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Global circumferential strain in patients with ischemic heart disease

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The authors declare no competing interests.

Abbreviations
2D-ST: two-dimensional speckle-tracking
GCS: global circumferential strain
LVEF: left ventricular ejection fraction
NSCAD: non-significant coronary artery disease
SCAD: significant coronary artery disease

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ABSTRACT

Introduction: Cardiovascular diseases are the top cause of death in Cuba as well as in most developed countries. Two-dimensional speckle-tracking (2D-ST) echocardiography is a recent technique in the evaluation of cardiac function.
Objectives: To determine the relationship between global circumferential strain (GCS) measured through 2D-ST echocardiography and the state of coronary circulation in patients with ischemic heart disease.
Method: An analytical, cross-sectional study was carried out on 55 patients with indication of coronary angiography, who underwent echocardiography to measure the GCS through 2D-ST at the Centro de Investigaciones Medico Quirúrgicas (CIMEQ, Havana, Cuba), during one year. Two groups were created: with significant coronary artery disease (SCAD = 32) and non-significant coronary artery disease (NSCAD = 23). The statistical package for the social sciences (SPSS) was used to analyze the results.
Results: Mean age was higher in the SCAD group (55.6 ± 9.3 vs. 61.8± 8.8, p=0.014). Men with SCAD (47.3%), patients with high blood pressure (SCAD=90.6% and NSCAD=65.2%, p=0.02) and smokers (SCAD=59.4% and NSCAD=17.4%, p=0.002) predominated. The most frequent diagnosis was chronic stable angina (87%). Three-vessel disease predominated in the SCAD group (75%). The GCS was lower in the SCAD group [(-19.5.0±3.8 vs. -25.2±5.7, p=0.033); area under the curve=0.208]. There were no differences in GCS according to the number of significantly diseased vessels.
Conclusions: The results found do not justify the use of GCS through 2D-ST echocardiography to discriminate the presence or nor of SCAD.
Keywords: Ischemic heart disease, Myocardial ischemia, Bidimensional speckle-tracking echocardiography, Global circumferential strain, Cardiac performance

Deformación miocárdica (strain) circunferencial global en pacientes con cardiopatía isquémica

RESUMEN

Introducción: Las enfermedades cardiovasculares constituyen la primera causa de muerte en Cuba y la mayoría de los países desarrollados. La ecocardiografía con rastreo de marcas o speckle-tracking bidimensional (ST-2D) es una técnica reciente en la evaluación de la función cardíaca.
Objetivo: Determinar la relación entre la deformación miocárdica (strain) circunferencial (GCS) medida por ST-2D y el estado de la circulación coronaria, en pacientes con cardiopatía isquémica.

Authors' contribution
IRF and APB: Idea and design of the research; obtaining, analyzing and interpreting the data, as well as writing the manuscript.
AND, AYRN and OAAM: Analysis and interpretation of data as well as collaboration in writing the manuscript.
All authors critically reviewed the manuscript and approved the final report.

Método: Se realizó un estudio analítico, transversal, con 55 pacientes con indicación de coronariografía a los que se les realizó ecocardiograma para medir la GCS mediante ST-2D, en el Centro de Investigaciones Médico Quirúrgicas (CIMEQ, La Habana, Cuba), durante un año. Se crearon dos grupos: con enfermedad coronaria significativa (ECS=32) y no significativa (ECNS=23). Se utilizó SSPS para análisis de los resultados.
Resultados: La edad promedio fue mayor en 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 ECS predominó la enfermedad de tres vasos (75%). La GCS fue menor en ECS [(-19,5±3.8 vs. -25,2±5,7; p=0,033); área bajo la curva = 0,208]. No hubo diferencias en GCS, según el número de vasos significativamente enfermos.
Conclusiones: Los resultados encontrados no justifican el empleo de la GCS por ST-2D para discriminar la presencia o no de ECS.
Palabras clave: Cardiopatía isquémica, Isquemia miocárdica, Ecocardiografía con speckle-tracking bidimensional, Deformación miocárdica circunferencial, Función cardíaca

INTRODUCTION

Cardiovascular disease is the top cause of death in most developed countries. There are multiple resources devoted to cardiology research to reverse such unfavorable statistics[1]. Currently, for this cause alone, more than 20,000 Cubans die annually[2].

