Study of longitudinal myocardial deformation in patients with ischemic cardiopathy

Estudio de la deformación miocárdica longitudinal en pacientes con cardiopatía isquémica

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Abstract

Introduction: Cardiovascular diseases are the leading cause of death in Cuba and most of the developed countries. Two-dimensional speckle tracking echocardiography (2D STE) is a recent technique in the evaluation of cardiac function.

Objectives: The objectives of this study were to determine the relationship between myocardial deformation measured by 2D speckle tracking (2D ST) and coronary circulation in patients with ischemic heart disease, in the CIMEQ, for 1 year.

Material and method: An analytical and cross-sectional study was carried out with 55 patients with an indication for coronary angiography who underwent 2D echocardiography and 2D ST study with longitudinal strain measurement (LSM). Two groups: significant coronary disease (SCD = 32) and not SCD (NSCD = 23) were created. SSPS was used to analyze the results.

Results: The average age was higher in SCD (55.6 ± 9.3 vs. 61.8 ± 8.8 , $p = 0.014$). Men with SCD (47.3%), hypertensive (SCD = 90.6% and NSCD = 65.2%, $p = 0.02$), and smokers (SCD = 59.4% and NSCD = 17.4%, $p = 0.002$) predominated. The most frequent diagnosis was chronic stable angina (87%). Three-vessel disease (75%) prevailed in SCD. The LSM was lower in SCD (-20.0 ± 3.2 vs. -22.1 ± 3.6 , $p = 0.035$; AUC = 0.458). There were no differences in LSM according to the number of significantly diseased vessels. **Conclusions:** The results found do not justify the use of 2D ST to discriminate SCD.

Key words: Ischemic cardiopathy. Two-dimensional speckle tracking echocardiography. Longitudinal myocardial deformation. Cardiac function.

Resumen

Introducción: Las enfermedades cardiovasculares constituyen la primera causa de muerte en Cuba y la mayoría de los países desarrollados. La ecocardiografía con speckle tracking bidimensional (ST 2D) es una técnica reciente en la evaluación de la función cardíaca. **Objetivos:** Determinar la relación entre la deformación miocárdica medida por ST 2D y el estado de la circulación coronaria en pacientes con cardiopatía isquémica, en el CIMEQ, durante un año. **Material y método:** Se realizó un estudio analítico y transversal con 55 pacientes con indicación de coronariografía sometidos a ecocardiograma bidimensional y estudio de ST 2D con medición de la deformación longitudinal (DLG). Se crearon dos grupos: enfermedad coronaria significativa (ECS = 32) y no significativa (ECNS = 23). Se utilizó SSPS para análisis de los resultados. **Resultados:** La edad

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promedio fue mayor en la ECS (55.6 ± 9.3 vs. 61.8 ± 8.8 ; $p = 0.014$). Predominaron los hombres con ECS (47.3%), los hipertensos (ECS = 90.6% y ENCS = 65.2%; $p = 0.02$) y los fumadores (ECS = 59.4% y ENCS = 17.4%; $p = 0.002$). El diagnóstico más frecuente fue la angina crónica estable (87%). En la ECS predominó la enfermedad de tres vasos (75%). La DLG fue menor en la ECS [$(-20.0 \pm 3.2$ vs. -22.1 ± 3.6 ; $p = 0.035$); AUC = 0.458]. No hubo diferencias en la DLG según el número de vasos significativamente afectados. **Conclusiones:** Los resultados encontrados no justifican el empleo del ST 2D para diferenciar la ECS.

Palabras clave: Cardiopatía isquémica. Ecocardiografía con speckle tracking 2D. Deformación miocárdica longitudinal. Función cardíaca.

Introduction

Cardiovascular diseases are the leading cause of death in most developed countries¹. At present, more than 20,000 Cubans die every year only for this cause².

Ischemic heart disease is a condition in which myocardial perfusion and tissue oxygenation are compromised, causing changes in the ventricular function³.

Assessing the effect of ischemic heart disease on cardiac function is one of the systematic objectives of echocardiography laboratories⁴. The most widely used echocardiographic variable to quantify left ventricular (LV) systolic function is the LV ejection fraction (LVEF), and its determination by echocardiography crucially depends on the operator's expertise, in addition to being modified by significant intraobserver and interobserver variability⁵.

