Effects of Vasoactive Drugs on the Relationship between ECG-pulse Wave Delay Time and Arterial Blood Pressure in ICU Patients

W Zong, GB Moody, RG Mark

Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA, USA
Cardiology Division, Beth Israel Deaconess Medical Center, Boston, MA, USA

Abstract

This study focused on the relationship between arterial blood pressure (ABP) and the delay time from ECG to radial pulse (PWDT) with and without vasoactive drugs, to learn if PWDT could be a useful monitoring parameter yielding information complementary to that obtained from ABP. Fourteen ICU patient records from the MIMIC Database were used as subjects. Automated QRS detection and ABP pulse detection algorithms were employed to obtain the PWDT between the onset of each ECG QRS and the foot of the following ABP pulse. We found an approximately linear relationship between smoothed PWDT and smoothed systolic (or diastolic) ABP, with no significant correlation between changes in vasoactive drug levels and changes in the relationship (slope or intercept) of PWDT and ABP.

1. Introduction

Vasoactive drugs modulate ABP by acting on the peripheral resistance vessels that are at the level of arteriolar beds. Both vasoconstrictors and vasodilators may also significantly modulate the smooth muscle tone in larger muscular arteries. The state of vascular tone is of considerable clinical interest because it may, together with knowledge of ABP, allow one to differentiate among the causes of hemodynamic abnormalities (e.g., different clinical conclusions would be drawn for low ABP with low vascular tone versus high vascular tone).

The size and elasticity of the arteries determine pulse wave velocity (PWV). It is well known that the nonlinear elastance of blood vessels causes them to become incrementally stiffer at higher distensions (higher ABPs). Thus, PWV increases as ABP rises. Changes in arterial smooth muscle tone will also change vessel diameter and elasticity at any given ABP and would be expected to change PWV according to the Moens-Korteweg equation for thin-walled elastic vessels [1]:

$$v = \sqrt{Eh/2\rho r} \quad (1)$$

where v is the pulse wave velocity; E is the Young's modulus, which represents the stress/strain ratio (i.e. the elasticity) of the vessel wall; h is the wall thickness; ρ is the blood density; and r is the inner radius of the vessel.

The ECG-ABP pulse wave delay time (PWDT) includes the pulse wave transmission time from aorta to radial artery as well as the pre-ejection period (PEP) of the heart. PWDT is closely related to PWV. Many investigators have studied the relationship between PWV and ABP using pulse wave transit time (PWTT) [2, 3, 4] and also the ECG-ABP pulse delay time (PWDT) because of its ease of measurement [5, 6]. Previous studies were mainly focused on comparing differences of PWV changes between normal and hypertension, or on investigating the determinants (such as age, pressure, and cholesterol) of PWV. This study focused on the relationship between PWDT and ABP with and without vasoactive drugs, to learn if these drugs (at dosages used in the ICU) measurably affect the mechanical properties of the arteries, and to learn if PWDT could be a useful monitoring parameter yielding information complementary to that obtained from ABP.

2. Materials and methods

2.1. Subjects

Fourteen records of ICU patients from the MIMIC database [7] were selected and processed in this study. The selected patients (8 males and 6 females, aged 21 to 92) had clinical problems that included sepsis, CHF/pulmonary edema, bleed, MI/cardiogenic shock, angina, and respiratory failure. During the recording period, five of these patients received vasoconstrictors

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(Levophed and/or Neosynephrine), four were treated with vasodilators (Nitroglycerine), and the other five were not given vasoactive medications. The patient records contain multi-lead ECGs, radial ABP, pulmonary arterial pressure (PAP), a plethysmograph signal used by the ICU monitor to derive oxygen saturation, and an impedance-based respiration signal; they also include extensive clinical data including patient history, lab results, and medications. Each record is between 20 and 60 hours long, and is stored on a CD-ROM. The ECG signals were digitized at 500 Hz, and the other signals at 125 Hz, with 12-bit resolution. The recording bandwidths of the ECG and ABP signals were 0.5-40 Hz and 0.1-20 Hz respectively.

