

Pulse wave analysis

Michael F. O'Rourke and David E. Gallagher

Pulse wave analysis in historical times Interpretation of the arterial pulse has been an important part of the medical examination from ancient times. Graphic methods for clinical pulse wave recording were introduced by Marey in Paris and by Mahomed in London last century. Mahomed showed how such recordings could be used to detect asymptomatic hypertension, and used them to chart the natural history of essential hypertension and to distinguish between this condition and chronic nephritis. Interest in arterial pulse analysis, as applied by Mahomed, lapsed with the introduction of the cuff sphygmomanometer 100 years ago.

Modern pulse wave analysis Analysis of the arterial pulse is now regaining favour as limitations of the cuff sphygmomanometer are better recognized (including the ability only to measure extremes of the pulse in the brachial artery). In addition, high-fidelity tonometers have been introduced for very accurate, non-invasive measurement of arterial pulse contour, and there is now a better understanding of arterial hemodynamics, and appreciation of disease and aging effects in humans. It is now possible to record the pulse wave accu-

rately in the radial or carotid artery, to synthesize the ascending aortic pulse waveform, to identify systolic and diastolic periods and to generate indices of ventricular-vascular interaction previously only possible with invasive arterial catheterization. Pressure pulse wave analysis now permits more accurate diagnosis and more logical therapy than was ever possible in the past.

Journal of Hypertension 1996, 14 (suppl 5):S147-S157

Keywords: transfer function, impedance, ventricular-vascular interaction, sphygmogram, applanation tonometry

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Conflict of interest: M.F.O'R. has an interest in PWV Medical (Australia) and EMTS (USA), companies associated with pulse analysis systems.

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'Our old ally the pulse ranks the first among our guides; no Surgeon can despise its counsel, no Physician shut his ears to its appeal. Since then the information which the pulse affords is of so great importance and so often consulted, surely it must be to our advantage to appreciate fully all it tell us, and to draw from it every detail that it is capable of imparting.'

F.A. Mahomed, 1872 [1]

Introduction

While the arterial pulse is the most fundamental clinical sign in medicine, identifies the physician in works of art and forms the crest of the Royal College of Physicians of London, modern physicians pay scant attention to it and usually use it only for determining heart rate. Physicians dealing with hypertension are content to measure just the highest (systolic) and lowest (diastolic) value of the brachial pressure pulse in diagnosing and treating this condition. Even when monitored directly in operating theatres and critical care areas, anesthetists and intensivists show little interest in the waveform and base their judgements on values of systolic, diastolic and mean pressure.

With respect to the arterial pulse, modern clinical practice has not advanced in 150 years, despite advances in other areas, and the new methods which have been developed to measure, analyse and interpret the arterial pulse. The aim of this review is to trace developments in this area in the past 150 years, and to suggest how clinically important information can be gleaned from studies of the arterial pulse.

Classical sphygmography

In his classic work, Richard Bright [2] identified increased arterial tension from 'hardness' of the arterial pulse, and correctly attributed left ventricular hypertrophy and vascular damage to high arterial pressure. Working at the same hospital (Guy's) in London, and initially whilst a medical student, Mahomed sought to identify patients with increased arterial pressure through graphic registration of the pulse [1,3,4]. He improved on the technique initially developed by Marey in Paris [5] and introduced a quantitative sphygmogram in which the 'hold down' force on the radial artery could be measured. Mahomed went on to describe the typical pressure pulse in arterial hypertension, stressing that the most important fea-

ture of the pulse was not the 'hold down' force, but the contour of the wave, with relative prominence of the secondary systolic or 'tidal' wave, caused by wave reflection (Fig. 1).

'1. Pressure above 1 ounce and sometimes as high as 10 ounces is employed to develop the pulse-tracing to its greatest extent.

2. The percussion wave is usually well marked and distinctly separated from the tidal.

3. The dicrotic wave is very small and often scarcely perceptible; the vessels, however, are full during the diastolic period, and collapse slowly.

4. The tidal wave is prolonged and too much sustained.

...The most constant of these indications is the prolongation of the tidal wave; and one or all of the other characters may under certain conditions be absent.'

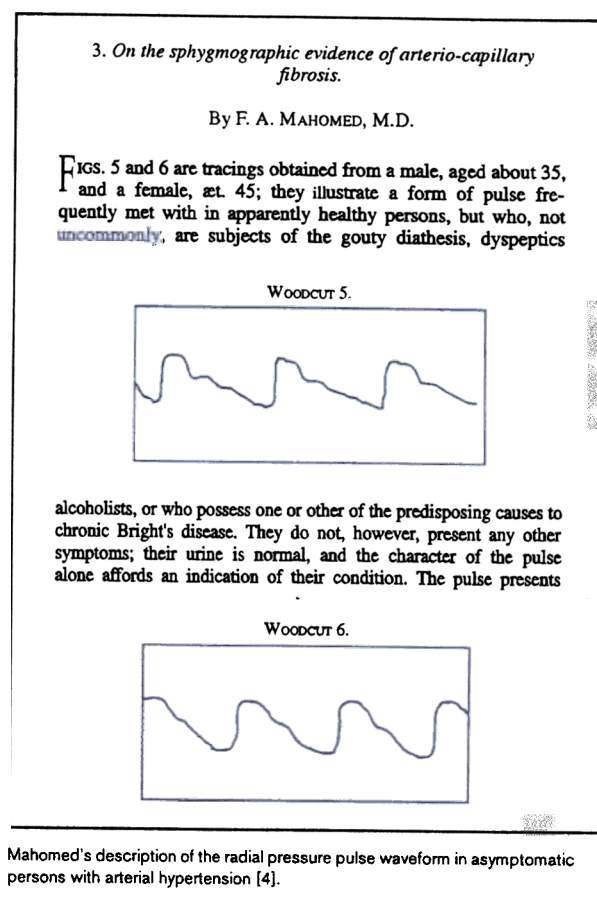
On the basis of this work, Mahomed went on to chart the natural history of what we now call 'essential hypertension' and to separate this from hypertension caused by glomerulonephritis (Bright's disease).

