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# The degree of heart rate asymmetry is crucial for the validity of the deceleration and acceleration capacity indices of heart rate: A model-based study

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ABSTRACT

The deceleration capacity (DC) and acceleration capacity (AC) of heart rate are a pair of indices used for evaluating the autonomic nervous system (ANS). We assessed the role of heart rate asymmetry (HRA) in defining the relative performance of DC and AC using a mathematical model, which is able to generate a realistic RR interval (RRI) time series with controlled ANS states. The simulation produced a set of RRI series with random sympathetic and vagal activities. The multi-scale DCs and ACs were computed from the RRI series, and the correlation of DC and AC with the ANS functions was analyzed to evaluate the performance of the indices. In the model, the HRA level was modified by changing the inspiration/expiration (I/E) ratio to examine the influence of HRA on the performances of DC and AC. The results show that on the conventional scales ($T=1$, $s=2$), an HRA level above 50% results in a stronger association of DC with the ANS, compared with AC. On higher scales ($T=4$, $s=6$), there was no HRA and DC showed a similar performance to AC for all I/E ratios. The data suggest that the HRA level determines which of DC or AC is the optimal index for expressing ANS functions. Future clinical applications of DC and AC should be accompanied by an HRA analysis to provide a better index for assessing ANS.



## 1. Introduction

Heart rate variability (HRV) is a powerful tool for evaluating the autonomic nervous system (ANS) non-invasively. Various HRV measures serve as reliable prognostic indicators of cardiovascular morbidity and mortality [1]. A depressed HRV is observed in post-myocardial infarction (MI) [2,3], chronic heart failure (CHF) [4,5], and diabetes mellitus [6,7]. However, despite its wide application, one shortcoming of HRV is its limited ability to discriminate the sympathetic and vagal activities of the ANS [1,8,9]. Further, many HRV calculations are sensitive to artifacts and ectopic beats in the RR interval (RRI) time series [10,11]. Novel techniques are therefore required to assess ANS functions more accurately.

The deceleration capacity (DC) and acceleration capacity (AC) of heart rate are two new indices used to evaluate ANS functions [12]. The selection of the time and wavelet scales in their calculation allows the generation of multi-scale DC and AC indices for assessing the activities of the sympathetic and vagal branches of the ANS [13,14]. It was previously reported that the DC and AC can predict mortality in post-MI patients [12,13], detect the physiological status in fetuses [15–20], and diagnose various cardiovascular diseases (CVDs) [21,22].

Despite the successful clinical application of the DC and AC, their prognostic and diagnostic ability for CVDs remains controversial. A large-scale multicenter clinical trial found that the DC was superior to the AC for predicting mortality among post-MI patients [12]. By contrast, it was found that the AC outperforms the DC in discriminating between healthy young and old subjects [23], in diagnosing dilated cardiomyopathy patients [21], and in monitoring fetal status [18,20]. Others studies reported that the DC and AC have similar abilities to predict risk in post-MI patients [13], perform closely in detecting fetal status [17,19], and express close degrees of correlation with respect to ageing [24].

Discrepancies between the DC and AC have been largely attributed to their distinct associations with the ANS: DC is associated with vagal activity, and AC with sympathetic activity [18,21,25]. By contrast, our recent theoretical study found that both short-term DC and AC solely reflect vagal activity, while both

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long-term DC and AC reflect sympatho-vagal balance [14]. These findings suggest that the two indices reflect the same aspects of the ANS, while the scales determine whether they reflect sympathetic or vagal activity. Consequently, the paradox in the relative performance of DC and AC remains unresolved, and an interpretation of their distinctiveness is highly necessary.

Heart rate asymmetry (HRA) may provide an explanation for the different capabilities of DC and AC. Deceleration and acceleration rates are asymmetrical [26–28]. Because the calculation of DC and AC relies, respectively, on an deceleration- and acceleration-related anchor-point selection [29], asymmetry in the rates may affect the performance of the indices. The present study seeks to investigate whether the significance of DC and AC is affected by the mode of HRA. A mathematical model was adopted to generate an RRI time series that is realistic in the context of HRV properties, DC and AC values, and the HRA phenomenon. The model also allows an adjustment of the cardiac sympathetic and vagal activity levels, as well as the respiratory period and the inspiration/expiration (I/E) ratio, and can thus yield an RRI time series with controllable physiological conditions for the purpose of further investigation.

## 2. Methods

### 2.1. Model description

The model is based on that of Ursino and Magosso [30,31], improved for displaying respiration-induced HRV. Ursino and Magosso considered the role of the baroreflex and lung-stretch receptor in heart rate regulation. Their model is superior to other ANS models [32–35] in terms of simulating the HRV power-spectral density (PSD), which is also crucial for our study. It has been applied to study physiological problems [36,37] and serves as the basis for cardiac regulation in an integrative model of the cardiopulmonary system [38].

The model consists of two parts: a hemodynamic model, which simulates pulsatile pressure and flow in the human circulatory system, and an ANS model, which regulates the heart period, peripheral resistance, venous unstressed volume, and heart contractility. The mechanisms relating to heart-period regulation are described below. Details of the other parts of the model were previously reported [30,31].

