This educational guide outlines the development and clinical applications of Pulse Wave Analysis. It has resulted from written contributions by an honorary advisory group each involved in aspects of the management and prevention of cardiovascular disease.

The objective has been to produce an understandable and interesting document that can be updated at intervals with useful information from the world literature.

The adoption of innovative technology in the routine practice of medicine requires objective and protracted appraisal. In the development of new medical technology a compelling influence is the need to visually represent, quantify and to store what would otherwise be only observer subjective information. This is true for PWA that has evolved from a mechanical recording of the peripheral pulse with a slow response time in the 19th century into a sophisticated computer-based non-invasive method for the accurate recording of both peripheral and central pulse profiles. Based on current world experience, this document introduces how the technology should be used in the management of a range of macrovascular, hypertensive and cardiac problems.

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Introduction

A growing number of risk factors including diabetes, hypercholesterolaemia, smoking, hypertension, and age have been linked to the adverse cardiovascular endpoints of heart attack, stroke and heart failure.

Importantly, it is known that these risk factors lead to an increase in arterial stiffness. Increased arterial stiffness accelerates the speed at which the left ventricular ejection pressure wave travels through the arteries, and leads to an earlier return of the reflected pressure wave back to the left ventricle. The reflected pressure wave starts to arrive more and more during systole, where it augments the late systolic pressure (afterload) on the left ventricle. Because the wave is therefore arriving less during diastole, it reduces the coronary artery perfusion pressure during this critical period. Therefore, increased arterial stiffness leads to a greater risk of:

- angina and heart attack (by reducing coronary artery perfusion pressure during diastole)
- stroke (by increasing central pulse pressure)
- heart failure (by increasing left ventricular load).

Arterial stiffness can be increased by three key mechanisms:

1. A breakdown of the elastic structure (elastin fibres) in the arterial walls. This is a function of cumulative cycles and artery wall pulsatility, and is the prime cause of increasing stiffness in the aorta with ageing.
2. Damage to the endothelium/smooth muscle mechanism by which arterial stiffness is dynamically controlled. This is the prime cause of arterial stiffness in the muscular conduit arteries.
3. An increase in mean arterial pressure, which increases the stiffness of an artery. This mechanism influences the entire arterial tree as a passive effect.

The process by which the arterial system interacts with the left ventricle and coronary arteries can be clearly visualised when the patient’s aortic root pressure waveform is available for analysis. SphygmoCor is a non-invasive device that enables this aortic root pressure waveform to be measured during a normal clinical consultation. The system elucidates the mechanisms that cause increased systemic arterial stiffness, and then provides a visual display of these parameters in relation to cardiovascular health.

History and Development

SphygmoCor is an integrated system of pulse wave analysis. It was developed from the concept that there is haemodynamic information contained in the shape of the arterial pressure pulse, which can be used to supplement the conventional measurement of blood pressure. The systolic and diastolic values of blood pressure are the maximum and minimum points of the pressure curve obtained in a peripheral location, usually the upper arm. However, similar values of systolic and diastolic pressures can be associated with many different pulse wave shapes, and these determine the type of interaction between the heart as a pump and the arterial system as the load. The elastic and geometric properties of the arteries cause the arterial pressure pulse to change its shape as it travels along the arterial tree, such that mean pressure is approximately similar along the large arteries of the arterial tree, but pulse pressure can be markedly different (see Section 2, Figure 2.1).

The graphical registration of the arterial pulse was the first physiological recording that was used for clinical diagnosis in the mid-to-late nineteenth century. Seminal work was done by a young and observant medical student in 1872, Fredrick Akbar Mahomed, at Guys Hospital in London. He first described the changes in the shape of the arterial pulse with age.

Illustration of the Sphygmograph developed by French physiologist Etienne-Jules Marey (as described by B. Sanderson in 1867 in “The handbook of the sphygmograph”, Hardwiche, London). The lower part shows the lever mechanism in profile.
The work of Donald McDonald and colleagues, conducted in the three decades after the Second World War, is fundamental to the development of the concepts underlying SphygmoCor. The first edition of the monograph of Blood Flow in Arteries was published in 1960 by McDonald, and the 4th edition was published 25 years after his death by Nichols & O'Rourke in 1998 as McDonald's Blood Flow in Arteries: Theoretical, experimental and clinical principles. This recent edition contains an entire chapter on 'sphygmocardiography', highlighting the connection between the early work on the arterial pulse, and the latest concepts of arterial haemodynamics.

Sphygmocardiography is defined as 'the study of the dynamic interaction of the left ventricle and the arterial system by analysis of the blood pressure waveform'. In relation to SphygmoCor, this involves the derivation of the central aortic pulse waveform from the recording of the pressure waveform in peripheral locations (eg the radial artery). 'Sphygmocardiography' is derived from the Greek term sphygmos for 'pulse'. Other derivative terms are 'sphygmograph' (a plot of the pulse waveform) and 'sphygmocardiograph' (a plot of the ventral pressure waveform, together with the derived indices from the waveform (eg pressure to first systolic shoulder, augmentation pressure, augmentation index, as illustrated in Section 2).

The main attribute of SphygmoCor is its ability to derive the central aortic pressure waveform non-invasively from the pressure pulse recorded at a peripheral site. Two specific things made this possible and contributed to the practical use of the device in both research and clinical situations: (i) the accurate recording of the peripheral pulse by means of applanation tonometry; and (ii) the use of a generalised transfer function of the upper limb across the adult population.

Detection of peripheral blood pressure waveforms

The peripheral pulse can be detected by a suitable transducer that can respond to dynamic changes in force or volume due to the expansion of the segment of artery underlying the transducer. There are many such devices, but what initiated the development of SphygmoCor was the use of the extremely sensitive pressure sensor used at the tip of catheters (eg Millar catheters) to obtain an accurate measurement of intravascular pressure during catheterisation procedures. It was found in initial experimental trials...
that if this element was pressed on the outside of the skin over an artery, and the artery was compressed slightly against a firm structure such as bone (Figure 1.3), the signal produced was similar to that of the intravascular pulse.

This, in fact, is the principle of applanation tonometry, which is used to measure intra-ocular pressure for the assessment of glaucoma and its response to treatment. The application of this principle to arteries, made it possible to obtain a high-fidelity signal without penetrating the skin or blood vessels. Following a liaison with Millar Instruments, a pencil-type hand-held probe was produced with the sensing element at the tip (Figure 1.3) so that a pulse could be obtained at peripheral locations (e.g., radial, carotid, femoral, dorsalis pedis arteries).

Since the development of the hand-held tonometry probe there have been many adaptations of the technique, including non-operator dependent devices.

Figure 1.3

Generalised Transfer Function

A transfer function defines the relationship between two parameters, the input and the output of any system. If the input signal is the aortic pressure pulse, and the output is the radial artery pressure pulse, then the transfer function of the connecting brachial arterial system (i.e., aorta to radial artery) can be obtained by relating the frequency components of the radial and aortic pulse wave (see further explanation in Section 2). A mathematical model can be constructed which describes the transfer function such that if one signal is available, then the other can be derived. This is the principle employed by SphygmoCor, where the aortic pulse is reconstructed from the non-invasive radial waveform.

