Blood Pressure Measurement Methodologies: Present Status and Future Prospects

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Abstract

The seminal advances of Riva Rocci made by introducing a brachial cuff with peripheral palpation, and of Korotkoff by auscultation of sounds associated with changes in arterial blood flow due to cuff pressure, have been the lynchpin of non-invasive measurement of blood pressure. Non-invasive quantification of blood pressure of the brachial artery has utility in risk prediction and hypertension management, despite inherent inaccuracies in the method, that an individual does not have a single blood pressure but a variability in blood pressure reflecting diurnal rhythm and physiological responses to daily life, and that brachial artery pressure may not be the precise pressure seen by the heart, kidney, and brain. This article discusses the inherent limitations of blood pressure measurement, the site of measurement, and currently largely ignored technical issues such as traceable calibration of blood pressure devices. The improvements in temporal resolution of blood pressure measurement with cuffless measurement of blood pressure are highlighted with the challenges of these techniques discussed. The future challenges are to obtain reliable continuous blood pressure measurements to quantify risk not only on blood pressure values but also on the entire beat-to-beat profile during daily living.

Key words: Aortic blood pressure, arterial pressure, brachial blood pressure, central blood pressure, cuffless blood pressure, measurement

Introduction

Arterial blood pressure, one of the most important clinical parameters, is also one that presents formidable challenges to obtain accurate non-invasive measurements. All non-invasive blood pressure quantification methods do not measure the actual blood pressure in arteries, but rely on factors that correlate with blood pressure to arrive at an estimate that has some correlation with, but is not equivalent to, the actual blood pressure. Blood pressure is also difficult to quantify as a single quantity as it is highly variable from day-to-day, throughout the day, minute-to-minute, and even from one cardiac cycle to the next. It is also difficult to quantify as arterial pressure varies throughout the vasculature such that there is no single blood pressure across the body at any 1 time. Despite these limitations, the current non-invasive methods of quantification of brachial artery systolic and diastolic blood pressure are highly useful in prediction of cardiovascular events and mortality.(1) As a result, non-invasive brachial artery systolic and diastolic pressure are the main measures guiding clinical decision on administration of antihypertensive therapy.

The following is a discussion on the current invasive and non-invasive methods of blood pressure quantification with a look toward the future of techniques in blood pressure quantification including continuous and cuffless approaches. It also covers issues that need to be addressed in quantifying blood pressure such as traceable calibration and addressing blood pressure variability.
Invasive Blood Pressure Measurement

The first reported instance of the direct measurement of blood pressure was by Reverend Stephen Hales in 1733, who observed the height of blood in a pipe inserted into the left crural artery of a conscious 14-year-old mare, tied down on her back [Figure 1]. The blood “rose in the tube 8 ft 3 in [185 mmHg] perpendicular above the level of the ventricle of the heart” and did “rise and fall at and after each pulse 2, 3, or 4 in [4–7 mmHg].” This was a direct measurement of pressure in the large arteries in relation to the reference level of atmospheric pressure and did not involve any principle of transduction with associated instrumentation and physical variables. All other reported blood pressures are either in some way transduced through a secondary surrogate measurement, as in the case of invasive blood pressure measurement, or estimated, as in the case of non-invasive measurement.

In humans, the closest measurement of direct blood pressure is obtained by placing a solid-state pressure sensor-tipped catheter in contact with the blood itself within the artery. With changing pressure, the transducer (usually a strain gauge) changes resistance (with the signal being an output voltage). Accuracy relies on reliable calibration of the transducer relating that change in resistance to a change in pressure. More common in the acute care scenario is the placement of a saline-filled line within the artery, and which is externalized to a pressure transducer and referenced to atmospheric pressure. Accuracy in this method also relies on reliable calibration of the transducer. Error can also be introduced by placement of the transducer as movement of the transducer upward or downward in relation to the artery will change the hydrostatic pressure within the fluid line, and thus the pressure measured. Even with correct calibration, errors can be introduced by the length of tubing between the signal (blood stream) and the pressure transducer, the compliance of the tubing, and/or microbubbles in the saline, all of which have the potential to alter the frequency response of the manometer system as a whole. A survey of 300 blood pressure measurements using a fluid line found 31% were underdamped, resulting in an overestimation of systolic blood pressure (compared to invasive solid-state pressure catheter) of 28 ± 16 mmHg and underestimation of diastolic blood pressure of −2 ± 11 mmHg.

