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Continuous Cardiac Output and Left Atrial Pressure Monitoring by Pulmonary Artery Pressure Waveform Analysis

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Abstract— **We introduce a novel technique for continuous (*i.e.*, automatic) monitoring of cardiac output (CO) and left atrial pressure (LAP) by mathematical analysis of a pulmonary artery pressure (PAP) waveform. To obtain an initial evaluation of the technique, we applied it to PAP waveforms obtained from nine critically ill patients and compared the resulting CO and LAP estimates with standard operator-dependent thermodilution and pulmonary capillary wedge pressure measurements, respectively. We report that the technique achieved an overall CO error of 17.2% and an overall LAP error of 15.8%. With further testing, the technique may ultimately be employed so as to permit, for the first time, continuous CO and LAP monitoring in critically ill patients.**

I. Introduction

CARDIAC output (CO) represents the total blood flow rate in the circulation, while left atrial pressure (LAP) generally indicates the blood pressure attained in the left ventricle during the cardiac filling phase. CO and LAP are two of the most important quantities to be able to monitor in critically ill patients, as they facilitate the diagnosis, monitoring, and treatment of various disease processes such as left ventricular failure, mitral valve disease, and shock of any cause. For example, a decrease in CO while LAP is rising would indicate that the patient is in left ventricular failure, whereas a decrease in CO while LAP is falling may indicate that the patient is going into hypovolemic shock.

The standard methods for monitoring CO and LAP in critically ill patients both involve the use of the balloon-tipped, flow-directed pulmonary artery catheter [1][2]. CO is specifically estimated according to the thermodilution method. This method involves injecting a bolus of cold saline in the right atrium, measuring temperature downstream in the pulmonary artery, and computing the average CO based on conservation laws. LAP is estimated through the pulmonary capillary wedge pressure (PCWP) method. This method involves advancing the catheter into a branch of the pulmonary artery, inflating the balloon, and measuring the resulting steady-state PCWP. In theory, PCWP should nearly equal LAP, since flow has ceased through the branch.

A major limitation of the thermodilution and PCWP methods is that they require an operator. Thus, these two methods are only employed every few hours. Moreover, several technical problems must be overcome in implementing the PCWP method such as partial wedging and balloon over-inflation [3][4]. Indeed, the developers of the PCWP method and the pulmonary artery catheter each reported that they could properly measure PCWP only about 75% of the time [2][5]. Similarly, technical problems are also encountered in implementing the thermodilution method in which variations in injectate volume, rate, and temperature introduce error in the measurement, which is known to be in the 10% range [6]. Perhaps, as a result of these shortcomings, the clinical benefit of the pulmonary artery catheter has yet to be clearly established [7].

On the other hand, the pulmonary artery catheter also permits continuous (*i.e.*, automatic) monitoring of pulmonary artery pressure (PAP). Since CO and LAP are both known to be significant determinants of PAP, it should, in principle, be possible to continuously monitor these two critical hemodynamic variables by mathematical analysis of a PAP waveform. Such an approach could be utilized in critically ill patients to, for example, assess the effects of interventions in real-time, provide an early indicator of deleterious hemodynamic events, save precious time in the busy intensive care unit (ICU), as well as circumvent the aforementioned technical problems in implementing the standard measurement methods.

We find only four papers in the literature for monitoring CO by PAP waveform analysis [8][9][10][11]. These papers described techniques that analyzed intra-beat PAP variations in which highly complex wave and inertial effects are prominent [12]. Perhaps, as a result, the techniques were shown to be inaccurate, especially during vascular interventions. On the other hand, there is substantial literature on estimating LAP through the end-diastolic PAP (*e.g.*, [1][13]). However, this simple analysis is not as accurate as PCWP [13] and is known to be unreliable during pulmonary hypertension [1]. We find only one paper in the literature describing a more advanced technique to estimate LAP, which specifically involved training a neural network to predict PCWP from a PAP waveform [14]. However, this technique was shown to be ineffective in subjects whose data were not utilized in training the network. Thus, no advanced technique based on first principles has been introduced in the literature to monitor LAP or both CO and LAP by mathematical analysis of a PAP waveform.

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In this paper, we introduce a technique for continuous monitoring of both CO and LAP by mathematical analysis of a PAP waveform over time scales greater than a cardiac cycle in which the confounding effects of wave and inertial phenomena are attenuated [12]. We then describe an initial evaluation of the technique with respect to pulmonary artery catheterization data from nine critically ill patients.

