

Clinical Research

Blockade of Angiotensin II at the AT1 Receptor During Acute Inferior Myocardial Infarction: Assessment by Tei Index

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Introduction: Extensive multicenter studies have shown the beneficial effects of blocking the renin-angiotensin system at the level of conversion of angiotensin I to angiotensin II (ACE inhibitors) as well as at the level of antagonism of angiotensin II AT1 receptors, using agents known as angiotensin receptor blockers. Although ACE inhibitors have been studied extensively and have become established as a supplementary treatment to conventional therapy of myocardial infarction, there are no data to show whether angiotensin receptor blockers have an equivalent effect in this condition. The purpose of this study was the assessment of the impact of the angiotensin receptor blocker irbesartan on the global left ventricular (LV) performance in patients (pts) with acute MI (AMI) of limited extension, focusing on the utility of the Tei index.

Methods: 40 pts (27 male) participated in this study. Their mean age was 60.15 ± 9.06 (SD) years, all with their first AMI restricted to the inferior wall (AMI-I). The pts were divided into two groups: a) 20 pts in the group with conventional treatment of AMI-I (CT) and b) 20 pts in the group which received irbesartan (75-150 mg) additionally to the previous treatment from the 3rd post-infarct day (IR). Twenty-four healthy individuals with similar age and sex distribution were used as a control group (CG). All pts underwent a complete echocardiographic examination and Tei index measurement at rest on the 8th post-infarct day. A similar examination was also performed in the healthy subjects. The t-test was used to compare the values between the groups studied and a value $p < 0.05$ was considered statistically significant.

Results: The index of pts with AMI-I (0.65 ± 0.03) was significantly greater than that of CG (0.45 ± 0.03) ($p = 0.0003$). The index of IR (0.53 ± 0.03) was significantly lower compared to that of CT (0.78 ± 0.05) ($p = 0.00005$), but was similar to that of healthy subjects ($p = \text{NS}$). Moreover, the administration of irbesartan caused a significant decrease in isovolumic relaxation time (114.7 ± 6.77 vs. 140.5 ± 6.92 ; $p = 0.003$) and isovolumic contraction time (52.0 ± 2.36 vs. 63.9 ± 3.45 ; $p = 0.005$) and a significant increase in ejection time (279.5 ± 6.58 vs. 256.05 ± 7.63 ; $p = 0.019$).

Conclusions: 1) Global LV function is impaired in pts with AMI-I. Therapy with irbesartan restores this dysfunction within a short time period. 2) Irbesartan accelerates LV relaxation, which indirectly improves LV systolic function through the improvement of the remodeling process.

Ongoing multicenter studies, such as GISSI-3, SAVE, AIRE, ISIS-4, SOLVD, and many others¹⁻¹¹ conducted during the past two decades have proved how remarkably helpful are

the agents that block the renin-angiotensin system at the point of angiotensin I hydrolysis to angiotensin II in patients with myocardial infarction (MI). Their successful use in both the early³⁻⁵ and

late^{2,3,8,10} phase of MI has led to their establishment as an important addition to our therapeutic armamentarium.

Recently, the worldwide scientific community has been attracted by a new class of drugs that attack the renin-angiotensin system more selectively. The advent of angiotensin II receptor I (AT₁) blockers has created new opportunities. These agents are extraordinarily well tolerated and their action through direct blockade of AT₁ receptor is an important therapeutic step, since there is growing evidence of non ACE-dependent pathways for angiotensin generation. We are now beginning to see the beneficial results of large studies of angiotensin receptor blockers in a wide range of patients with hypertension^{12,13}, heart failure^{14,15} and vascular diseases^{16,17}. Despite this remarkable record of success in the aforementioned conditions we still do not have data to recommend their use in patients with MI.