'These persons appear to pass on through life pretty much as others do and generally do not suffer from their high blood pressure except in their petty ailments upon which it imprints itself...as age advances the enemy gains accession of strength...the individual has now passed forty years, perhaps fifty years of age, his lungs begin to degenerate, he has a cough in the Winter time, but by his pulse you will know him...Alternatively, headache, vertigo, epistaxis, a passing paralysis, a more severe apoplectic seizure, and then the final blow'.

He also showed that similar changes are seen in the arterial pulse with aging, and noted that the secondary systolic or tidal wave is normally more prominent in central (carotid) than in the brachial or radial arteries. Mahomed's contribution to this field was recognized in two recent reviews [6,7]. It was very influential at the time, and formed the basis of Broadbent's book on the pulse [8], and Mackenzie's later work [9]. At the turn of the century, medical texts and journal articles were liberally illustrated with sphygmograms.

Introduction of the sphygmomanometer cuff to clinical practice in the early 1900s led to a decline of interest in sphygmography. The technique of pulse wave recording was difficult and time consuming; recordings often showed artifacts, and were not easy to describe or characterize. The cuff provided numbers which came to be linked in a simplistic way to cardiac strength (systolic pressure) and arteriolar tone (diastolic pressure) [10]. Pseudoscience had arrived with numbers, and an era followed in which high systolic pressure was considered good (since it inferred a strong and healthy heart), but high diastolic pressure was considered bad, and the diagnostic requirement for hypertension (since it inferred high arteriolar tone and vascular resistance). This era ended with

Fig. 1.



appreciation of Framingham data, and with the Systolic Hypertension in the Elderly Program and other trials in the 1980s which showed a very strong association between systolic blood pressure and cardiovascular events [11,12].

Classical sphygmography enjoyed a brief period of popularity in the 1970s before widespread use of echocardiography, to measure systolic time intervals. Recordings were made with a microphone or similar device from the carotid artery in the neck. Changes in systolic time intervals (increase in pre-ejection period, decrease in ejection time) were associated with systolic left ventricular dysfunction and decreases in diastolic period, especially with tachycardia, were associated with increased potential for myocardial ischemia [13,14]. This work has recently been rekindled with the demonstration of the critical importance of diastolic time during exercise in patients with angina pectoris and (often) relatively mild coronary atherosclerosis [15].

The arterial pulse is of complex shape, varies with age, differs in different arteries, and changes markedly with physiological

and pharmacological interventions. Hence advances in pulse wave interpretation had to await the development of accurate high-fidelity instruments for invasive and non-invasive pressure wave recording, and for a deeper understanding of arterial hemodynamics to be achieved. This occurred with the introduction of catheter-tip manometers by Murgu and Millar [16] and of practical tonometers [17–19], and with the full development of methods to characterize and analyze the arterial pulse in the frequency as well as the time domain [20].

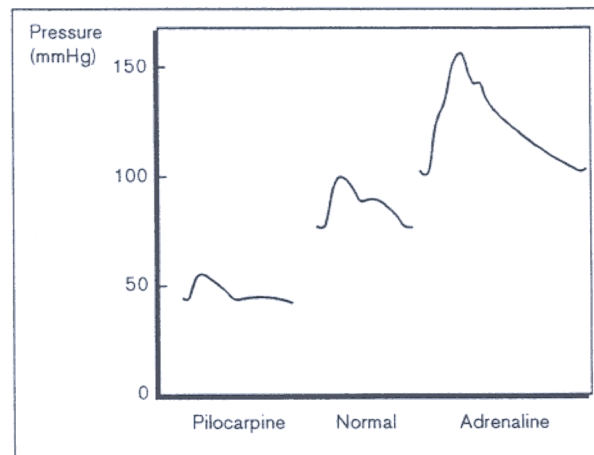
Analysis in the frequency domain

This field was opened by the experimental and theoretical work of McDonald, Womersley and Taylor at St Bartholomew's Hospital, London, during the 1950s [21,22]. Crucial to progress was the demonstration by Womersley that the non-linearities in pressure–flow relationships were small, so that the arterial system could realistically be regarded as a linear system. Pressure and flow waves were broken down into component harmonics, and their relationships were expressed as transfer functions. These techniques were used to characterize pressure–flow relationships at the one site as vascular impedance and pressure waves at different sites as a pressure transfer function. This work permitted the study of wave transmission and wave reflection in a quantitative fashion, and led to more sophisticated approaches using impulse responses and inverse Fourier transformation.

With respect to arterial hypertension, it was shown that the characteristic pulse wave changes as described by Mahomed (Fig. 1) can be created in experimental animals (Fig. 2) by infusion of vasoconstrictor agents [23,24], and that these were associated with changes in ascending aortic impedance, with impedance curves shifting upwards and to the right (i.e. to higher frequencies; Fig. 3) [24,25]. The changes in pulse wave contour and in impedance could readily be explained on the basis of increased stiffness of the aorta and early return of wave reflection [24,25]. The increased prominence of the 'tidal' wave and disappearance of the diastolic wave can be attributed to the same phenomenon: increased aortic tension and stiffness, with increased pulse wave velocity and early return of wave reflection, so that the reflected wave moves from diastole to systole. These changes are most apparent in the aorta and central arteries, and more subtle in peripheral arteries since, as observed by Mahomed, and confirmed by others [26,27], the amplitude of the secondary systolic (or tidal) wave is invariably greater in central than in peripheral arteries.

