Assessment of Left Ventricular Diastolic Function using Phonocardiogram Signals: A Comparison with Echocardiography

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Abstract— **This paper presents a fully-automated end-to-end phonocardiogram(PCG)-based wearable system capable of providing echocardiography-like metrics for left ventricular (LV) diastolic function assessment. Proxy metrics for five echocardiographic parameters were calculated based on physiologically-motivated features extracted from PCG signals using noise-subtraction, heartbeat-segmentation, and quality-assurance algorithms. The clinical value of these proxy metrics was evaluated using the latest American Society of Echocardiography/European Association of Cardiovascular Imaging guidelines for evaluation of LV diastolic function. When tested on a group of n=34 patients, proxy metrics successfully identified LV diastolic dysfunction in a n=29 subset with 87.5% accuracy, and elevated LV filling pressures in a n=17 subset with 75% accuracy.**

Clinical Relevance— **This fully-automated phonocardiogram-based wearable system provides metrics for heart failure screening with an accuracy comparable to that of echocardiography.**

I. INTRODUCTION

Left ventricular (LV) diastolic dysfunction characterized by impaired LV relaxation and increased LV stiffness is one of the biggest causes for the development of heart failure [1][2]. In patients with suspected heart failure, evidence of this dysfunction is often determined using echocardiography and subsequent cardiac catheterization [1]. Echocardiographers compute several 2-dimensional or Doppler parameters to assess LV dimensions, wall motion, ejection fraction, and valvular blood-flow patterns [2]. Cutoff values for each parameter are then analyzed to grade the level of diastolic dysfunction and to estimate LV filling pressures [2]. The accuracy of echocardiographic parameters is greatly influenced by suboptimal signal acquisition and inter-observer variability, and regular quality assurance programs involving echocardiographer education are therefore required [3][4].

Presented here is a fully-automated phonocardiogram (PCG)-based wearable system that can compute proxies for echocardiographic parameters for the purpose of assessing LV diastolic function. These proxy metrics are calculated from PCG signals using features that characterize physiological phenomena such as cardiac pressure gradients, muscle motion and blood flow [5]. The goal of this study is to compare these proxy metrics to echocardiographic parameters for heart failure diagnosis. Section 2 (Methods) describes data collection, data processing, feature extraction, proxy-metric computation and validation algorithms. Section 3 (Results) discusses the physiological meaning of features, evaluates relationships between each echocardiographic parameter and its proxy, and analyzes diagnostic outcomes. Section 4 (Discussion) summarizes the utility and impact of this system.

II. METHODS

A. Patient Population and Data Collection

The study population consisted of adult inpatients (n=34) scheduled for right heart catheterization at the Oregon Health & Science University Hospital (Portland, OR, USA) (IRB Number: 19067). Subjects included 13 females and 21 males between 24 and 85 years old (mean age of 62 ± 17 years, age data available for n=23 subjects) with LV ejection fraction values between 5 and 78% (mean ejection fraction of 49 ± 19%, data available for n=30 subjects). Echocardiographic reports consisting of 2-dimensional and Doppler parameters from a transthoracic examination performed in close proximity to the right heart catheterization were obtained for each subject. Each report included one or more of five parameters based on the quality of the echocardiographic study (Table 1).

Synchronous PCG and Electrocardiogram (ECG) signals were acquired from each patient lying supine on the catheterization laboratory patient bed. PCG signals were acquired at a sample rate of 512 Hz using three acoustic sensors placed at the aortic, pulmonic, and mitral auscultation locations [6]. Each sensor consisted of an electret microphone housed in an ABS-plastic body covered by a 0.4 mm-thick nitrile membrane at one end [7]. ECG signals were acquired at a sample rate of 300 Hz using three electrodes placed proximally at the two upper limbs and lower left abdomen. Depending on catheterization lab schedule, signal acquisition lasted between 4 and 80 minutes per subject, and these signals were then stored for offline analysis in Matlab (MathWorks, MA, USA).

