Noninvasive Determination of Age-Related Changes in the Human Arterial Pulse

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Arterial pressure waves were recorded noninvasively from the carotid, radial, femoral, or all three of these arteries of 1,005 normal subjects, aged 2–91 years, using a new transcutaneous tonometer containing a high fidelity Millar micromanometer. Waves were ensemble-averaged into age-decade groups. Characteristic changes were noted with increasing age. In all sites, pulse amplitude increased with advancing age (carotid, 91.3%; radial 67.5%; femoral, 50.1% from first to eighth decade), diastolic decay steepened, and diastolic waves became less prominent. In the carotid pulse, there was, in youth, a second peak on the downstroke of the waves in late systole. After the third decade, this second peak rose with age to merge with and dominate the initial rise. In the radial pulse, a late systolic wave was also apparent, but this occurred later; with age, this second peak rose but not above the initial rise in early systole, even at the eighth decade. In the femoral artery, there was a single systolic wave at all ages. Aging changes in the arterial pulse are explicable on the basis of both an increase in arterial stiffness with increased pulse-wave velocity and progressively earlier wave reflection. These two factors may be separated and effects of the latter measured from pressure wave-contour analysis using an “augmentation index,” determined by a computer algorithm developed from invasive pressure and flow data. Changes in peak pressure in the central (carotid) artery show increasing cardiac afterload with increasing age in a normal population; this can account for the cardiac hypertrophy that occurs with advancing age (even as other organs atrophy) and the predisposition to cardiac failure in the elderly. Identification of mechanisms responsible offers a new approach to reduction of left ventricular afterload. (Circulation 1989;80:1652–1659)

Although the arterial pulse is the most fundamental of physical signs and has been used by clinicians for hundreds of years, it was not until the last century that the contour of the pressure pulse was first recorded noninvasively in humans. The sphygograph introduced by Marey in 1860 was sufficiently simple to be applied in clinical practice; this was done by Mahomed, who, utilizing the instrument, first described the clinical entity of essential hypertension, and by Mackenzie, who described changes in both pulse contour and rhythm observed in his general practice. This early work on pulse-contour recordings was soon eclipsed by the introduction of the now ubiquitous sphygmomanometer. Despite classic texts on the pressure pulse contour by Mackenzie and by Wiggers, written in the early twentieth century, the sphygmomanometer was readily embraced as being more “scientific” because it was able to quantify blood pressure in terms of systolic and diastolic numbers. This ascendancy of sphygmomanometric values was also due to an absence of theory to describe or interpret the pulse contour, an inability to use pulse recordings usefully in clinical practice, and to problems with artifacts inherent in the available mechanical recording systems. Thus, the use of the sphygmograph in describing pressure-pulse waves declined, even as Einthoven’s electrocardiograph was being quickly accepted for its description of waves of electric activity.

With subsequent clinical use of the sphygmomanometer, brachial arterial pressure has been described in terms of the two extremes between which it fluctuates, the systolic and diastolic pressures, and aging changes characterized as an increase in systolic pressure with little change in diastolic pressure within the brachial artery. Furthermore, it has been assumed that such change is the same in

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all arteries. The effects of advancing age on the arterial pulse contour, however, have not been precisely defined.

The aim of this study was to document age-related changes in the arterial pulse contour, both in the central and peripheral arteries, using an instrument that would noninvasively register pressure wave contour without artifact and with such accuracy that characteristics of the contour could be clearly and quantitatively defined, much as we can now clearly define features of electrocardiographic waves. Such precisely documented changes in the normal pulse with age will allow valid determination of the effects of disease states on the pressure wave contour.