Considering these factors along with a previous study of ours¹⁸ including patients with acute MI (AMI) of limited extension and preserved left ventricular (LV) function who received the ACE-inhibitor perindopril, in the present study we aimed to examine the effect of the angiotensin receptor blocker irbesartan on global LV function in a similar group of patients using the same protocol. It was focused on the use of the well known Doppler index of global myocardial performance (Tei index). This index has been proved to be superior to the conventional Doppler parameters in the identification of patient groups^{19,20}. It has also been reported as a non-geometric measure of global LV function²⁰⁻²⁴ and has been well associated with the accepted systolic and diastolic hemodynamic parameters^{22,24}. Moreover, its prognostic value has been proved in the clinical settings of cardiac amyloidosis²¹, dilated cardiomyopathy^{25,26}, and primary pulmonary hypertension²⁷, as well as recently in MI²⁸⁻³³. Additionally, it is an easily obtainable and reproducible^{23,29} index, unaffected by variations in blood pressure^{21,23} or heart rate^{21,23,34} and independent of ventricular geometry, age^{35,36}, sex³⁵, afterload³⁷, while it seems relatively stable despite preload changes in the supine position³⁸.

Material and methods

This study included 40 patients (27 males), of mean age 60.15 ± 9.06 (SD) years, suffering their first uncomplicated AMI restricted to the inferior wall of the LV (AMI-I). The characteristic precordial pain,

accompanied by electrocardiogram findings favoring inferior infarction and diagnostic serial changes in biochemical cardiac markers, were considered as criteria of the existence of AMI-I. In our protocol the determination of localized AMI-I was based on clinical and electrocardiographical criteria. All cases referred to patients with ST-segment elevation in leads II, III, avF. Three groups were defined: A) 20 patients (12 males) of mean age 60.68 ± 1.88 (SD) years receiving the conventional treatment for AMI-I (CT); B) 20 patients (15 males) of mean age 59.8 ± 2.61 (SD) years receiving in addition to the conventional treatment the angiotensin receptor blocker irbesartan, in a dose of 75-150 mg, once daily, beginning on the third post infarction day (IR) (dose titration was proportional to baseline supine systolic blood pressure values for better tolerance and elimination of hypotensive complications); C) 24 healthy subjects of similar age and gender distribution who served as a control group (CG). The individuals in the control group had no history or symptoms suggestive of cardiovascular disease and their physical, electrocardiography and echocardiography examinations were normal. Apart from our experience regarding the specific patients' data¹⁸, reasons of ethics defined the selection of this particular group. We considered this protocol to be ethical since the administration of an ACE-inhibitor would not deprive these patients of a globally acceptable benefit. On the contrary, providing them a medicine with similar action (protection against angiotensin harmful effect), would be equally beneficial.

All patients underwent an intensive echocardiography examination and all the conventional systolic and diastolic Doppler parameters were measured, as well as the index, on the eighth (8.07 ± 0.96) post-infarct day, in fasting condition and at midday. A similar examination was also performed on all healthy subjects. Conventional treatment for AMI-I was considered the per os administration of β -blockers and aspirin and the intravenous infusion of nitrates and heparin. Both groups of patients were treated with the same pharmaceutical regimen of each drug category. Administration of nitrates was interrupted on the third post-infarct day. Thrombolytic therapy was administered to 7/20 (37%) of the CT group patients and to 8/20 (40%) of the IR group. A history of hypertension existed in 14/20 (70%) and 10/20 (50%) patients of the above groups respectively. Individuals with absolute or relative contraindications for the use of angiotensin receptor

blockers, such as prolonged (>1 hour) severe hypotension (systolic blood pressure <100 mmHg), a history of previous MI, coexistent right ventricular infarction, physical signs or clinical manifestations of congestive heart failure (>Killip class I), sustained angina pectoris, atrial fibrillation, left bundle branch block, mechanical complication of AMI requiring any prompt surgical intervention, history of previous percutaneous coronary intervention or coronary artery bypass grafting, and coexistence of any valvulopathy more severe than mild, were excluded from the study.

