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A comparision of left ventricular functions after acute myocardial infarction receiving different reperfusion therapy

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ABSTRACT

It is demonstrated that primary angioplasty is more effective than thrombolytic therapy on the clinical outcomes in ST- segment elevation acute myocardial infarction (STEMI). The aim of this study was to compare the effects of reperfusion therapies on left ventricular systolic and diastolic functions.
We assigned 114 patients (19 female, mean age 60.2 ± 10.7 years, and 95 male, mean age 53.6 ± 11.0 years) with first STEMI treated with primary angioplasty (n=54) or thrombolytic drug therapy (n=60) in accordance with selection criteria. Assesment of LV systolic function was done by wall motion score index (WMSI) and left ventricular ejection fraction (LVEF). Left ventricular diastolic function was evaluated by the pulsed Doppler technique. WMSI was significantly lower in angioplasty group (1.31 ± 0.30) compared to thrombolysis group (1.45 ± 0.40) ($p<0.01$). LVEF did not differ between treatment groups (50 ± 9 % vs 47 ± 8 %, $p>0.05$). The frequency of diastolic dysfunction tended to lower in angioplasty group but the difference was not significant (50% vs 62%, $p>0.05$). Nevertheless, rates of restrictive filling pattern cases was significantly higher in thrombolysis group (7% vs 22%, $p<0.05$). There was a significant difference for E/A ratio between two groups (0.99± 0.38 versus 1.20± 0.60, $p<0.05$).
The results showed that the left ventricular systolic and diastolic functions were preserved with STEMI treated by primary angioplasty. This may contribute to better clinical outcomes in patients with STEMI treated with primary angioplasty.

1. Introduction

Modern management of acute myocardial infarction is estabish on clinical evidence from randomised controlled trials. Reperfusion therapy using either intravenous thrombolytic agents or primary angioplasty is established therapy for acute myocardial infarction (AMI) (Milavetz et al., 1998). Meta-analyses of clinical trials which compared primary angioplasty with thrombolytic therapy have been shown significant reduction in rates of mortality, reinfarction, total stroke and hemorhagic stroke with angioplasty (PCAT Collaborators, 2003; Keeley and Grines, 2004). Early and effective flow through the infarct-related artery has a paramount importance for limitation of infarct size and preservation of left ventricular function in patients with AMI (de Boer et al., 1994).

Left ventricular systolic and diastolic functions were predictors of the clinical outcomes in patients with AMI (Keeley and Grines, 2004; Azevedo et al., 2004). Reducing myocardial ischemia by revascularization in early period of AMI, improves left ventricular systolic functions, but its effect is unclear on diastolic functions (de Boer et al., 1994). However, the link between left ventricular function and clinical outcome has not been satisfaying demonstrated in the nowadays. The aim of this study was to compare the effects of reperfusion therapies on left ventricular systolic and diastolic functions by echocardiogarpic indexes.

2. Experimental procedure

Study population

This study consisted of 116 consecutive patients (99 male, 55+ 11 years) admitted to the coronary care unit with a first acute ST-segment elevation myocardial infarction. The STEMI patients were prospectively enrolled in our clinic. STEMI was defined according to the WHO criteria with a typical chest pain, ST segment elevation> 1 mm in contiguous leads and elevation of creatine kinase isoenzyme MB (CKMB) at least two times. The exclusion criteria were as follows; previous AMI, previous coronary artery bypass grefting or coronary intervention, atrial fibrillation, inadequate view of echocardiography, chronic renal insufficiency, presence of mechanical complications. Written informed consent was optained from all patients

Clinical characteristics

All of the patients were treated by either primary angioplasty or thrombolytic therapy and patients were assigned into two groups: angioplasty group (n=54); and thrombolysis group (n=60). Reperfusion strategies in each patient were determined by recommendation of ACC/AHA guidelines for the management of patients with STEMI (Antman et al., 2004). Initial fibrinolytic therapy were chosen in patient with low bleeding risk who present very early after symptom onset (<2 to 3 hours) and who have longer delay to PCI (>120 minute). Of these patients, 54 were treated with primary angioplasty and 60 had thrombolytic agents. Low-flow nasal oxygen, oral aspirin (300 mg), intravenous nitroglycerin, beta-blocker, angiotensin converting enzyme inhibitors were administered to patients without contrandications in each group. Heparin was given according to treatment group to which the patients was assigned. CKMB levels were measured in blood samples to enzymatic estimation of infarct size.