Ischemic heart disease is a disease in which there is an alteration of myocardial perfusion and tissue oxygenation, which leads to changes in the ventricular function[3]. Assessing the impact of ischemic heart disease on the cardiac function is one of the routine goals of echocardiography laboratories[4]. The most widely used echocardiographic variable to quantify the left ventricular systolic function is its ejection fraction (LVEF); its determination by echocardiography crucially depends on the expert knowledge of the operator and, in addition, it is affected by a significant intraobserver and interobserver variability[5].

The general function of the LV is the result of the contraction and relaxation of a complex architecture of myocardial fibers, a contraction that determines changes in the size and shape of the LV that are the result of simultaneous longitudinal shortening, circumferential rotation and radial thickening of the myocardium[6,7].

Echocardiography with analysis of the myocardial strain has become a routine technique for the evaluation of different heart diseases. The study by means of tracing marks or points (two-dimensional speckle-tracking [2D-ST]) has emerged as a novel technique for the quantitative evaluation of the myocardium's global and segmental function. Alterations in its strain usually appear before visual alterations in the regional movement of the myocardial wall, which gives value to their study[8,9]. Techniques such as 2D-ST have improved the non-invasive assessment of myocardial strain compared to the conventional two-dimensional ones, and provide accurate information in the initial phases of myocardial diseases[10]. The strain data is obtained by means of an automatic measurement, frame by frame, of the distance between two points of each segment of the LV during the cardiac cycle, in three dimensions (radial, circumferential and longitudinal)[11,12].

Conventional coronary angiography, although it is a generally safe research method, is not exempt from complications, besides having high costs[13,14]. Therefore, simple, non-invasive methods are needed to improve the selection and prognosis of patients referred for this angiographic procedure[4].

Many studies support the usefulness of the technique, in at rest conditions, for the identification of patients with high-risk ischemic heart disease, determined by the presence of left main coronary artery disease or three-vessel disease. It is not well-known whether radial and circumferential strains can predict the presence, extent, and location of significant coronary artery disease. Recent publications deny its usefulness in this context[15,16], motivations that have led to this work in order to determine the relationship between circumferential myocardial strain —measured by 2D-ST— and the state of the coronary circulation, in patients with suspected ischemic heart disease.

METHOD

An analytical cross-sectional observational study was carried out between January 2016 and January 2017, at the *Centro de Investigaciones Médico Quirúrgicas (CIMEQ),* in Havana, Cuba. The population of study was represented by all those patients who attended the hemodynamics laboratory for coronary angiography with the clinical diagnosis of ischemic heart disease. The sample consisted of 55 patients who met the following criteria: over 18 years of age, optimal acoustic window for echocardiography, and signing the informed consent to participate in the research.

Patients with oncological diseases, severe valvular heart disease, impaired contractility at rest, heart rhythm disorders, and those where accurate echocardiographic images were not obtained to complete the study, were excluded.

Variables

The following variables were studied: age, sex, atherogenic risk factors, presence and extent of coronary artery disease, and affected artery; as well as those related to the M-mode echocardiogram, two-dimensional and myocardial strain, whose normal values were taken into account, according to the recommendations for the quantification of cardiac chambers in adults of the American Heart Association and the European Association of Cardiovascular Imaging[17].

Echocardiogram

Study participants were examined by transthoracic echocardiography, using a commercial EPIQ7 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).

Two-dimensional (gray scale) projections were obtained with an apical (four- and two-chamber, and long-axis views) and parasternal approach (long-axis and short-axis views at the mitral valve, papillary muscles, and apex). Records of three consecutive cardiac cycles of each projection were obtained, while the patient maintained the apnea at the end of expiration. Special care was taken to obtain correct apical and parasternal images using standard anatomical landmarks.

The analysis of the speckle-tracking images was performed with the commercial software QLab (Philips Medical Systems). Short-axis projections were used for the measurement of the segmental and global circumferential strain. The program automatically marked the endocardial and epicardial borders, and automatically divided each echocardiographic view into several of the 17 segments that are related to the perfusion territory of the epicardial arteries. In addition, it provided automated confirmation of the 2D-ST scan (which was verified by the operator) and generated strain values, expressed in global and segmental percentages. If there were more than three of the 17 LV segments with inadequate tracing, the patient was excluded from the study. The myocardial strain values are presented in the form of curves and a polar map, or a bull's-eye diagram (**Figure 1**).

