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Noninvasive Assessment of the Digital Volume Pulse Comparison With the Peripheral Pressure Pulse

Sandrine C. Millasseau, Franck G. Guigui, Ronan P. Kelly, Krishna Prasad, John R. Cockcroft,
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Abstract—The digital volume pulse can be recorded simply and noninvasively by photoplethysmography. The objective of the present study was to determine whether a generalized transfer function can be used to relate the digital volume pulse to the peripheral pressure pulse and, hence, to determine whether both volume and pressure pulse waveforms are influenced by the same mechanism. The digital volume pulse was recorded by photoplethysmography in 60 subjects (10 women, aged 24 to 80 years), including 20 subjects with previously diagnosed hypertension. Simultaneous recordings of the peripheral radial pulse and digital artery pulse were obtained by applanation tonometry and a servocontrolled pressure cuff (Finapres), respectively. In 20 normotensive subjects, measurements were obtained after the administration of nitroglycerin (NTG, 500 μ g sublingually). Transfer functions obtained by Fourier analysis of the waveforms were similar in normotensive and hypertensive subjects. In normotensive subjects, transfer functions were similar before and after NTG. By use of a single generalized transfer function for all subjects, the radial and digital artery pressure waveforms could be predicted from the volume pulse with an average root mean square error of 4.4 ± 2.0 and 4.3 ± 1.9 mm Hg (mean \pm SD) for radial and digital artery waveforms, respectively, similar to the error between the 2 pressure waveforms (4.4 ± 1.4 mm Hg). The peripheral pressure pulse is related to the digital volume pulse by a transfer function, which is not influenced by effects of hypertension or NTG. Effects of NTG on the volume pulse and pressure pulse are likely to be determined by a similar mechanism. (*Hypertension*. 2000;36:952-956.)

Key Words: plethysmography ■ hypertension, essential ■ pulse ■ nitroglycerin ■ tonometry

A digital volume pulse (DVP) can be obtained by measuring infrared light transmission through the finger (photoplethysmography).¹⁻³ The pioneering work of Takazawa et al⁴ has shown that the DVP resembles the carotid pressure wave and varies, as does the carotid pressure wave, with vasodilator and vasoconstrictor drugs. Analysis of this pulse waveform has been used to characterize the effects of aging and of vasodilator drugs on the circulation.⁴ However, the physical characteristics that determine the volume pulse waveform are not fully understood. By contrast, the peripheral pressure pulse derived from the radial or digital artery has been subject to much analysis by O'Rourke and colleagues,⁵⁻⁷ who have established that the peripheral pressure pulse is influenced by pressure wave reflection mainly from the lower body and by pressure wave velocity. Transmission along the upper limb also influences the radial or digital artery pressure pulse (P_{rad} and P_{dig} , respectively), but this influence remains approximately constant across subjects and during the administration of systemically acting vasodilator drugs.⁸ Thus, changes in the peripheral pressure pulse are determined mainly by changes in pressure wave reflection within the trunk and lower body.⁵⁻⁷ The nitrovasodilator

nitroglycerin (NTG) reduces wave reflection, producing marked changes in the character of the pulse wave at doses that produce only minor changes in heart rate and blood pressure.⁹⁻¹¹ The DVP also shows characteristic changes in response to NTG.^{2,3} The major change in both pressure and volume waveforms is a decrease in the height of the diastolic component of the waveform and the inflection point (IP) preceding this.¹² However, the quantitative relationship between the DVP and peripheral pressure pulse waveforms and the relative effects of NTG on these waveforms is unknown. The purpose of the present study was to characterize the relation between the DVP measured by photoplethysmography and peripheral pressure pulse waveforms obtained by radial artery tonometry and by a servocontrolled digital artery pressure cuff (Finapres). We derived individual transfer functions (ITFs) and generalized transfer functions (GTFs) relating the volume waveform to the pressure waveforms and used a GTF to examine the accuracy with which the pressure waveforms could be predicted from the volume waveform. We did this under resting conditions in both normotensive and hypertensive subjects. In normotensive subjects, we also measured volume and pressure waveforms after NTG to

