Abnormalities of the Systolic Time Intervals Obtained by Electronic Stethoscope in Heart Failure

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Citation

Abstract

We studied the systolic time intervals, using the electronic stethoscope in 55 patients with systolic heart failure and 60 normal subjects. The measured systolic intervals were: QS1 (onset of the QRS to first heart sound S1), S1S2 (cardiologic systole: S1 to S2), QS2 (electromechanical systole: onset of the QRS to S2), CSI (cardiologic systole index: ratio of the observed S1S2 to a predicted S1S2, adjusted by heart rate), ESI (electromechanical systole index: ratio of the observed QS2 /predicted QS2) and QS1/S1S2 index. In the heart failure we observed relevant prolongation of the QS1, reduction of the CSI and increase in the QS1/S1S2. In the HF with QRS ≥ 120 ms (n=23), the QS1 and ESI were augmented in relation to HF with QRS< 120 ms. There were correlations between these alterations in CSI and QS1/S1S2 and the NYHA class and between the QS1/S1S2 and the ejection fraction by echocardiogram.

INTRODUCTION

The systolic time intervals (STI) obtained from simultaneously recorded electrocardiogram, heart sounds and carotid pulse tracing, constituted the first non invasive technique to assess cardiac function. The ratio of the pre-ejection period by the left ventricular ejection (PEP/LVET) is a validated measurement of left ventricular (LV) systolic performance. This ratio increased significantly in the heart failure with depressed LV systolic function through a raise in the PEP and a fall of LVET [1].

Echocardiography is a valuable technique to assess the cardiac function, but requires specialized training for image acquisition and interpretation, presents relative high costs and limited accessibility in many countries [2]. Thus the development of cost-effective diagnostic tools to evaluate the cardiac function remains important.

Electronic stethoscopes make it possible to play back sounds and provide visual display in a computer [3]. The simultaneous use of a single-lead ECG in time waveform (phonocardiogram) allows the measurement of some systolic time intervals.

The present study aims to evaluate the time intervals obtained by electronic stethoscope in patients with heart failure (HF) due to systolic LV dysfunction. The objective is to contrast this evaluation with data obtained from normal subjects; comparing the relation between the STI and the heart functional class by New York Heart Association (NYHA), the ventricular function and left-sided conduction delay.

METHODS
PATIENTS

In this observational and prospective study, it was consecutively selected 55 patients with signals and symptoms of heart failure, an increase of the LV dimensions and a systolic LV dysfunction: LV ejection fraction less than 50% as detected by echocardiography.

They had been included patients interned for a heart failure exacerbation or stable patients of clinic. Patients were included if in sinusal rhythm. Exclusion criteria included acute coronary syndrome, use of pacemaker or implantable defibrillator, presence of significant heart murmur (> 3+/6), active infection and use of the continuous intravenous therapy. The patients underwent the phonocardiogram by electronic stethoscope between June 2006 and March 2007.

A group of 60 normal individuals (30 men and 30 women),

with ages varying from 26 to 80 years old, served as the control group. They were selected among volunteers and patients who showed up for check-up consultations. The control group had normal clinical history, physical examination, ECG and echocardiography evaluations. None of the control patients used cardiovascular medication.

The HF and control patients were available at the University Onofre Lopes Hospital. The study was approved by the local ethics committee. All patients provided written informed consent.

PHONOCARDIOGRAM

The phonocardiograms were obtained using the electronic stethoscope Master Elite and software Meditron Analyser 4.0 (Welch Allyn inc, Skaneateles Falls, NY), a PC-based software that captures sound waves with a synchronized ECG signal. The system is comprised of an electronic stethoscope, a module for acquisition of the electrocardiogram, and a laptop. The files are 10 seconds long and were saved as Microsoft® wav in a computer hard disc to offline analysis.

The procedure was made with the patient in supine position and quiet respiration. The stethoscope was appropriately placed in mitral area. The stethoscope used simultaneous cardiac auscultation to allow the examiner to detect the adequate area.

The measurements were realized by the software in standard waveform. The cursors provided the automatic record of the time intervals. The time intervals were obtained by averaging five or more selected cardiac cycles, excluding the premature beats and pauses. The HR was determined as the mean value of ten sinusal cardiac cycles with the cursor positioned in the R peak wave. All intervals were measured in milliseconds.

The following basic time intervals were measured:

QS1: the interval obtained from the onset of the QRS complex to the first high-frequency vibrations of S1 (mitral component).

