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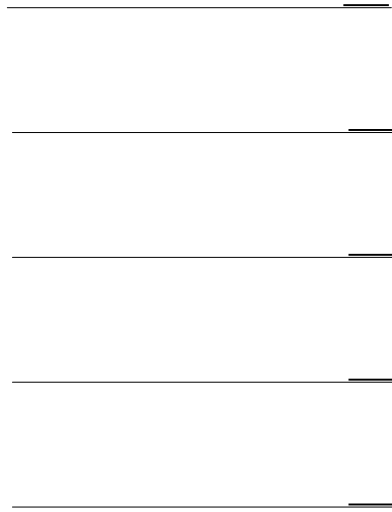


가

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2002 8

•



2002 6 20

- -

: (myocardial fractional flow reserve)  
가

가 가

가

가

: 2000 9 2002

12 ( 11 ,  $60.1 \pm 10.0$  )

16 ( 12 ,  $57.1 \pm 11.0$  )

, . 47

2.5 (1 , 27 )

2.5 (2 , 20 )

(Pa)

(Pd)

(Pd/Pa)

: 1 (15 27 , 24 ) 2 (13 20 , 16 )  
 (55 ± 10 : 63 ± 10 , p < 0.05), [ 6  
 (22%): 13 (65%), p < 0.01] , , ,  
 . 1 2 (2.7 ± 0.8 :  
 2.0 ± 0.4; p < 0.05), (0.81 ± 0.17 : 0.90 ±  
 0.06; p < 0.05)  
 가 . 1  
 (Pearson 0.55, p <  
 0.05), 2  
 가  
 (Pearson < 0.35, p 0.05).  
 : 2.5  
 가 ,  
 .  
 가 .

---

: , , ,

	-----	1
	-----	3
	-----	4
	-----	5
	-----	6
	-----	7
I.	-----	8
II.	-----	10
A.	-----	11
B.	-----	11
C.	-----	12
D.	-----	12
E.	-----	13
III.	-----	14
A.	-----	14
B.	-----	14
C.	-----	14
D.		
	-----	15
IV.	-----	16
V.	-----	20
	-----	21
	-----	26

FFR<sub>myo</sub>: (myocardial Fractional Flow Reserve)

IRA: (Infarct-Related Artery)

CFR: (Coronary Flow Reserve)

1 : ,  
2.5

2 : 2.5

PTCA: (Percutaneous TransCoronary Angiogram)

DST: (Diameter Stenosis)

MLA: (Minimal Luminal Area)

r-AST: (reference Area Stenosis)

Pa: (mean aortic pressure)

Pd: (mean coronary pressure, lesion distal)

ROC : Receiver Operating Characteristic curve

IVUS: (IntraVascular UltraSound)

SPECT: Single Photon Emission Computed Tomography

TIMI: Thrombolysis in Myocardial Infarction trial

RLA: (Reference Luminal Area)

AUC: ROC (Area Under Curve)

CI: (Confidence Interval)

QCA: (Quantitative Coronary Angiography)

EDRF: Endothelial Derived Releasing Factor

AMI: Acute Myocardial Infarction



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- a) with normal microvascular resistance and intramyocardial vascular pool without microvascular injury
- b) with increased microvascular resistance and decreased intramyocardial blood pool in AMI with microvascular injury.

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가

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,

I.

가 ,

가 가

가 .<sup>1</sup>

가 (Intravascular ultrasound)

가 ,  
가 .<sup>2-4</sup> 가  
(Coronary Flow Reserve)

(Myocardial Fractional Flow

Reserve) .

가

가 .<sup>5-8</sup>

,<sup>9,10</sup> ,<sup>11,12</sup> ,<sup>13</sup> (preload)<sup>14</sup> 가

,<sup>15</sup> ,<sup>16</sup> ,<sup>17</sup>

가

SPECT

0.75 .<sup>18</sup> ,

가  
가 ,

가  
,  
,

가

가

,

.

## II.

2000 9 2002

가

30% TIMI (Thrombolysis

in Myocardial Infarction trial) grade 3 가

1 (

2.5 )

2 ( 2.5

) . 30

가 가 16

30

2mm ST ,

creatine kinase MB isoform 3 ,

12

( 80 mmHg ), ,

( ), ,

,

A .

