

A NONINVASIVE METHOD FOR CHARACTERIZING VENTRICULAR DIASTOLIC FILLING DYNAMICS

R. Mukkamala, R. G. Mark, R. J. Cohen

Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA, USA

Abstract— We developed a novel method for estimating a single parameter (τ_D) which summarizes the diastolic filling dynamics of the ventricle that governs the effects of diastolic filling time on stroke volume. The method involves the analysis of beat-to-beat fluctuations in heart rate, arterial blood pressure, and left ventricular stroke volume, each of which may be measured noninvasively in humans. In order to evaluate the method, we constructed a computational model of the human cardiovascular system. We applied the method to data generated from the computational model and found close agreement between the estimated and actual τ_D . We also demonstrated with computational model examples that the method could be utilized to monitor increasing degrees of cardiac tamponade and mitral stenosis, two cardiovascular disease processes which prohibit the ventricles from filling adequately. This model-based study motivates the experimental validation of the method.

Keywords— system identification, cardiovascular modeling, ventricular diastolic compliance

I. INTRODUCTION

Cardiac tamponade, restrictive cardiomyopathy, and mitral stenosis are examples of disease processes which prohibit the ventricles from filling adequately. In this paper, we present a method for the quantitative characterization of ventricular diastolic filling dynamics which requires beat-to-beat measurements of heart rate (HR), arterial blood pressure (ABP), and left ventricular stroke volume (SV). These measurements may be obtained non-invasively in humans with, for example, Doppler ultrasound and Finapres techniques. The method may therefore potentially provide a powerful means for monitoring patients who are being treated for these cardiovascular disease processes. The method also complements another algorithm that we previously developed which requires the same beat-to-beat measurements but characterizes the total peripheral resistance baroreflex [1].

Ventricular diastolic filling dynamics are highly complex and are determined by a multitude of parameters. This may be illustrated with Fig. 1 which includes a sketch of right ventricular stressed volume as a function of time ($Q_{rv}(t)$). This sketch indicates that the diastolic filling time period (T_D) may be divided into three phases. In phase 1, the tricuspid valve opens initiating rapid passive filling from the right atrium to the right ventricle. The dynamics involved in this phase are principally determined by the right atrial and ventricular diastolic compliances and the small tricuspid resistance. Phase 2 then follows with slower passive filling from the systemic veins to the right ventricle via the right atrium with the dy-

namics largely determined by the right atrial and ventricular diastolic compliances, the tricuspid resistance, and the relatively larger systemic venous resistance. Finally, in phase 3, rapid active filling from the contracting right atrium to the right ventricle occurs with the dynamics predominantly determined by right ventricular diastolic compliance, the time-varying compliance of the right atrium during systole, and the tricuspid resistance.

The sketch in Fig. 1 indicates that $Q_{rv}(t)$ rises from its end-systolic value (Q_{rv}^{es}) to its end-diastolic value (Q_{rv}^{ed}) over T_D . If T_D were infinitely long, $Q_{rv}(t)$ would rise to a maximum value (Q_{rv}^{max}) that is usually established by the product of the right ventricular diastolic compliance and the pressure in the systemic veins which is essentially constant due to its large compliance. A unique exponential function may be fit to T_D , Q_{rv}^{es} , Q_{rv}^{ed} , and Q_{rv}^{max} as shown in the figure. The time constant of this exponential is a simple, scalar parameter which summarizes ventricular diastolic filling dynamics. We refer to this parameter as the effective ventricular diastolic filling time constant (τ_D). This time constant may be thought of as the product of a lumped resistance and a lumped compliance. For example, τ_D would decrease with right ventricular diastolic compliance and increase with tricuspid resistance. Therefore, τ_D could be utilized as a means for monitoring changes in these resistances and compliances.

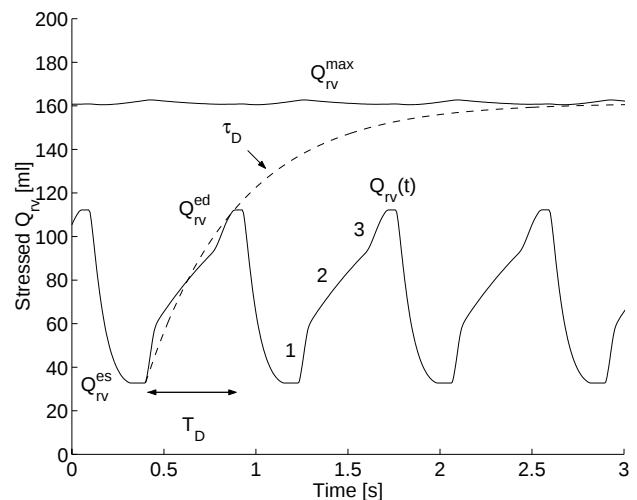


Fig. 1. Definition of a scalar parameter τ_D which summarizes ventricular diastolic filling dynamics.

