conversely, decreasing cuff pressure is applied in response to decreasing peripheral artery pressure. The cuff pressure waveform required to maintain a flat PPG waveform closely approximates the systemic arterial pressure waveform.[62]

Although a control loop modifying finger bladder pressure in response to changes in a PPG tracing can estimate the shape of a peripheral arterial pressure waveform (i.e., measuring the *qualitative* aspects of the systemic arterial BP tracing), more work is needed to provide *quantitative* measures of systolic, diastolic, and MAPs. Again, previously established principles are helpful. Yelderman and Ream[33] demonstrated that the amplitude of pressure changes detected in a BP cuff is near-maximal when the cuff is inflated at or near MAP. By measuring the amplitude of the PPG waveform distal to a finger cuff while applying a *constant* pressure to the finger cuff, then changing the pressure in either direction such that the amplitude of the PPG waveform is maximal, MAP can be estimated.

Because MAP changes over time, volume clamp BP monitors have to periodically recalibrate themselves to reidentify MAP. When an external pressure cuff reaches MAP, the arterial wall stress is minimized, and the artery beneath the cuff is said to exist in an "unloaded" or "unstretched" state. As external pressure decreases, the forces intrinsic to the arterial wall take over the pressure "load," gradually increasing the arterial wall stress required to maintain vessel shape.[63,64] To keep the underlying artery in an unstretched state, volume clamp devices modify cuff pressure periodically, analyzing the PPG to identify the pressure needed to produce an unstretched artery (i.e., the point at which PPG amplitude is maximal). Wesseling combined the volume clamp technique with Peñáz' feedback loop, producing the Finapres™ (Finapres Medical Systems BV, Amsterdam, The Netherlands) device.[63,65,66]

Modern volume clamp BP monitors use slightly different techniques to achieve vascular unloading. The ClearSight™ (Edwards Lifesciences, Irvine, CA) device, which was developed as the Nexfin® (BMEYE, Amsterdam, The Netherlands) device, is a direct extension of Wesseling's Finapres device and the "Physiocal" (physiologic calibration) algorithm to

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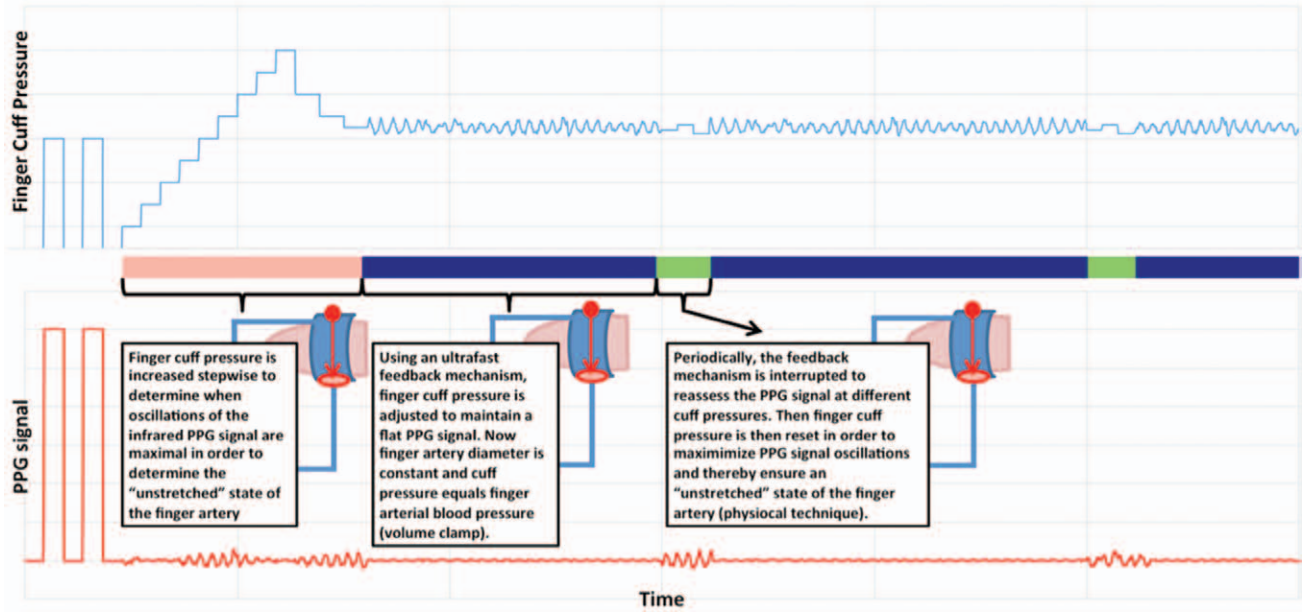