Coronary angioplasty procedure

Coronary angiography (Siemens Artist, Acompc ver. 1.1) was performed in angioplasty group patients before and after the procedure without ventriculography. Coronary angiography was not performed in patients treated with thrombolytic agents in the acute phase of myocardial infarction unless recurrent ischemia. Angioplasty procedures were performed using the Judkins technique with a 6-7 French (Fr) guiding catheter via the femoral artery approach. A bolus of 75–100 IU/kg of heparin was administered after securing arterial access achieving an activated clotting time of at least 300 seconds. Oral 300-600 mg loading dose of clopidogrel was administered to these patients. Platelet glycoprotein IIb/IIIa-receptor blockers (tirofiban) were administered (70%) at the discretion of the physician.

The infarct-related artery was treated if it was totally occluded, if there was a culprit lesion with stenosis of more than 50 percent of the luminal diameter, or if it had a flow grade of less than 3 according to the Thrombolizis in Myocardial Infarction (TIMI) classification. Stenting of the culprit lesion was attempted in all patients, unless the vessel had a diameter of less than 2 mm and stent-like results (two patients) after balloon angioplasty. Also direct stenting was performed in 8 patients. The duration of each inflation was at least 30 s (30–60 s) and mean inflation pressure 12 atm (8–15 atm). Angioplasty for non-infarct-related arteries did not performed.

Thrombolytic therapy protocol

Thrombolytic agents were administered to patients in whom primary angioplasty not recommended by ACC/AHA guidelines (Antman et al., 2004). The patients received either streptokinase (86%) or tissue-type plasminogen activator [tPA] (14%). Streptokinase was given intravenously 1.5 Million Units within a period of 60 minutes. Accelerated t-PA an intravenous bolus of 15 mg, followed by an infusion of 0.75 mg per kilogram of body weight [not to exceed 50 mg] over a 30-minute period and then 0.50 mg per kilogram [not to exceed 35 mg] over the next 60 minutes, for a maximal total dose of 100 mg was given.

Echocardiographic examination and Doppler measurement

Two dimensional and Doppler echocardiographic examination were performed with a Vingmed cardiac ultrasound unit using a 2.5 MHz transducer. Echocardiographic examination was performed 3 (2–4) days after AMI and the results were assessed by two cardiologist. Assesment of LV systolic function was done by Wall motion score index (WMSI) and left ventricular ejection fraction (LVEF). WMSI and LVEF were measured in all patients by two-dimensional echocardiography to assess the left ventricular systolic function. Left ventricular wall motion was analyzed according to the 16-segment model and global wall motion score index was calculated. LVEF was estimated using Simpson's method (Schiller et al., 1989).

Left ventricular diastolic function was evaluated by the pulsed Doppler technique. The mitral inflow velocity pattern was recorded from the apical four chamber view by placing the sample volume between the tips of the mitral leaflets during diastole. Three consecutive beats were measured and averaged for each measurement. Diastolic filling indexes, including the peak transmitral velocity of early rapid filling wave (E), peak velocity of late filling wave (A), the E/A ratio and mitral deceleration time (DT) were analysed. Echocardiographic measurements were applicable in 114 patients. One patient was excluded as the mitral flow did not measurable due to fusion of the Doppler waves. Other patient was died 12 h after AMI.

Diastolic dysfunction was diagnosed in the presence of one of the following diastolic pattern; 0.75<E/A<1.5 and DT >150 was defined normal filling pattern, E/A less than 0.75 was defined as impaired relaxation pattern, 0.75<E/A<1.5 and DT <150 ms was defined as pseudonormal pattern and E/A>1.5 was defined as restrictive filling pattern (van Kraaijn et al., 2002; Khouri et al., 2004). These diastolic patterns were considered as from low to high level of the severity of diastolic dysfunctions respectively.

Statistical analysis

All data are expressed as mean ± SD. The statistical analysis were performed using the Statistical Package for Social Sciences software (SPSS Inc. Chicago, Illinois, USA). Differences between mean values in the two groups were compared using by Student's t-test and Mann-Whitney nonparametric test. The frequencies between the two groups were compared by the chi-square test. The association of WMSI with mean CKMB levels was analysed with the use of Pearson correlation. P value of less than 0.05 was considered as statistically significant.