S1S2 (cardiologic systole): the interval demarcated by heart sounds [4] , measured from the first high-frequency vibrations of S1 to the first high-frequency vibrations of S2 (aortic component).

QS2 (electromechanical systole): the time interval obtained from the onset of QRS complex to high-frequency vibrations

of S2. It was obtained by addiction: QS1 + S1S2.

Heart rate (HR): obtained from the relation: 60000/RR interval.

Regression equations relating HR and systole duration (S1S2) were obtained in the control group.

From these STI we calculated auxiliary indices as follows:

Cardiologic Systole Index (CSI): ratio of the observed S1S2 to a predicted S1S2 for given HR calculated by the regression equation.

Electromechanical Systole Index (ESI): ratio of the observed QS2 to a predicted S1S2 for given HR calculated by the regression equation.

QS1/S1S2 Index: ratio of the QS1 by the S1S2.

The time intervals were measured by a blind observer of the heart failure condition, the echocardiographic measurements and the clinical findings.

ELECTROCARDIOGRAM (ECG)

All patients underwent a 12-lead ECG. The HF patients were classified by the QRS duration in narrow (<120 ms) and wide QRS (?120 ms) based on the ECG and by the measurement of QRS duration in the single-lead ECG in the phonocardiogram.

ECHOCARDIOGRAPHY

A two-dimensional guided M-mode echocardiography with the use of commercially available echo-machine and a 3.5 MHz linear array transducer was performed on each subject. All measurements were made according to the American Society of Echocardiography [5] . LV measurement was obtained at end diastole and end systole in the parasternal long axis view. Left ventricular function was evaluated by visual estimation and the ejection fraction was calculated by M-mode echocardiography by Teicholtz.

STATISTICAL ANALYSIS

Analyses were performed with MedCalc version 9.2.1.0 (MedCalc Software, Belgium). Continuous variables were expressed as means ± standard deviation. Variables with normal distributions were compared by unpaired t-test and by Mann-Whitney to variables with abnormal distributions. The correlation to analyze the degree of association between two variables was made by the calculation of the Pearson coefficient (r), when the distribution was normal. Linear

regression analysis was used between the systolic time intervals and the HR. Two-tailed p values <0.05 were retained for statistical significance.

RESULTS

Phonocardiograms with adequate quality to make measurements were obtained in 55 of the 59 (93%) patients with HF. The HF patients were 29 to 86 years old. There were 29 men and 26 women, with NYHA functional class II to IV due to coronary artery disease (n=22), idiopathic dilated cardiomyopathy (n=18), hypertensive cardiopathy (n=10), alcoholic cardiomyopathy (n=3) and Chagas disease (n=2). Twenty seven were inpatients with heart failure exacerbation and 28 were stable outpatients. Twenty three patients (42%) had conduction delay with QRS duration of 120 ms or more, with complete left bundle branch block (LBBB) in 19 patients.

This study showed that in patients with heart failure due to systolic dysfunction, there is a relevant increase of the both the QS1 interval and the QS1/S1S2 ratio, as well as a reduction of the cardiologic systole (Table 1 and Figure 1).

Figure 1

Table 1: Parameters in the control group and patients with heart failure

Parameter	Control n=60	HF n=55	P value
AGE (years)	54.1 ± 12.4	58.1 ± 11.9	0.09
EF*	71.3 ± 7.5	35.5 ± 7.0	<0.001
QS1	41.5 ± 7.6	73.0 ± 13.4	<0.001
CSI*	1.0 ± 0.04	0.90 ± 0.1	<0.001
ESI**	1.0 ± 0,04	1.01 ± 0.09	0.2
QS1/S1S2***	0.12 ± 0.02	0.25 ± 0.06	<0.001

Values expressed as mean ± SD. HR denotes heart rate (beats/min).

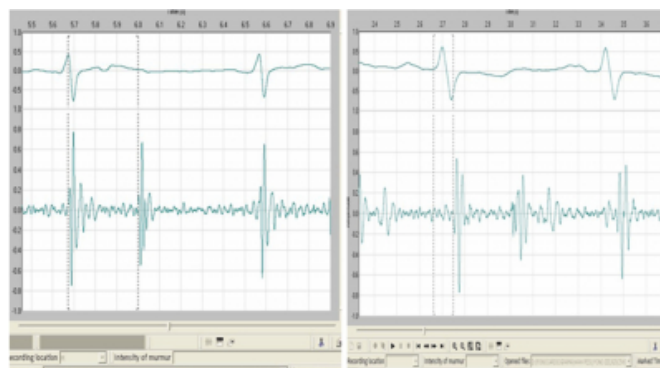*Ejection fraction calculated by M-mode echocardiography by Teicoltz.