LVEF provides a general index of the LV chamber function, without taking into account the relative role of the different components of myocardial function (deformation in different directions and rotation), which can be affected at varying degrees, despite the LVEF continuing at normal values^{6,7}.

Echocardiography with myocardial strain analysis (two-dimensional speckle-tracking echocardiography 2D STE) has become a regular technique for the evaluation of different heart diseases. The study by means of the tracking of acoustic markers has emerged as a novel technique for quantitative evaluation of myocardial global and segmental function. Myocardial strain alterations usually occur before visual alterations in myocardial wall regional movement, which confers value to their study^{8,9}.

Techniques such as STE have improved myocardial strain non-invasive evaluation in comparison with conventional 2D approaches and provide accurate information at myocardial diseases initial phases¹⁰. Data on strain are obtained by automated, frame by frame measurement of the distance between two points of each LV segment during the cardiac cycle in three dimensions (radial, circumferential, and longitudinal)^{11,12}.

Coronary angiography has been the invasive diagnostic technique par excellence in the anatomical study of coronary artery disease. Although generally, this is a safe investigation, it is not free of complications, in addition to its cost being elevated^{13,14}. Therefore, simple and non-invasive methods are required, which improve the selection and prognosis of patients referred for coronary angiography⁴. Despite the numerous works that confirm the usefulness of the technique in resting conditions, recent publications question it in this context^{15,16}, this has led to the performance of this work, the purpose of which was to determine the relationship between myocardial strain measured by 2D speckle tracking electrocardiography and coronary artery circulation status in patients with suspected ischemic heart disease.

Material and method

A cross-sectional, analytical, and observational study was carried out during the months from January 2016 to January 2017 at the CIMEQ hospital. The sample included all patients with a clinical diagnosis of ischemic heart disease who attended the hemodynamics laboratory to undergo coronary angiography. The final sample was comprised of 55 patients based on the following criteria: age older than 18 years, patients with an optimal acoustic window and individuals who signed the informed consent; patients with oncological diseases, severe valve disease, impaired contractility at rest, and heart rate disorders were excluded from the study.

The following variables were studied: age, gender, atherogenic risk factors, presence of coronary artery disease, extension, and affected artery, as well as those related to M-mode and 2D echocardiogram and myocardial strain, whose normal values were taken into account according to the American Heart Association and the European Association of Cardiovascular Imaging recommendations for the quantification of cardiac chambers in adults¹⁷.

Study participants were examined by transthoracic echocardiography using the EPIQ7 commercial ultrasound system (Philips Medical Systems) equipped with a 2.5-MHz transducer. All images were obtained with the same frame rate (50-80 frames/s). The moment of aortic valve closure was determined when the movement of the said valve was examined in the long axis apical projection.

The analysis of the speckle tracking images was carried with the QLab commercial software. 4C, 2C, and 3C apical projections were used for segmental and global longitudinal strain (GLS) determinations. The program automatically marked endocardial and epicardial borders, in addition to automatically splitting each echocardiographic projection and considering segmentation in 17 segments that are related to epicardial arteries perfusion area. This provided an automated tracking confirmation, expressed in segmental and global percentages. The myocardial strain values are presented in the form of a bullseye diagram (polar map).

Coronary angiography protocol

For the diagnostic coronary angiography, the common techniques of this procedure were used. The Integrus HM 3000-Philips equipment (Medical Systems-Nederland B. V.) was used. The Phillips quantification program was used for the Integrus line in the quantitative coronary angiography.

Statistical analysis

Statistical analysis was carried out with the help of the Statistical Package for the Scientific System SPSS package. Kolmogorov-Smirnov test was used to assess the normality of variables. Summary measures were used for qualitative data (ratios and percentages) and quantitative data (arithmetic mean and standard deviation). The Chi-square test was used for the comparison of groups with qualitative variables. Student's t-test was used to compare continuous variables (according to the characteristics of their distribution) between two groups, and a one-factor ANOVA was used for comparison between more than two groups. A value of 0.05 was taken as a significance point.

Ethical aspects

The research respected the ethical bases of imaging examination in human subjects. The free acceptance

of the patient, previously informed, that he would undergo harmless diagnostic procedures, was obtained.