3. Results

Clinical characteristics

The clinical characteristics of subjects are summarized in Table 1. Baseline clinical characteristics were similar in both groups. A total of 114 patients who had STEMI were screened for inclusion. Two patients were excluded (see above). The time from the onset of symptoms to initiation of reperfusion treatment did not differ in two groups (4.12± 3.04 h vs 4.40± 2.43h, p>0.05). There was no difference between two groups in terms of rates of location of AMI. Anterior location AMI was observed in 29 cases in angioplasty group and 32 cases in thrombolysis group (Table 1).

Table 1. Baseline clinical characteristics in patients with primary angioplasty and thrombolytic groups.

	Angioplasty (n=54)	Thrombolysis (n=60)	*p Value*
Age(years)*	54±12	56±11	ns
Male	46(85%)	49 (81%)	ns
BMI(kg/m2)*	27.0±4.4	26.7±4.5	ns
Diabetes mellitus	15(28%)	12(20%)	ns
Hypertension	21(39%)	17(28%)	ns
Smoking	32(59%)	39(65%)	ns
History of family	18(33%)	18(30%)	ns
Hyperlipidemia	8(15%)	8(13%)	ns
LVMI (g/m2)*	92±34	105±42	ns
Heart rate(beats/min)*	75±13	78±14	ns
Peak CKMB (U/L)*	300±209	326±202	ns
Systolic blood pressure(mmHg)*	112±12	113±14	ns
Diastolic blood pressure(mmHg)*	70±8	69±10	ns
Anterior location of infarct	29(55%)	32(53%)	ns
Time from the onset of symptoms to initiation of treatment (hr)*	4.12±3.04	4.40 ±2.43	ns
Medication			
Beta-blocker	50(93%)	56(93%)	ns
Aspirin	54(100%)	60(100%)	ns
ACE inhibitor	47(87%)	55(92%)	ns

*Values are mean ± SD; BMI = Body mass index; ACE = Angiotensin converting enzyme; LVMI = Left ventricle mass index; CKMB = Creatin kinase isoenzyme MB; ns= p>0.05.

There was no statistical difference between two group according to success of reperfusion treatment (p=0.148). Successful revascularization (TIMI flow grade ≥ 2) was observed in 50 (92%) patients in angioplasty group. Successful thrombolysis was observed in 49 (81%) patients in thrombolysis group, which it was evaluated with clinical parameters such as relief of pain, ST segment resolution and early peak in CKMB level.

Systolic functions

WMSI was significantly lower in angioplasty group (1.31 ± 0.30) compared to thrombolysis group (1.45 ± 0.40) (p<0.01). LVEF did not differ between treatment groups (50 ± 9 % vs 47 ± 8 % p>0.05). The significant correlation was found between CKMB levels and WMSI in thrombolysis group (r =0.510, p<0.001), but this correlation was not observed in primary angioplasty group (p>0.05) (Fig. 1).

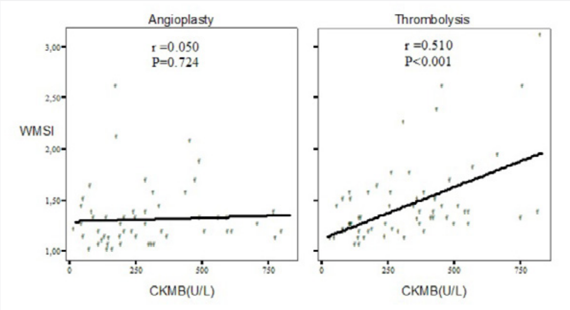

Fig. 1. The relationship between creatin kinase MB (CKMB) and wall motion score index (WMSI).

Diastolic functions and Doppler measurements

Table 2 shows the Doppler derived diastolic parameters. There was no difference between two groups according to E wave and A wave velocity. E wave velocity was 0.62± 0.16 m/s and 0.67± 0.18 m/s, (p>0.05) in angioplasty and thrombolysis group, respectively. Also A wave velocity was 0.65± 0.14 m/s in angioplasty and 0.62± 0.19 m/s in thrombolysis group (p>0.05). But, there was a significant difference for E/A ratio between two groups (0.99± 0.38 versus 1.20± 0.60, P<0.05). DT was 169 ± 61 ms in primary angioplasty group and 163 ± 59 ms in thrombolytic group (p>0.05).

