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A Model-based Study of Relationship between Timing of Second Heart Sound and Systolic Blood Pressure

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Abstract—The onset of second heart sound is triggered by the closure of aortic valve due to the interaction of left ventricle and arterial system. Noninvasive experiments found that RS_2 defined by the time delay from the peak of ECG R wave to the onset of the second heart sound had a close inverse correlation with arterial systolic blood pressure. However, no theoretical study has been carried out to investigate the underline connections between them. A modified model of heart-arterial system is proposed in the present study. In this model the heart is described as a pressure source depending on time, ventricular volume, outflow, and heart rate, and the arterial system as a nonlinear system incorporating a pressure-dependent compliance. Simulation results show that the modified model is able to reflect the cardiovascular function qualitatively. The results also demonstrate that RS_2 is inversely correlated with aortic blood pressure under the effect of changing peripheral resistance, heart rate and contractility. The present study gives insight into the significant functional relations between the parameters characterizing the cardiovascular system and hemodynamics characteristics and provides an interpretation of the experimental observation on the relationship between RS_2 and aortic blood pressure.

I. Introduction

The heart sounds result from the interplay of the dynamic events associated with the contraction and relaxation of the artia and ventricles, the valve movements and the blood flow [1]. The first heart sound (S1) occurs at the onset of ventricular contraction during the closure of the mitral and the tricuspid valves. The second heart sound (S2) marks the end of ventricular systole and the beginning of the ventricular relaxation, following the closure of the aortic and pulmonary valves. The diagnostic value of heart sound has been recognized and used for primary screening of various heart diseases for long time. With the development of phonocardiogram, the timing of heart sound has been utilized in cooperation with electrocardiogram (ECG) and carotid pulsation to measure systolic time intervals (STI) which was established as a noninvasive test of cardiac function [2, 3].

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The interest of this study lies on the relationship between the timing of second heart sound and systolic blood pressure in aorta. The onset of second heart sound corresponds to the closure of the aortic valve at the end of ventricular systole when the aortic pressure exceeds ventricular pressure. The results of previous noninvasive experiments demonstrated that RS_2 that is defined by the time delay from the peak of ECG R-wave to S2 has a close inverse correlation with arterial systolic blood pressure (SBP) [4]. The finding has shown great promise for developing a noninvasive and cuffless blood pressure monitoring technique based on the timing information of heart sounds.

The objective of this study is to give insight into the underline mechanism that determines the relationship between systolic blood pressure and RS_2 by means of a mathematical model analysis. In this paper, we develop a new mathematical model to describe the heart-arterial interaction, in which the relation between SBP and RS_2 is investigated under varying peripheral resistance, arterial compliance, heart rate, contractility and end-diastolic volume.

II. Materials and Methods

A. A Modified Heart-Arterial Model

The present study proposes a modified model of heart-arterial system. The electrical analog of this model is presented in Fig.1. In this modified model, the left ventricle is described as pressure source rather than an elastic chamber via the well-known time-varying elastance model. The concept that describe ventricular pressure as a function of time and ventricular volume was first derived by Mulier from experiments on the isolated dog heart [5, 6]. The effect of ejection and heart rate was later introduced into the model by Danielsen and Ottesen [7, 8]. Therefore, the left ventricle is

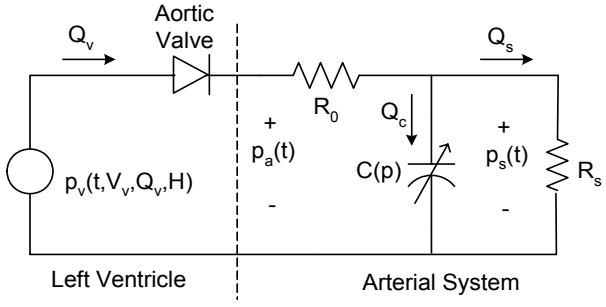


Fig.1. The electrical analog of a modified model of heart-arterial system proposed in the present study.

described as a pressure source depending on time *t,* ventricular volume V_v, outflow Q_v and heart rate H as

$$p_v(t,V_v,Q_v,H)=a(V_v-b)^2+(cV_v-d)F(t,Q_v,H) \quad (1)$$

where

$$F(t,Q_v,H)=f(t,H)-k_1Q_v(t)+k_2Q_v^2(t-\tau),\qquad \tau=\kappa t. \quad (2)$$

and *f(t, H),* the activation function, is a continuous function as

$$f(t,H)=\begin{cases} p_p(H)\dfrac{(t-\alpha)^n(\beta-t)^m}{n^n m^m[(\beta-\alpha)/(m+n)]^{m+n}}, & \alpha\le t\le\beta(H) \\ 0, & \beta(H)\le t\le t_h \end{cases} \quad (3)$$

where

$$\beta(H)=\frac{n+m}{n}\left\{t_{p,\min}+\left[\frac{\theta^v}{H^v+\theta^v}\right](t_{p,\max}-t_{p,\min})\right\}-\frac{\alpha m}{n}, \quad (4)$$

and

$$p_p(H)=p_{p,\min}+\left[\frac{H^\eta}{H^\eta+\phi^\eta}\right](p_{p,\max}-p_{p,\min}). \quad (5)$$