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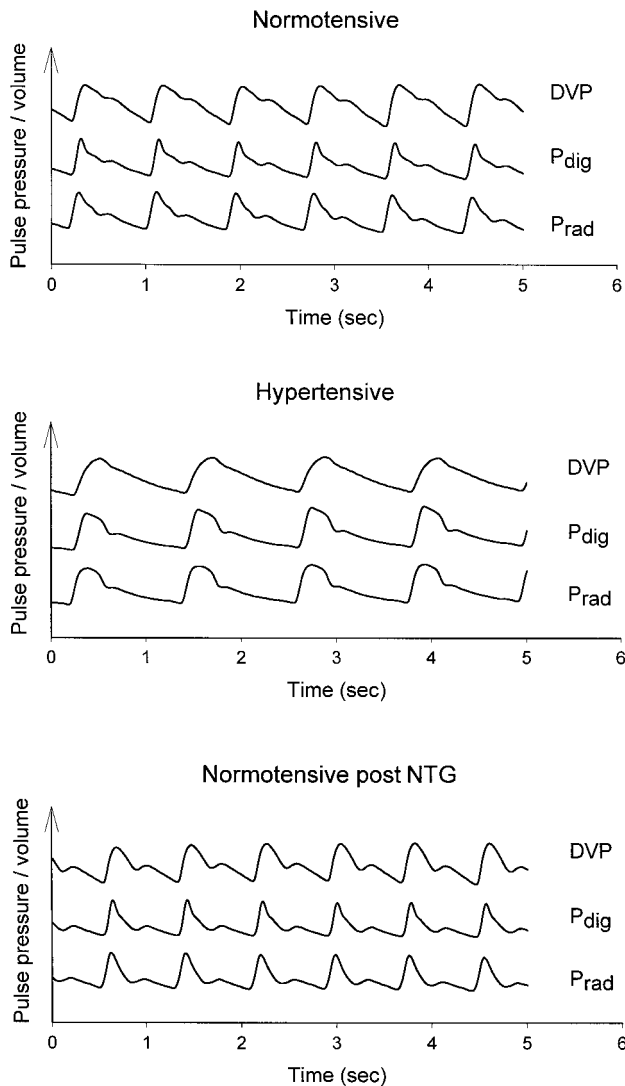


Figure 1. Typical DVP, P_{dig} , and P_{rad} waveforms recorded by photoplethysmograph, Finapres, and radial tonometer, respectively, in a normotensive subject, hypertensive subject, and after nitroglycerin (NTG, 500 μg sublingual) in a normotensive subject.

establish whether NTG produced a change in the relationship between the volume and pressure pulses.

Methods

Subjects

Healthy normotensive ($n=40$) and hypertensive ($n=20$) subjects aged 24 to 80 years were recruited from the local community and from the hypertension clinic at Guy's and St Thomas' Hospital. Healthy subjects had no previous history of hypertension or cardiovascular disease and were normotensive (office blood pressure $<140/90$ mm Hg) at the time of the study. Blood pressure (mean \pm SD) was $118 \pm 11/67 \pm 9$ mm Hg. Hypertension was diagnosed on the basis of ≥ 3 measurements of office blood pressure $>140/90$ mm Hg separated by at least 1 week. None of the hypertensive subjects had clinical evidence of cardiovascular disease other than hypertension. Twelve were receiving antihypertensive therapy at the time of the study (diuretics, 7 of 12; β -adrenoreceptor antagonists, 5 of 12; α -adrenoreceptor antagonists, 1 of 12; ACE inhibitors, 3 of 12; angiotensin II receptor antagonists, 2 of 12; and calcium channel blockers, 4 of 12). Blood pressure at the time of the

study in the hypertensive subjects was $152 \pm 14/92 \pm 12$ mm Hg. The study was approved by St Thomas' Hospital Research Ethics Committee, and all subjects gave written informed consent.