In the organization of our study we preferred to calculate the index not during the hyperacute phase of AMI-I, when LV systolic dysfunction is predominant^{39,40}, but during the acute phase, when diastolic dysfunction is present as a later consequence of compensatory hypertrophy during the LV remodeling process^{39,40}. Considering the aforementioned findings as well as the ones of our previous study¹⁸, where it was shown that the dominant modification in the setting of AMI of limited size was the prolongation of relaxation, we assumed that time of index measurement to be a convenient one for the assessment of irbesartan's impact on LV remodeling.

The echocardiographic examination (m-mode, 2-dimensional, and Doppler) was performed using a commercially available ultrasound instrument, ATL-UM9 (Advanced Technology Laboratories) with a phased array transducer of 2.5 MHz. With the patient in the left lateral decubitus position, we used the parasternal long-axis view at the mid-left ventricular level to measure the end-diastolic diameter. From the same view at the aortic level, atrial diameter was assessed by m-mode. Ejection fraction (EF) was estimated using Bullet's formula. The assessment of LV filling pattern was realized using the apical four chamber view with the pulsed wave Doppler sample volume positioned at the tips of the mitral leaflets, in the center of the flow stream, during diastole⁴¹. The following parameters were measured: a) transmitral peak rapid filling velocity (E wave), b) peak atrial filling velocity (A wave), c) E/A ratio, d) E wave deceleration time (Edt) (the time interval from the apex of the E wave to the point where the decline of E wave meets the baseline). Additionally, from the apical five chamber view with the pulsed wave Doppler sample volume positioned in the LV outflow tract where both mitral inflow and aortic outflow patterns are recordable, we obtained the LV isovolumic relaxation time

(IRT), the interval between the end of the aortic flow and the onset of the mitral inflow^{41,42}. The aforementioned method for the study of LV diastolic function is widely accepted, and has been well correlated with radionuclide and angiographic techniques^{42,43}. Moreover, from the apical five chamber view with the pulsed wave Doppler sample volume positioned firstly in the LV outflow tract and then below the aortic valve, we measured the systolic parameters isovolumic contraction time (ICT), the time interval between mitral valve closure and aortic valve opening, and the ejection time (ET), the interval from opening to closure of aortic valve. Finally we calculated the index. This index involves both systolic and diastolic time intervals and is calculated mathematically using the formula $\text{index} = (a - b)/b$, where "a" is the time interval from the cessation to onset of mitral inflow, and "b" is the ET of the LV. These time intervals are calculated from the time intervals of mitral inflow and LV outflow tract velocities, with the use of pulsed Doppler. In the interval "a" are included the time intervals of ICT, IRT and ET, which constitute established indexes of systolic and diastolic LV function. Therefore, if we subtract from the interval "a" the interval "b" which is the ET, the sum ICT+IRT remains as numerator of the fraction and the index can be expressed by the formula $\text{index} = (\text{ICT} + \text{IRT})/\text{ET}$ (Scheme 1). All Doppler measurements were calculated at the end of expiration from an average of 5 consecutive cycles. The study protocol was approved under the ethical rules of our country, according to the treaty of Helsinki.

