Mechanical Dispersion

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Introduction

The sudden death is the most severe and fearsome outcome of myocardial infarction, happening in nearly 50% of post-infarction deaths, and being mainly brought about by complex ventricular arrhythmias[1, 2]. In industrialized countries, post-infarction sudden death and cardiac arrest surpass all the other causes of death together. In the 1990s, in the United States, there were over 450,000 cases of sudden death yearly[3].

Cardiac arrhythmias after myocardial infarction may be monomorphic tachycardia, triggered by a reentry mechanism or polymorphic ventricular tachycardias and ventricular fibrillation, caused by dispersion of repolarization[4]. The post-infarction remodeling brings about regional or intramural reentry mechanisms, which include ischemic myocardium regions and infarction scars not electrically excitable. The left ventricular (LV) dilation, accompanied by decreased function, also predisposes to electrical heterogeneity, characterized by temporal dispersion of repolarization, which favors the occurrence of reentry arrhythmias[5].

Several methods may be used to stratify the risk of patients after myocardial infarction to present severe arrhythmias and sudden death. The ejection fraction (EF) is considered an important marker of heart failure and cardiovascular mortality, but is relatively insensitive for predicting arrhythmias[6]. The electrocardiographic evaluation by surface mapping and 12-lead electrocardiography (ECG) may reveal electrical instability upon measurement of the QT interval, presenting high sensitivity (92%) and specificity (81%) to predict sudden death[7]. Recently introduced, the mechanical dispersion of myocardial strain, measured by cardiac strain, presents good sensitivity and excellent specificity to identify arrhythmic events, mainly if associated with global longitudinal strain (GLS)[8, 9].

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The myocardial depolarization happens in a sequential and harmonic manner to the helical bands of the normal heart. This translates into synchronic strain of the myocardial segments along all the anatomical axes (longitudinal, circumferential and radial), with straight gap, which may be measured by the standard deviation of the time between QRS and the strain peak of each segment, referred to as mechanical dispersion (MD). Because longitudinal strains are more stable and precise, they are preferred for MD tests. Most cardiac strain test software performs this calculation automatically.

Initially applied for indicating implantable defibrillators, MD has had its use widened, currently including cardiomyopathies, valvular heart diseases, pressure overloads and evaluation of left ventricular function[10, 11].

Description of the works reviewed

Preliminary data[8] obtained in 85 patients who had myocardial infarction, with percutaneous implantation of implantable cardioverter defibrillator (ICD), reviewed over an average period of 2 to 3 years, revealed that 38 of them presented at least one event of arrhythmia, needing for device activation. The selection of patients for implantation of ICD abided by primary prevention criteria (44 patients with EF < 35% with at least 40 days after infarction or EF < 40% associated with non-sustained ventricular tachycardia) or secondary prevention (41 survivors of cardiac arrest or patients with sustained ventricular tachycardia). This study excluded patients with atrial fibrillation, left bundle branch block, prior myocardial revascularization or valvular heart diseases with clinical consequences higher than moderate. All patients were subject to coronary angiography, 49 of them undergoing percutaneous angioplasty. Four patients had undergone surgical revascularization after implantation of ICD and one patient was subject to treatment with thrombolytics after undergoing acute myocardial infarction. In 31 patients, coronary lesions were not adequate for revascularization. The control groups were formed by 20 patients who had myocardial infarction, but not met the inclusion criteria for ICD implantation, and 24 healthy volunteers.

In all patients and controls, 12-lead ECG was performed, the correct QT interval was calculated for heart rate. In the echocardiographic study, the EF was calculated by the Simpson method and the GLS was measured based on the average of strain obtained in 16 myocardial segments, excluding the segments with post-systolic contraction and not analyzable. The MD was obtained calculating the standard deviation of the starting time of QRS until the maximum peak of strain of the 16 myocardial segments, including the segments with post-systolic contraction and excluding the non-analyzable segments.

Keywords

Echocardiography/methods; Myocardial Infarction/complications; Arrhythmias/Pathophysiology; Ventricular Tachycardia; Systolic Volume.

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Manuscript received on December 13, 2014; manuscript revised on February 03, 2014; accepted on May 06, 2014.

DOI: 10.5935/2318-8219.20140022

The clinical data did not reveal a significant difference between the two groups of patients with ICD (with and without arrhythmic events) and the patients without ICD, with regard to age, heart rate, duration of QRS, medication, type and extent of infarction and the interventional therapy. The EF was smaller in groups with ICD than in the group without ICD, and both of these groups were smaller than the group made up of volunteers. The data of GLS and MD was showed in Table 1. This data highlights the increase of the MD time in patients with ICD which presented arrhythmias during evolution. MD values higher than 70 ms presented sensitivity of 65% and specificity of 92% to predict arrhythmias in patients who underwent myocardial infarction. Figure 1 represents the calculation of MD in a normal individual and in a patient having myocardial infarction with increased MD.

