Automativ assessment of systolic cardiac performance using PEP/LVET index

A Mohamed Sameh¹, M A Abbas²*, M Hazem³, and M H. Abd Elazeem¹
¹Electronics and Communication Dept., Arab Academy for Science, Technology and Maritime Transport.
²Biomedical Engineering Dept., Military Technical College.
³Cardiology Dept., El-Galaa Family Armed Forces Hospital Cairo, Egypt.

*Corresponding author: abbassma@mtc.edu.eg

Abstract. Congestive cardiac failure is one of the deadliest diseases in the world, with more than 26 million patients. Echocardiogram and angiography consider as the gold standards for heart failure diagnosis. Nevertheless, they are not commonly used for long-term follow up as they need highly skilled and experienced operator. In this paper, a simple and low-cost system for automatic assessment of systolic cardiac performance using systolic cardiac intervals is presented. The proposed system utilized electrocardiogram (ECG) and phonocardiogram (PCG) to calculate pre-ejection period (PEP) and left ventricle ejection time (LVET). The ratio between PEP and LVET was computed to assess the performance of the systolic cardiac function. ECG and PCG were acquired using a commercial stethoscope which was modified to convert PCG auscultation to electrical signals. ECG and PCG signals were digitized and transferred to a personal computer. A custom MATLAB application was designed to display the acquired ECG and PCG, and to compute PEP, LVET, and PEP/LVET ratio. The system was tested on 17 healthy subjects and results showed high agreement between the systolic heart function status assessed by the proposed system and the corresponding echocardiography results. These results imply that the proposed system could be used for long-term follow up for patients with congestive heart failure.

1. Introduction
Congestive heart failure due to coronary artery disease or hypertension is affecting more than 26 million adults [1]. In Middle East, coronary artery disease is the major risk factor for heart failure[2]. Heart failure due to cardiac muscle dysfunction can be assessed by measuring systolic time intervals [3, 4]. Systolic time intervals including aortic pre-ejection period (PEP), defined as the time interval between the onset of left ventricle depolarization (i.e. onset of Q-wave or R-wave [5] on electrocardiogram) and aortic valve opening (i.e. peak of the first heart sound (S1) on the phonocardiogram), and left ventricle ejection time (LVET), defined as the period between the opening of aortic valve and its closure times (i.e. the peak of S1 and the negative peak of the second heart sound (S2)) [6]. Using the ratio between PEP and LVET (PEP/LVET index), healthy and unhealthy
cardiac muscles can be discriminated [7]. Normal ventricle exhibits longer LVET and shorter PEP than abnormal ventricle [6].

Echocardiography is considered the gold standard for systolic cardiac dysfunction assessment [3, 8]. In echocardiograph, PEP/LVET ratio can be measured accurately using simultaneous recording of cardiac mechanical and electrical activity using M-mode and electrocardiograph (ECG), respectively [3]. However, its usage is limited by cost and complexity as it requires highly trained and experienced physicians. Other methods for measuring systolic time intervals using simultaneous acquisition of ECG, phonocardiogram (PCG) [9, 10] or carotid arterial pulse tracings [11] were proposed to provide initial judgment of patient heart health. However, these approaches relied on manual and non-real time computations.

In this paper, a real-time automated system for evaluating systolic cardiac function is presented. The proposed system acquires ECG and PCG signals for each patient then systolic cardiac intervals, particularly PEP and LVET, are calculated. The designed system consisted of a commercial digital stethoscope, signal conditioning and acquisition circuits (for PCG and ECG), and a custom MATLAB program to automatically measure PEP, LVET, and PEP/LVET index. The ultimate goal of this work is to implement a compact cardiac assessment system, that could be used by patients who suffers from congestive heart failure for long-term follow-up.

2. Methods
In this section the overall design of the proposed system and the experiments are discussed in detail. Block diagram of the proposed system is shown in Fig.1.