The characteristics of the transfer function are determined by the physical properties of the arterial system, such as arterial diameter, wall elasticity, wall thickness, amount of branching, and the condition of the peripheral vascular beds. Of course not all brachial vasculature is identical in all adults, and it is expected that there would be some difference in the overall transfer function among individual subjects. However, it was found that the main components of the transfer function do not change markedly between normal adults with age for example, such that it would give large errors in the derived waveforms. Studies of pulse wave velocity (a parameter which is related to arterial stiffness) in hundreds of people have shown that most of the age changes occur in the aortic trunk, and not in the arteries of the arm (Figure 1.4).
Another piece of evidence in support of a generalised transfer function came with the observation that the transfer function did not differ markedly in normal conditions and in conditions of vasodilatation following administration of nitroglycerin. This then made it possible to utilise the concept in a practical way to determine aortic pressure non-invasively in a range of situations. While there has been some discussion on the use of a generalised transfer function, recent evidence is emerging that the general transfer function concept can even apply to analysis of finger volume pulses.

Validation

The study by Chen et al validated the use of the generalised transfer function under normal conditions, and when there are marked changes in blood pressure following a valsalva manoeuvre (Figure 1.5).

The study reports results of invasive central aortic pressure measured by micromanometer and radial pressure by automated tonometry in 20 patients at steady state and during haemodynamic transients (Valsalva manoeuvre, abdominal compression, nitroglycerin, or vena caval obstruction) (Figure 1.6). A generalized transfer function was determined from the average of individual transfer functions. The generalized transfer function estimated central arterial pressures to 0.2±3.8 mm Hg error and augmentation index (see 2.3.3) to within ±7%. The study shows that individual transfer functions were only marginally superior to the generalized transfer function for reconstructing central pressures (Figure 1.6).

Further evaluation of the technique has shown a very good correlation between the derived and measured central aortic systolic pressure. Various studies have reported a good correlation between the augmentation index determined from measured (y) and derived (x) aortic pressure waveform: y = 0.92x + 0.24; r = 0.75; p<0.001.

Results from validation study by Chen et al comparing derivation of aortic pressure using a generalised transfer function.Measured aortic pressure (dotted line) and aortic pressure derived from the radial pulse (solid line) using a GTF. Lower panels show individual pressure tracings at rest (left) and reduced preload (right).

Results from validation study by Chen et al showing regression analyses for systolic, diastolic, and pulse pressures during haemodynamic transients (eg valsalva manoeuvre). A = pressure measured in the radial artery (horizontal axis) compared with pressure measured in the central aorta (vertical axis). Note the markedly reduced systolic and pulse pressure in the central aorta compared with the radial artery while there is little difference in diastolic pressure. B = aortic pressure derived from the radial artery using the generalised transfer function (GTF) (horizontal axis) compared with pressure measured in the central aorta (vertical axis).
Limitations

The use of the transfer function does not depend on the shape of the aortic pulse. For example, if there is incompetence of the aortic valve, the aortic pulse waveshape will be changed, and of course, so will the radial pulse. In these situations SphygmoCor can be used to analyse the radial pulse, since there is no real modification of the arterial properties. However, if the radial pulse is modified due to severe obstruction of any part of the brachial arterial system, SphygmoCor cannot be used in these situations to derive aortic pressure.

1.3.3 Reproducibility

Reproducibility of central aortic pressure and pulse wave velocity measurements with SphygmoCor depend on the quality of the data recorded. The essential element is to obtain an accurate radial pulse waveform, from which all parameters are derived. As with any technique, results of reproducibility will depend on both the stability of subjects physiological status and operator skill. Clinical studies have shown that the technique is highly reproducible. For further details, refer to Appendix 7.1.

References

6. Kelly MP, Gibbs HK, O'Rourke MF, et al. Nitroglycerin has a more favorable effect on left ventricular afterload than apparent from measurement of pressure in a peripheral artery. European Heart J, 1990; 1: 138-144.
Performing and Understanding Measurements taken with SphygmoCor

2.1

The Pressure Pulse Waveform

One of the most basic physiological properties of the arterial pulse is that the shape becomes modified as it travels along the arterial tree. The amplitude generally increases, and the pulse waveform features are altered. For example, the peripheral pulse tends to have a narrower and sharper systolic peak than the central pulse.¹ ³

The normal pulse pressure amplification between central and peripheral locations, which can be quite marked, will depend on the heart rate. As the heart rate increases the peripheral pulse pressure can be approximately three times that at the aorta⁴ ⁶ as seen during exercise and with other causes of increased heart rate. At normal heart rates, the pulse pressure at the brachial artery (where it is normally measured) is 20-50% greater than that at the aorta, although this is dependent on age, with a greater difference in pulse pressure seen in the young compared to the elderly.² The increased arterial stiffness in the elderly leads to increased wave reflection, which increases central pulse pressure (see Section 2.3).

Conventional measurement of cuff blood pressure in the brachial artery does not take into account these two essential properties of the arterial pressure pulse. These are:

(i) the pulse amplitude increases at it moves away from the heart (Figure 2.1).
(ii) the amplification of the pressure pulse increases with heart rate in the normal population (Figure 2.2).

This means that:

- the conventional pressure measurement, which gives only the maximum (systolic) and minimum (diastolic) values of the peripheral pressure pulse, is not an accurate measure of the pressure load on the heart;
- any intervention that causes an increase in heart rate can cause a significant overestimation.

These features can be accounted for by analysing the information present in the pressure pulse waveform itself.

![Figure 2.1](image1)

*Change of pressure wave contour along the aortic trunk and peripheral arteries recorded in adult human subjects aged 24, 54 and 68 years. The amplification of the pulse towards the periphery decreases with age. The arrow on the waveforms indicates the first systolic inflection corresponding to the beginning of the reflected wave at different positions in the arterial tree. Note that this point tends to occur earlier in systole with advancing age.¹*

![Figure 2.2](image2)

*Amplification of the pressure pulse between the central aorta and radial artery with heart rate. The data were obtained with SphygmoCor in over 200 subjects and amplification calculated as the ratio of radial/central aortic pulse pressure. For a reference heart rate of 60 beats/min, the amplification increase is approximately 1% per beat/min.*
Central Aortic Pressure from the Peripheral Pulse

The SphygmoCor system incorporates the actual pulse recorded at the radial artery and the properties of the transfer function between the aorta and the radial artery to estimate central aortic pressure non-invasively. When considering the transfer function, the input is considered to be the aortic pulse and the output the peripheral pulse. However, if the inverse of the transfer function is used as a mathematical model, then the input is the peripheral pulse and the output will be the aortic pressure.

The radial pulse is detected by a non-invasive high fidelity sensor using applanation tonometry (similar to the technique used for measurement of intra-ocular pressure - see Section 1). The waveform is calibrated using systolic and diastolic pressure values from conventional cuff measurement and SphygmoCor derives a complete waveform for the whole cardiac cycle for the aortic pulse (Figure 2.3). An average waveform is calculated from the ensemble average of a series of contiguous pulses.\(^1\)\(^,\)\(^6\)\(^,\)\(^7\)

Once the aortic pulse is derived, a number of features can be extracted to enable calculations to be made, which cannot be made from the peripheral pulse or from the conventional measurement of brachial blood pressure.

