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Magnetic Resonance Imaging in prognostic stratification of patients with Acute Myocardial Infarction

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Abstract

Purpose: The purpose of this study was to verify the role of cardiac magnetic resonance imaging in prognostic stratification of patients with acute myocardial infarction (STEMI) treated with primary angioplasty (PCI). **Materials and Methods:** During the years 2012 and 2013, 36 patients treated with primary angioplasty were selected in order to be examined with magnetic resonance imaging in acute stage (within 6 days) and at a later stage after 6-7 months. The MR protocol included SSFP sequences, T2Black-Blood FAT SAT for edema evaluation and contrastographic IRGE sequences for the evaluation of delayed enhancement. The ejection fraction in acute and follow-up was considered as the fundamental parameter of prognostic stratification. In addition, by using post-processing dedicated tools, the following data was extrapolated: the end-diastolic volume, the amount of edema and scar, then correlated to the ejection fraction. **Results:** In acute phase, the end-diastolic volume, edema and the delayed enhancement (DE) presented variable correlation with ejection fraction (r = 0.58, and 0.80 0.69); while after 6 months, the correlation between the end-diastolic volume, delayed enhancement and ejection fraction was 0.64 and 0.87. None of the patients presented edema in chronic phase. **Conclusions:** The data of our study suggest that MRI is an important prognostic stratification tool in patients with STEMI, especially for the significant correlation between ejection fraction and the amount of delayed enhancement.

Keywords: STEMI, Infraction, Magnetic Resonance, SCAR, Prognostic Stratification.

Introduction

Acute myocardial infarction (AMI) is the most frequent cause of morbidity and mortality worldwide. The true incidence of this disease is difficult to determine, mostly for the non-unique use of diagnostic criteria and the not optimal overlap between the hospital discharge data and the diagnostic criteria adopted. Community studies have shown that the death rate of patients with suspected myocardial infarction or acute coronary syndrome is particularly high within the first two hours [1]. This rate appears to have slightly changed in recent years [2]; while oppositely, there has been a marked reduction in mortality among patients who reached the hospital.

Before the introduction of Coronary Care Units in the 60's,in-hospital mortality approached 25-30%.

With the widespread dissemination of hemodynamic laboratory, secondary prevention, antithrombotic and thrombolytic therapy, mortality within 1 month was reduced to 4-6%, as shown by recent large-scale randomized trial in which as treatment, thrombolysis and/or primary angioplasty were used [3,4].

Most ST-segment Elevation Myocardial Infarctions (STEMI) are caused by occlusion of a coronary artery. Coronary occlusion and reduction in blood flow are usually due to rupture of an atherosclerotic plaque with the consequence of formation of an occluding thrombus, while the concomitant coronary vasoconstriction and/or microembolization can act as aggravating factors of the clinical conditions. Infrequently, in the other hand, a thrombus can be formed as a result of endothelium surface erosion even in the absence of plaque.

The risk of plaque rupture depends on plaque composition, its vulnerability (plaque type) and the degree of stenosis [5]. Over 75% of infarctions causing thrombus are formed on plaques responsible for a mild or moderate stenosis. Nevertheless, also plaques responsible for severe stenosis can rupture causing coronary occlusion [6].

For patients with clinical and instrumental presentation of STEMI such as: persistent ST segment elevation or left bundle branch block of new onset, the indication is to perform an early reperfusion, either mechanical or pharmacological, within 12 hours of the onset of symptoms.

The primary Percutaneous Coronary Intervention (PCI) is defined as an angioplasty or stenting without previous or concomitant fibrinolytic therapy and it is the main therapeutic choice, when it can be preformed quickly in a specialized center. This approach has proven successful both in terms of safety and to ensure the coronary reopening, as well as avoiding hemorrhagic risks related to the fibrinolysis. A meta-analysis of 23 randomized clinical trials with 7739 patients showed how the primary PCI has led to a lower rate of premature death (7% vs 9%, $p = 0.0002$), non-fatal re-infraction (3% vs 7%, $p < 0.0001$) and stroke (1% vs. 2%, $p = 0.0004$) compared to fibrinolytic therapy [7].