Pressure and Volume Pulse Recording

Photoplethysmographic digital volume was determined by use of an infrared light-emitting diode (940 nm) and phototransistor (Micro Medical) applied to either side of the index finger of the right hand. Applanation tonometry was used to record P_{rad} by use of a piezo-resistive cantilever transducer (Millar SPT 301, Millar Instruments) applied over the radial artery of the left arm. P_{dig} was measured noninvasively by use of a servocontrolled pressure cuff device¹³ (Finapres 2300, Ohmeda) applied to the middle finger of the right hand. Previous studies have shown that changes in pressure recorded by the tonometer^{14,15} and Finapres¹⁶ accurately reflect changes in intra-arterial blood pressure. Signals from all transducers were amplified, displayed in real time, digitized, and recorded via a 12-bit analog-to-digital converter (sampling frequency 100 Hz). Further digital signal processing was performed offline. Brachial artery pressure (left arm) was measured by use of an automated oscillometric method (Dinamap, Critikon). Because the purpose of the present study was to compare the shape of the waveforms, all waveforms were normalized to the same amplitude (nominally equal to brachial artery pulse pressure).

Protocol

Subjects rested supine in a temperature-controlled laboratory ($26 \pm 1^\circ\text{C}$) for 30 minutes. Simultaneous pressure and volume waveforms were recorded for 30 seconds at 5-minute intervals for 15 minutes. In a subset of 20 of the normotensive subjects, NTG (500 μg) was then administered sublingually, and further simultaneous volume and pressure recordings were obtained 3 minutes after NTG when the effects of NTG were maximal.

Data Analysis

Pressure and volume waveforms in the time domain for each individual were ensemble-averaged (with periodicity normalized to 1 second by scaling the time axis). ITF relating P_{rad} to the DVP waveform and relating the P_{dig} waveform to the DVP waveform in the frequency domain were determined from fast Fourier transforms (FFTs) of waveforms for each individual: $\text{ITF}(P_{\text{rad}}/\text{DVP}) = \text{FFT}(P_{\text{rad}})/\text{FFT}(\text{DVP})$ and $\text{ITF}(P_{\text{dig}}/\text{DVP}) = \text{FFT}(P_{\text{dig}})/\text{FFT}(\text{DVP})$.

The first 10 harmonics of each waveform were used for this analysis because higher harmonics do not contribute significantly.^{5,17,18} ITFs were determined at baseline and 3 minutes after NTG administration (when changes due to NTG were maximal) by use of a minimum of 6 consecutive stable cycles obtained from all 3 transducers. GTFs for resting waveforms and 3 minutes after NTG administration were derived by averaging ITFs at baseline and after NTG administration. The mean GTF for all subjects was used to predict pressure waveforms from the volume waveforms. The agreement between predicted and measured waveforms was quantified by the root mean square (RMS) difference between the 2 signals. In addition, we measured the height of the IP and compared changes in IP in the predicted and measured waveforms after NTG administration. The IP was defined as the point immediately preceding the second peak of the waveform (occurring in early diastole), at which the first derivative of the volume signal was maximum and was expressed as a percentage of the waveform amplitude.¹²

Statistical Analysis

Results are presented as mean \pm SD. ANOVA (for repeated measures where appropriate) was used to compare differences in IP and RMS errors between the groups and waveforms. A value of $P < 0.05$ was taken as significant.

