Comparison of Systolic Time Interval Measurement Modalities for Portable Devices

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Abstract— **Systolic time intervals (STI) have shown significant diagnostic and prognostic value to assess the global cardiac function. Their value has been largely established in hospital settings. Currently, STI are considered a promising tool for long-term patient follow-up with chronic cardiovascular diseases. Several technologies exist that enable beat-by-beat assessment of STI in personal health application scenarios. A comparative study is presented using the echocardiographic gold standard synchronized with impedance cardiography (ICG), phonocardiography (PCG) and photoplethysmography (PPG). The ability of these competing technologies in assessing the pre ejection period (PEP) and the left ventricle ejection time (LVET) is given a general overview with comparative results.**

I. Introduction

Myocardial relaxation and contraction are governed by intracellular recycling of calcium ions. The timings of these basic cardiac events are directly related to the health of the cardiac cells [1] and determine the ability of the myocardium to achieve blood delivery according to the metabolic requirements of the organs. Of major importance are the systolic and diastolic timings of the left ventricle, since it is this ventricle's function to insure the blood flow in the systemic circulation. This ventricle acts like a pump with two main functions [2]: the systolic ejection and the diastolic filling. Systolic ejection is preceded by the electro-mechanical delay and by the isovolumetric contraction time (IVCT). These two time intervals compose the pre-ejection period (PEP), which is the time interval between the start of ventricular depolarization and the moment of aortic valve opening. The left ventricle ejection time (LVET) is defined as the time interval of left ventricular ejection, which occurs between the opening of the aortic valve and its subsequent closure. Diastolic filling is preceded by the isovolumetric relaxation time (IVRT).

Clinically accepted descriptions of systolic function of the left ventricle are the velocity of pressure rise, the velocity of ejection, the extent of ejection and the ejection fraction [3]. Diastolic function may be assessed by the velocity of pressure decline, the filling velocity or by the diastolic pressure-volume relation. These function indicators can be readily obtained using invasive as well as non-invasive procedures (e.g. echocardiography, which is the current gold standard for systolic time intervals measurement) in in-hospital settings, which are not adequate for daily applications in home settings as required for long-term patient follow-up with chronic cardiovascular disease. An adequate alternative to evaluate the global cardiac function in this type of application scenarios is the use of systolic time intervals (STI) [4,5].

Several measurement modalities are currently being considered in the literature to assess STI for home settings or other clinical scenarios where mobility is recommended, ranging from photoplethysmography (PPG) [14], radial pulse pressure [15], phonocardiography (PCG) [17] and impedance cardiography (ICG) [16].

Given that systolic time intervals are highly correlated to fundamental cardiac functions, in this paper the goal is to compare the performance of some of the most pertinent modalities for measuring STI that are applicable for portable devices in home or mobile contexts. In order to achieve this goal, a data collection study was conducted using synchronized acquisitions of echocardiogram-ICG-PCG-PPG signals.

The remaining of the paper is organized as follows: in section II some clinical background on the diagnostic and prognostic value of STI is discussed. Section III presents the experimental design of the study and the data analysis procedure. In section IV the main results are presented and discussed. Finally, in section V the main conclusions are presented.

II. Clinical Background

In the mid 20th century IVCT and PEP were studied extensively as measures of cardiac systolic function, whereas LVET was applied as a surrogate of left ventricle stroke volume. A healthy heart exhibits a short PEP and a long ejection time [5], while myocardial dysfunction prolongs PEP and shortens LVET. This has led to the introduction of the PEP/LVET index to assess the systolic function of the heart.