Frequency of LV diastolic dysfunction is presented in Fig. 2. There was no difference between two groups in terms of frequency of diastolic dysfunction (p>0.05). LV diastolic dysfunction was observed in 27 patients (50%) in angioplasty group and 37 patients (62%) in thrombolysis group. The number of patients in different LV filling pattern is presented in Table 2. LV diastolic filling abnormality in patients treated with angioplasty was mostly impaired relaxation (n=13) and pseudonormal pattern (n=10), while it was equally distributed in patients treated with thrombolytic agents between impaired relaxation (n=11), pseudonormal pattern (n=13) and restrictive filling pattern(n=13). However the number of patients with restrictive filling pattern are very low (n=4) in angioplasty group. Primary angioplasty resulted in a reduced number of patient with LV restrictive filling pattern compared to thrombolytic therapy (p<0.05).

Table 2. Echocardiographic variables

Variable	Reperfusion strategy: Primary angioplasty (n=54)	Reperfusion strategy: Thrombolysis (n=60)	*p Value*
LVEF (%)	50±9	47±8	ns
WMSI	1.31±0.30	1.45±0.40	<0.01
E (cm/s)	0.62±0.16	0.67±0.18	ns
A (cm/s)	0.65±0.14	0.62±0.19	ns
DT(ms)	169±61	163±59	ns
E/A	0.99±0.38	1.20±0.60	<0.05
Diastolic dysfunction patterns (n,%)			
impaired relaxation pattern	13 (24%)	11 (18%)	ns
pseudonormal pattern	10 (19%)	13 (22%)	ns

Values are mean ± SD; E= Peak transmitral velocity of early rapid filling wave; A= Peak velocity of late filling wave; DT= mitral deceleration time; LVEF= left ventricular ejection fraction; WMSI= wall motion score index; ns= p>0.05.

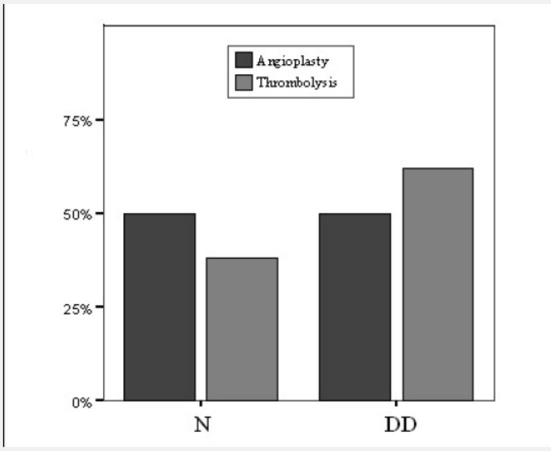

Fig. 2. The frequency of diastolic function in patients treated with primary angioplasty and thrombolytic agents. N: Normal diastolic function, DD: Diastolic dysfunction.

4. Discussion

Our study shows that primary PCI has a more beneficial effect on left ventricular functions using the echocardiogarphic index in STEMI patients. These favourable results has been observed especially systolic function by assesed WMSI and diastolic dysfunction by restrictive filling abnormalities.

Diastolic dysfunction after AMI has a prognostic information provided by the diastolic assessment independent from that derived from the systolic evaluation alone (Poulsen et al., 2001; Azevedo et al., 2004) and it has been shown that diastolic dysfunction plays an important role in the development of clinical heart failure following AMI (Poulsen et al., 1987). Moreover, ischaemic injury after AMI affects both systolic and diastolic function. Indeed, it has been demonstrated that the phenomenon of myocardial stunning has both a systolic and a diastolic component (Azevedo et al., 2004). Myocardial stunning and hibernation have been observed after PTCA and thrombolysis in AMI (Kloner and Jenning, 2001).

Mechanical reperfusion seems to exert more favorable effects on early LV filling abnormalities after AMI compared with thrombolysis, probably because of an anti-remodelling effect of the open infarct-related artery (Cerisano et al., 2001). In the present study, the effect of primary angioplasty on LV diastolic functions have been investigated in the early phase of AMI using transmitral flow velocities by Doppler echocardiography. Two-dimensional echocardiography is an excellent method for diagnosing systolic dysfunction, and Doppler echocardiography has become well accepted as a reliable, reproducible and practical noninvasive method for diagnosing and longitudinal follow-up of patients with diastolic dysfunction (Nishimura and Tajik, 1997). In our study, the number of cases with diastolic dysfunction were lower in primary angioplasty group. But, there are no significantly differences between two group in diastolic dysfunction frequency. However the frequency of restrictive filling pattern were found higher in thrombolysis group than angioplasty group. Additionally, mean E/A ratio was significantly elevated in thrombolysis group. This is may be due to the high number with the restrictive filling pattern in these patients. However the deceleration time was decreased in thrombolysis group, indicative of a restrictive filling pattern, but it was not significant. The patients with a restrictive LV filling pattern after early phase of AMI have a poor clinical outcome, even if treated with primary angioplasty (Garcia-Rubira et al., 1997; Cerisano et al.,2001). Thus, our results suggest that primary angioplasty was more effective than thrombolytic therapy on preservation for restrictive filling pattern in early phase of AMI. The protective effect of primary angioplasty on restrictive filling pattern may contribute to the better clinical outcomes.

