Diagnosis of mitral insufficiency using impedance cardiography technique ICG

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Abstract

Impedance cardiography (ICG) is a non-invasive tool for assessing the hemodynamic parameters. It has been used for diagnosing several cardiovascular diseases, such as heart failure, cardio-myopathy, and valvular diseases. Particularly, the valvular heart disease is characterized by the damage in one of the four heart valves: the mitral, aortic, tricuspid or pulmonary valves. The mitral valve insufficiency and the aortic valve stenos are the most frequent valve diseases in the world. In this paper, we propose to diagnosis the mitral valve insufficiency using the impedance cardiography technique. The study group consisted of 40 subjects (20 control subjects and 20 patients with mitral insufficiency). A parameter "I" is calculated from the impedance cardiogram waveform and it is used to differentiate control subjects from patients with mitral insufficiency. The parameter "I" was related significantly to the abnormalities of the impedance cardiogram waveform. For patients with mitral insufficiency, "I" was higher than for the healthy subjects with a difference ratio of 89% (p<0.001). To improve the diagnosis, we determined the stroke volume, cardiac output, and other hemodynamic parameters for the two groups of subjects. Finally, we concluded that we could identify, easily, patients with mitral insufficiency based on the abnormalities of the impedance cardiogram tracings and a characteristic parameter "I".

Keywords: Impedance Cardiography, mitral insufficiency, hemodynamic parameters, parameter "I"

Introduction

Impedance cardiography (ICG) is a simple, non-invasive, and cost effective technique for assessing stroke volume (SV), cardiac output (CO) and others hemodynamic parameters [1]. In order to establish its validity, ICG has been widely compared to several methods which measure stroke volume and cardiac output [3], such as echo-cardiography [4, 5], thermodilution [6,7], and the Fick method [8]. Impedance cardiography has been used for many clinical purposes. It has been used for diagnosing several cardiovascular diseases such as heart failure [9-10] and myocardial infarction [11]. Moreover, it has been used to detect ischemia [12]. Furthermore, it may be useful to examine the effect of different diseases of the autonomic nervous system like the Parkinson's disease [13, 14], for monitoring pregnant women [15, 16], for diagnosis and treatment of patients with hypertension [17, 18]. Likewise, it has been used to monitor surgical operations [19, 20] and dialyzed patients [21, 22].

Mitral Insufficiency (MI), called also mitral regurgitation, is defined as systolic retrograde flow from the left ventricle into the left atrium [23]. MI is the most-frequent valvular heart disease in the world and it is constituted as the second most prevalent valve disease after aortic valve stenosis. The major complication of MI is heart failure, pulmonary hypertension, atrial fibrillation, and death [24]. There are several diagnostic tools in assessing Mitral Insufficiency such as the chest X-ray, the echocardiography, and catheterization. The most interesting diagnostic technique that can provide important information about MI is echo-cardiography, especially the Doppler echocardiography [25–27]. However, this technique is expensive and often not necessary for making a diagnosis [28]. Otherwise, there are few studies, which discussed the ability of the impedance cardiography method to diagnose Mitral Insufficiency. Karnegis *et al.* have calculated an index from the ICG tracings, which may be useful in identifying patients with mitral regurgitation [29]. Schieken *et al.* have determined a mitral regurgitation fraction that is the ratio of the areas of the first systolic and diastolic waves [30]. Viscor *et al.* have discussed the ability of impedance cardiography to measure the change of stroke volume during a Mueller maneuver in patients with mitral regurgitation [31].

Some literature reviews have affirmed that the waves A and O in the ICG waveform were considered as a marker of the mitral insufficiency pathology. Lababidi *et al.*, Takada *et al.* and other groups have demonstrated that the amplitude of the wave A is highly correlated to the left atrial ejection fraction [39]. On the other hand, the maximum of the wave O coincides with the opening of the mitral valve in patients with mitral stenosis [40] and the increase of O-wave size has been marked in patients with mitral valve pathology [41]. Thus, the amplitude of the A and O waves can facilitate the diagnosis of the mitral valve diseases.