Aortic Pressure Waveform

The shape of the aortic pressure pulse is a result of the ventricular ejection and the physical properties of the arterial system. The load on the ventricle during ejection is described by the pressure during systole. In the absence of wave reflection, the shape of the pressure wave during systole is determined by the ejection wave and the elastic and geometric properties of the ascending aorta. If there is no wave reflection, the shape of the pressure and flow look quite similar.\(^1\)

The contracting ventricle of a normal heart is able to eject blood under a range of pressure loads, so even if the pressure is changed, the form of the ejection wave is quite similar. If wave reflection occurs during systole, it will increase the pressure against which the ventricle has to eject its contents. Thus, in addition to having the values of systolic and diastolic pressure in the aorta, knowledge of the pressure waveform will facilitate analysis of the coupling between the ejection heart and the pressure load. These parameters can be extracted from the features of the aortic waveform such as the first systolic inflection (P1), the systolic peak (P2), the relative difference between the two in terms of pressure augmentation, the pressure at the end of systole, and the relative area during systole and diastole (Figure 2.4). The way these parameters are determined by SphygmoCor is addressed in the following sections.
Categories of pressure pulse waveforms (A, B, C)

Generally, the aortic pressure waveform can be divided into three broad categories, labelled as Type A, B and C. These indicate different degrees of wave reflection primarily due to arterial stiffening. This may occur physiologically with age or pathologically in disorders such as hypertension, diabetes or hypercholesterolaemia (Figures 2.5a and 2.5b). They are described in terms of the feature of augmented pressure:

**Type A**
- Early systolic shoulder; late systolic peak
- Positive augmentation pressure

**Type B**
- Zero augmentation pressure

**Type C**
- Peak pressure coincides with peak flow; late systolic shoulder; no augmentation pressure; negative augmentation index (AI) - see Section 2.3.3

Augmentation pressure

The ejection of blood from the ventricle into the aorta generates an aortic pressure pulse. In many cases the timing of peak pressure does not coincide with the timing of peak flow, such that peak pressure may occur later. In this event, there is usually a systolic shoulder on the ascending limb pressure curve which coincides with peak flow, then a rise in pressure to the systolic peak (Figure 2.5b). This increase in pressure is described as the ‘augmentation pressure’ (Figure 2.6) and is predominantly due to the reflected components of the original pressure pulse generated by ventricular ejection. The speed of the pulse in arteries is normally such that the reflection occurs in the diastolic phase but it can return during systole, while the aortic valve is still open, thus increasing the afterload pressure against which the heart has to eject blood.3,8

The amount of augmentation increases as the arteries stiffen. In the young (15-25 years) it is common to see no augmentation. That is, peak pressure coincides with peak flow, and the systolic shoulder occurs after the peak. This would seem to be an important characteristic in differentiating cases with similar central systolic and diastolic pressures but different pulse patterns during systole. Augmented pressure during systole produces a different loading pattern on the myocardial fibres, even if peak systolic values are identical.9

This situation can only be identified by analysis of the whole central wave form and not by the conventional means of blood pressure measurement.
Augmentation Index

The amount of augmentation pressure is quantified in terms of the relative change over the whole pulse. That is, once the early systolic shoulder (peak, P1) and the peak, or late systolic shoulder (P2) are identified, the absolute augmentation is calculated ($\Delta P = P2 - P1$) and an augmentation index (AI) is defined (Figure 2.7). SphygmoCor defines this in two ways: i) relative to P1 (ie AI 1 = $\Delta P / P1$) and ii) in relation to the pulse pressure (PP) (ie AI 2 = (PP/P1). Both give similar information, but expressed in different forms.

Subendocardial viability ratio (SEVR)

From the derived aortic pulse, calculations can be made which make use of the waveform features. By transferring the ejection duration determined from the peripheral pulse, the area under the systolic (AS) and diastolic (AD) part of the curve can be calculated. AS has been shown to be related to the work of the heart and to oxygen consumption (commonly known as the Tension Time Index). AD is associated with the pressure and time for coronary perfusion, thus is related to the energy supply of the heart. The ratio of supply and demand is termed the Subendocardial Viability Ratio or the Buckberg Index (ie, SEVR = AD/AS). It has been shown that when SEVR is below unity (or 100%), the layers of the subendocardium are underperfused (Figure 2.9).

SEVR for normal conditions is usually high (~130-200%). However, it can decrease markedly with high heart rates or high systolic pressures. In measurements there is considerable variability in SEVR. However, if low values are consistently found in patients with known coronary artery disease, this may indicate the potential for aggravating subendocardial ischaemia due mainly to reduction in diastolic perfusion time. Thus, this simple non-invasive measurement contributes to the decision-making process for specific therapeutic interventions and for further investigations in patients at risk of ischaemic events.
Subendocardial viability ratio (SEVR)

References

3.1 Introduction

Cardiovascular damage is the final common pathway for a number of diseases. One of the most difficult challenges for the practitioner treating a patient with cardiovascular risk factors is to establish a diagnosis early, in order to allow pre-emptive action to be taken. In the patient with established disease, it would be of great assistance to have treatment directed appropriately at the physiological vascular abnormality.

Clinical examination of the cardiovascular system typically includes measurement of the pulse rate and character, measurement of blood pressure and cardiac auscultation. Further information can be gained by echocardiography, and by invasive haemodynamic monitoring. There is great potential value in a non-invasive tool to augment information gleaned from the clinical examination. Applanation tonometry, permitting accurate description of peripheral pulse wave characteristics and pulse wave velocity, and extrapolation of findings to central cardiac and aortic physiological events, is such a tool.

Medical disorders with clear potential cardiovascular complications provide the greatest opportunity for using applanation tonometry. These include:

- Hypertension (including essential and secondary causes, and hypertension complicating pregnancy)
- Left ventricular hypertrophy (LVH) and failure
- Systolic heart failure
- Diabetes mellitus
- Renal disease
- Hyperlipidaemia

In some of these disorders, there is already compelling evidence for the use of pulse wave velocity measurements. In this section of the guide, evidence is presented for pulse wave velocity in several disease states. Where available, the value of measurements in guiding diagnosis and/or therapy is presented. In some areas, studies are incomplete and therefore no specific recommendations can yet be made. As such information is acquired it will be reviewed for future editions of the guide.
Significance

Chronic elevation of arterial blood pressure is the most common medical problem in the developed world. It leads to unacceptable morbidity and mortality due to target organ damage, which is frequently accentuated by other cardiovascular (CV) risk factors. Systolic, and to a lesser extent, diastolic pressure rise with age such that 50% of the population aged 65 and over is at risk. There is a continuous relationship between blood pressure and the risk of cardiovascular events, and based on an ideal maximum target pressure of 140/90 mmHg (high normal), 70% of patients currently receiving antihypertensive therapy are inadequately or poorly controlled.

Detection

Despite extensive clinical and population studies, the specific physical properties of the arterial pulse that are most closely associated with the risk of target organ damage continue to be debated. In ageing societies, elevated systolic pressure has been identified as more important than elevated diastolic pressure. However, recent CV risk studies suggest that pulse pressure could be the most important variable. This implies that at a particular level of elevated systolic pressure, risk could increase as diastolic pressure decreases. This has been confirmed in several risk analysis trials, but does not deny that diastolic pressure above 90 mmHg (high normal) is a strong separate risk predictor and requires therapeutic intervention irrespective of the systolic pressure.

The association between pulse pressure and cardiovascular risk has implications for the choice of antihypertensive therapy (see Treatment Objectives, Section 3.2.5). Studies leading to these conclusions have been based on conventional sphygmomanometry arm pressures, usually in the clinic setting and taken in the sitting position. Sphygmomanometry is convenient and when clinic pressures are confirmed with occasional ambulatory and home values, most physicians would conclude that effective monitoring and management of hypertension are achievable.