	Seldinger	Judkins
Philips BH 3000	H3000	DCI system (Philips Medical Systems, Eindhoven, Netherlands)
	quantitative coronary analysis system	
	(minimal luminal diameter)	(percent diameter stenosis)
	.	(heparin) 5000u

B .

0.014  
(30-40 MHz. 2.9-3.2 F, monorail type. Boston Scientific Co.)

200ug

motorized

pullback device 0.5mm , S - VHS

computer assisted planimetry

10mm 가 (reference luminal area) , 가 (minimal luminal area) , (reference area stenosis) .

C .

0.014 (Doppler FloWire<sup>®</sup>,  
Cardiometrics, Mountain View, CA, USA)

24 - 48ug  
15 MHz pulsed doppler velocimeter (FloMap<sup>®</sup>, Cardiometrics,  
Mountain View, CA)  
(average peak velocity)

가

**D.**

(0.014 inch fiberoptic pressure monitoring wire,  
Radi Medical System, Up-psala, Sweden)

24 - 48ug

(Pd)

(Pa)

(Pd/Pa)

**E.**

±  
chi-square student t-test



curvilinear(quadratic) regression analysis .

0.75

receiver operating characteristics(ROC) curve analysis

Area Under Curve(AUC)

p 0.05 .

### III.

#### A.

28 ( 23 ,  $57 \pm 10$  )  
47 (Table 1). 1  
2 (55 ±  
10 :  $63 \pm 10$  ,  $p < 0.05$ ), 가 [ 6 (22%) : 13  
(65%),  $p < 0.01$  ] , ,  
(Table 2).

#### B.

(reference diameter),  
(lesion length), , (Ejection fraction)  
가 (Table 3).

#### C.

,  
가 .  
1 (2.7 ± 0.8 : 2.0 ± 0.4;  
 $p < 0.05$ ), (0.81 ± 0.17 : 0.90 ± 0.06;  $p < 0.05$ )  
(Table 4).

#### D.

가

2

1

1

가

0.50

가 (Table 5). 1

(Y) ( ) Y = 0.6200

+ 0.0690 - 0.0035 <sup>2</sup>(Rsq = 0.389, p<0.05) , (Y)

( ) Y = 0.9235 - 0.0007 + 0.000026 <sup>2</sup>,

(Rsq = 0.61, p<0.05) (Fig 1, 2).

1 0.75

ROC . 0.75

77.4% ( 90.0%, 75.0%, AUC 0.850 ±

0.094; 95% CI: 0.665 - 1.035) (Fig 3).

IV .

가 가 가  
 . 가 가  
 가 .<sup>19</sup> 가가 가  
 가 가  
 20 가 .  
 가 가  
 가 2,3 ,  
 가 가 .<sup>21,22</sup>  
 가 .  
 가 가  
 23,24 , 가 가  
 ,  
 .<sup>25</sup>  
 , 가 1

18,26

가

. Pijls Bech <sup>27</sup>

0.75

가

ROC

0.75

Takagi <sup>28</sup> 60% ( 92%, 88.5%), de Bruyne <sup>33</sup> 66% ( 74%, 94%), Briguori <sup>34</sup> 70% ( 100%, 68%)

1 (CFR 2.5)

0.75 77.4% ( 90.0%, 75.0%, AUC 0.850 ± 0.094; 95% CI: 0.665 - 1.035)

(Fig 3).

가

. Bartunek <sup>27</sup>

가

가 (r=0.82)

Takagi <sup>28</sup>

가

(r=0.62, r=0.60. p<0.0001).

가

(r=0.92)

.<sup>29</sup> Hanekamp <sup>30</sup> 30

(quantitative coronary angiography; QCA)

91%

QCA

46%, 48% .

, Caymaz <sup>31</sup>

66% 67% 0.78 0.63

가 de Bruyne <sup>32</sup>

SPECT 가

가 가

67% 68% 가

0.52 0.67 가

가 가

1

0.50 가 , 2

가 . 2 ,

83%

0.70 0.98

(Fig 4, 5).