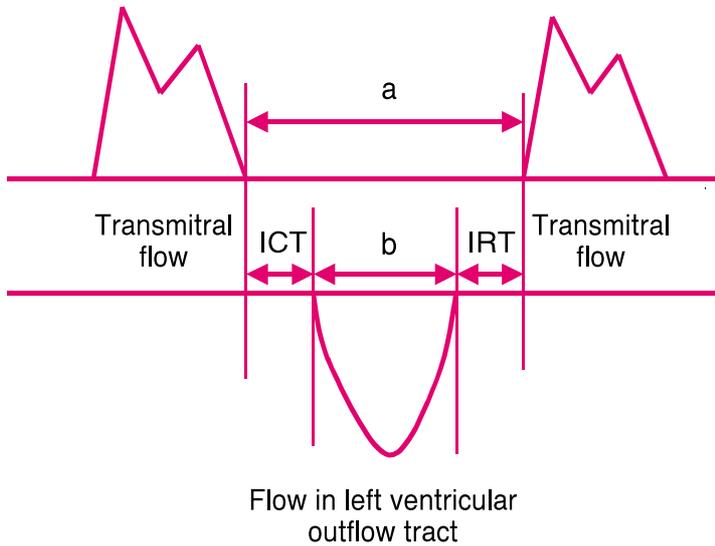
Statistical analysis

All the quantitative clinical results are expressed as mean value (MV) ± standard error (SE). The t-test was used for the comparison of quantitative observations and the χ^2 test to compare qualitative characteristics. A p value <0.05 was considered statistically significant.

Results

The clinical characteristics and general echocardiographic findings of healthy subjects and patients with AMI-I are given in table 1: The three studied groups were comparable regarding age, gender, heart rate and LV end diastolic diameter. The two groups of patients were also comparable regarding

$$\text{Index} = (a-b)/b = (\text{ICT} + \text{IRT}) / \text{ET}$$



Scheme 1. Scheme for the measurements of Doppler time intervals. The index is defined as $(a-b) / b$, where a is the interval between cessation and onset of the mitral inflow and b is the ejection time (ET) of left ventricular outflow. Isovolumic relaxation time (IRT) is the interval between the aortic valve closure and the onset of mitral valve flow. Isovolumic contraction time (ICT) is the interval between the cessation of mitral inflow and the onset of aortic valve flow.

thrombolysis and history of systemic hypertension. The systolic blood pressure of healthy subjects was significantly higher than that of the patient groups, whereas the systolic blood pressure of IR group subjects (112.0 ± 2.60 mm Hg) was similar to that of the CT group (113.4 ± 3.55 mm Hg) ($p = \text{NS}$). The EF was in normal limits in all patients with AMI-I. It did not differ between patients of the IR group and CT group ($p = \text{NS}$) but it was significantly lower compared to that of normal individuals.

Variance of Doppler parameters and Tei index in studied groups: Although the isovolumic contraction time of normal subjects was similar to that of the IR group ($p = \text{NS}$), it was significantly shorter than that of CT patients ($p = 0.037$). Moreover, isovolumic contraction time was significantly shorter in patients of the IR group than in the CT group ($p = 0.005$), (Table 2, Figure 1). The ejection time was significantly prolonged in healthy subjects compared to patients. In addition IR group subjects

Table 1. Comparison of the basic clinical characteristics and the general echocardiographic findings of subjects in the three groups studied: 24 healthy subjects as a control group (CG), 20 patients with AMI-Inferior (AMI-I) given irbesartan (IR) and 20 patients with AMI-I receiving only conventional treatment (CT).

	CG (MV±SE) n=24	IR (MV±SE) n=20	p	CG (MV±SE) n=24	CT (MV±SE) n=20	p	IR (MV±SE) n=20	CT (MV±SE) n=20	p
Age (years)	59.2±1.72	59.8±2.61	NS	59.2±1.72	60.68±1.88	NS	59.8±2.61	60.68±1.88	NS
Female / Male	9/11	5/15	NS	9/11	8/12	NS	5/15	8/12	NS
Heart rate (b/m)	67.7±2.98	71.9±2.40	NS	67.7±2.98	70.1±3.42	NS	71.9±2.40	70.1±3.42	NS
Systolic BP (mmHg)	128.5±3.06	112.0±2.60	0.0007	128.5±3.06	113.4±3.55	0.002	112.0±2.60	113.4±3.55	NS
Diastolic BP (mmHg)	79.0±1.48	71.75±1.86	0.013	79.0±1.48	76.3±2.44	NS	71.75±1.86	76.3±2.44	NS
LVd (cm)	4.86±0.13	4.98±0.12	NS	4.86±0.13	4.91±0.14	NS	4.98±0.12	4.91±0.14	NS
LAd (cm)	3.59±0.09	3.99±0.10	0.003	3.59±0.09	4.08±0.10	0.0003	3.99±0.10	4.08±0.10	NS
Ejection fraction (%)	73.8±1.55	60.0±6.03	0.03	73.8±1.55	56.2±3.21	0.0000	60.0±6.03	56.2±3.21	NS