Figure 4. Finger blood pressure measurement using photoplethysmography using the volume -clamp and physiocal approaches. Figure used with permission from Springer. Bartels K, Thiele RH. Advances in photoplethysmography: beyond arterial oxygen saturation. Can J of Anaesth 2015;62:1313–28. © Springer 2015.[68]

achieve vascular unloading. The Physiocal strategy induces periodic, stepwise bladder pressure changes and simultaneously reanalyzes the PPG waveforms. If alternate pressure settings result in larger PPG amplitudes, the feedback set point is adjusted to ensure a maximally unloaded state of the finger artery[63] (Fig. 4).

The Continuous Noninvasive Arterial Pressure (CNAP®; CNSystems, Graz, Austria) device uses the "Vasomotoric Elimination and Reconstructed IdentiFication of the Initial set point" (VERIFI) algorithm to unload peripheral arteries, coupled with an upper arm oscillometric BP monitor for calibration. The CNAP is designed to account for the fact that no feedback mechanism can be completely instantaneous (thus introducing error because of the time lag between the cuff and the PPG signal detector).[b] To generate an initial BP measurement and identify the "set point," the VERIFI algorithm relies on a brachial artery cuff–Noninvasive Blood Pressure (NIBP). The volume clamp (finger bladder) is still used to approximate the BP waveform by maintaining constant blood volume as a function of time, V(t). However, the VERIFI algorithm uses a different set point calibration strategy than the Physiocal solution.[67]

Like musical notes, physiologic waveforms (e.g., BP) can be described as the sum of a series of sine waves, each with its own amplitude, frequency, and phase shift. The dominant waveforms, whose frequencies center around multiples of the fundamental frequency, are known as "harmonics."[3] The VERIFI algorithm decomposes the volume signal, V(t), into frequency components using frequency domain analysis (e.g., Fourier transformation). Pulsatile volume, $V_{AC}(t)$, low frequency volume, $V_{LF}(t)$, and very low frequency volume, $V_{VLF}(t)$, are isolated. Because volume changes are a function of pressure changes, volume and pressure can be related to each other by the degree of amplification, also known as "gain" (G, analogous to the resistance in Ohm's law). Gain is assumed to be zero at very low frequencies, but at the "pulsatile" and low frequencies (G_{AC}, G_{LV}, respectively) can be determined by comparing various fixed cuff pressures to the signal amplitude and developing a transfer function (T) relating the 2 (Fig. 5).[67] For a comparison of the features of the Nexfin/ClearSight and CNAP devices, see Table 2.[68]

Clinical Considerations and Accuracy

As with sphygmomanometry and oscillometry, volume clamp devices require peripheral perfusion and blood flow to estimate BP. In theory, just as the pulse oximetry waveform (which is derived from both red and infrared PPG signals) is affected by extreme vasoconstriction, temperature changes, and other physiologic disturbances, the same should be true of volume clamp estimates of BP.

The impact of vasomotor tone on this class of devices has been studied. An early analysis of the Finapres device during surgery found that half of the measurements were conducted in a state of vasoconstriction (defined as a PPG amplitude reduction of at least 50% [PPG amplitude is generally considered an acceptable surrogate measure for vasomotor tone[69]]). This small study, in which 378 paired measurements were made in 6 subjects, suggested that the discrepancy between volume clamp and oscillometric devices was dependent on peripheral perfusion.[70] Interestingly, a direct comparison between the Finapres and the invasive measurements suggests that the thumb is the optimal site for finger arterial BP measurements, presumably because of the larger arterial cross-sectional area and better perfusion.[71]

In a meta-analysis of studies comparing commercially available noninvasive arterial BP measurements with invasive measurements, the overall random-effects pooled SD was 9.4 mm Hg for MAP using the CNAP, slightly worse than the 8.4 mm Hg reported for all noninvasive devices overall.[41] This study

[b]Available at: http://www.cnsystems.com/Innovation/Cnap-Technology. Accessed February 1, 2016.