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In practice, it is not feasible to measure directly τ_D because of the difficulty in establishing $Q_{rv}^{\max}$. However, in the next section, we describe one method to measure τ_D indirectly from measurements that may be obtained noninvasively in humans.

II. METHOD

The method is based on the assumption that a small step increase in HR would decrease SV in the steady-state due solely to the reduction in T_D . The other determinants of steady-state SV, namely $Q_{rv}^{\max}$ and Q_{rv}^{es} , would be relatively unaffected primarily because systemic venous compliance is large and pulmonary arterial resistance and right ventricular end-systolic compliance are small. By further assuming a single time constant model of ventricular diastolic filling dynamics, steady-state SV may then be written according to the following equation:

$$SV = SV_{\max}(1 - e^{-T_D/\tau_D}), \quad (1)$$

where $SV_{\max} = Q_{rv}^{\max} - Q_{rv}^{\text{es}}$ and is assumed to be constant for small HR changes. This equation indicates that τ_D may be determined from two steady-state pairs of T_D and SV measurements through solution of the following nonlinear equation:

$$\frac{SV_1}{SV_2} = \frac{1 - e^{-T_{D,1}/\tau_D}}{1 - e^{-T_{D,2}/\tau_D}}. \quad (2)$$

The two steady-state pairs of measurements may be obtained by slightly varying the mean HR with a pacing protocol. However, they may also be determined from a single pair of beat-to-beat measurements of HR and left ventricular SV obtained during normal, resting conditions in which the fluctuations in these variables are small. The idea here is to establish the first pair with the mean values of HR and SV ($SV_1 = \overline{SV}$, $HR_1 = \overline{HR}$) and the second pair by identifying the transfer function between the fluctuations in HR and the fluctuations in SV ($HR \rightarrow SV$) and computing its DC value (G) – the steady-state SV response to a unit step increase in HR. That is, $SV_2 = \overline{SV} + \sigma_{HR}G$ and $HR_2 = \overline{HR} + \sigma_{HR}$, where σ_{HR} is the standard deviation of HR. For small changes in HR, $T_{D,(1,2)}$ may be approximated from $HR_{(1,2)}$ with the scale factor $(1 - 0.4/\sqrt{\frac{60}{HR}})$ [2]. The parameter τ_D may then be determined with the bisection method from these two steady-state pairs and (2). The standard deviation of τ_D may be analogously estimated with the standard deviation of the estimate of G .

In order to identify reliably $HR \rightarrow SV$, it is necessary to measure and account for ABP fluctuations which also contribute to *left ventricular* SV fluctuations through mechanical afterload and baroreflex effects. This may be achieved by simultaneously identifying the transfer function between ABP fluctuations and SV fluctuations ($ABP \rightarrow SV$) from the beat-to-beat measurements as depicted in the block diagram in Fig. 2. The term N_{SV}

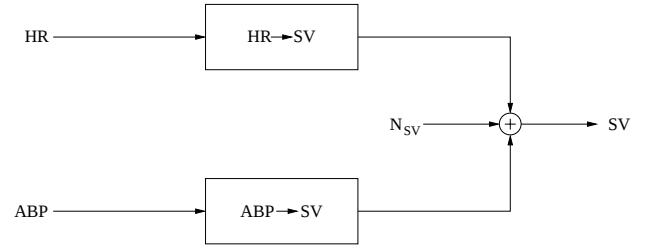


Fig. 2. Identification method for establishing the two steady-state pairs of HR and SV values.

in the block diagram is also estimated from the beat-to-beat measurements and represents the residual variability in SV not accounted for by HR or ABP fluctuations.

The block diagram in Fig. 2 is mathematically represented by an autoregressive moving average (ARMA) difference equation of the following form:

$$SV(t) = \sum_{i=1}^m a_i SV(t-i) + \sum_{i=0}^n b_i HR(t-i) + \sum_{i=0}^p c_i ABP(t-i) + W_{SV}(t), \quad (3)$$

where t is discrete time and W_{SV} is the residual error. The three sets of parameters $\{a_i, b_i, c_i\}$ completely specify the transfer functions characterizing $HR \rightarrow SV$ and $ABP \rightarrow SV$, while the residual error together with the set of parameters $\{a_i\}$ fully define N_{SV} [3]. The values of the parameters are determined from six minute segments of zero-mean HR, ABP, and SV sampled at 0.5 Hz by minimizing the variance of the residual error in conjunction with an ARMA parameter reduction algorithm [3]. The mean of the estimate of G is then given by $\frac{\sum_{i=0}^n b_i}{1 - \sum_{i=1}^m a_i}$, while its standard deviation may be approximated as described in [2], [3].