B. Data Processing and Feature Extraction

Noise artifacts from motion, speech and other sources were removed from raw PCG signals by first applying a fourth-order Butterworth band-pass filter with cutoff frequencies of 25 and 140 Hz, and then applying a spectral noise subtraction algorithm commonly used in speech processing [8]. The start

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*Research supported by Sensydia Corporation through the University of California Los Angeles. The authors had full access to data, devices and materials used in this study and take full responsibility for the integrity of data, accuracy of analyses and interpretation of outcomes.

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978-1-7281-1990-8/20/$31.00 ©2020 IEEE

TABLE I. SUMMARY OF PARAMETERS AVAILABLE IN ECHOCARDIOGRAPHIC REPORTS

Parameter	Description	Observed Range	Number of Subjects
Peak E velocity	The peak early diastolic flow velocity measured at the mitral valve leaflet tips	0.42 – 1.55 m/s	26
E/A ratio	The ratio of early-to-late peak diastolic flow velocities measured at the mitral valve leaflet tips	0.66 – 3.66	18
e’ velocity[a]	The average early diastolic flow velocity measured at the mitral valve annulus	0.03 – 0.17 m/s	23
Peak TR velocity	The peak regurgitant systolic jet velocity measured at the tricuspid valve	2.07 – 3.71 m/s	22
LAVi	The maximum left atrial volume indexed to body surface area	14.2 – 85.8 ml/m^2	25

a. Derived indirectly by dividing each peak E velocity parameter value by the available tissue Doppler imaging E/e’ ratio parameter value.

and end times of individual heartbeats in both the raw and denoised-PCG signals were determined using the ECG signal as a reference [9]. PCG signal segments corresponding to the diastolic interval, first heart sound (S1), systolic interval, and second heart sound (S2) were then identified for each heartbeat by leveraging the short-time periodicity of successive cardiac cycles [10][11]. A heartbeat was identified as a quality heartbeat if its signal: (1) had both S1 and S2 successfully identified, (2) had systolic and diastolic intervals free of signal excursions, and (3) had a heartbeat duration within ± 20% of the median beat duration for the subject. To account for variations in underlying physiology, the feature extraction process utilized either raw or denoised PCG signals belonging to either all or exclusively quality heartbeats.

Physiological principles measured by each echocardiographic parameter were used to guide feature exploration [2]. Three types of features were extracted from PCG signals and later used to compute proxy metrics. These included an amplitude feature, a frequency feature and a spectral entropy feature. For calculating the amplitude feature, a Hilbert transform [12] was applied to the selected PCG signal followed by a fourth-order Butterworth low-pass filter with cutoff frequency of 51 Hz. The amplitude feature was calculated as the 60th percentile value of this signal envelope. This feature was used to compute the proxy metric for Peak E velocity. For calculating the frequency feature, a 64-point discrete Fourier transform was computed from the selected PCG signal after the application of a Hamming window. The frequency feature was the center of mass of the frequency distribution between 16 and 160 Hz. This feature was used to compute proxy metrics for e’ velocity and LAVi. The spectral entropy feature was calculated as the negative product of the signal probability distribution estimate with its logarithm [13]. This feature was used to compute proxy metrics for E/A ratio and peak TR velocity. The final feature value for each subject was calculated by taking the mean feature value of select heartbeats for that subject. A summary of features used for each echocardiographic parameter is shown in Table II.

TABLE II. SUMMARY OF FEATURES USED TO COMPUTE PROXIES FOR ECHOCARDIOGRAPHIC PARAMETERS

Parameter	Feature used to Compute Proxy Metric
Peak E velocity	Ratio of pulmonic-to-aortic diastolic amplitude for denoised signal in quality heartbeats
E/A ratio	Ratio of early-to-late pulmonic diastolic spectral entropy for raw signal in quality heartbeats
e’ velocity	Aortic late-systolic frequency center of mass for denoised signal in all heartbeats
Peak TR velocity	Ratio of pulmonic-to-aortic diastolic interval spectral entropy for denoised signal in quality heartbeats
LAVi	Mitral early-diastolic frequency center of mass for raw signal in all heartbeats

C. Proxy Metric Computation and Statistical Analysis

The per-subject feature values were plotted against their echocardiographic parameters, and the proxy metric was estimated for each subject using a linear fit. The proxy metric was adjusted by subtracting the linear model’s intercept and dividing by its slope, and any proxy values outside physiologically-feasible ranges were truncated accordingly.