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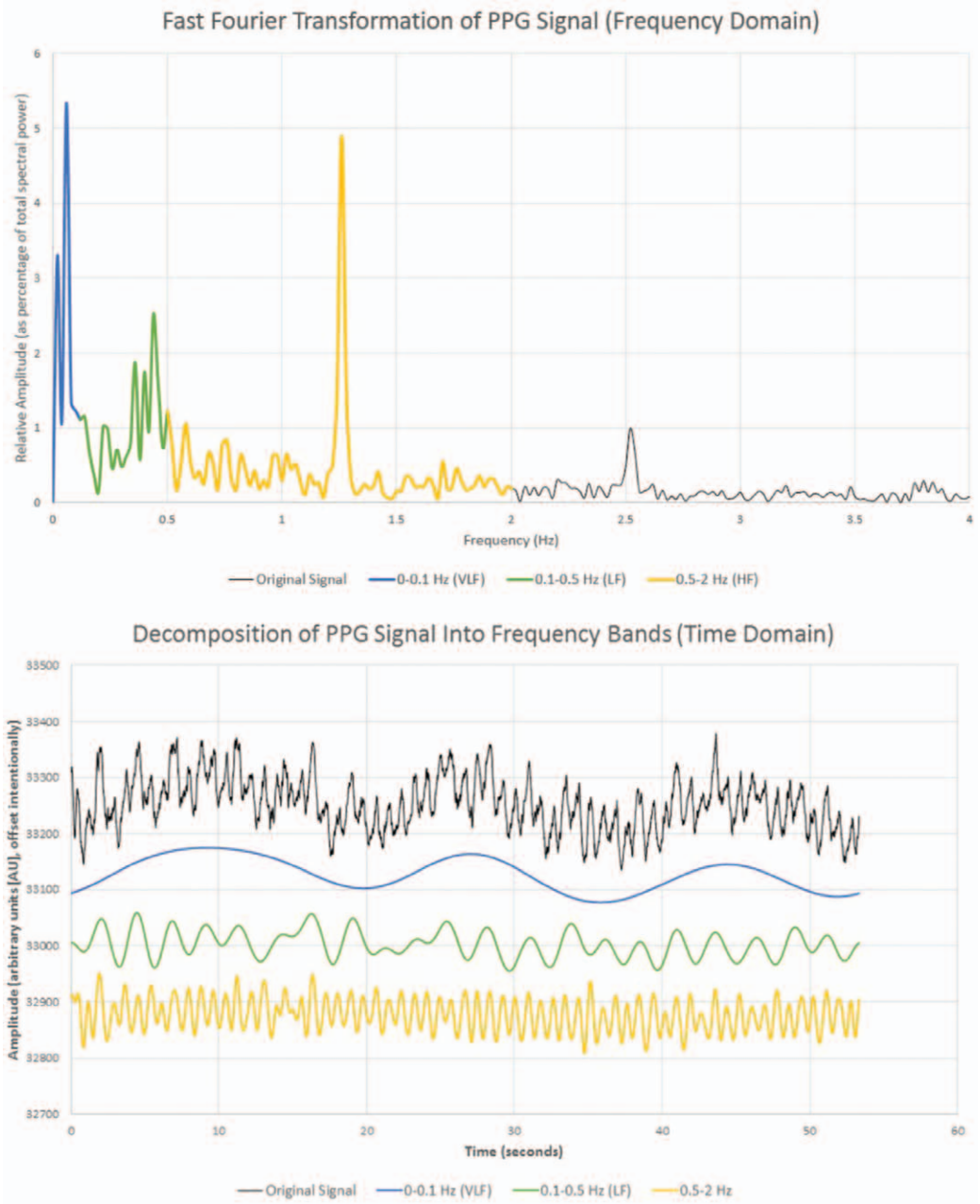