Coronary angiography protocol

Classic techniques were used in this study to carry out the diagnostic procedure, with an INTEGRIS HM3000 - PHILIPS MEDICAL SYSTEMS - NEDERLAND B.V. equipment; the Phillips quantification program was used for the INTEGRIS line in the quantitative coronary angiography.

Statistical analysis

The statistical analysis was carried out using the Statistical Package Scientific System SPSS (v. 18). The Kolmogorov-Smirnov test was used to evaluate the normality of the variables. Summary measures were used for qualitative (ratios, percent) and quantitative data (arithmetic mean and standard deviation). The χ^2 was used to compare groups with qualitative variables. The Student's t test was used for the comparison of continuous variables (according to the characteristics of their distribution) between two groups and one-way ANOVA (ANalysis Of VAriance), for the comparison among more than two groups. The value 0.05 was taken as the significance level.

Ethical aspects

In the research, the ethical bases of human examinations were respected and the free acceptance of the patient (consent) was obtained, previously informed that the echocardiogram was a safe diagnostic procedure.

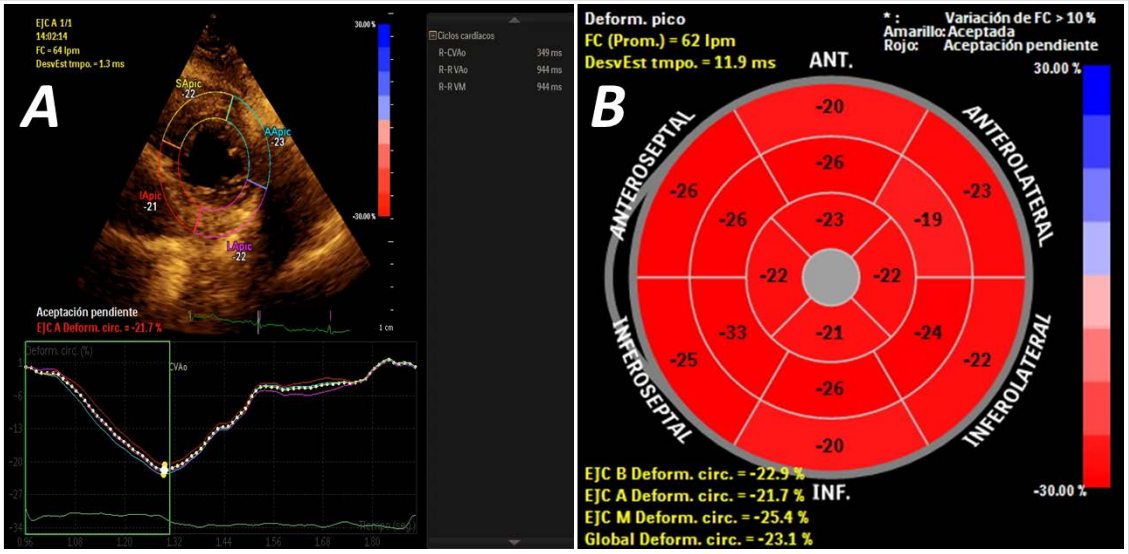

Figure 1. Circumferential myocardial strain values. **A.** Parasternal short axis view of the left ventricle. **B.** Diagram of the polar map (bull's-eye diagram).

RESULTS

A total of 55 patients were studied, 38 (69.1%) of them male. The mean age was 59 years. There were 32 (58.2%) cases with significant coronary artery disease (SCD) and almost half of those researched (47.3%) were men with SCAD (**Table 1**). The mean age was significantly higher in the patients with SCAD (55.6±9.3 *vs.* 61.8± 8.8; p=0.014).

Within the two groups, the patients had an average body mass index above 25 kg/m^2, with no differences between them. During the time the echocardiographic research was carried out, the stability of the hemodynamic variables (heart rate and blood pressure) could be verified between the patients in both groups.

The cardiovascular risk factors evaluated were all more frequent in the group of patients with SCAD. The one that presented more frequently, both in patients with SCAD and in those with non-significant coronary disease (NSCAD), was the high blood pressure (HBO); although it was more frequent (90.6%) among the former. It is striking that almost 60% of those who presented SCAD were smokers, with an important difference between the two

Table 1. Characterization of patients according to the presence of significant or non-significant coronary artery disease.