Next, the clinical value of proxy metrics was evaluated using an algorithm described in the joint recommendations of the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI) in 2016 [2]. The first part of this algorithm was designed to use peak E velocity, e’ velocity, peak TR velocity and LAVi to identify subjects with LV diastolic dysfunction in the presence of normal LV ejection fraction values (Fig. 1A). The second part of the algorithm was designed to use the above 4 parameters along with E/A ratio to estimate the mean left atrial pressure (as an indirect measure of LV filling pressure) for subjects with reduced ejection fraction values or those with normal ejection fraction values in presence of underlying myocardial disease (Fig. 1B). Ground truth diastolic dysfunction and left atrial pressure diagnoses were obtained

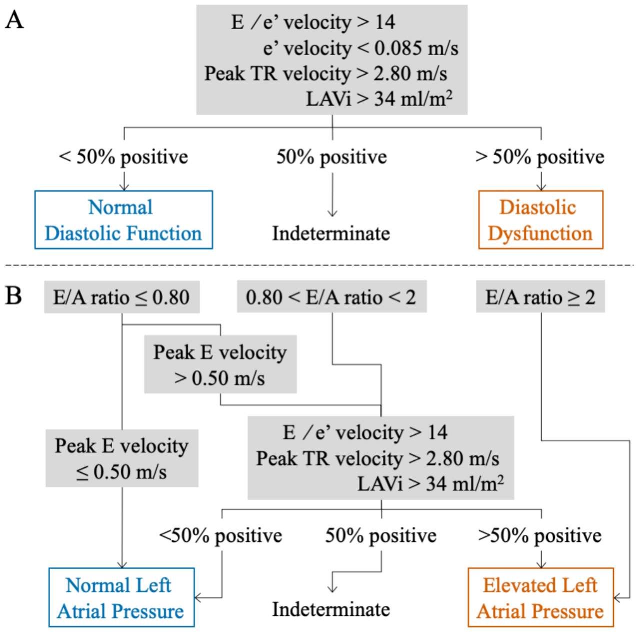

Figure 1. The algorithm described in the joint recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging in 2016 for evaluation of LV diastolic function (A) and estimation mean left atrial pressure as a reliable approximation of LV filling pressure (B). Cutoff value for “average” e’ velocity was chosen as the mean of those for “septal” and “lateral” e’ velocities.

for each subject using their echocardiographic parameters irrespective of ejection fraction. These diagnoses were either “afflicted” (indicating diastolic dysfunction or elevated left atrial pressure), “normal” or “indeterminate”, with the “indeterminate” result indicating that the parameters available for diagnosis were discordant and that the subject required analysis beyond the scope of the algorithm [2][14]. For subjects with “afflicted” or “normal” ground truths, corresponding diagnoses were obtained using proxy metrics. The accuracy of diagnosis was then evaluated by verifying algorithm outcomes using proxy metrics against echocardiographic parameter-based ground truths, and by calculating the sensitivity and specificity for diastolic dysfunction and elevated left atrial pressure diagnoses.

III. RESULTS

Noise-subtraction, heartbeat segmentation, feature extraction and proxy metric computation proceeded in a fully-automated manner. The extracted features directly characterized physiological phenomena otherwise measured by echocardiographic parameters:

- The relative aortic diastolic signal amplitude provided an indirect estimation of the early-diastolic pressure gradient between the left atrium and left ventricle [15]. Greater diastolic amplitudes were seen for subjects with larger peak E velocity values.
- Identification of diastolic signal segments with low spectral entropy enabled detection of LV filling-related muscular contractions. A ratio of early-to-late pulmonic diastolic signal spectral entropy was therefore used to calculate the proxy for E/A ratio.
- LV hemodynamic forces responsible for early-diastolic mitral annulus deflections were indirectly gauged by calculating the aortic end-systolic signal frequency center-of-mass. Subjects with high e’ velocity values due to larger mitral annulus deflections correspondingly showed greater low-frequency signal content.
- The pulmonary artery systolic pressure as calculated from the peak TR velocity was indirectly measured using the pulmonic diastolic signal spectral entropy [2]. Subjects with greater peak TR velocity values, and therefore higher pulmonary artery pressures, showed larger spectral entropy values indicative of turbulent blood flow.
- The size of the left atrium as measured by LAVi was estimated by calculating the amount of low-frequency content in the mitral diastolic signal. Subjects with larger left atria had larger muscle mass and therefore displayed greater muscle-motion related low-frequency signal content.