Figure 5. Decomposition of a standard pulse oximetry signal into three bands: a very low frequency band (0-0.1 Hz), a low frequency band (0.1-0.5 Hz), and a pulsatile band (0.5-2 Hz). Figure used with permission from Springer. Bartels K, Thiele RH. Advances in photoplethysmography: beyond arterial oxygen saturation. Can J Anaesth 2015;62:1313–28. © Springer 2015.[68]

did not specifically analyze data for the Nexfin or ClearSight devices. Because a true gold standard is readily available (direct arterial catheterization), volume clamp devices will always be *less* accurate than the gold standard. The important clinical question is how well the volume clamp devices agree with direct catheterization, and how this compares with other noninvasive devices (e.g., oscillometry). However, as examined in an aforementioned study comparing oscillometry and direct arterial catheterizations, as the true BP deviated from the mode, oscillometric performance deteriorated, particularly at the extremes (hypertension, hypotension) when accurate measurements matter the most.[40]

There have been multiple comparisons of volume clamp devices with direct arterial catheterization. Because this body of work spans several decades, not all of them use the same statistical techniques. More modern studies use the limits-of-agreement approach. Overall, these data suggest performance that is at least comparable to oscillometric techniques, although there are no large, retrospective comparisons available to validate the prospective observations in the real-world clinical environment (Table 3).[72–96]

Arterial Catheterization

Background

In addition to giving the clinician a near-instantaneous measurement of systolic, diastolic, and MAPs, arterial catheterization also allows for convenient, periodic blood sampling

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Table 2. Comparison of Nexfin to CNAP Volume Clamp Devices

Characteristic	CNAP	Nexfin/ClearSight
Fingers used	2	1–2
Algorithm to continuously recalibrate blood pressure (account for changes in vasomotor tone)	VERIFI	Physiocal
Algorithm for stroke volume	Pulse contour analysis using CNCO algorithm and biometric or manual calibration	Pulse contour analysis and biometric calibration

Comparison of Nexfin to CNAP Volume Clamp Devices for the continuous measurement of both blood pressure and stroke volume. Note that while both devices rely on the volume clamp technique, they employ different algorithms to consistently measure blood pressure in the setting of changing vascular tone and apply different arterial waveform analysis algorithms for the estimation of stroke volume.

CNAP = continuous noninvasive arterial pressure; CNCO = continuous noninvasive cardiac output; VERIFI = Vasomotoric Elimination and Reconstructed IdentiFication of the Initial set point.

(e.g., for the measurement of arterial blood gases). Analysis of >12,000 surgical cases at an Academic Medical Center in the United States revealed that 16% of patients were monitored with an arterial catheter.[97] By 1990, >8 million had been placed.[98]

A variety of algorithms designed to measure stroke volume (SV) and fluid responsiveness (e.g., pulse pressure variation, SV variation) based on sophisticated analysis of the arterial waveform have been developed.[99] Until the appearance of the volume clamp technique devices on the market, noninvasive estimates of SV, pulse pressure variation, and SV variation required placement of an intraarterial catheter. Now, with the availability of the ClearSight and the CNAP, the same algorithms can be applied to an arterial pressure waveform derived from the volume clamp technique. At present, there are insufficient clinical data to comment on the relative accuracy of noninvasive SV derived from directly or indirectly measured arterial pressure waveforms.

That said, volume clamp devices, which seem to outperform automated oscillometric techniques in terms of accuracy and measurement frequency, may one day change the anesthesiologist's decision-making process with regard to BP monitoring.[100] This is particularly important, as the complications associated with percutaneous cannulation of a systemic artery, including infection, pseudoaneurysm formation, nerve injury, permanent arterial occlusion, or hematoma formation, are increasingly appreciated.[101–103]

Arterial BP is most commonly measured at the radial, brachial (or axillary), and femoral sites, with the radial being most common.[103] As described earlier, the BP waveform is a function of both incident and reflected waves and is dependent on arterial compliance, branch points, and distance from the left ventricle. Thus, different arteries produce different BP tracings within the same individual.