Non-invasive brachial blood pressure estimation

Any quantification of blood pressure that is not invasive is estimation, by definition. All non-invasive methods use signals that can be correlated, with varying accuracy, to blood pressure. Non-invasive methods do not provide an actual measurement of blood pressure.

The uncalibrated pressure pulse waveform (sphygmography) was first transduced by Marey and Mahomed. The first non-invasive blood pressure estimation was reported in 1896 by Riva Rocci. He reported using a pressurized cuff wrapped around the upper arm to occlude the brachial artery, then deflating the cuff and associating the cuff pressure with systolic pressure at the first appearance of the pulse palpated distal to the cuff. In 1905, Korotkoff extended this technique by application of the stethoscope to the brachial artery distal to the cuff to identify characteristic sounds associated with systolic and diastolic pressure.

These methods of blood pressure estimation were not proposed because of their absolute correlation with invasive measurement of brachial artery blood pressure. Rather, the methods rely on logical assumptions that underlie all cuff-based blood pressure estimates:

1. That the pressure in the cuff is the pressure applied to the brachial artery.
2. That cuff pressures above systolic pressure collapse the artery and occlude blood flow.
3. That cuff pressure at, or, marginally below systolic pressure allows blood to intermittently flow in the artery, giving rise to characteristic sounds and a palpable pulse distal to the cuff.
4. That cuff pressure at, or marginally below diastolic blood pressure is reliably associated with the disappearance of sounds or characteristic muffling of the sounds.

Figure 1: The evolution of blood pressure measurement. (1733) Adapted from Cuzzort’s impression (printed in the Medical Times, 1944) of Stephen Hales and assistant measuring the blood pressure of a horse, here shown taken from the left crural artery as described by Stephen Hales (original shown taken from the left carotid artery). (1896) Riva Rocci’s method (later auscultation as described by Korotkoff) of relating pulse related phenomenon to the pressure within a cuff around the upper arm. (1976) The first commercial oscillometric blood pressure devices were the Device for Indirect Non-invasive Automatic Mean Arterial Pressure (DINAMAP) 825. Model 845XT shown here. (1993) The first commercial device to measure blood pressure without a cuff was the Casio BP-100.
Although the technique of brachial artery auscultation is the reference standard for non-invasive quantification of blood pressure, Korotkoff himself saw the limitations and difficulty of quantifying blood pressure, captured in the title of his seminal work proposing auscultation, “A contribution to the problem of methods for the determination of blood pressure.”[8] There are varying theories as to the source of the Korotkoff sounds, especially during the supposed systolic pressure.[9] The more common theory is that the first Korotkoff sound is due to arterial wall movement when blood begins to flow through the previously occluded artery, and subsequent Korotkoff sounds are due to fluid (blood) turbulence.[9]

The characteristic sounds, first described by Korotkoff, do not correspond exactly with the systolic and diastolic pressure within the brachial artery. Systolic pressure is underestimated, on average, by 6 mmHg (95% CI –8 to –4 mmHg) and diastolic pressure overestimated by 6 mmHg (95% CI 4–8 mmHg).[10] This discordance between invasively measured blood pressure and non-invasively estimated blood pressure is not constant, varying greatly between people and within the individual under different physiological conditions.[11]

The reasons for this disparity between measured blood pressure and non-invasively estimated blood pressure are unknown but will relate to errors in the previously outlined assumptions. Modeling suggests that physiological differences in arterial wall properties can alter pressure estimates using a brachial cuff by up to 20%[12] due to transmission of the cuff pressure to collapse and occlude the artery. The transmission of cuff pressure to the artery is one of the potential causes for the historical inaccuracy of wrist cuff blood pressure devices with the radial artery being bordered by the ulna and radius bones. It has been suggested that accurate positioning of the cuff and scaling the cuff width to an individual’s wrist diameter may overcome these problems.[13]

Due to ease of use, oscillometry is a highly popular method of non-invasive quantification of brachial blood pressure. The underlying principle is identical to that proposed by Riva Rocci, but relies on detection of small oscillations in the cuff pressure due to volumetric changes in the brachial artery[14] and association of changes in the amplitude or shape of those small oscillations with the systolic and diastolic pressure. The point of maximum oscillations will occur when the arterial wall is unloaded, that is, when the transmural pressure is zero and the cuff pressure corresponds to the mean arterial pressure. This has been demonstrated in an idealized model[15] but suffers from the same limitations as the auscultatory technique insofar that it assumes the cuff pressure is entirely and uniformly transmitted to the artery.