Primary angioplasty should be performed within two hours from the first medical contact, and it is known to be the first-choice treatment for patients in cardiogenic shock [8]. Except for this last class of patients, during the acute phase, only the coronary responsible for the acute injury should be treated, leaving for a later stage the completion of the revascularization of any other eventual significant injuries.

Numerous imaging techniques nowadays, contribute to the study of acute and chronic ischemic heart disease, including: Echocardiogram, Single Photon Emission Computed Tomography (SPECT), Positron Emission Tomography (PET), Computed Tomography (CT); among these methods, Cardiac Magnetic Resonance (CMR) is the technique which in recent years has had the largest growth, due to the many information it can provide.

The study of function and cardiac anatomy with MRI was introduced in clinical practice since 2001 when the SSFP sequences (Steady State Free Precession) GE-derived were released in commercial [9]. Cardio-MRI study in patients with already treated and stabilized acute myocardial infarction, can be used as innovative instrument of prognostic stratification and evaluation of possible complications, allowing additionally, a differential diagnostics in all the clinical cases in which coronary angiography shows intact coronary arteries, ECG alterations or increase of cytolysis index, such as troponins.

Among the clincal cases mentioned above, we would like to note in particularly the myocardium-pericarditis and the syndromic cases of Tako-tsubo.

Currently, the implanted stents are manufactured with special materials that undergo a very limited heating process, reducing the risk of overheating or possible secondary thrombosis. This latest innovation has allowed to overcome the safety problem of coronary revascularization.

In this study 36 patients with STEMI type acute myocardial infarction were prospectively and consecutively included, these patients were assessed by Cardiac Magnetic Resonance (CMR) within 6 days of stent implantation and later on, with the same protocol, went through follow-up after 6-7 months. The study was approved by the Ethics Committee of our Institution.

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Materials and Methods

Sample Description

36 patients (33 males and 3 females) were the subject of this prospective study , all of them had a STEMI type acute myocardial infarction and underwent a control examination after 6-7 months.

It should be noted that the study was carried out in two different moments:

- Within 6 days after primary percutaneous coronary intervention.
- Follow Up 6-7 months after the acute event.
- On average, the study in the acute phase was carried out 3-6 days after the primary angioplasty.

Exclusion criteria were:

- Hemodynamically unstable or uncooperative patients;
- Claustrophobia; It should be noted that the examination of cardio-resonance often causes a strong anxious emotional reaction linked to claustrophobia.
- creatinine clearance < 30 ml/min;
- Patient’s Denial of consent;
- Severe obesity.

Control examination at 6 months was performed on average after 193 days; the causes of non-implementation of follow-up (in 4 patients, therefore not included into the study) were:

- Denial of the patient (1 case);
- Pacemaker implantation not compatible with MRI (3 cases).

Study Protocol and used sequences

For the CMR examination and the subsequent post-processing analysis, the following devices were used:

- Magnetic Resonance Equipment (1.5-T MRI Signa HDX, GE Medical Systems, Milwaukee, Wisconsin), with coil surface dedicated to 8 channels.
- Steady-State Free Precession Sequences (SSFP).
- T2-weighted Black-Blood-FAT SAT Sequences
- Inversion-Recovery Gradient-Echo Sequences (IRGE Delayed Enhancement (DE) after administration of contrast medium Gadovist ® (Gadobutrol, Bayer Schering Pharma, Germany), 0.1 mmol/kg.
- Post Processing software Package dedicated for the analysis of medical images Cardiac (Segment ®, Medviso, Lund-Sweden).

The study protocol included the following steps:

- Initial localization and cardiac study of long axis (2-3-4 chambers) performed with Steady-State Free Precession (SSFP) in respiratory apnea, preferentially expiratory.
- CINE sequences of short axis performed with SSFP to evaluate the kinetics and the function. The package set consists of 10 mm slices with 0 mm gap.
- For the assessment myocardial edema, BBT2 FAT SAT sequences set for TR of 2800-3000 msec and TE of 80-100 msec were used; Therefore we have chosen a sampling on two or three TR to lengthen the TR interval while TE were set manually for 80-100 msec (fig. 1a-1b).