Procedure

Arterial cannulation can be performed using a variety of techniques. The simplest strategy is to insert a 20-gauge (or smaller) catheter directly into the artery and "thread" the catheter off a needle and into the artery. Some clinicians prefer to "transfix" the artery with a needle and catheter, remove the needle, and retract the catheter backward until it resides in the vessel lumen, after which a guidewire can be inserted through the catheter and into the artery. For particularly challenging patients, the Seldinger technique can be used, in which a needle is inserted into the vessel, a guidewire is threaded through the needle and into the vessel, the needle is removed, and the catheter is threaded into the vessel (over the wire). Identification of the artery may be facilitated by using ultrasound guidance.[104] A meta-analysis of 7 trials including 482 patients suggested that ultrasound-guided radial artery cannulation increased the first-attempt success rate, as well as decreasing the number of attempts, time to success, and rate of hematoma formation.[105]

Some clinicians use the "Allen test" to evaluate collateral flow to the hand before cannulating the radial artery. This test is performed by occluding arterial inflow into the hand (by compressing both the radial and the ulnar arteries simultaneously) while asking the patient to create a fist, thereby exsanguinating the palm. After opening the hand and releasing the pressure over the ulnar artery (but maintaining pressure over the radial artery), a qualitative sense of the adequacy of ulnar flow can be gained by observing how quickly the palm returns to color. Although the Allen test seems logical, it is not clear that reason and reality have aligned, because large analyses including several thousand patients have questioned the predictive ability of the Allen test.[106,107] Furthermore, it is now appreciated that the radial artery can often be harvested for coronary bypass surgery, despite an abnormal Allen test, and this has prompted some investigators to look for alternative testing modalities.[108,109]

Equipment

Intraarterial pressure is measured using a strain gauge, the essential component of which is a thin metal wire whose resistive properties change as it is stressed. By building strain gauges into a Wheatstone bridge circuit, changes in strain can be measured as electrical current through the bridge fluctuates. These changes in current can be translated into pressure changes by "zeroing" the transducer. Importantly, current intraarterial pressure monitors measure the pressure of a fluid-filled column that is in hydrostatic continuity with the blood stream. Thus, the physical attributes of the measuring system—in particular, the length, diameter, and stiffness of tubing—can potentially affect the measured BP waveform.

The fluid-filled transduction systems that are commonly used to transmit intravascular pressure changes to a Wheatstone bridge strain gauge can be described as "underdampened, second-order dynamic systems."[110] Three parameters define the performance characteristics of these systems: mass (of fluid), elasticity (of tubing), and friction (primarily between the fluid and the tubing). Every fluid-filled tubing system has a *natural frequency* (f_n), that is, a frequency at which a pressure pulse will oscillate within the system, and a *damping coefficient* (ζ), a measure of how quickly an oscillating waveform will decay. Fluid-filled transduction systems are "underdampened" because a pressure pulse will oscillate at the natural frequency of the system before decay. Rigid, short, narrow diameter tubing more rapidly transmits pressure waveforms, effectively

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Table 3. Mean Arterial Blood Pressure Measured by Volume Clamp (ClearSight/Nexfin or CNAP) Versus Intraarterial Technique

