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Early Detection of Hemorrhage via Central Pulse Pressure Derived from a Non-Invasive Peripheral Arterial Blood Pressure Waveform

Guanqun Zhang, *Student Member, IEEE*, Kathy L. Ryan, Caroline A. Rickards, Victor A. Convertino, and Ramakrishna Mukkamala, *Member, IEEE*

***Abstract*—There is a profound need for early and convenient detection of hemorrhage in both civilian and military medicine. Due to wave reflection timing, central pulse pressure (PP), but not peripheral PP, is a surrogate of stroke volume (SV) and therefore an early marker of blood loss. However, only peripheral PP is convenient to measure. We tested an adaptive transfer function technique for deriving the central arterial blood pressure (ABP) waveform from a non-invasive peripheral ABP waveform in healthy humans subjected to lower body negative pressure (LBNP), a safe model of early hemorrhage. Our results showed that the derived central PP provided an earlier and more sensitive marker of progressive LBNP and a far more accurate measure of SV than measured peripheral PP.**

I. Introduction

Hemorrhage is a common malady in various patient populations including the critically ill and combat casualties. So, the ability to detect hemorrhage early – when intervention is most effective – carries great value. Unfortunately, due to compensatory physiologic mechanisms, arterial blood pressure (ABP) and other convenient vital signs are often late markers of blood loss [1–4]. Although stroke volume (SV) is known to provide an early indication of hypovolemia, it is difficult to measure directly.

Pulse pressure (PP) has long been regarded as a surrogate of SV [5] and could therefore represent a convenient approach for achieving sensitive detection of hemorrhage. However, this approach is hampered by arterial wave reflection. That is, when the heart ejects blood, a pressure wave is initiated that travels through the arteries. When the wave reaches the arterioles, a significant part of the wave is reflected back towards the heart. As a result, the ABP waveform at a given arterial site arises as the sum of the forward and backward traveling waves at that site. Since wave reflection occurs mainly at the arterioles, there is little time delay between the forward and backward waves in a peripheral artery. So, summing the backward wave to the forward wave increases peripheral PP (see Fig. 1). Moreover, the magnitude of the backward wave relative to the forward wave increases with total peripheral resistance. Peripheral PP accordingly increases with vasoconstriction and decreases with vasodilation. By contrast, the forward and backward waves in the central aorta are shifted by the time it takes for the wave to travel from the central aorta to the periphery and back. Consequently, adding the backward wave with the forward wave has much less impact on central PP (see Fig. 1). In sum, because of wave reflection timing, only central PP is a surrogate of SV [6], [7]. On the other hand, only peripheral PP can be conveniently measured.

Previously, we developed an adaptive transfer function technique to derive the central ABP waveform from a peripheral ABP waveform [8]. We validated this technique as applied to invasive peripheral ABP waveforms against high fidelity central ABP waveforms from animals during a broad array of interventions. In the current study, we applied the same technique to non-invasive peripheral ABP waveforms from healthy humans subjected to lower body negative pressure (LBNP), a well-established laboratory model of early hemorrhage [9]. We then compared the derived central PP and the measured peripheral PP in terms of their ability to detect the SV and cardiac output (CO) reductions induced by progressive LBNP.

II. Methods

A. Adaptive Transfer Function Technique

Our adaptive transfer function technique is illustrated in Fig. 2 and described in detail elsewhere [8]. Briefly, the arterial tree is modeled as m parallel, uniform, and frictionless tubes with terminal loads. The i^{th} tube represents the wave travel path between the central aorta and the i^{th} peripheral artery. Each tube has constant characteristic impedance (Z_{ci}) and allows waves to travel along the entire tube with constant time delay (T_{di}). The i^{th} terminal load represents the arterial bed distal to the i^{th} peripheral artery. Each terminal load has frequency-dependent impedance characterized by peripheral resistance (R_i), peripheral compliance (C_i), and Z_{ci}.

According to this model, a peripheral ABP waveform ($p_{pi}(t)$) is related to the central ABP waveform ($p_c(t)$) through a transfer function defined in terms of T_{di}, R_iC_i, and $Z_{ci}C_i$ (see

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G. Zhang is with the Department of Electrical and Computer Engineering, Michigan State University, East Lansing, MI 48824, USA (e-mail: zhanggu2@msu.edu).