Results

Typical volume and pressure waveforms are shown in Figure 1. P_{rad} and P_{dig} waveforms were in close agreement in all

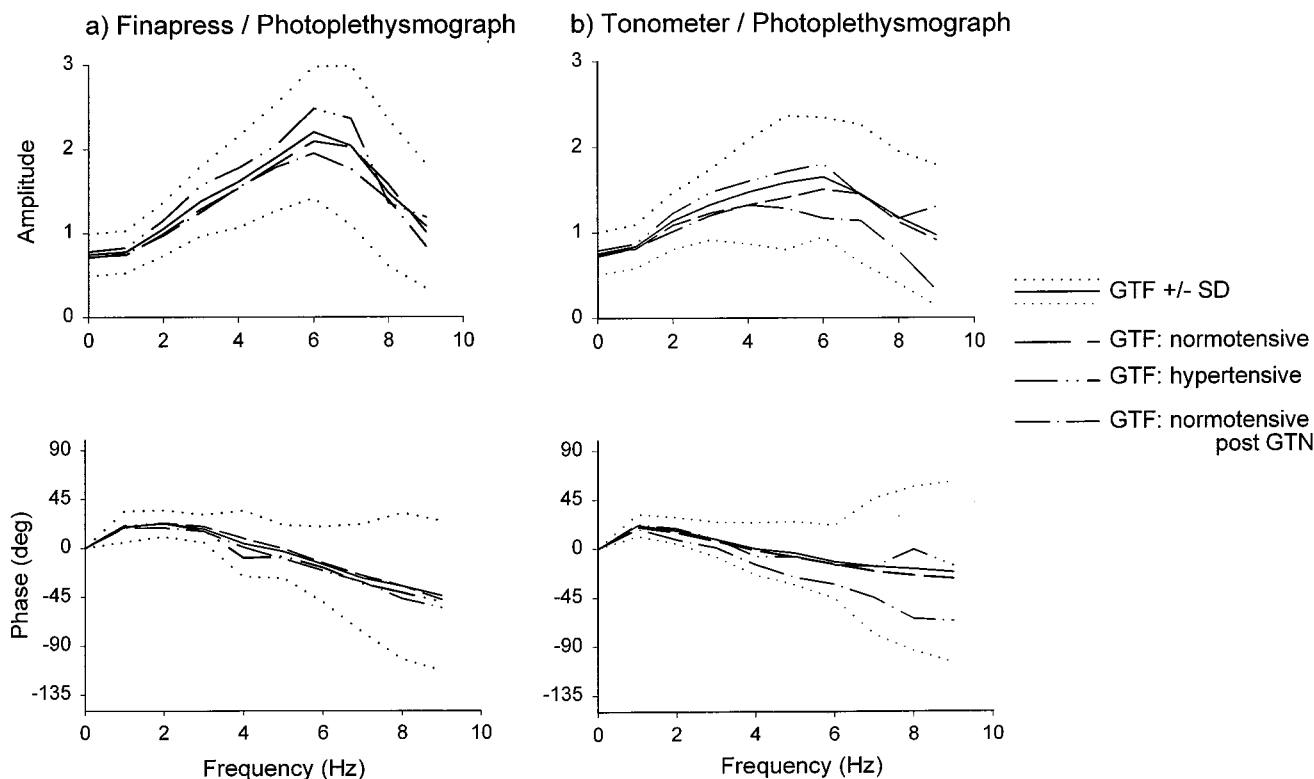


Figure 2. GTFs, shown as amplitude and phase for the pressure/volume relation for the relation between P_{dig} and DVP waveforms in normotensive subjects ($n=40$), hypertensive subjects ($n=20$), and after NTG ($500 \mu\text{g}$ sublingual) in normotensive subjects ($n=20$) (a) and the relation between P_{rad} and DVP waveforms in the same groups (b). The solid line is the mean transfer function for all subjects.

subjects. The mean RMS error for the difference between P_{rad} and P_{dig} waveforms was 4.4 ± 1.4 mm Hg (mean \pm SD for all subjects). The volume signal differed from the pressure signals (Figure 1), with the main difference being in the height of the diastolic component of the waveform and the IP preceding the diastolic component. The IP of the DVP waveform ($62 \pm 12.9\%$, mean \pm SD for normotensive subjects) was higher than that of the P_{rad} waveform ($35 \pm 7.8\%$, $P < 0.001$ for the comparison with the volume IP) and that of the P_{dig} waveform ($36 \pm 9.9\%$, $P < 0.001$ for the comparison with the volume IP). There were subtle differences in the waveforms between hypertensive and normotensive subjects, with a tendency for the IP to be higher in hypertensive subjects (Figure 1).

