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A Human Cardiopulmonary Model: Extension to LV Dysfunction

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Abstract

We update a cardiopulmonary (CP) model previously developed by our group, more convincingly validate the model with additional hemodynamic and echocardiographic data, and demonstrate the utility of the model by extending it to the simulation of left ventricular diastolic dysfunction (LVDD) via a simple parameter change. The model has considerable potential for the characterization of complex cardiopulmonary diseases such as right or left ventricular failure, valve dysfunction, primary pulmonary hypertension, and acute respiratory distress syndrome (ARDS).

Introduction

Critical care physicians are increasingly interested in using integrated human cardio-pulmonary (CP) models as diagnostic tools [1, 2, 3, 4]. Our group has contributed [5, 6, 7] by developing a human CP model that simulates normal hemodynamics, whole-body and cerebral gas exchange, and both baro- and chemoreceptor reflexes. The model can simulate complex CP interactions, such as those occurring during the Valsalva maneuver [5], thigh-cuff deflation [7], and simulated apnea [6]. Our present report updates and validates the model with a variety of hemodynamic and echocardiographic data taken from the medical literature, and with high fidelity, micromanometer (Millar Instruments, Inc., Houston, TX) pressure tracings simultaneously recorded from the right and left ventricles of a normal patient undergoing cardiac catheterization (data from Brooke Army Medical Center (BAMC) Archive in San Antonio, TX). We will refer to the model reported in [7] as "the original" CP model, and to the presently reported, updated version as "the revised" CP model.
[1]

Model Review and Structural Change

Our circulatory system sub-model consists of four regional blood flow circuits, systemic, pulmonary, cerebral and coronary characterized as multi-segmental compartments populated with resistive (R), compliant(C) and inertial (L) elements. The mechanics of the lungs and airways are characterized in terms of a lumped two compartment model, whereas gas exchange (O_2 and CO_2) across lung, brain and whole-body tissue beds, is simulated by solving the diffusion equation in the appropriate compartment model. Venous return from the major tissue compartments is collected at the right atrium and blood gases are mixed in that compartment. Gas transport delay is implemented via the time required for flow through the circulatory pathways. Neural control of heart rate, contractility and vasomotor tone is mediated via baro- and chemo-receptive feedback.

With one exception the structure of the revised model is equivalent to that of the original model, and that is the original model did not provide for gas mixing in the right atrial compartment. That has been resolved in the revised model. In manually fitting measured data, we have used changes in model parameter values, particularly associated with the heart sub-model, to achieve good fits. Three types of data have been employed to help validate the model: (a) simultaneous high fidelity pressure recordings from a normal patient (BAMC Archive); (b) measured pressure and echocardiographic flow velocity waveforms reported in the literature, and (c) measured input impedance plots for the pulmonary and systemic circulations reported in the literature.

Results

Figure 1 shows the pressure-volume loop of a normal heart (solid lines in panels A and B). In particular, we are able to fit both simultaneously measured right and left ventricular pressure data waveforms (Fig. 1 C and D, respectively), while generating tricuspid and mitral flow waveforms that are typical of a normal subject (Fig. 2). Model-generated pulmonary and central venous flow waveforms are also shown in that figure (panels C and D). For example, the calculated E/A ratio of model-generated mitral flow waveforms is in the range 1-1.5 and agrees well with normal values. The S/D ratio associated with the modeled pulmonary venous flow waveform is 1.15 –1.5 which is also typical of a normal human [8]. Table 1 lists the model-generated human CP function values, which

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mimic well those of a normal patient.

