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Estimation of Cardiac Output and Total Peripheral Resistance in Preterm Infants by Arterial Waveform Analysis

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***Abstract*—This study investigated whether arterial blood pressure waveform analysis could be useful for estimating left ventricular outflow (LVO) and total peripheral resistance (TPR) in preterm infants. A cohort of 27 infants were studied, with 89 measurements of left ventricular outflow (LVO) using Doppler echocardiography and arterial pressure using catheters, performed in 0, 12, 24 and 36 hours after birth. TPR was computed as mean arterial pressure divided by LVO. The diastolic decay rate (1/τ) was obtained via fitting an exponential function to the last one third of each arterial pulse, with the mean rate computed from 50 pulses selected from each infant. This decay rate was considered to be inversely related to TPR while positively related to LVO. The results of regression analysis have confirmed that the diastolic decay rate had significant positive and negative relationships with LVO and TPR respectively($r = 0.383$, $P = 0.0002$ and $r = -0.379$, $P = 0.0002$ respectively). These preliminary results demonstrated the potential utility of arterial pressure waveform analysis for estimating LVO and TPR in preterm infants, but more advanced multi-parameter models may be needed to improve accuracy of the estimation.**

I. Introduction

Cardiac output (CO) and total peripheral resistance (TPR) are two important parameters of the cardiovascular system. Measurement of these two parameters can provide valuable information for the assessment and management of patients needing intensive care, including preterm infants in the neonatal intensive care unit (NICU) [1, 2]. For example, high CO and low TPR are symptoms of sepsis, which is a common cause of mortality and morbidity in preterm infants, particular those with very low birth weight (VLBW) [1]. A substantial drop in CO (>50%) has been associated with a high risk of mortality in these infants with sepsis [1]. Furthermore, the measurement of systemic hemodynamics can facilitate the development of better therapeutic strategy for these infants, including the use of volume expansion and inotropes [2]. In the present NICU setting, the assessment of CO and TPR requires the measurement of left ventricular outflow (LVO) or right ventricular outflow (RVO) using ultrasound Doppler echocardiographic waveforms. However, such measurement requires specialized skill and equipment, and cannot be performed continuously.

In this study, the estimation of LVO and TPR was performed by analyzing the rate of blood pressure decay in the diastolic portion of the arterial pulse wave. This has been associated with TPR in the Windkessel model, and has been utilized in the study of animals and adult patients [4,5]. However, whether this arterial waveform parameter is useful for monitoring preterm infants has not been previously investigated. The results from the current study would help to establish the potential utility of the diastolic decay rate parameter for assessing LVO and TPR in preterm infants.

II. Methods

A. Subjects

All the data were collected in the NICU at the Nepean Hospital in Sydney, Australia. The study was approved by the Sydney West Area Health Service Human Research and Ethics Committee and informed parental consent was obtained in all cases. The study cohort comprised a convenience sample of 27 early low birth weight infants with gestational age <30 wks. The demographic characteristics of the studied infants are as follows (mean±SD): 17 males 12 females, gestational age 26.7±1.8 wks (range 24-30 wks), birth weight 1010.7±346.3 g (range 520-1929 g).

Physiological data were collected from the infants at four different time periods: 1-3 hours after birth (27 babies), 12 hours after birth (24 babies), 24 hours after birth (20 babies) and 36 hours after birth (18 babies). Thus a total of 89 measurements were used in the modeling.

B. Measurement and protocol

A Vivid 7 Dimension ultrasound scanner (GE Health Care, Rydalmere, Australia) was used with a 5–7 MHz sector cardiac probe incorporating pulsed wave and continuous Doppler echocardiographic waveforms. All ultrasounds were performed by the same investigator (M.T.).

LVO was obtained by measuring the aortic valve annulus diameter in the parasternal long axis view, and then velocity time integrals (VTI) were obtained with a minimum of 5 consecutive aortic pulsed Doppler waveforms from an apical long axis view [3].

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C. *Arterial pressure waveform analysis*

The Arterial blood pressure (ABP) pulses of preterm infants typically follow an exponential decay during each diastolic interval. According to the Windkessel model of the systemic circulation that comprises elements of arterial resistance (R) and arterial compliance (C), the time constant of this exponential decay (τ) corresponds to RC [4, 5] Assuming that C was similar amongst the infants (as C changed mainly with age and the infants should have very compliant arteries at birth), while R could vary greatly depending on the infants' condition, the main determinant of τ would be R. CO (measured as LVO here) was related to R via the relationship R = MAP/CO, thus we would expect a relationship between CO and 1/τ. In addition, there may be a stronger relationship between CO and MAP/τ, assuming that τ represents R.

