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ORIGINAL ARTICLE
Coronary artery disease

Coronary microcirculatory dysfunction can be assessed by positive dicrotic wave and amplitude index on resting distal coronary pressure waveform, a newly developed index

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Aims Some lesions have high resting distal coronary pressure/aortic pressure (Pd/Pa) despite low fractional flow reserve (FFR). This study aimed to assess microcirculatory dysfunction as a possible basal mechanism.

Methods and results Patients were grouped into two according to coffee intake (caffeine 222 mg) before coronary angiography. Through an adenosine-induced Pd/Pa decrease, amplitude index was calculated by dividing the difference between the highest pressure after the inflection point and the minimal diastolic pressure by the pulse pressure on the Pd waveform. In 130 coronary lesions (caffeine group, $n = 69$; non-caffeine group, $n = 61$) from 113 patients, the amplitude index through the adenosine-induced Pd/Pa decrease in all lesions was 0.54 ± 0.11 at resting Pd/Pa and 0.44 ± 0.12 at FFR ($P < 0.0001$). The positive dicrotic wave distribution on a maximal hyperaemia (FFRnicr)–resting Pd/Pa graph was analysed. In lesions with FFRnicr <0.80 on the FFRnicr–resting Pd/Pa graph, the resting Pd/Pa was divided into three zones based on Pd/Pa values: high-remaining, intermediate, and low. The high-remaining zone had a higher amplitude index than the intermediate zone (0.60 ± 0.09 vs. 0.48 ± 0.12; $P < 0.005$); the low zone lesions had no inflection point (no amplitude index). The high-remaining zone correlated with a larger positive dicrotic wave than the intermediate zone (94 vs. 30%; $P < 0.005$). Most lesions in the high-remaining zone corresponded to the caffeine group.

Conclusion In severe coronary stenosis, a high-remaining resting Pd/Pa with a high amplitude index or a positive dicrotic wave on the resting Pd waveform suggests microcirculatory dysfunction, such as insufficient arteriolar dilation reactive to myocardial ischaemia.

Registration UMIN000046883.

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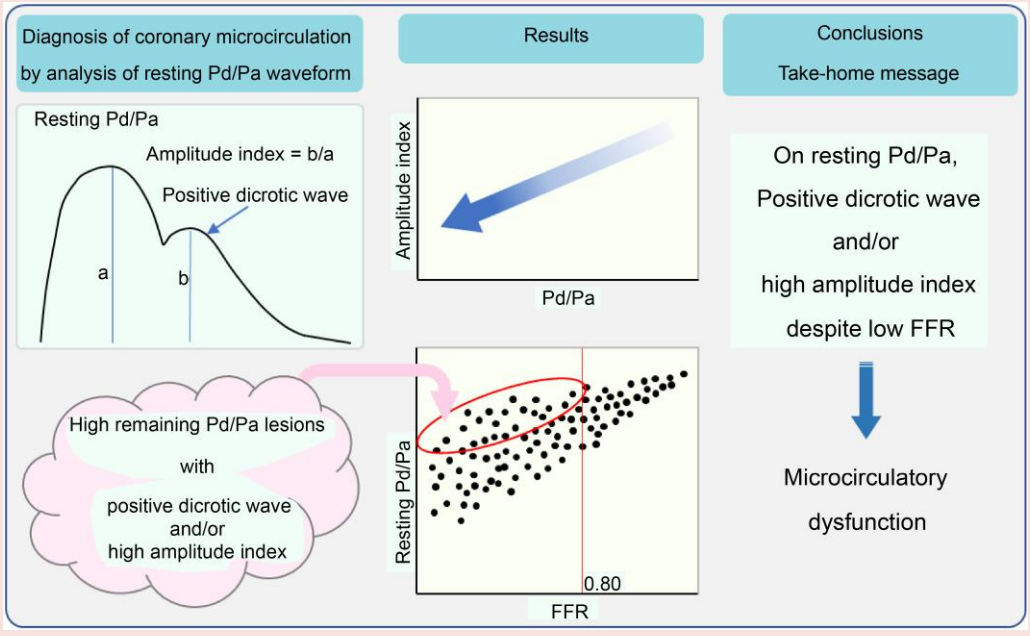
Graphical Abstract



Keywords Coronary microcirculatory dysfunction • Dicrotic wave • Amplitude index • Resting Pd waveform

Introduction

Pressure examinations have been used to assess the functional significance of coronary stenosis,[1–4] and fractional flow reserve (FFR) is considered the gold standard for decision-making in percutaneous coronary intervention (PCI).[5] An FFR of 0.80 is the cut-off value for PCI indication,[6,7] and an FFR of 0.75 is the cut-off value for myocardial ischaemia, compared with standard non-invasive tests.[8] FFR is measured in maximal hyperaemia[9] and reflects the balance between blood supply through stenotic lesion and blood pooling in maximally dilated arterioles. Meanwhile, resting distal coronary pressure/arterial pressure (Pd/Pa) reflects the balance between blood supply and blood pooling under the natural or basal condition of arterioles.[8,9] Blood supply before PCI depends not only on epicardial coronary stenosis but also on reactive arteriolar dilation to myocardial ischaemia.[10] Following a successful PCI, blood supply depends largely on arteriolar condition. As a result, estimating coronary microcirculatory tendency before PCI is extremely important.