Limitations

Among the limitations of the research, it is important mentioning that the sample employed is small since it consisted of patients undergoing coronary angiography at CIMEQ hemodynamics laboratory, which is a site that receives the least amount of emergency cases in Cuba.

Results

Fifty-five patients were studied, out of which 38 (69.1%) were male. The mean age was 59 years. There were 32 (58.2%) cases with significant coronary disease (SCD). Almost half of the patients corresponded to men with SCD (47.3%). Mean age was significantly higher in patients with SCD (55.6 ± 9.3 vs. 61.8 ± 8.8 ; $p = 0.014$).

The evaluated cardiovascular risk factors were all more common in the group of subjects with SCD. The risk factor that was most often observed, both in individuals with SCD and in those who had non-SCD (NSCD), was high blood pressure (HBP), although it was more common among the former (90.6%). Of note, almost 60% of those who had SCD were smokers, with a marked difference between both groups ($p = 0.002$).

Regarding the clinical diagnosis, cases with stable chronic angina were more common (48 patients, 87.2%), which represented more than three-quarters of all patients.

Of the individuals with SCD, a predominance of those with three-vessel arterial disease, which was present in 75% of them, was observed. The echocardiographic variables used for the evaluation of the LV systolic and diastolic functions showed no differences of interest between both groups, which show their homogeneity in that sense. The fact that the patients selected in the research had a normal LVEF stands out (Table 1).

Table 2 and figure 1 show GLS mean and standard deviation values based on the presence or not of SCD. GLS was lower among patients with SCD than among those who had NSCD (-20.0 ± 3.2 vs. -22.1 ± 3.6 ; $p = 0.035$). This variable had the same behavior when analyzed by 2C (-19.7 ± 4.5 vs. -23.0 ± 4.1 ; $p = 0.008$), 4C (-20.7 ± 3.7 vs. -21.6 ± 3.6 , $p = 0.381$), and 3C views (-19.4 ± 3.1 vs. -22.2 ± 4.8 , $p = 0.016$). Although there are differences between both groups, there are values that overlap with each other, which makes it difficult finding a cutoff value to differentiate them.

Table 1. Echocardiographic variables according to coronary artery disease severity

Echocardiographic variables	NSCD (n = 11) Mean ± SD	SCD (n = 25) Mean ± SD	p
Septum diastole	10.8 ± 2.5	11.3 ± 1.8	0.415
Septum systole	15.6 ± 2.9	15.1 ± 2.4	0.961
Posterior w. diastole	10.3 ± 1.3	11.3 ± 2.4	0.075
Posterior w. systole	15.7 ± 2.2	16.9 ± 3.6	0.248
LV diastole	45.8 ± 4.9	45.8 ± 6.4	0.998
LV systole	29.3 ± 5.2	30.5 ± 7.9	0.537
EDV	88.5 ± 27.9	99.9 ± 36.0	0.552
ESV	37.0 ± 14.4	40.1 ± 20.1	0.773
LVEF (Simpson)	55.5 ± 7.5	61.6 ± 7.5	0.183
FS	34.9 ± 7.4	34.8 ± 8.2	0.878
EDV	83.1 ± 32.8	93.9 ± 23.9	0.458
ESV	30.8 ± 11.8	36.4 ± 11.4	0.125
LVEF	62.6 ± 8.3	60.7 ± 6.5	0.371
E-wave	72.7 ± 13.5	82.1 ± 19.1	0.127
A-wave	72.2 ± 14.9	80.6 ± 20.3	0.157
E/A ratio	1.0 ± 0.3	1.1 ± 0.5	0.594
MPV	49.7 ± 24.1	47.0 ± 12.0	0.794
e'	10.2 ± 3.6	9.6 ± 4.4	0.468
s'	6.7 ± 1.5	7.2 ± 2.4	0.265
E/e'	8.1 ± 3.7	9.7 ± 4.0	0.650

Posterior w. diastole: posterior wall in diastole; Posterior w. systole: posterior wall in systole; EDV: end-diastolic volume; ESV: end-systolic volume; FS: fractional shortening; MPV: mitral valve flow propagation velocity.

