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Assessment of hemodynamic load components affecting optimization of cardiac resynchronization therapy by lumped parameter model*

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Abstract—**Timing of biventricular pacing devices employed in cardiac resynchronization therapy (CRT) is a critical determinant of efficacy of the procedure. Optimization is done by maximizing function in terms of arterial pressure (BP) or cardiac output (CO). However, BP and CO are also determined by the hemodynamic load of the pulmonary and systemic vasculature. This study aims to use a lumped parameter circulatory model to assess the influence of the arterial load on the atrio-ventricular (AV) and inter-ventricular (VV) delay for optimal CRT performance.**

The model consists of variable elastance components to simulate both left and right ventricles as well as the interventricular septum. The pulmonary and systemic circulations are modeled by lumped parameter Windkessel elements using resistors, inductors and capacitors to represent vascular resistance, blood inertia and arterial and venous compliance, including the coronary circulation. Optimal CRT performance was determined by varying AV and VV delay and the critical delay was obtained for the maximum value of CO. The maximal (optimal) central systolic blood pressure (SBP) was also used to assess the potential use of non-invasive continuous pressure for CRT optimization

Model calculations were made for maximal (optimal) CO and SBP with changes in systemic compliance (Cas) and peripheral resistance (Ras). Simulations with the circulatory model indicate that arterial loading parameters have an intrinsic effect on the timing for optimal CRT performance, with a greater relative impact on VV compared to that on AV delay. Load parameter changes for SBP give similar results to using CO as an optimizing parameter, although differences occur with changes in Ras.

I. Introduction

Cardiac resynchronization therapy (CRT) is a device based procedure using biventricular pacing in conditions of heart failure associated with asynchronous contraction of left and right ventricles. Setting of optimum atrio-ventricular (AV) and inter-ventricular (VV) conduction times is often done using echocardiography to maximize atrial inflow [1] and so maximizing cardiac output, or using peripheral pulse measures to maximize arterial pulse pressure [2-4]. However, even with attempts at optimizing timing parameters, not all subjects obtain benefits in terms of increased ejection fraction and improved ventricular function from the different optimal delay strategies [5].

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In addition to the optimum time delays for atrial and ventricular filling and contraction to achieve maximal cardiac output (CO), cardiac ejection is also influenced by the arterial load from both the pulmonary and systemic vasculature. The arterial load is determined by the steady component comprising peripheral resistance, and a pulsatile component related to the elastic properties of the large conduit arteries [5]. Hence, with a given set of AV and VV delay times optimized for particular values of load parameters, CRT performance would be altered with changes in either peripheral resistance or arterial compliance or both. To investigate the relationship of changes in load parameters with AV and VV delays to achieve maximal CRT performance, a closed loop model of the pulmonary and systemic circulation was constructed using lumped parameter representation of the arterial load and variable elastance for cardiac chambers and interventricular septum with addition of the Frank-Starling law.

II. Methods

A. Arterial Section of Circulatory Model

The arterial system in this simulation was constructed by use of the classic 4 element Windkessel model with inductor (Las, blood inertia) in series with characteristic impedance (Zas, vascular resistance) (WK4s), in which the two hemodynamic parameters as variables are systemic arterial compliance (Cas) and systemic peripheral resistance (Ras) (Fig. 2a). The contractile function of the atria, ventricle and septum was simulated by variable capacitors in the electric circuit using time-varying elastance characteristics [6].

Intrinsic relationships of the Frank-Starling mechanism and VV delay associated with ventricular inotropy were also simulated. This feedback was made by the addition of functions that describe the relationships: (1) the increase in venous return flow causes the elevation in maximum and minimum ventricular contractility; (2) the VV delay resulting in a lag for ventricular contraction (Fig. 1) is associated with decreases in maximum ventricular contractility.

