Do Indices of Coronary Conductance After Reperfusion Reflect the Extent of Salvaged Myocardium?

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SUMMARY

Existing indices of coronary conductance (hyperemic flow-versus-pressure slope index, FPSI, and zero flow pressure, Pzf) have been developed as measures of microcoronary resistance. These indices, however, refer to cases of normal hearts, and there are no reports studying these indices following acute myocardial infarction. In this study, we investigated whether FPSI and Pzf truly measure the extent of myocardial salvage after successful reperfusion therapy. We also developed a new index of zero pressure flow, Fzp.

Nineteen patients who underwent successful reperfusion therapy to the proximal portion of the left anterior descending artery (LAD) were studied.

After successful reperfusion therapy, a Doppler wire was placed into the LAD. Aortic pressure was recorded in real time. Results from the aortic pressure and flow meter were combined to produce FPSI, Pzf, and Fzp. All cases underwent a resting thallium (Tl) and BMIPP scintigram within five days of successful reperfusion therapy. Infarcted myocardium was estimated using a severity score calculated from the Tl scintigraphy (TlSS), and the BMIPP (BMIPPSs) was estimated using a severity score. Patients with a TlSS/BMIPPSs ratio of less than 0.4 were assigned to the successful salvage group (group S), while the others were assigned to the failed salvage group (group F).

FPSI of group F was 1.91 ± 0.26 m/sec and of group S was 0.92 ± 0.43 m/sec (P < 0.01). Pzf of group F was 51 ± 3 mmHg and of group S was 51 ± 5 mmHg (NS). Fzp of group F was -98 ± 16 cm/sec and of group S was -46 ± 4 cm/sec (P < 0.05).

FPSI and the new index of Fzp were useful in estimating the extent of myocardial salvage. Our results suggest that the Pzf index could not differentiate between the two groups. (Jpn Heart J 2004; 45: 387-396)

Key words: Doppler wire, Reperfusion therapy, Coronary conductance, Salvaged myocardium
It is vital in acute-phase therapy for acute myocardial infarction to attempt reperfusion as early as possible. Primary percutaneous transluminal coronary angioplasty (PTCA) offers a useful means of doing this. The reported benefits of early successful reperfusion therapy include reduction in infarction area, prevention of reinfarction, and decreased mortality. Despite successful early reperfusion, however, left ventriculography in the chronic phase sometimes reveals cases where there is hardly any contraction of myocardium in the infarcted area.

In this study of patients with an anteroseptal myocardial infarction, we inserted a Doppler wire immediately after successful reperfusion to investigate whether or not coronary conductance indices derived from instantaneous measurement of coronary blood flow and aortic pressure reflect the degree of salvaged myocardium as measured by acute myocardium scintigraphy.

**Methods**

The subjects were 19 patients (14 males and 5 females, average age, 64 ± 2 years) who were diagnosed as having suffered an acute anteroseptal myocardial infarction within 12 hours of onset. The culprit lesions underwent successful reperfusion therapy, after which we measured coronary flow and pressure. As well as the diagnosis of acute myocardial infarction, at least one of the following three symptoms also had to be present: chest pain lasting 30 minutes or more, ST elevation in two or more leads, or a twofold or greater increase in CKMB level. After diagnosis of acute myocardial infarction, the culprit lesion of the coronary artery was expanded, leaving a residual stenosis of 25% or less. Cases with significant stenosis in front of or behind the culprit lesion of the coronary artery were excluded. We also excluded patients who were in shock or who underwent intra-aortic balloon pumping.

We obtained the informed consent of the patients and their families to obtain Doppler wire measurements. After confirming the dilatation, we inserted a Doppler wire (Flowire®, manufactured by JOMED Co, Ltd.) into the distal site of the lesion, and measured the velocity of the coronary blood flow. We also measured the instantaneous aortic pressure at the catheter edge. From the coronary blood flow velocity and the aortic pressure waveform, we derived a pressure-flow velocity loop using the method of Mancini, et al. We calculated the flow versus pressure slope index (FPSI: cm/sec/mmHg) from the slope of the end-diastolic loop, by defining the pressure at which flow velocity became zero as zero-flow pressure (Pzf: mmHg) and the flow at which pressure became zero as zero-pressure flow (Fzp cm/sec). Fzp is a new index of coronary conductance and we estimated its usefulness for the first time. We derived the deceleration time (DT: sec), defined as the time taken for attenuation of diastolic blood flow, from the maxi-
mal blood flow velocity of the coronary blood flow waveform. We also serologically examined maximum CKMB (IU/L).

Within five days following successful reperfusion, we carried out myocardial scintigraphy using thallium (Tl) and BMIPP. Using the methods of Prigent, et al\(^5\) and Sarai, et al\(^6\), we calculated the severity score for each patient according to Tl (TISS) and BMIPP (BMIPPSS). We then classified the subjects into the successful salvage myocardium group (S) and failed salvage myocardium group (F) according to the following formula\(^7\):

- **Group S:** TISS/BMIPPSS < 0.4
- **Group F:** TISS/BMIPPSS \(\geq 0.4\)

Data are shown as the average plus or minus standard error. Student's t-test was used. A \(P < 0.05\) was taken as the significance level for any differences.

