Review Article

# Cardiovascular Simulation of Heart Failure Pathophysiology and Therapeutics

DARSHAN DOSHI, MD, MSc,[1] AND DANIEL BURKHOFF, MD, PhD[1,2]

*New York, New York; Framingham, Massachusetts*

**ABSTRACT**

Mathematical modeling and simulation allows for an in-depth examination of the cardiovascular system and provides the opportunity to develop deeper understanding. This review summarizes recent efforts at modeling the cardiovascular system and how these models have been useful in providing greater comprehension of the pathophysiology of heart failure, explaining the hemodynamic impact of various heart failure devices, predicting the hemodynamic effects and clinical outcomes of certain heart failure clinical trials, and perhaps aiding in patient selection for new therapies. The potential future use of these models in clinical research and clinical practice are also discussed. (*J Cardiac Fail 2016;22:303–311*)
**Key Words:** Cardiovascular modeling, simulation, hemodynamics.

The heart and vasculature have been the topic of research for more than a century, with countless efforts made to mathematically model their properties. More than 50 years ago, researchers also started focusing on coupling vascular and cardiac models to understand the determinants of key clinically important hemodynamic parameters.[1] These models have undergone tremendous evolution over the years. Some of the more recent embodiments start with mathematical representations of myocyte function based on actin-myosin interactions, ion channel function, ion metabolism (sodium, calcium, potassium, etc.), and models of signaling pathways.[2] Based on those building blocks, a heart with realistic chamber geometries, myocyte fiber orientations, and valves is constructed. That model heart then interacts with complex models of the pulmonary and systemic vascular systems.[3] Some of these models even include short- and long-term adaptations based on simulated autonomic nervous systems and molecular responses of the heart, vasculature, and kidneys to acute and chronic mechanical and neurohormonal stimuli.[4] Such models require significant computing power and computing time and are not readily available or convenient for real time use.

In contrast, simpler models employing high-level phenomenological descriptions of heart chamber properties based on pressure-volume relationships and 0-order representations of the vascular systems have also been developed.[5,6] Although these simpler models provide less detailed predictions of pressure and flow waveforms, they have shown great flexibility in simulating the hemodynamics of a very wide range of heart failure–related disease states and therapies while retaining the ability to be run in real time, even on desktop, laptop, and mobile devices.

This review summarizes the current status of these recent efforts at *simple* cardiovascular modeling and how they have been useful in providing insights into pathophysiology of heart failure, explaining hemodynamic impact of different heart failure devices and surgeries, predicting the hemodynamic effects and outcomes of certain clinical trials, and guiding selected aspects of patient selection for new therapies. The potential future uses of these simpler models in clinical research and clinical practice are discussed.

## Overview of *Simple* Cardiovascular Models

Modern simulations of the cardiovascular system have their origin in the work of Guyton, who described the systemic and pulmonary vascular systems by series of resistance and compliance elements.[7] Suga and Sagawa introduced the *time-varying elastance* model to describe the time-dependent, load-

*From the [1]Columbia University Medical Center/New York-Presbyterian Hospital, New York, New York and [2]HeartWare International, Framingham, Massachusetts.*

Reprint requests: Daniel Burkhoff, MD, PhD, Columbia University Medical Center, 177 Fort Washington Ave, New York, NY 10032. Tel: +1 201 294 6081; Fax: (917) 398-1690. E-mail: Db59@columbia.edu (D. Burkhoff).

