Is there a need for another model on the pulsatile nature of coronary blood flow?

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In this issue of the American Journal of Physiology-Heart and Circulatory Physiology, Huo and Kassab (5a) present an elegant study describing and modeling pulsatile behavior of the coronary circulation. A Womersley-type mathematical model was developed to analyze pulsatile blood flow in diastole during maximal coronary dilation. This model, which provides an analytical solution of time-varying flow in the entire coronary arterial tree, was based on previously measured morphometric data (6, 7). The morphometric information was used to calculate pressures and cross-sectional area in the coronary tree. The model was solved to allow prediction of impedance, pressure distribution, and the pulsatile flow throughout the entire coronary arterial tree. Certain aspects of the model were validated by experimental measurements in six diastolic arrested, vasodilated porcine hearts. The authors found superb agreement between theory and experiment. Other aspects of the model (pulse wave) were supported by previously published steady-state models. The model also predicted that the phase angle of flow decreased along the trunk of the major coronary artery and primary branches toward the capillary vessels. On the basis of the extensive analysis, the authors conclude: “this study represents the first, most extensive validated analysis of Womersley-type pulse wave transmission in the entire coronary arterial tree down to the first segment of capillaries” (5a).

The literature is replete with models of the coronary circulation that have described everything from the phasic nature of coronary perfusion to control of coronary blood flow (5, 14). This prompts the question: what is the benefit of yet another model that describes the phasic nature of coronary blood flow? Our answer to this question is intuitively obvious: models are necessary and important instruments to understand, predict, and test the nature of an unknown system, vis-à-vis, the dynamic nature of phasic myocardial perfusion. It is amazing to note that in the early 21st century, we have known the human genome for approximately 4 years, and technological developments have recently enabled the culture of an artificial organ, but science has yet to understand the basis of phasic coronary blood flow that occurs during the cardiac cycle.

Investigators have been able to study the microcirculation of the beating heart on the epicardial and endocardial surfaces and have measured a variety of parameters ranging from diameters (3, 12), pressures (3, 12, 15), flow velocities (1, 13), and intercapillary differences (10), but to date, measurements of microvascular dynamics of coronary vessels imbedded in cardiac muscle have escaped investigation. However, we would be remiss to not mention that Mori and colleagues (11) reported measurements of diameters of intramural small coronary arteries during the cardiac cycle by using monochromatic synchrotron radiation. Nonetheless, despite these myriad advances, one can ask, why does this important aspect of understanding the regulation of coronary blood flow (mechanical effects of the beating heart) remain unknown? In our opinion the answer is simple, but the solution is difficult. We believe there are two components to the answer. First, the heart moves. Second, the vessels that matter (those subjected to the mechanical force of contraction) are imbedded in muscle. Thus, to understand how cardiac contraction confers phasicity to coronary blood flow, one needs to view small microvessels (both arterioles and venules) within muscle of the beating heart; and of course, measurements of pressure in microvessels would become imperative also. The process of cardiac contraction impedes such measurements. For example, visualization of the coronary microcirculation using intravital microscopy is complicated by the fact that when an image is being magnified 100 times, motion is magnified by the same amount. Most investigators have used a variety of approaches to compensate for cardiac motion, including stroboscopic illumination (3, 12), floating objectives (1, 9), image conduits (8), and/or three-dimensional micromanipulators to move a micropipette in conjunction with the beating heart (3, 12). Importantly, examination of the microcirculation within the left ventricular wall has not yet been accomplished, nor is it yet possible; this highlights the role of models in furthering our understanding of coronary hemodynamics.

The model presented by Huo and Kassab (5a) offers interesting and important predictions about coronary hemodynamics during phasic coronary blood flow and fills a void, at least theoretically, in understanding this basis. Despite this importance, caveats of this, or any model, must be highlighted, because they could illustrate problems with experimental data or limitations of the model. For example, Fig. 12 of this study (5a) offers predictions about phasic pressure and flows throughout the coronary tree. The question that we have about such model information is the discrepancy from published results. For example, two studies report significant pressure losses in vessels greater than 100–140 μm in diameter (3, 12), whereas one reports minimal pressure dissipation in vessels of this size (14). Yet the model predicts minimal pressure losses in vessels down to ~70 μm in diameter, which is at odds with the results in two reports. Figure 12 and many of the others from this study (i.e., Figs. 5–7 (Ref. 5a) illustrate continuous forward coronary flow throughout the cardiac cycle as measured experimentally and predicted by the model. Many groups have reported negative flows during systole in the coronary circulation and microcirculation (1, 4); thus, there is likely an incorrect assumption made by the model calculations and an unknown variable influencing the experimental values. Another observation made in the study (5a) is that peak flow rate in the left coronary circulation coincides with peak pressure measured at the inlet both in the absence (Fig. 5) and presence (Fig. 8) of...
myocardial contraction. Even more disturbing is that their model predicts this type of behavior (Fig. 8C of Ref. 5a).

Another limitation of the model should be mentioned; namely it makes no prediction about endocardial-epicardial variations in pressures, flows, and impedances. The systolic-diastolic excursion in flow and diameters are greater in the endocardium than the epicardium (16), and modeling the contractile influences of systole at varying depths throughout the wall of the heart is critical for this understanding. Moreover, even the distribution of vascular resistance is different between the epicardial and endocardial microcirculations (2), and the model oversimplifies this issue.

Admittedly, one could find discrepancies from published results with any model predicting the phasic nature of coronary hemodynamics, but this does not necessarily mean the model is invalid. Experiments are subject to error, and satisfaction of Heisenberg’s Principle of Uncertainty, i.e., the nature of the experiment should not influence the outcome of the results, is not always met! Thus understanding differences between predictive models with published results is paramount to furthering our understanding of the intricacies of coronary physiology and the best way to understand the basis by which mechanical activity of the heart confers phasic properties to coronary blood flow.

REFERENCES