**RESULTS**

The clinical characteristics of the patients are shown in Table. There were no significant differences between the two groups with respect to gender, age, or time to reperfusion. There was no difference in TIMI grade between the two groups.

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Rep.time = reperfusion time; FPSI = flow versus pressure slope index; PZF = pressure of zero flow; FZP = flow of zero pressure; DT = deceleration time.
1) FPSI, Pzf, and Fzp

As shown in Figure 1, FPSI was $1.91 \pm 0.26$ cm/sec/mmHg in group F and $0.92 \pm 0.43$ cm/sec/mmHg in group S. The slope for group F was significantly steep ($P < 0.01$). As shown in Figure 2, Pzf was $51 \pm 3$ mmHg in group F and $51 \pm 5$ mmHg in group S. There was no significant difference between the two groups with respect to Pzf. As shown in Figure 3, Fzp was $-98 \pm 16$ cm/sec in group F and $-46 \pm 4$ cm/sec in group S. The Fzp of group F was deeper ($P < 0.05$).

2) Deceleration time (DT)

As shown in Figure 4, DT was $280 \pm 20$ msec in group F and $540 \pm 50$ msec in group S. Group F showed a significantly shorter mean deceleration time ($P < 0.01$).

Figure 1. Comparison of coronary flow versus pressure slope index (FPSI) between group F and group S.

Figure 2. Comparison of zero flow pressure (Pzf) between group F and group S.
Maximum CKMB: As shown in Figure 5, maximum CKMB levels in group F and group S were 405 ± 73 IU/L and 161 ± 33 IU/L, respectively. Maximum CKMB was significantly higher in group F ($P < 0.05$).

Representative cases: Representative cases of group F and S are illustrated in Figures 6 and 7. Figure 6 shows a case in whom the myocardium scintigraphy result in the acute phase was 0.1 by TISS/BMIPPSS, and who was assessed as belonging to group S. FPSI was 0.97 cm/sec/mmHg, Pzf was 64.9 mmHg, and Fzp was -66.9 cm/sec. Figure 7 shows a case with a myocardium scintigraphy result of 0.74 by TISS/BMIPPSS who was assessed as belonging to group F. FPSI of acute myocardial infarction was 2.60 cm/sec/mmHg, Pzf was 49.5 mmHg, and Fzp was -19.0 cm/sec.
Figure 5. Comparison of serum cTnMB between group F and group S.

Figure 6. A typical example from group S. FPSI = 0.97 cm/sec/mmHg, Pzf = 64.9 mmHg and Fzp = -61.5 cm/sec.

Figure 7. A typical example from group F. FPSI = 2.60 cm/sec/mmHg, Pzf = 49.5 mmHg and Fzp = -128.3 cm/sec.
DISCUSSION

In patients with acute myocardial infarction, it is believed that early reperfusion leads to reduced infarction size, reduced mortality, and prevention of myocardial remodeling. Immediately after successful reperfusion therapy, it has not previously been possible to estimate how much the myocardium was salvaged using coronary angiography. Based on our investigations, we conclude that FSI and the new index Fzp are useful measures of myocardial rescue following reperfusion therapy.

Shibata, et al compared coronary blood flow waveforms immediately after successful acute reperfusion with myocardial scintigraphy, and reported that average systolic peak velocity (ASPV) and diastolic/systolic velocity ratio (DSVR) indicated the amount of salvaged myocardium.\(^7\) Kawamoto, et al used echocardiograms and reported that local cardiac contractility after one month correlated well with average systolic peak velocity (ASPV) and deceleration time (DT).\(^8\) Our results in this study also show that DT was significantly shorter in patients with failed salvaged myocardium. ASPV and DSVR require careful measurement. Hori, et al have reported that in cases of coronary fistula, the proximal average peak velocity was higher than the distal portion, because of shunt flow.\(^9\) ASPV appeared higher and DSVR appeared lower.

Maximum CKMB was significantly higher in group F. This suggests that more extensive myocardial necrosis occurred in group F, and agrees with the finding of Kawamoto, et al that DT becomes shorter at this time. It is well known that the coronary blood flow waveform immediately after successful reperfusion correlates well with chronic cardiac contractility. As DT is affected by heart rate, however, it is possible that DT shortens with increased pulse rate. It is widely assumed that DT reflects myocardial damage following acute myocardial infarction, but we were uncertain of the significance of DT. Indices of coronary conductance have been shown to reflect the status of the coronary microcirculation.