Table 2. Relationship of global longitudinal and segmental strains according to coronary artery disease severity

Speckle tracking longitudinal variables	NSCD (n = 23) Mean ± SD	SCD (n = 32) Mean ± SD	p
GLS	-22.1 ± 3.6	-20.0 ± 3.2	0.035
2C GLS	-23.0 ± 4.1	-19.7 ± 4.5	0.008
4C GLS	-21.6 ± 3.6	-20.7 ± 3.7	0.381
3C GLS	-22.2 ± 4.8	-19.4 ± 3.1	0.016

GLS: global longitudinal strain; 2C GLS: 2-chamber global longitudinal strain; 4C GLS: 4-chamber global longitudinal strain; 3C GLS: 3-chamber global longitudinal strain.

Figure 2 shows the receiver operating characteristic (ROC) curve for SCD prediction through GLS. The area under the curve is low, which does not allow establishing

Figure 1. Myocardial global longitudinal strain according to coronary artery disease severity. **Figure 2.** Receiver operating characteristic curves for significant coronary disease prediction.

values to define patients with degrees of sensitivity and specificity that enable using the technique for that purpose.

When myocardial GLS was analyzed according to the number of vessels with angiographically significant lesions, it was noticed that there were no between-group differences in any of the cases (Fig. 3).

Table 3 shows average strains of cardiac segments related to main epicardial arteries possible irrigation territories: anterior descending, circumflex, and right

Figure 3. Myocardial global longitudinal strain based on the extent of coronary artery disease.

Table 3. Myocardial segments average strain in relation to the coronary artery irrigation area and coronary artery disease severity

Speckle tracking variables	NSD Mean ± SD	SD (n = 32) Mean ± SD	p
	n = 25	n = 28	
Anterior descending Longitudinal strain	-21.6 ± 3.5	-19.9 ± 3.4	0.093
	n = 31	n = 22	
Circumflex Longitudinal strain	-20.7 ± 3.4	-19.1 ± 3.3	0.113
	n = 32	n = 21	
Right coronary Longitudinal strain	-19.6 ± 3.4	-17.9 ± 2.7	0.092

NSD: non-significant disease; SD: significant disease.

coronary artery, according to a previously established and apparently uniform anatomical pattern. The segments related to significantly compromised arteries had lower longitudinal strain mean values than those that had no arteries with significant obstruction, although they did not show statistically significant differences.

Discussion

The male gender predominated in this study, which is consistent with the fact that the highest proportion of

patients were aged 50-69 years, an age period where cardiovascular diseases are more common in men since women are more protected by known hormonal factors at this stage of life^{18,19}.

This result is consistent with those obtained by groups of the Institute of Cardiology and Cardiovascular Surgery (ICCCV – *Instituto de Cardiología y Cirugía Cardiovascular*), the Ameijeiras Hospital, and Cardio-centro Ernesto Guevara, from Villa Clara, both in patient gender and ages²⁰⁻²².

Among the subjects with SCD, a high prevalence of risk factors was identified. HBP was the most frequently identified. Blood pressure figures are correlated with the incidence of coronary artery disease and cerebrovascular disease^{23,24}.

According to the results of the 3rd National Survey on Risk Factors (III ENFR – *III Encuesta Nacional Sobre Factores de Riesgo*), HBP global prevalence in Cuba is 30.9% in the population ≥ 15 years, with an increase from 55 years onward. These results are similar to those published in most European countries^{1,25}.

Smoking is an important risk factor related to endothelial damage and the formation of plaques in the coronary arteries. Actually, 29% of deaths due to ischemic heart disease have tobacco as the main cause²⁵⁻²⁷.

The fact that three-quarters of patients have a clinical diagnosis of stable chronic angina is of great importance when interpreting the results since the study sample was made up of patients undergoing coronary angiography at CIMEQ hemodynamics laboratory, a

site where acute patients are less frequent, and their representation within the sample was therefore lower.

Three-quarters of the subjects with SCD that were investigated had the three-vessel disease, which is related to a higher proportion of ischemic myocardium and; therefore, it would justify the performance of coronary angiography inpatient risk stratification⁴.

