UNIVERSITA' DEGLI STUDI DI PISA

Dipartimento Cardio Toracico e Vascolare

Corso di Dottorato di Ricerca in Fisiopatologia e Clinica dell'Apparato Cardiovascolare e Respiratorio

Tesi di Dottorato

Early evaluation of global, regional and intramyocardial left ventricular function after acute myocardial infarction with a new ultrasonic software

Relatore:
Prof. Vitantonio Di Bello

Candidato:
Dott. Stefano Stroppa

CONTENTS

Introduction	page 3
Aim	page 9
Materials and methods	page 10
Results	page 25
Discussion	page 35
Conclusions	page 41
Abbreviations	page 43
Tables	page 45
References	page 60

INTRODUCTION

Acute myocardial infarction (AMI) can be defined in different ways in relation to its clinical, elettrocardiographic, echocardiographic, biochemical and phatologic characteristics[1]; instead, it is widely accepted that the term myocardial infarction reflects the death of cardiac myocytes caused by prolonged ischaemia.

An acute coronary syndrome (ACS) is nearly always caused by a sudden reduction in coronary blood flow caused by atherosclerosis with trombosis superimposed with or without concomitant vasoconstriction[2].

In the presence of clinically appropriate symptoms two categories of patients may be encountered: patients with persistent ST segment elevation or (or so presumed) new left bundle branch block (STEMI) and patients without ST segment elevation, i.e. ST segment depression or T wave abnormalities[3] (NSTEMI).

Persistent ST segment elevation generally reflects acute total coronary occlusion and the great majority of these patients show a typical rise

of myocardial necrosis biomarkers and progress to Q-wave myocardial infarction; the therapeutic goal is rapid, complete and sustained recanalization of infarct vessel by fibrinolytic treatment or primary percutaneous coronary intervention (PCI)[3].

Echocardiography is a quick, repeatable, non invasive diagnostic technique playing a pivotal role in the diagnosis and follow-up of ACS. Echocardiography allows to estimate severity and extension of coronary artery disease and to obtain prognostic informations that may influence the terapheutic choices. An accurate analysis of left ventricular function, global and regional, is useful to evaluate the anatomical injury and the complications of AMI.

In patients with STEMI, several randomized clinical trials have demonstrated an improved residual left ventricular function and a better clinical outcome after mechanical[4,5] [PCI or, in a limited number of patients, coronary artery by-pass surgery (CABG)] or pharmachological[6-8] (fibrinolysis) restoration of patency of the infarct vessel and myocardial tissue reperfusion.

The degree of recovery of left ventricular function after STEMI is related to the quickness and effectiveness of coronary reperfusion and consequently, to real infarct size[9].

The necessary time for a complete functional recovery really differ among patients and, in a single patient, is variable depending on myocardial segments. Several studies with repeated echocardiograms have demonstrated the restoration of left ventricular function since 24 hours to ten days after coronary reperfusion; although, in the presence of stunned myocardium, three or four weeks may be necessary[10].

Echocardiography is important for the evaluation of left ventricular remodeling after ACS both during acute phase, and short and long term follow up; in fact, after effective coronary reperfusion, left ventricle dimensions are constant or reduced in the first three months after STEMI, while increase in patients that have not received an effective myocardial tissue reperfusion[11]. The patency of the infarct vessel is also linked to the improvement of regional function and to the reduction of dilatation of left ventricle since one to six months from symptoms onset[12,13].

Prognosis after AMI is related to the severity of left ventricular systolic impairment (infarct size) and to the presence and extension of residual myocardial ischemia[14]; in facts, an infarcted area of more than 35% of whole left ventricle identifies patients at high risk of further events (reinfarction and death), with a percentage of mortality of 50% in the first month after AMI[15].

Several multivariate analyses have demonstrated that wall motion score index (WMSI) and left ventricle ejection fraction (LVEF) are important predictors of major adverse cardiovascular events (MACEs) and provide an accurate risk assessment (even more than haemodinamic parameters[16-20]). After STEMI, high values of WMSI identify patients at high risk of early in-hospital death, heart failure and fatal arrhythmias[21].

Left ventricle ejection fraction (LVEF), expression of global systolic function, is another very reliable parameter for long-term prognosis after AMI; in a population of 512 AMI patients, end-systolic area and left ventricle systolic function calculated on the basis of echocardiogram performed eleven days and one year after symptoms onset, were the stronger predictors of death and MACEs[22].

Another important relief during the acute phase of AMI is the presence of hyperkinesis of myocardial segments not related to the infarct vessel; the absence of compensatory hyperkinesis is expression of multivessel coronary disease[21,23,24] and is associated with an higher incidence of death, reinfarction and heart failure[25].

Actually, evaluation of left ventricular function can be performed with several echocardiographic methods: M-mode, two dimensional (2D) and Doppler [pulsed-wave (PW), continuous-wave (CW) and color] echocardiography, three dimensional (3D) echocardiography, backscatter, automatic border detection (ABD) and left ventricular opacification (LVO), color kinesis and tissue doppler imaging (TDI). Echocardiographist experience (operator-dependence) partially limits the use of this tecnique in the diagnosis, risk assessment and follow up of AMI.

The increasing potentiality and flexibility of digital techniques are only partially utilized in acquisition, recording and off-line analysis of echocardiographic data, but it is easy to forecast a future dominant role of these methods in ultrasonic imaging.

The achievement of concrete progress in real-time echocardiographic imaging is due to a better comprehension of interactions between ultrasounds and tissues and to a better knowledge of formation, enhancement, analysis and quantification of ultrasonographic images.

The interest in the availability of a quantitative method using an echocardiogram can be attributed to three main reasons: a) qualitative methods for the appraisal of left ventricular function are subjective and difficult to reproduce, b) a wide inter-operator variability in identifying events that materialize in a short period of time (< 80 msec) and finally, c) it is extremely difficult to single out the onset and duration of two or more occurrences that take place simultaneously.

AIM

Aim of the study were the validation and use of a new ultrasonic software for semi-automatic evaluation of global and regional left ventricular function in patients with STEMI.

Moreover, this software was used to analyze the myocardial deformation (strain) and systolic and diastolic local velocities at infarcted and peri-infarcted region level; the aim of this evaluation was to identify the most important functional parameters for short and long term prognosis after STEMI.

MATERIALS AND METHODS

Study population

We analyzed 39 patients (mean age 59 ± 13 years, 76.9% men), admitted to the intensive coronary care unit of the Cardiac, Thoracic and Vascular Department of Pisa University Hospital with a diagnosis of STEMI.

STEMI was defined according to the European Society of Cardiology/American College of Cardiology and American Heart Association/American College of Cardiology criteria[1,26].

The selection did not require the approval of the Institutional Ethical Committee because patients' name were not revealed and echocardiographic evaluation was performed within our standard diagnostic method without any additional procedure for the patient. All patients, however, were informed about and agreed to data collection and study execution. All available clinical data were collected and stored in an appropriate database.

Inclusion criteria of study patients were:

- a prior diagnosis of STEMI;
- a TIMI-3 (angiographic evidence of grade 3 coronary flow proposed by the Thrombolysis in Myocardial Infarction study group) flow of the infarct-related coronary artery after primary or rescue PCI;
- an adequate acoustic window.

Patients with malignancies, sepsis, immunologic disease, chronic renal failure (serum creatinine ≥ 2.5 mg/dl), advanced liver disease, central nervous system damage, severe anemia (Hb ≤ 10 g/dl) and aged more than 85 years were excluded.

77% (31 patients) and 13% (8 patients) were treated with primary and rescue PCI respectively. Twenty-three, 5 and 11 patients showed one-, two, and three-vessel coronary disease respectively; a complete myocardial revascularization (during the first week after STEMI) was performed in 9 out of 16 patients with multivessel coronary disease.

After initial treatment (primary or rescue PCI), medical long-term therapy was administered according to clinical findings and physician judgment.

Briefly, aspirin, clopidogrel, angiotensin-converting enzyme inhibitors, 3-hydroxy-3-methylglutaryl coenzime A reductase

inhibitors (statins) and β-blockers were administered as standard therapy to all patients (except contraindications).

Study procedures

All study patients were submitted to conventional echocardiography [M-mode, 2D and Doppler (PW, CW and color)] performed with a "Sequoia" echograph equipped with "4S" transducer at intensive coronary care unit admittance time [time 0 (t0)], three days [time 1 (t1)] and six days [time 2 (t2)] from symptoms onset.

We obtained mono dimensional echocardiographic images by short and long axis parasternal view and two dimensional echocardiographic images by two, four and five apical chamber views. Left ventricular diameters, interventricular septum and posterior wall thickness were measured according to the American Society of Echocardiography criteria[27]; end-diastolic and end-systolic volumes and global ejection fraction of left ventricle were obtained with Simpson's rule formula[28].

Left ventricular mass (LVM) was calculated with Devereux's formula (Penn Convention)[29], indexed for body surface ($LVMi_{bs}$) and height ($LVMi_{h}$)[30,31].