LV diastolic function is determined by the energy dependent deactivation of contractile elements in the sarcomere (relaxation) and the passive properties of the ventricle during filling (compliance) (Bayata et al., 2000; Moller et al., 2003). Both myocardial relaxation and compliance are affected by ischemia, but the predominant diastolic abnormality is the impaired relaxation (Poulsen et al., 1997). The effect of percutaneous transluminal coronary angioplasty (PTCA) on LV diastolic function has been investigated in a number study. The studies showed that early or late improvement in LV diastolic function following PTCA. A study by Schanwell et al. (2001) showed an early improvement of LV diastolic function 48 hours after stent implantation. They reported that there was no significant short-term (48 hours) improvement of diastolic function. Joserich et al. (1990) found that LV diastolic filling is more pronounced within 24 hours after angioplasty, compared to 3 hours after PTCA. Klisiewicz et al. (2002) reported that LV diastolic functions were improved following angioplasty in 1 to 6 months after AMI, these patients were evaluated with the tissue Doppler Imaging. In contrast, Ricou et al. (1992) reported the persistence of diastolic filling abnormalities 3 months after angioplasty in patients with isolated coronary stenosis and normal systolic function. However the primary angioplasty and thrombolysis were not compared in these studies and there are limited information available regarding to diastolic functions in the early phase of AMI.

Despite the greates. reperfusion rates associated with primary angioplasty, a difference in left ventricular ejection fraction have not always revealed among patients treated with primary angioplasty and lytics (Berger and Gersh, 2001). In our study, primary angioplasty brings out a better preserved myocardial systolic function compared to patients who received thrombolytic therapy. This systolic preservation has been observed as wall motion score index, though left ventricular ejection fraction was slightly increased in primary angioplasty group. Semiquantitative assessment of regional systolic function using wall motion score index is an alternative to LVEF for the assessment of left ventricular systolic function. Moller et al. (2006) were found a close negative correlation between LVEF and WMSI in AMI patients and they have showed the predictive power of WMSI for prognostic information is greater than LVEF.

In study by Ottervanger et al. (2001), the patients treated with primary angioplasty showed a significant improvement almost 50% in left ventricular systolic functions after 6 months. But no data was available about diastolic dysfunction in their study.

In our study, the enzymatic estimation of infarct size by CKMB was significantly correlated with WMSI in thrombolysis group, but no correlation was observed in angioplasty group. The preservation of systolic functions associated with angioplasty may be independent of enzymatic elevations. In addition, the elevation of enzymes in patients with primary angioplasty may not reflect the severity of myocardial damage.

Some trials reported that the primary angioplasty showed a more beneficial effect in patients with anterior infarct location (de Boer et al., 1994; Ottervanger et al., 2001). However, the almost equal number of patients in two groups with anterior wall AMI in our study, may show that the effect of primary angioplasty on LV diastolic function are independent of the location of AMI.

Limitations

In the current study, diastolic functions were assessed only by standart traditional Doppler filling indices. We did not use the new echocardiographic applications such as flow propagation velocity by colour M-mode Doppler echocardiography, mitral annulus velocities by tissue Doppler echocardiography and pulmonary venous flow velocities. Furthermore, invasive haemodynamic measurements were also not performed. Echocardiographic examination was not performed before and after angioplasty or thrombolysis because this treatment regimens were urgent. Therefore diastolic functions did not compared before and after the procedures.

Conclusions

Primary angioplasty is more effective than thrombolytic therapy in reducing short-term and long-term major adverse cardiac events. The primary mechanism of benefit of primary angioplasty may be related to early restoration of coronary flow. However, differences in outcomes is influenced not only by systolic functions, but also by the diastolic functions; especially restrictive filling pattern. In consequence, the primary angioplasty seems to have more favorable effects on restrictive filling abnormalities after early phase of AMI. This protective effect may contribute to better clinical outcomes in patients with AMI treated by primary angioplasty.

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