AMI=acute myocardial infarction, BP=blood pressure, LVd=left ventricular end diastolic diameter, LAd=left atrial dimension, p= statistical significance, NS= statistically not significant. $p < 0.05$ statistically significant. MV±SE=mean value±standard error.

Table 2. Comparison of systolic and diastolic Doppler parameters as well as Tei index of 24 healthy subjects (CG), 20 patients with AMI-Inferior (AMI-I) given irbesartan (IR) and 20 patients with AMI-I receiving only conventional treatment (CT).

Doppler Variables	CG (MV±SE) n=24	IR (MV±SE) n=20	p	CG (MV±SE) n=24	CT (MV±SE) n=20	p	IR (MV±SE)	CT (MV±SE) n=20	p
ICT (ms)	55.2±2.47	52.0±2.36	NS	55.2±2.47	63.9±3.45	0.037	52.0±2.36	63.9±3.45	0.005
ET (ms)	305.2±5.98	279.5±6.58	0.009	305.2±5.98	256.05±7.63	0.000002	279.5±6.58	256.05±7.63	0.019
Wave E (m/sec)	0.79±0.04	0.70±0.05	NS	0.79±0.04	0.59±0.04	0.004	0.70±0.05	0.59±0.04	NS
Wave A (m/sec)	0.68±0.04	0.83±0.05	0.023	0.68±0.04	0.75±0.05	NS	0.83±0.05	0.75±0.05	NS
Ratio E/A	1.20±0.05	0.91±0.09	0.010	1.20±0.05	0.88±0.11	0.005	0.91±0.09	0.88±0.11	NS
IRT (ms)	95.7±2.70	114.7±6.77	0.026	95.7±2.70	140.5±6.92	0.000001	114.7±6.77	140.5±6.92	0.003
Edt (ms)	194.5±7.58	244.7±11.25	0.002	194.5±7.58	234.21±12.85	0.017	244.7±11.25	234.21±12.85	NS
Doppler-index	0.45±0.03	0.53±0.03	NS	0.45±0.03	0.78±0.05	0.00000	0.53±0.03	0.78±0.05	0.00005

ICT=Isovolumic contraction time, ET=Ejection time, IRT=Isovolumic relaxation time, Edt=Deceleration time of E wave, (AMI and statistics as in table 1).

showed longer ejection time than patients of the CT group (Table 2, Figure 1). The isovolumic relaxation time was significantly shorter in normal subjects than in patients, but subjects of the IR group had a significantly shorter isovolumic relaxation time compared to the subjects of CT group (Table 2, Figure 1). The E/A ratio was higher in healthy subjects than in patients, but there was no significant difference between the two groups of patients (Table 2). Fur-

thermore, the Tei index of healthy subjects (0.45 ± 0.03) was significantly lower than that of patients of the CT group (0.78 ± 0.05) ($p=0.000000$) but was similar to that of patients of the IR group (0.53 ± 0.03) ($p=NS$). The index of patients in the IR group was significantly lower than that those in the CT group ($p=0.00005$) (Figure 2, Table 2).