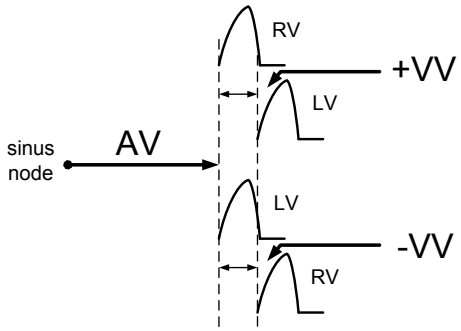

Figure 1. Diagram of AV and VV delay and ventricular contraction. A positive VV delay indicates left ventricle (LV) contracts after the right ventricle (RV).

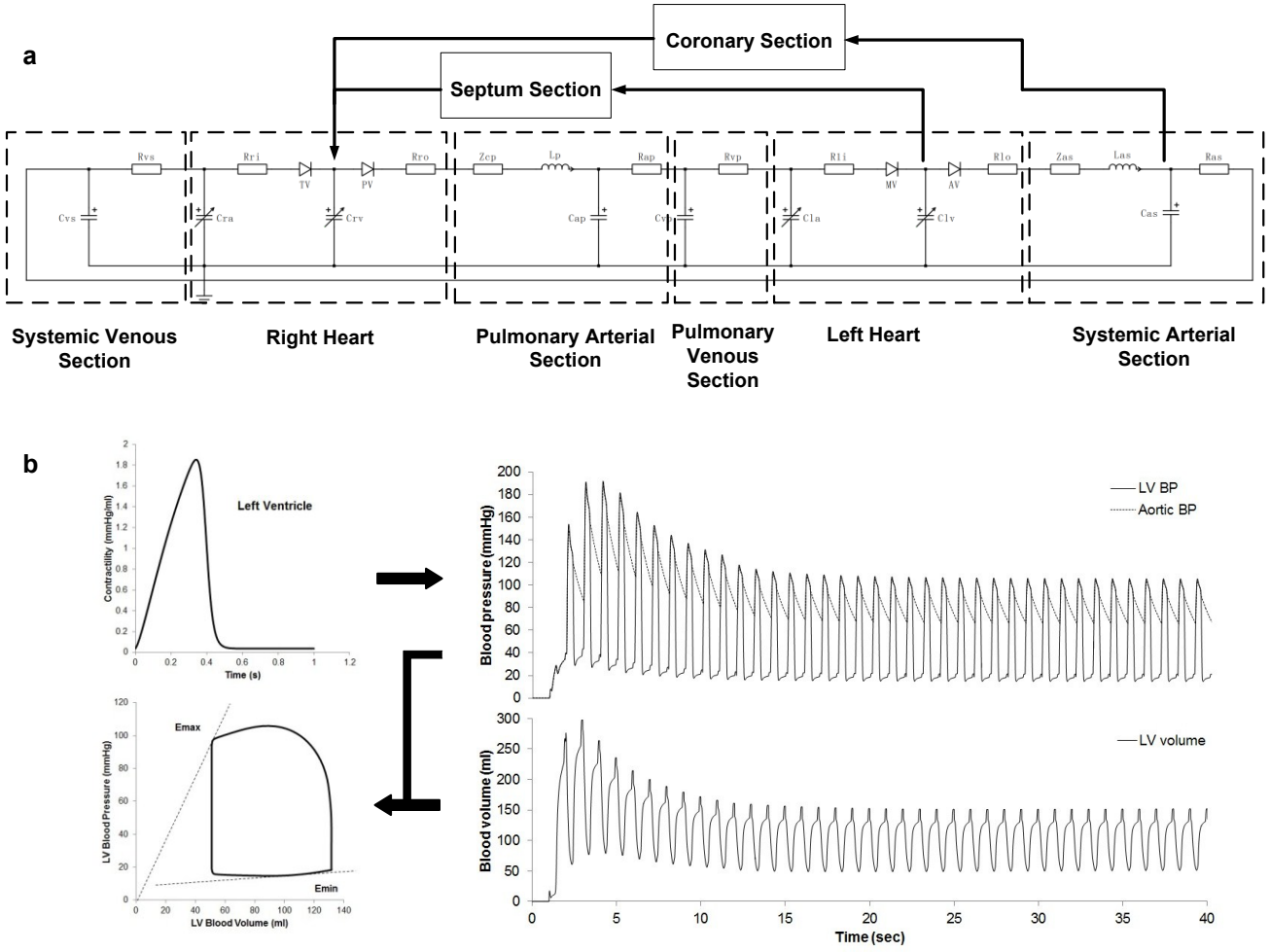

Figure 2. (a) The electric circuit representation of the closed loop cardiovascular model. The left and right heart are represented by variable capacitors. Systemic and pulmonary arterial sections and systemic and pulmonary veous sections are represented by Windkessel components. The septum section was also constructed by a variable capacitor with a reduced range of the time-varying elastance compared with that of the atria and ventricle. The coronary system was modeled similarly to previous studies [9]. (b) Typical simulation of the model, stabilized blood pressure and volume pulses occure at approximately 15 second into the simulation. The LV pressure-volume loop was obtained from pulses in the stable region.

B. CRT Optimization Criteria

To simulate optimal CRT performance, the range of CO obtained with variation of load parameters was normalized by the highest value of CO. This is standard practice with respect to AV and VV delay. Recently, this has been tested by using peripheral SBP by non-invasive techniques and comparable results were