But what is missing from this current practice is a clear understanding of why, in particular patients, systolic, diastolic or pulse pressures are elevated and the consequences this can have for drug selection and prognosis. This insight requires quantitative information relating to stroke volume, large artery stiffness and peripheral vascular resistance. Thus, systolic pressure is influenced directly by stroke volume and vascular stiffness. But while diastolic pressure rises with increasing peripheral resistance to blood flow and also when neurohormonal factors increase the heart rate, it actually falls as large artery stiffness increases. This results from the faster ‘run-off’ of the stroke volume from the main arteries due to their reduced visco-elastic properties and inability to retain the ejected volume. Information relevant to these variables, and to the cause of increased pulse pressure and consequently CV risk, can be derived non-invasively and conveniently from pulse wave analysis (PWA).

Pulse wave analysis

Using the SphygmoCor system of pulse wave analysis, the hallmark of increasing arterial stiffness is an augmentation of central aortic systolic peak pressure due to an increased pulse wave velocity and rate of wave reflection (see Section 2). This has secondary effects on cardiac work and coronary perfusion that can become decisive factors for left ventricular function. In the routine management of hypertension, PWA at intervals together with sphygmomanometry permits the physician to identify more accurately the physical cause and progressive consequences of the hypertension. With this information the selection of therapy appropriate to the specific causation, whether systolic, diastolic or pulse pressure is more informed.
Typical waveforms in hypertension

Young normotensive

Note: Narrow radial peak. Late systolic shoulder in aortic pulse is lower than the early systolic peak (negative augmentation).

Middle aged normotensive

Note: Wide radial systolic peak. Late systolic peak in aortic pulse is higher than early systolic shoulder (positive augmentation).

Elderly normotensive

Note: Increased late systolic shoulder in radial pulse. Increased late systolic augmentation in the aortic pulse.
Young hypertensive

Note: Prominent late systolic shoulder in the radial waveform. Presence of late systolic augmentation in the aortic pulse.

Middle aged hypertensive

Note: Increased late systolic shoulder in the radial waveform. Increased late systolic augmentation in the aortic pulse.

Elderly hypertensive

Note: Exaggerated increase in late systolic peak in radial waveform is higher than earlier systolic shoulder, in contrast to young and middle aged hypertensive pulse. This is associated with prominent augmentation of late systolic aortic pulse. Note also the relative reduction in pressure during the diastolic phase indicating reduced coronary artery perfusion pressure.
Treatment objectives

Assuming there are no associated conditions accentuating CV risk, such as diabetes, the general objective in all hypertension management is to reduce systolic/diastolic pressures to below 140/90 mmHg. However, the increasingly common problem of isolated systolic hypertension with increased pulse pressure requires further consideration. In these patients, the target should be achieved without reducing diastolic pressure further, thus avoiding the risk associated with high pulse pressure. The ideal drug in this situation would be one that reduces large artery stiffness, pulse wave velocity and augmentation pressure (as monitored by PWA) but without decreasing peripheral vascular resistance. Of the commonly used agents, calcium channel blockers (CCBs) and inhibitors of the renin-angiotensin system (ACE inhibitors, angiotensin II receptor antagonists) are recommended, but are not specific and do not act selectively to increase large artery compliance. Low dose nitrates, not currently recognised for the routine management of hypertension, do increase large artery compliance and have been shown to reduce pulse wave velocity. Further aspects and future prospects relating to the rational selection of drugs to correct the pulse profile are outlined in Section 4.

Summary

- 70% of patients receiving antihypertensive therapy are inadequately controlled
- Pulse pressure is an important determinant of cardiovascular risk
- PWA enables the physical cause of hypertension to be accurately identified
- Specific treatment programs can be developed and monitored based on PWA results
- Central aortic pressure derived from SphygmoCor is expected to relate more closely to hypertension, morbidity and mortality than conventional brachial artery pressure measurements alone

References

Significance of left ventricular hypertrophy (LVH) and failure (LVF)

LVH is a powerful risk indicator in hypertension and constitutes a major independent risk factor for sudden death, myocardial infarction, stroke and ischaemic heart disease. LVH also predicts the eventuality of ventricular failure.

The major cause of LVH is essential hypertension which is initiated by increased peripheral vascular resistance and with time is compounded by increasing stiffness of the main conduit arteries due to secondary structural changes. Aortic stiffness, by increasing pulse wave velocity, has two potentially serious consequences for LV function:

1) Central systolic pressure is augmented by the earlier return of the reflected wave which increases the ventricular after-load and systolic work and decreases late systolic flow (Figure 3.3.1).

2) Diastolic coronary perfusion time is reduced due to the augmented and protracted systole while coronary perfusion pressure is also lowered due to the shift in the timing of the returning reflected wave from diastole into systole (see Section 2).

These are important compromising factors for ventricular function and contribute to a slowly developing vicious cycle that will ultimately result in left ventricular failure.

Detection

LVH is routinely confirmed by non-invasive imaging and electrocardiography but it is surprising that these methods cannot provide insight into the progression of events described above. To reveal the impact of increased pulse wave velocity on cardiac function requires the recording of the central arterial pressure profile at intervals during the management of the complaint.

3.3

Left Ventricular Hypertrophy and Failure

400 600 800 1,000 (ms)

90
80
70
60
50
40
30
20
10

Increased effects of wave reflection associated with arterial stiffness are seen in the augmented late systolic peak in the radial waveform (left) and derived aortic waveform (right).
Pulse wave analysis

PWA using SyphgmoCor enables an accurate determination of central aortic pressures non-invasively via the transfer function. The sequential measurements of central pulse pressure profile, augmentation index and subendocardial perfusion ratio (see Section 2) quantifies the factors listed above that can be the main contributors to the development of LVH and ultimately ventricular failure.

A main characteristic of early left ventricular failure is the loss of contractile power to cope with increased impedance to ejection. The impedance resides both at the arteriolar level and in the central arteries. In heart failure the arterioles are constricted due to increased neurohormonal influences and central pressures may be augmented due to slower systolic ejection and aortic stiffness each causing the reflected wave to lie within the systolic period. (Figure 3.3.1)

Treatment objectives for LVH and failure using SyphgmoCor

Treatment is directed to reverting the progression of events described above and again this can only be monitored by a technique that allows assessment of central arterial pressure profiles. For LVH, the objective is to determine the presence and then to reduce the degree of systolic augmentation. This is true also for ventricular failure but with failure there is additional concern to obtain evidence of increased contractility, increased late systolic flow and improved subendocardial perfusion. Reducing mean arterial pressure by any means will improve aortic compliance and potentially reduce pulse wave velocity but without altering the degenerative structural wall changes that have occurred to that time. There are currently no drugs available to reverse these changes but their progression should be decreased by pressure control. On the other hand vasodilator drugs reduce impedance to ventricular ejection and improve late systolic flow.

Summary

- LVH is a major risk factor for cardiovascular disease and predicts the development of LV failure.
- Traditional methods to detect LVH do not provide information about the arterial dynamics that determine LVH.
- PWA enables direct assessment of the severity of central aortic pressure elevation, and thus the development of LVH.
- PWA can accurately assess the effects of drug treatment for LVH.
- PWA can reveal the haemodynamic basis for ventricular failure and follow its therapeutic correction.