As coronary stenosis progresses, arterioles in the related myocardial region dilate in proportion to ischaemia, resulting in a decrease in resting Pd/Pa.[10] However, some lesions have a high-remaining resting Pd/Pa despite myocardial ischaemia.[1,3–5] These lesions show a large diremption from FFR and make a large dispersion between resting Pd/Pa and FFR on the FFR–resting Pd/Pa graph. We hypothesized that either inadequate reactive arteriolar dilation in response to myocardial ischaemia or microvascular constriction may be the cause of this substantial diremption. Advanced examinations, such as coronary flow reserve (CFR)/index of microcirculatory resistance (IMR) measurement, are performed to assess coronary microcirculation[11]; however, despite being a useful assessment method, it is time consuming and requires more effort and a large catheter.

As we have considered that arteriolar conditions can induce changes in the shape of the pressure waveform, we focused on the inflection point and dicrotic wave on the resting Pd waveform. We developed a simple amplitude index on the resting Pd waveform and hypothesized that we could diagnose lesions with microcirculatory dysfunction based on the change in shape of the resting Pd waveform, which reflects arteriolar condition. This study aimed to clarify the cause of a large diremption of resting Pd/Pa from FFR using the caffeine-loading method to induce artificial coronary arteriolar constriction. In addition, we aimed to analyse the utility of the amplitude index, which we developed for assessing coronary microvascular dysfunction.

Methods

Patients

The flowchart of this study is shown in *Figure 1*. We enroled patients with stable angina and suspected myocardial ischaemia. Patients with severe acute coronary syndrome such as acute, impending myocardial infarction, and acute myocardial infarction were excluded. We also excluded those with severe valvular diseases, especially aortic valvular diseases, because those diseases influence systemic and coronary arterial pressure and waveform. Those with severe congestive heart failure with left ventricular ejection fraction <0.20 were also excluded because we cannot stop their medications before catheterization. Patients on haemodialysis were also excluded.

Patients undergoing coronary angiography (CAG) were instructed not to consume coffee or caffeine-containing foods for 24 h before the procedure. When patients were prepared for catheterization, we explained the study to each patient and offered them the option of consuming caffeine before the procedure. The patients who agreed to have caffeine were given coffee containing 222 mg of caffeine (UCC Black Non-sugar®; UCC Ueshima Coffee Co., Ltd, Kobe, Japan) before entering the catheterization laboratory. The remaining patients entered the laboratory without consuming coffee. Patients underwent coronary pressure examination when CAG revealed the presence of coronary stenosis (diameter stenosis >50%). Before the pressure examination, patients were divided into two groups: caffeine and non-caffeine.

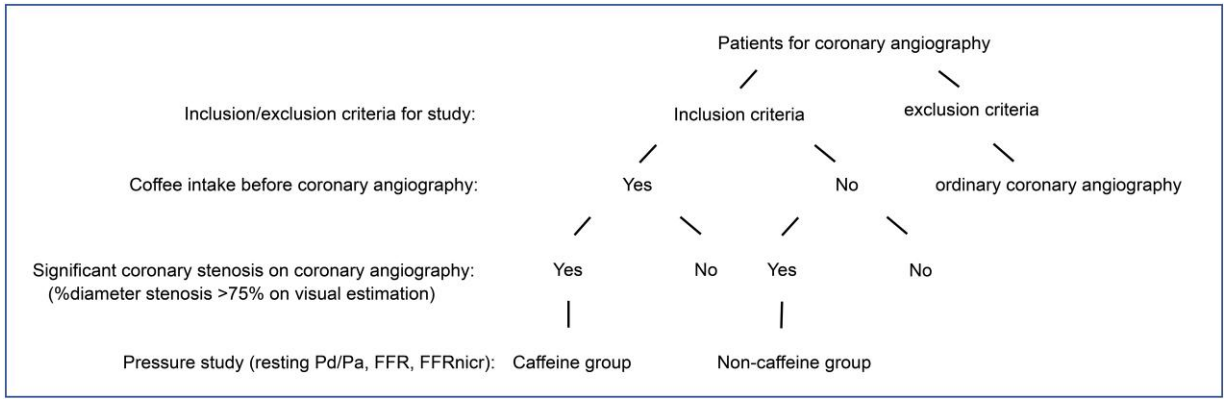


Figure 1 Study flowchart.