From each cardiac pulse of the pressure waveform, the diastolic decay time constant (τ) of the Windkessel model was determined by fitting an exponential function to the diastolic period, which was approximated by the last one third of the pulse period [4]. The fitted curves are illustrated in Fig. 1. A direct way of extracting the exponential time constant was to take the logarithm of both pressure and time and carry out linear regression, then the slope of the regression would be 1/τ, termed the diastolic decay rate. Fig. 1a shows an example of a relatively slow decay rate (long time constant) whereas Fig. 1b shows an example of a fast decay rate (short time constant). This slope parameter was first determined in each set of measured data by taking the mean value of 50 pulses. Finally, the relationship of CO (and TPR) with 1/τ was examined by linear regression using the 89 sets of measurements, and the corresponding correlation coefficient r was computed.

As a comparison, another parameter given by the product of pulse pressure and heart rate (PP × HR) was derived, and its relationship with CO was examined. This parameter has previously been used to track CO changes in adult subjects [6].

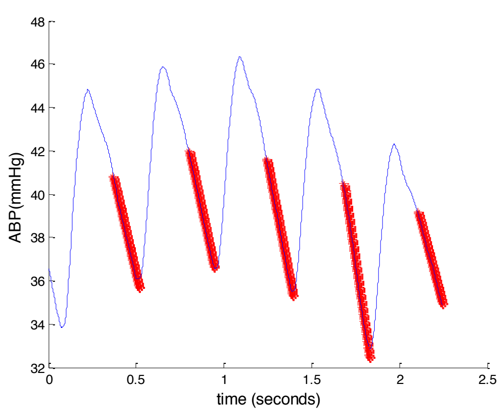

Fig. 1a. Arterial blood pressure (ABP) pulses with the fitted exponential functions, for one subject with a diastolic decay rate of 0.44 Hz (time constant of 2.3 s).

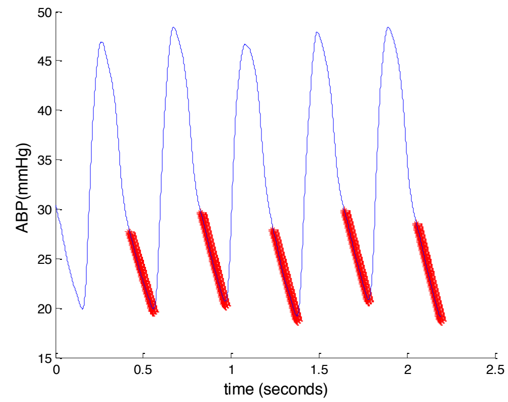

Fig. 1b. Arterial blood pressure (ABP) pulses with the fitted exponential functions, for one subject with a diastolic decay rate of 1.24 Hz (time constant of 0.8 s).

III. Results and Discussion

The results of regression analysis demonstrate that the diastolic decay rate 1/τ had a significant positive relationship with LVO (r = 0.383, P = 0.0002), and negative relationship with TPR (r = -0.379, P = 0.0002). The corresponding scatter plots are shown in Figs. 2 and 3. It was noted that one subject had a much higher decay rate (1/τ = 1.8 Hz) compared to others, and if this subject was neglected the correlations would become stronger (for LVO, r = 0.435, P = 0.00002; for TPR, r = -0.437, P = 0.00002). Overall, the results have shown that the diastolic decay rate parameter was potentially useful for providing information about LVO and TPR in the preterm infants. Although the correlations were not high, the scatter plots (Figs. 2 and 3) seem to suggest that the relationships between the variables may be better described by a more complex nonlinear function rather than a simple linear one. This could be further explored in future to improve the accuracy of estimation.

The individual exponential fit to the ABP pulses displayed high R^2 (0.99 ± 0.01), which provided justification of the Windkessel model for the analysis of pressure waveforms in infants. While previous studies have demonstrated the utility of the Windkessel-model based approach for the hemodynamic monitoring of animals and adult patients [4,5], the current study was the first to demonstrate its potential value for the assessment of preterm infants in the NICU setting. It has been suggested that in normal adults, the presence of arterial pulse wave reflection may affect the accuracy of the Windkessel model [5]. However, it appears that in the preterm infants, wave reflection is not prominent as the arterial pulses often do not display clear secondary peaks (Fig. 1). This may explain the good fit achieved by a simple Windkessel model.