References

Systolic Heart Failure

Significance

Coronary artery disease is the most common cause of myocardial systolic dysfunction in Western society. This dysfunction can include ischaemia in the absence of infarction, and sometimes in the absence of symptoms of inadequate coronary perfusion. Transient loss of nutritional support for myocardial relaxation and contraction can result in prolonged functional impairment without loss of cellular integrity.

Systolic heart failure may result from a variety of conditions including myocyte loss, impaired myocyte function, interstitial or pericardial structural alterations that affect ventricular function, and electrical disturbances that impair pump function.

Detection

Systolic heart failure is characterised by reduced exercise capacity resulting from dyspnoea or fatigue. The signs and symptoms of heart failure relate not only to the abnormality of cardiac function but also to a wide variety of systemic responses that alter the vascular tone and neurohormonal milieu. It is these complex physiological responses that make heart failure such a multifaceted syndrome.

Pulse wave analysis

The use of sphygmonometry to identify patients with low subendocardial perfusion ratio (SEVR) can be helpful in preventing ischaemic induced systolic dysfunction.

In systolic heart failure, increased arterial stiffness and early wave reflection result in a reduction of late systolic blood flow, and vasodilator drugs targeted at large arteries will be of benefit by increasing late systolic flow rather than late systolic pressure.

Treatment

Acute drug administration has been demonstrated to alter pulsatile loading conditions in patients with heart failure. Both nitroprusside and dobutamine can decrease aortic afterload in patients with heart failure.

Management of the systolic dysfunction therefore includes efforts to treat the reversible causes of heart failure and to use drugs to improve left ventricular function through the optimisation of central haemodynamics and neurohormonal function.
References

Use of Sphygmocor in Diabetes Mellitus

Diabetes mellitus (type II diabetes) is parallel with obesity and is increasing in incidence and prevalence throughout the developed world.\(^1\)

Not only is diabetes associated with microvascular disease, but also with an increase in macrovascular disease. The American Heart Association has gone so far as to say ‘diabetes is a cardiovascular disease’.\(^2\)

Atherosclerosis is more common, more generalised and occurs at an earlier age in diabetic subjects than in the population at large.\(^3\) The resultant high risk of major cardiovascular complications is exacerbated further by its common associations with hypertension and hyperlipidaemia. Aggressive lowering of blood pressure in this situation undoubtedly results in prevention of vascular disease.\(^4\)

Even after correction for blood pressure, those with type II diabetes have increased left ventricular mass,\(^5\) and a high incidence of heart failure.\(^6\) This suggests a role for increased vascular stiffness, augmenting central systolic pressure.\(^7\)

The significance of the atherogenic dyslipidaemia of diabetes is shown clearly by results from the FINMONICA Study,\(^8\) describing an almost 50% death rate within 12 months of myocardial infarction in both male and female diabetics under the age of 65 years, almost double the rates of non-diabetic subjects. Effective treatment of hyperlipidaemia in diabetic patients was of great value in both primary and secondary prevention of cardiovascular disease, both in the CARE study\(^9\) and in the Scandanavian Simvastatin survival study (4S).\(^10\)

A small study by Goodfellow and colleagues,\(^11\) utilising a combination of techniques, showed increased vascular stiffness early in the course of type II diabetes. Using Sphygmocor, these findings were later confirmed in a larger study.\(^12\) It is likely that this stiffness is related to endothelial dysfunction rather than structural vascular alterations - this in turn raises the possibility that it is reversible. Since direct measurement of endothelial function in vivo is invasive and expensive, reliable and reproducible surrogate measures are of great clinical value. They have the potential for use in population screening for risk detection, as well as for use in monitoring responses to therapeutic manipulation in individual patients.

Candidates for causation of endothelial dysfunction and vascular disease are many, including hyperglycaemia, insulin resistance, abnormal lipid metabolism and the presence of advanced glycation end products. Each of these is susceptible to a variety of potential therapeutic or preventive manipulations.

The value of techniques to analyse the peripheral arterial pulse wave in detection and assessment of the severity of these abnormalities is dealt with in detail elsewhere in this manual, and a broader perspective is described in ‘Diabetes: Current Perspectives’.\(^13\) Insulin administration has been shown to cause endothelial dependent vasodilatation,\(^14\) associated with a reduction in central aortic pressure augmentation.\(^15\) It is likely therefore that Sphygmocor will have a role in patients with newly diagnosed diabetes, in the detection of early cardiovascular disease (Figure 3.5.1). Further, it is likely to be of assistance in evaluation of responses to control of hyperglycaemia, hyperlipidaemia and hypertension, and in tailoring of individual therapeutic regimens.

![Figure 3.5.1](image-url)

**Figure 3.5.1**

Note: Normal values of peripheral blood pressure. Elevated late systolic shoulder in radial pulse associated with a high calculated aortic augmentation index of 39%. This value lies outside the confidence intervals for the patients’ age. This together with relatively long systolic duration (41% of cardiac cycle) results in elevated systolic load on the heart, resulting in a relatively low SEVR of 127%. These indices calculated by Sphygmocor indicate that left ventricular load could be increased even at normal blood pressure.
Summary

- Diabetes is a cardiovascular disease
- Diabetic patients have increased vascular stiffness that contributes to increased LV mass and heart failure.
- SphygmoCor can monitor and quantify the onset of these changes.

References

Pulse wave analysis and renal failure

Cardiovascular complications are a major cause of morbidity and mortality in patients with renal failure. Deaths due to myocardial infarction and stroke are more frequent in haemodialysis patients than in the total population. Methods which permit simple but accurate assessment of cardiovascular status are therefore important. Arterial stiffness, determined by a variety of methods, is undoubtedly increased in renal failure. Aortic stiffness, determined by measurement of aortic pulse wave velocity (PWV) (via Doppler ultrasonography) is a strong independent predictor of all-cause and cardiovascular mortality in patients on chronic haemodialysis. The same group has recently reported that aortic PWV index (calculated as measured PWV - theoretical PWV) has greater predictive power than blood pressure or pulse pressure measurements.

Techniques to allow non-invasive and simple measurement of these haemodynamic variables are necessary before they can be included in routine clinical assessment of cardiovascular risk. There is now good evidence that central aortic pulse wave information can be acquired from examination of the pulse wave characteristics of medium sized peripheral arteries by applanation tonometry. Carotid artery tonometry measurements in non-diabetic haemodialysis patients have shown markedly increased PWV and augmentation index (AI).

Acquisition of similar information from the radial artery would further simplify assessment of pulse wave characteristics. Radial artery tonometry has the potential problem of previous and current vascular access, which will alter the measurements made in the arm. Interpretation of measurements also demands understanding of the acute effects of dialysis, in particular of rapid fluid balance shifts.

The first report on radial artery tonometry findings in patients on regular maintenance haemodialysis appeared recently. The authors describe pre- and post-dialysis values in 51 subjects with a wide range of pre-dialysis pulse waveforms (Figures 3.6.1 and 3.6.2), and several different patterns of response to the blood pressure and volume effects of dialysis therapy.

The clinical significance of these acute changes has yet to be determined, as has the most appropriate timing of measurements to determine the longer term prognosis of cardiovascular disease in this complicated patient population.
References


Summary

- Arterial stiffness is increased in patients with renal failure
- Aortic stiffness is a strong independent predictor of mortality in patients on chronic haemodialysis
- PWV and AI are increased in non-diabetic haemodialysis patients
- Haemodialysis may have a positive impact on arterial haemodynamics

Figure 3.6.2
Representative pulse wave form from a subject showing raised brachial artery blood pressure levels (top) and abnormal aortic function (bottom) (AGI of +31%). Adapted from reference 5.

