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Effects of Eptifibatide on the Microcirculation After Primary Angioplasty in Acute ST-Elevation Myocardial Infarction: A Trans-Thoracic Coronary Artery Doppler Study

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1. Introduction

1.1 Extent of disease

Cardiovascular atherosclerosis is the most common disease in the industrial countries. In the United States of America more than 1 million patients every year are admitted to the coronary care unit with suspected acute myocardial infarction (Yusuf et al, 2004; American Heart Association, 2007). The incidence of acute myocardial infarction in USA is 865000, 565000 of them new infarctions annually. In Europe, the situation is similar to the USA, however in northern countries the incidence is higher than in southern countries (Lopez et al, 2006). In the emerging market economies in Eastern Europe, higher cardiovascular mortality is found. The burden of cardiovascular and coronary heart disease in developing countries is approaching that in developed countries. Thus the problem is a worldwide problem and international joint efforts are needed in order to treat this still prevalent disease.

Mortality of acute myocardial infarction is decreasing steadily. This decrease is related to reduction in the prevalence of disease in some countries, improvement of primary prevention and secondary prevention as well as treatment of the acute event (Hunink et al, 1997; Cooper et al, 2000).

1.2 Contemporary treatment

Primary percutaneous coronary intervention (PCI) is the treatment of choice in acute ST elevation myocardial infarction (Grines et al, 1993; Zijlstra et al, 1993; GUSTO, 1997; De Luca et al, 2004).The objective of primary PCI is to restore myocardial perfusion in the coronary bed distal to the occluded culprit artery. The TIMI classification (Chesebro et al, 1987) and myocardial blush grades (van't Hof, 1998; Gibson et al, 2000; Stone et al, 2002) used to assess epicardial coronary artery flow and myocardial perfusion after primary PCI

predict outcome after the procedure. However, the TIMI flow and myocardial blush grades are semi-quantitative, invasive, not easily repeatable, and do not reflect subsequent events and processes at the level of the coronary artery and microcirculation. Thus, even with successful primary PCI and the high rate of patency of the culprit artery, left ventricular functional recovery is limited and not well predicted (Stone et al, 1997; Zijlstra et al, 1997).

1.3 Limitations and problems of contemporary treatment

The main goal of primary PCI is to open the occluded epicardial coronary artery, and thus to re-establish blood flow to the jeopardized myocardium. In order to nourish the myocardium, blood must flow through the epicardial coronary artery segments, resistance vessels, arterioles and capillaries before reaching venules and veins. The epicardial coronary arteries are larger than 400 um, serve as conduit vessels and their diameter is regulated by shear stress and do not contribute significantly to pressure drop. Coronary resistance vessels with diameter between 100 and 400 um are affected myogenically mainly by shear stress and luminal pressure. Resistance coronary vessels with diameter less than 100um are sensitive to local tissue metabolism and directly control perfusion to the low pressure capillary bed nourishing the myocardium. Myocardial capillary density is 3500/mm^2 with inter-capillary distance of 17 um , greater in the subendocardium than in the subepicardium (Canty, 2008).

Microvascular injury is the leading cause for the decreased myocardial perfusion observed in about 80% of patients after successful PCI (Gibson et al, 2000; Stone et al, 1997; Zijlstra et al, 1997; Kondo et al, 1998). Various factors contribute to the limited myocardial perfusion, including micro-emboli, platelets, white blood cells, ischemic necrosis, and reperfusion injury(Chesebro et al, 1987; van't Hof, 1998; Gibson et al, 2000; Stone et al, 2002).

1.4 Detection of dysfunction of the microcirculation

As already mentioned, myocardial blush grade as assessed in the catheterization laboratory evaluates the function of the microcirculation.

Extent of resolution of ST-segment elevation after primary angioplasty is an adequate indicator of the function of the microcirculation and myocardial perfusion.

Measurement of coronary flow velocities using Doppler wire and pressure recordings to assess severity of coronary artery stenoses are invasive procedures in addition to other disadvantages (Iliceto et al 1991; Erbel et al, 1991; Kozakova et al, 1994; Donohue et al, 1993; Miller et al, 1994; Di Carli et al, 1995).

Trans-esophageal echocardiography visualizes only the proximal coronary arteries and Doppler sampling is feasible in less than 70% of patients (Joye et al, 1994; Kern et al 1995; Abizaid et al, 1998).