K. L. Ryan is with the United States Army Institute of Surgical Research, Fort Sam Houston, TX 78234, USA (e-mail: kathy.ryan@amedd.army.mil).

C. A. Rickards is with the University of Texas at San Antonio, San Antonio, TX 78249 (e-mail: caroline.rickards@us.army.mil).

V. A. Convertino is with the United States Army Institute of Surgical Research, Fort Sam Houston, TX 78234, USA (e-mail: victor.convertino@amedd.army.mil).

R. Mukkamala is with the Department of Electrical and Computer Engineering, Michigan State University, East Lansing, MI 48824, USA (phone: 517-353-3120; fax: 517-353-1980; e-mail: rama@egr.msu.edu).

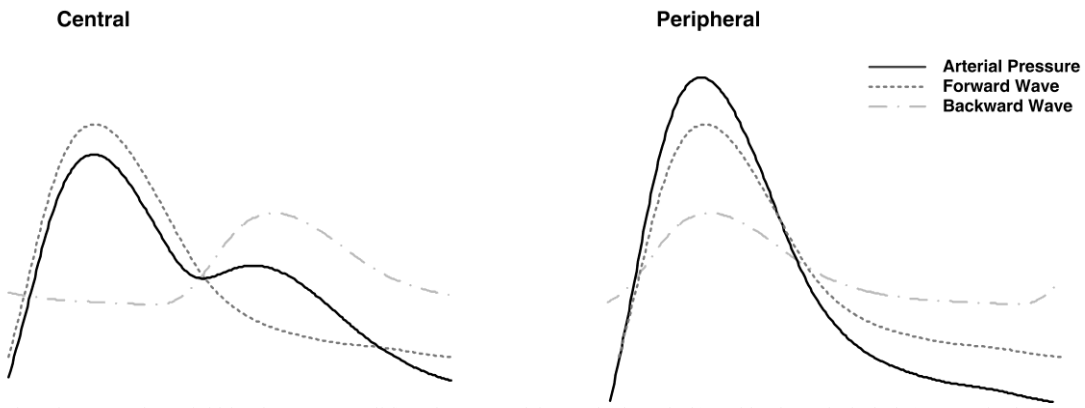

Figure 1. Sample plot of measured arterial blood pressure (solid) and computed forward (short dash) and backward (dash dot) waves in the central aorta and a peripheral artery.

peripheral ABP→central ABP transfer function in Fig. 2). The three unknown parameters are estimated from $p_{pi}(t)$ by exploiting the fact that central aortic blood flow (ABF) is negligible during diastole. Thus, the flow at each tube entrance in the model (central ABF component ($q_{ci}(t)$)) may likewise be small during this time interval. That is, according to the model, $p_{pi}(t)$ is related to $q_{ci}(t)$ through a transfer function also defined in terms of T_{di}, R_iC_i, and $Z_{ci}C_i$ (see peripheral ABP→central ABF transfer function in Fig. 2). These common parameters are estimated by finding the peripheral ABP→central ABF transfer function, which when applied to $p_{pi}(t)$, optimally fits $q_{ci}(t)$ (scaled by Z_{ci}) to zero over its diastolic intervals. This optimization is achieved via a nonlinear least squares search over a physiologic range of the parameters. The optimization is facilitated with an initial measurement of T_{di} (i.e., pulse transit time between the central aorta and peripheral artery measurement site), which sets the search range for this key parameter.

Finally, the peripheral ABP→central ABP transfer function with the estimates of T_{di}, R_iC_i, and $Z_{ci}C_i$ is applied to $p_{pi}(t)$ so as to derive $p_c(t)$.

B. *Experimental Data*

De-identified physiologic data from humans subjected to a well-established LBNP protocol to simulate hemorrhage and resuscitation were studied [10]. The data collection procedures were approved by the Institutional Review Board of the Brooke Army Medical Center. The procedures pertinent to this particular study are briefly described as follows. Five young, healthy humans in the supine posture were secured in an LBNP chamber. Instruments were positioned for measurement of various physiologic variables including a non-invasive impedance cardiography (ICG) waveform and a non-invasive finger ABP waveform (Finometer, TNO-TPD Biomedical Instrumentation, Amsterdam, The Netherlands). The physiologic variables were recorded at a sampling frequency of 500 Hz during a five-minute baseline period and following sequential exposure to increasing levels of LBNP up to at least 60 mmHg for five minutes each. After termination of LBNP and a five-minute equilibration period, the physiologic variables were recorded for an additional five-minute recovery period.