**Methods**

**The Instrument**

To document aging changes in pulse contour in large numbers of the general population, an accurate noninvasive method of measuring pressure-pulse waves was needed. The instrument devised is a pencil-shaped probe held on the skin over the maximal arterial pulsation either by hand or by a micromanipulator. The probe incorporates a Millar micromanometer in its tip and has the same high fidelity response as conventional Millar catheters.6 Use of the probes is based on the principle of applanation tonometry, as is used in ocular tonometry for registration of intraocular pressure. Essentially, if one can flatten or applanate (Figure 1) the curved surface of a pressure-containing structure, then the circumferential stresses in the wall of the structure are balanced and the pressure registered by the sensor is the true intra-arterial pressure.7,8 Like echocardiography and other noninvasive diagnostic techniques, applanation tonometry requires some training but readily can be mastered. Having located the point of maximal arterial pulsation, the probe is placed over the vessel and pressed down on the artery against underlying bone. If no flattening is achieved, no consistent signal can be registered. Excessive flattening produces a distorted signal. Recordings are taken only when a reproducible signal is obtained with high amplitude excursion. Large amounts of overlying tissue make optimal waveforms harder to obtain; the technique is best applicable to superficial, large arteries such as the radial, carotid, and femoral. The sensor is a stiff ceramic beam on which are mounted piezoresistive elements forming two arms of a Wheatstone bridge. The remaining two arms are housed in the connector. This is attached to a standard Millar preamplifier box that amplifies the induced voltage change by a factor of 100. This amplified, electrically calibrated signal was then recorded on magnetic tape. The accuracy of the probe has been previously validated in animals and in human subjects with indwelling radial artery lines.9 Comparisons were made between directly and indirectly recorded radial artery pressure waves in 62 humans, between directly and indirectly recorded femoral pressure waves in three dogs, and between directly recorded ascending aortic pressure waves and indirectly recorded carotid pressure waves in 17 humans. Comparison both in the time domain and by spectral analysis show excellent correspondence with theoretic predictions. The tonometer provides a high fidelity recording of arterial pressure wave contour under a wide variety of clinical conditions and pulse pressures. The stringent requirements delineated by more recent theoretical studies8 apply to internally calibrated systems attempting to obtain accurate noninvasive measurements of absolute systolic and diastolic pressure levels. When, however, applanation tonometry is used to record pressure wave contour to supplement sphygmomanometric readings, these exacting conditions are not necessary. Accurate recordings of wave contour can indeed be achieved under standard clinical conditions.

The tonometer voltage signal registers a pressure wave with harmonic content that does not significantly differ from that of an intra-arterially recorded wave.9 The output of the Millar preamplifier box electrically calibrates the signal in mm Hg (1 mV/mm Hg) in the same way as the conventional Millar unit. The use of the tonometer on an exposed vessel indeed records a waveform of amplitude virtually identical to that recorded intra-arterially.9 Percutaneous use of the probe records morphological features of the wave that are accurately reproduced over a wide range of pulse pressures9 although absolute pulse pressure recorded might be less reliable. Accordingly, the output of the instrument is reported in this manuscript with an arbitrary amplitude scale of millivolt (mV) units.

**Registration and Analysis**

Waveforms were recorded on an FM TEAC magnetic tape recorder, digitized by a 12-bit analog to digital converter with an acquisition rate of 1 kHz and entered into storage on disk by an IBM-AT computer. For each subject studied, six to eight

**Figure 1. Diagram of applanation tonometry process.** Flattening of curved pressure containing structure allows accurate registration of transmitted pressure, because stresses inherent in wall of curved surface are balanced when it is flattened.
Consecutively recorded pulses were averaged, their alignment being triggered at the occurrence of the maximum rise time determined by the smoothed first differential of the signal (dP/dt). The averaged pulse was then taken as the representative pulse for that individual. An ensemble average of similar representative waves from 30–70 other subjects in the same age decade was obtained to form a representative wave and 2 SDs for that particular age decade. Thus, a series of decade waves was established, each being the average of approximately 50 representative waveforms from individuals of similar age. Subjects with heart rates greater than 100 beats/min were excluded to avoid excessive truncation of the age-decade wave (to that of the subject with the shortest heart period) during the averaging process.

Carotid waveforms were further analyzed to measure the “shoulder” and “peak” of the waves. Such analysis of wave contour has been done previously by Murgo et al.\textsuperscript{10} and Takazawa\textsuperscript{11} for invasively recorded ascending aortic waves and, also, by Fujii et al.\textsuperscript{12} for noninvasively recorded waves. We defined the augmentation index for each wave as the ratio of height of the peak above the shoulder of the wave to the pulse pressure (Figure 2). This can be done from visual inspection as has been used previously.\textsuperscript{10–12} Such identification, however, can be highly subjective because the shoulder is often not a clearly defined point but sometimes a less well defined plateau region on the systolic upstroke. We, therefore, chose to identify the shoulder automatically from the time derivative of the pressure wave, as herein described.