Recent technologic advances in trans-thoracic echocardiography made Doppler sampling of coronary artery velocities possible (Voci et al, 1998; Caiati et al, 1999; Hildick-Smith et al, 2000; Higashiue et al, 2001; Pizzuto et al, 2001; Takeuchi et al, 2001). Contrast agents may

enhance the detection rate of coronary velocities (Abizaid et al, 1998; Caiati et al, 1999), however, an experienced operator is essential.

Sampling of blood velocities in the left anterior descending coronary artery is successful almost in all patients. The advantages of Doppler sampling of coronary artery blood velocities is that it is non-invasive and can be repeated easily in the coronary care unit. As we demonstrated recently using transthoracic Doppler, the function of the microcirculation is dynamic and changes after primary angioplasty (Sharif et al, 2008; 2010). After primary coronary intervention in acute myocardial infraction the microcircirculation may improve or deteriorate. Therefore, transthoracic Doppler sampling of coronary artery velocities is even more important than other methods for the evaluation of the function of coronary microcirculation.

1.5 Possible solution for coronary microvascular dysfunction

After having the epicardial coronary artery treated and well open, according to the mechanisms of microcirculatory dysfunction, platelet micro-emboli and changes in platelet activity may have an impact on myocardial perfusion. Therefore, in the present study we examine the effects adjuvant treatment with glycoprotein 2b3a receptor blockers on the function of the microcirculation after primary angioplasty in the setting of acute anterior ST-elevation myocardial infarction.

2. Methods

Forty five consecutive patients with acute ST elevation anterior myocardial infarction undergoing primary PCI were enrolled in the study. All fulfilled the following criteria: 1) First anterior wall ST segment elevation myocardial infarction (STEMI). 2) Primary PCI within 12 hours of the onset of symptoms. 3) Routine informed consent to perform primary PCI. Anterior STEMI was defined as continuous chest pain for at least 30 minutes and ST elevation of at least 2.0mm in ≥2 contiguous precordial ECG leads. Exclusion criteria included one of the following clinical or angiographic findings: Prior bypass surgery, previous anterior STEMI, significant left main artery disease, failed primary PCI.

2.1 Primary PCI

Primary PCI was performed in standard fashion. All subjects were treated with oral clopidogral (600 mg) and aspirin (300 mg) in the emergency department. Thirty one patients were treated with an intravenous bolus injection of heparin (50-70 U/Kg) to achieve coagulation time of ≥ 250msec, Fourteen patients were treated before angioplasty with intravenous eptifibatide as 2 boluses of 180ug/kg, ten minutes apart, and a maintenance infusion at a rate of 2ug/kg/min for 24 hours, and 500 units heparin/hour. Coronary angiography and primary PCI were performed subsequently. Bare metal stents were deployed by high-pressure implantation techniques. Low magnification angiogram at either the right 30 º or 90 º lateral projections with prolonged cine was performed to optimize myocardial blush grade (MBG) documentation at the end of the intervention as previously described (van't Hof et al, 1998). All patients were treated with clopidogrel and aspirin for 12 months after the procedure.

2.2 Echocardiography

All patients had complete Doppler echcardiographic studies, within the first 6 hours after primary PCI, 48 hours later, and 5 days after the intervention.

Siemens, Acuson Sequoia echocardiographic system, California, equipped with 3.5-7MHZ transducers was used. All patients had complete Doppler echcardiographic studies, within the first 6 hours after primary PCI, 48 hours after primary PCI, and 5 days after primary PCI.

In order to obtain LAD flows, the color Doppler Nyquist limit was set at 17 cm/sec or power Doppler modality was applied. Systematic attempt to get LAD-color flow were performed. From low parasternal short axis view, search for diastolic color flow in the anterior interventricular groove followed by clockwise rotation was performed, while form apical foreshortened two chamber views LAD diastolic flow was located in the interventricular groove and the counterclockwise rotation of the transducer was performed. Colour Doppler sampling was easy to achieve, branches could be seen (figure 1) and margins of colour jet well delineated allowing measurement of jet width (figure 2).

Fig. 1. Colour Doppler of the LAD and diagonal branch

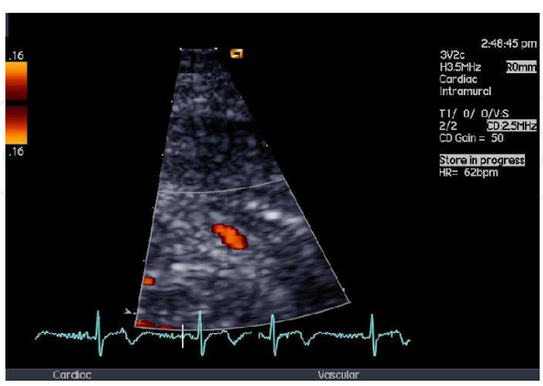

Fig. 2. Colour Doppler of the LAD allowing measurement of jet width

Pulsed-wave Doppler sampling was consistent (figure 3), with dominant diastolic component and clear envelope easy to trace (figure 4) and well demonstrated systolic component (figure 5).