Figure 3.6.1
Representative pulse wave form from a subject with normal brachial artery blood pressure levels (top) and virtually normal aortic function (bottom) (AGI of +2%). Adapted from reference 5.
Cardiovascular function in normal human pregnancy

Extensive information from invasive and non-invasive studies regarding the haemodynamic alterations of the normal human pregnancy has been available for many years. These studies demonstrate an increase in plasma volume, stroke volume, heart rate, and cardiac output, plus a fall in total peripheral resistance and systolic and diastolic blood pressures.

Cardiovascular function in human pregnancy complicated by pre-eclampsia

Maternal vascular function is abnormal in pre-eclampsia. In addition to hypertension, there is:

i) volume contraction

ii) increased total peripheral vascular resistance

iii) increased uterine artery resistance

iv) increased maternal vascular reactivity to external pressor substances.

A recent report utilising finger photoplethysmography has also described calculation of indices related to pressure wave reflection and large artery stiffness. The calculated values were increased in women with pre-eclampsia, in keeping with the concept of increased vascular stiffness in pre-eclampsia. Again, the parameters measured, while undoubtedly related to PWV, arterial stiffness and pressure wave reflection, suffer from the potential effects of extraneous stimuli on the local digital circulation.

Using a combination of procedures (two-dimensional M-mode echocardiography, oscillometric brachial artery blood pressure measurement, ECG, Doppler estimation of ascending aortic blood flow velocity, and subclavian artery pulse wave tracings), a group from the University of Chicago described an increase in arterial compliance in normal human pregnancy, and both a delay and a reduction in the magnitude of peripheral arterial wave reflection. These changes were felt to represent adaptations in both conduit and peripheral arteries, and help to accommodate the increased plasma volume and the efficiency of ventricular-arterial coupling and diastolic perfusion pressure. Unfortunately, women with pre-eclampsia or chronic hypertension were excluded from this study. A specialised in-house apparatus was used to acquire the subclavian artery pulse wave information, and the methodology is therefore not applicable to routine clinical practice.

Non-invasive in vivo assessment of arterial compliance and cardiovascular load in pregnancy

A variety of non-invasive methods have been developed to allow better description of cardiovascular physiology in vivo. These involve measurement of the arterial pulse waveform from a medium-sized or small peripheral artery, and calculation of central arterial pressure characteristics. Some of these techniques have been examined in normal and/or hypertensive pregnancy. Reproducible assessment of wave propagation and reflection, which are major components of pulsatile arterial load, would give information about vascular stiffness, pulse wave velocity, central aortic pressure augmentation, and hence cardiac afterload.

Early work in pregnant women by Hon et al described the development of a non-invasive pressure transducer for application to the finger, permitting the recording of peripheral pulse wave patterns. From these recordings and simultaneous ECG tracings, information was gained about pulse wave velocity (PWV) and about the associations of different pulse wave contour patterns with pregnancy outcomes. There are a number of publications from this group describing the patterns observed both in normal pregnancy and in hypertensive pregnancy of different causes. However, the measurements made are potentially affected by local circulatory changes in the hand. The device is not yet commercially available in Australia, and is being evaluated in ongoing studies in various international centres.
Potential applications of SphygmoCor to normal and hypertensive pregnancy

We hypothesise that in pre-eclampsia, because of the combination of vasoconstriction and small vessel disease secondary to coagulation activation, there will be a detectable increase in both PWV and augmentation index (AI), the latter increasing sharply in proportion to clinical severity. It is likely that some pregnant women with chronic hypertension also have increased PWV.

We hypothesise that this will be the subgroup which develops superimposed pre-eclampsia, which is characteristically very rapidly progressive when it occurs on a background of chronic hypertension. We therefore suggest that measurements of either AI or PWV will be of value in assessing the clinical severity and the likelihood of complications such as pulmonary oedema, and may help to guide therapy for these patients.

Increased vascular reactivity, increased uterine artery resistance, increased BP measured by ambulatory BP monitoring, and a reduction in plasma volume all precede the development of pre-eclampsia. Therefore, it is possible that the PWV and AI values may be detectably abnormal prior to the clinical appearance of the disorder. It is not known yet whether this is so, or whether the measurements will be a reliable predictor of pre-eclampsia. It is also not known whether this will be a useful prognostic indicator in women with early disease.

Current research is underway to assess PWV in normal women at different stages of pregnancy to establish baseline ranges. Future investigations will examine women with hypertension.

A recent study illustrates the potential use of pulse wave analysis in pregnant patients, highlighting the effect of normal pregnancy on pulse pressure (Figure 3.7.1), and augmentation pressure and augmentation index (Figure 3.7.2).

**Figure 3.7.1**

The effect of normal pregnancy on pulse wave pressure measured at radial artery and derived by SphygmoCor at the aorta. Values are shown (mean, 95% CI) for women at 25-28 weeks amenorrhoea, and for non-pregnant women. The wider pulse pressure at the radial artery, well described in normal pregnancy (p<0.05), is not seen centrally.

**Figure 3.7.2**

The effect of normal pregnancy on augmentation (mmHg) and augmentation index (%). Values are shown (mean, 95% CI) for women at 25-28 weeks amenorrhoea, and for non-pregnant women. Augmentation and augmentation index are significantly lowered in normal pregnancy (p<0.01), reflecting peripheral vasodilatation.
Summary

• Maternal vascular function is abnormal in pre-eclampsia
• There is likely to be increased PWV and AI in patients with pre-eclampsia
• Measurements of PWV may be valuable for assessing the clinical severity or pre-eclampsia

References

**Effects of Drugs on Central Pressure**

### Introduction

In routine clinical practice, the selection of drugs for the treatment of hypertension and/or cardiac contractile failure requires knowledge of their established effects on systolic and diastolic brachial artery pressure, cardiac ejection and excitability, autonomic function and heart rate. In particular, awareness of cardiovascular, cerebrovascular and renal outcome statistics from long term treatment studies is required.

There is little opportunity to improve on such evidence-based criteria unless a patient's individual cardiovascular characteristics are more fully explored and then progressively monitored. This is particularly true when systolic hypertension and cardiac contractile impairment are specifically aggravated by decreased vascular compliance (i.e. increased arterial stiffness).

Central arterial systolic pressure increases not only as a direct function of the ventricular ejection properties and vascular conduit stiffness, but also indirectly through vascular stiffness, which causes increased velocity of the pulse wave propagation and reflection. This can lead to potentially dangerous augmentation of central systolic peak pressure, limiting cardiac ejection and exposing central and cerebral vessels to higher than anticipated pressures. The augmentation can account for as much as 40% of the central pulse pressure in older patients with isolated systolic hypertension. However it is specifically reducible in individual patients with drugs that modify the velocity and size of the pulse wave and its reflection.

In order to apply these haemodynamic principles responsibly in practice, published evidence regarding the different classes of drugs should be carefully considered, particularly:

- The acute effects of the drug on peripheral (i.e. brachial) and central arterial wave forms. This information allows functional information about both aortic and systemic arterial stiffness to be assessed, as well as the degree of augmentation of the central pulse due to reflection, and the timing of the reflected wave.
- Evidence that these initial changes are maintained with long-term administration.
- Multicentre outcome studies in which drugs that decrease central arterial pulse augmentation, or at least retard the progression of vascular stiffness, provide better statistical associations with reduced morbidity and mortality than brachial artery pressure alone.