![Proposed ECG and PCG signals acquisition system](image)

**Figure 1.** Proposed system block diagram

2.1. Experiments
Seventeen healthy subjects ($N = 17$), all male, with average age of 26.41 ± 4.7 years and body mass index of 25.58 ± 1.9 Kg/m² were enrolled in the experiments conducted in El-Gala Family Armed Forces Hospital. All subjects had to agree on a verbal consent before starting the experiments. For each subject, systolic time intervals, including PEP, LVET, and PEP/LVET index were measured using the proposed system and echocardiography.

2.2. Echocardiography
Echocardiography was employed using Echo VIVED e95 (GE medical system, Horten, Norway) with
M5Sc-D sector transducer (1.4 – 4.6 MHz, 120° field of view, and 30 cm depth) incorporated with three ECG electrodes. Each subject was laid in his left lateral position with his left arm placed behind his head. The transducer was positioned by the cardiologist along the parasternal long-axis view. The ultrasound scanner was adjusted to the pulsed Doppler mode. The sweep speed was adjusted to 66.67 mm/s. ECG electrodes were connected in the same configuration as the proposed system to extract ECG signal of Lead I. According to the pulsed Doppler images, PEP and LVET were measured for each subject.

2.3. The Proposed system

2.3.1. Signals extraction and acquisition Signals extraction was carried out using a commercial digital stethoscope, which provided one lead ECG (Lead I) and mechanical heart sound signals. Heart sound signals were converted to electrical signal and processed using commercial microphone breakout circuit. Extracted ECG and PCG signals were digitized using 10-bit analog-to-digital converter and stored on 2 GB secure digital (SD) memory card with sampling rate of 782 Hz. Stored signals were transmitted to a personal computer connected to the acquisition circuit using serial communication (RS232 protocol 8N1-baud rate 115200 bps) for further processing.

2.3.2. Automatic calculation of systolic cardiac intervals A custom MATLAB program was implemented to retrieve stored ECG and PCG signals from the acquisition circuit through serial communication interface. Retrieved ECG and PCG signals were band-pass filtered from 10 to 20 Hz and 30 to 150 Hz [10], respectively. Both filtered signals were normalized. For the normalized ECG signal, QRS-complex was detected using Pan-Tompkins detection algorithm [12] using MATLAB [13]. Normalized PCG signal was smoothed using Savitzky-Golay filtering to mitigate the high-frequency noises in the signal [14, 15]. Hilbert transform was employed to get the envelope of the smoothed PCG signal. Then, the peak of S1 (i.e. first positive peak) was annotated within 50 ms from the onset of the annotated R-wave. Peak of S2 was annotated by searching for the first negative peak within 250 ms form S1. Finally, PEP and LVET values were calculated based on the annotated R-wave, S1, and S2 signals for all detected R peaks for each subject. For each subject, PEP and LVET values were averaged and the PEP/LVET index was calculated. The flow chart of the algorithm used for the proposed system to calculate the PEP/LVET index is shown in Fig.2.

2.4. Statistical analysis

Mean and standard deviation values for PEP, LVET, and PEP/LVET index were calculated for all subjects tested by either echocardiography or the proposed system.

A post hoc analysis for correcting the calculated PEP, LVET, and PEP/LVET index was carried out using the heart-rate (HR) and QRS-complex time width ($W_{QRS}$) measured for each subject [3], as shown in Eq. (1)-Eq. (3). Heart-rate was calculated by inverting the time interval measured between two successive R-peaks detected by the algorithm and multiplied by 60 to get the HR in beat per minute (bpm) units. QRS-complex time width was measured for each detected R-peak. Mean and standard deviation values for HR and $W_{QRS}$ were calculated for all subjects.

\[
P_{EP} = 0.46 \times W_{QRS} + PEP \quad (1) \\
LVET_{c} = 1.5 \times HR + LVET \quad (2) \\
PEP/LVET_{c} = 0.017 \times W_{QRS} + PEP/LVET \quad (3)
\]