In our modified model, the left ventricular model is coupled to a nonlinear model of arterial system which consists of three elements: characteristic impedance of the proximal aorta R_0, total peripheral resistance *Rs*, and a pressure-dependent compliance *C(p)* [9] described as

$$C(p(t))=a\cdot e^{bp(t)}. \quad (6)$$

In the present study, mechanical interactions between the left ventricle and the vascular system are idealized with the following assumptions: 1) aortic pressure p_a is equal to the left ventricular pressure p_v; and 2) aortic valve is closed when the flow rate into the aorta from the left ventricle is equal to zero. During the ejection phase, the ventricular pressure p_v and aortic pressure p_a are guided by

$$\begin{cases} \dfrac{dp_s}{dt}=-\dfrac{R_s+R_0}{R_0R_sC(p_s(t))}+\dfrac{1}{R_0C(p_s(t))}p_v(t,V_v,H,Q_v), \\ \dfrac{dV_v}{dt}=\dfrac{p_s(t)}{R_0}-\dfrac{p_v(t,V_v,H,Q_v)}{R_0}, \\ p_a=p_s(t)-R_0Q_v. \end{cases} \quad (7)$$

They can be solved numerically by prescribing the end-diastolic volume and diastolic blood pressure. An iteration process is applied. The iteration continues until the difference in DBP of aortic pressure between two successive iteration loops is less than 1%.

B. Simulation

We performed a numerical simulation of this modified model to mimic the pressure and flow in left ventricular and proximal aorta. The control parameter values of a dog heart used in ventricular pressure model were: a = 0.007 mmHg/ml^2, b = 5 ml, c = 3.5 mmHg/ml, d = 1 mmHg, n = 2.05, m = 3.68, α = 0s, $t_{p,min}$ = 0.1859, $t_{p,max}$ = 0.2799, φ = 1.66, υ =9.9, $p_{p,min}$ = 1, $p_{p,max}$ = 1.372, θ = 1.83, and η = 17.5. By varying the parameter value, it is possible to study separately the influence of each parameter on the mechanical interactions and the relationship between SBP and RS_2.

III. Results

A. The Effect of Changing Peripheral Resistance

The peripheral resistance was varied from 1.5 mmHg·s/ml to 12 mmHg·s/ml while the characteristic impedance, heart rate and parameters for pressure-dependent compliance were constant. The instantaneous ventricular pressure, ventricular volume, aortic pressure and aortic flow under different resistance are shown in Fig. 2. The start point of time axis corresponds to the peak of ECG R wave. It is worth noting that the ventricular volume after the closure of the aortic valve marked by the gray dash line is of no meaning because the ventricular filling during the relaxation phase is not taken into account. The results shown in Fig. 2 agree with a previous study on ventricular-arterial system interaction by imposing simulated arterial hydraulic impedance on an excised canine ventricle [10]. As shown in Fig.3 (a), RS_2 changes inversely with SBP when peripheral resistance is changing.

B. The Effect of Changing Arterial Compliance

The pressure-dependent arterial compliance described by Eq.6 is characterized by parameter *a* and *b*. A smaller *a* indicates a stiffer arterial system. In simulation, the parameter

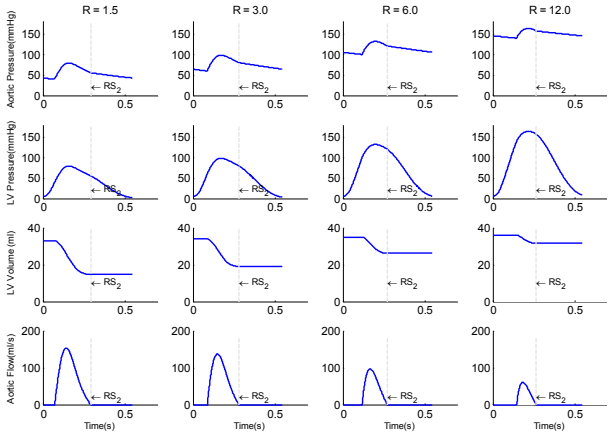


Fig.2. Effects of changing peripheral resistance (Rs) on ventricular pressure, ventricular volume, aortic pressure and aortic flow waveform. The parameters for the pressure-dependent compliance (a = 1.3 ml/mmHg and b = -0.0138 mmHg^{-1}), characteristic impedance (R_0 = 0.2 mmHg·s/ml) and heart rate (110beats/min) are constant.