It has been suggested that repeated episodes of transient myocardial ischemia generate small degrees of myocardial stunning, which, despite not being sufficient to produce visual disturbances in segmental contractility, can modify longitudinal strain. This justifies the numerous studies that have been carried out comparing myocardial strain at rest between patients with SCD and subjects with NSCD^{10,13,28,29}.

Amundsen et al.³⁰ validated the application of 2D STE for clinical use by providing precise measurements, which turned it into a potential patient-bedside clinical tool to quantify myocardial regional function.

In the research that was carried out, myocardial GLS values were observed to be lower in patients with SCD in comparison with those with non-significant disease, which is consistent with several published studies^{10,13,28,29,31}.

Biering-Sorensen et al.³² found that, in patients with suspected stable angina, GLS was significantly lower in subjects with CAD in comparison with those who did not have it.

On the other hand, Choi et al.³³ proposed its usefulness to predict trunk or three-vessel disease, where, depending on the area under the curve, a -17.9% value could be used to differentiate severe CAD with sensitivity and specificity of 79%.

Although the difference between groups is significant in the study, it is important to note that, in the group of patients with NSCD, there are patients with possible microvascular damage, slow coronary flows, or lesions in one or more coronary arteries that do not exceed 50% of the vessel lumen, they are essentially sick patients, and the myocardial strain values may therefore be decreased (Figs. 4 and 5), and maybe they overlap with those with significant coronary lesions. The presence of risk factors causes a disruption in the myocardial interstitial matrix due to microvascular ischemia, fibrosis, and collagen substitution, which can lead to microscopic changes in the myocardial fiber that generates subclinical myocardial dysfunction, potentially detectable through the study of myocardial strain³⁴.

Based on the above, it can be explained that, when analyzing the ROC curve, the area under it does not justify the application of the tool to discern between the patient with significantly compromised coronary arteries

Figure 4. Myocardial global longitudinal strain polar map in a patient with a clinical diagnosis of progressively-worsening angina.

Figure 5. Cardiac catheterization image in a right coronary artery with the slow coronary flow.

and the patient in whom the coronaries may be normal or slightly obstructed, given that the values overlap between each other.

Regarding myocardial strains, and in relationship with epicardial arteries and their possible irrigation areas, although they were lower in the segments related to arteries with significant block, their differences were not relevant in statistical terms. Coronary anatomy is variable,

and assessing the territorial function according to a specific vascular area may therefore not reflect the true coronary artery distribution. Norum et al.³⁵ published similar results.

Although the body of evidence for its use in usual clinical echocardiography is much less than that of LVEF, GLS measurements have been shown to be robust and reproducible in several studies. GLS is a stronger predictor of all causes of mortality in comparison with LVEF, according to 16 studies with a total of 5721 patients³⁶. However, LVEF is still the main parameter for heart function evaluation. GLS is particularly important in patients with normal or minimally decreased LVEF since it is more sensitive for myocardial disease early detection^{37,38}.

However, its implementation and widespread use are still not possible, especially because there is no current agreement on its usefulness due to the variability in software and vendors, in addition to the need to unify criteria with regard to its performance by vendors of equipment capable of performing it¹⁰.

Finally, the greatest benefit of using 2D ST is that it makes echocardiography more objective and quantitative, which turns it into a more complete and accurate heart examination. Many complementary studies can be expensive. Despite current technological limitations, it is likely that GLS will become a standard clinical tool in the near future, inasmuch as imaging experts gain confidence in its measurement and clinicians become more familiar with its value. To be effective in terms of cost, echocardiography should be a definitive study³⁷. The use of 2D ST is a big step in that direction.

In the research conducted in patients with ischemic heart disease, men in the sixth decade of life were predominant. The most common risk factors were HBP and smoking, with the latter being present in more than half the patients with SCD. The highest proportion of patients had a clinical diagnosis of stable chronic angina. The 2D echocardiography values showed similar data in patients with NSCD and SCD. The GLS values were lower in subjects with SCD, as well as the segmental values in relation to the affected arteries. There were no differences in GLS according to the number of significantly compromised vessels. Despite the above, the modest results do not justify the use of 2D ST to differentiate CAD.

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Conflicts of interests

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patients or subjects referred to in the article. This document is in the possession of the corresponding author.

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