Study	Patient population	Device	Bias, mm Hg	SD (95% CI), mm Hg
Stover et al. (2009)[72]	Critically ill (n = 10)	Nexfin	2	8 (−13.7 to 17.7)
Biais et al. (2010)[73]	Major vascular surgery (n = 25)	CNAP	1.8	10.3 (−18.4 to 22)
Hofhuizen et al. (2010)[74]	Pediatric congenital heart surgery (n = 10)	Nexfin	0.19	2.7 (−5.1 to 5.5)
Jeleazcov et al. (2010)[75]	Elective abdominal surgery, cardiosurgery, or neurosurgery (n = 88)	CNAP	1.6	11 (−20 to 23.2)
Martina et al. (2010)[76]	Cardiopulmonary bypass (n = 18)	Nexfin	−1.3	6.5 (−14 to 11.4)
Schramm et al. (2011)[77]	Transfemoral aortic valve implantation with sedation (n = 29)	CNAP	−0.8	15 (−30.2 to 28.6)
Fischer et al. (2012)[78]	Post-cardiac surgery intensive care (n = 44)	Nexfin	4.6	6.5 (−8.1 to 17.3)
Garnier et al. (2012)[79]	Pediatric intensive care (n = 41)	Nexfin	−2.6	7.7 (−17.7 to 12.5)
Hahn et al. (2012)[80]	Elective surgery with general anesthesia (n = 100)	CNAP		
		50 patients with standard software	2.9	10.6 (−17.9 to 23.7)
		50 patients with modified software	3.1	9.5 (−15.4 to 21.6)
Ilies et al. (2012)[81]	Surgery with general anesthesia (n = 85)	CNAP		
		Induction of anesthesia	10.2	11.3 (−10.8 to 32.3)
		Maintenance of anesthesia	4.3	10.4 (−16.1 to 24.7)
Jagadeesh et al. (2012)[82]	Cardiac surgical intensive care (n = 30)	CNAP	−0.04	2.05 (−4.1 to 4)
Martina et al. (2012)[83]	Cardiac surgery (n = 50)	Nexfin	2.2	6.4 (−10.3 to 14.7)
Broch et al. (2013)[84]	Cardiac surgery (n = 50)	*Nexfin versus femoral*		
		Pre-CPB	6.2	11.7 (−16.7 to 29.2)
		Post-CPB	9.7	11 (−11.9 to 31.3)
		Nexfin versus radial		
		Pre-CPB	10.9	13 (−14.6 to 36.5)
		Post-CPB	13.5	11.3 (−8.6 to 35.7)
Dewhirst et al. (2013)[85]	Pediatric surgery in the prone position (n = 20)	CNAP	−0.26	6.1 (−12.18 to 11.67)
Gayat et al. (2013)[86]	Surgery with general anesthesia (n= 52)	CNAP	8	14 (−18 to 35)
Hohn et al. (2013)[87]	Critically ill surgical (n = 25)	Nexfin	6	12 (−18 to 30)
Schramm et al. (2013)[89]	Elective transfemoral aortic valve implantation with monitored anesthesia care (n = 33)	CNAP	4	11.3 (−26.1 to 18.1)
Ameloot et al. (2014)[90]	Critically ill (n = 45)	Nexfin	2.3	12.4 (−22 to 26.6)
Ilies et al. (2015)[91]	Cardiovascular surgical critical care (n = 104)	CNAP	6.1	7.6 (−10.1 to 22.4)
Kumar et al. (2015)[92]	Cardiac surgery (n = 60)	CNAP	0.02	5.68 (−11.12 to 11.17)
Tobias et al. (2014)[93]	Severely obese adolescents and young adults undergoing weight loss surgery (n = 18)	CNAP	0.6	8.6 (−16.2 to 17.4)
Vos et al. (2014)[94]	Elective general surgery (n = 110)	Nexfin	2	9 (−15 to 19)
Wagner et al. (2015)[95]	Intensive care unit (n = 38)	CNAP	1	9 (−16 to 19)
Weiss et al. (2014)[96]	Elective surgery (n = 31) 11 time points	Nexfin		
		T-1 (n = 31)	7	14 (−21 to 34)
		T0 (n = 31)	7	16 (−24 to 38)
		T1 (n = 31)	7	14 (−21 to 35)
		T2 (n = 31)	7	17 (−26 to 40)
		T3 (n = 31)	5	12 (−18 to 29)
		T4 (n = 31)	7	11 (−15 to 30)
		T5 (n = 31)	8	12 (−15 to 31)
		T6 (n = 30)	8	13 (−18 to 34)
		T7 (n = 26)	9	15 (−20 to 39)
		T8 (n = 26)	8	13 (−17 to 33)
		T9 (n = 26)	9	17 (−24 to 41)

CI = confidence interval; CNAP = Continuous Noninvasive Arterial Pressure; MAP = mean arterial blood pressure.

Comparison studies of intraarterial blood pressure versus blood pressure measured using volume clamp technology (ClearSight/Nexfin or CNAP). If either 95% CI or SD were not reported, the missing values were calculated using the formula CI = Bias ± 1.96 × SD. Bias was recalculated from the published data as necessary to standardize: Bias = $MAP_{volume\ clamp} - MAP_{intraarterial}$ for all studies reported.

increasing the natural frequency. Dampening is a function of energy loss, which occurs primarily because of friction. Air bubbles, tubing kinks, stopcocks, and other irregularities can alter the physical characteristics of the tubing system and distort the recorded waveform.