Initial variables	Coronary artery disease		p
	Non-significant (n=23)	Significant (n=32)	
Age (years)	55.6 ± 9.3	61.8 ± 8.8	0.014
Male	12 (21.8%)	26 (47.3%)	
BMI (kg/m^2)	26.5 ± 4.1	26.1 ± 3.5	0.780
Heart rate	64.6 ± 10.5	66.8 ± 11.5	
Systolic HBP	130 ± 8.9	131 ± 6.7	0.335
Diastolic BP	81 ± 10	80 ± 11	0.350
Risk factors			
Smoking	4 (17.4)	19 (59.4%)	0.002
High blood pressure	15 (65.2%)	29 (90.6%)	0.020
Dyslipidemia	6 (26.1%)	11 (34.4%)	0.512
Obesity	4 (17.4%)	8 (25.0%)	0.500
Diabetes mellitus	3 (13.0%)	9 (28.1%)	0.182
Clinic			
Chronic stable angina	21 (91.3%)	27 (84.4%)	0.002
Unstable angina	2 (8.7%)	5 (15.6%)	
Extension			
One-vessel disease	-	4 (12.5%)	0.273
Two-vessel disease	1 (4.3%)	4 (12.5%)	
Three-vessel disease	-	24 (75.0%)	

Values show mean ± standard deviation and n (%).
BMI, body mass index; BP, blood pressure

Table 2. Echocardiographic variables according to coronary artery disease.

Echocardiographic variables	Coronary artery disease		*p*
	Non-significant (n=11)	Significant (n=25)	
Diastole IVS (mm)	10.8 ± 2.5	11.3 ± 1.8	0.415
Systole IVS (mm)	15.6 ± 2.9	15.1 ± 2.4	0.961
Diastole PW (mm)	10.3 ± 1.3	11.3 ± 2.4	0.075
Systole PW (mm)	15.7 ± 2.2	16.9 ± 3.6	0.248
Diastole LV (mm)	45.8 ± 4.9	45.8 ± 6.4	0.998
Systole LV (mm)	29.3 ± 5.2	30.5 ± 7.9	0.537
LVEDV (ml)	88.5 ± 27.9	99.9 ± 36.0	0.552
LVESV (ml)	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
LVED volume (ml)	83.1 ± 32.8	93.9 ± 23.9	0.458
LVES volume (ml)	30.8 ± 11.8	36.4 ± 11.4	0.125
LVEF (%)	62.6 ± 8.3	60.7 ± 6.5	0.371
E wave (cm/s)	72.7 ± 13.5	82.1 ± 19.1	0.127
A wave (cm/s)	72.2 ± 14.9	80.6 ± 20.3	0.157
E/A ratio	1.0 ± 0.3	1.1 ± 0.5	0.594
e' (cm/s)	10.2 ± 3.6	9.6 ± 4.4	0.468
s' (cm/s)	6.7 ± 1.5	7.2 ± 2.4	0.265
E/e'	8.1 ± 3.7	9.7 ± 4.0	0.650

Values show mean± standard deviation.
FS, fractional shortening; IVS, interventricular septum; LVEF, left ventricular ejection fraction; LVTDV , left ventricular end-diastolic volume; LVTSV, left ventricular end-systolic volume; PW, posterior wall

groups (p=0.002).

Regarding the clinical diagnosis, patients with stable chronic angina were more frequent (48 [87.2%]), representing more than three-quarters of all those researched. Among the patients with SCAD, there was a predominance of those with three-vessel artery disease, present in 75% of them (**Table 1**).

The echocardiographic variables used to evaluate the systolic and diastolic functions of the left ventricle did not show any differences of interest between the two groups, which demonstrate their homogeneity in this regard. The fact that the patients selected for the research had a normal LVEF is highlighted (**Table 2**).