### Measurement and Justification of Augmentation Index

From invasive ascending aortic pressure and flow velocity data previously reported,\textsuperscript{13} we have noted there exists a correspondence between the peak of flow and the shoulder of pressure. The shoulder of the pressure wave is defined as the first concavity on the upstroke of the wave. We analyzed the initial pressure rise from the late systolic peak that occurs in middle aged and older subjects.\textsuperscript{10} A computer algorithm was written to identify this shoulder in a more objective, automated way than visual inspection by using time derivatives of the pressure wave. Reanalysis of the invasive data was performed to ascertain the relation between the shoulder of the ascending aortic pressure wave, the time derivatives of pressure, and the peak of simultaneously recorded flow. The simultaneously recorded pressure and flow-velocity data were digitized at 0.01-second intervals and were plotted with the first four derivatives of pressure. When plotted against pressure derivatives, the timing of the shoulder was reliably indicated by a local minimum in the first derivative that was in the range from 0 to 50 msec of the peak of flow (the mean estimate from interpolation between sample points determined from 13 patients) being 27 msec once correction had been made for the frequency response of the flowmeter (10 msec).

To simplify the algorithm for detection of this point, higher-order derivatives were used to identify the zero-crossing point equivalent to the local minimum of the first derivative. The first zero crossing of the fourth derivative (in a direction from above to below the zero line) corresponded to the beginning of the pressure wave upstroke (line AA, Figure 3). The second zero crossing in the same direction corresponded to the shoulder at the beginning of the second wave, which constituted the late systolic peak (line BB, Figure 3). A good correlation was found between the time to the second zero crossing of the fourth derivative (x) and the timing of the peak of flow (y) in the patients studied (y=0.91+1.31x; R=0.75).

Such a relation between peak flow and the shoulder of the pressure wave is to be expected if the shoulder of the wave indicates the pressure rise resulting from peak flow input into the vasculature before the effects of wave reflection,\textsuperscript{10,13,14} Hence, we decided to use the algorithm as described to...
detect the contribution of wave reflection to changing carotid pulse contour. The method used is automatic and excludes subjective bias. It identifies a point on the pressure wave very close to peak flow in the ascending aorta, and is justifiable on the theoretical basis of wave travel and reflection in the aorta.

**Subjects**

Volunteers studied were from the out-of-hospital community-based population considered to represent the normal population. Volunteers were Caucasians from both urban and rural areas who were 2–91 years old. They were screened on the basis of cardiovascular history and examination; those with valvular heart disease or chronically treated cardiovascular disease were excluded. Subjects found to have mild hypertension (diastolic blood pressure >95 and <105 mm Hg), 4.8% of the sample, were included in analysis as part of the spectrum in the general population. Radial pressure waveforms were obtained from 420 subjects (207 men and 213 women), of whom 38 were smokers; carotid waveforms were from a further 407 subjects (181 men and 226 women), of whom 82 were smokers; and femoral waveforms were from 178 subjects of similar age (110 men and 68 women), of whom five were smokers. Of all the subjects studied, 28 were on monotherapy for hypertension at the time of study.

**Statistical Analysis**

Statistical analysis was performed using a two-tail unpaired Student's t test with a significant difference being at the level of \( p \) equaling less than 0.05.

**Results**

The radial pulse contour recorded in 420 subjects showed characteristic changes with increasing age (Figure 4). The radial pulse contour in children shows multiple prominent fluctuations. With advancing age, these become less distinct and the systolic peaks progressively broader, although the maximum still usually occurs in early systole. In contrast, the carotid wave recorded in 407 subjects shows not so much a broadening but the emergence of the late systolic peak, which determines the systolic pressure level (Figure 5). With increasing aging, the principal change in the carotid pulse is a progressive rise in the second systolic peak that, after the third decade, merges with and dominates the initial rise. The femoral waveforms (Figure 6) also show a progressive rise in the systolic wave and loss of any diastolic wave.