Type of LV diastolic dysfunction detected in patients of groups studied: In ten (25%) of the

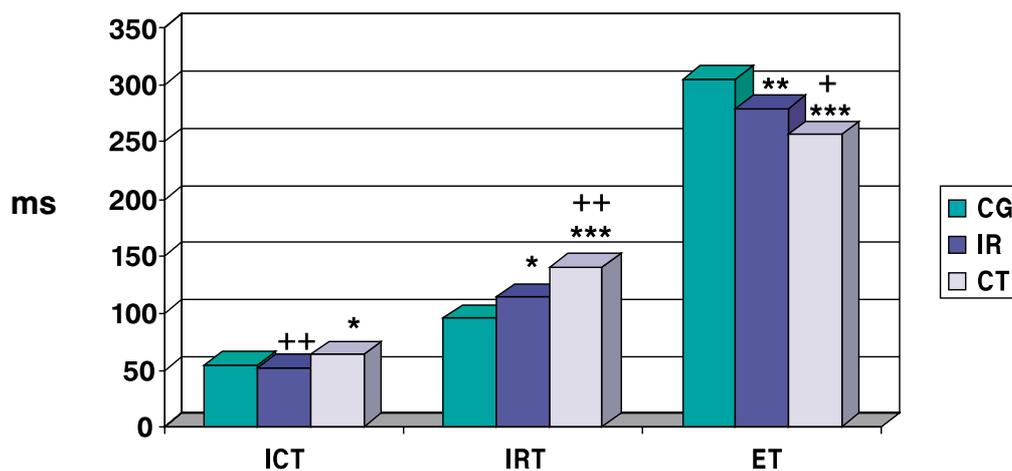


Figure 1. Comparison of Doppler time intervals between normal subjects (CG), patients (pts) with acute inferior myocardial infarction (AMI-I) who received the conventional treatment (CT) and pts with AMI-I who received irbesartan additionally to conventional treatment (IR). Left ventricular (LV) isovolumic relaxation time (IRT) in pts with AMI-I was significantly prolonged and ejection time (ET) significantly shortened compared to the values in normal subjects. The administration of irbesartan induced significant improvement of these parameters. Moreover, LV isovolumic contraction time (ICT) in CG was significantly shorter than that in CT whereas it was similar to the value in IR. Therapy with irbesartan significantly reduced this time interval. The * symbol denotes comparison between CG and the IR and CT groups, the + symbol comparison between IR and CT group. The number of symbols suggests the statistical significance: *, += $p < 0.05$, **, += $p < 0.01$, ***, += $p < 0.001$.

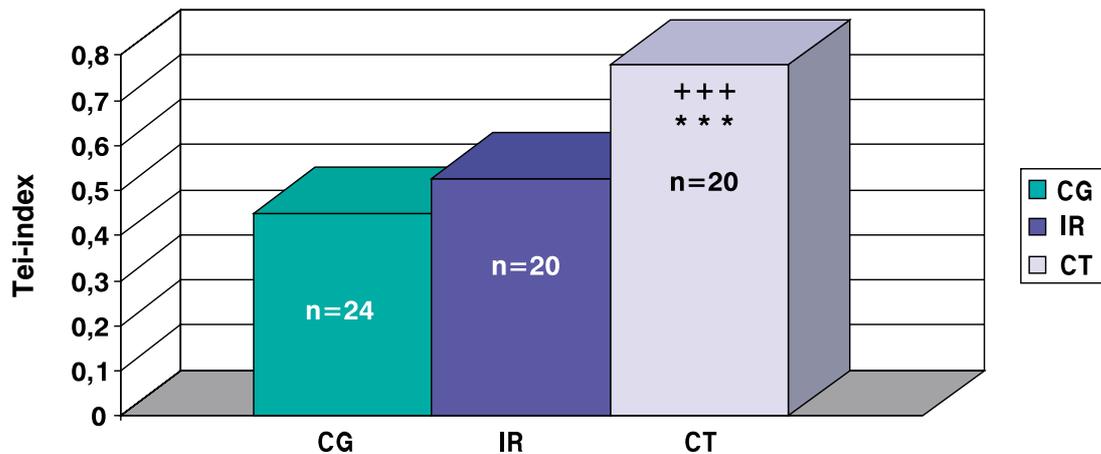


Figure 2. Comparison of Doppler Index (DI) of global myocardial performance between normal subjects (CG), patients with acute inferior myocardial infarction (AMI-I) who received conventional treatment (CT) and patients with AMI-I who received irbesartan additionally to conventional treatment (IR). DI of CG was significantly lower compared to that in CT but similar to that in IR. Administration of irbesartan substantially improved the index value. The * and + symbols and the statistical significance differences as in figure 1.