Figure 1: (a) BBT2 FAT-SAT sequences -short axis: septum edema – front part; (b)BBT2 FAT-SAT sequences-long axis: septum edema – front part.

The Inversion-Recovery Gradient-Echo (IRGE) DE sequences were captured by slice thickness of 10 mm and gap of 0 targeted for biventricular coverage with a temporal interval around 7-10 minutes after administration of intravenous bolus of 0.1 mmol/kg of body weight of diethylenetriamine pentaacetic acid (gadolinium), (Gadovist ®, Gadobutrol, Bayer Schering Pharma, Germany), followed by saline infusion. (fig. 2).

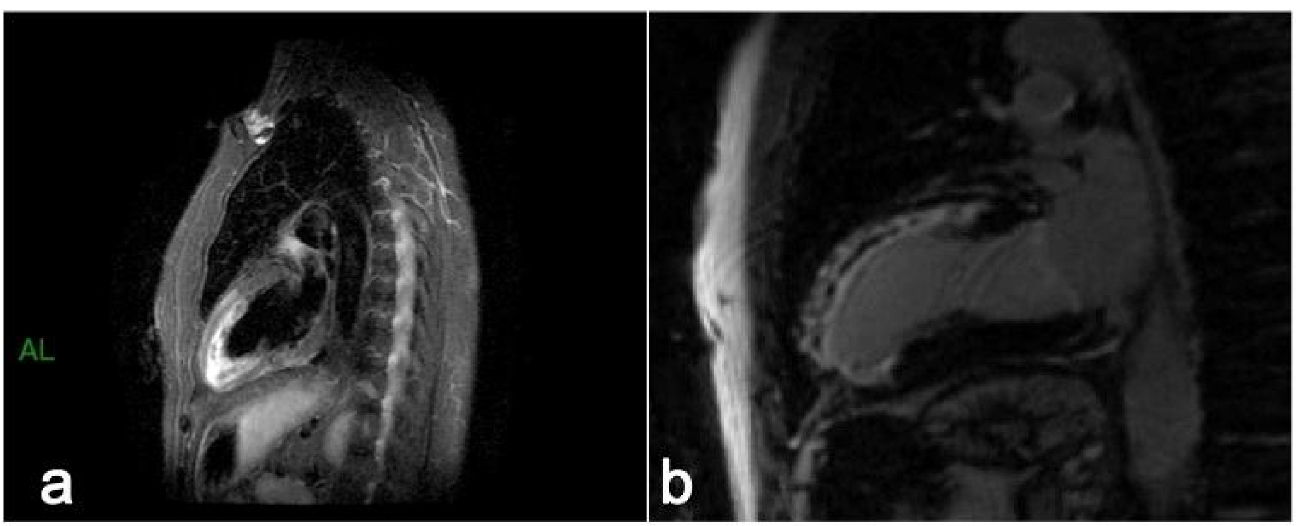

Figure 2: (a) post processing segment: quantification tool of edema (gr and % of the total mass); (b) short axis acute infarct; delayed transmural enhancement anterior wall post–contrastographic IRGE sequences: delayed transmural enhancement of anterior wall and entire apex with areas of no-reflow.

Post-Processing Study

For the evaluation and post-processing study of this type of pathology, SEGMENT® software, company MEDVISO (Lund) [10] has been used, which in additionally for the usual tools for the kinetics and cardiac function study, features also the most distinctive and innovative tools for quantification of edema and scar, according to precise and reproducible quantitative measures.

Once the images has been acquired, the post-processing elaboration phase started, in order to obtain all necessary measurements and quantification.