Depending on the complexity of the BP waveform, as many as 10 harmonics may be required to accurately reproduce the BP.[3,110] Because the human heart rate is approximately 1 to 2 Hz (60–120 beats/min), higher-order harmonics may approach 20 Hz in frequency. To faithfully reproduce these higher-order harmonics, a natural frequency as high as 40 Hz is needed. The natural frequency of systems used clinically can be considerably lower than this.[111]

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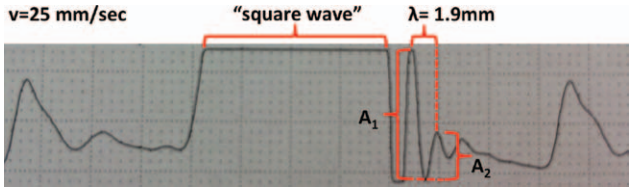

Figure 6. Flush test. The natural frequency (fn) is the frequency at which the pressure pulse will oscillate within the system and can be calculated from: fn = v/λ. The damping coefficient (ζ) is a measure of how quickly an oscillating waveform will decay and is dependent on the ratio of successive amplitude ratios (e.g. A1/A2).[110]

Thus, waveform distortion is a function of both f_n, and ζ, as well as the complexity and component frequencies of the pressure waveform (with more complex, higher-frequency waveforms being more prone to distortion). Acceptable combinations of f_n and ζ, which lead to accurately reproduced waveforms, are referred to as having adequate dynamic response. To assess f_n and ζ, the "flush test" can be used. Rapid introduction and removal of a high-pressure pulse (known in engineering lexicon as a "square wave") into the transducing system will lead to a characteristic, oscillatory waveform that reverberates at f_n and diminishes over time in accordance with ζ (Fig. 6).

Interpretation

Measurement of intraarterial BP is relatively straightforward if the aforementioned principles on which the measurement system is based are understood. One common mistake is to attribute high systolic BPs to "whip" or an under-responsive system. Although it is possible for an under-responsive system to augment pulse pressure (thus raising systolic pressure and lowering diastolic pressure), this theory can be tested by performing a flush test, measuring both assess f_n and ζ and plotting the performance characteristics of the transduction system on a dynamic response map. In reality, it is *normal* for pulse pressure to increase as the measurement site moves distally, particularly in patients with noncompliant vasculature. This widened pulse pressure should initially be assumed to be real and only attributed to suboptimal equipment after a determination of both f_n and ζ has been made.

The BP waveform can be mathematically decomposed into a series of sine waves, each described by their amplitude, frequency, and phase shift. This is accomplished using a computational technique called "fast Fourier transformation." The fundamental frequency of the BP waveform is the heart rate (for a heart rate of 80 beats per minute, the fundamental frequency is 1.33 Hz or 1.33 beats per second). When "harmonic" waves are added to the fundamental wave, the true shape of the waveform is more accurately approximated.

Complications

Although pseudoaneurysm formation, nerve injury, permanent arterial occlusion, and hematoma formation are known complications of intraarterial catheterization, the risk of infection is increasingly appreciated.[101–103] An analysis of over 200 published studies on infectious complications associated with intravascular devices estimates an infection rate of 1.7 per 1000 catheter-days for arterial catheters, when compared with 0.5 per 1000 for peripheral IV catheters and 2.7 per 1000 for nontunneled central venous catheters.[102] A large, factorial trial analyzing the impact of dressing changes and chlorhexidine-impregnated sponge use on both central venous *and* arterial catheters demonstrated a substantially lower rate of bloodstream infections (hazard ratio, 0.39; 95% CI, 0.17–0.93), suggesting that these devices should be placed on all arterial catheters.[112]

FEEDBACK LOOPS, GAIN, AND BP CONTROL

Assuming that anesthesiologists desire to maintain BP within some prespecified range, a feedback loop must be established among the patient, the BP monitor, and the anesthesiologist. Feedback loops are well described in the engineering literature.[113] A rudimentary feedback loop consists of a measurable variable (e.g., temperature), a method of measurement (e.g., thermometer), and a response (e.g., heating or cooling). The "set point" is the ideal value for the measured variable (e.g., 37°C). In the simplest feedback loop, the response is linearly related to the difference between the measured *process variable* and the set point. The magnitude of the response, indexed to this difference (known as an *error value*), is known as *gain*. This type of system is often referred to as a proportional–integral–derivative controller.