In **table 3** and **figure 2** are shown the means and standard deviation of the values of the global circumferential strain (GCS) in relation to the presence or not of SCAD. The GCS was lower (absolute values) in the SCAD for both, global strain (-19.5±3.8 *vs.* -25.2±5.7; p=0.003) and basal (-17.7±6.2 *vs.* -21.7± 7.1; p=0.045) mean (-17.0±4.3 *vs.* -24.2±7.5; p=0.001) and apical segments (-23.7±7.5 *vs.* -29.6±9.1; p=0.036); as well as for the different segments of the left ventricle compared individually, although in the comparison by segments, the differences were not statis-

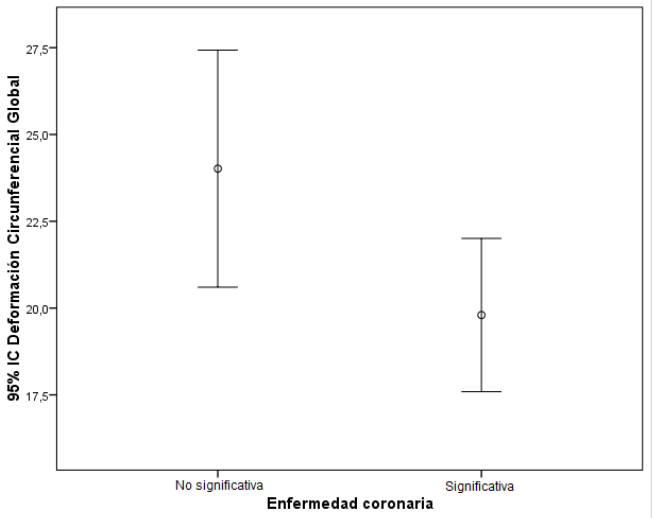

Figure 2. Global circumferential myocardial strain according to the severity of the coronary artery disease.

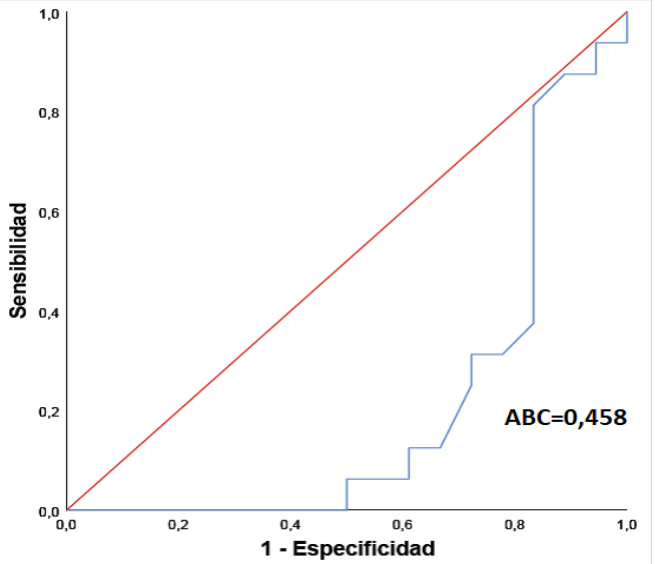

Figure 3. ROC curve of the global circumferential strain for predicting significant coronary artery disease.

Table 3. Relationship of global and segmental circumferential strains according to coronary artery disease.

Circumferential speckle-tracking variables	Coronary artery disease		p
	Non-significant (n=23)	Significant (n=32)	
GCS	-25.2 ± 5.7	-19.7 ± 3.8	0.003
Basal GCS	-21.7 ± 7.1	-17.7 ± 6.2	0.045
Medial GCS	-24.2 ± 7.5	-17.0 ± 4.3	0.001
Apical GCS	-29.6 ± 9.1	-23.7 ± 7.5	0.036
Basal segments			
Anterior septal	-22.5 ± 7.8	-18.6 ± 6.2	0.108
Anterior	-22.2 ± 7.9	-17.9 ± 6.5	0.084
Anterior lateral	-21.3 ± 5.2	-17.0 ± 8.4	0.072
Inferior septal	-21.7 ± 6.5	-18.0 ± 6.7	0.108
Inferior	-20.2 ± 7.3	-16.1 ± 6.7	0.088
Inferior lateral	-20.1 ± 7.0	-16.3 ± 6.4	0.103
Medial segments			
Anterior septal	-25.6 ± 7.6	-17.6 ± 4.8	0.001
Anterior	-24.6 ± 7.6	-18.1 ± 5.9	0.007
Anterior lateral	-24.8 ± 8.4	-17.6 ± 4.7	0.004
Inferior septal	-25.9 ± 8.0	-19.9 ± 5.3	0.013
Inferior	-22.7 ± 7.7	-16.4 ± 7.0	0.015
Inferior lateral	-24.5 ± 8.4	-15.8 ± 6.8	0.002
Apical segments			
Septal	-30.2 ± 8.8	-24.5 ± 6.5	0.035
Anterior	-30.3 ± 8.4	-25.0 ± 6.6	0.041
Inferior	-28.2 ± 10.4	-25.2 ± 7.5	0.331
Lateral	-29.6 ± 8.6	-23.9 ± 6.2	0.029

Values (%) are expressed in mean± standard deviation.
GCS: global circumferential strain

tically significant. Despite existing differences between the two groups, there are values that overlap between them, which makes it difficult to find a cut-off value to differentiate them.