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Several authors (e.g. [4]) have proposed heart rate compensation mechanisms to correct time intervals in order to reduce the variance of the index. It should be mentioned that PEP and LVET are affected independently by several hemodynamic and electrical variables, which also tend to increase variability. More recently, Mancini *et al.* [6] and Tei *et al.* [7] proposed the myocardial performance index (MPI), i.e. (IVCT+IVRT)/LVET, to assess the left ventricle function. The rationale behind this index was (i) to combine in one index the ability to characterize both systolic and diastolic function of the left ventricle and (ii) to eliminate the influence of the electro-mechanical activation delay which tends to be prolonged in patients with left bundle branch block. The MPI has been shown to have prognostic value for several cardiac conditions [8][9][1]. More recently, Gillebert *et al.* [3] and Dandel *et al.* [10] have pointed out that there are limits for the MPI, since there are complex systolic interrelationships that might mask MPI and, therefore, the diastolic function should be assessed separately.

The left ventricle time intervals have found other important clinical applications. PEP and LVET are dependent on the LV load. PEP has been used to derive surrogates for continuous blood pressure (e.g. [18]). PEP has also been extensively applied for vascular and hemodynamic state characterization using the pulse transit time (PTT) principle. One popular measurement principle of PTT uses the pulse arrival time compensated by PEP [11][12]. PTT has received considerable attention in the medical and biomedical literature for its dependence on key physiological variables such as peripheral resistance, atrial compliance and blood pressure. It has been extensively considered by the research community in several clinical applications, such as systolic and mean arterial blood pressure monitoring [11] and sleep apnea [13].

III. Methods

A. Data Collection

The data collection study was conducted at the Centro Hospitalar de Coimbra and involved 17 volunteer students. The data collection study aimed at the simultaneous collection of heart sounds (PCG), impedance cardiogram (ICG), photoplethmogram (PPG) and echocardiography (echo). A synchronous ECG with each of the above signals was also acquired and served as a reference signal for co-registration. The population was not balanced for gender (14 male and 3 female). The average HR during data collection was 72.94 ± 9.87 bpm. All persons involved in this study did not have any known congenital or other heart disease. The biometric characteristics of the population were (values are reported in the form mean ± std):

- Age: 22.53 ± 3.81 years
- BMI: 23.27 ± 2.15 Kg/m^2

The measurement protocol was conducted by an authorized medical specialist and consisted of synchronous acquisitions of echocardiography (alternately Doppler and M-mode), ICG, PPG and heart sound (LSB – left sternum border and apex). All subjects were placed in supine position during the measurements and signal acquisition was performed at rest. No pacing was performed for respiration during data acquisition. The acquisition was performed under controlled temperature (approx. 22ºC) and in a quiet and relaxed environment. The following signals have been acquired:

- Echocardiography and ECG using a Siemens Acuson CV70 device. This device produces a DICOM output with images of time resolution equivalent to 272 Hz.
- PCG and ECG: a Meditron Stethoscope and Analyzer were applied to record PCG and ECG at 44.1 kHz. The bandwidth of the PCG sensor is 20 kHz.
- PPG and ECG: a vital sign monitor from HP has been used.
- ICG and ECG: these signal were obtained using a Niccomo device from Medis.

The echocardiographic data was annotated under the supervision of a clinical expert. A thorough description of the annotation and processing steps followed can be found in [19]. The database is composed by 564 heard beats with annotated aortic valve opening and 358 beats with annotated aortic valve closing moments using echocardiography as a reference. The later is lower than the former, since in M-mode echocardiography, the closing of the aortic cusps is not always visible.

B. Data Processing

In this study PEP is defined as the time interval between the ECG's P-peak and the opening moment of the aortic valve. The left ventricle ejection time is defined as the time interval between the aortic valve opening and its subsequent closing. It becomes clear that the key events to be detected are the opening and the closing movements of the aortic valve. As already mentioned, there are several technologies that might be applied for this goal. In this paper we consider the following, which are among the most promising for personal health applications:

Impedance cardiography: there are several possible definitions for ICG characteristic points to capture the aortic valve events. The opening of the aortic valve is usually associated to the B-point [21]. However, some authors (e.g. [20]) suggest using the zero-crossing to the left to dZ/dt_{max}. More recently, a new definition for this point was suggested based on echocardiography-ICG analysis [22]. In this study we present results for each of these alternative definitions of markers to capture the aortic opening event. These are obtained with the algorithms reported in [20], [21] and [22], respectively. The measurements achieved by the Niccomo ICG monitor from Medis are also shown. A comparative analysis of the performance of the aforementioned algorithms in identifying the X-point (aortic valve closing event) is also presented. This enables to measure both PEP and LVET.