patients with AMI-I the normal LV diastolic function was preserved (6/20 in IR group, 4/20 in CT group). Only 17 (42%) patients demonstrated decreased peak filling rate pattern (9/20 in IR group, 8/20 in CT group). Twelve (30%) patients had an impaired LV relaxation filling pattern ($E/A < 1$, $DT > 220$ ms, $IRT > 105$ ms, 5/20 in IR, 7/20 in CT)⁴⁴. Only one patient (2.5%) in the CT group showed a restrictive LV filling pattern (shortened DT and higher E/A ratio).

Discrimination between groups of patients: The Tei index, isovolumic contraction time and ejection time distinguished the groups of patients ($p=0.00005$, $p=0.005$, $p=0.19$, respectively) (Table 2), while ejection fraction (Table 1), E/A (Table 2) and Edt (Table 2) were unable to achieve this.

Discussion

As is well known, AMI causes various degrees of LV systolic and diastolic dysfunction. The use of the Tei index, a method which shows good association with overall myocardial function²⁰⁻²⁴, seems reasonable in the detection of the impact of various regimens on LV global performance in patients with AMI. As was stated in the introduction, although many trials have indicated a significant benefit of angiotensin II inhibition at the level of AT1 receptors¹²⁻¹⁷ there are not sufficient data to support their favorable impact on

patients with AMI. Therefore, in the present study we compared the Tei index as well as the standard echo Doppler parameters in 20 patients with AMI-I treated only with the conventional treatment, 20 patients who received irbesartan in addition to the above therapy, and 24 healthy subjects of similar age and gender. The aim of the study was the evaluation of the effect of irbesartan on the global LV function.

The isovolumic relaxation time interval of patients with AMI-I was significantly longer than that of healthy subjects. This could be attributed to the development of LV compensatory hypertrophy during the remodeling process following AMI. This finding is consistent with our previous studies in patients after AMI^{18,19}, as well as with other studies of patients with cardiac amyloidosis²¹ and dilated cardiomyopathy²⁵. There was some discrepancy between our study and that of Poulsen et al²⁸, who reported that the isovolumic relaxation time of patients with AMI was similar to that of normal individuals. The following observations could be a reasonable explanation for this disparity: a) The material in the Poulsen et al study comprised a great number of patients suffering anterior AMI, and also individuals with a prior history of infarction. As anticipated, this material presented more severe LV dysfunction with higher filling pressures, resulting in reduction of isovolumic relaxation time in comparison with our material. b) The echocardiographic

examination in the Poulsen et al study was performed during the hyperacute phase of myocardial infarction²⁸ (within 1 hour of the patients' admission to the coronary care unit). As is widely accepted, LV systolic dysfunction seems to predominate in this period, while the impairment of relaxation has not yet developed^{39,40}. In contrast, our patients were assessed in the acute phase of MI (on the 8th post-infarct day), when the disorder in relaxation has already emerged as a consequence of the LV remodeling process^{39,40}. This significant increase of isovolumic relaxation time in our patients supported our hypothesis that relaxation impairment would be present at the moment of index calculation and is consistent with the aforementioned studies^{39,40} and a previous study of our own¹⁸. Irbesartan administration resulted in a significant reduction of isovolumic relaxation time, improving LV diastolic function in patients of the IR group compared to CT patients. Taking into account that systolic blood pressure was similar in the two patient groups, it seems that the favorable impact of irbesartan was achieved through its direct tissue effect on LV remodeling, regardless of its hemodynamic action. This observation is consistent with a previous finding of ours regarding the efficacy of perindopril¹⁸ (an ACE inhibitor) in similar patients. The common finding of these studies is that the inhibition of the renin-angiotensin system at any level in patients with preserved systolic LV function, does not work through the regulation of water and sodium metabolism or through the control of loading conditions (through the circulating renin-angiotensin-aldosterone system). Instead, the direct interaction with tissue renin-angiotensin and kinin/kininases systems seems more relevant.