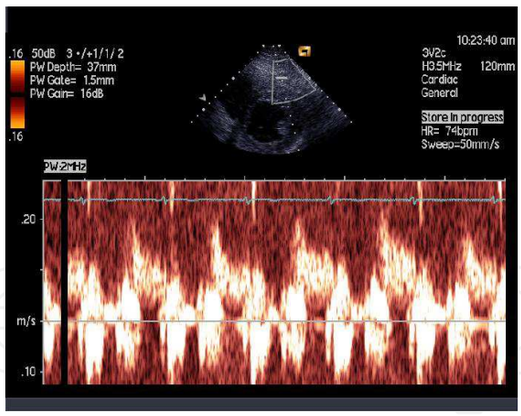

Fig. 3. Consistent pulsed-wave Doppler sampling of LAD blood velocity

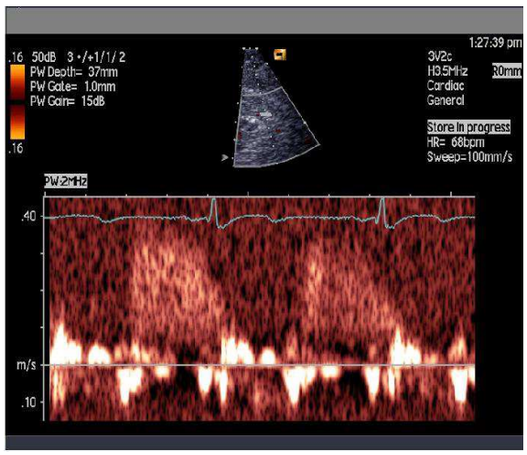

Fig. 4. Pulsed-wave Doppler of LAD blood velocity with dominant, easy to trace diastolic component

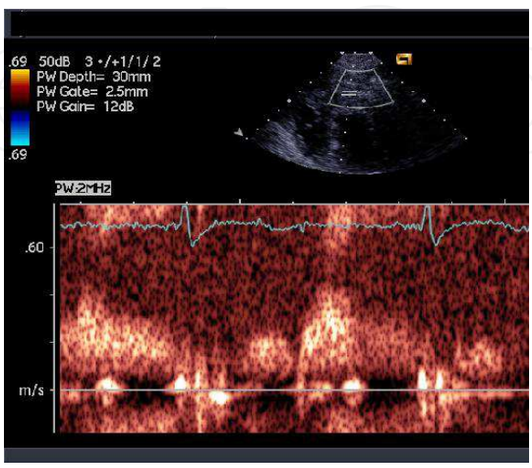

Fig. 5. Pulsed-wave Doppler of LAD blood velocity with prominent systolic flow

2.3 Echocardiographic measurements

Chamber diameters and usual measurements were performed according to recommendations of American Society of Echocardiography. Ejection fraction of LV (LVEF) was measured from biplane apical views.

For the calculation of wall motion score index

$$LV-WMSI=\frac{\sum score\ of\ 16 segments}{16} \quad (1)$$

assigning a value of 1 for normal LV wall motion, 2 for hypokinesis and 3 for akinesis. Using the same values of wall motion scores, LAD 9 segmental score index was calculated as:

$$LAD-WMSI=\frac{\sum score\ of\ 9 segments}{9} \quad (2)$$

2.4 Velocity of the LAD and measurements

In order to obtain LAD flows, the color Doppler Nyquist limit was set at 17 cm/sec. From low parasternal short axis view, search for diastolic color flow in the anterior interventricular groove followed by clockwise rotation was performed, while form apical foreshortened two chamber views LAD diastolic flow was located in the interventricular groove and the counterclockwise rotation of the transducer was performed.

Parameters of LAD velocity patterns were averaged from 3 beats, all in sinus rhythm. Diastolic LAD deceleration Time (DDT) was measured as the time from peak diastolic velocity to the intercept of tangent of the velocity envelope with baseline. Pressure half time (P1/2T) (msec) was determined as the time for peak diastolic velocity to decrease to $1/\sqrt{2}$ of its initial value. In addition, search for LAD early systolic flow reversal with early systolic negative velocity (ESFR) was performed.