II. Mathematical Analysis Technique

Our technique for continuously monitoring CO and LAP from a PAP waveform represents an extension to a technique we previously developed for continuously monitoring CO by long time interval analysis of a systemic arterial pressure waveform [15][16]. Below, we describe the underlying concepts of the extended technique and then outline its mathematical steps.

Our technique is based on the Windkessel model of the pulmonary circulation in Fig. 1a. This model predicts that PAP should decay like a pure exponential during each diastolic interval with a time constant (τ) equal to the product of the pulmonary arterial resistance (PAR) and the pulmonary arterial compliance (PAC). The model further predicts that the exponential pressure decay should equilibrate towards average LAP rather than zero pressure. Thus, the Windkessel model here suggests that both τ and average LAP may be determined from a PAP waveform by fitting a mono-exponential function plus a constant term to each of its diastolic intervals. Moreover, assuming PAC is relatively constant over a wide pressure range, CO may be subsequently determined to within a constant scale factor of 1/PAC subtracting LAP from the mean PAP (MPAP) and dividing this difference by τ.

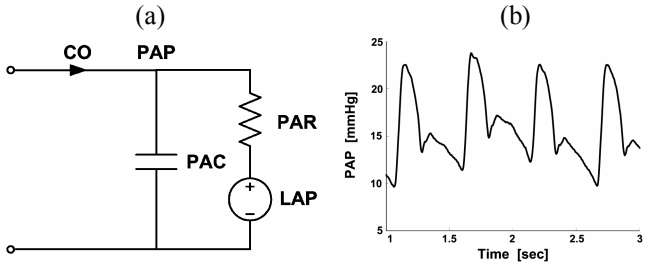

Fig. 1. (a) Windkessel model of the pulmonary artery pressure (PAP) waveform. (b) Experimental PAP waveform. CO is cardiac output; PAC, pulmonary arterial compliance; PAR, pulmonary arterial resistance; and LAP, left atrial pressure.

However, pure exponential diastolic decays are generally not apparent in experimental PAP waveforms (Fig. 1b) [10] due to complex wave reflections and inertial effects in the pulmonary circulation [12]. On the other hand, as we and other researchers have previously discussed, the confounding wave and inertial dynamics may be faster than the exponential Windkessel dynamics in the pulmonary circulation [12][15][16]. This concept implies that if pulsatile activity abruptly ceased, then PAP would eventually decay like a pure exponential and ultimately equilibrate to LAP once the faster wave and inertial dynamics vanished. Thus, the Windkessel model of Fig. 1a is a more valid representation of the long time scale or beat-to-beat variations in the PAP waveform.

Our technique therefore analyzes the PAP waveform over long time intervals (seconds to minutes) in order to determine the pure exponential decay and equilibrium pressure that would eventually result if pulsatile activity suddenly ceased. More specifically, average LAP and the response of PAP minus average LAP to a single, solitary cardiac contraction (h(t) in Fig. 2) are simultaneously estimated by optimal fitting or prediction of ~6 min contiguous segments of a PAP waveform. Then, the Windkessel time constant τ is determined by fitting a mono-exponential function to the tail end of h(t) once the faster wave and inertial effects have vanished (Fig. 2). Finally, proportional CO is computed via Ohm's law (Fig. 2). The technique, which is illustrated in Fig. 2, is specifically implemented in four mathematical steps.

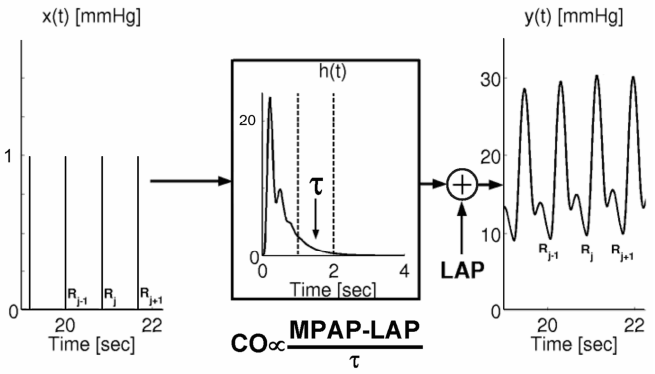

Fig. 2. Illustration of how the mathematical analysis technique determines the time constant τ of the Windkessel model in Fig. 1, average left atrial pressure (LAP), and proportional cardiac output (CO) from a pulmonary artery pressure (PAP) waveform. R_j is the time of the electrocardiogram R wave for the j^{th} beat; x(t), a constructed cardiac contractions signal; y(t), a PAP waveform; h(t), an estimated impulse response coupling x(t) to y(t)-LAP; and MPAP, mean PAP.