In short axis cine-SSFP sections, end-diastolic, end-systolic volumes, left and right ventricular ejection fraction were calculated, using as benchmark the Maceira normality benchmarks [11]. By using the dedicated sequences, the extent of myocardial edema, scar tissue (SCAR) and microvascular obstruction (MO) were calculated; expressed in grams and as a percentage of the total left ventricular mass (fig. 3).

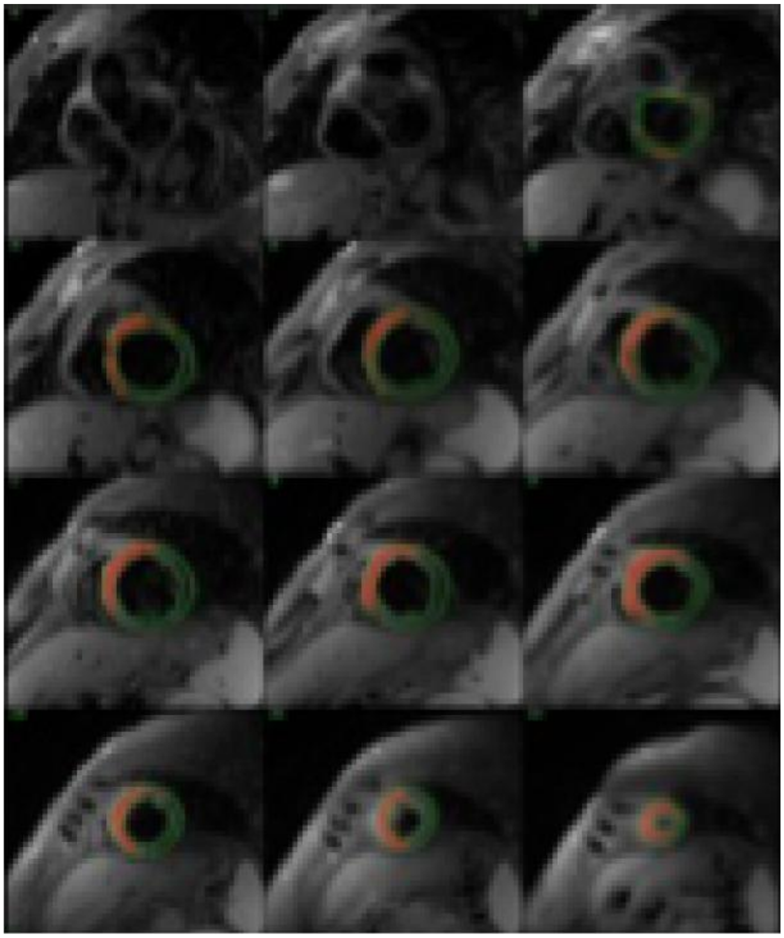

Figure 3: long axis; delayed transmural enhancement anterior part. Post-contrastographic IRGE sequences: delayed transmural enhancement of anterior wall and entire apex with areas of no-reflow.

Our interest principally, was to select specifically which parameters derived from these software tools could be actually useful for a correct prognosis determination and in particular, it was decided to explore whether there was a direct correlation between specific parameters derived from post processing calculations such as:

In acute phase:

Indexed End-Diastolic Volume (VTDi) with Ejection Fraction (EF).

Edema/myocardium at risk (MAR) with Ejection Fraction (EF).

Scar Area (SCAR) with Ejection Fraction (EF).

While at follow-up, the following parameters were correlated:

Indexed End-Diastolic Volume (VTDi) with Ejection Fraction (EF).

Scar Area (SCAR) with Ejection Fraction (EF).

Statistical Analysis

In order to evaluate the correlation of the data listed above, we used Bland-Altman statistical analysis; which indeed, allows to obtain a value expressed in the same units of the measured variable, allowing a direct interpretation. The Bland Altman method interprets the variability in terms of concordance between the two observers: the variability decrease with the increasing of the concordance.