, 1 2

가 가

EDRF (Endothelial Derived Releasing Factor)

<sup>36</sup>

가 가 .

(microvascular blood

pool)

(Fig 6).

가 , 가

0.75

가

가 가

2.5

가

V.

2.5

가 ,

.

가

.



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- ABSTRACT -

**Analysis of factors effecting myocardial fractional flow reserve**

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**Background and Purpose:** Previous studies reported that myocardial fractional flow reserve (FFR<sub>myo</sub>) is a reliable functional index of epicardial stenosis severity, and showed significant correlation with other stress tests and anatomical stenosis severity in patients with angina pectoris. However, an important conceptual limitation of FFR<sub>myo</sub> is microvascular disease. The objective of this study was to evaluate the influence of microvascular integrity on FFR<sub>myo</sub>.

**Materials and Methods:** The study population consisted of 12 patients with AMI and 16 patients with angina pectoris. We performed intravascular ultrasound (IVUS) and intracoronary pressure and flow measurement before and after coronary stenting. The 47 data points are divided into two groups; post-stent coronary flow reserve (CFR) or CFR without PCI  $\geq 2.5$  (Group 1), and post-stent CFR  $< 2.5$  (Group 2). CFR, FFR<sub>myo</sub>, IVUS minimal luminal area (MLA), and reference area stenosis (r-AST) were calculated.

**Result:** There was no significant difference in angiographic and IVUS stenosis severity between Group 1 and Group 2. CFR was higher in Group 1 than in Group 2 ( $2.7 \pm 0.8$  :  $2.0 \pm 0.4$ ;  $p < 0.05$ ), and FFR<sub>myo</sub> was lower in Group 1 than in Group 2 ( $0.81 \pm 0.17$  :  $0.90 \pm 0.06$ ;  $p < 0.05$ ). There were

significant correlation between IVUS stenosis severity and FFR<sub>myo</sub> in Group 1 (correlation coefficient -0.54,  $p < 0.01$ ), however, not in Group 2 (correlation coefficient -0.25,  $p > 0.05$ ).

**Conclusion:** FFR<sub>myo</sub> was poorly correlated with anatomic stenosis severity in patients with impaired microvasculature integrity. This study suggests that the reliability of FFR<sub>myo</sub> for clinical decision making in patients with impaired microvascular integrity needs further investigation.

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**key words:** Myocardial fractional flow reserve, coronary flow reserve, intravascular ultrasound, microvascular integrity.

**Table 1. Basic Characteristics of the study population**

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Clinical Diagnosis	
Acute Myocardial Infarction	12
Angina Pectoris	16
Age(yrs)	57 ± 10
Risk Factors	
Hypertension	14 (50%)
Smoking	21 (75%)
Total cholesterol (mg%)	187 ± 35
Target Artery Studied	
Left anterior descending artery	20
Left circumflex artery	4
Right coronary artery	4
Infarction related artery	8
Stent Implantation	27

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**Table 2. Comparison of Basic characteristics of study groups**

	Group 1	Group 2
Patients (Male : Female)	27 (24 : 3)	20 (16 : 4)
Age (years)*	55 ± 10	63 ± 10
Acute Myocardial Infarction**	6 (22.2 %)	13 (65.0 %)
Risk factor		
Hypertension	13 (48.1 %)	7 (35.0 %)
Smoking	19 (70.4 %)	9 (45.0 %)
Hypercholesterolemia	8 (29.6 %)	2 (10.0 %)
TG (mg/dL)	165.8 ± 117.5	149.6 ± 46.2
TC (mg/dL)	185.2 ± 40.3	190.4 ± 29.7
HDL-C (mg/dL)	43.1 ± 9.7	39.0 ± 6.0
LDL-C (mg/dL)	113.3 ± 40.1	123.1 ± 38.4
Target artery		
Left main	0 ( 0.0 %)	1 ( 5.0 %)
Left anterior descending artery	19 (70.4 %)	11 (55.0 %)
Left circumflex artery	3 (11.1 %)	2 (10.0 %)
Right coronary artery	5 (18.5 %)	6 (30.0 %)