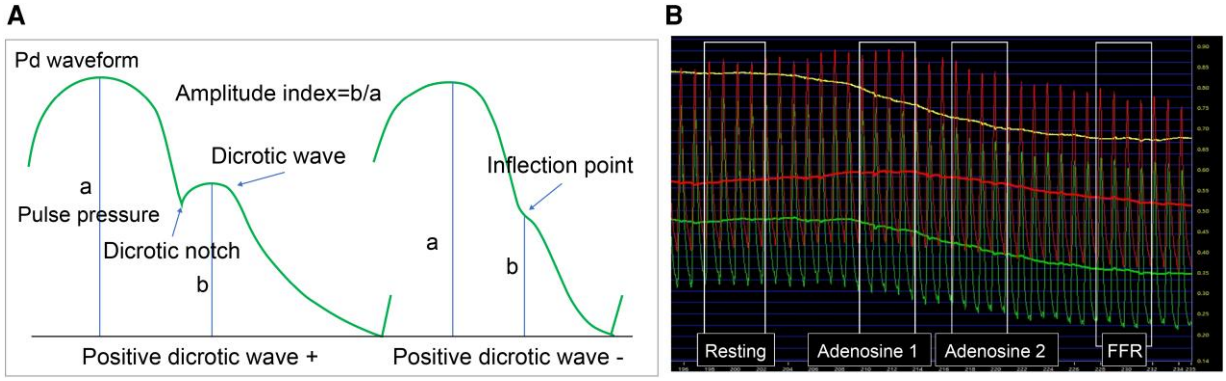


Figure 2 Definition of the amplitude index and analysis of the distal coronary pressure waveform. (*A*) Definition of the amplitude index. (*B*) Analysis of the resting distal coronary pressure waveform. Each of the four heartbeat cycles in four sections (resting, adenosine 1, adenosine 2, and fractional flow reserve) was analysed.

This study was approved by the local ethics committees and conformed to the tenets of the Declaration of Helsinki on human research. The study was registered with the UMIN Clinical Trials Registry (UMIN000046883). All patients provided written informed consent after the protocol and potential risks were explained.

Coronary angiography

We used 4 Fr diagnostic catheters and a non-ionic contrast medium (Iopamiron®; Bracco, Milan, Italy). We intravenously administered 100 IU/kg of heparin prior to CAG. Three cardiologists with 32, 23, and 14 years of experience visually assessed the severity of the coronary stenosis.

Pressure study

Coronary pressure examination was performed using Quantien™ (St. Jude Medical/Abbott, St. Paul, MN, USA). After calibration and equalization of a 0.014 inch pressure guidewire (Certus™ and Aeris™; St. Jude Medical/Abbott), we administered an intracoronary bolus of nitrates and advanced the wire to the distal portion beyond the stenotic lesion. We measured, in turn, the resting Pd/Pa and FFR, and an additional 2 mg nicorandil was administered through intracoronary injection during FFR measurement (FFRnicr) for maximal hyperaemia. Fractional flow reserve was assessed by continuous intravenous infusion of 140 μg/kg/min adenosine, which was increased to 180 μg/kg/min, as needed.

Definition of inflection point, amplitude index, and positive dicrotic wave

We exported the pressure data from Quantien™ as a spreadsheet and imported them on an Excel sheet for analysis (Microsoft, Redmond, WA, USA). The Pa, mean Pa, Pd, mean Pd, and Pd/Pa were recorded every 10 ms. In the resting Pd pressure data sheet, the inflection point, including the dicrotic notch, was determined according to the fluctuation of pressure decreasing speed (dP/dT). We calculated the dP/dT as the difference between the present pressure and the next. The Pd pressure usually decreases rapidly in the late systolic phase and slows down. The pressure point where the dP/dT changes from negative to positive was defined as the dicrotic notch. Meanwhile, the slowed down pressure is often accelerated again, resulting in no formation of a dicrotic notch. We defined this dP/dT changing point from slowdown to acceleration as inflection point. When we found plural points or confusable points in one waveform, we analysed consecutive three waveforms and determined the mean value as the inflection point. When the inflection point could not be clearly determined on the early diastolic phase, we defined the wave as a monophasic waveform.[12] A positive dicrotic wave was defined as a wave with a higher pressure than the dicrotic notch pressure. The amplitude index was calculated as the ratio of the difference between the highest pressure after the inflection point and the minimal diastolic pressure to the pulse pressure [(highest pressure after the inflection point – minimal diastolic pressure)/pulse pressure] (*Figure 2A*).