2.2. Procedure

Two computer algorithms, one for detecting the QRS onset in the ECG, and another for detecting the pulse onset in the ABP, were used to obtain the series of time delays (PWDT) between the beginning of each QRS complex and that of the following ABP pulse. The ABP pulse detection algorithm also measured the systolic and diastolic pressure values of each ABP pulse. PWDT, systolic ABP (ABP_{sys}) and diastolic ABP (ABP_{dias}) were resampled at uniform intervals of 1.024 seconds after smoothing by averaging over a 64 beat moving window. The relationships between smoothed PWDT, ABP_{sys}, and ABP_{dias} were studied at varying vasoactive drug levels.

2.3. Detection algorithms

The **QRS detection algorithm** we used is based on a nonlinear-scaled ECG curve length feature [8], in order to locate the QRS onset with high accuracy. This algorithm was previously evaluated with 150 normal and abnormal QRS complexes from patient ECG records in the MIT-BIH Arrhythmia Database; the mean absolute difference and standard deviation of the QRS onset detection from manual measurements of normal beats were 0.4ms and 2.4ms respectively [8].

The **ABP pulse detection algorithm** identified the time of ABP pulse arrival as a point at the onset of the pulse wave, so as to avoid the effects of pressure wave reflection. The algorithm constructed an ABP template during its learning period (the first 15 beats). An algorithm based on the ABP signal slope was used to get the approximate onset points of the ABP pulse. The detected onset points were verified manually. After ten ABP pulse onsets were obtained in this way, the corresponding ABP pulse waveforms were averaged (over a 480ms window beginning 160ms

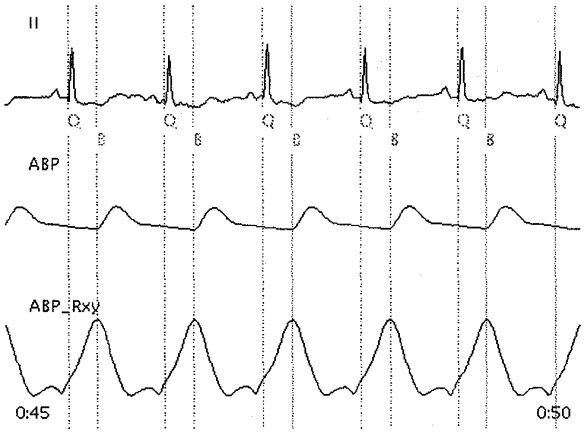

Figure 1: Measurement of PWDT from ECG (lead II) and ABP. ABP_Rxy is the CCF; PWDT is the interval between Q and B.

before the onset), to create a template representing the typical ABP pulse. For the remainder of the recording, the template was shifted, point by point, in the neighborhood of each detected pulse wave, and at each step, a linear cross correlation coefficient function (CCF) was calculated. The CCF value is between -1 and +1. A threshold of 0.92 was used to define a search window for the ABP pulse, within which the maximum CCF is taken to coincide with ABP pulse arrival. Since each beat produces a similar ABP pulse waveform, template matching gives a high precision result indicating the arrival time of the ABP pulse. This fiducial mark need not be the exact onset of the ABP pulse wave; it suffices to locate a stable point in the vicinity of the onset, since the most useful information is the change of the arrival time of ABP pulse. Figure 1 shows the fiducial marks obtained in a typical case.

3. Results

The 14 patient records were processed as described above, and for each record, time series of smoothed ABP (systolic and diastolic) and PWDT measurements were calculated and matched with time series of vasoactive drug levels. Figure 2 shows PWDT, ABP_{sys}, ABP_{dias}, and vasodilator (Nitroglycerine) drug level for MIMIC record 230. Figure 3 shows PWDT and ABP for another record.