### Nitric oxide donors

Acute studies using various nitric oxide (NO) donor preparations (e.g. nitroprusside in hypertensive patients) have shown that augmentation of the central systolic pressure is consistently abolished. This is evident with both invasive and non-invasive assessment, and is seen with or without a fall in brachial artery pressure. The acute beneficial effect of nitrates may be due not only to a reduction in total vascular stiffness or pulse wave velocity, but to a reduction in the size of the component of the wave complex reflected from peripheral arteries larger than arterioles.

Long-term non-invasive observations (e.g. 34 weeks on isosorbide mononitrate) in elderly hypertensives have confirmed that the reduction in central systolic pressure is sustained, but to date, morbidity and mortality outcome comparisons of pulse wave analysis with brachial pressures are not available.

### Dihydropyridine calcium channel blockers, alpha adrenergic blockers and hydralazine

This heterogenous group of antihypertensive drugs are classified by their main site of action, and act primarily by decreasing peripheral arteriolar resistance. They have been shown to reduce brachial artery pressure and augmentation of the central pulse both acutely and long-term in middle-aged essential hypertensives.

Studies have shown that the calcium blocker nifedipine completely abolished augmentation by apparently reducing pulse wave velocity, vascular stiffness, and wave reflection. Any drug that decreases mean arterial pressure will also reduce pulse wave velocity acutely as wall tension decreases in central vessels. In addition, drugs that tend to increase heart rate, such as hydralazine, will reduce augmentation irrespective of their other actions due to a faster systolic ejection, allowing the main component of the reflected wave to fall in the post-systolic peak period. Conversely, drugs that increase systolic ejection time, which can occur with calcium blockers, may negate the beneficial effects of the reduced pulse wave reflection. To date, no outcome data using this insight from pulse wave analysis are available for this group of agents.
**ACE inhibitors and AT1 receptor blockers**

ACE inhibitors and AT1 receptor blockers act on the tone in muscular arteries and arterioles. Interfering with the actions of angiotensin decreases blood pressure without changing heart rate. Pulse wave changes with these agents are similar to those seen with calcium blockers, i.e. reduced pulse wave velocity, vascular stiffness, wave reflection and central augmentation. These drugs appear to be the most beneficial for reducing the morbidity and mortality associated with hypertension, and the application of pulse wave analysis to long-term outcome studies is presently being assessed. The possibility that these drugs retard or improve vascular pathology and therefore the compliance properties of the main conduit vessels in the long-term seems likely.

**Diuretics and combination therapy**

The effect of diuretics alone on pulse wave analysis has not been seriously studied. These agents are not expected to produce significant changes on pulse wave, since they act acutely through fluid reduction and cardiac output and long-term by moderate reductions in peripheral resistance. In combination with calcium blockers or ACE inhibitors, the salutary effects of the primary antihypertensive drug on the central pulse wave are not obviously improved, but long term studies with diuretics alone are required.

**Beta-receptor blockers**

Beta-receptor blockers adversely affect pulse wave reflection characteristics in the short term and are manifestly less active than other antihypertensives in the long term. This may be due to:

- bradycardia with increased systolic ejection time
- vasoconstriction in some vascular beds increasing pulse wave reflection
- lack of direct effect on vascular compliance.

Despite these features, beta blockers have been repeatedly shown to improve outcome statistics, especially in combination with diuretics. However, they are not as beneficial as ACE inhibitors in hypertension which may be partly accounted for by their failure to reduce augmentation of the central pulse.

**Summary**

- Drugs that modify the velocity and size of the pulse wave and its reflection can effectively reduce augmentation of central systolic pressure
- Evidence regarding the effects of different drug classes on peripheral and central arterial waveforms should be carefully considered when applying haemodynamic principles in clinical practice
- Nitric oxide preparations, calcium channel blockers, ACE inhibitors and angiotensin II receptor blockers have been shown to abolish augmentation by reducing pulse wave velocity, vascular stiffness and wave reflection
- The application of PWA to long-term outcome studies with various agents is currently being assessed

**References**

Case Studies

SphygmoCor in Clinical Practice: Nitroglycerin for Angina

Case Study 1

Patient: GTN

Presents with acute angina and is given a sublingual capsule of nitroglycerin. SphygmoCor studies are done as a control, and then every 30 seconds for 3 minutes, to derive calibrated aortic pressure waveforms.

Waveform Analysis

This SphygmoCor display shows the dramatic reduction in aortic systolic peak pressure due to arterial vasodilation (reduction in aortic pressure augmentation, or “afterload”).

Parameter Trend Analysis

This SphygmoCor display plots the changing aortic parameters over time for the seven nitroglycerin studies above.
Summary

The use of PWA provided additional valuable information to guide treatment in this patient. It demonstrates clearly the effects of nitroglycerin, where as little change could be seen in peripheral blood pressures.

This case demonstrates the importance of central pressures in optimising drug choice, drug dose and drug combinations to achieve best results.

Notes
SphygmoCor in Clinical Practice: Hypertension

Case Study 2

First visit: October 1997

Patient: DH
Female aged 89, with 10-year history of mild hypertension.

PWA (see Figure 5.1): AG 21 mm; SVR 120%; ED 42%

ECG: L ant hemiblock
Echo: EA reversal, mild LVH, diastolic dysfunction, normal systolic function
Ex ECG: NAD
VO2 max: 15 ml/kg/min
Glu: 4.8

Plan: stop diltiazem; start atenolol

Blood Pressure 166/87 (121) mmHg
1st, 2nd Peak 36%ED, 53%ED
Aug. Index 102% (P2/P1)
Maximum dP/dt 1178 mmHg/s

Blood Pressure 155/92 (121) mmHg
1st Peak 36%ED, 102 ms
2nd Peak 72%ED, 203 ms
Augmentation +25 mmHg

CENTRAL HAEMODYNAMIC PARAMETERS

Radial Pulse Waveform

Aortic Pulse Waveform

Pressure Data

Pulse Height (PH) 63 mmHg
P1 Height (P1-DP) 42 mmHg
Augmentation (AG) +21 mmHg
Aug. Index (P2/P1, AG/PH) 152%, +33%
Mean Press. (Syst/Diast) 135/112 mmHg
End Systolic Pressure 140 mmHg

TIMING DATA

Heart Rate, Period 89 bmp, 674 ms
Eject. Duration (ED) 42%, 280 ms
Diast. Duration 58%, 394 ms
Buckberg. SUR (Ad/As) 120% (3986/3308)
- Systolic Area/min 3308 mmHg. s/m
- Diastolic Area/min 3986 mmHg. s/m

EXPERIMENTAL DATA

Waltz. Index 102% (P2/P1, AG/PH)
Blood Pressure 166/87 (111) mmHg
Aug. Index 102% (P2/P1)
Maximum dP/dt 1178 mmHg/s

Figure 5.1
SphygmoCor in Clinical Practice: Hypertension

Non-smoker
Examination NAD
Rapid pulse, HR 93
Height: 148 cm; weight: 53 kg;
BMI: 24
Medication: diltiazem hydrochloride
180 mg
Sitting BP: 150/95 mmHg; Lying
BP: 166/87 mmHg