2.5 LAD Flow measurements

Diameter of the jet of blood velocity through the LAD (D), heart rate (HR) and diastolic time velocity integral ($TVI_{Diastole}$) of the pulsed-wave Doppler were used to calculate blood flow in the LAD according to the following formula (3):

$$Diastolic\ LAD\ Flow=\pi\frac{D^2}{4}\times HR\times TVI_{Daistole} \quad (3)$$

2.6 Angiographic analysis

Coronary angiograms were reviewed by two experienced interventional cardiologists. TIMI (thrombolysis in myocardial infarction) and MBG (myocardial blush grade) were evaluated pre and post- PCI. TIMI-0: no antigrade flow beyond the occlusion; TIMI-1: contrast passes through the occlusion but do not opacify the distality entirely; TIMI-2: contrast passes through the obstruction and opacify the distal coronary bed slower than normal or clears slower than normal; TIMI-3: prompt contrast opacification and clearance of the distal coronary bed (Chesebro et al, 1987). MBG was evaluated as: MBG-0: minimal or no

myocardial blush; MBG-1: myocardial staining persists on the next injection; MBG-2: myocardial staining with slow washout and persists markedly at the end of injection; MBG-3: normal myocardial staining and clearance with only mild staining at end of injection (van't Hof, 1998; Gibson et al, 2000; Stone et al, 2002).

2.7 Statistical analysis

Statistical analyses wee conducted using SPSS software version 13. All values were expressed as means and standard deviations. Two-tailed student's-t test was performed to compare changes in DDT and P1/2T, considering $p<0.05$ as statistically significant. Assessment of clinical utility of flow parameters was done by calculating sensitivity, specificity, positive and negative predictive values as well as diagnostic accuracy. Correlation coefficients and their p value were calculated to evaluate the relation of LAD flow parameters with LV systolic function parameters pre-discharge (5 days after PCI).

3. Results

3.1 Angiographic results

Average TIMI and myocardial blush grades (MBG) before angioplasty were not different between patient who were treated with epitifibatide compared to those in whom the medicine was not administrated (table 1). However, TIMI=0, was observed in 33% with eptifibatide compared to 55% in those without. In both groups TIMI and MBG grades improved after the PCI. TIMI grade after the intervention was higher in subjects who were treated with epifibatide, however, MBG was not different.

	TIMI Pre-PPCI	**TIMI Post-PPCI**	**TIMI p-(Pre/Post)**	**MBG Pre-PPCI**	**MBG Post-PPCI**	**MBG p-(Pre/Post)**	**Diastolic LAD Flow (ml/min)**
EPT-Yes	1.07±1.07	2.43±0.5	0.0004	0.71±1.07	1.93±0.73	0.002	49±26
EPT-NO	0.94±1.2	2.28±0.6	1.3×10^{-9}	0.52±1.06	2.25±0.9	6×10^{-9}	35±17
P (Yes/No)	0.7	0.049		0.57	0.22		0.09

Table 1. Pre and Post PCI, TIMI and MBG and Diastolic LAD Flow

3.2 Feasibility and examples of LAD Doppler velocity sampling

Sampling of LAD blood velocities was possible at all occasions in all the patients. Colour-Doppler jet of blood velocity through the LAD had distinct boarders and measurement of diameters was possible with inter and intra-observer variability of 0.1±0.05mm and 0.15±0.07mm. Inter and intra-observer variability of LAD velocities were 2±0.4 and 1.5±0.2 cm/sec and of time velocity integrals 0.4±0.1 and 0.3±0.1cm, and of pressure half time 10±3 and 8±3 msec In figure 6, an example of a patient with acute anterior STEMI after primary angioplasty and bare metal stent implantation in the LAD. The velocity profile demonstrates prolonged diastolic deceleration time (more than 600msec) and forward systolic flow. In this patient left ventricular systolic function improved and left ventricular ejection fraction at

discharge was normal. In figure 7, an example of a patient with unfavorable LAD blood velocity profile after primary angioplasty and bare metal stent implantation in a patient with acute anterior STEMI. Short diastolic deceleration time (less than 600msec) and early systolic flow reversal are demonstrated. In this patient left ventricular ejection fraction was reduced at admission and did not improve later.