Proxy metrics could not be calculated for all subjects due to occasional signal quality deficiencies associated with measurement in the noisy catheterization laboratory environment. Peak E velocity and peak TR velocity proxies were unavailable for 6 subjects each, e’ velocity for 3 subjects, and LAVi for 1 subject. The linear relationship between each proxy metric and its corresponding echocardiographic parameter along with Bland-Altman analysis results are detailed in Fig. 2 and Table III.

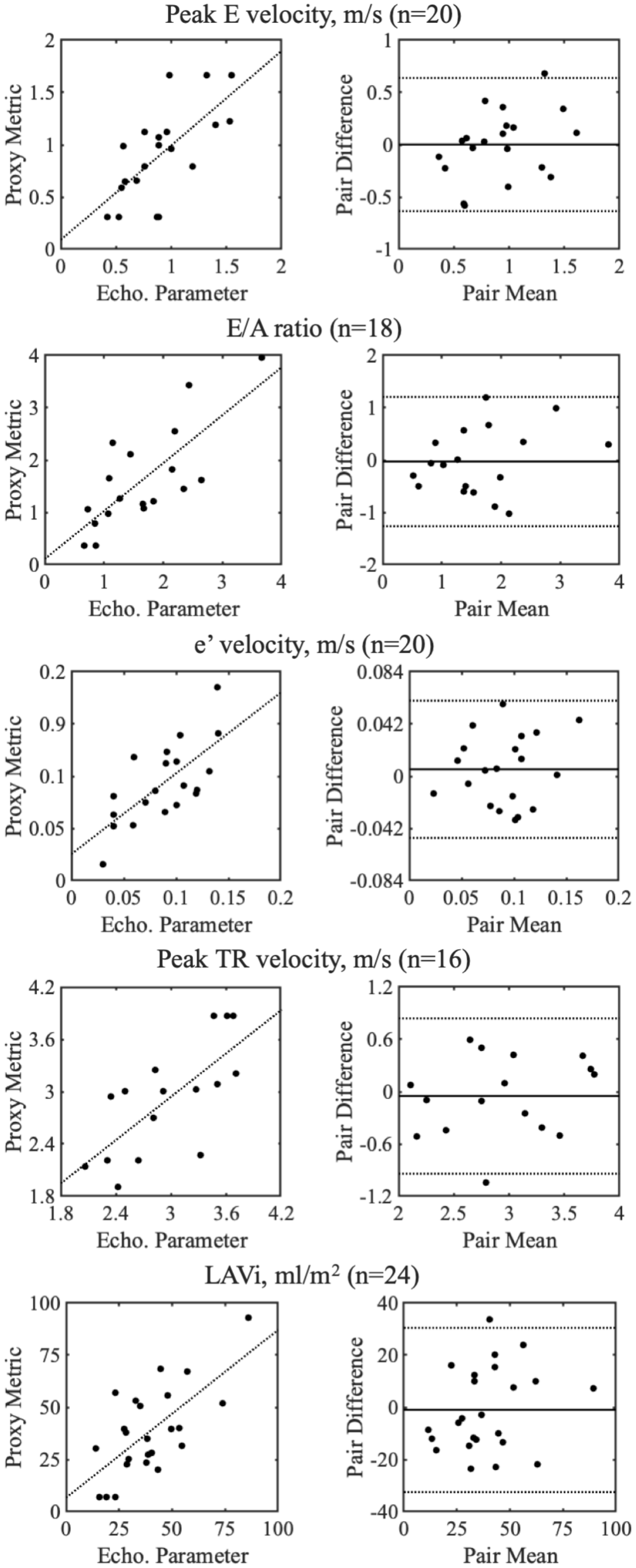

Figure 2. Proxy metric vs echocardiographic (Echo.) parameter scatter plots (left column) and Bland-Altman plots (right column) for peak E velocity, E/A ratio, e’ velocity, peak TR velocity and LAVi. Markers represent subjects. Scatter plots show dotted linear regression line, and Bland-Altman plots show bias (solid line) and 95% limits of agreement (dotted lines).