*CSI: ratio of the observed S1S2 to a predicted S1S2 for given HR calculated by the regression equation.

** ESI: ratio of the observed QS2 to a predicted QS2 for given HR calculated by the regression equation.

*** QS1/S1S2: ratio of the QS1 by the S1S2.

Figure 2

Figure 1: Phonocardiograms of the two men. Left: Normal subject, with the following measurements: QRS-96 ms, FC-68 bpm (RR=878 ms), QS1=37 ms, S1S2=327 ms, CSI=0.97 e QS1/S1S2=0.11. Right: patient with idiopathic dilated cardiomyopathy and severe systolic dysfunction, functional class III (NYHA). Measurements: QRS=105 ms, HR=83 bpm (RR interval of 721 ms), QS1=86 ms (showed), S1S2=265 ms, CSI=0.84 and QS1/S1S2=0.32. There is a third heart sound (S3).

The regression equations and the duration of S1S2 and QS2, reveal differences between men and women:

1- Male: QS2 =488-1.65 HR and S1S2=428-1.35 HR (r^2 =0.60, p<0.001);

2- Female: QS2 =553-2.3 HR (r^2 =0.77, p<0.001) and S1S2 =498-2.1 HR (r^2 =0.71, p<0.001).

The regression equations were used in the determination of the predicted values of the S1S2 and QS2 and of the indices CSI and ESI in every situation. Therefore, the value of the CSI and ESI were adjusted by HR and sex.

In all cases the relation between the S1S2 and the HR represents linear regression equations. In the example of the Figure 1 (right): S1S2=265 and HR=83, the predicted S1S2 was calculated by the equation S1S2=428-1.35*HR =428-1.35*83=315.9, then CSI=265/315.9=0.84.

The relationship between the QS1 and the HR was described by the equation: 65-0.3 HR (r^2 =0.21, p<0.001) regardless of genre. As the QS1 changes slightly with the HR increase, this equation can be dismissed. The QS1/S1S2 index is not influenced by heart rate (r=0.048, p=0.74).

The normal values of the systolic time intervals (5th and 95th percentiles), obtained in the normal control group, were: QS1=30 to 54 ms; CSI=0.93 to 1.06, ESI=0.94 to 1.06 and QS1/S1S2 index=0.08 to 0.16. There are no significant differences of the QS1, ISC, ESI and QS1/S1S2 between the

sexes.

The QS1 was prolonged (>54 ms) in 53 of the 55 HF patients (96%) and normal (? 54) in 57 subjects (95%) of the control group. The QS1/S1S2 index was abnormal (>0.16) in 53 patients with HF (96%) and normal (? 0.16) in 59 subjects of the control group (98%).

We generally observed a visible difference between the phonocardiogram of the HF patients and of the normal subjects. In the normal subjects, the onset of S1 occurs simultaneous or near the R peak. In contrast, in HF patients the onset of S1 is often delayed in relation to the R peak when the QRS complex is positive, as shown by the vertical lines (Figure 1).

The QS1 and systole duration (CSI and ESI) were significantly greater in patients with HF and prolonged QRS, when compared with a subgroup with a narrow QRS (Table 2).

Figure 3

Table 2: Comparative parameters in patients with heart failure with narrow QRS and wide QRS

Parameter	HF with QRS<120 n=32	HF with QRS ≥120 n=23	P value*
HR	76.0 ± 12.3	81.6 ± 15.5	0.28
NYHA class	2.7 ± 0.7	2.7 ± 0.8	0.98
EF	35.8 ± 7.0	35.1 ± 7.0	0.73
QRS	95.6 ± 10.4	149.1 ± 15.1	<0.001
QS1	69.1 ± 10.8	78.3 ± 14.9	0.01
CSI	0.88 ± 0.06	0.95 ± 0.13	0.01
ESI	0.98 ± 0.06	1.06 ± 0.10	<0.001
QS1/S1S2	0.24 ± 0.04	0.26 ± 0.08	0.19

NYHA-New York Heart Association functional class. Other abbreviations as in the Table 1.
* Two-tailed p values (independent samples).

Overall, in the patients with HF there was correlation between the systole, when measured by CSI, and the QRS duration (r=0.52, p=0.0001, respectively). The QS1/S1S2 was prolonged in the two subgroups, without statistical difference.