Relying on an algorithm (usually proprietary and unreleased by the device company, but sometimes published[16]) to estimate systolic and diastolic pressure, the technique has the advantage that it can be automated and the measurement itself is user-independent. However, the timing of measurements, positioning of the patient, and use of the automated device is not user-independent and is still subject to errors. A recent study evaluating medical students’ ability to take blood pressure with an automated device found that on average less than 40% of the criteria for good blood pressure measurement were met.[17] Only 1 of the 159 students tested was able to take a blood pressure measurement correctly and according to guidelines.[17]

At the time of invention of oscillometric blood pressure devices, the use of auscultation for quantification of blood pressure was ubiquitous and long-standing clinical guidelines[18] using auscultation values of blood pressure were in place. Despite auscultation not accurately estimating invasive blood pressure, oscillometric devices were, and still are, validated against auscultation estimation of blood pressure so that the blood pressure values provided are consistent with those in guidelines. However, this also means that the oscillometric technique has the same error in estimating invasive blood pressure as auscultation does. The agreement between oscillometric and auscultation itself is highly variable, with a greater than 10 mmHg difference between oscillometric quantified blood pressure and auscultation quantified blood pressure in 15% of measurements for systolic blood pressure and 6% of measurements for diastolic blood pressure.[19]

Efforts were made in the last century to standardize validation of blood pressure quantification against auscultatory quantification of blood pressure measurement. Several guidelines on how to validate blood pressure devices were created.[20-22] All were largely similar and more recently an effort was announced[23] to consolidate the several guidelines into a single standard, ISO 81060-2:2018.[24] Not all blood pressure devices sold have been validated, and the Lancet Commission on Hypertension[25] has recommended that government regulatory authorities adopt a requirement for blood pressure devices to be validated.[26]

Validation studies are peer reviewed. However, these validation studies usually occur outside of the international measurement framework and in laboratories that do not have accreditation, and thus are not privy to the same scrutiny that is standard in other industries, sciences, and in retail,[27] with issues as fundamental as traceable calibration of references devices not addressed.

Validation occurs within the limits of variability of the technique. There is variability between oscillometric and auscultatory quantification of blood pressure.[19] In part, this is likely due to auscultation being highly variable in reliably quantifying brachial blood pressure as measured invasively.[11] The disparity between oscillometric and auscultation measurement may therefore be a result of the limitations of accuracy of auscultation for blood pressure quantification.

**Calibration**

Regardless of the method used to estimate blood pressure, pressure needs to be transduced. In the case of cuff techniques, it is the pressure of the air within the cuff that is transduced. Conventionally, this was done by coupling the bladder of air with a column of mercury, with the height of mercury within
that column giving the pressure. The high density of mercury as compared to water allows for the pressure to be read in an easy-to-handle device that can sit on a desk. This gave rise to the expression of blood pressure in mmHg rather than in Système International (SI) units (also accepting that SI units were proposed in the 20th century, after the advent of blood pressure measurement).

Mercury columns, often perceived as ground truth for pressure measurement, can deteriorate with age and give erroneous readings. In a 2002 inspection of mercury sphygmomanometers, 28% had an error of 4 mmHg or more and 7% an error of 6 mmHg or more. The impact of such systematic errors is substantial. It is estimated that systematic errors due to non-calibrated devices are responsible for 28% of undetected hypertensive cases and 31% of false diagnoses of hypertension.

Due to issues of safety, there is now a movement away from mercury devices. In general, a piezoelectric sensor is coupled with the air in the brachial cuff (non-invasive measurement) or a fluid line internalized to the artery (invasive measurement). When released from the factory, this sensor has been calibrated to provide an accurate transduction of pressure. With time, the sensitivity of the sensor can change, and recalibration is required. Annual calibration checks are recommended with the calibration check being performed with traceable measurement (documented, unbroken chain through national measurement institutes to the international standard) by an accredited laboratory. This does not occur often. Of 271 general practices surveyed across England and Wales, one (0.4%) regularly calibrated their blood pressure devices and 34 (12.5%) had at some point had their blood pressure machines calibrated by a drug company representative.