The main aim of our study is to compare the change of impedance cardiogram waveforms in control subjects and patients with mitral insufficiency. Firstly, we propose to discuss the amplitudes of A-wave and O-wave. Then, we suggest calculating a parameter "I" that can facilitate the diagnosis of mitral valve diseases. Furthermore, we determine hemodynamic parameters for improving the comparison between the ICG tracings and for evaluating the importance of the proposed parameter "I".

Materials and methods

Subjects

A total of forty subjects participated in this study; twenty control subjects (10 males and 10 females) having an average age of 30 ± 10 years (ranging from 21 to 49 years), and twenty patients with mitral insufficiency (10 males and 10 females) having an average age of 44 ± 8 years (ranging from 24 to 50 years). We selected for this work patients with isolated mitral insufficiency, the patients who had additional diseases were excluded.

Measurements

The ICG recording method used in this study consists of applying a low level current and high frequency (1 mA, 30 kHz), through two electrodes placed in front of and above the leading edge of the heart, respectively. Two other electrodes are placed on the chest of the patient at the level of the aorta, 2 or 3 cm apart permitting registration of impedance variation of the explored thoracic region. During the signal recording, the patient must lie supine, relaxed and in expiratory apnea for a period of 10 seconds [32]. Figure 1 shows the electrode configuration for the measurement of the ICG signal.
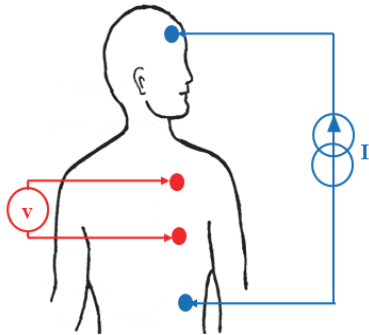

Fig.1: Electrodes configuration for the measurement of the ICG signal.

ICG signal

The typical ICG waveform and its characteristic points are shown in Figure 2. A, B, C, X and O are the main characteristic points of the ICG trace. These points are related to distinct physiological events in the cardiac cycle. The description of those points is presented in Table 1.
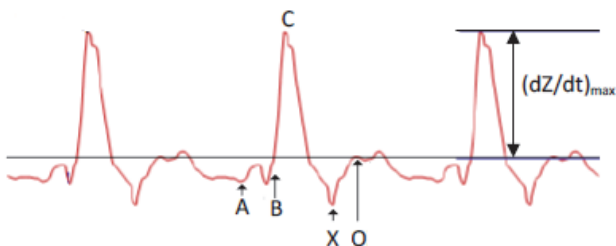

Fig.2: A typical ICG signal.

Table 1. Characteristic points on the ICG signal

Characteristic points	Description
A	Is the beginning of electromechanical systole. It is associated with the atrial contraction.
B	Appears simultaneously with the opening of the aortic valve. The precise identification of a B point is important for accurate calculation of stroke volume and cardiac output [33]. It denotes the beginning of the ejection time. It has been reported that the marker of this point is not always apparent [34] and it may occur at any point on the ascending portion of the signal before the (dZ/dt) max [35, 36].
C	Is taken at the peak of the ICG signal and it corresponds to the ventricular contraction. The amplitude of this point is used to calculate the stroke volume and cardiac output.
X	Is the lowest point after the peak and it is associated with the closure of the aortic valve. It indicates the end of the systole [37].
O	Is associated with changing of the volume during the diastolic phase of the cycle and the maximal opening of the mitral valve [37].

Hemodynamic parameters

The main hemodynamic parameters that can be estimated from the ICG signal are the Heart Rate (HR), the Ejection Time interval (LVET), the Stroke Volume (SV) and the Cardiac Output (CO). The LVET, described as Left Ventricular Ejection Time, is the time interval measured from the B point to the X point; this parameter is used to estimate stroke volume and cardiac output. Moreover, the stoke volume is the volume of blood pumped by the left ventricle during one contraction cycle. Furthermore, the cardiac output is the volume of blood ejected by the heart into the systemic circulation during 1 min [33].