We evaluated PW Doppler parameters of transmitral flow velocity: E peak (velocity peak of transmitral flow in early diastole), A peak (velocity peak of transmitral flow during atrial systole), E/A ratio, mitral acceleration time (from baseline to E peak), mitral deceleration time (from E peak to baseline) and isovolumetric relaxation time (IVRT).

Regional wall motion was studied after subdivision of left ventricle in 16 segments according to the American Society of Echocardiography Guidelines[27].

We attribute to each segment a systolic wall thickening score as follow:

- normokinesia (point 1);
- hypokinesia (points 2);
- akinesia (points 3);
- dyskinesia (points 4).

The degree of wall motion abnormality was categorized adding up the score of each segment and dividing the result by total number of evaluated segments [according to wall motion score index (WMSI)][32]. Two dimensional echocardiographic images, obtained by 2,4,5 apical chamber views, were transferred to a personal computer and analyzed off-line with a new software “DIOGENE” (AMID technology, Italy). “DIOGENE” provides global and regional LVEF evaluation through automatic border detection searching for each single points the maximum likelihood in the greyscale pattern over its neighbourhoods in the following frames. With “Diogene” the endocardial border is not determined by software, but it’s traced on a single frame by an expert operator and then it’s followed by software during the acquired cardiac cycles (Figure 1).

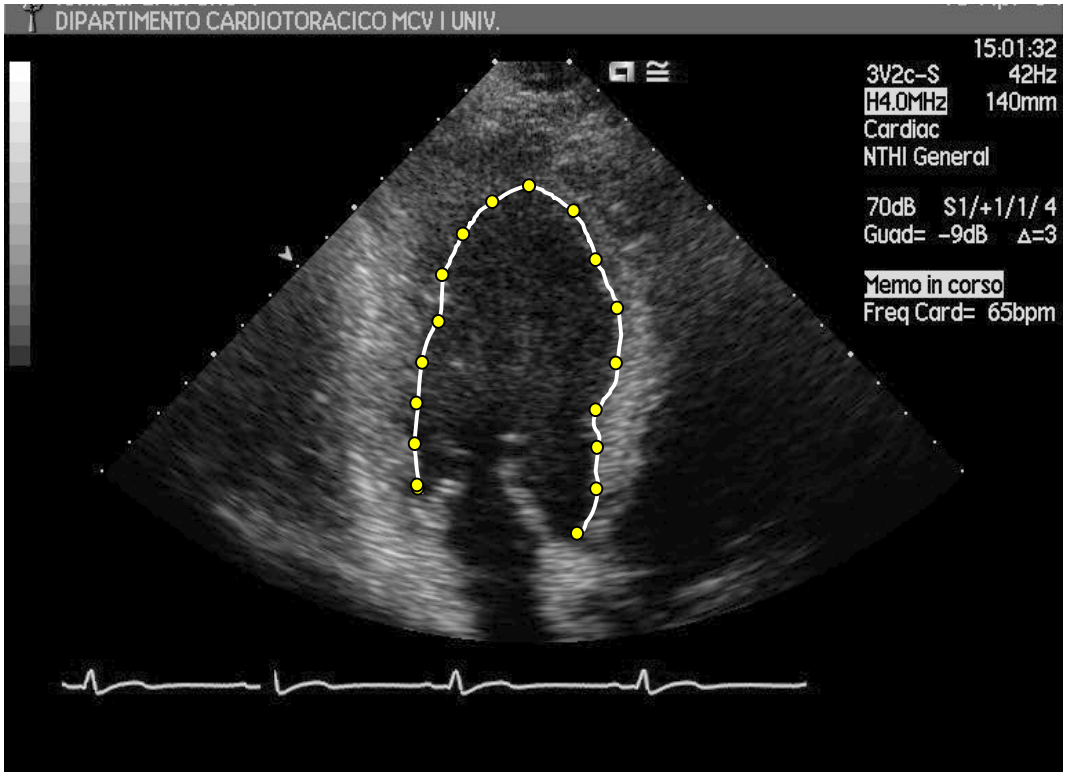

Figure 1: endocardial border layout on four apical chamber view.

Using DIOGENE software, ambiguities of a total automatic approach are eliminated and a more careful check is possible.

Endocardial border, drawed on a sigle frame, is identified by a series of single points and then it's followed by software frame by frame.

Calculation of traced points shifting, frame by frame during cardiac cycle, provides velocity vector data, peculiar of the motion of the same points[33,34].

Unlike TDI, velocities calculated with “DIOGENE” are vectorial (two components) and not dependent on the ultrasonic angle of incidence. After definition of endocardial border in every frame, left ventricular volumes are calculated according to Simpson’s rule formula[28], using 64 equally-spaced disks between mitral floor and apex; with this method, “DIOGENE” is able to calculate both global and regional (16 segments) systolic funtion of left ventricle.

With the same technique it’s possible to investigate shifting and velocity vectors of points in the myocardial thickness, permitting the evaluation of two parameters, expression of average behaviour of wall thickness: strain and strain-rate, strictly linked to intramyocardial regional function[34,35-39].

Strain can be defined the deformation of an object indexed for its original shape. Strain of a monodimensional element is the ratio between change of its lenght after stress and its original lenght: $\Delta = (L - L_0)/L_0$ (Figure 2).

Strain of a two-dimensional element provides a monoaxial deformation along two orthogonal directions (Figure $2_{1\text{-}2}$) and angular changes between these two axes (Figure $2_{3\text{-}4}$). Strain of a two-

dimensional element is a matrix with four indexes of deformation: two axial indexes and two angular indexes. This matrix is named tensor of deformation, with dimensions 2x2.

Likewise strain of a three-dimensional element is delineated by nine indexes of deformation: three axial indexes and six angular indexes. Tensor of deformation have dimensions 3x3.

In this study we considered the mono-dimensional deformation of a segment of left ventricular wall, belonging to the endocardial border traced point by point.

Deformation of evaluated segments depends on their endocardial border location and time. If we know istant by istant start and end-time segment deformation of the process we can define instantaneous deformation of the segment at t time such as: $\Delta(t) = [L(t) - L(t_0)\ ]/\ L(t_0)$.

Moreover, the deformation at generical instant t can be expressed referring to the deformation at the immediately former instant: $d\Delta(t) = [L(t+dt) - L(t)\ ]/\ L(t)$.

In this way, total deformation of a segment between two instants $t_0 - t_1$ is the addition of single deformations at time intervals dt, in which the

interval $t_0 - t_1$ is resolved. Deformation so calculated is named *natural deformation*. Natural deformation is the most adequate to assess wide deformations like that during contraction and relaxation phases of cardiac cycle.

Strain is a measure of the evaluated segment own activity and it is strictly linked to tissue effective contractility.

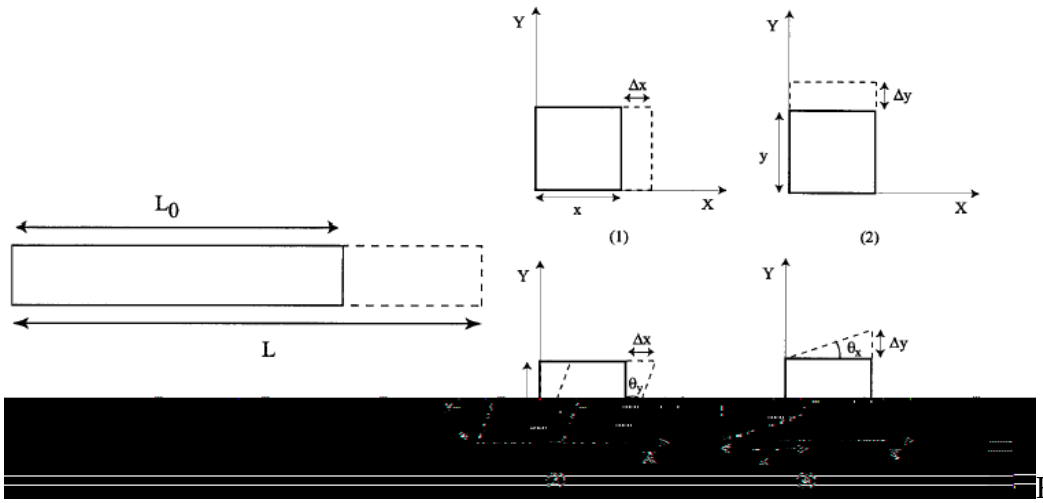

Figure 2: strain concept illustration.

Strain rate is expression of the velocity of deformation and it's measure unit is s^{-1}; strain rate is calculated with the first derivative of deformation (strain) in the time.

Instantaneous strain rate is defined with the formula $\varepsilon(t) = L'(t)/L(t)$: $L'(t)$ is the deformation rate in the unit time and $L(t)$ is the instantaneous lenght of evaluated segment.