In another recent study[9], the authors analyzed the hypothesis that GLS could be measured based on the size of infarction and that MD would be an important predictor of sudden death or malignant ventricular arrhythmias after myocardial infarction, through evaluation of the heterogeneity of the myocardial strain. Risk stratification is rather significant during the cases of admission with acute myocardial infarction, as sudden death and severe arrhythmias typically happen close in time and after discharge. The primary outcome of this study, which involved 988 patients over a period of two years and a half, was sudden death, admission due to proven ventricular arrhythmia or appropriate discharge of ICD (only in patients with implantation due to primary prevention). Patients were divided in three groups, according to GLS: 330 patients with GLS > -15.5%, 329 patients with GLS between -15.5% and -12.0% and 329 patients with GLS < -12%. The age of the last group of patients was significantly higher than that of the two first groups. There were no differences relating to sex, incidence of hypertension, diabetes and previous infarction, as well as the treatment prior to infarction. The groups showed a significant increase of the functional classification (Killip) proportionally to a smaller GLS, as well as the increase of heart rate, duration of QT interval, percentage of cases with QRS > 120 ms and incidence of ST-segment elevation. The echocardiographic data showed a gradual increase of the LV dimensions and of the mass index, and decrease of ejection fraction and increase of MD.

During the study, 80 deaths happened, 26 out of which due to sudden death. Three patients had severe ventricular arrhythmia or were resuscitated after cardiac arrest, and 30 patients were subject to ICD over the study period. The analysis of strain to predict sudden death or ventricular arrhythmias showed decrease of GLS and increase of MD in connection with the increase of age, presence of comorbidities, width of QRS, extent of infarction, Killip classification and LVEF. The patients who had sudden death

Table 1 – Echocardiographic data of healthy volunteers, patients with prior myocardial infarction without ICD, patients with ICD without arrhythmic events and patients with arrhythmic events (adapted from Haugaa KH et al. JACC Imaging, 2010; 3:247)

	Volunteers (n = 23)	Prior MI without ICD (n = 20)	ICD without events (n = 47)	ICD with events (n = 38)	P-value
GLS (%)	-21.6 ± 2.8	-15.9 ± 2.5	-11.2 ± 4.0	-10.0 ± 3.7	<0.001
MD (ms)	22 ± 10	45 ± 15	56 ± 13	85 ± 29	<0.001

MI: Myocardial infarction, ICD: Implantable Cardioverter Defibrillator; GLS: Global Longitudinal Strain; MD: Mechanical Dispersion.

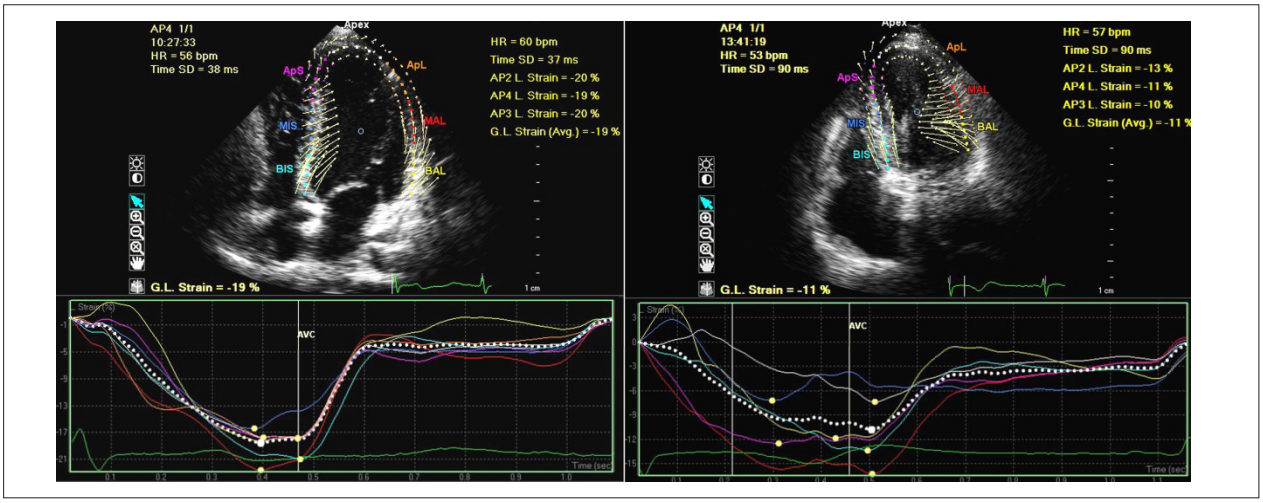

Figure 1 – *Left: GLS in a normal individual, showing the standard deviation of strain times (MD = 37 ms). Right: GLS in patient with anterolateral myocardial infarction that presented multifocal ventricular extrasystoles. One can note the decrease of global strain (-11%) and increased MD (90 ms) with several strain peaks happening after the closing of aortic valve (CVA).*