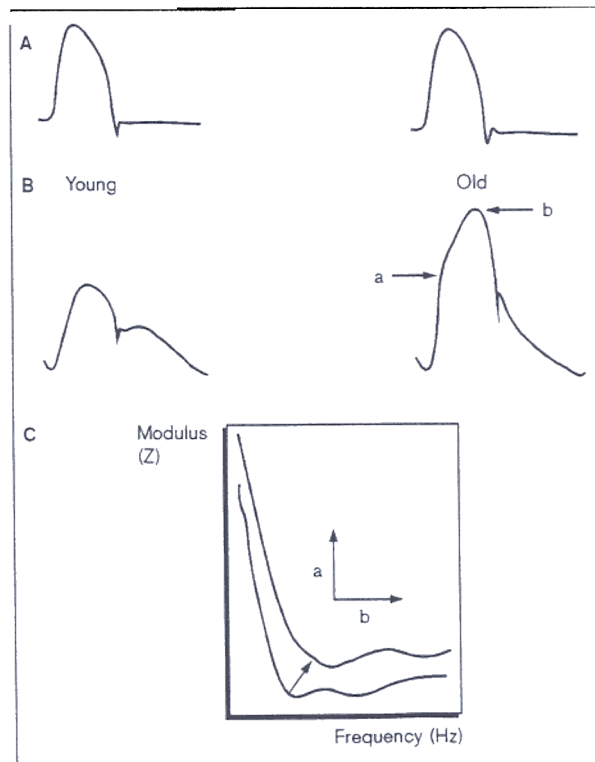
These points have been confirmed repeatedly in humans, where ascending aortic pressure and flow waves are recorded and expressed as vascular impedance. Hypertensive subjects show considerable augmentation (amplitude of the 'tidal' wave) and show the characteristic impedance changes which are apparent in experimental animals during infusion of pressor agents, and are consistent with aortic stiffness and early return of wave reflection [28,29]. Antihypertensive therapy offsets these adverse effects on arterial stiffness and early wave reflection [28–32]. The most extensive recent studies on ascend-

Fig. 2.



Pressure wave contour in the ascending aorta of a rabbit under normal conditions, with pressure reduction induced by infusion of pilocarpine and with increased pressure caused by infusion of adrenalin. From [24].

Fig. 3.



Schematic diagram of flow waves (A) and pressure waves (B), in the ascending aorta of a young human subject (left) and in an older person with isolated systolic hypertension (right). C, Ascending aortic impedance modulus plotted against frequency, and with this shifted upwards and to the right, by regional aortic stiffening (a), and by early return of wave reflection (b). From [24].

ing aortic impedance in humans have been conducted by Chen and colleagues from Taiwan, and have shown, as predicted, evidence of reduction in wave reflection during therapy with an angiotensin converting enzyme (ACE) inhibitor and calcium channel antagonist, but evidence of increased wave reflection with a beta-blocking agent [29–32].

While characteristic changes in ascending aortic impedance have been demonstrated repeatedly in hypertensive subjects, and are attributable to increased aortic pulse wave velocity, there is virtually no change in the relationship between arterial and peripheral (upper limb) pressure waves, as expressed as the transfer function (Fig. 4). We have exploited this constancy of transfer function in the upper limb so as to generate the central aortic pressure wave from the radial pressure wave. This is discussed below.

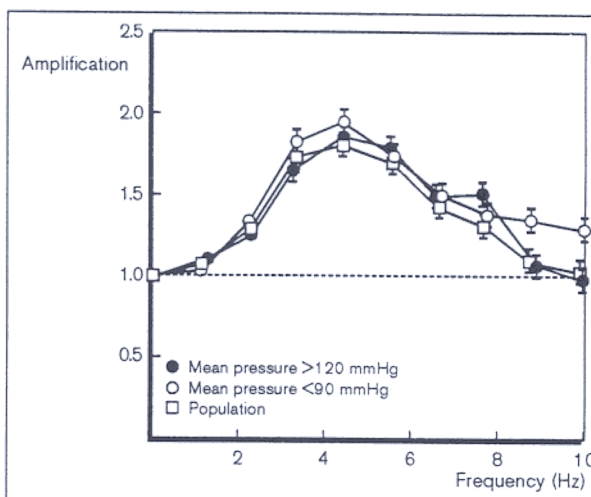
Computer modelling studies provide support for the experimental findings and clinical observations described above. Virtually all wave reflection as seen at the heart comes from the lower body and appears to arise from the lower aorta [34–36]. With aging and in hypertension, earlier wave reflection is attributable to greater stiffness of the aorta and a greater degree of dilation of the proximal as compared to the distal aorta (which shifts the resultant reflecting site to a more proximal location) [20]. The transfer function in the upper limb is altered somewhat by different interventions but hardly at all under 3–4 Hz where most components of the pressure pulse reside [37]. Hence transmission in the upper limb is reasonably approximated by a generalized transfer function.

These basic points explain much of what follows in this article. The gross increase in ascending aortic impedance at low frequencies (less than 4 Hz) causes substantial change, with marked augmentation of the aortic pressure wave [20]. These changes are attributable to aortic stiffening. On the other hand, and in stark contrast, there is little or no change in upper limb pressure transfer function with age or with hypertension at frequencies under 4 Hz [20,33,37].