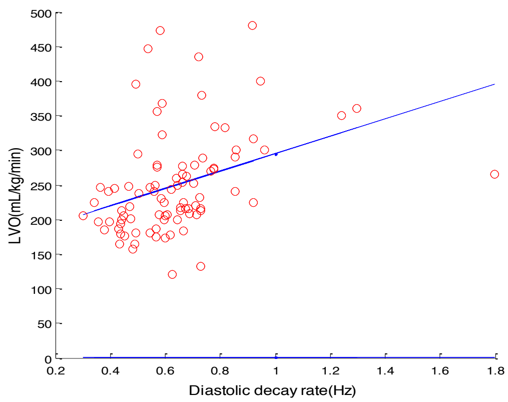

Fig. 2. Left ventricular outflow (LVO) versus diastolic decay rate (1/τ) in the cohort of preterm infants.

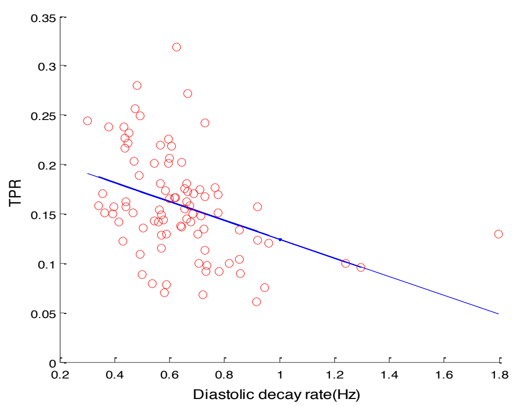

Fig. 3. Total peripheral resistance (TPR) versus diastolic decay rate (1/τ) in the cohort of preterm infants.

The parameter MAP/τ (MAP × diastolic decay rate) had lower correlation with LVO (r = 0.266, P = 0.012) compared with 1/τ, as shown in Fig 4. If the outlier with a very high decay rate (1/τ = 1.8 Hz) was excluded, the correlation became higher (r = 0.299, P = 0.0046). According to the model, MAP/τ should have a stronger relationship with CO compared with 1/τ, but the data seemed to suggest otherwise which was unexpected. Another arterial waveform parameter PP × HR did not show any significant correlation with LVO (r = 0.066, P = 0.54). Thus this parameter is probably more suitable for monitoring intra-subject change [6] but not for estimating CO in a group of preterm infants.

Many extremely low birth weight infants have impaired cerebral autoregulation (some with a complete absence of autoregulation) and thus a pressure passive cerebral circulation. Intracranial haemorrhage is more likely in this state of pressure passive circulation. Routine methods of estimating cardiac function in these preterm infants are dependent on echocardiographic estimates of volumetric flow or M-Mode estimates of ejection fraction. There are obvious limitations with the need of appropriately trained clinicians to perform these examinations and those measurements are valid for the short time period of the examination. There is thus an urgent need to explore new methods of continuous estimates of cardiac function to support clinical decisions to treat hypotension and support vulnerable cerebral circulation.

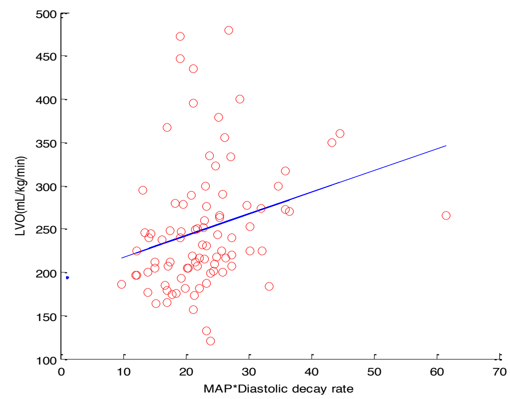

Fig. 4. Left ventricular outflow (LVO) versus the product of mean arterial pressure and diastolic decay rate (MAP/τ) in the cohort of preterm infants.

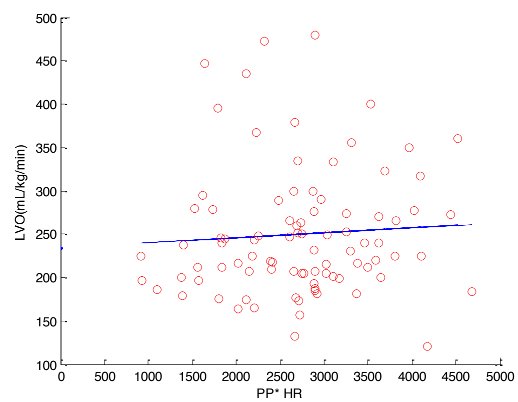

Fig. 5. Left ventricular outflow (LVO) versus the product of pulse pressure and heart rate (PP × HR) in the cohort of preterm infants.

IV. Conclusion

The preliminary results from this study demonstrated the potential utility of arterial pressure waveform analysis for estimating LVO and TPR in preterm infants. However, to further improve the accuracy and robustness of the estimation, more advanced multi-parameter models may be needed. Such models could include additional physiological parameters such as heart rate as well as incorporating possible nonlinear relationships between the parameters.

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