In **figure 3** is displayed the ROC (Receiver Operating Characteristic) curve for SCAD prediction from GCS. The area under the curve is low, which does not allow setting values to define patients with levels of sensitivity and specificity that allow the technique to be used for that purpose. When analyzing the GCS, from the number of vessels with angiographically significant lesions, it was found that there were no differences between the groups in any of the cases (**Figure 4**).

The average strains of the cardiac segments related to the possible irrigation territories of the main epicardial arteries, —anterior descending, circumflex and right coronary arteries— which have a previously established and supposedly uniform anatomical pattern (**Table 4**), show that those segments related to significantly diseased arteries had lower mean GCS values than those without significant obstruction, although this result was not statistically relevant.

DISCUSSION

In this study carried out in patients with suspected ischemic heart disease, males predominated, what is related to the fact that the largest proportion of the patients were between 50 and 69 years of age, at which time cardiovascular diseases are more frequent in men, since women are more protected by known hormonal factors at this stage of life[18,19]. This result coincides with those obtained by groups from the *Instituto de Cardiología y Cirugía Cardiovascular (ICCCV),* of the Hospital Hermanos Ameijeiras, both in Havana, and the *Cardiocentro Ernesto Che Guevara*, in Villa Clara, both with respect to sex and age of patients[20-22].

With no differences between the groups, it is noteworthy that the averages of body mass index placed

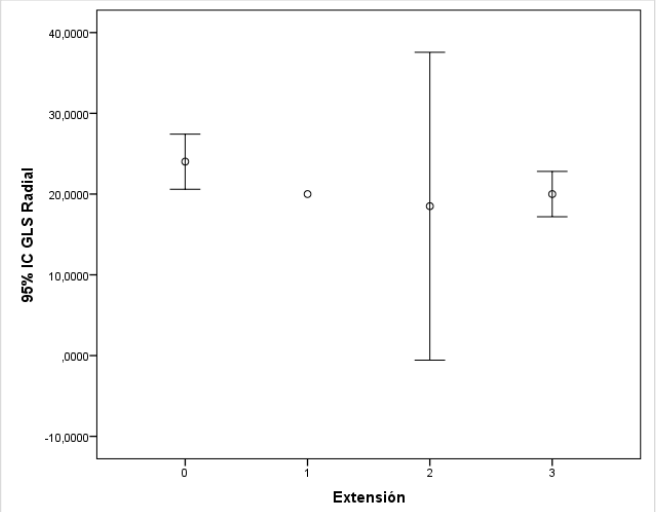

Figure 4. Global circumferential myocardial strain according to the extent of the coronary artery disease.

Table 4. Average strains of myocardial segments, according to the territory of irrigation of the coronary artery and coronary artery disease.

Speckle-tracking variables	Coronary artery disease		p
	Non-significant	Significant	
Left anterior descending artery	**n=25**	**n=28**	
GCS (%)	-20,7±4,6	-19,1±4,4	0,907
Circumflex artery	**n=31**	**n=22**	
GCS (%)	-17,8±8,7	-12,9±10,1	0,096
Right coronary artery	**n=32**	**n=21**	
GCS (%)	-19,4±3,7	-18,1±2,6	0,192

GCS: global circumferential strain

the patients within the overweight category. According to WHO data, Cuba reported, until 2008, a prevalence of obesity for adults aged 25 years or more of 27%, and 14% for women and men, respectively[23].

A high frequency of cardiovascular risk factors was found among sick patients with SCAD. High blood pressure was found the most. Blood pressure figures, both systolic and diastolic, correlate with the incidence of coronary and cerebrovascular disease[24.] According to the results of the III National Survey on Risk Factors (III ENFR, after its abbreviation in Spanish), in Cuba, the global prevalence of HBP is 30.9% in the population ≥ 15 years, with an increase after 55 years old. Results similar to those shown in most European countries[1,25].