III. CARDIOVASCULAR SYSTEM MODEL

A computational model of the cardiovascular system provides a convenient means for evaluating the method, because it would be possible to establish the actual τ_D according to Fig. 1. To this end, we constructed a computational model of the human cardiovascular system that is capable of reasonably emulating experimental beat-to-beat hemodynamic variability. The model includes three major components: a heart and circulation, a short-term regulatory system, and resting physiologic perturbations.

The heart and circulation is a lumped parameter model which includes eight compartments representing the left atrium and ventricle, the right atrium and ventricle, the systemic arteries and veins, and the pulmonary arter-

ies and veins. Each compartment consists of a linear or nonlinear resistance and a linear or nonlinear compliance with an associated dead volume. The compliances of the ventricular and atrial compartments vary over each cardiac cycle so as to drive blood flow in the model.

The short-term regulatory system consists of arterial and cardiopulmonary baroreflexes as well as a direct neural coupling mechanism between respiration and heart rate. The arterial baroreflex maintains ABP through the control of HR, ventricular end-systolic compliances, systemic arterial resistance, and systemic venous dead volume, while the cardiopulmonary baroreflex senses right atrial transmural pressure and manipulates systemic arterial resistance and systemic venous dead volume.

The resting physiologic perturbations include fixed-rate respiratory activity which impinges upon the heart and circulation through intrathoracic pressure – the reference pressure of the pulmonary, atrial, and ventricular compartments – as well as the direct neural coupling mechanism. The resting physiologic perturbations also include a broadband stochastic disturbance to systemic arterial resistance which is primarily responsible for generating low frequency (0.04-0.1 Hz) fluctuations through a model resonance phenomenon as well as a $1/f$ stochastic disturbance to HR which initiates very low frequency (<0.04 Hz) variability. Further details of the computational model are provided in [2].

IV. MODEL RESULTS

Fig. 3 illustrates the results of the application of the method to the computational model generated data in terms of the estimated versus actual τ_D . The actual τ_D was varied by adjusting the right ventricular diastolic compliance and the tricuspid resistance of the computational model. The estimates are shown in terms of their $\text{mean} \pm \text{standard deviation}$ as determined from 20 different realizations of computational model generated data. The solid trace is the identity line, and the dashed trace is the line of best fit. The results here suggest that τ_D may be reliably estimated from experimental data to the extent that the computational model coincides with reality.

Fig. 4 illustrates an example of how the method would perform in the case of cardiac tamponade which was implemented in the computational model by decreasing both ventricular diastolic compliances. The figure here illustrates that the estimated τ_D ($\text{mean} \pm \text{standard deviation}$) successfully decreases with right ventricular diastolic compliance (C_{rv}^D). Fig. 5 illustrates an example of how the method would perform in the case of mitral stenosis which was implemented in the computational model by increasing the mitral resistance (R_{mitral}). The figure illustrates that the estimated τ_D ($\text{mean} \pm \text{standard deviation}$) successfully increases with R_{mitral} . Importantly, in order to monitor changes in C_{rv}^D and R_{mit} by conventional methods, invasive measurements would be

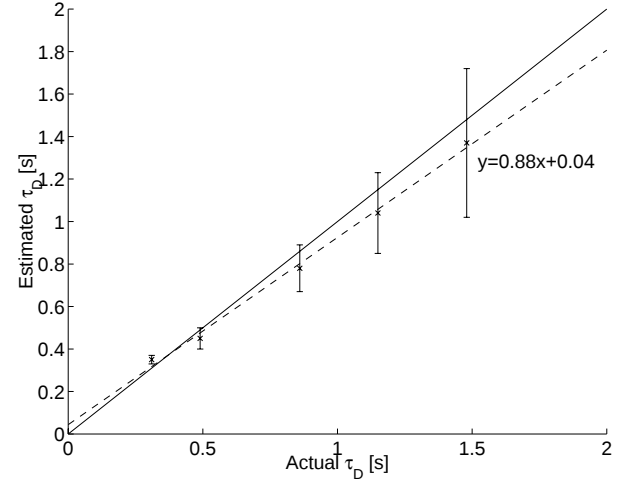


Fig. 3. Computational model results. See text for details.

required.