Strain rate is a measure of deformation in the time and it expresses shortening velocity for lenght of myofibril. Mean strain rate of a Δr long segment at the instant t is defined with the following formula: $\varepsilon(t) = [v(r + \Delta r) - v(r)]/ \Delta r$ (Figure 3).

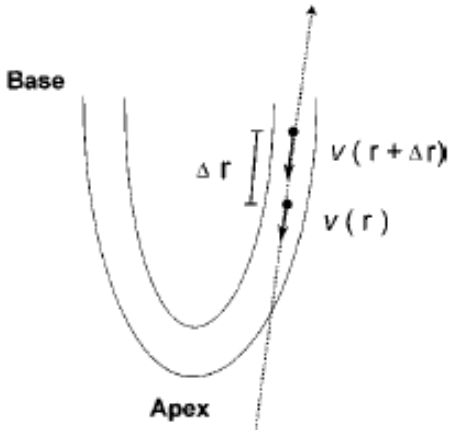

Figure 3: strain rate concept illustration.

Strain rate is zero for equal velocities of deformation in the two points; if the difference $v(r+\Delta r) - v(r)$ is positive we have traction, otherwise we have compression.

In this way, in every patient after STEMI, we evaluated (by two, four and five apical chamber views) longitudinal strain of some regions of left ventricle (figure 4).

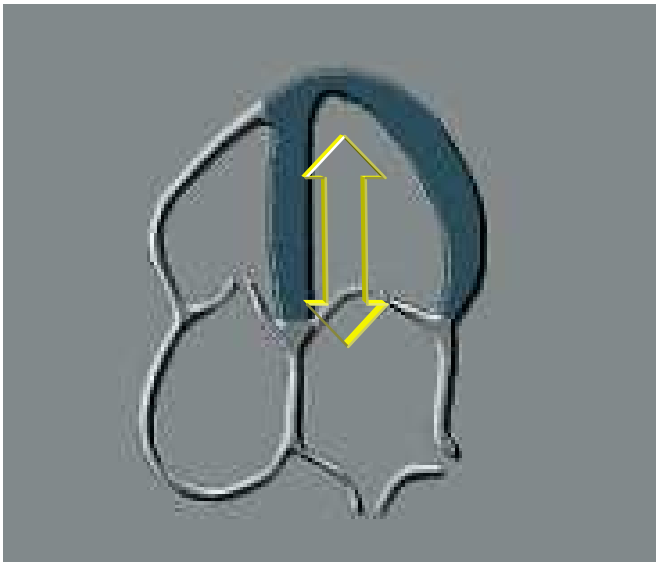

Figure 4: longitudinal strain.

In figure 5 we can observe an example of “Diogene” elaboration relative to intra-myocardial velocities and strain and strain rate behaviour. The curves of velocities (left ordinate in cm/s) and strain (right ordinate in %) time variation are reported in the low diagram; likewise the curves of velocities (left ordinate in cm/s) and strain rate (right ordinate in s^{-1}) time variation are reported in the high diagram.

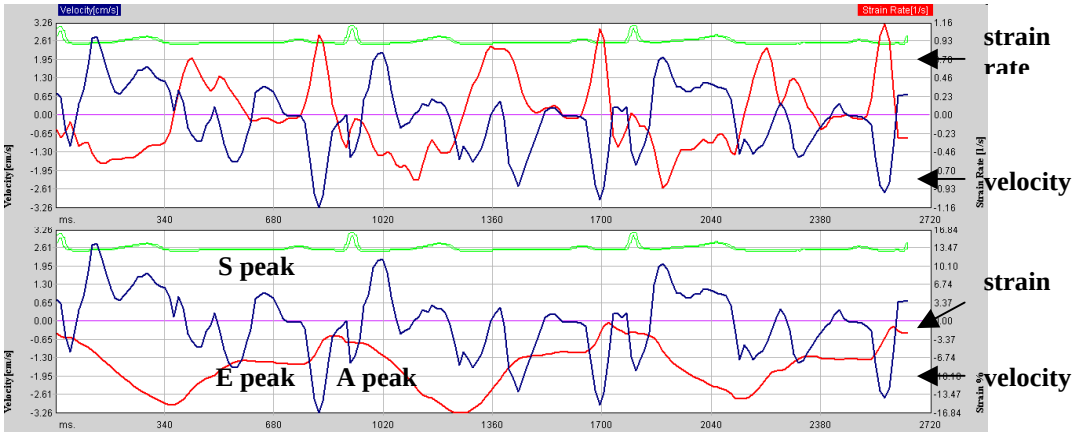

Figure 5: velocity, strain and strain rate time variations.

With “Diogene” in all study patients we obtained end-diastolic volume (EDVc), end-systolic volume (ESVc), global ejection fraction (EFc) and regional ejection fraction (EFr) of the sixteen segments of left ventricle at t0, t1 and t2.

In this way we identified myocardial areas with different behaviour: 1- akinetic areas at t0, t1 and t2 (infarcted areas); 2- areas in wich EFr has improved (stunned myocardium); 3- areas in wich EFr has impaired (extension of ischemia); 4- “healthy” areas not injuried by ischemia.

“Diogene” marks EFr with different values and colours: 1- EFr > 35% (green colour) is normal; 2- 15% < EFr < 35% (red colour) is expression of an hypokinetic segment; EFr < 15% (blue colour) is expression of akinesia (Figure 6).

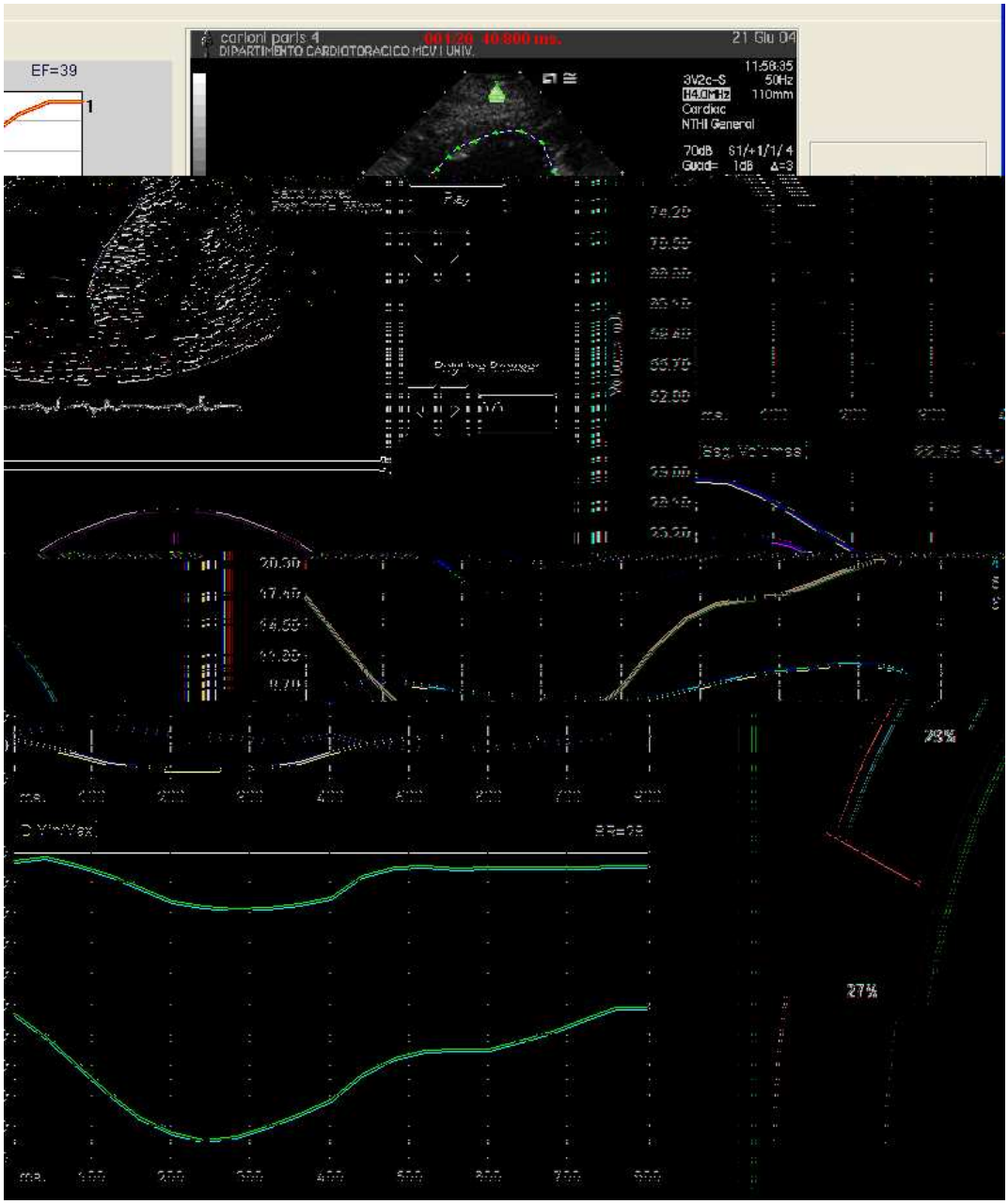

Figure 6: EFr calculation with “Diogene”.