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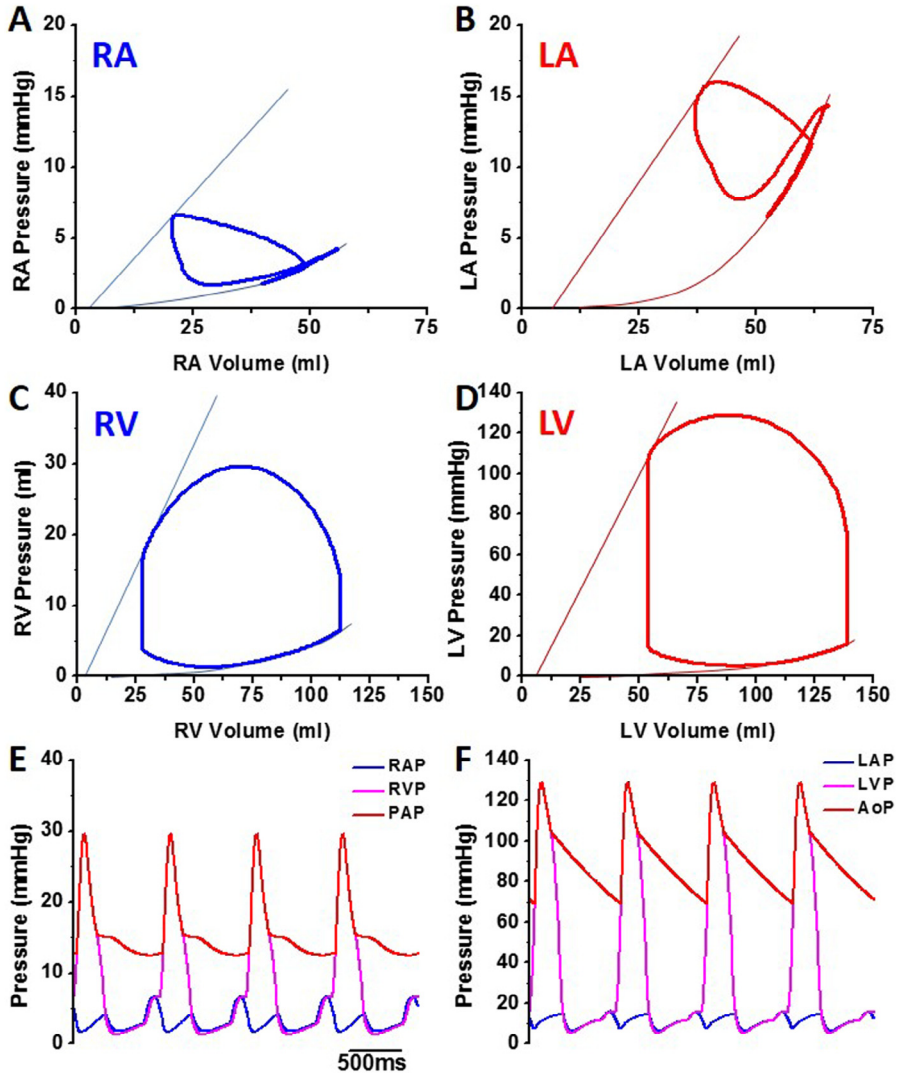


**Fig. 1.** RA, LA, RV, and LV pressure-volume loops generated from the cardiovascular model with normal parameter values (A–D). Time course of right- and left-sided pressures shown in E and F, respectively. LA, left atrial; LV, left ventricular; RA, right atrial; RV, right ventricular.

independent dynamics of atrial and ventricular contraction.[8,9] Sunagawa and colleagues[5] coupled the time-varying elastance model of the heart to the Guytonian model of the vasculature systems, which led to the ability to describe the time-dependence of pressure, flow, and volume waveforms in the ventricles, atria, arteries, and veins. Collectively, these efforts provided the foundation for developing comprehensive, integrated models of the complete cardiovascular system in health and disease, including the introduction of certain types of devices (e.g., blood pumps), valve lesions, and shunts. The details of the model have been provided previously[6] (including the differential equations underlying the model) and are summarized more fully in the online supplemental material. The differential equations describing such models can be solved with simple mathematical techniques yielding a multitude of outputs, including the pressure-volume loops from each of the 4 chambers (Fig. 1); time-dependent tracings of pressures, flows, and volumes; and all of the possible hemodynamic parameters derived from these signals. Note in Fig. 1 (in which all loops and time-dependent tracing are derived directly from the simulation) that the pressure-volume loops of the normal right ventricle and of each atrium are significantly different than those of the more familiar normal left ventricle, and that these simulated loops have all key characteristics of directly measured loops reported in the literature.[10,11]

## Potential Applications of Cardiovascular Modeling

There are at least 4 interrelated areas where cardiovascular hemodynamic modeling is of potential clinical utility: (1) clarifying fundamental hemodynamic principles related to pathophysiology of disease and therapeutic approaches; (2) predicting the hemodynamic effects and outcomes of certain clinical trials; (3) assisting in device development; and (4) guiding selection of cardiovascular therapeutics in individual patients. A summary of key applications and, when available, references that provide data to support conclusions derived from the model are summarized in