obtained using CO or SBP as optimizing variables, particularly when changes in Ras were not large [7]. The empirical time widely accepted as the optimal value of AV and VV delay in clinical practice is 120 ms (AV) and 0 ms (VV). These values were used such that when one was varied, the other was maintained at the constant value.

C. Simulation procedure

We simulated the possible alterations of the curve of CO with respect to AV and VV delay by changing the value of Cas and Ras. The values of the parameters were in the range of 1-10 ml/mmHg for Cas and 0.5-1.9 mmHg·s/ml for Ras. Apart from the changes and variations of right and left ventricular contractility from the feedback interrelations, all

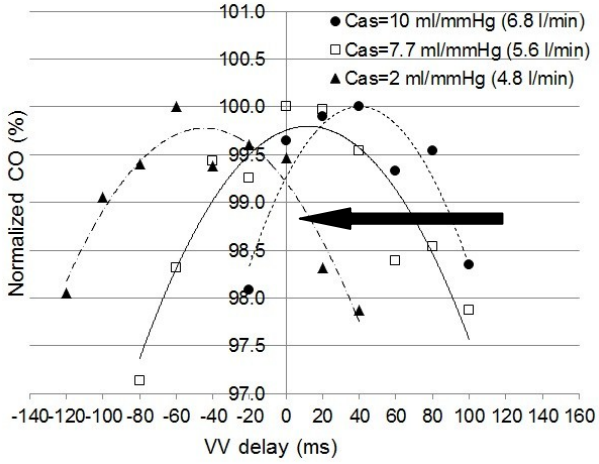

Figure 3a. Increase in arterial stiffness (reduction of Cas) casues a left shift in VV delay (shorter delay) of maximal (optimal) CO.

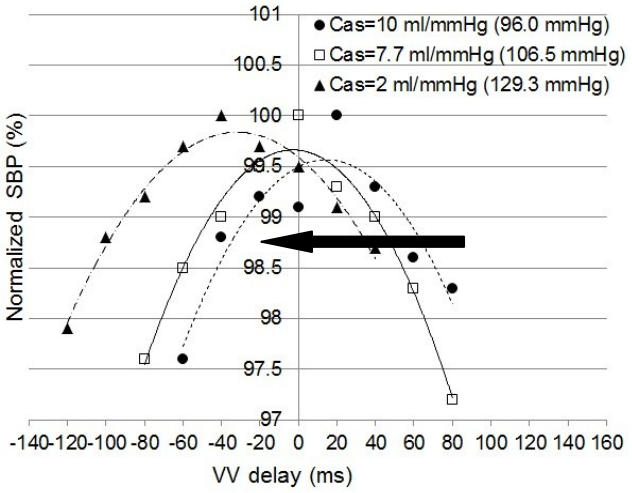

Figure 3b. Increase in arterial stiffness (reduction of Cas) casues a left shift in VV delay (shorter delay) of maximal (optimal) SBP.

other hemodynamic parameters were constant. Central aortic SBP value was calculated for utilization as an optimization criterion in addition to CO. Significant differences of the comparison were considered as $p < 0.05$ in Student's t-test.