We studied intra-myocardial function of four areas, according to the values obtained with the software and the infarct coronary vessel: 1- a first infarcted area, akinetic or severely hypokinetic at all evaluation

times; 2- a second infarcted area, akinetic or severely hypokinetic, that only in nine patients showed an improvement of EFr with recovery of a normal value at t2; 3- a peri-infarcted area that showed a variable behaviour (improvement of EFr in 32 patients; light worsening in seven patients); 4- “healthy” area not injuried by ischemia, that showed a normal EFr at all evaluation times.

In every area, “Diogene” provided strain and strain rate of evaluated segment and intra-myocardial velocities of each point selected for vectorial analysis (three points for every segment): S peak (systolic peak), E peak (proto-diastolic peak), A peak (end-diastolic peak)[40-42] (Figure 5).

Patients of the study were divided onto two groups according to LVEF percent variation, obtained with conventional echocardiography: group 0 (20 patients, 80% men) with improved or constant ejection fraction and group 1 (19 patients, 74% men) with LVEF impairment.

Inter-individual and intra-individual variability of values obtained with manual and semi-automatic method was very low. Evaluated parameters correlation was between 0.9 and 0.93 referring to inter-

individual variability values and between 0.89 and 0.94 referring to intra-individual variability values.

Statistical analysis

Continuous variables are expressed as mean values and standard deviation. Analysis of variance for repeated measures and Tukey test were performed to evaluate echocardiographic parameters longitudinal differences (at t0, t1 and t2). Student's t-test for not-paired data was performed for cross comparison between group 0 and group 1. We used analysis of variance for repeated measures according to Bland-Altmann method to evaluate semi-automatic method repetibility, with an intra and inter-class coefficient.

All calculation were performed using SPSS/PC+11-5 statistical software.

Linear regression method was performed to obtain echocardiographic parameters correlation coefficients. The results were considered significant when the p value was < 0.05.

RESULTS

Study patients were divided into two different groups in relation to LVEF values obtained with conventional echocardiography at t0, t1 and t2 evaluation: group 0 patients showing improved or constant LVEF (t0 vs t2: 46.88 ± 4.26 vs 54.38 ± 5.85%; $p < 0.05$) (Figure 7), and group 1 patients showing LVEF impairment (t0 vs t2: 54.00 ± 6.48 vs 49.11 ± 2.57%; $p < 0.01$) (Figure 8)

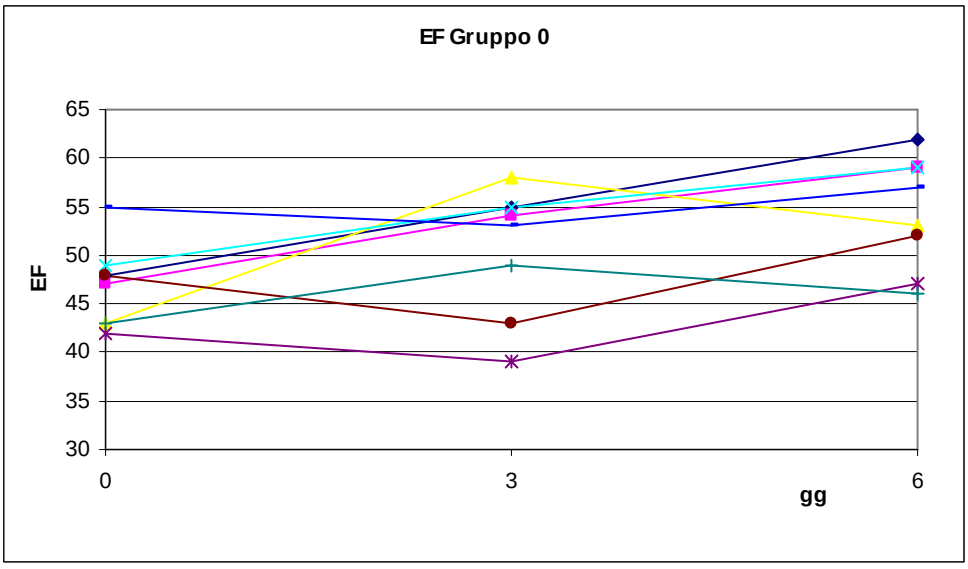

Figure 7: time course variation of LVEF in group 0. LVEF values are expressed as percentage.

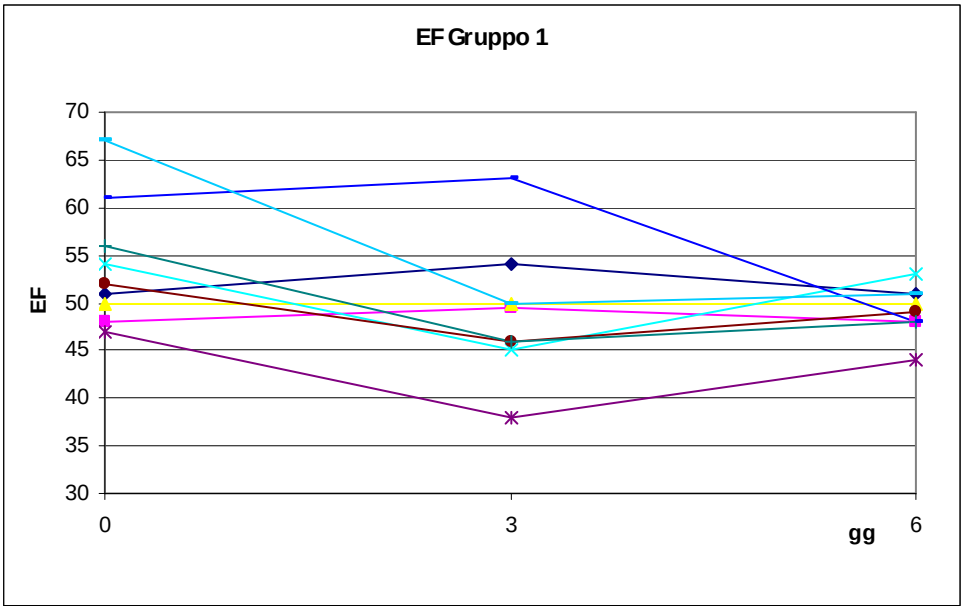

Figure 8: time course variation of LVEF in group 1. LVEF values are expressed as percentage.

Age, body mass index (BMI), body surface, heart rate, systolic and diastolic arterial pressure, cardiac damage serum markers (except Troponin I peak value significantly higher in group 1) were similar between group 0 and 1 (Table 1).

Correlations between Troponin I peak value and EDV, ESV, EF, EDVc, ESVc and EFc were evaluated at t0, t1 and t2; we observed a significant correlation between I Troponin peak value and EF at t2 ($p < 0.02$) and EFc at t2 ($p < 0.05$).

The same values were compared with intra-myocardial indices and showed a significant correlation with the value of strain peak at first infarcted region level at t2 ($p < 0.01$) and with strain rate at second infarcted region level at t2 ($p < 0.03$).

CKMb peak values were similar between group 0 and group 1; nevertheless they correlated with EF at t2 ($p < 0.02$), EFc at t2 ($p < 0.05$) and strain peak of first infarcted region at t2 ($p < 0.01$).

Coronary angiography was performed in all study patients. In group 0 ten patients showed a single-vessel coronary artery disease, while five patients showed a two and three-vessel coronary artery disease. We observed in 14 patients occlusion of left anterior descending artery and in six patients the occlusion of left circumflex artery. Primary PCI of “culprit” lesion was performed in all group 0 of patients; we completed myocardial revascularization in eight patients with multi-vessel coronary artery disease during the first week after AMI. In group 1, 15 patients showed a single-vessel coronary artery disease, while four patients showed a three-vessel coronary artery disease (in these patients only PCI of “culprit lesion” was performed). We observed in eight patients the occlusion of left anterior descending

artery, in eight patients the occlusion of left circumflex artery and in three patients the occlusion of right coronary artery. Primary PCI of "culprit" lesion was performed in eleven patients, while rescue PCI was reserved for eight patients.

Left ventricular dimensions obtained in M-mode, LVM and trans-mitral flow velocity were similar between group 0 and group 1 at t0 (Table 4).

Referring to left ventricular volumes and global ejection fraction obtained with conventional echocardiography (Table 2) we observed: 1) EDV did not significantly differ between group 0 and group 1; 2) ESV and EF at t0 were respectively higher ($p < 0.02$) and lower ($p < 0.02$) in group 0, while EF at t2 was higher ($p < 0.04$) in group 0.

Analysis of EDV, ESV and EF at t0, t1 and t2 showed an opposite behaviour between group 0 and group 1.