We chose episodes with different drug levels and plotted the PWDT versus ABP_{sys} and ABP_{dias}, to observe whether there are any changes in the relation of PWDT versus ABP. Figure 4 shows episodes from record 230. From such plots for our 14 cases, we found

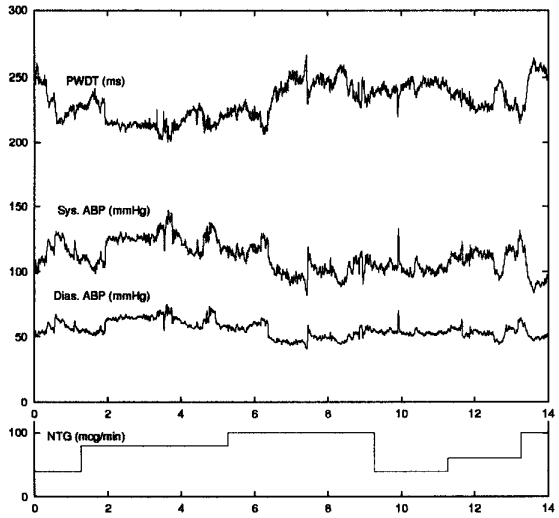

Figure 2: Plot of smoothed PWDT, ABP, and Nitroglycerine (NTG) level from a 15-hour segment of MIMIC record 230. Note the strong anticorrelation bewteen smoothed PWDT and ABP at all levels of NTG. The horizontal axis indicates elapsed time in hours from the beginning of the record.

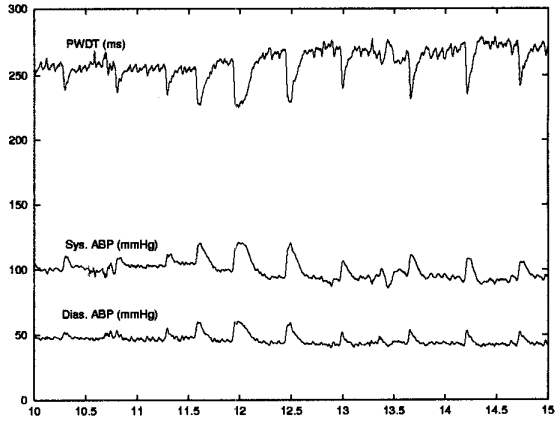

Figure 3: Relationship between PWDT and ABP during a 5-hour segment of MIMIC record 212. During this interval, the patient received IV Neosynephrine at an approximately constant rate.

that there was a strongly linear relationship between PWDT and ABP_{sys} or ABP_{dias}. In each case, we identified the longest interval of uninterrupted signals (between 3 and 15 hours), and performed linear regression over the entire interval (see Table 1 for the results and Figure 4 for examples of the least-squares fitted lines). We also fitted lines to overlapping one-hour segments within each of the 3- to 15-hour intervals in order to assess the variability of the slope and intercept of the fitted lines over time. We found no significant correlation between changes in drug levels and changes in the relationship (slope or intercept) between PWDT and ABP_{sys} (or ABP_{dias}), indicating that vasoconstrictors and vasodilators, at the dosages used in the ICU, did not measurably affect PWDT.

4. Discussion

The effects of vasoactive drugs on the relationship between PWDT and ABP in ICU patients were investigated in this study. Averaged PWDT and ABP values were used since the beat to beat values of PWDT and ABP fluctuate due to noise or physiological dynamic change and are not suitable for our purpose on drug effects.

PWDT includes the left ventricular PEP plus the pulse wave propagation time, thus representing PWV in part. Although it would be desirable to study PWV