III. Results

Increase in arterial stiffness (reduction in Cas) causes left shifts in the VV delay time for maximal CO and SBP (Fig 3a and 3b; actual value of maxima are given in parenthesis). Quantitively, the decrease in Cas is associated with a relatively earlier activation of the left ventricle compared to right ventricular activation (a negative VV delay indicates that the right ventricle contract after the left ventricle as shown in Fig 1.). The sensitivity of the optimum VV delay is higher for CO compared to SBP optimization (Fig 4a). Whereas the effects of Cas on VV delay is linear (Fig 4a), the effect with changes of Ras is non-linear (Fig 4b). For Ras the CO and SBP optimization showed similar features except with an offset of Ras, where similar VV delay is obtained for a lower Ras when optimized for maximal SBP.

Changes in Cas and Ras had smaller relative effects on AV delay (Fig 5a and 5b) compared to effects on VV delay (Fig. 4). Although the AV range was relatively small, changes in Cas were associated with opposite directional changes in AV for SBP and CO optimization (slopes of 1.4 vs -0.3 repectively, Fig. 5a). This was not seen for Ras where the trend was in the same direction (Fig 5b). The average delay value (mean ± SD, ms) of the estimated optimal AV was 88.4 ± 3.8 (CO) vs 57.9 ± 4.5 (SBP) ($p < 0.05$) for changes in Cas and 90.3 ± 12.1 (CO) vs 58.2 ± 8.7 (SBP) ($p < 0.05$) for Ras. These were within the clinial range [3].

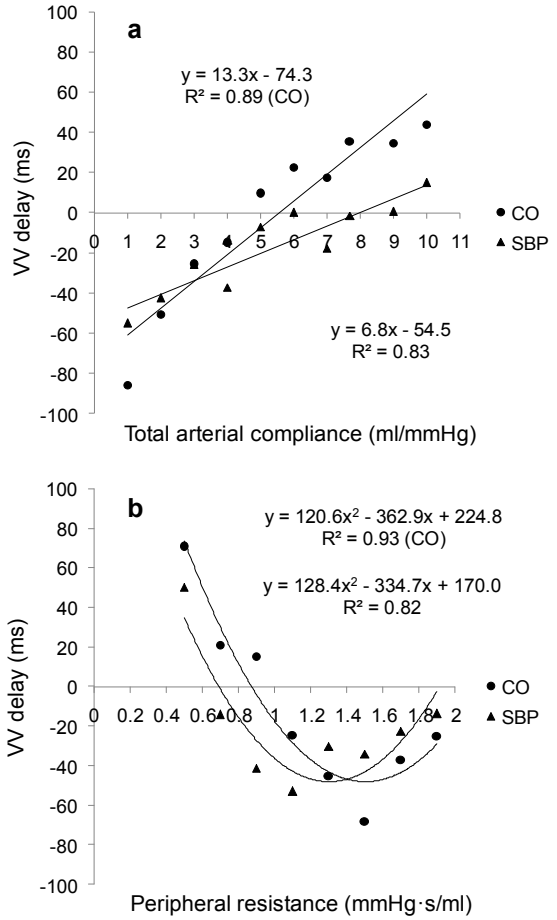

Figure 4. The responses of maximal (optimal) CO and SBP with respect to VV delay as functions of Cas (a) and Ras (b) Functions are fit with linear regression (Cas) or polynomials (Ras) (x, y: horizontal and vertical axes)