The hemodynamic model, outlined in Fig. 1, includes the four chambers of the heart, the pulmonary circulation, and the systemic circulation. The chambers and the vessels are represented by a Windkessel compartment with a hydraulic resistance element and a compliance element. An inertial element is also included for the systemic and pulmonary arteries. The extravascular pressures for all the vessels in the thoracic and abdominal cavities are set to the breath-dependent intrathoracic pressure $P_{thor}(t)$ and the abdominal pressure $P_{abd}(t)$, respectively, to take account of the mechanical effect of respiration on the cardiovascular system. $P_{thor}(t)$ and $P_{abd}(t)$ are calculated as [31]

$$P_{thor}(t)=\begin{cases} -\Delta P_{thor}\cdot\alpha\cdot\dfrac{T_{resp}}{T_i}-4 & 0<\alpha<\dfrac{T_i}{T_{resp}} \\ -\Delta P_{thor}\cdot\alpha\cdot\dfrac{T_i+T_e-\alpha\cdot T_{resp}}{T_e}-4 & \dfrac{T_i}{T_{resp}}<\alpha<\dfrac{T_i+T_e}{T_{resp}} \\ -4 & \dfrac{T_i+T_e}{T_{resp}}<\alpha<1 \end{cases} \quad (1)$$

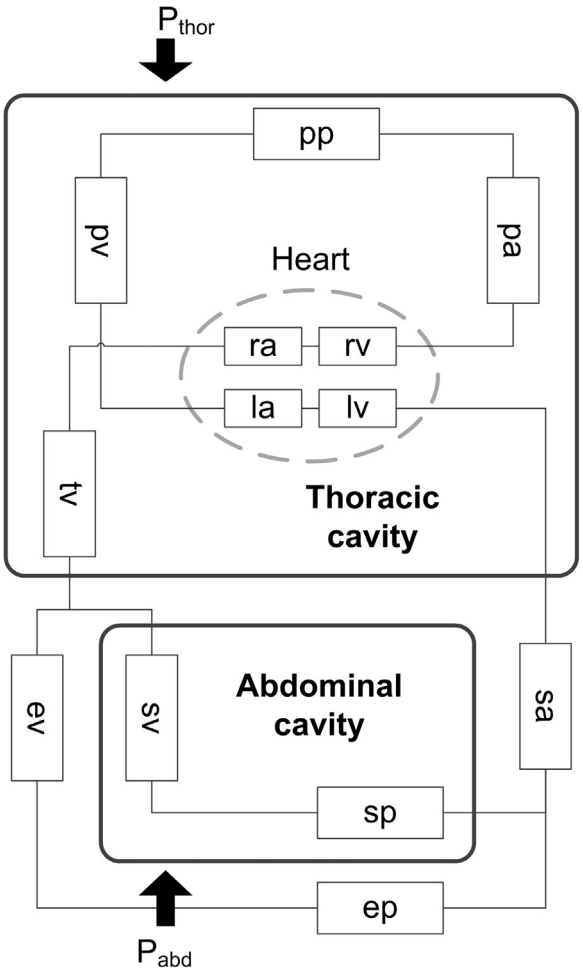


**Fig. 1.** Hemodynamic model. Each block represents a vessel segment or a heart chamber. ra: right atrium, rv: right ventricle, la: left atrium, lv: left ventricle, sa: systemic arteries, sp: splanchnic peripheral circulation, sv: splanchnic venous circulation, ep: extrasplanchnic peripheral circulation, ev: extrasplanchnic venous circulation, tv: systemic thoracic veins, pa: pulmonary arteries, pp: pulmonary peripheral circulation, pv: pulmonary venous circulation. $P_{thor}$: pressure in the thoracic cavity, the extravascular pressure for the vessels in the thoracic cavity. $P_{abd}$: pressure in the abdominal cavity, the extravascular pressure for the vessels in the abdominal cavity.

$$P_{abd}(t)=\begin{cases} -2.5\cdot\alpha\cdot\dfrac{T_{resp}}{T_i/2} & 0<\alpha<\dfrac{T_i/2}{T_{resp}} \\ -2.5 & \dfrac{T_i/2}{T_{resp}}<\alpha<\dfrac{T_i}{T_{resp}} \\ -2.5\cdot\alpha\cdot\dfrac{T_i+T_e-\alpha\cdot T_{resp}}{T_e} & \dfrac{T_i}{T_{resp}}<\alpha<\dfrac{T_i+T_e}{T_{resp}} \\ 0 & \dfrac{T_i+T_e}{T_{resp}}<\alpha<1 \end{cases} \quad (2)$$

where $T_{resp}$ is the respiratory period, and $T_i$ and $T_e$ are the durations of inspiration and expiration, respectively. $\Delta P_{thor}$ is the difference between the pressures at the end of the inspiration and the steady state. The basal value for $\Delta P_{thor}$ is 5 mm Hg [31]. The parameter $\alpha$ indicates a proportion of the respiration cycle, with a value of 0 indicating the beginning of the inspiration. $T_p = T_{resp} - T_i - T_e$ describes the duration of the expiratory pause.

Fig. 2 depicts the model of heart-period regulation. The heart period is controlled jointly by the sympathetic and vagal activities through their responses to the stimuli from the carotid baroreceptors (CBR) and the lung-stretch receptors (LSR). The governing