Table 1 Patient characteristic

	Caffeine group (56 patients)	Non-caffeine group (47 patients)	P
Age (years)	70.3 ± 10.5	71.1 ± 11.9	ns
Male (%)	71%	66%	ns
BMI (kg/m^2)	24.4 ± 3.5	23.9 ± 3.6	ns
Risk factors *n* (%)			
Hypertension	37 (66%)	28 (60%)	ns
Diabetes	24 (43%)	23 (49%)	ns
Dyslipidaemia	31 (55%)	23 (49%)	ns
Smoking	21 (38%)	15 (32%)	ns

BMI, body mass index; ns, not significant.

Table 2 Coronary angiography results

	Caffeine group (69 lesions)	Non-caffeine group (61 lesions)	P
Lesion distribution			ns
LAD	36 (52%)	39 (64%)	
LCX	13 (19%)	9 (15%)	
RCA	20 (29%)	13 (21%)	
% diameter stenosis	67.0 ± 15.5	69.2 ± 14.8	ns

Values are presented as mean ± standard deviation or *n* (%).
ns, not significant; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

Analysis of the resting distal coronary pressure waveform

We analysed the adenosine-induced decrease in the resting Pd waveform (*Figure 2B*, green wave). Each of the four heartbeat cycles in four sections (resting, adenosine 1, adenosine 2, and FFR) were analysed. The amplitude index was calculated using the Pd pressure data on the Excel sheet. The means of the four amplitude indexes and the mean Pd/Pa in each section were recorded.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation and compared using a *t*-test, paired *t*-test, or parametric Wilcoxon test, as appropriate. Categorical variables are expressed as percentages and analysed using Fisher's exact test. We quantified the relationship between resting Pd/Pa and FFR or FFRnicr using the coefficient of determination (R or R^2). An FFR of 0.75 was considered the cut-off value for myocardial ischaemia, and an FFR ≤0.80 was the cut-off value used for PCI indication. A $P < 0.05$ was considered significant. All statistical analyses were performed using MedCalc (MedCalc Software, Mariakerke, Belgium) and SPSS version 23.0 (IBM Japan, Ltd, Tokyo, Japan).

Results

Patient characteristics and coronary angiography

We enroled 130 lesions from 113 patients (mean age, 70.3 ± 10.5 years; male, 68%) in this study. Of these patients, 58 were enroled in the caffeine group and 55 were enroled in the non-caffeine group. The patient characteristics of each group are presented in *Table 1*. One patient enroled in the caffeine group had an unstable angina. Among the 130 lesions, 6 (5%) were cases of post-PCI restenosis.

On CAG, the lesion distribution was 58% in the left anterior descending artery, 17% in the left circumflex artery, and 25% in the right coronary artery. There was no difference in mean diameter stenosis between the caffeine and non-caffeine groups (*Table 2*).

Pressure study

The elapsed time from coffee intake to pressure examination was 2.4 ± 1.9 h in the caffeine group. The elapsed time was 30–60 min in 6 lesions, 60–120 min in 43 lesions, 2–4 h in 12 lesions, and >4 h in 8 lesions.

Change in the shape of the resting distal coronary pressure waveform

Figure 3A shows a representative of a dicrotic notch and a positive dicrotic wave on the resting Pd waveform. The Pd waveform showed a rapid pressure decrease in the early diastolic phase and a decrease of the dicrotic wave (*Figure 3B*). White arrows indicate the inflection point, including the dicrotic notch. *Figure 3C* shows a monophasic waveform with a more rapid decrease in Pd pressure, where the inflection point cannot be clearly determined and the dicrotic wave has disappeared.

Distal coronary pressure/aortic pressure in the caffeine and non-caffeine groups

The Pd/Pa values of resting, adenosine 1, adenosine 2, FFR, and FFRnicr did not differ between the caffeine and non-caffeine groups (*Table 3*). However, the difference between FFRnicr and FFR (FFRnicr − FFR) was significantly larger in the caffeine group than in the non-caffeine group (−0.015 ± 0.017 and −0.005 ± 0.018, respectively, $P < 0.005$), suggesting insufficient arteriolar dilation induced by adenosine in the caffeine group. *Figure 4* shows the FFR–resting Pd/Pa relationship. There was a large dispersion of resting Pd/Pa in severely stenotic lesions, and most of the lesions with high-remaining resting Pd/Pa were those in the caffeine group (brown circle).