Applanation tonometry

Applanation tonometry, applied to arteries [17] has revolutionized the old technique of sphygmography by providing high-fidelity signals which, under ideal conditions, are identical to those recorded within an artery [18,19,38]. Tonometry is widely used for recording intra-ocular pressure and is based on the theoretic principle that when the surface of a rounded chamber or vessel is flattened, tangential pressures are normalized, and a sensor on the flattened surface will record the pressure within the chamber. Theoretic principles are degraded by the presence of tissue between the sensor and arterial wall, with consequent inability to achieve ideal applanation under all circumstances. However tonometry has been shown to give an excellent representation of the intra-arterial pressure wave when used by an experienced operator on a suitable subject. Pressure excursion (pulse pressure) is usually measured with a fair degree of accuracy [39], but the actual systolic and

Fig. 4.



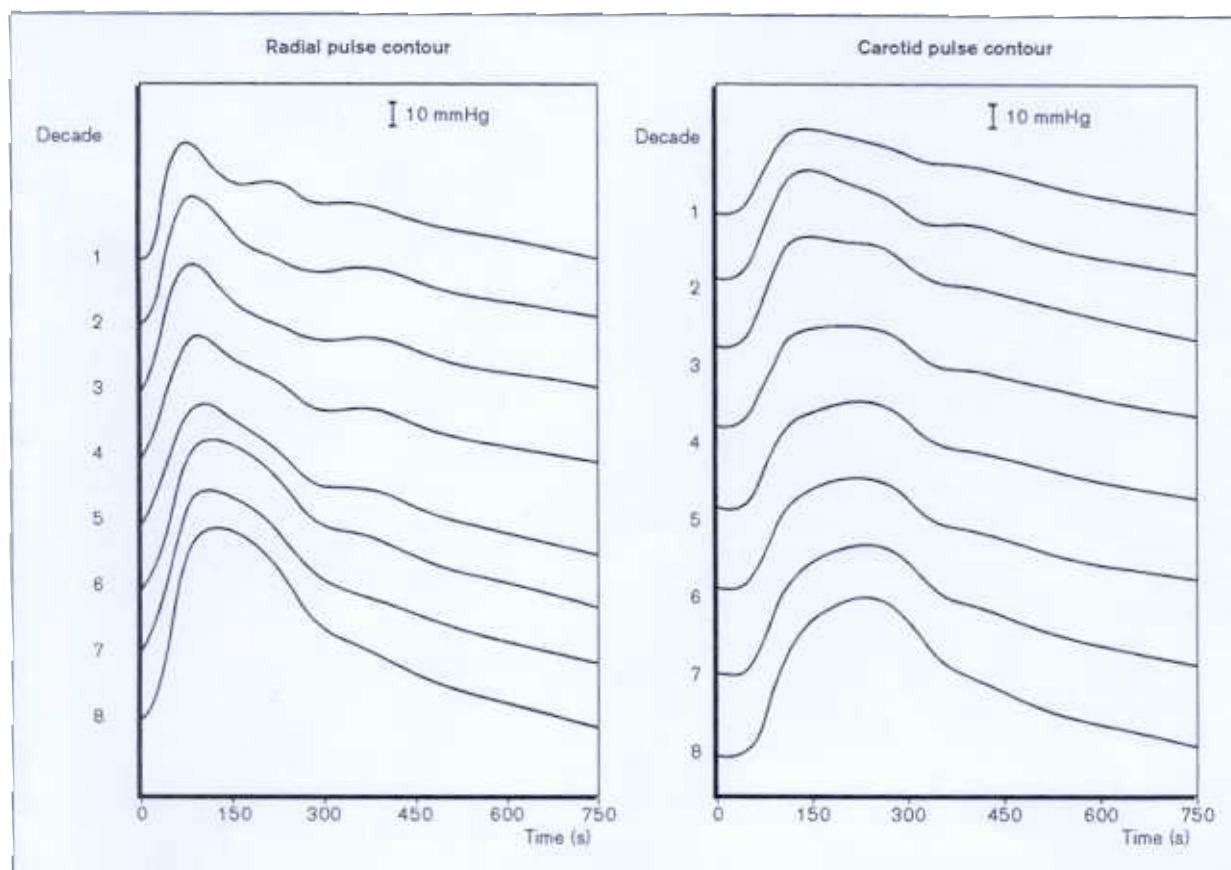
Overall transfer function between carotid artery and radial artery in 439 human subjects plotted with upper (>120 mmHg) and lower (<90 mmHg) quartiles of mean pressure. No difference was observed between groups. From [33].

diastolic pressures vary with the 'hold down' pressure applied to the sensor by the operator. While confident about wave shape, we have not been happy with absolute pressure and have calibrated the radial pressure wave against the sphygmomanometrically determined brachial pressure, so ignoring the (small) degree of amplification between the brachial and radial sites. Calibration of the carotid pressure wave is more complex [20,33].

Radial and carotid pressure waves

Kelly *et al.* [26] reported a study of carotid, radial and femoral pressure waves in 1005 normal human subjects (Fig. 5). There are progressive changes in wave contour at the carotid and radial sites with aging. The principal change is with the secondary systolic wave. In young adults this is well below the peak of the radial wave, but rises progressively to approach the wave peak by the eighth decade of life. In the radial artery of young adults, the late systolic wave is followed by a third distinct wave in early diastole. The performance of a Valsalva maneuver readily confirms that these two waves (late systole and early diastole) are indeed just one and represent the 'echo' of the original systolic wave [40]. They appear as two by interposition of the incisura caused by aortic valve closure. During a Valsalva maneuver, the two waves (incident and reflected) are seen distinctly as reflection is delayed by decreased aortic pulse wave velocity and as systole is shortened by reduced venous return. The wave shape comes to resemble a damped sinusoid (Fig. 6). The sharp dip between the secondary waves is caused by aortic valve closure, and its identification permits ejection duration to be determined accurately from the peripheral radial artery pulse [20,41]. The carotid pulse has a higher late systolic shoulder at any age (as first described by

Fig. 5.