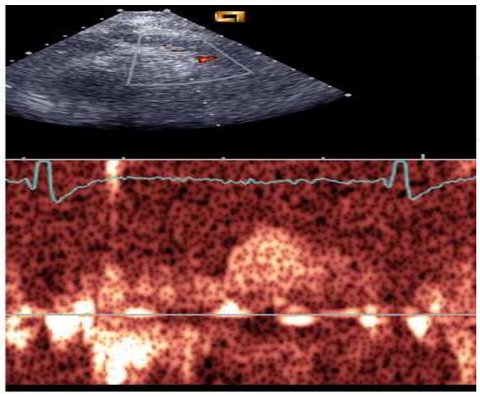

Fig. 6. Favourable LAD blood velocity profile with prolonged diastolic deceleration time and forward systolic flow.

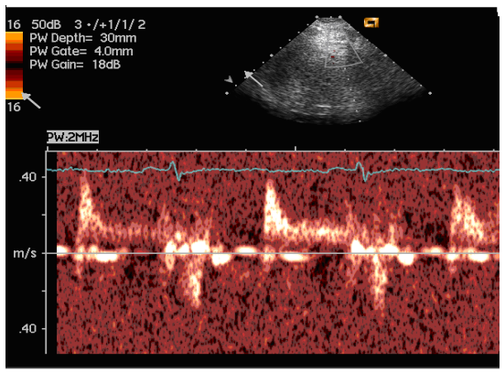

Fig. 7. Unfavourable LAD blood velocity profile with reduced diastolic deceleration time and early systolic flow reversal.

3.3 LAD velocity profiles

Early systolic flow reversal did not occur with eptifibatide while it was noticed in 6 (17%) in those without, $p<0.05$ (table 2).

	ESFR Early	ESFR 48 Hr.	ESFR 5 Days
EPT-Yes	0	0	0
EPT-No	6	4	2

Table 2. LAD Systolic Flow Reversal

Diastolic deceleration time of LAD flow averaged 629±238 msec in patients treated with eptifibatide and 593±344 msec in those without, p=0.7 (figure 8). Short (<600msec) diastolic deceleration time occurred in 6 (40%) of those treated with eptifibatide, compared to 12 (39%) in those not treated, p=ns (figure 8).

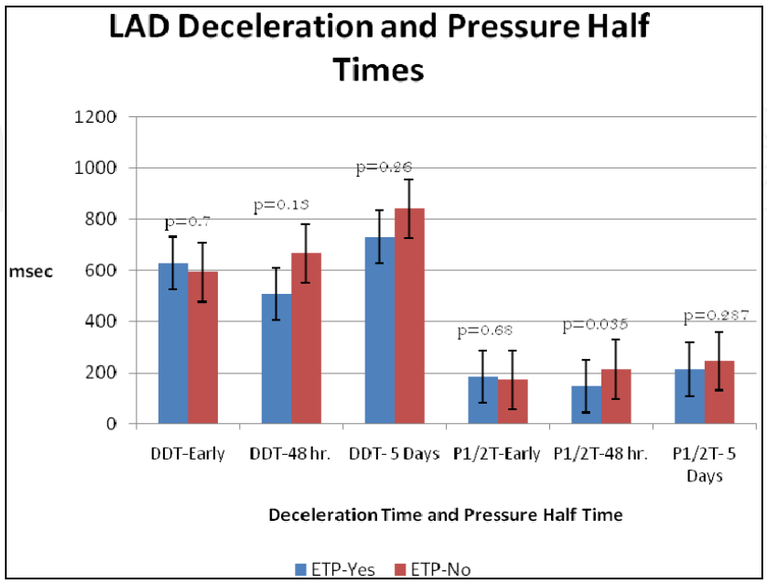

Fig. 8. Histogram of diastolic deceleration time and pressure half time of LAD blood velocity profiles in patients with and those without eptifibatide treatment.

Patients treated with eptifibatide had higher diastolic velocities, 39±11 cm/sec, vs 31±9 cm/sec, p=0.043 and tended to have higher diastolic LAD flows, 49±26 ml/min, vs 35±17 ml/min, p=0.09 (figure 9).