Amplitude index based on the resting distal coronary pressure waveform during the adenosine-induced decrease in distal coronary pressure/aortic pressure

Sixteen examinations were not suitable for exact analysis because of drifting, large pressure fluctuation, extreme Mayer waves (apparent and cyclic pressure fluctuation induced by the sympathetic nerve activation), inadequate saline flush during observed phase, and so forth; thus, they were excluded from the analysis. Finally, we analysed the pressure data in 114 lesions (caffeine group, $n = 58$; non-caffeine group, $n = 56$).

The amplitude index on the resting Pd waveform is shown in *Figure 5*. The amplitude index of all lesions was 0.54 ± 0.11 in resting, 0.51 ± 0.10

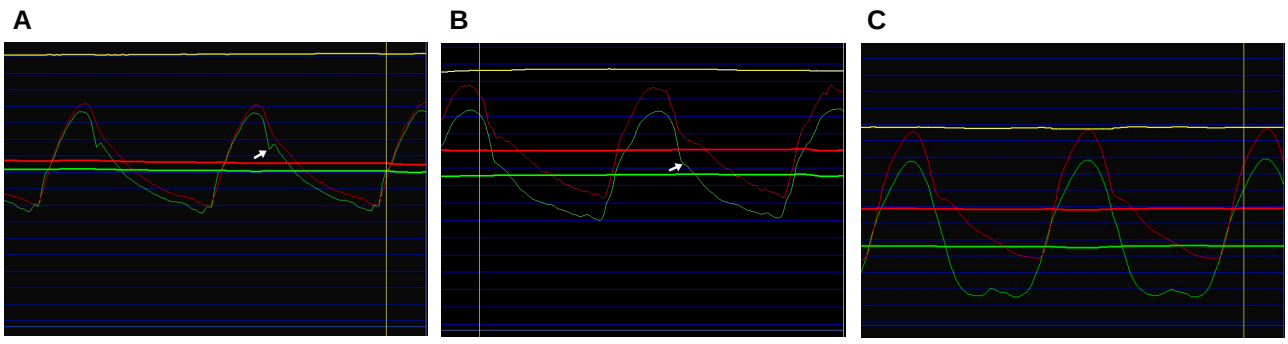


Figure 3 Representatives of the distal coronary pressure waveform. (*A*) Dicrotic notch and a positive dicrotic wave. (*B*) Non-positive dicrotic wave. White arrows indicate the inflection point, including the dicrotic notch. (*C*) Monophasic waveform; the inflection point cannot be clearly identified in this case.

Table 3 Distal coronary pressure/arterial pressure results

	Resting Pd/Pa	Adenosine 1 Pd/Pa	Adenosine 2 Pd/Pa	FFR	FFRnicr	FFRnicr–FFR
All lesions (105 lesion)	0.923 ± 0.070	0.885 ± 0.067	0.850 ± 0.079	0.811 ± 0.089	0.803 ± 0.093	−0.010 ± 0.022
Caffeine group (55 lesions)	0.922 ± 0.085	0.884 ± 0.071	0.856 ± 0.082	0.814 ± 0.105	0.799 ± 0.102	−0.015 ± 0.017*
Non-caffeine group (50 lesions)	0.925 ± 0.053	0.892 ± 0.062	0.860 ± 0.075	0.815 ± 0.083	0.810 ± 0.096	−0.005 ± 0.018

FFR, fractional flow reserve.
*$P < 0.005$ vs. non-caffeine group.

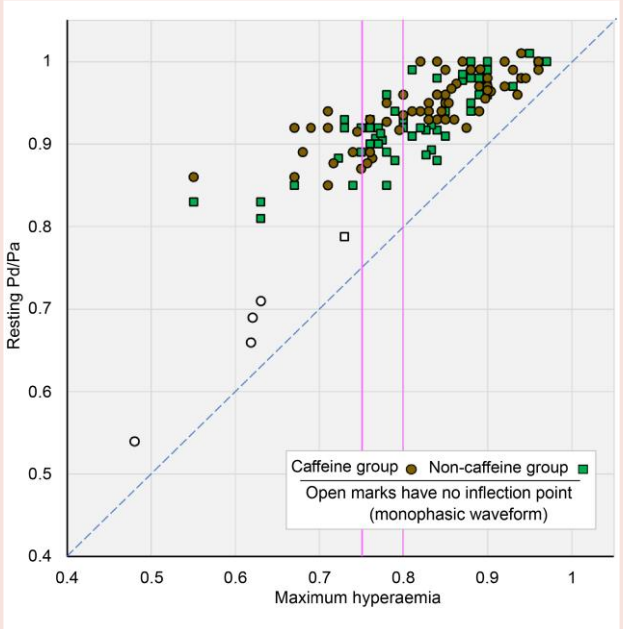


Figure 4 Relation between maximal hyperaemia and resting distal coronary pressure/arterial pressure. A large dispersion of resting distal coronary pressure/arterial pressure was observed in severely stenotic coronary lesions (fractional flow reserve < 0.75).

in adenosine 1, 0.48 ± 0.11 in adenosine 2, and 0.44 ± 0.12 in FFR, and the values significantly decreased proportionally with the Pd/Pa values (*Figure 5A*). Similar findings were observed in the caffeine and non-caffeine groups (*Figure 5B* and *C*). Although the amplitude index of the FFR was the same in the caffeine and non-caffeine groups, the amplitude index of resting was higher, albeit not significantly, in the caffeine group than in the non-caffeine group.