Change in contour of the radial and carotid pressure waves in normal human subjects with age. Data ensemble-averaged into decades. Published with permission of the American Heart Association [26].

Mahomed in 1874). This approximates the height of the initial wave in the fourth decade of life, then increases progressively thereafter. The amplitude of the secondary systolic wave can be expressed as augmentation [26]. This is positive from around age 25 years in the ascending aorta, from about 35 years in the carotid artery and over 70 years in the radial artery. At any age, and at any site, augmentation is increased by hypertension. Since augmentation is due to wave reflection from the lower body, it is also influenced by body height, being more prominent in persons of short stature [39], and in infants and children [42,43].

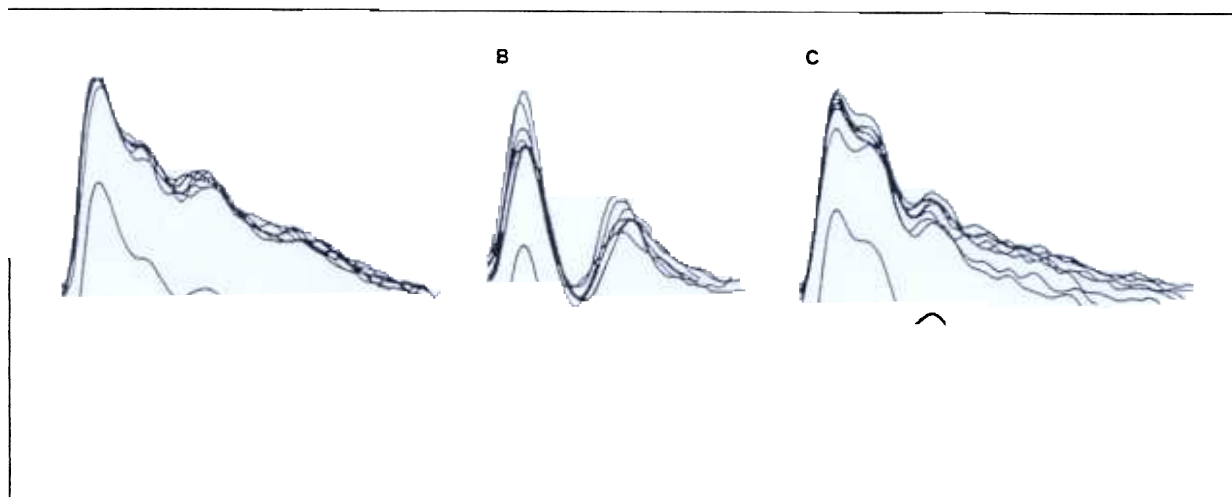
Changes in ascending aortic augmentation from a reduction in wave reflection in the trunk can be inferred from change in contour of the radial artery pressure wave. A decrease, delay or disappearance of the secondary systolic ('tidal') wave in the radial artery corresponds with similar changes in the carotid and aortic wave (Fig. 7) and signifies a decrease in central systolic pressure, even if the peak recorded pressure in the brachial or radial artery does not change [44]. Such a change in

the radial pulse wave with nitroglycerine was first noted by Murrell in 1879 [45]. It appears that the beneficial effects of nitrates on left ventricular load have been systematically underestimated over the years in consequence on complete reliance being placed on cuff sphygmomanometric systolic values [44,46].

Synthesis of the ascending aortic pressure wave

The constancy of the relationship between augmentation in central and peripheral arteries with age, and with nitroglycerine (Figs 5 and 7), provided the first clue that the pressure transfer function between central and peripheral upper limb arteries may be sufficiently consistent for the central wave form to be synthesized from the radial or brachial wave. This was tested in 14 patients studied at cardiac catheterization with aortic, brachial, radial (and carotid) waves recorded before and after nitroglycerine, and the relationship expressed as pressure transfer function. This was of similar appearance in all patients, and changed little after nitroglycerine [37] (Fig. 8). Similar results had been reported previously under control

Fig. 6.



Exaggerated diastolic pressure waves in the radial artery of a human subject during the Valsalva maneuver. The tracings are taken (A) under control conditions, (B) during the phase of peak strain and (C) after termination of the maneuver. Individual successive waves are plotted above, with the ensemble-averaged wave shown below. From [40].

conditions by Lasance *et al.* [47] in 68 patients studied at cardiac catheterization, and subsequently by Gallagher [33] through analysis of carotid and radial pressure waves in 439 normal subjects and patients with a variety of diseases, and under different conditions (Fig. 4).

Using the generalized transfer function we had generated, we then tested these on all the data available in the literature where central aortic and radial or brachial waves had been recorded simultaneously. We used the recorded peripheral wave to synthesize a central aortic wave, and then compared this against what had actually been recorded in the aorta. The agreement was good, especially for systolic pressure which had differed by up to 80 mmHg in the published data (Fig. 9). Subsequent validation studies have provided similarly good results [48,49].

The transfer function has now been incorporated into a commercially available system which permits the central aortic pulse wave to be synthesized in real time [50] (Fig. 10). For this system, the radial, brachial or carotid transfer function can be selected, and applied appropriately to recorded data. The synthesized ascending aortic pressure wave is similar, as are indices derived therefrom, irrespective of the site from which pressure waves are recorded [20,48].