\*: p < 0.05,

\*\* : p < 0.01

Group 1: Post-stent CFR or CFR without percutaneous coronary intervention 2.5

Group 2: Post-stent CFR < 2.5

TC: total cholesterol,

TG: triglyceride,

HDL-C: high density lipoprotein cholesterol,

LDL-C: low density lipoprotein cholesterol

**Table 3. Comparisons of angiographic findings between group 1 and group 2**

	Group 1	Group 2	p-value
Reference diameter (mm)	3.58 ± 0.32	3.43 ± 0.47	NS
Lesion length (mm)	13.0 ± 5.0	11.3 ± 3.3	NS
MLD (mm)	2.24 ± 1.15	2.05 ± 1.10	NS
DST (%)	38.89 ± 31.58	39.88 ± 32.38	NS
LV Ejection fraction (%)	72.2 ± 9.6	66.7 ± 15.0	NS

Group 1: Post-stent CFR or CFR without percutaneous coronary intervention 2.5

Group 2: Post-stent CFR < 2.5

MLD: minimal luminal diameter,

DST: diameter stenosis

LV: left ventricular

**Table 4. Comparisons of functional and luminological severity of stenosis between group 1 and group 2**

	Group 1	Group 2	p-value
Patients	27	20	
CFR	2.7 ± 0.8	2.0 ± 0.4	0.010
b-APV (cm/s)	16 ± 5	18 ± 8	NS
h-APV (cm/s)	39 ± 17	34 ± 10	NS
FFRmyo	0.81 ± 0.17	0.90 ± 0.06	0.035
h-Pa (mmHg)	98 ± 14	98 ± 16	NS
h-Pd (mmHg)	80 ± 19	88 ± 16	NS
IVUS characteristics			
Vessel area (mm <sup>2</sup> )	10.0 ± 5.0	15.4 ± 5.2	NS
Minimal luminal area (mm <sup>2</sup> )	5.1 ± 3.5	5.2 ± 2.9	NS
r-Area stenosis (%)	69 ± 17	66 ± 16	NS

Group 1: Post-stent CFR or CFR without percutaneous coronary intervention 2.5

Group 2: Post-stent CFR < 2.5

CFR: coronary flow reserve,

b- : baseline,

h- : hyperemic

APV: average peak velocity,

FFRmyo: myocardial fractional flow reserve

Pa: mean aortic pressure,

Pd: mean coronary pressure, lesion distal

IVUS: intravascular ultrasound

r-AST: reference area stenosis

**Table 5. Correlation coefficient between IVUS parameters and FFRmyo**

	Group 1	Group 2
MLA (mm <sup>2</sup> )	0.55 (p<0.005)	0.35 (p>0.05)
r-AST (%)	-0.54 (p<0.01)	-0.25 (p>0.05)