Phonocardiography: The first (S1) and the second (S2) heart sounds encode information related to the movement of the aortic valve cusps. A modified version of the algorithm reported in [17] is applied to extract PEP and LVET using heart sounds. The aortic valve opening event is captured from S1 using a Bayesian approach. The closing event of this valve is measured at the beginning of the S2.

Photoplethmography: A PPG signal can be exploited to yield an estimation of LVET from a peripheral site. There is no known solution to get a PEP estimation due to the propagation delay of the arterial pulse from the heart to the considered PPG site. For LVET estimation, the PPG waveform analysis is based on its successive derivatives up to the fourth order, similar to the approach described in [14]. The systolic ejection onset is determined at the time achieving the maximum of the third derivative along the up-rising wave of the main PPG pulse. The end of the systolic ejection is computed from several features including the slope, curvature and third derivative. The LVET estimation is obtained with a rule-based decision logic, taking account of the morphology of the falling part of the pulse, e.g., the presence or absence of a secondary pulse depending on the relative timing of the reflected wave.

IV. Results and Discussion

The results achieved in this comparative study are shown in table 1 and table 2 for PEP and LVET, respectively. The shown statistics were obtained using all the available individual heart beats. The estimation errors were always calculated using the subtraction between the measured value, x, in each modality and the echo reference, x_{Echo}, i.e. x-x_{Echo}. In both tables, the abbreviation "*Abs. Est. Error*" stands for average absolute estimation error, i.e. the average of $|x\text{-}x_{Echo}|$, whereas "*Est. Error*" identifies the average estimation error measured using x-x_{Echo}. Furthermore, regarding the results reported for ICG, abbreviations ICG_{ZC}, ICG_{Onu} $ICG_{Carvalho}$ and $ICG_{Niccomo}$ are used for the characteristic points calculated with the algorithms reported in [20], [21], [22] and the Niccomo ICG monitor from Medis.

As can be observed, the best overall performance is achieved using heart sound to measure STI. PCG enables the assessment of both PEP and LVET, hence it might be applied to assess the systolic function of the myocardium as well as to estimate the stroke volume. Furthermore, it exhibits among the smallest estimation errors in the study for both STIs. Regarding PEP, PCG exhibits the smallest absolute estimation error and dispersion. As can be observed in table 1, the systematic measurement bias of PEP based on the PCG modality is negligible (0.7 msec.), namely if it is compared to the other competing modalities which exhibit significant systematic biases. However, it exhibits the smallest correlation coefficient with respect to the gold standard (0.54 vs. 0.75 in ICG_{ZC}).

As for LVET measurement, it is observed that in the current study PPG achieved the best absolute estimation error (e.g. 11.5 msec vs. 14.4 msec. achieved with PCG). It should be mentioned that the statistics concerning PPG were calculated on a much smaller database, since only 112 heart beats with synchronized PPG were available. Hence, these results might be biased due to selection bias or sampling variability. However, our LVET PPG results are comparable in accuracy with those published in [14]. The PPG performance outperforms all other modalities regarding the error dispersion as well as in systematic bias. It should be mentioned that for LVET almost all other modalities exhibit non negligible systematic biases.

TABLE I
SUMMARY OF RESULTS FOR PEP. ρ - CORRELATION WITH ECHOCARDIOGRAPHY.

Parameter	Est. Error (msec.) (average ± std)	Abs. Est. Error (msec.) (average ± std)	ρ
ICG_{ZC}	-7.2 ± 28.6	23.9 ± 17.2	0.75
ICG_{Onu}	16.5 ± 16.7	19.9 ± 13.4	0.68
$ICG_{Carvalho}$	5.8 ± 14.0	12.4 ± 8.7	0.54
$ICG_{Niccomo}$	9.8 ± 21.4	19.3 ± 13.4	0.58
PCG	0.7 ± 11.0	9.0 ± 6.4	0.54

TABLE II
SUMMARY OF RESULTS FOR LVET. ρ - CORRELATION WITH ECHOCARDIOGRAPHY.