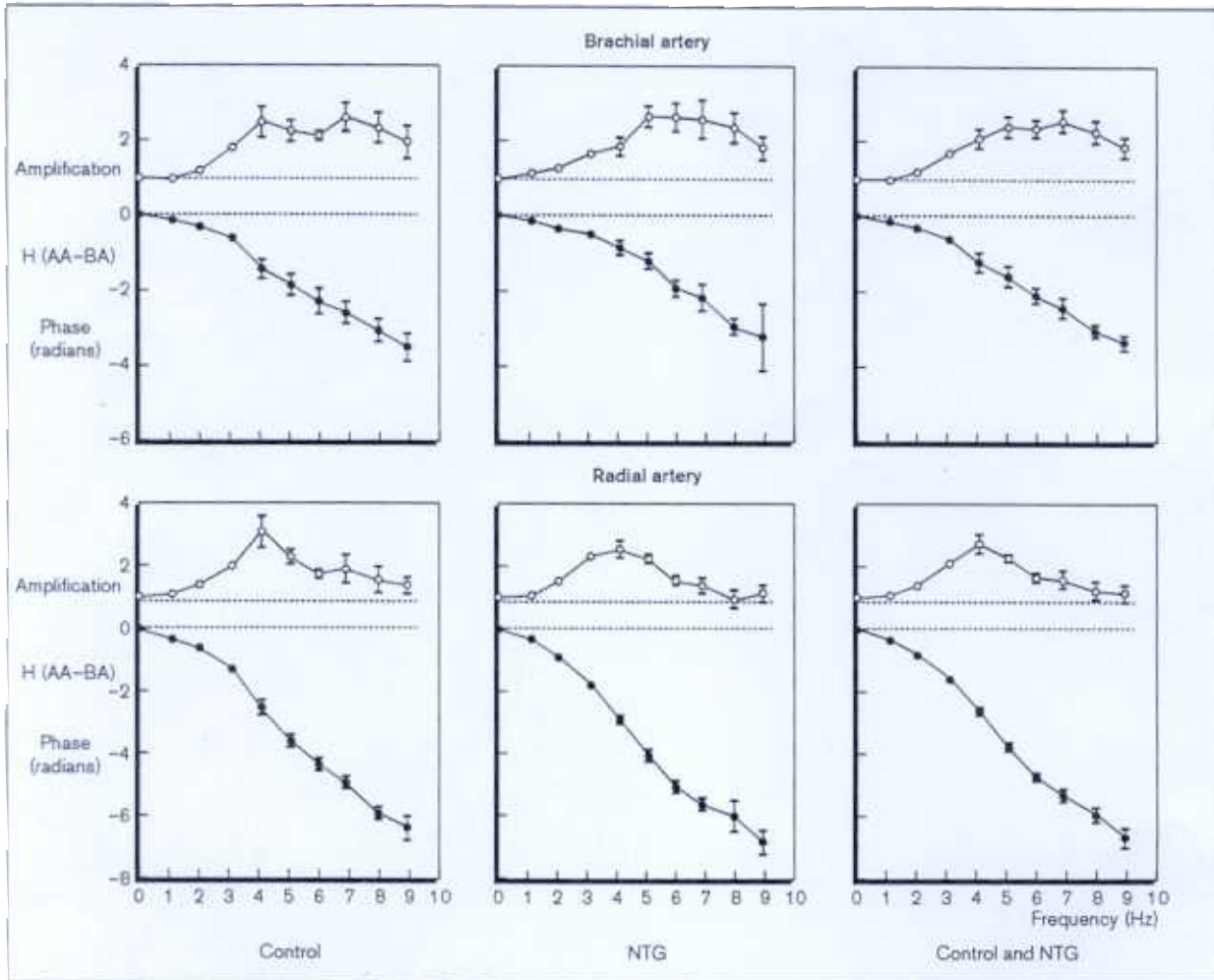
Interpretation of the synthesized central aortic pressure wave

The process described (Fig. 10) shows a series of recorded pressure waves and a series of synthesized aortic waves, together with a single ensemble-averaged peripheral and aortic wave. Both are calibrated by assuming (for the radial) that

systolic and diastolic pressures are the same as recorded by cuff sphygmomanometer, and (for the aorta) that there is no significant mean pressure drop between this and the peripheral vessel. The wave foot and incisura of the recorded wave are identified by differentials, and the cardiac cycle is separated into systolic and diastolic periods. These values are printed as are aortic mean systolic and mean diastolic pressure, together with diastolic pressure time integral (DPTI) and systolic pressure time integral (SPTI). DPTI is a determinant of myocardial blood supply and SPTI a determinant of myocardial blood requirement. The quotient (DPTI/SPTI) is expressed as subendocardial viability ratio (after Buckberg *et al.* [51,52]), and is related to subendocardial ischemia. Pressure wave augmentation of the synthesized wave is determined by identification of the tidal wave foot (again by differentials) and expressed as a percentage of pulse pressure, of the wave amplitude up to this inflection, or in mmHg. The maximal pressure change over time is measured for the systolic pressure upstroke of the peripheral pressure wave.