Group 1: Post-stent CFR or CFR without percutaneous coronary intervention 2.5

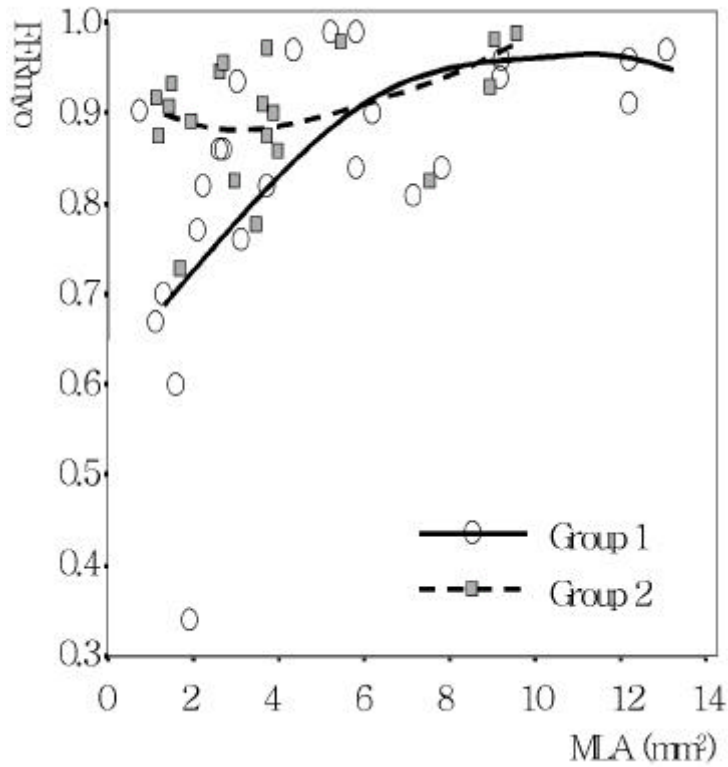
Group 2: Post-stent CFR < 2.5

MLA: minimal luminal area,

r-AST: reference area stenosis

IVUS: intravascular ultrasound

FFRmyo: myocardial fractional flow reserve



**Fig. 1. Plot showing quadratic correlation between FFRmyo and minimal luminal area (MLA) assessed by IVUS.**

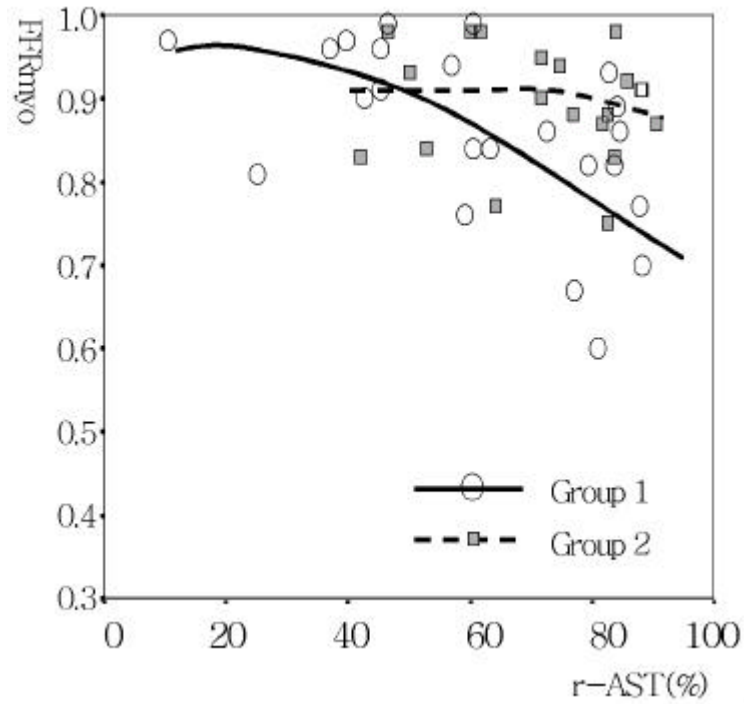
FFRmyo: fractional flow reserve, IVUS: intravascular ultrasound

Group 1: Post-stent CFR or CFR without percutaneous coronary intervention  $\geq 2.5$

$$Y = 0.6200 + 0.0690 \cdot X - 0.0035 \cdot X^2, R_{sq} = 0.389, p < 0.05$$

Group 2: Post-stent CFR  $< 2.5$

$$Y = 0.8972 - 0.0113 \cdot X + 0.0019 \cdot X^2, R_{sq} = 0.153, p > 0.05$$



**Fig. 2. Plot showing quadratic correlation between FFRmyo and reference area stenosis(r-AST) assessed by IVUS.**

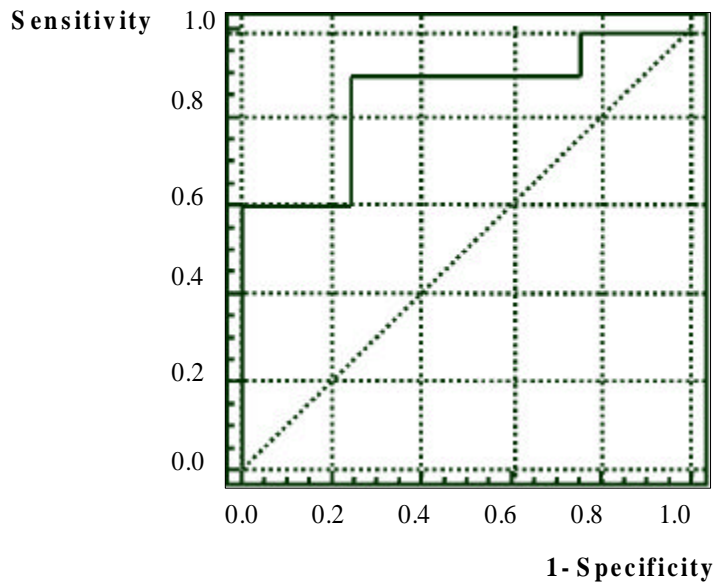
FFRmyo: fractional flow reserve, IVUS: intravascular ultrasound

