Analysis of Serial Coronary Artery Flow Patterns Early after Primary Angioplasty: New Insights into the Dynamics of the Microcirculation

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Abstract

Background: The temporal behavior of the coronary microcirculation in acute myocardial infarction may affect outcome. Diastolic deceleration time and early systolic flow reversal derived from coronary artery blood flow velocity patterns reflect microcirculatory function.

Objectives: To assess left anterior descending coronary artery flow velocity patterns using Doppler transthoracic echocardiography after primary percutaneous coronary intervention, in patients with anterior AMI.

Methods: Patterns of flow velocity patterns of the LAD were obtained using transthoracic echocardiography-Doppler in 31 consecutive patients who presented with anterior AMI. Measurements were done at 6 hours, 36–48 hours, and 5 days after successful PPCI. Measurements of DDT and pressure half times (Pt½), as well as observation for ESFR were performed.

Results: In the first 2 days following PPCI, the average DDT (600 ± 340 msec) was shorter than on day 5 (807 ± 332 msec) (P < 0.012). FVP in the first 2 days were dynamic and bidirectional: from short DDT (< 600 msec) to long DDT (> 600 msec) and vice versa. On day 5 most DDTs became longer. Pt½ at 6 hours was not different than at day 2 (174 ± 96 vs. 193 ± 99 msec, P = NS) and became longer on day 5 (235 ± 98 msec, P = 0.012). Bidirectional patterns were also observed in the ESFR in 6 patients (19%) at baseline, in 4 (13%) at 36 hours, and in 2 (6.5%) on day 5 after PPCI.

Conclusions: Flow velocity patterns of the LAD after PPCI in AMI are dynamic and reflect unpredictable changes in microcirculation.

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Primary percutaneous coronary intervention after the onset of acute myocardial infarction has been shown to achieve a higher rate of recanalization and a lower rate of complications as compared with pharmacological thrombolysis [1-3]. However, even with successful PPCI and the high rate of patency of the culprit artery, left ventricular function recovery is limited [2-4]. Using different methods, decreased myocardial perfusion was found in approximately 80% of patients who underwent PPCI and predicted adverse long-term outcome [5-9]. After PPCI, the leading cause for myocardial hypoperfusion is microvascular damage, secondary to multiple factors including embolization and reperfusion injury [5-15]. Kawamoto et al. [16] used Doppler guide wire to study coronary flow velocity patterns immediately after successful PPCI and found that coronary blood flow velocity patterns had distinct characteristics that correlated with the severity of microvascular damage [16].

In this study, we used Doppler transthoracic echocardiography to study coronary flow velocity patterns and their temporal dynamics to gain insights into the coronary microcirculation function in consecutive patients who underwent PPCI.

Patients and Methods

From January 2004 to January 2005, 31 consecutive patients who presented with first anterior ST elevation myocardial infarction were treated with PPCI and recruited to the study. Anterior STEMI was defined by continuous chest pain for at least 30 minutes accompanied by ST segment elevation of at least 2.0 mm in ≥ 2 contiguous precordial electrocardiography leads. Exclusion criteria included prior bypass surgery, previous anterior STEMI, significant left main artery disease and failed PPCI. All patients underwent a Doppler transthoracic echocardiography study of the left anterior descending artery blood FVP within 6 hours after successful PPCI, and then at 36–48 hours and 5 days after PPCI.

PPCI

PPCI was performed in a standard fashion. Briefly, patients were pretreated with an intravenous bolus of heparin (50–70 U/kg) to achieve a coagulant time of 250 seconds, an oral load of clopidogrel (600 mg) and aspirin (300 mg) in the emergency department; the use of glycoprotein IIb, IIIa was left to the discretion of the attending physician. Patients then underwent cardiac catheterization and coronary angiography and PPCI was performed. Bare metal stents were deployed by high pressure implantation techniques. At the end of the procedure, a low magnification angiogram at either the RAO 30º or 90º lateral projections with prolonged cineangiography was performed to optimize myocardial blush grade documentation. Myocardial blush grade was assessed as previously defined [17]: 0 = no myocardial blush or contrast density, 1 = minimal myocardial blush or contrast density, 2 = moderate myocardial blush or

STEMI = ST elevation myocardial infarction
contrast density but less than obtained during angiography of a contralateral or ipsilateral non-infarct related coronary artery; 3 = normal myocardial blush or contrast density, comparable with contralateral or ipsilateral non-infarct related coronary artery. After completion of PPCI, patients were treated in the coronary care unit at the discretion of the attending physician. All patients were treated with a standard clopidogrel and aspirin regimen for the following 3 months.