Amplitude index and positive dicrotic wave on the maximal hyperaemia–resting distal coronary pressure/aortic pressure relationship

We divided all lesions in *Figure 3* into three zones based on resting Pd/Pa values: high-remaining, intermediate, and low resting Pd/Pa with no inflection point zone (*Figure 6A*, red, yellow, and green zones, respectively). In severely stenotic coronary lesions, the amplitude index was significantly higher in the high-remaining resting Pd/Pa zone than in the intermediate zone. In lesions with FFRnicr <0.75, the amplitude index was 0.60 ± 0.09 in the high-remaining zone and 0.48 ± 0.12 in the intermediate zone ($P < 0.05$). In lesions with FFRnicr <0.80, the amplitude index was 0.58 ± 0.05 in the high-remaining zone and 0.49 ± 0.10 in the intermediate zone ($P < 0.005$). Lesions in the low zone had no inflection points (monophasic Pd waveform).

Figure 6B shows the distribution of positive dicrotic waves. In lesions with FFRnicr <0.75, the high-remaining resting Pd/Pa zone contained significantly more lesions with a positive dicrotic wave than the intermediate zone (91 and 9%, respectively; $P < 0.01$). In lesions with

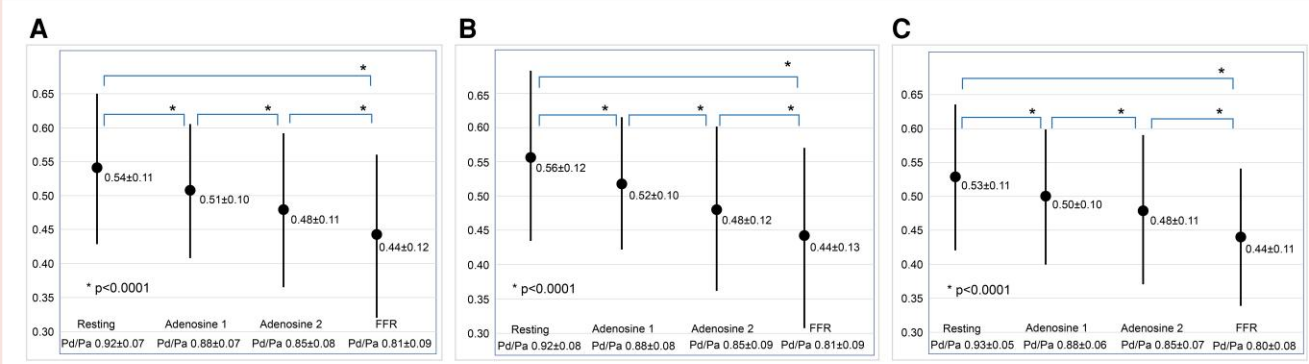


Figure 5 Adenosine effect on the amplitude index on the resting distal coronary pressure waveform. (*A*) All lesions. The amplitude index decreased proportionally with the distal coronary pressure/arterial pressure decrease. (*B*) Caffeine group. (*C*) Non-caffeine group.