Correlation analyses between uncorrected and corrected systolic time intervals (i.e. PEP, LVET, PEP/LVET index), measured by either the proposed system or echocardiography, were carried out using Pearson-test [16]. Also, correlation analyses between uncorrected and corrected systolic time intervals, and HR or $W_{QRS}$ were studied.
To assess the comparability between echocardiography and the proposed system, Bland-Altman (BA) analysis [17, 18] was employed for both uncorrected and corrected PEP/LVET index. The normality of data differences was tested using Shapiro-Wilk test [19] with the significance criterion $p<0.05$. Also, the intervals of agreement between the two methods were defined as the region where 95% of the data points should lie within $\pm 2\sigma$ of the mean difference (i.e. where $\sigma$ is the standard deviation).

**Figure 2.** Proposed system flow chart

### 3. Results

All subjects were investigated using both modalities to measure the systolic time intervals. Figure 3 shows a representative echocardiograph image for a subject under test. PEP and LVET were measured manually by an expert.

Figure 4 shows acquired and processed ECG and PCG signals for the same subject using the proposed system. The R-peak, S1, and S2 events were annotated on the ECG and PCG signals to determine the PEP and LVET time intervals. PEP and LVET values were calculated automatically in real time using the algorithm implemented and the PEP/LVET index was computed.

For all subjects investigated by echocardiography, the mean ± standard deviation for PEP was 34.88±4.09 ms, for LVET was 285.71±22.67 ms, and for PEP/LVET index was 0.12±0.02. However, for all subjects investigated by the proposed system, the mean ± standard deviation for PEP was 35.18±8.38 ms, for LVET was 315.38±23.12 ms, and for PEP/LVET index was 0.11±0.03. Whereas, the mean ± standard deviation for HR and QRS-complex time width was 69.83±12.4 bpm and 62.29±4.92 ms, respectively.

For all subjects investigated by echocardiography, the mean ± standard deviation for corrected PEP (PEPc) was 63.53±4.27 ms, for corrected LVET (LVETc) was 390.44±19.37 ms, and for corrected PEP/LVET (PEPc/LVETc) index was 1.18±0.08. However, for all subjects investigated by the proposed system, the mean ± standard deviation for PEPc was 63.83±9.29 ms, for LVETc was
420.13±24.48 ms, and for PEP/LVETc index was 1.17±0.09.

![Representative pulsed Doppler image showing the PEP and LVET time intervals](image1)

**Figure 3.** Representative pulsed Doppler image showing the PEP and LVET time intervals

![Representative ECG and PCG signals showing the PEP and LVET time intervals](image2)

**Figure 4.** Representative ECG and PCG signals showing the PEP and LVET time intervals
The proposed system showed high significant correlation between the two methods ($r = 0.95, p = 3.73 \times 10^{-9}$) as shown in Fig. 6.

Correlation analyses between uncorrected PEP, LVET, and PEP/LVET index, measured by the proposed system and echocardiography, showed no significant correlation between the two methods ($r < 0.4, p > 0.1$). For corrected PEP and LVET data, no significant correlation showed between the two methods ($r < 0.3, p > 0.2$), whereas, corrected PEP/LVET index showed high significant correlation between the two methods ($r = 0.96, p = 8.74 \times 10^{-10}$). However, no significant correlation found between either corrected and uncorrected PEP, LVET, and PEP/LVET index and HR. Significantly correlated data is shown in Table 1.