Doppler studies and analysis
Doppler TTE studies using the Siemens-Acuson Sequoia machine (USA) and 3.5-7 MHz transducers were performed at 6 hours, 36–48 hours and 5 days after PPCI in all subjects. In order to obtain left anterior LAD artery flow velocity patterns, the color Doppler Nyquist limit was set at 17 cm/sec. A low parasternal short axis view was used, followed by clockwise rotation of the transducer to search for color diastolic FVP of the LAD in the anterior interventricular groove. Alternatively, a modified fore-shortened apical two-chamber view followed by counterclockwise rotation of the transducer was used to pick the color diastolic flow of the LAD in the interventricular groove.

Coronary blood FVP analysis
The LAD and FVP analysis results were averaged from three consecutive heartbeats. Three parameters were measured [Figure 1]. First, diastolic deceleration time was measured as the time from peak diastolic flow velocity to the intercept of the tangent of the velocity envelope with baseline [Figure 1A]. Second, pressure half time (Pt½, msec) was determined as the time for the peak diastolic flow velocity to decrease to 1/2 of the initial value. Third, early systolic flow reversal was considered to be present if early negative systolic velocity was observed [Figure 1B].

Angiographic studies and analysis
Coronary angiograms were reviewed by two experienced interventional cardiologists who were blinded to the clinical and TTE findings. Both the TIMI grade flow and the myocardial blush grade were evaluated before and after the PPCI. The percent diameter stenosis and minimum lumen diameter of the culprit lesion were quantitatively analyzed offline by auto-edge detection with a validated technique (Horizon Clinicals, McKesson Corporation, USA) from the cineangiogram taken before and after the PPCI.

Statistics
Continuous data were reported as mean ± standard deviation. Analysis of variance was performed to compare DDT and Pt½ measurements at the different time points after PPCI. The Wilcoxon signed-ranked test was used to test for individual variability of DDT and Pt½. Statistical differences were considered significant at a value of $P < 0.05$.

Results
Patient and angiographic characteristics
Thirty one consecutive patients were enrolled in the study. The average age was 60.5 ± 11.5 years; 23 of the patients (74%) were male, body weight was 79.7 ± 14.6 kg. Risk factors for atherosclerosis included hyperlipidemia in 10 (32.2%), hypertension in 12 (38.7%), cigarette smoking in 10 (32.2%), diabetes mellitus in 3 (9.6%), family history of coronary artery disease in 5 (16.1%), and obesity in 5 (16.1%). Time from the onset of symptoms to catheterization laboratory was 3.1 ± 2.7 hours. All patients underwent successful PPCI of the LAD. The hemodynamic and
angiographic characteristics at the time of primary angioplasty are presented in Table 1. Baseline TIMI flow grade on arrival to the catheterization laboratory was 0.94 ± 1.2 and after angioplasty 2.89 ± 0.32. Baseline average myocardial blush grade was 0.52 ± 1.1 and average post-PPCI myocardial blush grade 2.3 ± 0.9. In 19 subjects the location of occlusion was in the proximal LAD and in 12 in mid-LAD. Type B2 infarct-related LAD lesion was found in 26 subjects and in 5 it was a type C lesion. Single-vessel disease was found in 19, double-vessel disease in 6 and triple-vessel disease in 6 subjects.

Doppler results
LAD flow velocity patterns were successfully obtained in all subjects. Inter and intra-observer variability of DDT was 14 ± 3 msec and 10 ± 4 msec, respectively, and of Pt½ 10 ± 3 and 8 ± 3 msec, respectively.

The DDT at 6 hours after PPCI (DDT1) was similar to that at 36–48 hours (DDT2) (600 ± 331 vs. 599 ± 340 msec, P = NS). At 5 days, the diastolic deceleration time (DDT3) was significantly longer (807 ± 332 msec, P < 0.002) [Figure 2]. Similarly, the Pt½ at 6 hours was not different from the 36–48 hour measurement (174 ± 96 vs. 193 ± 99 msec, P = NS), but was significantly longer at 5 days (235 ± 98 msec, P = 0.012)

Using the threshold set by Kawamoto et al., DDT = 600 msec [16], two types of LAD-FVP were observed at the 6 hour examination [Figure 2]. First, a prolonged DDT (DDT > 600 msec) was observed in 19 patients (61.3%). Second, a short DDT (DDT < 600 msec) was observed in 12 patients (38.7%). This group could be further divided by the presence of ESFR in 5 patients (16.1% of total) [17]. Two representative examples of the dynamic changes of the Doppler profile of the LAD are demonstrated in Figure 3.