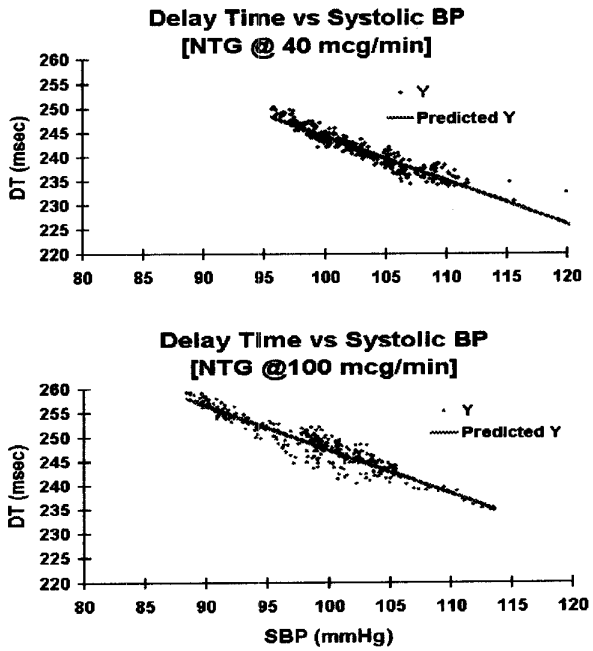

Figure 4: Examples of averaged PWDT vs. ABP in MIMIC record 230. Each plot shows 320 evenly-spaced samples over a period of one hour. The slopes of the least-squares fitted lines (Predicted Y) are nearly identical (-0.904 above, -0.906 below); there is a small but significant change in the y-intercept of about 3 ms. This change coincides with, but is not systematically related to, the change in drug level, as shown by further observations of this and other patients.

MIMIC record	PWDT vs ABP_{sys} r	PWDT vs ABP_{sys} slope	PWDT vs ABP_{dias} r	PWDT vs ABP_{dias} slope	Length (hours)
037	-0.903	-1.409	-0.870	-2.106	5.0
041	-0.926	-0.761	-0.855	-1.364	3.0
211	-0.949	-0.678	-0.701	-1.711	8.0
212	-0.922	-1.294	-0.869	-2.260	15.0
213	-0.911	-0.468	-0.862	-0.656	5.0
222	-0.801	-0.427	-0.673	-0.804	5.0
224	-0.916	-0.958	-0.832	-1.753	10.0
225	-0.891	-1.280	-0.758	-1.894	5.0
230	-0.943	-1.101	-0.748	-1.781	8.0
237	-0.826	-1.107	-0.481	-0.814	5.0
240	-0.955	-1.071	-0.882	-2.111	4.0
248	-0.934	-1.652	-0.285	1.982	8.0
413	-0.844	-1.002	-0.801	-1.554	12.0
446	-0.830	-0.748	-0.824	-1.205	5.5
Mean	-0.897	-0.997	-0.746	-1.288	7.0
SD	0.051	0.353	0.171	1.072	3.4

Table 1: Relationship between PWDT and ABP in 14 recordings from the MIMIC Database (see text).

or PWTT directly, those parameters are unavailable from the MIMIC database, reflecting clinical practice in long-term ICU monitoring.

It was considered that the smooth muscle tone might have a major influence on PWV. Bank et al. [9] investigated the direct effects of smooth muscle relaxation and contraction on in vivo human brachial artery. They applied 100μg Nitroglycerine to the artery in a 5mL bolus over about 2 seconds to make the artery relax, and applied 1.2μg Levophed in the same way to make the artery contract. The PWV in the artery decreased about 10% (from 15m/s to 13.3m/s) when this amount of Nitroglycerine was administered, but there was no significant change of PWV in response to Levophed applied locally. In contrast, the IV Nitroglycerine dosage used on the ICU patients in our study ranged from 40-150μg/min, less than a tenth of the amount used by Bank et al. Similarly, the IV Levophed dosage for the ICU patients usually ranged from 5-20μg/min, which was also much lower than that used by Bank.

From this analysis we might infer that the vasoactive drug dosages used in the ICU do not significantly change arterial wall properties or geometry, and thus do not change PWDT. Vasoconstrictors and vasodilators do change peripheral resistance and thus alter the vascular reflection coefficient. This should result in subtle changes in arterial pulse waveforms, which might be detectable by suitable pattern-recognition algorithms [10].

There is a strong linear relationship between the averaged PWDT and averaged ABP. From the results of the present study, PWDT does not give extra information about any possible small effects of vasoactive drugs on the properties of the arterial wall. In combination with periodic calibration using other methods, however, PWDT may be a useful surrogate for an invasive ABP measurement.

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Address for correspondence:
Wei Zong, Ph.D.
MIT Room E25-506B
Cambridge, MA 02139 USA
Email: wzong@mit.edu