First visit: October 1997

Presents with chest pain and
dyspnoea on exertion; dizziness
at times

Examination
Examination NAD
Rapid pulse, HR 93
Height: 148 cm; weight: 53 kg;
BMI: 24
Medication: diltiazem hydrochloride
180 mg
Sitting BP: 150/95 mmHg; Lying
BP: 166/87 mmHg

Plan: stop diltiazem; start atenolol
Review: March 1998

Dyspnoea improved, occasional chest pain
Examination NAD
Sitting BP: 165/80 mmHg; Lying BP: 158/70 mmHg
HR: 75
Meds: atenolol 25 mg, aspirin
HRV: normal

PWA (see Figure 5.2): AG 37 mm; ED 38%; SVR 126%

Plan: start diuretic (indapamide)
Review: October 1998

Dyspnoea stable, no further chest pain
Examination NAD
Sitting BP: 145/75 mmHg; Lying BP: 150/76 mmHg
HR: 64
HRV: normal
Meds: atenolol 25 mg; indapamide 2.5 mg; aspirin

PWA (see Figure 5.3): AG 29 mm; ED 36%; SVR 140%

Plan: start ACE inhibitor (for high augmentation pressure)
Review: April 1999

Dyspnoea stable
Examination NAD
Sitting BP: 126/76 mmHg; Lying BP: 130/76 mmHg
HR: 54
VO2 max 20 ml/kg/min
HRV: normal
Meds: atenolol 25 mg; trandolapril 1 mg; indapamide 2.5 mg; aspirin

PWA (see Figure 5.4): AG 21 mm; ED 31%; SVR 173%

Figure 5.4
Case Study 2 cont.

Review: May 2000

Dyspnoea on exertion worse

Examination NAD

Sitting BP: 135/68 mmHg; Lying BP: 135/73 mmHg

HR: 78

HRV: normal

Meds: trandolapril 1 mg; indapamide 2.5 mg; aspirin (stopped atenolol due to symptomatic bradycardia)

PWA (see Figure 5.5): AG 21 mmHg; ED 41%; SVR 121%

Plan: re-start low-dose atenolol
Summary

The use of PWA provided additional valuable information to guide treatment in this older patient. In particular, the low SVR at the first visit identified the need to reduce HR to optimise the coronary perfusion in this symptomatic patient who has evidence of diastolic dysfunction on echocardiography. The rate reduction achieved with atenolol resulted in a reduction in symptoms and an improvement in SVR. However, there was a dramatic increase in augmentation pressure which was not reflected by an increase in peripheral pressures. If left untreated, this may have worsened the diastolic dysfunction and caused increasing dyspnoea over time. Judicious use of a diuretic and an ACE inhibitor resulted in a reduction in augmentation pressure and maintenance of a normal SVR.

This case demonstrates the importance of central pressures in optimising drug choice, drug dose and drug combinations to achieve best results.

Notes
Reproducibility

Reproducibility of central aortic pressure and pulse wave velocity measurements with SphygmoCor depend on the quality of the data recorded. The essential element is to obtain an accurate radial pulse waveform, from which all parameters are derived. As with any technique, results of reproducibility will depend on the stability of subjects' physiological status and operator skill.

Reproducibility studies should be conducted by each operator, or groups of operators to determine the extent of variability inherent in the specific measurements. Clinical studies have shown that the technique is highly reproducible.

Three recent studies address the issue of reproducibility of parameters derived by SphygmoCor:

1. Filiposky et al studied 88 healthy subjects aged 19-53 years and determined the reproducibility of parameters estimated by pulse wave analysis (PWA), mainly of central systolic blood pressure in the aorta (CSP), central systolic pressure-time index (CSPTI), and central augmentation index (CAI). Variability within and among subjects was significantly different for peripheral systolic pressure (PSP) and for all the above-mentioned parameters (p < 0.0001 by ANOVA for all). Variability within and between observers did not show any trend for the variability to be dependent on the underlying mean value. PSP, CSP and CSPTI decreased significantly during one visit (by 4.6, 4.7 and 4.2%, respectively), PSP and CSP were higher at the first than at the second visit (by 2.2, 2.2%, respectively, and not significant for CSPTI), and there were also significant inter-observer differences in all the three parameters as one observer measured higher values (by 2.4, 3.2 and 6.0%, respectively). CAI did not change within and between visits; the same applied to the difference between PSP and CSP since these pressures always changed in parallel. The study concludes that PWA gives estimates of several parameters characterizing the pressure load of central circulation and the wave reflection. The reproducibility of CSP and CSPTI is similar to that of PSP. CAI and the difference between PSP and CSP is not influenced by order of measurement, of visit or by investigator.

2. Siebenhofer et al studied 33 healthy subjects of mean age 33 years (SD 10.3) and determined the inter-operator variability from 75 paired measurements. The table below summarises their results:

<table>
<thead>
<tr>
<th>SphygmoCor Parameter</th>
<th>Inter-operator variability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derived Systolic pressure</td>
<td>0.1 ± 1.7 mmHg</td>
</tr>
<tr>
<td>Derived Diastolic pressure</td>
<td>0.1 ± 0.7 mmHg</td>
</tr>
<tr>
<td>Augmentation index</td>
<td>0.4 ± 6.4 %</td>
</tr>
<tr>
<td>Subendocardial Viability Ratio</td>
<td>2.7 ± 15.4 %</td>
</tr>
</tbody>
</table>

3. O'Rourke and colleagues examined the typical coefficients of variability obtained in a representative reproducibility study, and these are outlined below.

Definitions

Coefficient of Variation CV (%) = 100 x standard deviation/mean.

Repeatability Repeatability was assessed in 18 subjects (age 22-57 yrs; 7 m, 11 f) with ten consecutive measurements at both the radial and carotid arteries.

Reproducibility Reproducibility was measured in 8 subjects (age 22-36 yrs; 2 m, 6 f) on four separate occasions over a 2-week period.

Interobserver variability This was assessed in 9 subjects (age 22-57 yrs; 5m, 4f) with measurements taken by three independent operators on the same occasion.

Right vs left radial waveforms Studies were also conducted in 45 subjects (24 on antihypertensive treatment; age 22-80 yrs) to assess the difference in derived parameters when recordings were taken from the left or right wrist.
Pulse wave velocity

SphygmoCor also performs measurements of pulse wave velocity as an index of arterial stiffness (see Section 2). This is associated with wave reflection phenomena and with the augmentation index (AI) of the central aortic waveform obtained by means of a transfer function from peripheral recordings of the arterial pulse. Reproducibility assessed through the Bland-Altman method with calculation of the repeatability coefficient was, following intra-observer comparison, for Brachial PWV: 1.64 m/sec (for a mean value of 8.65 ± 1.58 m/sec); and for aortic PWV: 2.34 m/sec (for mean value of 8.15 ± 3.01 m/sec). Corresponding data for between-observer values were 2.18 m/sec and 2.50 m/sec, respectively.

The augmentation index was analysed in terms of the relationship to pulse wave reflection and global arterial stiffness. Comparison between AI and aortic pulse wave velocity has shown a significant association, with a significant but relatively weak positive correlation found between AI and aortic PWV (r=0.29, p<0.005). However, the correlation increased when gender was considered. The role of height, heart rate and blood pressure, and the heritable component, as seen in twins, could partly explain this weak relationship.

References