After the administration of NTG to a subset of the normotensive subjects, systolic blood pressure fell by 1.2 ± 6.0 mm Hg ($P = \text{NS}$), and diastolic blood pressure fell by 5.2 ± 3.8 mm Hg ($P < 0.001$). NTG produced qualitatively similar changes in all 3 waveforms with a decrease in IP. Mean changes from baseline in IP after NTG administration were $22.9 \pm 4.9\%$, $11.3 \pm 4.7\%$, and $13.3 \pm 4.7\%$ units (each $P < 0.001$) for the DVP, P_{rad} , and P_{dig} waveforms, respectively.

GTFs relating the volume waveforms to the pressure waveforms for normotensive subjects, hypertensive subjects, and normotensive subjects after NTG administration are shown in Figure 2. Average pressure waveforms obtained by applying the GTF (derived from all subject groups) to the volume waveforms, together with measured waveforms, are

shown in Figure 3. Transformed volume waveforms were in close agreement with measured pressure waveforms in each artery. RMS errors between the pressure waveforms and between the transformed volume and pressure waveforms were similar and did not differ significantly between the various study groups (Table). RMS errors between transformed volume and pressure waveforms in treated hypertensive subjects did not differ significantly from those in untreated subjects. For all subjects, the mean RMS error for the difference between transformed volume and tonometer P_{rad} signals was 4.4 ± 2.0 mm Hg, and that for the difference between transformed volume and Finapres P_{dig} signals was 4.3 ± 1.9 mm Hg. These errors did not differ significantly from the RMS error between the measured P_{rad} and P_{dig} waveforms (4.4 ± 1.4 mm Hg). There was a small but significant difference in the change in height of the IP after NTG administration in the P_{rad} waveform predicted from the volume waveform and that obtained directly from the measured P_{rad} waveform ($15.4 \pm 4.1\%$ versus $11.3 \pm 4.7\%$, $P < 0.05$). The change in height of the IP after NTG administration in the P_{dig} waveforms predicted from the volume waveform was similar to that obtained from the measured Finapres waveform ($13.4 \pm 3.9\%$ versus $13.3 \pm 4.7\%$, $P = \text{NS}$).

Discussion

The relationship between noninvasive measurements of arterial pressure derived from the digital artery by the Finapres and from the radial artery by applanation tonometry with use