In order to compute the stroke volume, several equations have been proposed by; Kubicek [38], Stramek, Stramek-Bernstein [2], etc. In this work, the Stramek-Bernstein formula is used:

$$SV_{S-B} = \delta \frac{L^3}{4.25 \times Z_0} \, LVET \left(\frac{dZ}{dt}\right)_{max} \, (ml) \qquad (1)$$

Where δ is the weight correction for blood volume, L is the measured thoracic length between voltage sensing electrodes (cm), Z_0 is the basic impedance (Ω), $\left(\frac{dZ}{dt}\right)_{max}$ is

the maximum value of the ICG waveform (Ω/s), and LVET is the ejection time (s).

The cardiac output (CO) is related to stroke volume as follows:

$$CO_{S-B} = SV_{S-B} \times HR \quad (1 / min) \qquad (2)$$
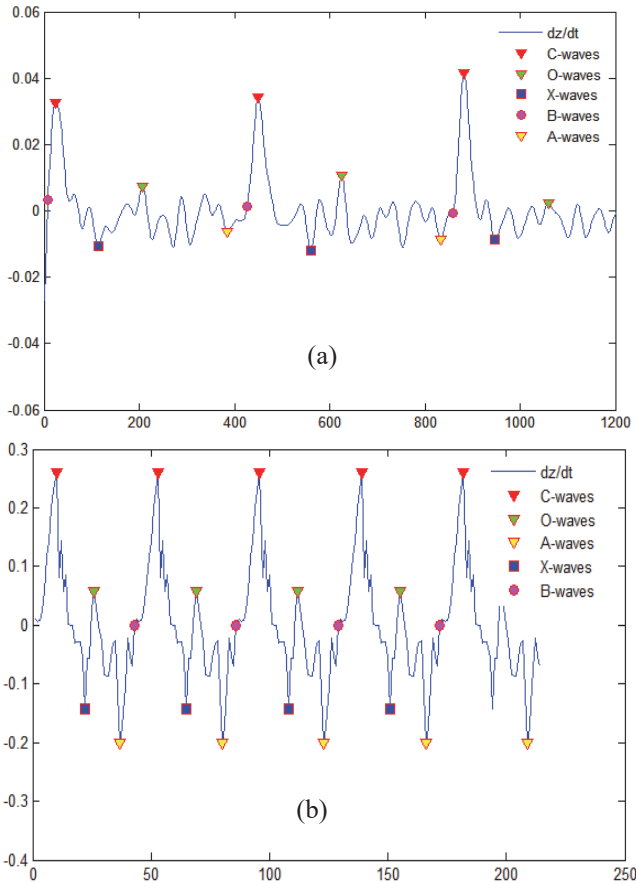
Where HR is the heart rate (bpm).

Fig.3: Impedance Cardiography traces recorded in (a) a control subject and (b) a patient with mitral insufficiency and the detection of the characteristic points (C-waves: red triangles, O-waves: green triangles, A-waves: yellow triangles, X-waves: blue squares, B-waves: pink circles).

Measurements

Throughout this study, a comparison is performed between control subjects and patients with mitral insufficiency. As a first step, the main characteristic points of the ICG waveform are detected by using Matlab software. Figure 3 presents two ICG traces recorded from a control subject (top strip) and from a patient with mitral insufficiency (bottom strip). Based in this figure and by visual inspection, we noticed that the shape of the ICG waveform in a patient with mitral insufficiency is different relative to the control subjects. Mainly, there is a distinct increase in the waves A and O for patients with MI. In order to quantify the increase

of A and O waves, the amplitudes of these waves are computed. Thereafter, a helpful parameter "I" is introduced that can distinguish between control subjects and patients with MI. This parameter is equal to the difference between the amplitudes of wave O and wave A (I=O-A). In the second step, the main hemodynamic parameters are computed and compared for the two groups of subjects.