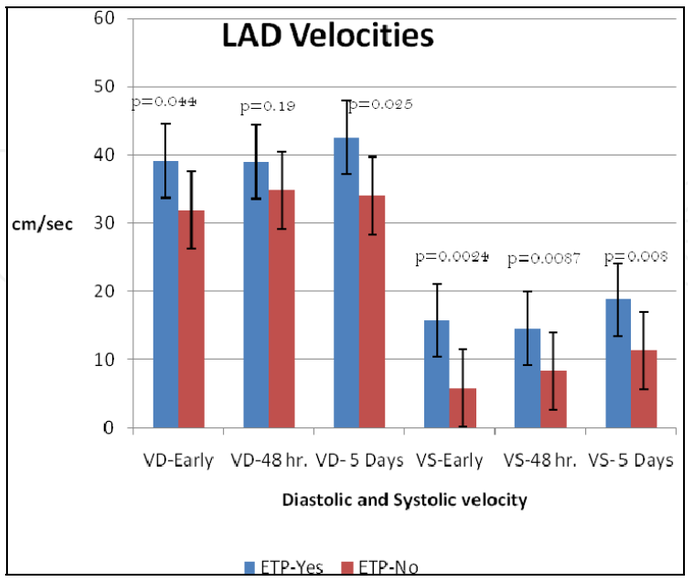

Fig. 9. Histogram of diastolic and systolic velocities of LAD blood velocity profiles in patients with and those without eptifibatide treatment.

3.4 LAD Flow

LAD flow tended to be higher early after primary angioplasty in subjects pre-treated with eptifibatide, however on the following evaluations during mid-hospital stay and pre-discharge diastolic flow in the LAD was similar in both groups.

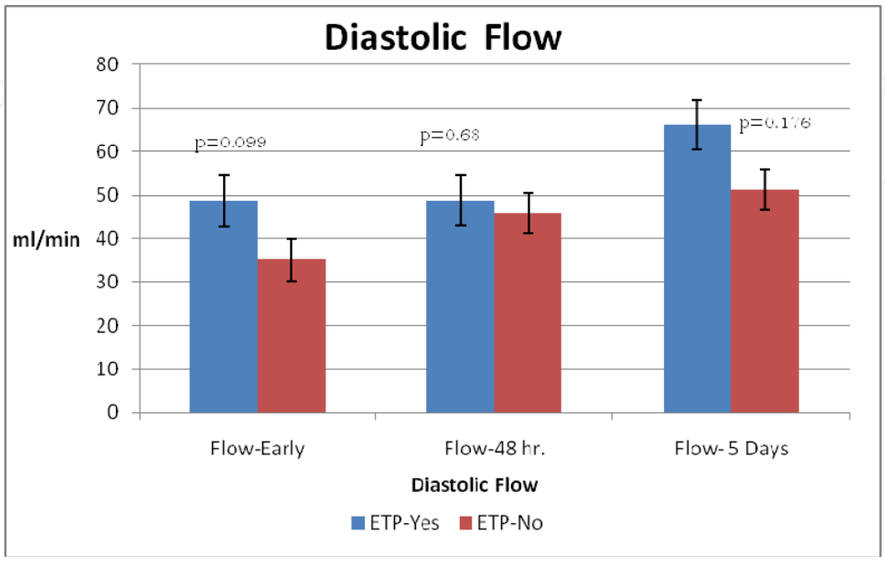

Fig. 10. Histogram of diastolic flow in the LAD in patients with and those without eptifibatide treatment.

3.5 Left ventricular systolic function

LVEF with epifibatide at baseline 37±6.5% was similar to that in those without, 36.7±4.4%, and at discharge, with epifibatide 43.8±8.2% and in those without 45±8.9%, p=ns.

	LVEF (%) Early	LVEF(%) 5 Days	LV-WMSI early	LV-WMSI 5 Days	LAD-WMSI early	LAD-WMSI 5 Days
EPT-Yes	37±6.49	43.8±8.2	1.68±0.17	1.49±0.295	2.15±0.2	1.83±0.43
EPT-NO	36.7±4.4	45±8.9	1.6±0.24	1.39±0.32	2±10.4	1.63±0.55
P (Yes/No)	0.79	0.687	0.296	0.282	0.165	0.258

Table 3. LV Systolic Function

4. Discussion

4.1 Brief summary of results

In this study, per-treatment of patients with acute anterior STEMI undergoing primary coronary angioplasty prevented severe dysfunction of the coronary microcirculation as

evidenced by absence of early systolic flow reversal in subjects treated with epitifibatide; however, less severe dysfunction of the microcirculation was not different between the groups since diastolic deceleration times by Doppler, and myocardial blush grades were similar. Moreover, diastolic maximal blood velocities early after PCI were higher in patients treated with eptifibatide but similar later on. Eptfibatide treatment was associated with a tendency of larger diastolic blood flow through the LAD but not later. All these changes with eptifibatide treatment did not affect left ventricular systolic function which was similar in both treatment groups, early after PCI and pre-discharge.