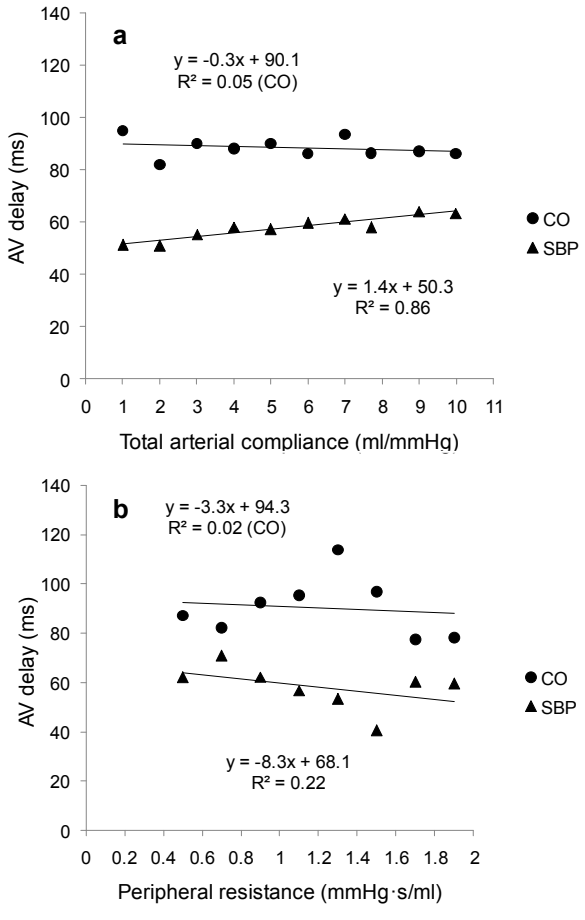

Figure 5. The trend of the responses of optimal AV delay occuring time from the changes in Cas (a) and Ras (b). The smaller effect could be observed both from CO and SBP estimation delay.

IV. Discussion

This study assessed the changes in arterial load parameters on AV and VV delay for optimum CRT performance. This was achieved by simulations using a lumped parameter circulatory model and maximizing the parabolic curve of CO and SBP. In patients on bi-ventricular pacing, this is achieved by assessing CO by echocardiography techniques [1]. In the last several years non-invasive techniques (e.g. Finometer and NICOM device) are emerging as possible means for non-invasive assessment using continuous pressure signals and estimated CO from those [6, 8]. This investigation showed the potential suitability for central aortic SBP as a hemodynamic parameter for optimization of CRT performance [5, 10, 11].

The changes of the two arterial load parameters selected in this simulation reflect the physiological range of the pulsatile characteristics in Cas and resistance properties in Ras. Decrease in Cas produces a left shift for the parabolic curve towards a shorter VV delay for optimal CRT performance. The scatter in the data seen in Figures 3, 4 and 5 was a result of the cardiac contractility being affected by venous return flow and the positive VV delay. However, this was not large and the data can be reliably represented by a parabolic function which enables the determination of peak CO for the estimation of optimal delays. For optimal AV delay with arterial load changes, the shorter conduction time estimated from SBP optimization compared with that from CO optimization may be of potential significance in strategies for clinical optimization of CRT performance. This was in line with our pilot data (unpublished) shows a more reliable effect from parameter SBP in reflecting arterial load alterations to AV and VV delay in the case of a distributed, transmission line model including the upper limb.

IV. Conclusion

The effect of the arterial load on optimization of AV and VV conduction times for CRT using CO and SBP measures was simulated with a circulatory model of the cardiac chambers, septum and pulmonary, systemic and coronary circulations. Simulation results show that the effects of changes in Ras and Cas are more pronounced for VV compared to AV delays for optimum CRT performance. While CRT and SBP optimization gives qualitatively similar results, quantitative differences in VV delay due to variation of Ras may be clinically relevant in the use of non-invasive continuous blood pressure signals for optimization of biventricular pacing and CRT performance. Application of this modeling analysis could be of benefit to those patients who do not respond favorably to conventional resynchronization therapy in quantitative localization of causes by minimally invasive or noninvasive assessment.

Acknowledgment

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