or severe ventricular arrhythmias compared to patients who did not undergo such events presented a lower EF (42.4% *vs*. 51.4%), decrease of GLS (-9.9% *vs*. -13.9%) and increase of MD (70.7 ms *vs*. 56.1 ms). EF < 35% was not capable of predicting the occurrence of the first outcome, as 67.6% of the sudden deaths or arrhythmias happened to patients who had EF > 35%. Only the GLS and MD showed independent prognostic information in the group with EF < 35%. After the adjustment of the multivariate analysis, MD was the single variable to predict arrhythmia during the clinical follow-up of patients (for each 10 ms of increase of MD: HR-95% CI -1.24 (1.07 - 1.43); p < 0.01). In patients with EF > 35%, only the diastolic dimension of LV and GLS had prognostic value, and there was no significant change of MD. This way, the study concludes that the early evaluation of GLS and MD in patients with acute myocardial infarction identifies the ones who can present sudden death or severe ventricular arrhythmias. It also demonstrates that GLS is an independent predictor of sudden death and severe ventricular arrhythmia after myocardial infarction, in a better way than any other echocardiographic variable, including EF. Additionally, it shows that MD, when associated with GLS, presents a strong prognostic value in patients with depressed ventricular function (EF < 35%).

Another recent study[10] performed experiments with pigs, which were subject to acute pressure overload by intra-aortic balloon occlusion, resulting in a 30% increase of systolic pressure and acute left ventricular dilation after 5 - 10 heartbeats. Grounded on the hypothesis that the pressure overload produces ventricular arrhythmias, the MD of three segments of the interventricular septum was analyzed before and after aortic occlusion, revealing a significant increase of the time for the strain peak and resulting in post-systolic contraction, increase of MD, decrease of longitudinal strain in all segments studied and incidence of premature beats in 33% of the cases. There were no changes in the QT interval of 12-lead ECG. The authors of the said study conclude that the acute increase of the left ventricular afterload increases MD and may play an important role in arrhythmias induced by increase of systemic pressure.

The last study reviewed uses MD to prevent arrhythmias in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC)[11]. It studied 69 patients, 42 out of which were symptomatic and 27 were asymptomatic relatives having genetic mutation. Forty healthy volunteers compose the control group. The variation of the RV areas was measured in the patients and controls. For analysis of strain, the strain of 16 LV segments and 3 segments of the RV free wall was obtained, calculating the GLS of LV and RV and the MD of both ventricles. The septal segments of RV were also analyzed to evaluate the differences of dispersion between the segments impacted (free wall) and not impacted (septum). All 42 patients with ARVC presented arrhythmias, and ICD was implanted in 39 patients. Two patients were responsive to the treatment with beta-blocker and one of the refused to be subject to ICD implantation.

The results showed that there was no significant different in LVEF between the healthy group and the group including symptomatic and asymptomatic patients. The variation of RV areas was decreased only in the symptomatic group. Table 2 shows the results of GLS of LV and RV and MD of the LV and RV. Figure 2 shows the longitudinal strain and MD of the RV in a healthy individual and in a patient presenting ARVC. The authors conclude that the increase of MD in patients presenting ARVC with arrhythmias may be correlated with the presence of ventricular tachycardia and ventricular fibrillation, a fact which is corroborated by the analysis of the multivariate logistic regression (for each 10 ms of increase of MD: HR-95% CI -1.66 (1.06 - 2.58); p < 0.03). The ROC analysis showed that the MD of 29 ms was the best cut-off value to identify arrhythmic events in the study participants. The increase of the MD found in asymptomatic individuals with the mutation may point to subclinical involvement. The decrease of GLS found in the right and left ventricles indicated that ARVC is a biventricular disease. The LV impairment happens to some cases of asymptomatic individuals presenting mutations and to most of the symptomatic patients.

Discussion

The death causes after myocardial infarction result from multiple factors, and the time elapsed between the start of pain and assistance is important. During the acute phase, mortality is usually associated with severe ischemia-induced arrhythmias, but other mechanical complications, such as ventricular or isolated muscle rupture, cardiac tamponade, septal defects and acute ischemic valvular dysfunction, may mimic sudden death due to arrhythmia, even if the heart rate is not indicative of ventricular fibrillation. The same picture may be observed in patients in cardiogenic shock due to extensive myocardial necrosis. After the acute phase is through, the post-infarction mortality is more connected to LV remodeling, where non-excitable areas of necrosis are mixed with areas with ischemia-induced arrhythmias owing to the reentry phenomenon. Another process is associated with ventricular cavity remodeling with progressive loss of function, decrease of cardiac output and congestive heart failure with formation of areas of fibrosis and the consequent non-homogeneity of repolarization, also inducing reentry arrhythmias.