Table 1. Representative results of the correlation analyses between the proposed system and corrected PEP, LVET, and PEP/LVET index. [$r(p$-value)]

|         | PEPC | LVETc | PEP/LVETc |
|---------|------|-------|-----------|
| $W_{QRS}$ | 0.51(0.03) | -0.06(0.83) | 0.96(8.7) |
| $\times 10^{-10}$ | | | |
| HR | -0.24(0.34) | 0.45(0.06) | -0.25(0.33) |

Correlation analyses between uncorrected PEP, LVET, and PEP/LVET index measured by the proposed system and WQRS showed insignificant low correlation ($r < 0.3, p > 0.2$), whereas, high significant correlation was found after correction for PEP/LVET index only ($r = 0.96, p = 8.74 \times 10^{-10}$). However, no significant correlation found between either corrected and uncorrected PEP, LVET, and PEP/LVET index and HR.

The differences between PEP/LVET index data, measured by the proposed system and echocardiography, passed Shapiro-Wilk test for normality with significance criterion equal to $p = 0.696$. Results of BA analysis showed that the PEP/LVET index values, automatically calculated by the proposed system (i.e. PEPS11), may be 0.07 below or 0.05 above the PEP/LVET index values measured by echocardiography as shown in Fig.5 and Fig.6.

4. Discussion

In this paper, a real-time automated system for evaluating systolic cardiac function was presented. The gold standard (i.e. Echocardiography) for congestive cardiac assessment was compared to our proposed system on clinical trials ($N = 17$) conducted in EL-Galaa Armed Forces Hospital. The proposed method showed acceptable performance as an initial indicator for heart health.

The proposed system was able to acquire and transfer ECG and PCG signals in real time to a computer for processing and for calculating systolic time intervals automatically. Echocardiograph images were hard to acquire and required a highly skilled person. Also, it was time consuming and not comfortable for the patient. That is why a simple method for heart health assessment is highly needed with high accuracy. Also, the proposed method can be developed to be portable (i.e. smaller size) and all the signal processing can be implemented on a chip. So, the patient would be able to use it anywhere.

The two methods showed no correlation between the measured PEP, LVET, and PEP/LVET index data signals. One reason could be the difficulty of acquiring ECG and PCG signals from obese and hairy subjects. Also, that may be a reason for the low correlation between the calculated PEP/LVET index for the two methods as shown in Fig.5. After correcting data acquired by both methods using HR and $W_{QRS}$, significant correlation was found for the PEP/LVET index. Although, correcting the PEP/LVET index enhanced the correlation between the two methods significantly, it didn’t affect the
BA analysis as shown in Fig.5 and Fig.6.

The PEP, LVET, and PEP/LVET index data calculated by the proposed system, showed no significant correlation with HR, even after correction. Similarly, results of the same analysis with WQRS showed no significant correlation between all calculated data. However, only PEP/LVET index showed significantly high correlation after correction. For the data calculated by echocardiography, significant correlation was found between uncorrected PEP and HR. While no significant correlation was found between the rest of uncorrected or corrected data and HR. Similarly, results for WQRS showed no significant correlation for all calculated uncorrected or corrected data, except for the corrected PEP/LVET index.

![Figure 5](image_url)

**Figure 5.** Plot of the correlation between PEP/LVET index measured by the proposed system and echocardiography (Left). Plot of differences between the proposed system and echocardiography vs. the mean of the two measurements for PEP/LVET index (Right). Where $r$, SSE, $y$, and KS are coefficient of correlation, sum of squared errors, linear regression equation, and Kolmogorov-Smirnov test, respectively.
Figure 6. Plot of the correlation between the corrected PEP/LVET index measured by the proposed system and echocardiography (Left). Plot of differences between the proposed system and echocardiography vs. the mean of the two measurements for the corrected PEP/LVET index (Right).

The study was limited by the population under investigation and the BMI. In the future, enrolling patients with heart failure history will be essential.

5. Conclusion

In this paper a real-time automatic system for systolic cardiac assessment was proposed. PEP and LVET time intervals for a group of healthy subjects were measured using the system and compared with echocardiography. Results showed high agreement between the proposed system and the gold-standard. These results imply that the proposed system could be potentially used for long-term follow up for patients with congestive heart failure.

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