Site of blood pressure measurement

Historically, non-invasive blood pressure has been taken as an approximation of brachial artery blood pressure as a matter of convenience and feasibility. There is no reason that brachial artery blood pressure is more important than blood pressure elsewhere in the body. It could be argued that the arterial pressure near the heart or in the brain is of greater consequence as these are sites of cardiovascular events. However, the main arteries of the heart and brain are not superficial and external pressure cannot be applied to them in the same way that it can in the brachial artery. Techniques for non-invasively estimating pressure in the aorta is addressed in this issue, where a transfer function applied to the peripheral arterial pressure waveform combined with cuff-based measurement of brachial blood pressure calculates the aortic pressure.

The site of blood pressure measurement is also important within brachial blood pressure measurements alone, with there being reported differences in blood pressure between the two arms, and this interarm difference being associated with greater cardiovascular risk and with cognitive decline. Interarm blood pressure difference does not appear to be associated with asymmetry in arm geometry, suggesting that it is not an artefact due to differences in the transmission of the cuff pressure to the artery. It may be that the interarm difference is an artefact due to pulse-to-pulse variability in blood pressure, with small differences in the timing of “simultaneous” blood pressure measurement in both arms resulting in a difference in estimated blood pressure. This theory has circumstantial evidence in that the interarm difference is not reproducible within individuals, yet is associated with end organ damage.

Blood pressure variability: What is someone’s blood pressure?

Systemic arterial blood pressure changes acutely. Blood pressure has a diurnal variability, variability with different life activities and stressors, and variability from one pulse to the next. Even if blood pressure can be measured accurately, and it is decided at which vascular site blood pressure is most important, it is still impossible to state that someone’s blood pressure is a set number due to the inherent and critical variability in blood pressure.

It is recommended in clinical evaluation of blood pressure that the blood pressure outside of the clinic be assessed either through use of a home blood pressure monitor or an ambulatory blood pressure monitor worn for a 24-h period. There is much controversy on the utility of visit-to-visit in-clinic blood pressure variability, night-time or daytime blood pressure, morning rise in blood pressure, and ambulatory variability in blood pressure in clinical assessment of risk and decision making in treating patients. With a greater number of blood pressure devices uploading patient data to internet-held databases, and with the increase in consumer-based blood pressure devices, the aggregation of data for individual patients suggests that a blood pressure profile, rather than a single blood pressure, is becoming increasingly available to the clinician. How to use that data in clinical assessment and treatment will require research-based consensus.

Continuous quantification of blood pressure

Continuous measurement of blood pressure, in terms of visualization of the continuous pressure pulse waveform, is usually only in the realm of research and has not found its way into clinical applications. In critical care scenarios such as anesthesia monitoring and intensive care, a near-continuous blood pressure will be provided in the form of systolic and diastolic pressure analyzed from an arterial line, updated pulse-by-pulse or at frequent intervals.

The only method for continuous blood pressure quantification is using an invasive approach. Servo-nulling of finger blood volume through changes in a pressure in a cuff around the finger has been investigated as a non-invasive approach to continuous blood pressure monitoring. It has been demonstrated to be relatively accurate in tracking changes in blood pressure, with an average offset from intra-arterial blood pressure of between 5 and 10 mmHg, but with significant between-individual variability. While useful in specifically designed research studies, the technique has not found value in critical care.
monitoring due to limitations in accuracy. The technique has found value in autonomic function testing, where quantification of acute blood pressure changes provides valuable information but does not warrant the risks and discomfort associated with an invasive blood pressure line.

**Blood pressure estimation without a cuff**

Oscillometric brachial cuff measurement is used to quantify blood pressure in the ambulatory scenario (when moving about) and during sleep. However, the technique has limitations in this setting being that: The participant still needs to be relatively still during the measurement; the measurement is intermittent (once over 15–30 min), not continuous; measurement during the night disturbs sleep resulting in a blood pressure measurement that may not be representative of nocturnal blood pressure; the wearing of the cuff and device throughout a 24-h period is uncomfortable.

These limitations could be addressed by estimation of blood pressure without a cuff. At present, devices designed to measure blood pressure without a cuff use either characteristics of an uncalibrated pressure waveform, or the pulse transit time to estimate blood pressure. As blood pressure increases, the arterial pressure waveform shape will change and the arteries will become stiffer, decreasing pulse transit time across a fixed distance. Such devices rely on a defined relationship between the measured parameter and blood pressure to estimate blood pressure. It has been established that this relationship differs between individuals and a fixed parameter-pressure relationship across the population is unlikely. For example, it is known that the relationship between pulse transit time and blood pressure has greater sensitivity for normotensive individuals than hypertensive individuals. The parameters used to quantify blood pressure without a cuff are even further removed from blood pressure than the non-invasive cuff-based approaches. It is therefore unlikely that the accuracy will be an improvement upon cuff-based devices.