Group 1: Post-stent CFR or CFR without percutaneous coronary intervention  
2.5

$$Y = 0.9235 - 0.0007 X + 0.000026 X^2, \text{ Rsq} = 0.61, p < 0.05$$

Group 2: Post-stent CFR < 2.5

$$Y = 0.9390 - 0.0012 X - 0.00002 X^2, \text{ Rsq} = 0.304, p > 0.05$$

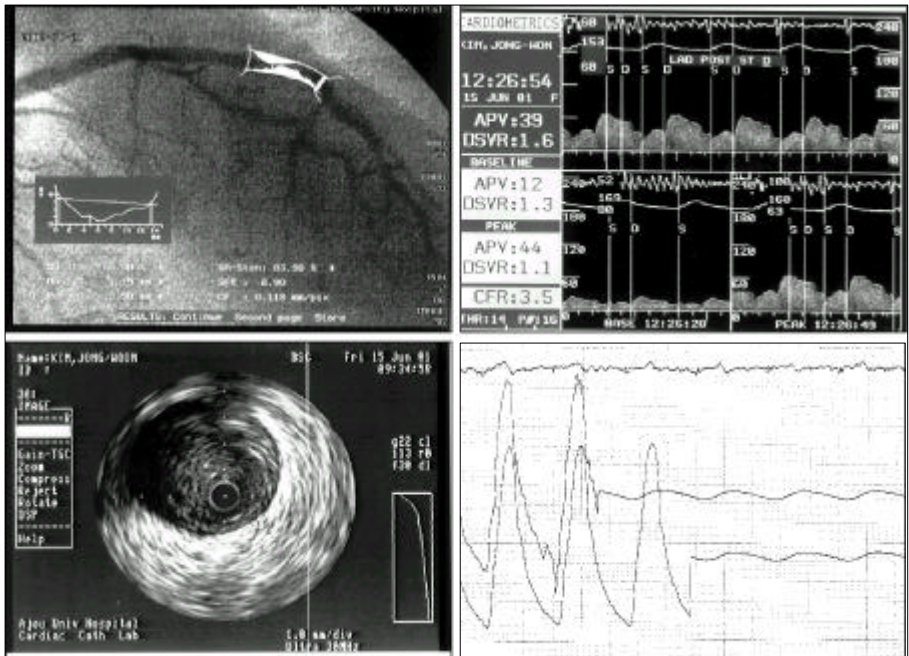


**Fig. 3. Receiver operating characteristic (ROC) curve analysis of reference area stenosis (r-AST) in group 1 (post-stent CFR or CFR without percutaneous coronary intervention 2.5)**