In group 0, EDV showed a not significant reduction, while ESV was significantly reduced ($p < 0.05$) and EF gradually increased ($p < 0.01$).

In group 1, EDV and ESV increased ($p < 0.04$ and $p < 0.01$ respectively), while EF showed t1 values significantly lower than t0 ($p < 0.04$) and t2 values similar to t1 ($p = ns$) (Table 2 and table 3).

Wall motion score index values showed a significant time-dependent reduction (t0 vs t2; 1.64 vs 1.53; $p < 0.01$) in group 0. Otherwise, in group 1 WMSI values gradually increased from t0 to t2 (1.55 vs 1.62; $p < 0.05$) (Table 7 e table 8).

With “Diogene” we automatically calculated left ventricular volumes and ejection fraction (Table 5 e table 6).

EFc values at t0 were significantly higher in group 1 compared with group 0. According to results obtained with conventional echocardiography, in group 0 EFc values gradually increased ($p < 0.04$) from t0 to t2, while in group 1 EFc showed t2 values significantly lower than t0 ($p < 0.04$).

Ejection fraction values, obtained with conventional echocardiography, and EFc values, calculated with “Diogene”, significantly correlate ($p < 0.001$) (Figure 9).

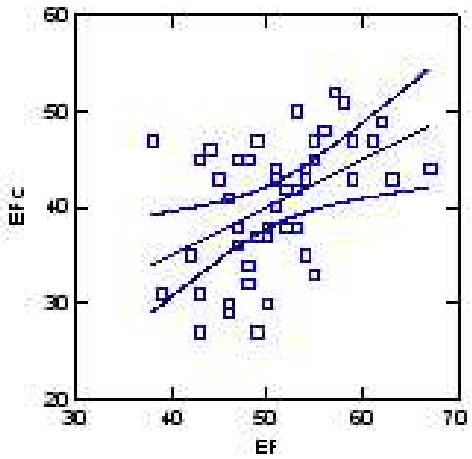

Figure 9: linear regression analysis for EF and EFc values.

In group 0, EDVc values were similar at all times, while ESVc values gradually decreased ($p < 0.05$). In group 1, EDVc and ESVc were increased since t0 to t2 with consequent left ventricular dilatation and dysfunction.

Correlation between EDV and ESV values, obtained with conventional echocardiography and with “Diogene” were statistically significant (EDV $p < 0.0001$; ESV $p < 0.001$) (Figure 10 and 11).

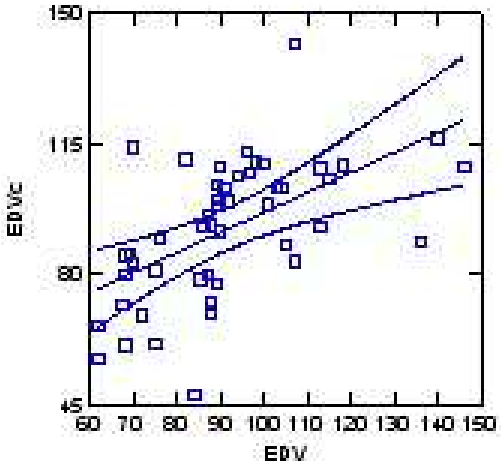

Figure 10: EDV and EDVc values correlation.

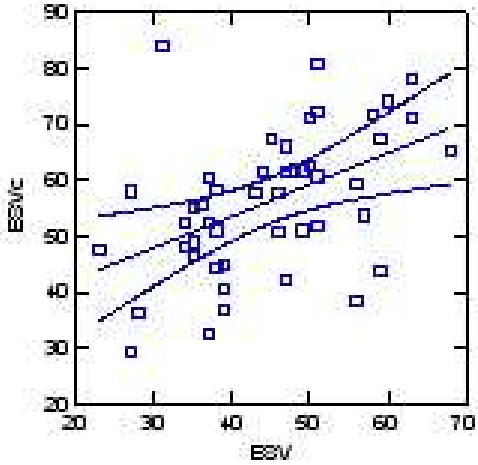

Figure 11: ESV and ESVc correlation.

With “Diogene” we studied systolic and diastolic intra-myocardial function of left ventricular four areas (two infarcted areas, a peri-infarcted area and an “healthy” area).

All evaluated parameters showed similar values between group 0 and group 1.

In relation to time course variation of every single value, in each group, we observed:

1- First infarcted area (Table 9 and table 10):

in group 0 strain and strain rate values were constantly similar. S peak values gradually decreased (t0 vs t2; 1.87 vs 1.44; $p < 0.04$), while E peak showed a significant reduction at t1 (t0 vs t1; -1.59 vs -0.7 $p < 0.01$) with similar values at t1 and t2 (t1 vs t2; -0.7 vs 0.78 p ns); A peak was steady.

In group 1 strain and strain rate values showed a significant reduction (t0 vs t2; strain: -16.9 vs -8.74, $p < 0.04$; strain rate: 0.71 vs 0.37, $p < 0.05$). S peak significantly differed with t1 values lower than t0 (t0 vs t1; 1.37 vs 1.01; $p < 0.05$) and a small improvement at t2 (t1 vs t2; 1.01 vs 1.06; p = ns). E peak and A peak were similar at the three evaluation times.

2- Second infarcted area (Table 11 and table 12):

in group 0 strain and strain rate values were similar at the three evaluation times. S peak improved (t0 vs t2; 1.46 vs 2.42; $p < 0.05$), while E and A peaks were stable.

In group 1 strain and strain rate did not significantly differ. S peak (t0 vs t2; 2.05 vs 1.17; $p < 0.05$) decreased and E peak (t0 vs t2; -2.32 vs -0.58; $p < 0.04$) gradually improved, while A peak was stable.

In this area we observed a different behaviour of mean systolic velocity between group 0 and group 1.

3- Peri-infarcted area (Table 13 and table 14):

in group 0 strain (t0 vs t2; -18.21 vs -21.25; $p < 0.05$) and strain rate (t0 vs t2; 0.56 vs 0.65; $p < 0.05$) values showed a significant improvement. S peak gradually improved ($p < 0.05$). We observed a normalization of diastolic parameters with increase of E peak (t0 vs t2; -1.43 vs -1.77; $p < 0.05$) and reduction of A peak (t0 vs t2; -2.16 vs -1.28; $p < 0.02$).

In group 1 strain (t0 vs t2; -15.07 vs -25.58; $p < 0.03$) and strain rate (t0 vs t2; 0.88 vs 0.35; $p < 0.05$) values showed a significant improvement. S peak gradually improved (t0 vs t2; 1.78 vs 2.41; $p < 0.05$). E peak showed an oscillating time course with t1 levels lower

than t0 and a significant increase at t2 (t1 vs t2; -1.1 vs -1.96; $p < 0.05$), while A peak was steady: impairment of diastolic phase persisted.

4- “Healthy” area (Table 15 and table 16):

in group 0 strain (t0 vs t2; -14.28 vs -21.04; $p < 0.05$) and S peak (t0 vs t2; 2.39 vs 3.38; $p < 0.05$) values were improved.

In group 1 all intra-myocardial function parameters not significant differed at the three evaluation times.

To evaluate the prognostic burden of strain and strain rate, we studied correlations between these values and EDV, ESV and EF values, obtained with conventional echocardiography and with “Diogene”.

We observed in the first infarcted area, a significant correlation between peak strain at t0 and ESV value at t2 ($p < 0.05$) and EFc value at t2 ($p < 0.05$). Another correlation was between peak strain at t2 and EF at t2 ($p < 0.01$).

DISCUSSION

End-diastolic and end-systolic volumes of left ventricle obtained with conventional two-dimensional echocardiography (Simpson's rule formula) are significantly correlated with the volumes obtained with ventriculography (cardiac catheterization) and myocardial scintigraphy.

In this study we compared left ventricular function parameters obtained by an expert operator with conventional echocardiography and with semi-automatic "Diogene" evaluation. We observed a significant correlation between values obtained with these techniques, showing the high reliability of semi-automatic method.

Preliminary partition of the patients in two groups, obtained by strength of left ventricular ejection fraction tendency to improve or to decrease, was performed with conventional echocardiography and was confirmed by the analysis of other important parameters commonly employed (Troponin I peak, WMSI, ESV).

First of all, patients of group 0, in those we observed an improvement of left ventricular ejection fraction and a reduction of ventricular volumes, were treated with primary PCI of the “culprit lesion”. This event can be explained with a greater effectiveness of primary PCI to preserve or to provide a further recovery of left ventricular volumes (especially end-systolic volume) and ejection fraction.

At t0 ESV and EF values significantly differ between group 0 and group 1, but they showed a following inverse time course.

In group 0, ESV and EF, at t0, were respectively higher and lower than in group 1. These values inverted at t2; ESV was lower in group 0 than in group 1, while EF was significantly higher in group 0.

The results of this study agree with other studies in those major predictors of adverse cardiovascular events after acute myocardial infarction were end-systolic area and global systolic function of the left ventricle[22].