Parameter	Est. Error (msec.) (average ± std)	Abs. Est. Error (msec.) (average ± std)	ρ
ICG_{Onu}	1.8 ± 46.2	39.1 ± 24.5	0.19
$ICG_{Carvalho}$	-23.6 ± 31.1	29.9 ± 25.1	0.36
$ICG_{Niccomo}$	51.2 ± 45.8	54.3 ± 42.1	0.27
PCG	-9.9 ± 16.3	14.4 ± 12.4	0.80
PPG*	0.9 ±14.2	11.5 ± 8.95	0.77

*Only applied over a subset of 112 beats where PPG was available.

In the present comparison study, the worst STI measurement results were achieved using the ICG, both for PEP as well as for LVET. For instance, the best PEP error measurement statistics achieved with the ICG modality is 38% higher compared to PCG, whereas for LVET it is observed that the lowest ICG estimation error is 180% higher compared to PPG. This is due to the difficulty to adequately detect the so-called X-point in ICG, since it is very prone to noise and respiration artefacts. It is also observed that significant variations in performance are observed with respect to the definition of the characteristic points. The conventional ICG characteristic point identification methods, i.e. the B-point [21] and the zero-crossing [20], exhibit significant biases with respect to the echocardiography reference in detecting both aortic valve related events. Furthermore, it is observed that these biases substantially differ, leading to significant over or underestimations of PEP and LVET. For this modality the best results are obtained using the characteristic point definition introduced in [22] which was based on synchronized echocardiography-ICG signals. As can be observed, using this method the smallest systematic bias as well as error dispersion in detecting the onset of the aortic valve open event is achieved. Regarding the detection of the aortic valve closing point, none of the ICG methods exhibit comparable performances to the PPG and the PCG methods. Most of the ICG algorithms exhibit very low correlation coefficients and very high systematic estimation errors and dispersions. Nevertheless, the achieved results suggest that the most stable estimation of this event using ICG seems to be attainable using the algorithm reported in [22].

It should be stressed that the apparently less favorable results of ICG might not generalize for all application scenarios and population characteristics. Elderly populations tend to exhibit significant changes in physiological characteristics that might have a significant impact on the performance of the measurement modalities. Body fat acts like a low-pass filter as well as a gain attenuator for heart sound. Its impact on the ability and accuracy in detecting the aortic valve movement from heart sounds is currently unknown. Elderly populations tend to exhibit significantly higher body mass indexes compared to the population used in the study. On the other hand, elderly populations tend to exhibit much stiffer arteries and higher blood pressures. Besides these factors, the optical transmittance of the skin changes with age. The impact of these factors on the shape of the PPG is significant and might affect the pulse shape (namely its reflection component as well as its amplitude).

V. CONCLUSIONS

This paper presents a comparative study on STI measurement using three different modalities, i.e. impedance cardiography, photoplethysmography and phonocardiography (heart sounds), with respect to the clinical gold standard - echocardiography. The criterion used in selecting the modalities for comparison was their non-invasive nature and their applicability for portable device design. The results achieved with PCG and PPG suggest that these modalities have the potential to build monitoring systems for long-term cardiac function follow-up. In fact, these modalities rely on bio-signals that can be easily measured non-invasively and with low intrusiveness. Furthermore, the current study demonstrates, that algorithms exist to accurately extract the systolic time intervals from these signals in order to enable proper systolic cardiac function assessment. The most inaccurate STI measurement results were achieved in this study using ICG. It seems that the characteristic points of this signals are significantly unstable. Nevertheless, the study was performed resorting to young population and these conclusions should be confirmed with unhealthy elderly populations, particularly with patients with cardiac diseases.

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