V. METHOD LIMITATIONS AND APPLICATIONS

Although the method performs quite well with respect to the computational model generated data, its potential applications are somewhat limited. Firstly, the definition of τ_D as depicted in Fig. 1 is not applicable for sufficiently fast ventricular diastolic filling dynamics such that the atrial contraction causes Q_{rv}^{ed} to exceed Q_{rv}^{max} . In this case, the estimated change in τ_D from one measurement period to the next may be misleading. However, the accompanying change in the SV measurement may aid in clarifying the actual change in τ_D .

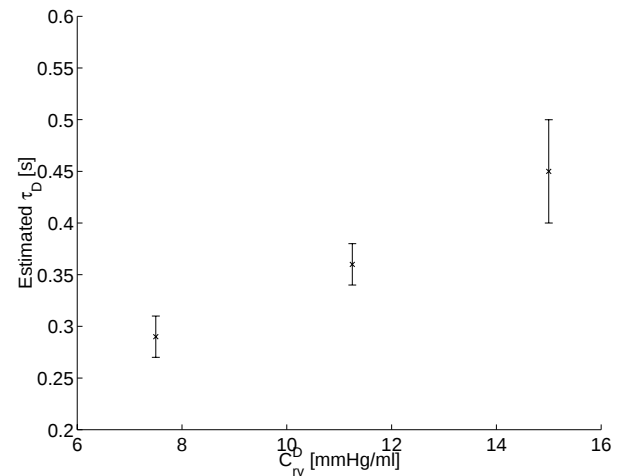


Fig. 4. Computational model example of cardiac tamponade monitoring. See text for details.

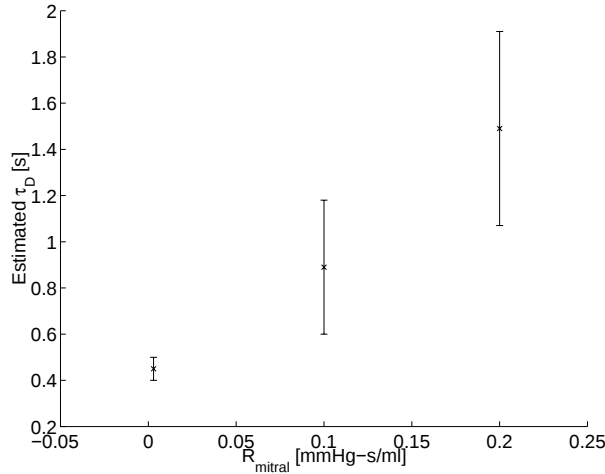


Fig. 5. Computational model example of mitral stenosis monitoring. See text for details.

Secondly, the method could not be used for diagnostic purposes. That is, a change in τ_D could be due to a change in the *state* of either a resistance or compliance. A τ_D change could also be due to a *shift in operating point* of either a resistance or compliance, since τ_D characterizes ventricular diastolic filling dynamics over a narrow range of operating points established by the size of the analyzed hemodynamic fluctuations. However, once the diagnosis is made, τ_D could then be used for monitoring purposes.

Finally, the estimated τ_D actually represents the diastolic filling dynamics of the ventricle which govern the effects of T_D on SV. Assuming that the right ventricular diastolic compliance and the lumped inflow resistance are both larger than their left ventricular counterparts (as is the case in the computational model), then τ_D normally characterizes right ventricular diastolic filling dynamics. This implies that the method *could not* be used to monitor isolated left ventricular diastolic compliance reductions (*e.g.*, hypertrophic cardiomyopathy, hypertrophy due to hypertension, left ventricular ischemia), because the slower right ventricle would govern the effects of T_D on SV in this case. However, the method *could* be used to monitor simultaneous reductions in both ventricular diastolic compliances (*e.g.*, cardiac tamponade, restrictive cardiomyopathy), isolated right ventricular diastolic compliance reductions (*e.g.* hypertrophy due pulmonary hypertension), and lumped inflow resistance increases (*e.g.*, stenosis of the tricuspid and mitral valves). We acknowledge that it may be possible to characterize τ_D and its associated operating point for each ventricle with beat-to-beat ventricular volume measurements obtained with B-mode echocardiography. However, this approach also has its disadvantages including exorbitant image processing.

VI. CONCLUSIONS

In this paper, we presented a method to estimate a parameter summarizing the diastolic filling dynamics of the ventricle which governs the effects of T_D on SV. The method requires beat-to-beat measurements of HR, SV, and ABP, each of which may be obtained noninvasively in humans. We validated the method against data generated from a computational model of the human cardiovascular system. The computational model-based validation motivates experimental evaluation of the method. This may be achieved, for example, by reducing the ventricular diastolic compliances in an animal model of cardiac tamponade and assessing whether the τ_D estimate is able to track these reductions.

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