Statistical Analysis

Data were expressed as mean ± standard deviation (SD). Student's t–test was used to evaluate the difference in parameters between two groups of subjects (control subjects and patients with MI). The Receiver Operating Characteristic (ROC) curve was utilized to evaluate the ability of the O-wave amplitude, the A-wave amplitude, and the diagnosis parameter "I" for discriminating between control subjects and patients with MI. The ROC curve was generated using the MedCalc software, version 16.8. The optimum cut-off, sensitivity (Se), specificity (Sp), negative predictive values (NPV), positive predictive values (PPV), and the area under the ROC curve (AUC) were calculated and compared. A p–value of p<0.05 was considered statistically significant.

Results

The A and O wave amplitudes, and the parameter "I" for control subjects and patients with MI are illustrated in Table 2. Student's t–test showed that there were highly significant differences between control subjects and patients with mitral insufficiency in O wave amplitude, A wave amplitude, and the characteristic parameter "I" (p<0.001).

The O, A, and "I" mean values significantly increased, by a percentage of 77%, 92%, and 89%, respectively, in patients with MI compared to those in the control group (Figure 4). In particular, the diagnosis parameter "I" significantly increased in patients with MI compared to control subjects (2.7±1.5 Ohm/s vs 25.3 ± 0.4 Ohm/s).

Table 2. ICG wave amplitudes for control subjects and patients with mitral insufficiency (mean± SD)

ICG waves	Control subjects	Patients with MI	t–values
O (Ohm/s)·10⁻³	1.2±1.2	5.3±0.4	14.4*
A (Ohm/s)·10⁻³	-1.5 ± 0.2	-20±0.004	403.5*
I (Ohm/s)·10⁻³	2.7 ± 1.5	25.3 ± 0.4	63.24*

Note: O: amplitude of O wave; A: amplitude of A wave; I: difference between the amplitudes of O and A waves; *p<0.001: the differences are highly significant.
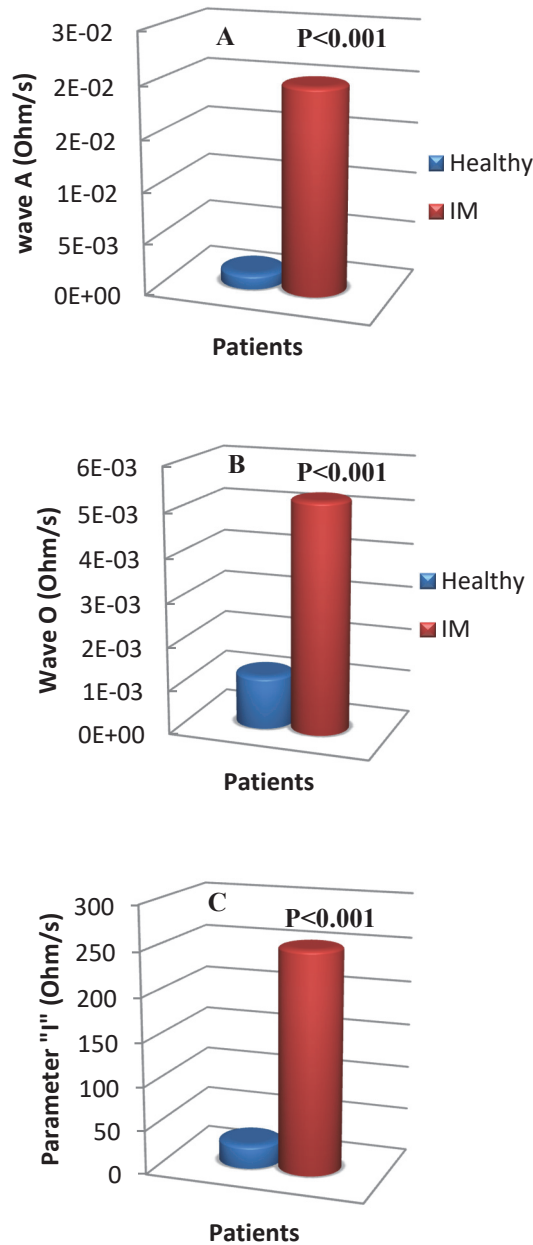
Fig.4: Difference between patients with mitral insufficiency (red) and control subjects (blue): (A) Histogram of the A-wave amplitude, (B) Histogram of the O-wave amplitude, (C) Histogram of the determined parameter "I".