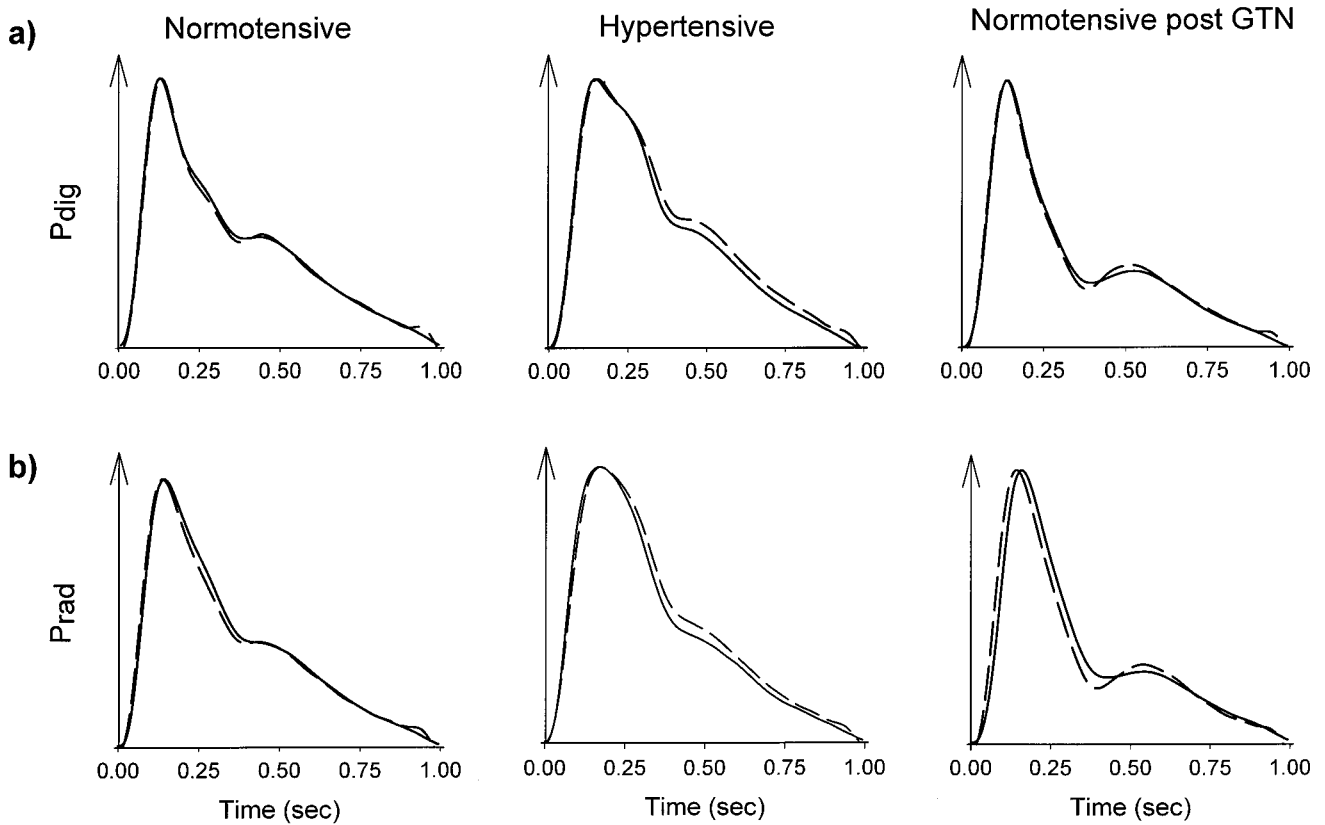


Figure 3. a, Average measured P_{dig} (solid line) and average P_{dig} predicted from DVP waveforms (dotted line) by use of the GTF (obtained from all subjects) in normotensive subjects ($n=40$), hypertensive subjects ($n=20$), and after NTG ($500 \mu\text{g}$ sublingual) in normotensive subjects. b, Average measured P_{rad} (solid line) and average P_{rad} predicted (dotted line) from DVP waveforms by use of the GTF in the same groups.

of a Millar tonometer has been previously investigated. Both instruments have been shown to provide waveforms that closely approximate intra-arterial pressure.¹⁴⁻¹⁶ In the present study, we obtained close agreement between waveforms derived from the tonometer and Finapres, as would be expected. The small discrepancy between the signals derived from the 2 instruments, represented by the RMS error of 4.4 ± 1.4 mm Hg, reflects the limits of accuracy of these devices in recording arterial pressure.^{15,19} The digital volume photoplethysmograph has not, hitherto, been used to derive a pressure waveform from the peripheral pulse. A simple GTF can be used to transform the volume pulse into the pressure pulse. In the present study, such a GTF has been successfully applied to predict the pressure pulse from the volume pulse

across a wide age range and in both normotensive and hypertensive subjects. The agreement between the transformed volume pulse and pressure pulse measured by either the Finapres or tonometer is similar to the agreement between the Finapres and tonometer. Moreover, the transfer function can also be used to predict the pressure pulse with similar accuracy after NTG administration, when large changes in both the volume and pressure pulse are observed. Thus, a simple linear relation exists between the shape of the DVP and that of the peripheral pressure pulse, which remains constant irrespective of the effects of hypertension or effects of vasodilation produced by NTG.