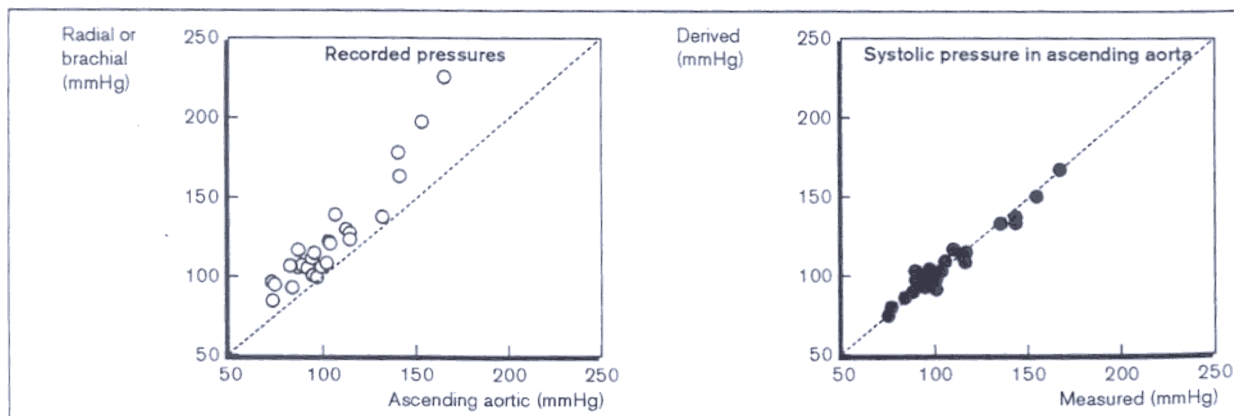
Clinical judgement is enhanced by interpretation of the synthesized aortic pressure waveform. Central pressure augmentation is increased with aging and hypertension, and is the major problem in systolic hypertension [53]. This is an appropriate target for antihypertensive therapy, and is reduced by drugs such as nitrates [20,45], ACE inhibitors [32,54], and calcium antagonists [20,31] which reduce wave reflection, sometimes without reducing systolic pressure in a peripheral artery [44,45]. Beneficial effects of therapy can be measured as a decrease in augmentation, a decrease in aortic systolic pressure and an increase in subendocardial viability ratio. This ratio is affected by change in heart period and ejection period

Fig. 8.



Calculated transfer function for pressure between the ascending aorta (AA) and brachial artery (BA) and between the ascending aorta and radial artery under control conditions, following administration of nitroglycerine (NTG) 0.3 mg sublingual and combined control and nitroglycerine data. From [37].

Fig. 9.

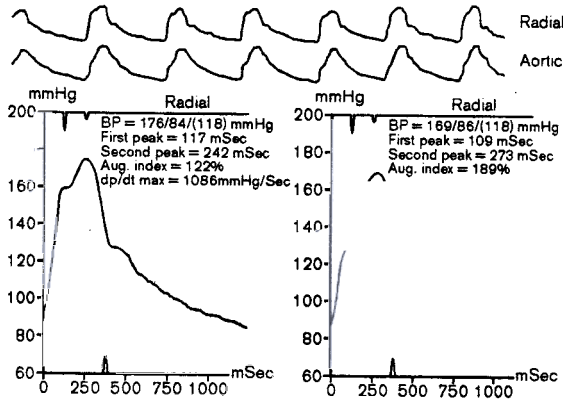


Relationship between measured ascending aortic pressure and measured radial or brachial artery systolic pressure (left), and the comparison between calculated ascending aortic systolic pressure and measured ascending aortic systolic pressure (right) for the same data using our generalized transfer function. Dotted line indicates the line of identity. From [37].

Ascending aortic waveform analysis

Patient ID = Operator ID = 0
 Patient name = Z G
 Sex = F Age = 69
 Address =
 Current medication = NIL

Date of inspection = TUE 02/NOV/1993 17:10
 Heart rate = 50 Bpm Ejection duration = 375 mSec Reference age = 80



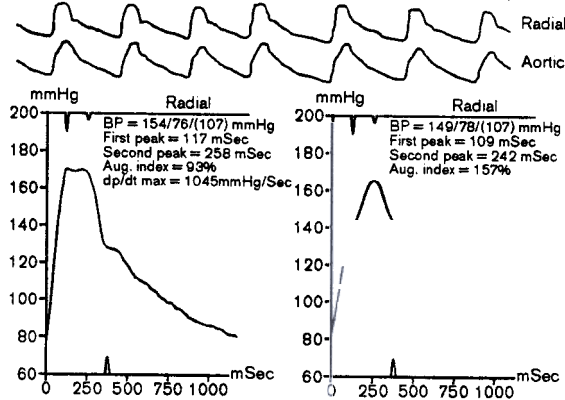
Central pressure indices

Augmented pressure = 38 mmHg
 Tension time index = 2691 mmHg.Sec/min
 Diastolic time index = 4433 mmHg.Sec/min
 Subendocardial viability = 165 %
 Mean systolic pressure = 144 mmHg
 Mean diastolic pressure = 107 mmHg
 End systolic pressure = 148 mmHg

Ascending aortic waveform analysis

Patient ID = Operator ID = 1
 Patient name = Z G
 Sex = F Age = 69
 Address =
 Current medication = PLENDIL

Date of inspection = TUE 07/DEC/1993 09:36
 Heart rate = 52 Bpm Ejection duration = 349 mSec Reference age = 70



Central pressure indices

Augmented pressure = 25 mmHg
 Tension time index = 2322 mmHg.Sec/min
 Diastolic time index = 4136 mmHg.Sec/min
 Subendocardial viability = 178 %
 Mean systolic pressure = 129 mmHg
 Mean diastolic pressure = 98 mmHg
 End systolic pressure = 132 mmHg

phymocardiogram reports. Analysis of radial pressure wave contour under control conditions in a patient with isolated systolic hypertension (left) and after 5 days treatment with 5 mg felodipine in the morning. The mean pressure fell from 118 to 107 mmHg and the calculated ascending aortic augmented pressure from 38 to 25 mmHg (see text for details).

as well as by change in central pressure, and is typically reduced by nitrates and ACE inhibitors, but may be increased with calcium channel antagonists when the heart rate increases with a disproportionate decrease in diastolic period [20]. Through this mechanism, the dihydropyridines, used alone, may predispose to myocardial ischemia.