Often the site of measurement of cuffless blood pressure devices is not the brachial artery. It must be considered whether the local vascular changes that are being interrogated are representative of blood pressure changes in the brachial artery, if it is the brachial artery blood pressure reference values that are to be estimated.

It should also be considered that if only one parameter is being measured (e.g., a single waveform feature or the pulse transit time) and both systolic and diastolic blood pressure are reported, how two parameters are estimated from one parameter. While there is some correlation between systolic and diastolic pressure, one cannot be predicted from the other. It follows that cuffless blood pressure devices reporting both systolic and diastolic pressure suffer from variability in accuracy or require further correlative inputs to predict both systolic and diastolic pressure with some accuracy.

The Food and Drug Administration (FDA) recently approved medical style devices marketed directly to the consumer (Apple Watch and AliveCor KardiaBand atrial fibrillation detection) as “de novo,” that is, not requiring equivalence to medical devices not marketed to consumers. In theory, this also opens the pathway for cuffless blood pressure devices marketed direct to consumers with differing criteria around accuracy to that of medical devices. This is important in considering the utility of consumer cuffless blood pressure in health decision making both on an individual level and at a population level using aggregated data. Separate to the FDA, the Institute of Electrical and Electronics Engineers have developed a standard for validation of cuffless blood pressure devices. The International Organization for Standardization is currently preparing a standard as well.

**Improvements in estimating true blood pressure**

The seminal advances of Scipione Riva Rocci made by introducing a brachial cuff with peripheral palpation, and of Nikolai Korotkoff by auscultation of sounds associated with changes in arterial blood flow due to cuff pressure, have been the lynchpin of non-invasive measurement of blood pressure. It was known from the very beginning that these techniques rely on the integrity of all components of the system to obtain a reliable estimate of arterial blood pressure by measuring cuff pressure. It is important to understand, the errors are not due to the actual measurement of pressure, that is, the manometric value of cuff pressure. This can be measured with high accuracy, the most accurate being the height of a column of fluid open to the atmosphere, as it is totally devoid of any process of transduction. The problem is the fiducial relationship of cuff pressure with arterial pressure. Indeed, the very first improvement that was required to the Riva Rocci sphygmanometer was to change the size of the cuff – the original cuff was not wide enough for uniform collapse of the brachial artery under the cuff.

Although the basis of sphygmanometry has not changed, there have been gradual improvements in cuff and internal bladder design so as to accommodate variable anatomy of the upper arm, use of microphones or flow sensing techniques, or even to visualize the Korotkoff sounds to obtain fiducial points in the brachial cuff pressure that correspond to systolic and diastolic pressure. Improvements in the oscillometric technique have included optimizing parameters for curve fitting to the oscillogram to obtain reliable coefficients for models estimating systolic and diastolic pressure.

Notwithstanding the many functional improvements made to the conventional brachial cuff measurement of blood pressure, the cuff pressure values generally tend to underestimate true intra-arterial systolic pressure. It is unlikely that any non-invasive technique will be able to obtain the true value of intra-arterial pressure with all measurements. However, it should be possible to design methodologies that will reduce the variability of the estimation so that true changes can be reliably estimated with achievable tolerances that are accepted by standards and regulatory agencies. Although, intermittent measurements of cuff-based methodologies have produced all the data on blood pressure for physiopathological associations of high blood
pressure and cardiovascular risk, the future challenges are to obtain reliable continuous blood pressure measurements so as to quantify risk not only on blood pressure values, but on the entire beat-to-beat profile during daily living.

Conclusions

It is undeniable that non-invasive quantification of blood pressure of the brachial artery has utility in risk prediction and hypertension management despite the inherent inaccuracies in the method compared to invasively measured blood pressure, and that brachial artery pressure may not be the precise pressure seen by the heart, kidney, and brain. Detailed guidelines exist around the validation of cuff-based blood pressure devices, and how to take measurements to obtain a seated resting value of blood pressure. More fundamental issues such as regular traceable calibration of devices, including in the laboratories performing validation studies, could be better addressed. Estimation of blood pressure without a cuff promises large gains in presenting a person’s blood pressure profile, rather than the broad method of stating a person has a single average blood pressure at rest. However, given that cuffless estimation of blood pressure relies on correlative parameters, accuracy of both clinical and consumer market devices should be carefully considered in employing these devices in clinical decision making and in research studies relying on aggregated data.

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