The same data are confirmed by the analisys of WMSI; it shows, since t0 to t2, an important reduction in group 0 and a signficant improvement in group 1.

The original side of the study is the possibility to analyze the intra-parietal segmental function of left ventricle with the semi-automatic approach. It expresses the deformability of evaluated segment (strain) and its rate of deformability (strain rate).

These parameters, calculated at the three evaluation times, are very interesting, because they are relatively independent of left ventricular pre-load and after-load; moreover they are independent of rotation and translation movements of the heart.

Furthermore “Diogene” provides to evaluate regional deformability of left ventricular walls, with the aim to identify ischaemic areas and to analyze residual function.

Semiautomatic evaluation of intra-myocardial function of the left ventricular four areas shows as following:

1- First infarcted area: in both described groups an oscillating but substantially stable course of the variables is observed. In group 1 actually inferior values are recorded, with reference to the deformability of the segment, regarding group 0; the strain peak clearly reduces.

2- Second infarcted area (close to zone 1): one first differentiation in the behaviour of the two groups is observed. In the group 0 strain values, strain rate, E and A peak are maintained stable in the time, while peak S, index of velocity of the movement of myocardial fibers in systolic phase, increases meaningfully, indicating a possible improvement of the functionality of such segment. A further reduction of peak S and E in the group 1 is observed, therefore a further worsening of the systolic and active diastolic function of the myocardium, that it could suggest an extension of the infarcted zone.
3- Peri-infarcted area: in both groups an improvement of the indices of intramyocardical function with increase of strain, strain rate and S peak, even if more emphasized in group 1. This appearing contradiction is imputable to the selection procedure of the surveying zones; perinfarctual zones have been chosen in some patients of group 0 that seem to worse ventricular function and, however, also in the other zones EF, between t0 and t2, turns out inferior in comparison the correspondent value in group 1. However an improvement clearly comes true, with trend to normalization, of the diastolic phase in group 0, while in group 1 it remains altered.

4- “Healthy” area: also in these myocardial segments, not interested from the ischemic event, the tendency to improvement of the deformability and systolic velocity in group 0 is observed, while in group 1 is recorded a substantial stability.

The more interesting potentiality of the employment of automatic techniques is, by far, the possibility to refer to the results of strain analyses, executed at t0, as predictive indices of ventricular remodelling six days after the acute event.

Such possibility is the consequence of the existing correlation between the peak values of strain in the first infarctual region, where the regional EF maintained less than 35%, and the values of EF to t2 and those of the end-systolic volume always to t2.

These considerations allow to employ the indices of strain to evaluate, already beginning at t0, patient’s probability to re-enter in the categories to greater risk of development of complications of AMI, suggesting a more aimed clinical monitoring and therapy.

Another important aspect is the meaningful correlation between the parameters of left ventricular function and peak values of troponin I,

CK-Mb and WMSI, that constitute important and well demonstrated prognostic indices.[16,22,43,44]

Peak values of troponin I and CK-Mb show a meaningful correlation with the values of strain peak in the first infartuated area at t2 and the peak of strain rate in the second infarctuated area at t2.

Limits of the semiautomatic method

Such method, being strongly innovative but with a rigorous scientific background, is influenced by the lack of one definitive validation according to standard techniques (ventriculography during cardiac catheterism, nuclear magnetic resonance).

Like all the techniques of automatic survey of the endocardic edge, also the technique we propose depends from the acoustic reflectivity of the subject.

At last the method is an off-line operation, that demands more time in comparison to an ultrasound scan routinely executed during the stay in hospital.

CONCLUSIONS

In this study a serial quantitative appraisal of the whole and regional left ventricular function has been executed in an automatic way through the employment of the “Diogenes” program . Data obtained from elaborations have been punctually compared with those corrispective ones obtained from an expert operator by means of conventional echordiographic techniques. The reliability of results elaborated from Diogenes is demonstrated from high existing correlation indices between the parameters of left ventricular function, calculated in semiautomatic modality and estimated by operator. According to the above-exposed data, “Diogene” program could be used to reduce the variability of measures, mainly imputable to the operator experience.

Obviously, our observations need further validation on large-size population.

Moreover, to confirm prognostic results, it would be of interest to extend study validity increasing over time analysis number after one, six months and one year after AMI.

ABBREVIATIONS

SAP: systolic arterial pressure

DAP: diastolic arterial pressure

EDD: left ventricular end-diastolic diameter

ESD: left ventricular end-systolic diameter

EDV: left ventricular end-diastolic volume

ESV: left ventricular end-systolic volume

EF: left ventricular ejection fraction

EDVi: left ventricular end-diastolic volume indexed for body surface

ESVi: left ventricular end-systolic volume indexed for body surface

FS= fractional shortening

IVSDD: inter-ventricular septum diastolic diameter

IVSSD: inter-ventricular septum systolic diameter

PWDD: posterior wall diastolic diameter

PWSD: posterior wall systolic diameter

LVM: left ventricular mass

LVMbs: left ventricular mass indexed for body surface

SV: stroke volume

HR: heart rate

IVRT: isovolumetric relaxation time

TOTDIAST: total diastolic time

EDVc: left ventricular end-diastolic volume calculated with “Diogene”

ESVc: left ventricular end-systolic volume calculated with “Diogene”

EFc: left ventricular ejection fraction calculated with “Diogene”

WMSI: wall motion score index

TABLES

Table 1: clinical and biochemical parameters.

	Group 0		Group 1		
	Mean	SD	Mean	SD	$p < 0.05$
SAP0	127.5	26.19	127.78	31.83	ns
SAP1	113.13	10.64	109.67	19.49	ns
SAP2	110	9.64	108.33	24.75	ns
DAP0	75	19.46	70	15.71	ns
DAP1	70	8.45	65.11	15.78	ns
DAP2	64.38	12.08	66.11	12.44	ns
Trop I peak	47.15	36.1	85.91	25.04	0.025
Miogl peak	1887.69	1716.78	1669.87	1242.31	ns
CKmbpeak	179.33	101.43	266.61	81.18	ns
HR	69.38	10.32	72.33	14.12	ns

Table 2: conventional echocardiographic parameters.

	Group 0		Group 1		$p < 0.05$
	Mean	SD	Mean	SD	
EDV0	98.5	22.63	85.03	17.18	ns
EDV1	92.81	26.18	87.1	12.53	ns
EDV2	90.75	21.01	92.33	15.48	ns
ESV0	51.75	9.79	38.78	10.37	0.018
ESV1	45.13	13.97	44.11	7.69	ns
ESV2	41.38	10	47.22	7.41	ns
EF0	46.88	4.26	54	6.48	0.017
EF1	50.75	6.61	49.06	6.88	ns
EF2	54.38	5.85	49.11	2.57	0.042
EDVi0	52.19	6.78	46.26	7.12	ns
EDVi1	49.15	9.49	47.7	6.45	ns
EDVi2	48.4	7.89	50.26	5.74	ns
ESVi0	27.59	3.64	21.06	4.97	ns
ESVi1	24.03	6.37	24.28	4.91	ns
ESVi2	22.25	4.9	25.77	3.27	ns

Table 3: intra-group analysis of conventional echocardiographic parameters.

	Group 0				Group 1			
p	0-1	1-2	0-2	glob	0-1	1-2	0-2	glob
EDV	0.05	ns	0.04	0.04	ns	ns	0.04	0.04
ESV	0.05	ns	0.04	0.05	ns	ns	0.01	0.01
EF	ns	ns	0.01	0.01	0.05	ns	0.04	0.04

Table 4: conventional echocardiographic performed at t0.

	Group 0		Group 1		$p < 0.05$
	Mean	SD	Mean	SD	
EDD	5.15	0.54	5.52	0.39	ns
ESD	3.56	0.64	3.65	0.37	ns
FS	31.03	9.11	35.1	5.19	ns
IVSSD	1.31	0.14	1.29	0.19	ns
IVSDD	1.04	0.25	0.97	0.16	ns
PWSD	1.44	0.32	1.4	0.18	ns
PWDD	0.98	0.12	0.93	0.12	ns
LVMbs	126.31	44.7	131.02	28.89	ns
SV	73.3	22.5	92.27	15.78	ns
E peak	0.68	0.15	0.65	0.11	ns
A peak	0.71	0.17	0.8	0.17	ns
E/A ratio	0.99	0.33	0.84	0.24	ns
IVRT	74.25	16.61	62.89	19.81	ns
TOTDIAST	443.25	111.21	419.11	75.34	ns

Table 5: left ventricular systolic function calculated with "Diogene".

	Group 0		Group 1		
	Mean	SD	Mean	SD	$p < 0.05$
EDVc0	94.72	22.9	85.74	15.4	ns
EDVc1	92.88	19.87	82.84	19.05	ns
EDVc2	96.4	11.86	100.86	19.8	ns
ESVc0	61.23	16.21	49.55	10.65	ns
ESVc1	55.98	13.76	56.68	14.22	ns
ESVc2	54.4	6.9	60.28	11.99	ns
EFc0	35.75	6.9	42.38	5.83	0.05
EFc1	40.38	8.43	40.38	5.29	ns
EFc2	43.75	7.55	36.13	4.19	0.04

Table 6: intra-group analysis of left ventricular systolic function calculated with “Diogene”.