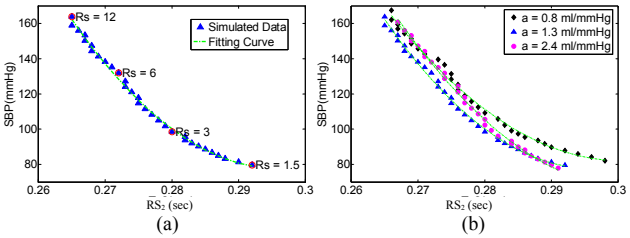


Fig. 3. (a) The relationship between SBP and RS_2: RS_2 changes inversely with SBP under the changing resistance. (b) The different arterial siffness slightly affects the relationship between SBP and RS_2 when peripheral resistance is changing

a was varied from 0.8 ml/mmHg to 2.4 ml/mmHg and the parameter *b* was varied from -0.202 $mmHg^{-1}$ to -0.0046 $mmHg^{-1}$. All other parameters were constant. It is found that pulse pressure, i.e. the difference between SBP and DBP, is elevated significantly as parameter *a* decreases. However, RS_2 is relatively insensitive to changes in SBP, particularly in arterial system of low or intermediate stiffness. On another hand, as shown in Fig.3 (b), the different arterial stiffness is found to affect the relationship between SBP and RS_2 slightly when peripheral resistance is changing.

C. *The Effect of Changing Heart Rate*

The heart rate was varied from 80 beats/min to 170 beats/min while parameters for pressure-dependent arterial compliance, peripheral resistance and characteristic impedance were kept unchanged. It is shown in Fig.4 that as heart rate increases SBP increases significantly while RS_2 is shorten. Simulation results also demonstrate that cardiac output (CO), which is the product of stroke volume (SV) and HR, increases with HR at low HR, is relatively insensitive to HR at intermediate HR, and decreases at high HR.

D. *The Effect of Changing Contractility*

Contractility is characterized by parameter *c* in left ventricular model. The parameter c was raised from 1.6 to 4.5 in steps of 0.1 in simulations. Other parameters were constant. As shown in Fig. 5 (a), RS_2 changes inversely with SBP as contractility is altered.

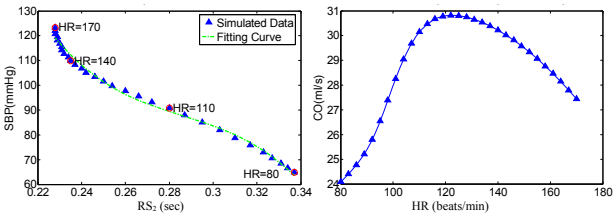
E. *The Effect of Changing End-diastolic Volume*

EDV was raised from 20 ml to 50 ml in steps of 1 ml while all other parameters were kept constant. Results shown in Fig. 5 (b) indicate that RS_2 is relatively insensitive to SBP variation induced by substantial changes in EDV.

IV. Discussion and Conclusion

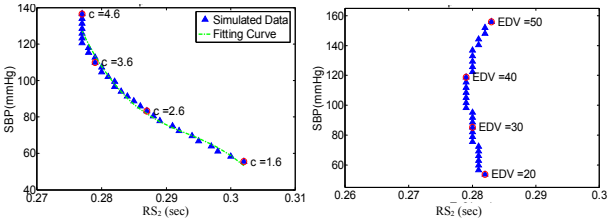
The modified model has provided several significant improvements in studying the heart-arterial interaction. First, the ejection effect including the negative and positive effect and arbitrary heart rate has been introduced. Second, the model separates isovolumic from ejecting properties which allows evaluate these ventricular properties individually. Third, the nonlinear nature of the arterial system has been taken into account. These improvements make it a good choice to study heart-arterial interaction under a variety of physiological conditions.

In the study of the effect of peripheral resistance and arterial compliance, we selected representative examples of data that were available from former studies in [10] to qualitatively validate the modified model. The model yielded a reasonable correspondence between simulated and measured data presented in [10], provided that model parameters are given reasonable values within physiological ranges. Furthermore, the trend that cardiac output changes responding to varying heart rate simulated by the modified model is in good agreement with clinical findings [11]. For this point of view, the modified model gives a better description of heart and arterial interaction than the model in which the ventricular pressure model is coupled to a linear arterial model with a constant compliance because the latter one failed to reflect the trend [7].