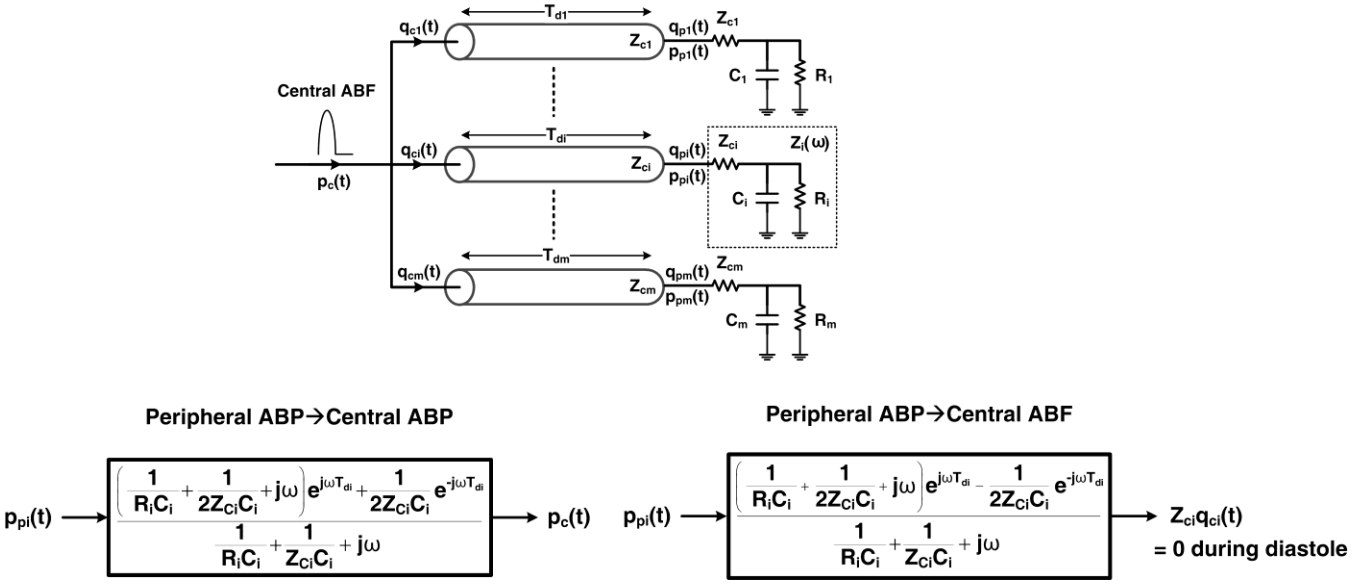

Figure 2. Adaptive transfer function technique for deriving the central arterial blood pressure (ABP) waveform from a peripheral ABP waveform. ABF is arterial blood flow; see text for remaining symbols.

C. Data Analysis

The adaptive transfer function technique was applied to the peripheral ABP waveforms during the baseline period, each LBNP level, and the recovery period. Since all subjects were young and healthy, the same initial T_{di} value was used for each subject. This value was specifically set to the group average baseline pulse transit time estimated from the ICG and peripheral ABP waveforms as described elsewhere [11]. (Note that a universal T_{di} value could potentially be used in a combat casualty care application wherein all subjects would likewise be young and healthy.) Central and peripheral PP were then respectively determined from the derived and measured ABP waveforms to obtain surrogates of SV. Both variables were also multiplied by heart rate (HR), as measured from the ABP waveform, to obtain CO surrogates.