Smoking is an important risk factor related to endothelial damage and plaque formation in the coronary arteries. Mortality from cardiovascular diseases has been shown to increase in smokers. In fact, 29% of deaths due to ischemic heart disease have tobacco as the main cause[25-27].

The fact that three-quarters of the patients have a clinical diagnosis of stable chronic angina is of great importance when interpreting the results, since these will be fundamentally related to their clinical status. The study population was made up of patients who underwent coronary angiography in the hemodynamics laboratory of the CIMEQ, a site where patients with acute coronary syndromes are less frequent; furthermore, these types of cases arrived at a time when it was difficult to perform the echocardiogram, as it was sometimes outside normal working hours; hence, its representation within the sample was lower.

Three-quarters of those analyzed with SCAD had three-vessel disease. In patients with a greater number of damaged vessels, the clinical picture is generally more diverse, with greater limitations in prognosis and quality of life, which is related to a greater proportion of ischemic myocardium and, thus, this would justify the performance of a coronary angiography in the stratification of the patient's risk and in the behavior to be followed, based on the current guidelines for action[4].

It is not possible to speak of ischemic heart disease without referring to the amount of phenomena and changes that are generated in relation to ischemia. Alterations in the myocardial strain usually appear before visual alterations in the regional movement of the myocardial wall, which gives value to their study[9]. This justifies the numerous studies that have been carried out comparing myocardial strain at rest between patients with SCAD and NSCAD[10,12,28,29].

Amundsen *et al.*[30] validated the application of the 2D-ST for clinical use by providing precise measurements, which made it a potential bedside clinical tool to quantify regional myocardial function. In the present research, it was found that GCS values were lower in patients with SCAD than in those with NSCAD, which is consistent with several published studies[10,29,31]. Although in the study, the difference between the groups is relevant, it is important to note that in the group of patients with NSCAD, there are patients with possible microvascular damage, slow coronary flows or with lesions in one or more coronary arteries that do not exceed 50% of the lumen of the vessel, but they are themselves sick patients, thus, myocardial strain values may be decreased and may overlap with those with significant coronary lesions. On the other hand, the presence of risk factors such as: diabetes mellitus, HBP and obesity causes 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 generate subclinical myocardial dysfunction, potentially detectable through the study of the myocardial strain[32].

The foregoing may explain that when analyzing the ROC curve, the area under it does not justify the application of the tool to distinguish between the patient with significantly diseased coronary arteries from those with normal coronary arteries or with non-significant lesions, since the values overlap each other. There were also no differences of interest between the GCS values according to the extent of the coronary disease, which does not coincide with several published studies[31,33]. In the authors' opinion, this result could be related to the size of the sample studied, where two thirds of the patients had three-vessel coronary disease.

Although myocardial strains, according to the epicardial arteries and their possible irrigation areas, were lower in the segments related to significantly obstructed arteries, their differences were not statistically relevant. The coronary anatomy is variable, hence, assessing territorial function according to a specific vascular territory may not reflect the true coronary artery distribution. Some areas may receive dual irrigation, including the development of collaterals. Norum *et al.*[12] describe similar results; on the other hand, Bakhoum *et al.*[34] studied the circumferential strain in patients with suspected stable coronary artery disease to predict the presence, extent and location of coronary obstruction, and found significantly lower GCS results in patients with trunk and three-vessel disease compared to those with normal coronary arteries or one- or two-vessel disease. (p=0.03 and p=0.00, respectively) [34].

The greatest benefit of using the 2D-ST is that it makes echocardiography more objective and quantitative, which determines a more complete and accurate cardiac examination. Many complementary studies can be expensive. Despite current technological limitations, GCS is likely to become a standard clinical tool in the near future, as imaging experts gain confidence in its measurement and clinicians become more familiar with its value. To be cost-effective, echocardiography must be a definitive examination. The use of 2D-ST is a big step in that direction[34].

CONCLUSIONS

In the patients studied with ischemic heart disease, men predominated in the sixth decade of life, as well as high blood pressure and smoking among the risk factors. The largest proportion of patients had a clinical diagnosis of stable chronic angina. Global circumferential strain values were lower in patients with significant coronary artery disease, but did not show relevant differences in relation to the number of significantly diseased vessels. Despite the above, the modest results do not justify the use of two-dimensional speckle-tracking to discriminate significant coronary artery disease.

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