4.2 Applicability of sampling of LAD blood velocities

Transthoracic Doppler sampling of coronary blood velocities is not mentioned or not stressed sufficiently in most textbooks of echocardiography. Thus, the importance of this study is related not only to the treatment of patients with acute STEMI. We found that sampling of LAD blood velocities was possible in all the patients and at all occasions. We believe that sampling of LAD blood velocities should be applied widely and repeated when needed and in all echocardiographic studies. In fact, electrocardiographic recording is performed when patients have chest pain, and in a similar fashion, echocardiography and sampling of coronary blood velocity may be performed in such patients in coronary care units.

4.3 Transthoracic Doppler sampling of LAD blood velocities and other methods

Measurement of coronary flow velocities using Doppler wire and pressure recordings to assess severity of coronary artery and microcirculation are invasive procedures in addition to other disadvantage (Iliceto et al 1991; Erbel et al, 1991; Kozakova et al, 1994; Donohue et al, 1993; Miller et al, 1994; Di Carli et al, 1995). Normal peak diastolic velocities in the present study were similar to those reported previously by invasive Doppler flowires (Ofili et al, 1993).

Trans-esophageal echocardiography visualizes only the proximal coronary arteries and Doppler sampling is feasible in less than 70% of patients (Joye et al, 1994; Kern et al 1995; Abizaid et al, 1998). Recent technologic advances in trans-thoracic echocardiography made Doppler sampling of coronary artery velocities possible (Voci et al, 1998; Caiati et al, 1999; Hildick-Smith et al, 2000; Higashiue et al, 2001; Pizzuto et al, 2001; Takeuchi et al, 2001). Contrast agents may enhance the detection rate of coronary velocities (Abizaid et al, 1998; Caiati et al, 1999), however, with increasing experience of the operator contrast agents are not needed.

4.4 Validity of LAD blood velocities and flow calculations

The range of the value of LAD blood velocities and time velocity integrals (Sharif et al, 2010) is similar to those found through cardiac valves with similar reproducibility and applicability. The diameter of the LAD and of the colour jet of blood flow through the vessel is in the range of diameter of vena contracta of regurgitant jets through cardiac valves. Moreover, LAD-colour jet diameter is similar to that of proximal iso-velocity surfaces of regurgitant jets through the mitral valve, so it can be applied in a similar fashion and

squared to calculate areas. Thus if blood velocities, and colour jet diameters of the LAD are similar to those of cardiac valves, then flow calculations should be of the same degree of validity.

4.5 Need for coronary blood velocity sampling in acute STEMI

Restoration of epicardial coronary artery flow by primary PCI in the setting of acute STEMI improves outcome (Shah et al, 2000), however optimization of myocardial tissue perfusion improves the prediction of outcome (van't Hof et al, 1998; Shah et al, 2000; van't Hof et al, 1997; Claeys et al, 1999; The TIMI Study Group, 19985; Gibson et al, 1996; 1999; 2001; de Lemos, 2001; Dörge et al, 2000). Despite these findings, still even with successful primary PCI and the high rate of patency of the culprit artery, left ventricular functional recovery is limited and not well predicted (Stone et al, 1997; Zijlstra et al, 1997).

Despite the value of myocardial blush grade in the evaluation of myocardial perfusion it is not repeatable because of its invasive nature. Resolution of ST-elevation also correlates with better myocardial perfusion, however it reflects only the stage immediately following the emergency PCI. As we have shown (Sharif et al, 2008) the function of coronary microcirculation is variable and may improve or worsen during the hospital stay after primary coronary angioplasty in patients with acute STEMI. Therefore, Doppler transthorcaic sampling of LAD blood velocities is important in such patients.

4.6 Diastolic deceleration time of LAD blood velocity curve (DDT) and the microcirculation

To understand the relation between DDT and coronary microcirculation, consider normal subjects where the intra-myocardial blood capacitance vessels fill during diastole without significant increase in intramural pressure, therefore the DDT is prolonged. When the capacitance vessels are partially obstructed with miroemboli there is impedance to flow in diastole, therefore the DDT is abbreviated (Kawamoto et al, 1999; Yamamaro et al, 2002). When the blockage of the microcirculation is more severe, the milking of blood in systole cannot proceed to the venules; instead, it is pushed back into the coronary artery and results in early systolic flow reversal (Kawamoto et al, 1999; Yamamaro et al, 2002).