Similar bidirectional patterns were observed for the ESFR. At baseline there were 6 patients (19%) with ESFR. At 36–48 hours follow-up we observed a resolution in 3 patients (50%) and a new appearance of the finding in one patient; thus at the second time point, ESFR was present in 4 patients (13%) of the total group. On day 5, only 2 patients (6.5%) still showed ESFR, and there was no new appearance of the finding.

Doppler results and other parameters
After angioplasty and stenting the LAD was wide open in all subjects and there was no significant difference between the angiographic lesion characteristics and diastolic deceleration time of the LAD. As seen in Table 1, heart rate was about 10 bpm lower in subjects with DDT > 600 msec. Blood pressure did not differ significantly. Left ventricular ejection fraction at presentation averaged 37.2 ± 6.5% and did not differ between the two groups. TIMI and myocardial blush grades before and after angioplasty and stenting the LAD were similar in patients with DDT > 600 msec and those with DDT < 600 msec.

Discussion
In this study we describe the temporal changes in coronary flow velocity pattern in patients with anterior STEMI immediately following primary PCI, using TTE. Like others, we use the coronary FVP to examine the function of coronary microcirculation in health and disease states [15–24]. According to our study, in the first 2 days following PCI the average diastolic deceleration times were shorter than when measured on day 5. FVP in the first 2 days were not static; bidirectional changes in FVP in the first 2 days, from short DDT (< 600 msec) to long DDT (> 600 msec) and vice versa, were observed. Only later, on day 5, was the overall trend towards longer diastolic flow periods. Thus, the observed early temporal behavior of FVP after PCI reflects dynamic changes in the microcirculation following successful PCI.

The relation between coronary artery FVP and function of the microcirculation can be explained by considering the spectrum of microcirculation. In normal subjects, the intramyocardial blood capacitance vessels fill during diastole without a significant increase in intramural pressure, therefore the DDT is prolonged. When the capacitance vessels are partially obstructed with
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Microemboli the flow in diastole is impeded, therefore the DDT is abbreviated \[16,19\]. 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 \[16,19\].

Previously invasive studies of coronary artery FVP were reported. Iwakura et al. \[15,21\] used Doppler guide wire to assess coronary FVP in patients immediately after PPCI and found that shorter DDT periods (< 600 msec) and the presence of ESFR were correlated with microvasculature damage. Using similar methods and patients, Kawamoto and team \[16\] showed that longer DDT (> 600 msec) correlated with improved myocardial salvage while shorter DDT (< 600 msec) represented greater microvasculature damage. Other groups also showed that after PPCI the presence of short DDT and the presence of ESFR are signs of microvasculature damage and may predict limited myocardial salvage \[20-23\].

Microvascular injury is the leading cause of the decreased myocardial perfusion observed in about 80% of patients after successful PPCI \[7,9-11\]. Various factors contribute to the limited myocardial perfusion, including microemboli, platelets, white blood cells, ischemic necrosis, and reperfusion injury \[5-8\]. Reduced myocardial perfusion correlates with reduced myocardial salvage, short- and long-term complications, and clinical outcome \[5,9-11\].

Coronary FVP studies thus far were performed using Doppler guide wire immediately after the PPCI, and thus offered only a single snapshot of the coronary FVP. Our data provide the opportunity to observe the temporal behavior of coronary FVP and the microcirculation, and reveal the dynamic nature of the coronary FVP, suggesting ongoing changes in the microcirculation during the first few days after PPCI. Hozumi and co-authors \[25\] also found that DDT of LAD velocity became longer during the first 2 weeks after PPCI in subjects with and in those without recovery of LV function. Distinct from the work of Hozumi, we report on changes in DDT of LAD velocity earlier, during the first 48 hours, and report on individual variability showing evidence for bidirectional changes. Factors causing microcirculatory damage immediately after PPCI are expected to diminish during the days after PPCI, which may improve the microcirculation as reported.
by others [25]. However, regional inflammation and perivascular edema, stretching and remodeling of the infarct region by normal adjacent myocardium may compress the microcirculation and may increase during the hours and days post-MI, which may worsen the status of the microcirculation. The balance between these opposing factors, the resolving intravascular microemboli, and the developing extravascular compression of the microcirculation may account for the bidirectional changes in function of the microcirculation after PCI.

The full clinical implications of the observed changes in coronary flow and the ability to manipulate these changes need to be fully evaluated in further studies. Our data suggest that TTE can be used as a simple bedside method to monitor the patient’s microcirculation after PCI. Furthermore, TTE can be used to evaluate the effects of therapeutic regimens aimed at ameliorating microvasculature perfusion.

References


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