All these factors lead to reflection about the methods that seek to stratify the risk of sudden death after myocardial infarction applying a one-variable model: the electrical dispersion of repolarization and its consequence, the mechanical dispersion of myocardial strain, i.e., work on the hypothesis that the post-infarction death is caused exclusively by arrhythmias. It is probably due to this that the sensitivity observed in the analyzed studies is not very high, mainly in patients with EF not so deteriorated. We found that, when MD is associated with GLS, the sensitivity increases considerably, given that GLS is a good parameter to estimate the left ventricular function, given that, when this function decreases to critical levels, it ultimately decreases the process of cardiac death. GLS is superior to EF because the latter is a generic measurement method that does not take into account segmental abnormalities, based on geometric extrapolation, even if resorting to the Simpson method. GLS, in turn, provides data obtained with the analysis of each myocardial segment, and is less influenced by the ventricular geometry and more independent from the load, better correlating with the amount of myocardial infarction.

Tabla 2 – Datos del strain en voluntarios sanos, mutantes asintomáticos y pacientes con CAVD sintomáticos (adaptado de Sarvari SI et al. Eur Heart J, 2013; 32:1089)

	Volunteers (n = 40)	Asymptomatic Individuals Presenting Mutations (n = 27)	ARVC (n = 42)	P-value Krustal Wallis
LV GLS (%)	-22.0	-20.0	-17.0	<0.001
RV GLS (%)	-25.0	-22.0	-19.0	<0.001
LV MD (ms)	20.0	38.0	60.0	<0.001
RV MD (ms)	13.0	35.0	52.0	<0.001

ARVC: Arrhythmogenic RV Cardiomyopathy; GLS: Global Longitudinal Strain; MD: Mechanical Dispersion.

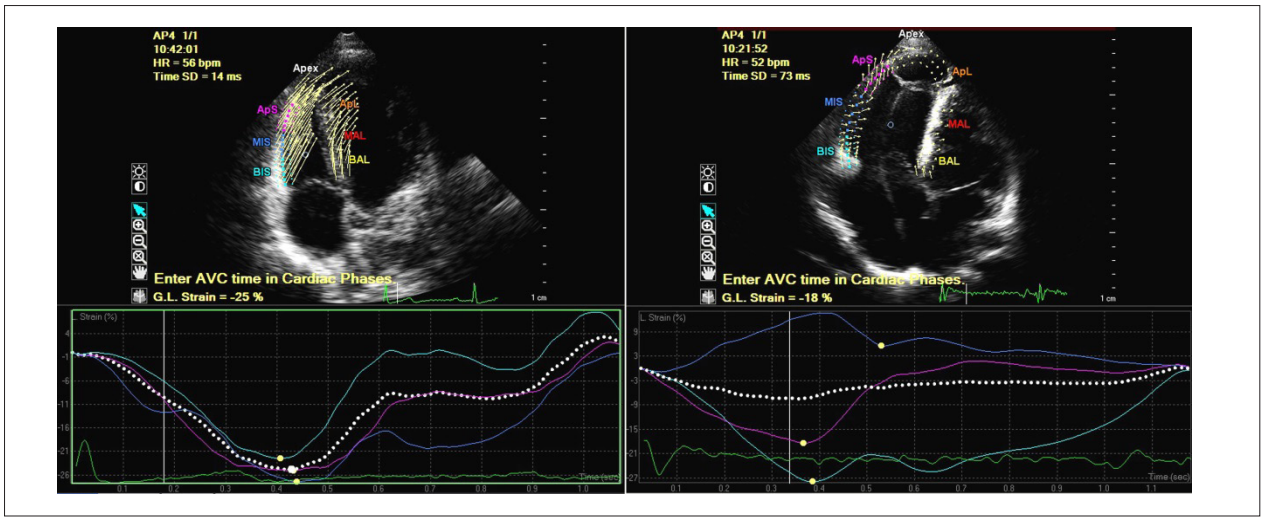

Figure 2 – *Left: Longitudinal strain of the RV free wall in a healthy individual with MD of 14 ms. Right: Longitudinal strain of the RV free wall in a patient with ARVC with decrease of strain and increase of MD (73 ms). Inside the right heart chambers, the ICD cable may be observed.*

Conclusion

The reviewed studies about mechanical dispersion provide a new method to stratify the risk of post-myocardial infarction sudden death, which may be significantly invaluable if used along with other data obtained by clinical and echocardiographic tests, such as functional classification, ECG data, QT interval, cavity dimensions, EF and, mainly, GLS, all of this associated with the early diagnosis and precise drug or interventional treatment of the acute myocardial infarction.

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