4.7 Mechanisms of dysfunction of coronary microcirculation after primary coronary angioplasty

After primary PCI, dysfunction of the microcirculation may develop as a result of periprocedural microembolization to the distal coronary artery bed. In addition, recently, evidence for the hypothesis that in situ inflammation and thrombosis contributes to dysfunction of the microcirculation after primary PCI was provided (Dörge et al, 2000). Despite the tendency of microemboli to dissolve after they developed during primary PCI, in situ microcirculatory thrombosis may account for worsening of microcirculatory function late after primary PCI. Thus not only early evaluation of the coronary microcirculation is important; in fact the worst coronary microcirculatory status like minimal diastolic deceleration time of LAD blood velocity seems to be even more important.

4.8 The logic and need for intense antiplatelet treatment in acute STEMI

Plaque disruption is considered to be the common substrate of acute coronary syndromes (Boersma et al, 2003). Consequently, the blood is exposed to a significant quantity of thrombogenic materials initiating platelet aggregation and the lumen of the coronary artery become obstructed by a combination of platelets, fibrin and red blood cells. Moreover, as mentioned previously, primary coronary angioplasty in patients with acute STEMI is associated with microembilzation rich with platelets to the distal coronary circulation. Therefore, the administration of rapidly acting powerful antiplatelet agent seems logical. Glycoprotein IIbIIIa receptor blockers fulfil these requirements.

4.9 The evidence of effectiveness of Glycoprotein IIbIIIa receptor blockers in acute STEMI

Thus, Abciximab (Neumann et al, 1998) maintained patency of large coronary arteries, but in addition was associated with higher coronary artery peak blood velocities and better left ventricular wall motion score index and higher left ventricular ejection fraction compared to heparin. Abciximab (de Lemos et al, 2000) was shown to improve both epicardial coronary artery flow and myocardial reperfusion as evidenced by resolution of ST elevation in patients with acute STEMI. Eptifibatide and tirofiban- small molecule Glycoprotein IIbIIIa receptor blockers- in a meta-analysis study were shown to be non-inferior to abciximab in patients with acute STEMI undergoing PPCI (Ottani et al, 2010). Eptifibatide was shown to be equal to abciximab as an adjunct to PPCI in acute STEMI and as effective in causing resolution of ST elevation (Zeymer et al, 2010) and reduced the rate one year mortality and re-infarction (Akerblom et al, 2010). Eptifibatide improved clinical outcome in patients with STEMI undergoing PPCI (Mahmoudi et al, 2011). In our study eptifibatide prevented severe dysfunction of coronary microcirculation after PPCI in acute STEMI which was not translated into better left ventricular systolic function. A larger number of patients may reveal such benefit in recovering left ventricular systolic function.

5. Summary and look to the future

Thus, transthoracic Doppler echocardiography is feasible and provides important information about the function of coronary microcirculation in patients with acute STEMI undergoing PPCI. Treatment with eptifibatide before primary angioplasty, prevented early LAD systolic flow reversal indicative of severe dysfunction of the microcirculation, increased diastolic LAD velocities and flows but did not increase left ventricular systolic function. Understanding mechanisms of dysfunction of the coronary microcirculation and implementation of newer strategies to treat microcirculatory dysfunction with transthoracic Doppler evaluation may improve the treatment of patients with acute STEMI undergoing primary angioplasty.

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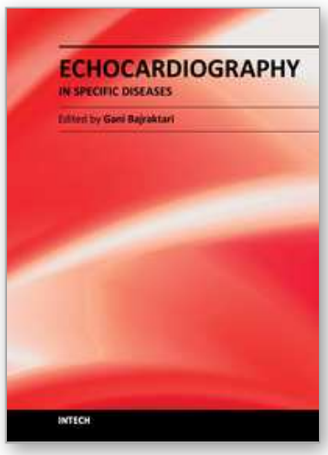

Echocardiography - In Specific Diseases

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The book "Echocardiography - In Specific Diseases" brings together contributions from well- known researchers from around the world, some of them specialized in imaging science in their clinical orientation, but also representatives from academic medical centers. Each chapter is structured and written to be accessible to those with a basic knowledge of echocardiography but also to be stimulating and informative to experts and researchers in the field of echocardiography. This book is primarily aimed at cardiology fellows during their basic echocardiography rotation, fellows of internal medicine, radiology and emergency medicine, but also experts in echocardiography. During the past few decades technological advancements in echocardiography have been developing rapidly, leading to improved echocardiographic imaging using new techniques. The authors of this book tried to explain the role of echocardiography in several special pathologies, which the readers may find in different chapters of the book.

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