The isovolumic contraction time of patients in the CT group was significantly prolonged and the ejection time in both the groups of patients with AMI-I was significantly shorter compared to the corresponding intervals of healthy individuals. These findings are consistent with our previous studies^{18,19}, with the Poulsen et al study²⁸ and with previous studies evaluating time intervals in myocardial infarction^{45,46}. They could be attributed to the reduced LV diastolic filling because of prolongation of the relaxation, which indirectly influences LV systolic performance. Irbesartan administration induced significant shortening of isovolumic contraction time and prolongation of ejection time through the aforementioned acceleration of relaxation and the subsequent indirect improvement of LV systolic function.

The changes of the Doppler time intervals that form components of the Tei index altered the value of the index accordingly in the study groups. Thus, the index of CT group patients was significantly higher compared to that of IR patients and healthy individuals. In contrast, the index of IR group patients did not differ from that of healthy subjects. These findings indicate that: a) the global LV function is impaired in patients after their first AMI-I when they receive only conventional treatment. This disorder is reflected in the value of the index and is consistent with previous studies by ourselves^{18,19} and other researchers^{28,30}; b) treatment with irbesartan results after a short time in the restoration of global LV function after AMI-I. This finding is in agreement with the results of our previous study¹⁸ concerning the effect of the ACE inhibitor perindopril on patients with AMI-I. The above data indicate that blockade of the renin-angiotensin system, irrespectively of the level of its completion, leads to a significant improvement of global LV function in patients with AMI of limited extent. It seems to be achieved through the extensive protection offered by the renin-angiotensin system inhibition against the destructive influence of angiotensin II.

Finally, the index was superior to its components in terms of the identification of the groups of patients. The latter was not achieved by the ejection fraction, the ratio E/A or the deceleration time of the E wave. This finding is in accordance with previous studies^{19,20} and emphasizes the importance of the index in this area, especially when applied to groups of patients suffering predominantly from diastolic dysfunction. In such a case the utility of the ejection fraction is negligible, as might be expected. This supremacy of the Tei index should be attributed to its ability to detect the variations in the aforementioned systolic and diastolic Doppler-parameters simultaneously. As a result it provides information concerning global LV function, which these parameters, like the systolic ejection fraction, are unable to offer by themselves.

Study limitations: The value of the index is significantly affected by preload³⁸. Nevertheless, this limitation does not appear to exist in supine patients with AMI³⁸. Moreover, a significant correlation of the Tei index with the LV diastolic filling pressure was found²³, a fact which attributes to the index an additional dependence on preload. In the present study all the subjects of the study groups were

supine. Because of this the reliability of our findings was not reduced by preload changes. Furthermore, nitrate administration to all patients who underwent echocardiographic evaluation was interrupted during the previous five days, while patients with clinical signs of heart failure (>Killip class I) were excluded. This measure contributed to the uniformity of our material as regards the LV filling pressure. Certainly, more studies are necessary to clarify the influence of loading conditions on the index value.

Our patients were studied only on the 8th post-infarct day and not later. There was no follow up to determine further information concerning the long term effectiveness of these regimens on the LV remodeling process and mortality. Certainly though, the current study suggests that therapy with irbesartan improves LV global performance in patients with AMI of limited extension.

Conclusions

It seems reasonable to conclude that: 1) global LV function is affected in patients with AMI of limited extension. Treatment with irbesartan restores impaired LV performance within a short time period. 2) Irbesartan administration directly accelerates relaxation, resulting in indirect improvement of LV systolic function. This benefit seems to derive from the direct tissue effect of this regimen during the process of LV remodeling, regardless of its hemodynamic action.

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