The ROC curve analysis results of the O-wave amplitude, A-wave amplitude, and the parameter "I" are shown in Table 3. For the O-wave, an optimum cut-off >3.64 Ohm/s had a sensitivity of 70%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 100%. The wave A (optimum cut-off ≤ -20 Ohm/s) and the parameter "I" (optimum cut-off > 5.44 Ohm/s), have the same statistical results (sensitivity, specificity positive predictive value, and negative predictive value of 100%). The AUC of the ROC curve for the O-wave amplitude, A-wave amplitude, and "I" were 0.96, 1 and 1, respectively (p < 0.0001) (Figure 5).

Table 3. ROC curve analysis of O-wave amplitude, A-wave amplitude, and the characteristic parameter "I"

Amplitude (Ohm/s)	AUC	P	Optimum cut-off	Se (%)	Sp (%)	PPV (%)	NPV (%)
O	0.96	<0.0001	>3.64	70	100	100	96.8
A	1	<0.0001	≤ -20	100	100	100	100
I	1	<0.0001	>5.44	100	100	100	100

Note: AUC: area under the ROC curve; Se: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value.
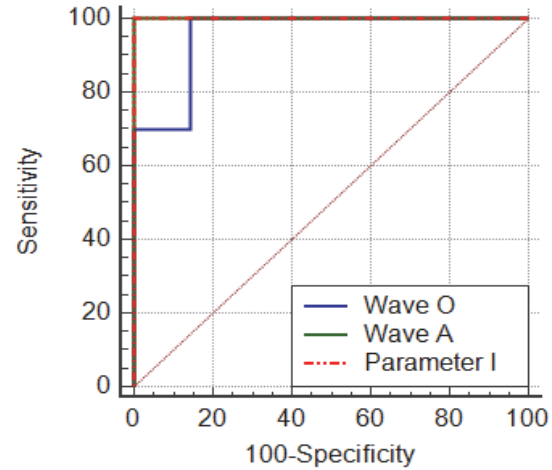

Fig.5: ROC curves for O- wave amplitude (AUC=0.96, p<0.0001), A- wave amplitude (AUC=1, p<0.0001), and the diagnosis parameter "I" (AUC=1, p<0.0001).

As a support for the obtained results, we calculated hemodynamic parameters for the two groups of subjects. The main hemodynamic parameters are the heart rate (HR), the left ventricular ejection time (LVET), the stroke volume (SV) and the cardiac output (CO). We found that, there were highly significant differences between the two groups of subjects in LVET, SV, and CO (p<0.001), but there was no significant difference between the mean heart rate values for control subjects and patients with MI (58±3 bpm vs 58±7 bpm) (Table 4). Figure 6 shows that the SV and CO significantly decreased on patient with MI compared to the control subjects.

Table 4. The computed hemodynamic parameters for control subjects and patients with mitral insufficiency (mean± SD)

ICG waves	Control subjects	Patients with MI	t–values
HR (bpm)	58±3	58±7	n/s
LVET (ms)	270 ± 110	500±76	7.50*
SV (ml)	113.8 ± 17.5	70.7 ± 12.2	8.81*
CO (l/min)	6.6±0.8	4.1±1.1	8.07*