For the variability estimation, Pearson correlation coefficient was used as an indicator of the correlation between measurements. This coefficient can have values ranging from -1.00 (between the two variables there is a perfect negative correlation) and + 1.00 (between the two variables there is a perfect positive correlation). A correlation equal to 0 indicates that between the two variables, there is no correlation. The statistical analysis, graphic representations, trend analysis and calculation of the correlation coefficient were performed using Microsoft Excel software ver. 14.

Results and Discussion

Results are shown in table 1. The MR Protocol was repeated in 36 patients at six months apart with the following results:

None of the patients, at the 6 months control, had the presence of infract edema and signs of microvascular obstruction (MO).

The data obtained from the comparative analysis between the 2 phases showed a reduction in the scar share between acute and chronic phase; on average by 3-4%. This fact is confirmed in recent studies in which it is suggested that, in an acute phase, due to their own unspecificity, the contrast medium spread nevertheless into the interstitium (volumetrically increased) for the presence of edema, while the actual scar tissue has a reduced extension volume.

Table 1: results (r = Pearson correlation coefficient).

Indexed Diastolic Volume	Acute EF	Chronic EF
Acute VTDi	0.58	0.57
Chronic VTDi	0.66	0.64
Acute Delay	0.80	0.77
Chronic Delay	0.00	0.87
Edema	0.69	0.58

In the acute phase, the indexed Diastolic Volume of left ventricle (VTDi), edema (MAr) and the Delayed Enhancement (DE), correlate with the Ejection Fraction (EF) with a closer correlation in reference to Delayed Enhancement (respectively r = 0.58, 0.69 and 0.80). These parameters evaluated in the acute phase were correlated with ejection fraction in 6 months (r = 0.57, 0.58, 0.77). Correlations between parameters obtained in the follow-up phase of VTDi and Delayed Enhancement with Ejection Fraction were respectively as follows: r = 0.64 and 0.87. Even in this case, the parameter of Scar/Delayed Enhancement presented significant correlation with the ejection fraction.

Conclusions

The results obtained in this study indicate specifically how Cardiac Magnetic Resonance imaging, used in the study of acute ischemic heart disease, is an instrument of great importance for the execution of therapeutic choices aimed at improving the life quality of the patient. Our work is a confirmation of the latest international literature, as it brings concrete evidence that some of the parameters obtained from the study with cardiac magnetic resonance imaging and post-processing support, are effectively usable for precise prognostic stratification of acute infarct.
Specifically, the correlations obtained based on the data analyzed, indicate how the quantification of ejection fraction represents today one of the most expressive parameters used for the clinical management of the patient.

It should be also noted that, according to the results acquired, the parameter that showed greater correlation with ejection fraction, both in the acute phase chronic phase was the scar parameter (charts 1-2-3).