First, a cardiac contractions signal is constructed by formation of an impulse train. Each impulse is located at the R-wave of a simultaneous surface electrocardiogram (ECG) measurement and has unity area.

Second, the PAP waveform segment (y(t)) is fitted according to the sum of an unknown constant term and the convolution between an unknown impulse response (h(t)) and the constructed cardiac contractions signal (x(t)). That is, the constant term and h(t) are estimated so as to permit the best fit or prediction of y(t) in the least squares sense. The estimated constant term represents the average LAP, while the estimated h(t) is defined to represent the PAP-LAP response to a single cardiac contraction. The impulse response h(t) and average LAP are specifically estimated with the following autoregressive exogenous input equation with constant term c:

$$y(t) = c + \sum_{k=1}^{m} a_k y(t-k) + \sum_{k=1}^{n} b_k x(t-k) + e(t), \qquad (1)$$

where e(t) is the unmeasured residual error, $\{a_k, b_k\}$ are unknown parameters, and m and n limit the number of these parameters (model order) [17]. For a fixed model order, the parameters including c are estimated from x(t) and y(t) through the least-squares minimization of e(t), which has a closed-form solution [17]. The model order is determined according to a heuristic technique introduced in [18]. With the estimated parameters, average LAP and h(t) are computed as follows:

$$LAP = \hat{c} / \left(1 - \sum_{k=1}^{m} \hat{a}_k \right), \qquad (2)$$

$$h(t) = \sum_{k=1}^{m} \hat{a}_k h(t-k) + \sum_{k=1}^{n} \hat{b}_k \delta(t-k), \qquad (3)$$

where ^ indicates estimates and $\delta(t)$ is the impulse function.

Next, τ is determined over the interval of the estimated h(t) ranging from one to two seconds following the time of its maximum value based on the exponential equation:

$$h(t) = Ae^{-t/\tau} + w(t). \qquad (4)$$

The parameters A and τ are estimated through the least squares minimization of the unmeasured residual error w(t), which has a closed-form solution after log transformation of h(t). In principle, accurate determination of τ as well as average LAP is achieved by virtue of h(t) reliably coupling the long time scale variations in x(t) to y(t)-LAP.

Finally, proportional CO is computed by dividing MPAP-LAP with τ. Note that the continuous proportional CO provided by the technique may be conveniently calibrated to continuous absolute CO with a single thermodilution measurement.

III. Methods

A. Pulmonary Artery Catheterization Data

The pulmonary artery catheterization data utilized here to initially evaluate the mathematical analysis technique were obtained from the MIMIC (Multi-parameter Intelligent Monitoring for Intensive Care) database, which is described in detail elsewhere and freely available on the web [19]. Briefly, this database includes 72 critically ill patient records, typically ranging from 24 to 48 hours in duration, that were archived from patient monitors in ICUs of the hospital formerly known as the Beth Israel Hospital, Boston, MA. Each of these records consists of continuous waveforms sampled at 125 Hz such as PAP and surface ECG leads as well as one-minute trends such as thermodilution CO, PCWP, and heart rate (HR). Fifteen of the 72 patient records were applicable for technique evaluation, as they included a PAP waveform and more than one reference thermodilution CO measurement (as the technique estimates changes in CO) and/or at least one PCWP measurement. Within each of these records, CO as well as PCWP were naturally changing due to disease progression and therapy.

Based on these 15 MIMIC patient records, we created a data set for technique evaluation as follows. First, we downloaded from these records all of the distinct, one-minute thermodilution CO and PCWP measurements and corresponding six-minute segments of the PAP waveforms. Then, we visually examined each of the PAP waveform segments and extracted the longest contiguous, artifact-free portion from each of these segments so as to benchmark the performance of the technique. Finally, we excluded from the study all PAP waveform segments that were less than 5 min in duration. A total of 26 pairs of artifact-free PAP waveform segments and reference PCWP from 5 patient records and a total of 52 pairs of artifact-free PAP waveform segments and reference thermodilution CO from 8 patient records remained for the subsequent evaluation of our technique. Table I summarizes the pulmonary artery catheterization data for each of these patient records.