The amplitude (pulse pressure) of the carotid wave increases by 91.3% from the first to eighth decade compared with a 67.5% increase in the radial pulse and a 50.1% increase in the femoral pulse. This greater increase is due to change in two parts of the carotid wave. After the third decade of life, a late systolic peak becomes dominant, which adds to the initial pressure rise and so defines the shoulder on the upstroke of the wave. The total 91% increase in carotid pulse pressure from the first to the eighth decade is due to an increase in both the rise to this initial shoulder (by an average 20 mV units or 53% of the increase) and the height of the late peak above the shoulder (averaging 18 mV units) (Table 1). This change in carotid pulse contour was quantified by the augmentation index.
measured by the algorithm developed using invasive aortic pressure and flow data. When this algorithm was applied to the carotid wave age-decade data, it was found that although the timing of the shoulder was within 14 msec for all eight decades (range, 102–116 msec, after the onset of systole), the height of the shoulder and the late peak both showed a substantial increase with age. (Table 1). The height of the shoulder increased from 39 to 59 mV units above diastolic pressure from the first to the eighth decade, whereas the late peak increased from less than 1 to 19 mV units above the shoulder. The corresponding augmentation index increased from 1.6% to 24.1%.

Changes in pressure-pulse contour are due to changes in the systemic vasculature itself or to differing flow input into the vasculature from the heart. Previous studies have shown that at rest there is little change in stroke volume or ejection fraction with increasing age. Aortic flow-velocity profile does not alter in contour with increasing age, although rate of flow acceleration and peak flow velocity are reported to decline with increasing age. We sought to verify that our study population concurred with these results by studying a sample of subjects using Doppler flow techniques. From the original cohort, a group of 12 older (>60 years) and 13 younger (<30 years) subjects were studied. Parameters compared were peak flow velocity (cm/sec), acceleration of systolic upstroke, and ejection time. This group spanned a wider range of age (19–80 years) than the data previously reported by Nichols et al. Ultrasonography was done with a Toshiba Sonolayer SSH 65 A phased array ultrasound and a 2.5-MHz pulsed-wave Doppler probe. Recordings were made with subjects in a supine, rested position. Recordings of ascending aortic flow were taken from the suprasternal notch (where sampling was done near the inner curvature at the aortic root), the right parasternal, and the apical positions. Signals analyzed were those that gave the best delineated velocity profile at any of the three positions.

As has been found by other workers, ejection time remained constant with increasing age, although peak flow velocity and acceleration did decline with increasing age (Table 2). As will be discussed, the changes in pressure wave contour with increasing age are explicable mainly on the basis of changes in the systemic vasculature with increasing age because there were few changes in flow input into the system as detected by ascending Doppler flow measurements (Figure 7).

### Discussion

These characteristic age-decade pulse waveforms represent the largest sample of noninvasive recordings of the pulse yet made in human subjects. The accuracy of the recordings is dependent on both the principle of applanation tonometry, which is based on well-established theory, and also the use of high fidelity Millar micromanometers incorporated into the tip of the probes. The technique has been shown to be accurate in registering intra-arterial pressure waves as compared in the time domain and by spectral analysis. Previous noninvasive pulse recordings have used wave tracings obtained by displacement of a volume of air or fluid contained in a capsule fixed over the arterial pulsation. Such volume displacement techniques are limited by...
movement artifact, by errors due to the large size of the capsule relative to the size of the artery, by inability to separate carotid and venous pulsations, by need for a significant “hold-down” force for optimal signal registration, and by a high damping coefficient causing attenuation of high frequency characteristics. Nevertheless, these techniques have given valuable information and extended the earlier work of Marey,1 Mahomed,2 and Mackenzie.3 In contrast to such capsules that rely on magnification of vessel wall displacement, tonometry is not dependent on volume changes. It requires minimal hold-down force and is much less subject to artifact related to placement over the pulse because the micromanometer in the tip of the probe is very small (0.5×1.0 mm, o.d.) compared to the diameter of the artery. Tonometry, thus, registers the arterial pressure pulse much as the clinician feels it by palpation.

The changes in the femoral pulse with age are characterized by a progressive increase in the size of the systolic peak with a resultant increase in pulse pressure, whereas diastolic fluctuations diminish. There are no secondary systolic fluctuations in the femoral pulse. In contrast, the carotid and radial waves show an increase in pulse amplitude with age, as well as important changes in the contour of secondary systolic fluctuations. The averaging process used to obtain age-decade waveforms resulted in obvious smoothing of high frequency components of the wave such as the incisura. Nevertheless, there is still a clear change in pressure wave contour with increasing age. There is a progressive rise in a late systolic fluctuation in both so that it becomes the late peak of pressure in the carotid artery after the third decade, and that becomes equal to the initial pressure peak in the radial pulse at the eighth decade. The result is a greater increase in carotid pulse pressure with increasing age than in either of the peripheral pulses because, in the carotid, the late peak is added to the initial pressure rise. The rise in this late systolic fluctuation in both the radial and carotid pulses is explicity due to faster return of wave reflection from the lower body. Such altered timing of wave reflection has been discussed at length elsewhere and is largely responsible for the suboptimal coupling of the vasculature to left ventricular function that is known to occur with increasing age.14