Note: HR: heart rate; LVET: left ventricle ejection time; SV: stroke volume; CO: cardiac output; * p<0.001: the differences are highly significant. n/s: not significant.
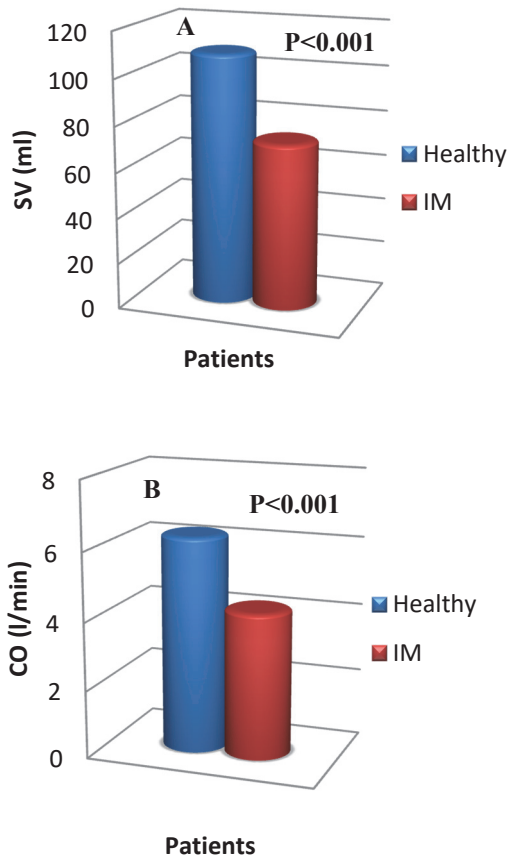
Fig.4: Difference between patients with mitral insufficiency (red) and control subjects (blue): (A) Histogram of stroke volume, (B) Histogram of cardiac output.

Discussion

The purpose of our study is to investigate the usefulness of the abnormalities of impedance cardiogram tracing in the diagnosis of mitral insufficiency disease (MI). The abnormalities of ICG waveforms were reproducible for each patient with MI. To facilitate the diagnosis of patients with MI, we proposed to discuss the amplitude of the A-waves and O-waves, and to calculate a characteristic parameter "I". As described above, the A-wave is associated with the atrial contraction and the O-wave is associated with the opening of the mitral valve. The parameter "I" was obtained from the difference between the O and A wave amplitudes (I= O-A) of the ICG tracings. Therefore, "I" is affected by the systolic and diastolic parts of the ICG tracing. The results of this study demonstrate that the O- and A- waves are marked as significant parameters in the distinction of the mitral insufficiency disease. Thus, "I" is considered as an efficient tool that can be used to diagnose patients with MI (the diagnosis parameter "I" had sensitivity and specificity of 100%).

In order to evaluate the obtained results, we compared the main hemodynamic parameters (SV, CO, and LVET) for the two groups of patients. We found that the SV and CO significantly decreased in patients with MI compared to the control subjects. In fact, previous studies have shown that the SV and the CO decrease in patients with MI; these results were correlated with catheterization [29, 30]. Hence, the analysis of hemodynamic parameters, especially the SV and the CO, has been found useful to diagnose the mitral insufficiency disease.

In order to diagnose pathologies, we suggest an automatical, simple, non-invasive, cheap and useful technique. The ICG technique has these characteristics, and it is selected to evaluate the performance of our study. Generally, the mitral insufficiency disease is diagnosed with Doppler echocardiography, which is expensive and requires expertise. Therefore, we used the impedance cardiography technique in order to facilitate the diagnosis. The results of the present study demonstrate that the ICG, especially the derived parameter "I", is considered as a simple and non-invasive tool for diagnosing the mitral insufficiency disease.

The main limitation of our study was the artifacts that can affect the shape of the ICG signal and can, therefore, affect the detection of the characteristic waves O and A. The motion and the respiration noises are the most discriminant kinds of artifacts in the ICG signal. Thus, an ICG signal denoising step is necessary to ensure better results for this present study. ICG signal denoising details have been published previously [42].

In the future research, we will investigate and try to determine a specific parameter to evaluate the severity of the MI diseases. In addition, a larger number of patient are needed in order to further quantify and recommend our method.

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