Using coronary conductance studies, we know that irreversible myocardial infarction is associated with major damage to the coronary microcirculation. In this study we looked at FSI and Pzf, which are reportedly more independent of heart rate and blood pressure than DT,\(^10\) and examined whether or not these indices could predict local cardiac contractility during the chronic phase of myocardial infarction. A good correlation was observed between DT and FSI in this study \((P < 0.01)\), however, because of similar heart rate and blood pressure in all cases. Bellamy examined the chronological correlation between pressure and flow volume of diastole, and reported that a linear relationship exists between them.\(^11\) The reciprocal of this linear gradient is equal to coronary resistance.
It is believed that perfusion pressure when the coronary blood flow ratio is reduced to zero cm/sec is not just the difference between coronary arterial pressure and right atrial pressure, but is strongly related to coronary arterial pressure which acts as coronary resistance.

The new index, \( Fzp \), is defined as the coronary artery flow when coronary blood pressure is reduced to zero mmHg. There may be reverse negative flow to the epicardial coronary artery from the intramyocardium. This phenomenon may be a reflection of increasing intramyocardial pressure exerted by the necrotizing myocardium. Yamamoto, et al reported that an increasing pressure derived fractional collateral blood flow index (PDCF) was associated with a predictor of poor LV recovery following reperfused AMI.\(^{12} \) PDCF was determined by simultaneous measurement of mean aorta pressure (\( Pa \)), distal coronary pressure during the balloon occlusion (\( Poc \)), and central venous pressure (\( CVP \)): \( \frac{(Poc - CVP)}{(Pa - CVP)} \). This implies that increasing intramyocardial pressure predicts poor LV recovery. We believe that a lower \( Fzp \) reflects higher PDCF.

When the coronary microcirculation is extensively damaged, blood flows from the epicardial side into the myocardium. When blood flow is low, blood is prevented from flowing into the myocardium. This is believed to be the reason for the acute decay observed during diastole. Additionally, FPSI rises significantly.

In summary, we consider that a short DT and acute FPSI predict extensive damage to the coronary microcirculation and limited blood inflow volume.

Bellamy did not address what occurs in acute myocardial infarction, and he did not report that \( Pzf \) correlates with intramyocardial pressure, even when myocardial infarction has caused destruction and inflammation of myocardial cells. In fact, no reports describing this phenomenon have been published. It is quite conceivable that in acute myocardial infarction, edema of the myocardium and interstitium in the infarction area,\(^9 \) or occlusion of the coronary microcirculation by leukocytes\(^{13,14} \) increase the intramyocardial pressure. However, our current results showed that \( Pzf \) showed no significant trend in either group.

For this reason, we had adopted the following model. As shown in Figure 8, we calculate \( Pzf \) from the primary pressure-flow volume correlation. This pressure-flow volume correlation is calculated from the primary equation \( y = ax - b \) (where \( a \) is inclination and \( b \) is intercept). \( Pzf \) is calculated as \( x_0 \) by setting \( y \) to zero; it can therefore be expressed as \( x_0 = \frac{b}{a} \). \( Pzf \) can therefore be regarded as an index with two independently variable factors: intercept (\( b \)) and inclination (\( a \)). Inclination (\( a \)) in this case means FPSI. Thus, to interpret \( Pzf \), it is necessary to consider the intercept (\( b \)). We calculated \( b \) for all cases in our study, assuming that \( b \) is zero pressure flow (\( Fzp: \text{cm/sec} \)), as shown in Figure 8. \( Fzp \) is \(-98 \pm 16 \text{ cm/sec} \) in group F and \(-46 \pm 4 \text{ cm/sec} \) in group S. Negative flow velocity was significantly faster in group F (\( P < 0.05 \)).
We have thus demonstrated that the lower \( b \) becomes, the greater the decrease in chronic LVEF becomes. Assuming that \( b \) represents negative flow velocity from the periphery of the myocardium to the central coronary artery, it became apparent that the larger this negative velocity becomes, the more chronically contractility decreases. During the acute phase of myocardial infarction, it is believed that the inclination (\( a \)) and intercept (\( b \)) of the primary line of the pressure-flow volume correlation vary independently of each other. To explain Pzf, which is a combination of these two independent variables, we believe that further elucidation of \( b \) is needed.

**Limitations of this investigation:** This study has two limitations. The first is that we did not investigate the influence of therapeutic agents, such as verapamil\(^{15}\) or nicorandil,\(^{16}\) on myocardial protection. It has been reported that the collateral circulation becomes an important factor for left ventricular function in the chronic phase,\(^{17}\) but we did not extend our study to investigate the degree of development of the collateral circulation. The second limitation was the preconditioning; we did not investigate whether or not patients had a prior history of angina pectoris. This condition may be an important factor in determining the extent of salvaged myocardium, and thus, further investigation is necessary.

**Conclusions:** We found that FPSI and the new index, Fzp, correlate significantly with the extent of myocardial salvage. On the other hand, we found no significant
correlation with salvage and Pzf. The reason for this difference is presumably because Pzf incorporates two independent variables.

REFERENCES