As aging occurs, there are dramatic changes in the vasculature that increase cardiac afterload.14,19 Both nonpulsatile (peripheral resistance) and pulsatile (characteristic impedance and wave reflections) components of arterial load increase with increasing age. The age-related increase in left ventricular pressure load is primarily due to increased aortic stiffness (characteristic impedance) that increases aortic and left ventricular pressure at its early systolic peak or shoulder and secondarily due to augmented early wave reflection that raises pressure from the shoulder to the late systolic peak.10,14 The results in Table 1 show these two effects on the carotid pressure pulse as they increase from the first compared with the eighth decade. In the intervening years, however, the increase in pulse pressure with increasing age is primarily due to an increase in wave reflection (height of the late systolic peak).

Although the 20-mV-units increase in shoulder height across the full age spectrum is consistent with the known increase in aortic stiffness of large arteries with increasing age, its constancy in middle age may be explained by the concomitant decrease in peak velocity that occurs with increasing age.16 Although, in middle years the progressive increase in arterial stiffness is balanced by a gradual decrease in peak flow from the heart, with the passage of time, the degenerative vascular changes are greater and, by the seventh and eighth decades, there is an increased characteristic impedance and consequent increased height of the shoulder above diastolic pressure. This study shows that, with increasing age, increased aortic stiffness and increased early wave reflection contribute approximately equally to ventricular load as assessed by the central pressure pulse (20 versus 18 mV units).

The increase in the late systolic pressure peak with increasing age is substantial and represents an increase of 25% of pulse pressure in the carotid artery between the ages of 30 and 60 years (Figure

![Figure 7](https://example.com/figure7.png)
in part, reversible by the use of nitroglycerin, which reduces the reflected wave component.13,23,24

These characteristic age-related changes in the pulse waveform have established a profile of normal-aging changes that will allow the effects of disease states to be more precisely defined. The increase in systolic and pulse pressure, particularly in the central carotid pulse, have important implications for the aging population. Increase in peak systolic pressure and increased pulsation around the mean pressure level result in increased cyclic stresses on the structure of arterial walls and account for the propensity of large arteries to rupture or develop atheromatous occlusive disease with increasing age.25 The findings in this study concur with previous epidemiologic data, showing the importance of systolic pressure as a risk factor for cardiovascular morbidity and mortality with advancing age.26,27 In addition, these findings provide important answers to the question posed by the most recent of these studies,28 regarding the determinants of systolic pressure levels in both central and peripheral arteries.

Furthermore, the fact that the radial pulse shows different but complementary changes to those in the carotid pulse has important implications for diagnostic approaches and treatment. It is clear that the increase in radial (and femoral) systolic pressures underestimate the age-related rise in central systolic pressure because it does not include the characteristic rise in the late systolic peak seen in the central arteries of mature adults. Hence, in subjects aged 40–70 years, measurements of sphygmomanometric pressure might substantially underestimate the effect of vasoactive drugs on ventricular afterload because a reduction in the late carotid pressure peak might occur with little or no change in peripheral systolic pressure. This is because, in the peripheral pulse, the reflected wave is on the downstroke of systole rather than at its peak and, although reduced by vasoactive drugs, it has little effect on peak systolic pressure. On the other hand, further investigation is warranted to see if a predictive index of central systolic pressure changes might be obtained from analysis of the late systolic fluctuation in the peripheral (radial) pulse waveform.

The determination of age-related changes in the arterial pulse by high fidelity applanation tonometry, thus, provides important supplementary information to that obtained by use of the sphygmomanometer. The use of this modern-day sphygmograph enhances new investigations of the ill effects of aging and disease states on cardiovascular function and extends the earlier observations of Mahomed,2 Mackenzie,3 and Freis et al.17

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**Figure 8.** Graph of augmentation index for carotid artery as function of age.

**Figure 9.** Scatterplot of augmentation index for ascending aorta as function of age; from data published by Murgio et al10 (●) and Takazawa11 (▲).
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