(a) (b)

Fig. 4 (a) The relationship between SBP and RS_2 under the changing heart rate. The parameters for the pressure-dependent compliance (a = 1.3 ml/mmHg and b = -0.0138 $mmHg^{-1}$), characteristic impedance (R_0 = 0.2 mmHg·s/ml), peripheral resistance (Rs = 3 mmHg·s/ml), and end-diastolic volume (EDV = 35 ml) are constant; (b) The changes in cardiac output (CO) with varying heart rate in a system with pressure-dependent compliance.



(a) (b)

Fig. 5 (a) The relationship between SBP and RS_2 under the changing contractility. The parameters for the pressure-dependent compliance (a = 1.3 ml/mmHg and b = -0.0138 $mmHg^{-1}$), characteristic impedance (R_0 = 0.2 mmHg·s/ml), peripheral resistance (Rs = 3 mmHg·s/ml), and end-diastolic volume (EDV = 35 ml) are constant; (b) The relationship between SBP and RS_2 under the changing EDV where contractile factor (c =3.5) was given and other parameters were kept constants as above.

Computational results presented above show that RS_2 changes inversely with SBP under the changing peripheral resistance, heart rate and contractility. A previous study based on a different model by Tözeren and Chien [12] also observed that an increase in peripheral resistance or ventricular contractility increases significantly both SBP and DBP and decreased duration of ejection phase, and the effects become more pronounced as heart rate was increased. Since the duration of ejection phase is the major portion of RS_2, it is suggested that our results is in good agreement with the previous study.

When other parameters are constant, the higher peripheral resistance results in a reduced ventricular outflow and thus an elevated SBP during ventricular ejection. Ventricular pressure drops rapidly after ventricular relaxation begins while the pressure in proximal aorta drops relatively slowly due to the high resistance. Consequently, the closure of aortic valve advances. Therefore, an inverse correlation between SBP and RS_2 was observed.

The mechanism that accounts for the effect of changing heart rate is straightforward. In an experiment on dogs in

1993, Regan et al. [13] found that peak isovolumic pressure is elevated and the pressure curve becomes narrower when heart rate increases. This phenomenon is probably due to an inability of the Na^+/K^+-ATPase to keep up with the sodium influx at higher heart rates, which leads to an accumulation of intracellular calcium via the sodium-calcium exchanger [14]. As heart rate increase, systolic pressure increase and pressure curve become narrower. The resultant RS_2 is shortened.

Changes in contractility are unique to cardiac muscle. An increase in contractility results in an increase in active tension at a given preload. Changes in contractility alter the rate of force and pressure development by the ventricle, and therefore change the rate of ejection. When the contractility is enhanced, the ventricle will develop a higher pressure during ejection and follow an accelerated rate of pressure drop during the relaxation. As a result, SBP is elevated and RS_2 is reduced.

Computational results also indicate that RS_2 is relatively insensitive to changes in SBP in conditions of altered arterial stiffness and EDV. The modified model introduces a pressure-dependent compliance which reflects the compliance changes due to acute changes in blood pressure. Arterial stiffness characterized by parameter *a* and *b* in the compliance model usually changes with aging, diseases or medication in long term. Thus, the alteration in arterial stiffness does not play an important role independently in determining the relationship between the SBP and RS_2. The effect of changing EDV in simulation results agrees with the previous study which found that the duration of the ejection phase decreases is insensitive to changes in end-diastolic volume [12]. It is partly because changes in EDV do not remarkably alter the time to peak pressure and the rate of pressure drop in ventricular relaxation.

Although the new model has demonstrated its ability to reflect the cardiovascular function faithfully in several aspects, this study, being a mathematical model study, inherently has some limitations. For example, the simulations are preformed in our study by altering a specific parameter and keeping other parameters constant. In an actual physiological case, a change in one of these parameters is usually accompanied by changes in several other parameters. However, the present model is useful to obtain significant functional relations between the parameters characterizing the cardiovascular system and hemodynamics characteristics.

In conclusion, the present study proposed a modified mathematical model of heart-arterial interaction to give insight into the connection between SBP and RS_2. Simulation results show that the modified model is able to reflect the cardiovascular function qualitatively. The results also demonstrate that RS_2 is inversely correlated with systolic blood pressure under the effects of changing peripheral resistance, heart rate and contractility. The present study provides an interpretation of the experimental observation on the relationship between RS_2 and systolic blood pressure.

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