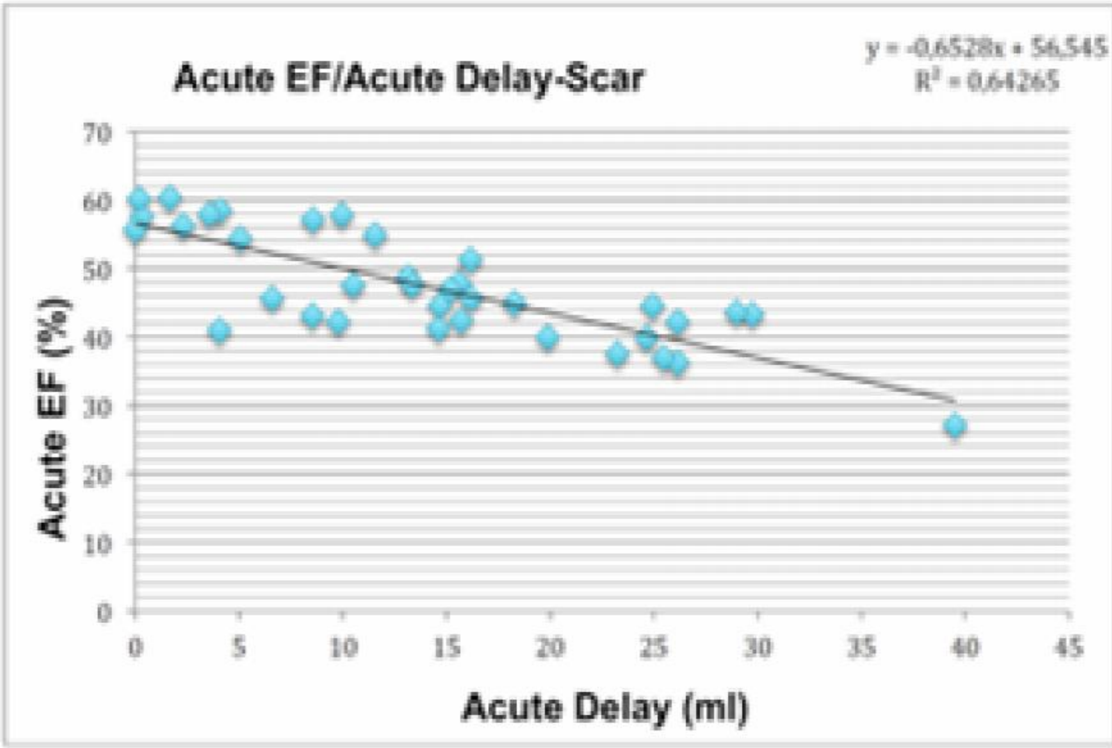

Chart 1: correlation Acute EF/Acute Delay-Scar.

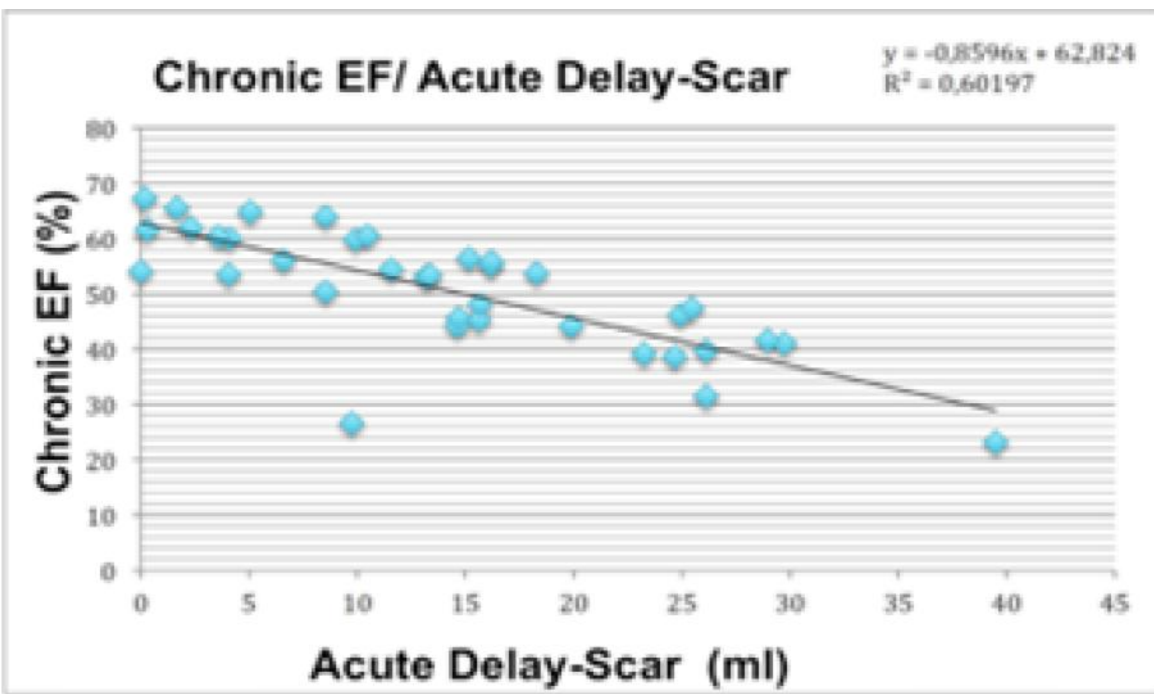

Chart 2: correlation Chronic EF/ Acute Delay-Scar.