	Group 0				Group 1			
p	0-1	1-2	0-2	glob	0-1	1-2	0-2	glob
EDV	ns	ns	ns	ns	ns	0.05	ns	0.05
ESV	ns	ns	0.05	0.05	ns	ns	0.05	0.05
EF	ns	ns	0.03	0.03	ns	ns	0.05	0.05

Table 7: wall motion score index.

	Group 0		Group 1		
	Mean	SD	Mean	SD	$p < 0.05$
WMSI0	1.64	0.23	1.55	0.15	ns
WMSI1	1.63	0.24	1.56	0.16	ns
WMSI2	1.53	0.24	1.62	0.27	ns

Table 8: intra-group analysis of WMSI.

	Group 0				Group 1			
p	0-1	1-2	0-2	glob	0-1	1-2	0-2	glob
WMSI	ns	0.05	0.01	0.02	ns	0.05	0.05	0.05

Table 9: intra-myocardial function parameters calculated with "Diogene" of the first infarcted area.

	Group 0		Group 1		$p < 0.05$
	Mean	SD	Mean	SD	
Strain peak 0	-12.2	7.88	-16.9	8.93	ns
Strain peak 1	-16.99	8.21	-7.54	6.14	ns
Strain peak 2	-18.55	9.07	-8.74	7.37	ns
Strain rate 0	0.64	0.27	0.71	0.54	ns
Strain rate 1	0.83	0.79	0.55	0.62	ns
Strain rate 2	0.51	0.49	0.37	0.22	ns
S peak 0	1.87	1.45	1.37	1.33	ns
S peak 1	1.67	1.59	1.01	1.05	ns
S peak 2	1.44	1.39	1.06	1.64	ns
E peak 0	-1.59	1.19	-0.64	0.68	ns
E peak 1	-0.7	0.76	-0.69	0.76	ns
E peak 2	-0.78	2	-0.72	0.91	ns
A peak 0	-1.82	1.44	-2	2.95	ns
A peak 1	-1.28	1.29	-0.87	1.06	ns
A peak 2	-2.14	3.1	-2.44	2.97	ns

Table 10: intra-group analysis of intra-myocardial function parameters calculated with "Diogene" of the first infarcted area.

	Group 0				Group 1			
p	0-1	1-2	0-2	glob	0-1	1-2	0-2	glob
S.peak	ns	ns	ns	ns	0.04	ns	0.05	0.04
S.rate	ns	ns	ns	ns	ns	ns	0.05	0.05
Speak	ns	ns	0.04	0.04	0.05	ns	0.05	0.05
Epeak	0.01	ns	0.01	0.01	ns	ns	ns	ns
Apeak	ns	ns	ns	ns	ns	ns	ns	ns

Table 11: intra-myocardial function parameters calculated with "Diogene" of the second infarcted area.

	Group 0		Group 1		$p < 0.05$
	Mean	SD	Mean	SD	
Strain peak 0	-20.9	7.77	-19.05	4.35	ns
Strain peak 1	-20.1	9.85	-16.4	6.08	ns
Strain peak 2	-19.27	6.18	-17.36	4.48	ns
Strain rate 0	0.76	0.63	0.58	0.55	ns
Strain rate 1	0.93	0.49	0.62	0.36	ns
Strain rate 2	0.89	1.12	0.89	0.88	ns
S peak 0	1.46	1.47	2.05	1.99	ns
S peak 1	2.31	1.57	1.78	1.45	ns
S peak 2	2.42	2.23	1.17	1.39	ns
E peak 0	-1.99	2.14	-2.32	1.57	ns
E peak 1	-1.67	1.03	-0.76	0.98	ns
E peak 2	-1.29	1.32	-0.58	1.29	ns
A peak 0	-2.95	3.49	-3.21	3.45	ns
A peak 1	-2.24	1.87	-2.26	2.52	ns
A peak 2	-1.3	1.24	-1.46	1.35	ns

Table 12: intra-group analysis of intra-myocardial function parameters calculated with "Diogene" of the second infarcted area.

	Group 0				Group 1			
p	0-1	1-2	0-2	glob	0-1	1-2	0-2	glob
S.peak	ns	ns	ns	ns	ns	ns	ns	ns
S.rate	ns	ns	ns	ns	ns	ns	ns	ns
Speak	0.05	ns	0.05	0.05	ns	0.05	0.05	0.05
Epeak	ns	ns	ns	ns	0.03	ns	0.04	0.04
Apeak	ns	ns	ns	ns	ns	ns	ns	ns

Table 13: intra-myocardial function parameters calculated with "Diogene" of the peri-infarcted area.

	Group 0		Group 1		$p < 0.05$
	Mean	SD	Mean	SD	
Strain peak 0	-18.21	13.49	-15.07	11.35	ns
Strain peak 1	-16.04	10.01	-14.7	6.38	ns
Strain peak 2	-21.25	4.26	-25.58	13.63	ns
Strain rate 0	0.56	0.23	0.88	0.5	ns
Strain rate 1	0.55	0.4	1.13	1.02	ns
Strain rate 2	0.95	0.55	1.35	0.98	ns
S peak 0	2.12	1.67	1.78	0.93	ns
S peak 1	1.89	1.35	2.24	1.39	ns
S peak 2	2.19	0.97	2.41	0.6	ns
E peak 0	-1.43	1.23	-2.19	1.6	ns
E peak 1	-1.58	1.21	-1.1	0.97	ns
E peak 2	-1.77	1.48	-1.96	1.33	ns
A peak 0	-2.16	2.09	-2.31	1.28	ns
A peak 1	-2.33	1.84	-1.76	2.19	ns
A peak 2	-1.28	0.96	-1.96	1.27	ns

Table 14: intra-group analysis of intra-myocardial function parameters calculated with "Diogene" of the peri-infarcted area.

	Group 0				Group 1			
p	0-1	1-2	0-2	glob	0-1	1-2	0-2	glob
S.peak	ns	ns	0.05	0.05	ns	0.04	0.02	0.03
S.rate	ns	0.05	0.05	0.05	0.05	ns	0.05	0.05
Speak	ns	0.05	ns	0.05	ns	ns	0.05	0.05
Epeak	ns	ns	0.05	0.05	0.04	0.05	ns	0.05
Apeak	ns	0.02	ns	0.02	ns	ns	ns	ns

Table 15: intra-myocardial function parameters calculated with "Diogene" of the "healthy" area.

	Group 0		Group 1		
	Mean	SD	Mean	SD	$p < 0.05$
Strain peak 0	-14.28	9.54	-19.48	10.41	ns
Strain peak 1	-25.43	7.75	-19.23	11.2	ns
Strain peak 2	-21.04	6.63	-28.66	16.8	ns
Strain rate 0	0.91	0.99	1.04	1.49	ns
Strain rate 1	1.34	1.11	1.06	1.03	ns
Strain rate 2	1.01	0.48	0.91	0.64	ns
S peak 0	2.39	0.71	2.99	0.88	ns
S peak 1	3.37	1.81	3.15	1.61	ns
S peak 2	3.38	1.27	3.87	2.2	ns
E peak 0	-2.16	1.49	-2.24	0.95	ns
E peak 1	-2.09	0.9	-2.01	1.62	ns
E peak 2	-1.93	1.43	-2.99	2.52	ns
A peak 0	-2.96	1.79	-4.03	3.6	ns
A peak 1	-3.9	1.77	-2.35	1.52	ns
A peak 2	-4.51	2.44	-2.86	1.89	ns

Table 16: intra-group analysis of intra-myocardial function parameters calculated with "Diogene" of the "healthy" area.

	Group 0				Group 1			
p	0-1	1-2	0-2	glob	0-1	1-2	0-2	glob
S.peak	0.05	ns	0.05	0.05	ns	ns	ns	ns
S.rate	ns	ns	ns	ns	ns	ns	ns	ns
Speak	0.05	ns	0.05	0.05	ns	ns	ns	ns
Epeak	ns	ns	ns	ns	ns	ns	ns	ns
Apeak	ns	ns	ns	ns	ns	ns	ns	ns

REFERENCES

[1] The Joint European Society of Cardiology/American College of Cardiology Committee. Myocardial infarction redefined – A consensus document of the Joint European Society of Cardiology/American College of Cardiology for the redefinition of myocardial infarction. – *Eur Heart J* 2000; 21:1502-13. (Also published in *J Am Coll Cardiol* 2000; 36:959-69).

[2] Davies MJ. – The pathophysiology of acute coronary syndromes. – *Eur Heart J* 2000; 83:361-6.