TABLE III. STATISTICAL MEASURES FOR PROXY METRICS

Proxy Metric	Number of Subjects	R^2-value	*p*-value	Bland-Altman Bias and Limits of Agreement
Peak E velocity	20	0.47	0.0009	0.00 ± 0.64 m/s
E/A ratio	18	0.58	0.0003	-0.03 ± 1.24
e' velocity	20	0.49	0.0006	0.01 ± 0.06 m/s
Peak TR velocity	16	0.51	0.0018	-0.05 ± 0.89 m/s
LAVi	24	0.44	0.0004	-1.0 ± 31.5 ml/m^2

Echocardiographic LV diastolic function ground truths were available for 29 of 34 subjects, where 12 subjects showed diastolic dysfunction and 17 showed normal function. Proxy metric-based diagnoses were "indeterminate" for 5 of these 29 subjects. For the remaining 24 subjects, sensitivity and specificity for detection of diastolic dysfunction were 70% and 100% (Fig. 3, left). Echocardiographic left atrial pressure ground truths were available for 17 of 34 subjects, where 11 subjects showed elevated pressures and 6 showed normal pressures. Proxy metric-based diagnoses were "indeterminate" for 5 of these 17 subjects. For the remaining 12 subjects, sensitivity and specificity for detection of elevated left atrial pressure were 75% and 75% (Fig. 3, right). The final diagnostic accuracy of proxy metrics was 87.5% for diastolic dysfunction and 75% for elevated left atrial pressures.

IV. DISCUSSION

The goal of this study was to compare PCG-based proxy metrics with echocardiographic parameters for LV diastolic function assessment using the 2016 ASE/EACVI algorithm. Proxy metrics identified LV diastolic dysfunction in 29 subjects with 87.5% accuracy, and elevated LV filling pressures in 17 subjects with 75% accuracy. These numbers were closely in line with those reported in reference studies comparing diagnostic accuracy of echocardiographic parameters with gold-standard invasive-catheter pressure measurements [16]. A potential source of error in proxy metric computation was that PCG signals were not recorded concurrently with echocardiographic parameters in order to minimize interference with the catheterization laboratory workflow. Proxy metric computation was based on well-established physiological principles, and the system operated in a fully-automated manner without expert supervision. Future studies can expand on subject count, include analysis of other parameters such as ejection fraction and afflicted conditions such as myocardial disease or valve disorders, and work on obtaining definite classifications for subjects with "indeterminate" LV function and filling pressure.

V. CONCLUSION

This PCG-based system shows potential to be used as a part of routine evaluation of patients presenting with symptoms of dyspnea or heart failure and can help them embark on an accelerated path of care.

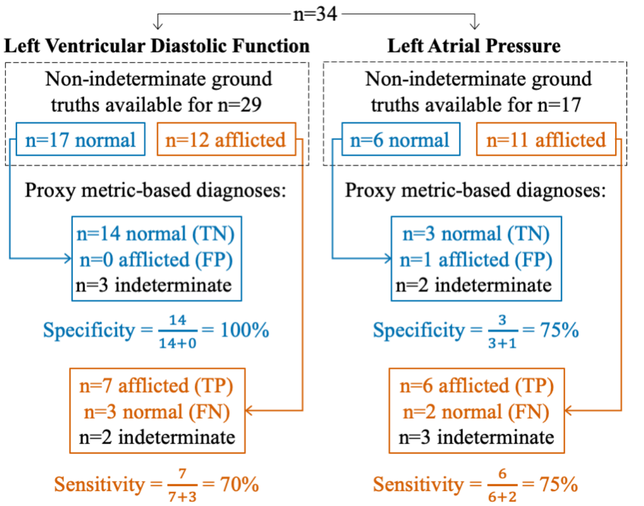

Figure 3. A summary of LV diastolic dysfunction (left) and elevated left atrial pressure (right) diagnoses for n=34 subjects. The overall diagnostic accuracy of proxy metrics was 87.5% for diastolic dysfunction and 75% for elevated left atrial pressures. (TN=True negatives, FP=False positives, TP=True positives, FN=False negatives).

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