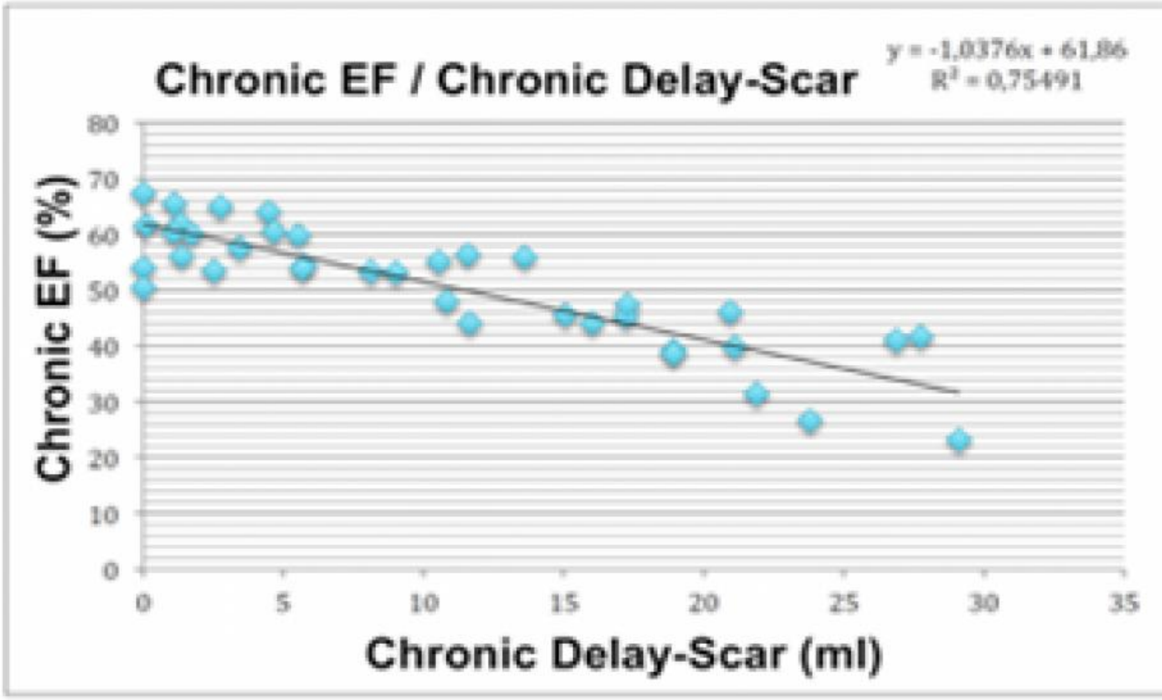

Chart 3: correlation Chronic EF / Chronic Delay-Scar.

As a matter of fact, our study has considerably confirmed that the progressive increase of the Scar is directly correlated with a worse prognosis in terms of survival and life quality of the patient. On the other hand, the gradual increase of the post-infarct scar is closely related to the time of myocardial revascularization. Therefore it is important to emphasize once again that, currently, the early revascularization is confirmed to be the only possible mode for myocardial functional recovery and consequently to improve clinical outcome.

It is necessary to note that the Magnetic Resonance in the study of this disease, compared with the other traditionally used methods, proves to be competitive. For example, comparatively to medical-nuclear imaging , Magnetic Resonance in addition to increased spatial resolution, has lower respiratory partial volume artifact, more accuracy for the detection of non-transmural myocardial infracts and more accurate grading of transmural necrosis or extension. It should also be noted that the study by functional magnetic resonance imaging is part of a more comprehensive approach that provides data on ventricular volumes and global function allowing the visualization and quantification of any associated valvular disease (for example: mitral regurgitation), as well as the demonstration of complications such as ventricular aneurysms or presence of blood clots.

Post infarct prognostic stratification is essential in case of STEMI type infarcts.

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