The CSI was significantly smaller in HF patients with NYHA class functional III or IV (n=28), in general patients interned with acute heart failure exacerbation, when compared with those with class II (n=27): 0.86 ± 0.08 vs. 0.96 ± 0.10, (p< 0.001), respectively. The QS1/S1S2 index also correlates with symptomatic status of the patients with heart failure as shown by their NYHA (median and interquartile range by rank sum tests): 0.26 (0.23 to 0.31) in the class III or IV patients and of 0.21 (0.18 to 0.25, p< 0.001) in class II. There was a correlation between this index and the ejection fraction available by M-mode echocardiography (r=-0.30, p=0.02). The QS1 was unrelated to the symptomatic status or degree of the LV dysfunction.

DISCUSSION

This study showed that patients with heart failure due to systolic dysfunction exhibit an increase of the QS1 interval, a reduction of the cardiologic systole and a meaningful increase of the QS1/S1S2 index. This is correlated with the symptomatic status of the patients and the degree of ventricular dysfunction.

These abnormalities noted in heart failure were not observed in patients with hypertension and chronic coronary artery disease in study using the similar methodology [6].

The prolongation of the QS1 in heart failure could, according Weissler et al [1], reflect an increased eletromechanical delay, which is greater when there is a left ventricular conduction disturbance. This study showed that the wide mean QRS observed, even in the HF subgroup with narrow QRS, contributed to the prolonged QS1. Burggraf [7] demonstrated, by echophonocardiogrphic study, a delay in mitral closure and an increase of the QS1 in LBBB compared with normal group. Rahko et al [8] observed a delay in the mitral and tricuspid closure related to the degree of systolic dysfunction and elevated filling pressure in congestive heart failure. The reversal closure sequence of the mitral and tricuspid valve was a common finding and, in contrast to what was reported by Burggraf, not related to the conduction delay. The reduction of the contractility may contribute to the increase of the QS1 by reducing the rising rate of ventricular pressure prior to the first heart sound.

In this study, a decrease in cardiologic systole was observed in the HF patients. The cardiologic systole was a little studded and a variable seldom obtained in the phonocardiography, in contrast to the eletromechanical systole (QS2). Lewis et al [9] observed the shortening of QS2 in the acute phase of myocardial infarction, which is related

to excessive adrenergic tone as assessed by urinary catecholamine excretion. The reduction of eletromechanical systole was documented after the administration of adrenergic agents [10] and after the use of atropine [11].

The notable increase of the sympathetic activity in heart failure, with elevations of the catecholamines, should be, at least in part, a factor participating in the shortening of cardiologic systole. In the study the CSI was shorter in the patients with HF class III or IV. On the other hand the reduction in CSI seen in the study may reflect the known reduction of the LVET in HF.

The ESI was significantly augmented in HF patients with a wide QRS complex interval (LBBB in 83% of the cases). This is in agreement with the observation that the LBBB is associated with significant later closing of the aortic valve and a relative reduction in the diastolic time and of the left ventricular filling [12]. These abnormalities (dyssynchrony) were corrected by the cardiac resynchronization therapy, having been documented the shortening of the QS2c after biventricular pacing system [13].

Ross et al observed strong associations between acoustic cardiographic parameters and left ventricular end-diastolic pressure, ejection fraction, and maximum contractility in patients with left ventricular systolic dysfunction underwent catheterization. Acoustic cardiographic is a system that records and algorithmically interprets the electrocardiographic and acoustic data. Shapiro et al [15] recently showed that the LV dysfunction index combining the phonoelectocardiographically measured data from the S3 and STI was a highly specific and moderately sensitive indicator of LV dysfunction.

The present study has certain limitations. The decreased amplitude of the first heart sound observed in HF patients with LBBB makes it difficult to measure the systolic time intervals. There was a time interval between the phonocardiogram and echocardiogram exams. This imposes certain limitations on the comparative analysis.

In addition, the normal value of the systolic time intervals and the regression equations may change in different populations.

Automatic determination of the intervals by software may be useful in this case. However, because the QS1 and S1S2 normally shorten proportionally with an increase of HR, the QS1/S1S2 ratio is not influenced by HR. This index has a narrow range in normal subjects. Similarly to PEP/LVET, it

is obtained by two components, with variation in opposite directions, from the heart failure with systolic dysfunction: the QS1 prolongs and the S1S2 shortens.

The parameters were obtained by a relatively simple method and with low cost equipment. This method can address and help bedside assessment of HF patients. Other potential applicability of the findings can be in the differential diagnosis of the systolic heart failure and diastolic heart failure.

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