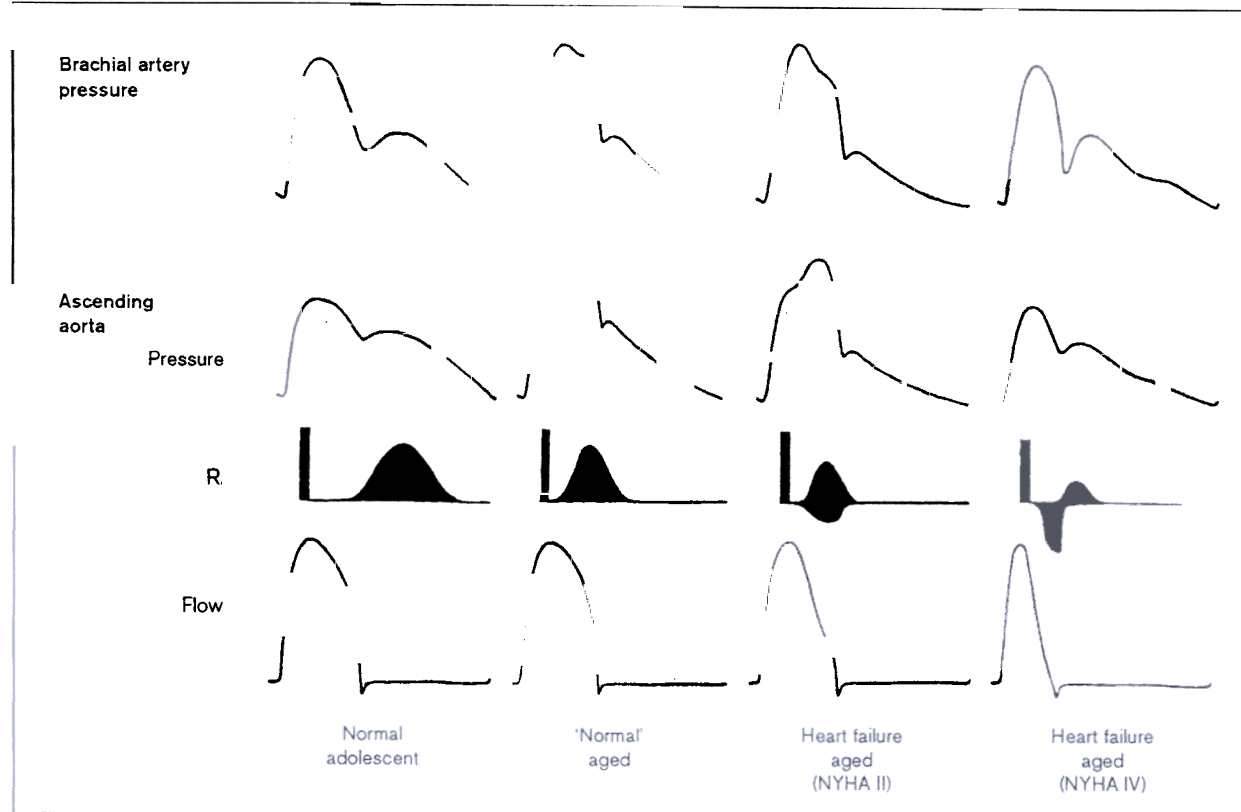
Ejection duration increases with age and in the presence of left ventricular hypertrophy and ischemia. Ejection duration is typically increased in diastolic dysfunction [55,56], but decreased in severe systolic dysfunction [57,58]. Measurement of ejection duration thus helps to separate systolic from diastolic dysfunction in the presence of cardiac failure, and may obviate the need for echocardiography. However, these conditions are often combined. In the presence of systolic dysfunction, and abbreviation of systole, systolic pressure augmentation is decreased and may indeed be absent when dysfunction is severe. Under these circumstances the aortic (and peripheral) pressure waves often assume a pronounced diastolic character as ejection duration is shortened and the diastolic

reflected wave exaggerated [57,58] (Fig. 11). These features, well known in the literature on systolic heart failure, are attributed to the heart behaving as a pressure source, unable to contract against the early wave reflection during the latter part of systole [57].

Analysis of the synthesized aortic pressure wave is also useful in pseudosystolic hypertension of youth [60]. In this condition, the ejection duration is relatively short, and the aortic synthesized pressure wave is entirely normal, but the brachial and radial peak is narrow and exaggerated as a consequence of pressure wave amplification. The problem is not with stiffened arteries (as in isolated systolic hypertension of the elderly) but rather the contrary, that the body is fully grown but the aorta and elastic arteries still have the high distensibility of infancy.

There are only limited data on all these issues, and explanations must be made with caution. However, it is clear that interpretation of wave shape adds substantially to the mea-

Fig. 11.



Effects of wave reflection on aortic pressure and left ventricular output with development of heart failure in a patient with isolated systolic hypertension. R., wave reflection (with effect on pressure shown as upward deflection, effect on flow as downward deflection); normal adolescent, control in early adulthood; 'normal' aged, arterial stiffening with normal ventricular contraction; heart failure aged (NYHA II), arterial stiffening with subclinical heart failure; heart failure aged (NYHA IV), arterial stiffening with severe heart failure; NYHA, New York Heart Association. From [57].

urement of wave peak and nadir only, and that modern instruments and hemodynamic principles open the way to more reliable and confident analyses than were ever possible in the past.

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