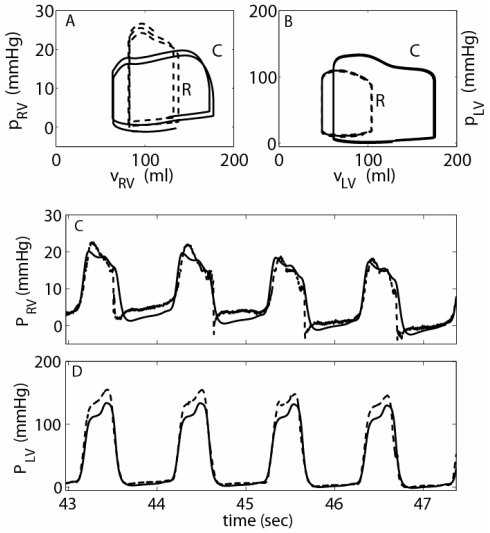

Figure 1 A and B: Pressure-volume loop for RV and LV, respectively (dashed lines are for LVDD). C and D: Model-generated normal human RV and LV pressure curves (dashed lines are from data). Respiratory variation evident.

Table 1: Average hemodynamic values over a full respiratory period in normal and LVDD (parentheses) cases.

Segment	AO	CV	PA	PC	PV
P (mmHg)	108 (94)	1.7 (0.6)	11.1 (19)	6.9 (16.4)	6.0 (15.9)
V (ml)	153 (95)	300 (272)	187 (235)	91.4 (111)	303 (376)

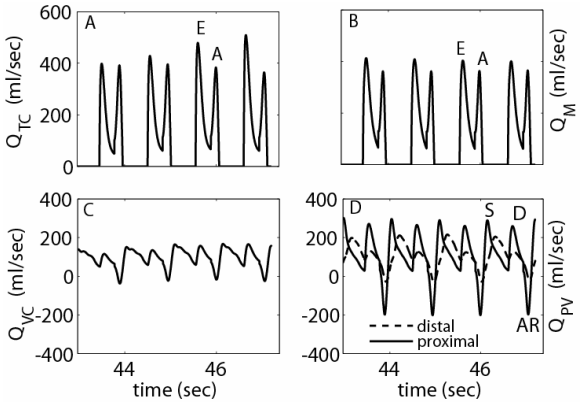

Figure 2 Model-generated valvular and venous flows. A: tricuspid flow; B: mitral flow; C: central venous flow; D: pulmonary venous flow.

Model Extension

As a preliminary application to disease cases, we have extended our model to simulate a special case of congestive heart failure, left ventricular diastolic dysfunction (LVDD). This is produced by using a single model parameter which effectively increases the stiffness of the end-diastolic pressure volume relationship (EDPVR). This is a restrictive (R) cardiac disease and its effect on ventricular pressure and volume is shown in Fig 1 A and B (loop R). This disease increases left ventricular (LV) filling pressure, which results in decreased stroke volume, cardiac output, and venous return. Heart rate (HR) is increased, as is LV diastolic pressure and pulmonary pressure (Table 2). In general, the simulated results clearly demonstrate the typical features of LVDD, such as pulmonary congestion and reduced SV with elevated pulmonary pressure and volume (table 2), while the compensatory neural feedback increases the HR significantly. The result closely mimics that of heart failure with a normal ejection fraction (HFNEF) [8, 9].

Table 2: Cardiac function in normal and LVDD (parentheses) cases.

HR (bpm)	SV (ml)	CO (l)	LVEF	RVEF
60 (69)	117 (55)	7.0 (3.8)	0.65 (0.54)	0.67 (0.39)

Conclusions

In conclusion, our human CP model is biophysically based and can easily be tuned to mimic different human CP states (normal or abnormal) with simple parameter changes. Model-generated results have been validated by hemodynamic and echocardiographic flow velocity data. The model can serve as a platform to analyze a wide range of complex problems due to the interaction of multiple organ systems (e.g., cardiovascular, respiratory and neural). . Although here we have mimicked LVDD using a rather simple parameter adjustment to the EDPVR, we propose that with appropriate adjustments to the heart and circulatory models, a variety of cardiovascular diseases can be mimicked providing testable hypotheses that might point to underlying biophysical mechanisms. Furthermore, new data can be

readily incorporated into the CP model because of its physiologic structure and physical parameters. Conceivably, it would be of considerable use in analyzing complicated diseases (*e.g.,* LV systolic dysfunction, RV failure, essential pulmonary hypertension, acute respiratory distress syndrome (ARDS)) and of assistance in their diagnosis and treatment.

Acknowledgements

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