III. Results

Fig. 1 illustrates a sample of the derived central and measured peripheral ABP waveforms. Consistent with known physiology, central PP was appreciably smaller than peripheral PP. Fig. 3 illustrates the group average results. Mean ABP was maintained with progressive LBNP indicating compensatory vasoconstriction. While peripheral PP decreased with increasing LBNP and then returned to its baseline value during recovery, central PP decreased earlier and showed superior discrimination of each LBNP level. Hence, central PP was a more sensitive marker of the simulated hemorrhage than peripheral PP. After multiplication with HR to obtain CO surrogates, only CO derived from central PP demonstrated a decline with progressive LBNP. Hence, central PP provided a considerably more accurate and sensitive indication of reduced SV than peripheral PP.

IV. Discussion and Conclusions

In summary, there is a profound need for early and convenient detection of hemorrhage in both civilian and military medicine. Central PP – as a surrogate of SV – can provide an early marker of blood loss, but only peripheral PP is convenient to measure.

We tested our previously developed adaptive transfer function technique for deriving the central ABP waveform from a peripheral ABP waveform in healthy humans subjected to a LBNP protocol. In this laboratory procedure, negative pressure is applied to the abdomen and lower extremities through a pressure chamber with an airtight seal so as to cause blood to pool in the lower body. A chamber pressure of -40 mmHg causes about a one liter shift of blood from the upper body to lower body [9]. As a result, similar to early hemorrhage, CO declines markedly even though mean ABP is maintained [12]. Our results showed that the derived central PP provided an earlier and more sensitive marker of LBNP and a far more accurate measure of reduced SV than measured peripheral PP. As predicted by wave reflection theory, the drop in peripheral PP due to a declining SV was

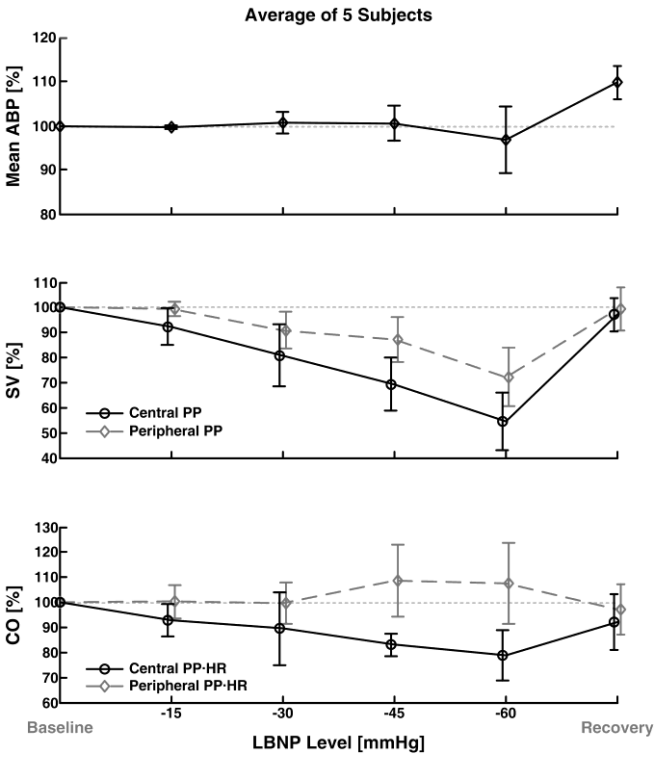

Figure 3. Mean ABP (top panel); stroke volume (SV – middle panel); and cardiac output (CO) at baseline, during LBNP, and recovery. SV and CO were calculated using central (solid lines) and peripheral (dashed lines) PP surrogates.

buffered by the compensatory vasoconstriction that occurred during LBNP. However, central PP was much less impacted by the rise in total peripheral resistance, presumably due to the significant time delay between the forward and backward waves in the central aorta.

This study improves upon our previous efforts to estimate SV and CO by long time interval analysis of a peripheral ABP waveform [10]. In particular, that technique estimates average CO over approximately 30-60 sec intervals. The technique described in the current study can potentially estimate beat-to-beat SV and could therefore detect rapid changes during hemorrhage and other physiologic conditions.

One limitation of our technique is that the PP surrogate of SV assumes instantaneous cardiac ejection. In the future, we plan to circumvent this assumption by estimating the Windkessel time constant via fitting an exponential to the diastolic decay of the derived central ABP waveform, which is less complicated by wave reflection than a peripheral ABP waveform.

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