In real life, there is often a time delay associated with the detection of an abnormality both in the measured variable and in the response (known as *response time*). In a fairly stable system with minimal response time, large amounts of gain can exert substantial control over the measured variable. However, if the response time is long (either because there is measurement delay or it takes time to affect the measured variable [e.g., application of heat to a cold patient]), it is possible for the system to be overgained, a situation in which an overly aggressive response destabilizes the system. Conversely, an undergained system may never exert control of the measured variable because the response is not effective enough. Ultimately, the stability of a simplified feedback loop system is a function of the inherent variability in the measured variable, response time, and gain.

Although, on the surface, this may seem to have only academic value, a thorough understanding of feedback loops is of great relevance to the anesthesiologist. For instance, an anesthesiologist who only administers 5-μg doses of phenylephrine may never be able to exert meaningful control over BP (nor will the anesthesiologist who administers 500 μg at a time). Similarly, BP stability is more easily achieved when near-instantaneous measures are used, as opposed to an oscillometric cuff that makes periodic measurements every 5 minutes. Also important is an appreciation for the lag time associated with these interventions; phenylephrine, for instance, takes 42 seconds to achieve peak effect.[114] Appreciation for these basic engineering principles among anesthesiologists is not widespread, and they are not part of the American Board of Anesthesiology content outline. Nonetheless, basic instruction on the principles of feedback loops may be a high-yield endeavor for anesthesiology trainees.

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Investigators at the University of California, Irvine, have taken the concept of feedback loops one step further and are attempting to "close the loop" using algorithms, which mimic the decision-making process used by individual anesthesiologists. The basic argument for this approach is that if some aspects of hemodynamic management can be easily standardized (e.g., giving IV fluid based on preestablished triggers), an automated feedback system that constantly monitors the measured variable (in this case, BP) will outperform a human being by minimizing response time, in addition to freeing up the anesthesiologist to focus on more cognitively challenging tasks. Preliminary work by this group has demonstrated feasibility and safety, but prospective comparisons between traditional, human-directed hemodynamic management and closed-loop hemodynamic management have yet to be undertaken.[115,116]

CONCLUSIONS

Periodic, quantitative measurement of BP in humans, predating the era of evidence-based medicine by over a century, is a component of the American Society of Anesthesiologists standards for basic anesthetic monitoring and is a staple of anesthetic management worldwide. Thus, it is unlikely that the clinical value of BP monitoring will ever be assessed in prospective fashion. Furthermore, adherence to traditional BP parameters complicates the ability of investigators to determine whether particular BP ranges confer any clinical benefits. The BP waveform is a complex amalgamation of both antegrade and retrograde (reflected) pressure waves and is affected by vascular compliance, distance from the left ventricle, and the 3D structure of the vascular tree. Accurate reproduction of this waveform requires an appropriately engineered monitoring system with a frequency response of up to 40 Hz. Oscillometry is the standard method of measuring BP semicontinuously in anesthetized patients and is the primary form of measurement in >80% of general anesthetics. Although these devices perform reasonably well when true MAP is approximately 75 mm Hg, a major shortcoming of oscillometry is its poor performance at the extremes. Another shortcoming of these devices is that they offer no information about the shape of the BP waveform. Two classes of devices have been developed to measure the BP waveform continuously, without requiring the placement of a catheter. Tonometric devices "touch" the radial artery by applying external pressure to the wrist. Volume clamp devices combine a rapidly responsive finger cuff to a finger plethysmograph in an effort to keep the radial artery in an "unstretched" state and the PPG flat; the finger cuff pressure required to do so closely approximates the radial artery pressure. The limits-of-agreement analyses of the latter 2 device classes using invasive measures as a reference standard are promising. Arterial catheterization remains the gold standard for accurate BP measurement, and understanding the measurement system is necessary for proper interpretation of the waveforms. In particular, the frequency response and damping coefficient of the fluid-filled tubing system can be used to measure the dynamic response of the system, and thus its adequacy for the accurate reproduction of complex waveforms. Fortunately, both the frequency response and the damping coefficient can be measured at the bedside using the flush test. Control of BP requires measurement, an algorithm (usually human-controlled) and an intervention. This can be described as a feedback loop, of which gain and response times are important variables that affect the stability of the measured variable (in this case, BP). Several investigators have begun "closing" this loop, effectively automating the human algorithms used to manage BP, allowing the anesthesia providers to focus their intellectual energy on other, more complex decisions and tasks.

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