[3] Van de Werf F, Ardissimo D, Betriu A et al. – Management of acute myocardial infarction in patients presenting with ST-segment elevation. – *Eur Heart J* 2003; 24:28-66.

[4] Canto JG, Every NR, Magid DJ et al. – The volume of primary angioplasty procedures and survival after acute myocardial infarction. National Registry of Myocardial Infarction 2 Investigastors. – *N Eng J Med* 2000; 342:1573-80.

[5] Bonnefoy E, Lapostolle F, Leizorovicz A et al. – Primary angioplasty versus pre-hospital fibrinolysis in acute myocardial infarction: a randomised study. – *Lancet* 2002; 360:325.

[6] Fibrinolitic Theraphy Trialists' (FTT) Collaborative Group. – Indications for fibrinolytic theraphy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. – *Lancet* 1994; 343:311-22.

[7] Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). – Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. – *Lancet* 1986; 1:397-402.

[8] Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). – Long-term effects of intravenous thrombolysis in acute myocardial infarction: final report of the GISSI study. – *Lancet* 1987; ii:871-4.

[9] Zabalgoita M, Ismaeil M. – Diagnostic and prognostic use of stress echo in acute coronary syndromes including emergency department imaging. – *Echocardiography* 2000; 17:479–93.

[10] Otto CM, Stratton JR, Maynard C, et al. – Echocardiographic evaluation of segmental wall motion early and late after trombolityc theraphy in acute myocardial infarction. The Western Washington Tissue Plasminogen Activator Emergency Room Trial. – *Am J Cardiol* 1990; 65:132–8.

[11] Picard MH, Wilkins GT, Ray PA, et al. – Progressive changes in ventricular structure and function during the year after acute myocardial infarction. – *Am Heart J*. 1992; 124:24–31.

[12] Jeremy RW, Hackworthy RA, Bautovich G, et al. – Infarct artery perfusion and changes in left ventricular volume in the month after acute myocardial infarction. – *J Am Coll Cardiol* 1987; 9:992–5.

[13] Siu SC, Nidorf SM, Galambos GS, et al. – The effect of late patency of infarct-related coronary artery on left ventricular morphology and regional function after trombolysis. – *Am Heart J* 1992; 124:265–72.

[14] Domingo E, Alvarez A, Garcia del Castillo H, et al. – Prognostic value of segmental contractility assessed by cross sectional echocardiography in first acute myocardial infarction. – *Eur Heart J* 1989; 10:532–7.

[15] Picard MH, Wilkins GT, Ray PA, et al. – Natural history of left ventricular size and function after acute myocardial infarction: assessment and prediction by echocardiographic endocardial surface mapping. – *Circulation* 1990; 82:484–94.

[16] Berning J, Steengaard-Hansen F. – Early estimation of risk by echocardiographic determination of wall motion index in an unselected population with acute myocardial infarction. – *Am J Cardiol* 1990; 65:567–76.

[17] Kan G, Visser CA, Koolen JJ, et al. – Short and long term predictive value of admission wall motion score in acute myocardial infarction: a cross echocardiographic study of 345 patients. – *Br Heart J* 1986; 56:422–7.

[18] Galasko Giw, Basu S, Lahiri A, et al. – A prospective comparison of echocardiographic wall motion score index and radionuclide ejection fraction in predicting outcome following acute myocardial infarction. – *Heart* 2001; 86:271–6.

[19] Nishimura RA, Tajik AJ, Shub C, et al. – Role of two dimensional echocardiography in the prediction of in hospital

complications after acute myocardial infarction. – *J Am Coll Cardiol* 1984; 4:1080–7.

[20] Bourdillon PD, Broderick TM, Sawada SG, et al. – Regional wall motion index for infarct and noninfarct regions after reperfusion in acute myocardial infaction: comparison with global wall motion index. – *J Am Soc Echocardiogr* 1989; 2:398–407.

[21] Sabia P, Afrookteh A, Touchstone DA, et al. – Value of regional wall motion abnormality in the emergency room diagnosis of acute myocardial infarction: a prospective study using two-dimensional echocardiography. – *Circulation* 1991; 84(suppl):185–92.

[22] St. John Sutton M, Pfeffer MA, Plappert T, et al. – Quantitative two dimensional echocardiographic measurements are major predictors of adverse cardiovascular events after acute myocardial infarction. – *Circulation* 1994; 89:68–75.

[23] Peels CH, Visser CA, Kupper AJ, et al. – Usefulness of two-dimensional echocardiography for immediate detection of myocardial ischemia in the emergency room. – *Am J Cardiol* 1990; 65:687–91.

[24] Shen WK, Khandheria BK, Edwards WD, et al. – Value and limitations of two-dimensional echocardiography in predicting myocardial infarct size. – *Am J Cardiol* 1991; 68:1143–9.

[25] Gibson RS, Bishop HL, Stamm RB, et al. – Value of early two dimensional echocardiography in patients with acute myocardial infarction. – *Am J Cardiol* 1982; 49:1110–9.

[26] Antman EM, Anbe DT, Armstrong PW, Bates ER et al. – ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial infarction). 2004. Available at www.acc.org/clinical/guidelines/stemi/index.pdf.

[27] American Society of Echocardiography Committee on standards, subcommittee on quantitation of two dimensional echocardiograms: recommendations for quantitation of the left ventricle by two dimensional echocardiography. – *J Am Soc Echocardiogr* 1989; 2:358–67.

[28] Zoghbi WA, Buckey JC, Massey MA, et al. – Determination of left ventricular volumes with use of a new nongeometric echocardiographic method: clinical validation and potential application. – *J Am Coll Cardiol* 1990; 15:610–5.

[29] Devereux RB, Lutas ME, Casale PN, et al. – Standardization of M-mode echocardiographic left ventricular anatomic measurements. – C*irculation* 1978; 58:1072–83.

[30] De Simone G, Daniels SR, Devereux RB, et al. – Left ventricular mass and body size in normotensive children and adults: Assessment of allometric relations and impact of overweight. – *J Am Coll Cardiol* 1984; 4:1222–30.

[31] Lauer MS, Anderson KM, Larson MG, et al. – A new method for indexing left ventricular mass for differences in body size. – *J Am Coll Cardiol* 1994; 74:487-91.

[32] Shiina A, Tajik AJ, Smith HC et al. – Prognostic significance of regional wall motion abnormality in patients with prior myocardial infarction; a prospective correlative study of two-dimensional

echocardiography and angiography. – *Mayo Clin Proc* 1986; 61:254-62.

[33] Bohs LN, Geiman BJ, Anderson ME et al. – Speckle tracking for multi-dimensional flow estimation. – *Ultrasonics* 2000; 38:369-75.

[34] D'Hooge J, Heimdal A, Jamal F et al. – Regional strain and strain rate measurements by cardiac ultrasound: principles, implementation and limitations. – *Eur J Echocardiogr* 2000; 1:154-70.

[35] Heimdal A, Støylen A, Torp H et al. – Real - time strain rate imaging of the left ventricle by ultrasound. – *J Am Soc Echocardiogr* 1998; 11:1013-9.

[36] Urheim S, Edvardsen T, Torp H et al. – Myocardial strain by Doppler echocardiography validation of a new method to quantify regional myocardial function. – *Circulation* 2000; 102:1158-64.

[37] Voigt JU, Arnold MF, Karlsson M et al. – Assessment of regional longitudinal myocardial strain rate derived from Doppler myocardial imaging indexes in normal and infarcted myocardium. – *J Am Soc Echocardiogr* 2000; 13:588-98.

[38] Pislaru C, Abraham TP, Belohlavek M. – Strain and strain rate echocardiography. – *Current Opinion in Cardiology* 2002; 17:443-54.

[39] Simmons LA, Weidemann F, Sutherland GR, et al. – Doppler tissue velocity, strain, and strain rate imaging with transesophageal echocardiography in the operating room: a feasibility study. – *J Am Soc Echocardiogr* 2002; 15:768-76.

[40] Jamal F, Strotmann J, Weidemann F, et al. – Noninvasive quantification of contractile reserve of stunned myocardium by ultrasonic strain rate and strain. – *Circulation* 2001;104:1059-65.

[41] Kukulski T, Jamal F, D'Hooge J, et al. – Acute changes in systolic and diastolic events during clinical coronary angioplasty: a comparison of regional velocity, strain rate and strain measurement. – *J Am Soc Echocardiogr* 2002; 15:1-12.

[42] Weidemann F, Dommke C, Bijnens B, et al. – Defining the transmurality of chronic myocardial infarction by ultrasonic strain rate imaging. Implications for identifying intramural viability an experimental study. – *Circulation* 2003; 107:883-8.

[43] Antman EM, Tanasijevic MT, et al. – Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. – *N Engl Med* 1996; 335:1342-49.

[44] Ohman E, Aramstrong P, Christenson R, et al. – Cardiac troponin T levels for risk stratification in acute myocardial ischemia. GUSTO-IIa Investigators. – *N Engl Med* 1996; 335:1333-41.