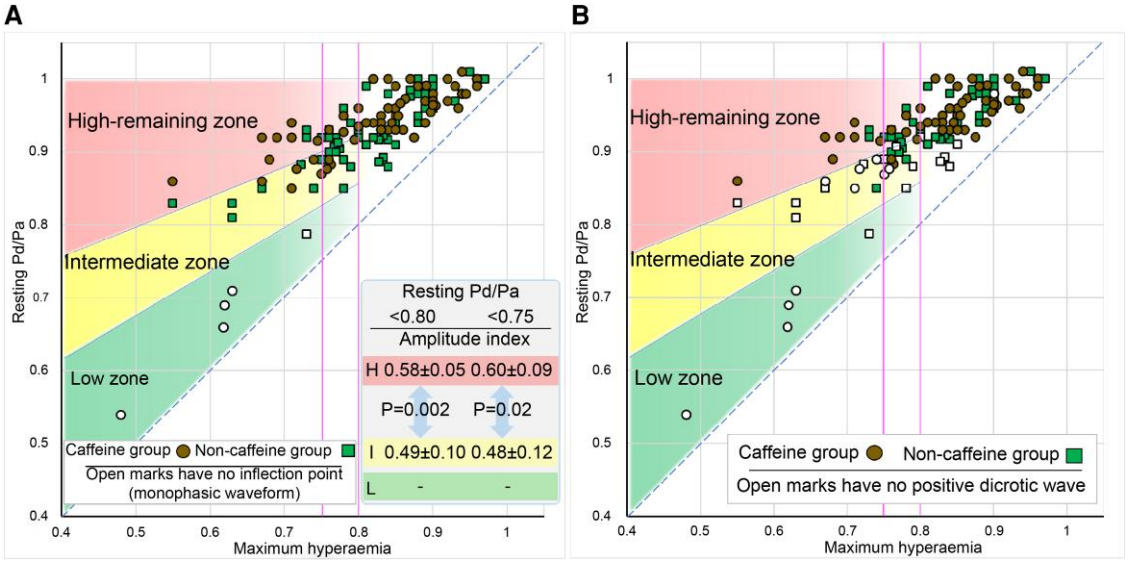


Figure 6 Amplitude index and positive dicrotic wave in three zones. (*A*) Amplitude index. (*B*) Distribution of a positive dicrotic wave. The graph field is divided into three zones: the high-remaining resting distal coronary pressure/arterial pressure zone (red), intermediate resting distal coronary pressure/arterial pressure zone (yellow), and the low resting distal coronary pressure/arterial pressure with no inflection point zone (green). The amplitude index is significantly higher in the high-remaining resting distal coronary pressure/arterial pressure zone than in the yellow zone.

FFRnicr <0.80, those with a positive dicrotic wave accounted for 94% in the high-remaining zone and 30% in the intermediate zone ($P < 0.005$). A positive dicrotic wave was not found on resting Pd/Pa <0.85 in either the caffeine or non-caffeine group.

Discussion

This study demonstrated that the amplitude index on the resting Pd waveform decreased in proportion to arteriolar dilation induced by adenosine, and that lesions with high-remaining resting Pd/Pa despite low FFRnicr (maximal hyperaemia) had a significantly high amplitude index and a positive dicrotic wave. Furthermore, most of those lesions were in the caffeine group, where arterioles were artificially constricted. These results suggest that a high amplitude index and a positive dicrotic wave indicate insufficient arteriolar dilation or microvascular constriction despite severe coronary stenosis.

Physiologically, peripheral coronary resistance is largely generated by arterioles, thus maintaining a relatively high myogenic tone at resting conditions.[13,14] Accordingly, vasodilating reserve can increase the blood supply three to five times the basal condition in response to largely increased oxygen demand.[15,16] Arteriolar dilation decreases resting Pd/Pa under epicardial coronary stenosis. Therefore, insufficient arteriolar dilation is considered to induce a high-remaining resting Pd/Pa despite a low FFRnicr.

Percutaneous coronary intervention indication has been determined by the results of pressure examinations.[6,7] However, a wide distribution of the resting Pd/Pa values on the FFR–resting Pd/Pa graph has been observed in previously reported resting physiologies.[1,3–5] The large dispersion between resting Pd/Pa and FFR makes the decision-making of PCI based on resting Pd/Pa difficult.

Vasoconstricting effects of caffeine and maximal hyperaemia

We artificially induced arteriolar constriction using caffeine. Patients in the caffeine group took 222 mg of caffeine 2.4 ± 1.9 h prior to pressure examination. This amount of caffeine is almost the same as that in one large cup of regular coffee. Caffeine inhibits vasodilation induced by adenosine as an antagonist on adenosine receptors.[17] As the effect of caffeine appears 30 min after intake, peaks after 60–120 min, and lasts for 2–4 h,[18] most of our patients (88%) were examined under caffeine effect.

There is a controversy over the vasoconstricting effect of caffeine and FFR.[19,20] In this study, the decrease in FFRnicr (maximal hyperaemia) from FFR was significantly greater in the caffeine group than in the non-caffeine group. Furthermore, FFRnicr was not different between the caffeine and non-caffeine groups (*Table 3*). These findings suggest that additional administration of nicorandil dilated arterioles that adenosine could not fully dilate. As a result, we chose additional administration of nicorandil on continuous adenosine infusion (FFRnicr) for maximal hyperaemia.