B. Data Analysis

After applying the technique to all 78 PAP waveform segments, the resulting proportional CO and absolute LAP estimates were quantitatively compared with their respective reference thermodilution CO and PCWP measurements as follows. First, the proportional CO estimates were scaled to have the same mean as the reference thermodilution CO within each patient record. Then, the root-mean-squared-normalized-errors (RMSNEs) between the calibrated CO and absolute LAP estimates and their respective reference measurements were computed. Finally, for comparison, the RMSNE between the mean end-diastolic PAP and their reference PCWP measurements was also computed.

IV. Results

Table I summarizes the results of the initial evaluation of the technique with respect to the MIMIC database. This table shows that the technique achieved an overall CO RMSNE of 17.2% (after a single calibration) and overall LAP RMSNE of 15.8%. Fig. 3 illustrates a visual example of these results from one patient record in which the calibrated CO and absolute LAP estimates are plotted against their respective reference measurements. For comparison, LAP estimation via mean end-diastolic PAP resulted in an overall RMSNE of 34.6%.

V. Discussion

We have introduced a novel technique to continuously monitor CO and LAP by long time interval analysis of a PAP waveform. To obtain an initial evaluation of the

technique, we have applied it to PAP waveforms from nine critically ill patients and have compared the resulting CO and LAP estimates with standard operator-dependent thermodilution CO and PCWP measurements, respectively. We note that the overall CO error of the technique was near the acceptable level of agreement of 15% proposed by Critchley et al. [20] (*i.e.*, sufficiently accurate for clinical use), while the LAP error of the technique was more than 50% smaller than the error of end-diastolic PAP estimates of LAP (see above). In the future, we plan to comprehensively evaluate the technique with respect to the MIMIC II database, which includes fully annotated hemodynamic records from thousands of ICU patients [21]. With future successful testing, the technique may ultimately be employed in critically ill patients so as to effectively automate the pulmonary artery catheter.

TABLE I
SUMMARY OF THE EVALUATION OF THE MATHEMATICAL ANALYSIS TECHNIQUE WITH RESPECT TO THE MIMIC DATABASE [19].

Patient Record	CO [L/min]	MPAP [mmHg]	PCWP [mmHg]	HR [BPM]	CO RMSNE [%]	LAP RMSNE [%]
253	---	23-41	13-26	54-72	---	13.2
410	4.3-6.8	19-23	---	60-90	7.9	---
411	3.2-4.6	30-37	---	58-60	13.8	---
456	4.4-8.5	22-33	13-22	78-108	14.6	11.4
474	3.8-4.9	21-26	9-14	84-108	19.8	12.7
476	3.8-4.8	15-20	---	102-108	25.8	---
482	4-4.3	25-28	13	84	5	33.5
484	5.1-6.8	28-31	---	84-96	7.4	---
485	3-4.1	23-44	19-30	102-114	19.7	16.3
TOTAL	3-10.5	15-44	9-30	50-116	17.2	15.8

CO is cardiac output; MPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; HR, heart rate; RMSNE, root-mean-squared-normalized error; and LAP, left atrial pressure.

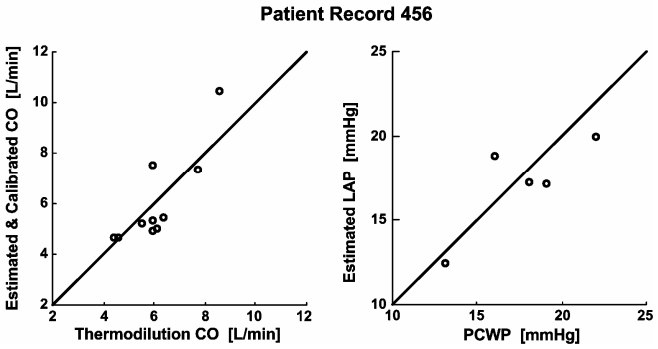

Fig. 3. Visual example of the results of the technique from one patient record in which the calibrated cardiac output (CO) and absolute left atrial pressure (LAP) estimates are plotted against reference thermodilution CO and pulmonary capillary wedge pressure (PCWP) measurements, respectively.

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