The major change in the peripheral pressure pulse after NTG administration is a lowering of the IP in the downslope of the waveform. Extensive theoretical and experimental work suggests that this results from reduced pressure wave reflection predominantly from the lower body.^{5,6} NTG also causes marked changes in the volume pulse. Indeed, in the present direct comparison, the change in the IP of the volume pulse after NTG administration was approximately twice that seen in the pressure pulses. Such changes in the volume pulse after NTG administration have been variously attributed to alterations in left ventricular preload or afterload,^{3,20,21} although no direct evidence has been presented to support these proposed mechanisms. The present study shows that the relationship between the pressure and volume pulse in the

RMS Error Between Pressure Waveforms

Subjects	P_{rad}/P_{dig}	P^*_{rad}/P_{rad}	P^*_{dig}/P_{dig}
Normotensive	4.28 ± 1.42	4.30 ± 2.03	3.89 ± 1.69
Hypertensive	3.74 ± 1.11	5.17 ± 1.88	4.07 ± 1.85
Normotensive after NTG	4.51 ± 1.31	5.24 ± 2.03	4.06 ± 1.56
All	4.41 ± 1.45	4.42 ± 1.96	4.33 ± 1.88

Values are mean \pm SD in millimeters of mercury. P^*_{rad} indicates radial pressure reconstructed from the volume pulse; P^*_{dig} , digital pressure reconstructed from the volume pulse.

frequency domain remains constant, irrespective of the effects of NTG. Thus, although the effects of NTG on the pressure and volume waveforms will vary in a complex manner depending on the amplitude of the various harmonics of the waveforms, the change in one waveform is uniquely related to that in the other and can be predicted by using a single GTF. Therefore, the effects of NTG on the volume and pressure pulse are likely to be caused by the same mechanism. The relationship between digital volume and pressure in the digital artery is determined by the impedance characteristics of vessels in the finger distal to the digital arteries. The constancy of the relationship between volume and pressure in the presence of large changes in both caused by NTG suggests that the effects of NTG on peripheral impedance characteristics of the finger are minor compared with changes in arteries in the lower body that alter wave reflection. This is consistent with the observation that the effects of NTG on pulse-wave transmission along the upper limb are minor compared with the effects on wave reflection from the lower body.⁸

Takazawa et al⁴ have recently shown that the DVP may be used to demonstrate changes relating to drug effects and aging. Their analysis involved the ratio of measurements obtained from the second derivative with respect to time of the DVP waveform. Although providing quantitative indices of drug effects and the effects of aging, the physical meaning of such measurements is difficult to interpret. The present study supports our previous findings that the simple measurement of DVP IP provides an index of pressure-wave reflection.¹² A number of investigators have shown that the central aortic pressure pulse can be derived from the peripheral pressure pulse.^{8,18,22} The present study suggests that such an analysis could equally be applied to the volume pulse. Although variance in transfer functions >6 Hz may limit the accuracy of such a secondary transformation, this may be offset by the similarity of the DVP to carotid artery pressure.⁵ Thus, central aortic pressure obtained from the DVP may be relatively independent of the exact form of a transfer function and, hence, allow semiquantitative effects of drugs on central pressure to be obtained without the need to use a transfer function. Measurement of the volume pulse offers a number of practical advantages over measurement of the pressure pulse. Photoplethysmography is inexpensive and, unlike tonometry, is operator independent. Furthermore, the technique is ideal for pharmacological studies in which continuous monitoring of drug effects is required. The only drawback with photoplethysmography relates to the damping of the signal as a result of peripheral vasoconstriction.³ In the present study, this was avoided by studying subjects in a warm laboratory. In conclusion, we have shown that the peripheral pressure pulse is related to the DVP by a transfer function that is not influenced by effects of hypertension or those of NTG. The effects of NTG on the volume pulse and pressure pulse are thus influenced by the same mechanism, likely to be a reduction in pulse-wave reflection. The volume pulse is likely to be useful in assessing the effects of drugs on pulse-wave reflection.

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