AUC (area under curve) :  $85.0 \pm 9.4 \%$ , 95 % C.I.: 0.67 1.04

Sensitivity: 90 %

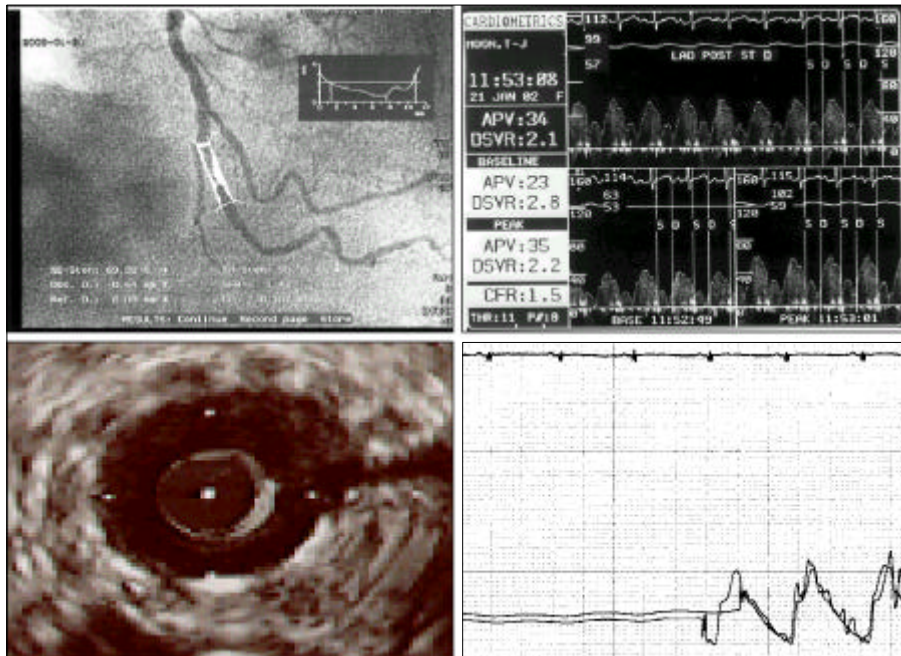
Specificity: 75 %



**Fig. 4. A case of acute myocardial infarction showing fractional flow reserve compatible with luminological severity.**

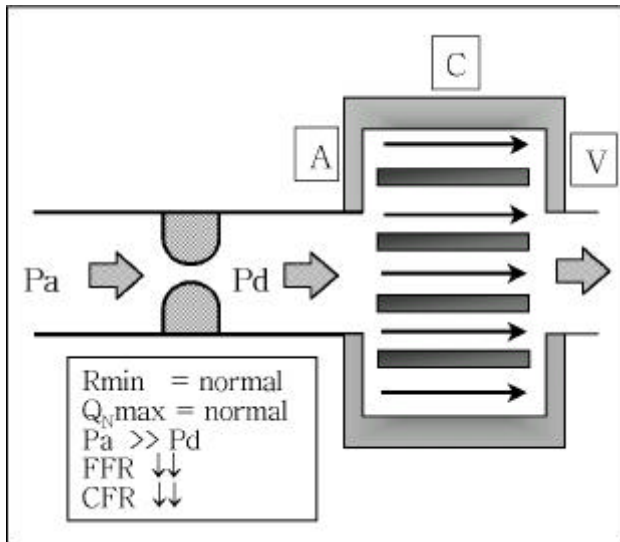
Top left, coronary angiography. Bottom left, intravascular ultrasound image show luminologically significant stenosis(reference area stenosis;r-AST = 83.3 %) of mid left anterior descending artery. Top right, post-stent coronary flow tracing shows functionally good pattern with coronary flow reserve(CFR) of 3.5. Bottom right, pre-stenting coronary pressure tracing shows functionally significant stenosis with fractional flow reserve(FFR) of 0.7





**Fig. 5. A case of acute myocardial infarction showing fractional flow reserve less severe than luminological severity.**

Top left, coronary angiography. Bottom left, intravascular ultrasound image show luminologically significant stenosis(reference area stenosis; r-AST = 83.9 %) of distal circumflex artery. Top right, post-stent coronary flow tracing shows impaired coronary flow reserve(CFR) of 1.5. Bottom right, pre-stent coronary pressure tracing shows functionally non-significant stenosis with fractional flow reserve(FFR) of 0.98.



**Fig. 6. Schematic illustration of the coronary stenosis and its dependent myocardial vascular bed**

Up, with normal microvascular resistance and intramyocardial vascular pool without microvascular injury

Bottom, with increased microvascular resistance and decreased intramyocardial blood pool with microvascular injury.

R<sub>min</sub>: minimal resistance of the myocardial vascular bed at a maximal arteriolar vasodilatation.

Q<sub>Nmax</sub>: maximum achievable myocardial flow if the coronary artery is normal.

Pa: mean aortic pressure during hyperemia

Pd: lesion distal mean coronary pressure during hyperemia

CFR: coronary flow reserve                      FFR: fractional flow reserve

A: arteriole,                      C: capillary bed during diastole,                      V: venule