Amplitude index and positive dicrotic wave for coronary microcirculation assessment

Arteriolar dilation decreases the dicrotic notch amplitude on the systemic arterial pressure waveform.[21] Under the basal condition of arterioles, early diastolic blood pressure decreases gradually. Arteriolar dilation induces a rapid decrease in early diastolic blood pressure, which lowers the dicrotic notch amplitude. At the same time, increased blood flow due to arteriolar dilation maintains blood pressure and inhibits a decrease in dicrotic notch amplitude. Hence, the dicrotic notch amplitude could be determined by the balance of these two factors. However, we believe that this mechanism would not work in stenotic coronary arteries. Because the blood supply through the stenosis cannot sufficiently increase to maintain early diastolic Pd pressure, arteriolar dilation might rapidly and directly decrease early diastolic Pd pressure. We suspect that arteriolar dilation is the main factor for the rapid decrease in early diastolic Pd pressure under severe coronary stenosis. Increased blood pooling capacity due to arteriolar dilation surpasses the reduced blood supply due to coronary stenosis, resulting in a significant decrease or disappearance of the inflection point and a positive dicrotic wave. Moreover, this mechanism would be apparent under a more severely stenotic coronary condition. *Figure 6* shows that lesions in the low resting Pd/Pa zone had no inflection point or positive dicrotic wave, indicating that a rapid decrease in Pd pressure led to their disappearance. Lesions in the intermediate resting Pd/Pa zone had a low amplitude index and a small number of positive dicrotic waves; meanwhile, lesions in the high-remaining resting Pd/Pa zone had a significantly higher amplitude index and a larger number of positive dicrotic waves than those in the intermediate zone. Furthermore, most lesions in the high-remaining resting Pd/Pa zone were those of the caffeine group, where arterioles were artificially constricted. The findings of this study indicate that arterioles in lesions with a high-remaining resting Pd/Pa zone are artificially constricted by caffeine or naturally constricted in the absence of caffeine despite myocardial ischaemia.

Another possible mechanism of these findings is increased vessel stiffness due to diabetes and/or advanced arteriosclerosis. Although it is difficult to make a conclusion in this study, the latter could be supported by other systemic factors or examinations.

Clinical implications

The amplitude index and positive dicrotic wave are simple and easy-to-use indexes; however, they cannot directly assess arteriolar condition. Regardless, these may be used as a clinical indicator of coronary microcirculatory condition.

In severely stenotic coronary lesions, when pressure examination shows high-remaining resting Pd/Pa with a high amplitude index, positive dicrotic wave, or both on the resting Pd waveform (*Figure 6*, high-remaining resting Pd/Pa zone), there is a high possibility of coronary microcirculatory dysfunction such as insufficient arteriolar dilation reactive to myocardial ischaemia or microvascular constriction. As a result, the patient may benefit from discontinuing coffee.

When arterioles are revealed to have a constrictive tendency, the blood supply cannot be maximized even after successful PCI. Therefore, additional drug therapy that dilates arterioles is recommended to maximize PCI effect.

Additional drug therapy to dilate arterioles can also maximize blood flow speed through treated coronary lesions. Therefore, there is a high possibility that increased blood flow speed can reduce the chance of subacute thrombosis in the stent; furthermore, increased blood flow speed could improve the morphology and function of regenerated endothelial cells, resulting in the prevention of restenosis.

Study limitations

This study had a small number of patients; hence, further studies with a larger patient group are needed. There is a possibility that patient's daily coffee-drinking habits influence the reaction to the caffeine effect. We have been investigating this aspect. Finally, the amplitude index is an indirect assessment of arteriolar condition; therefore, we need to link the amplitude index to another assessment method, for example, CFR/IMR, to improve the precision and utility of the index.

Conclusions

Some lesions with high-remaining resting Pd/Pa have a large diremption from FFRnicr (maximal hyperaemia) in severely stenotic coronary lesions. We tested whether the newly developed amplitude index and positive dicrotic wave can be used to diagnose coronary microcirculatory conditions. The amplitude index decreased in proportion to adenosine-induced Pd/Pa decrease. Most lesions with high-remaining resting Pd/Pa, despite low FFRnicr, have accompanying high amplitude index and/or positive dicrotic wave on the resting Pd waveform, suggesting a possibility of microcirculatory dysfunction such as insufficient arteriolar dilation reactive to myocardial ischaemia or arteriolar constriction. However, results of this study were not compared with established diagnostic measurements, such as CFR/IMR. Therefore, a validation study against those established measurements is needed to improve the precision and utility.

Lead author biography

Yoshiharu Fujimori, MD, PhD, is a cardiologist whose specialty is coronary intervention and angioscopy, especially diagnosing vulnerable coronary plaques by dye-staining angioscopy using Evans blue. Recently, he developed the saline-induced Pd/Pa ratio (SPR), a new and easy-to-use assessment method to diagnose the functional significance of coronary stenosis by using a bolus of intracoronary saline.

Data availability

The data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Conflict of interest: None declared.

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