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Pressure-wire based assessment of microvascular resistance using calibrated upstream balloon obstruction: a predictor of myocardial viability

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Abstract

Objectives—We assess microvascular integrity as a marker of myocardial viability after coronary stenting, using only a pressure guidewire.

Background—Microvascular integrity generally is not assessed using pressure-only guidewires because the transducer lies upstream of microvasculature. We partially inflate a balloon inside a coronary stent to achieve a specific normalized pressure drop at rest (distal coronary/aortic pressure=0.8) and then infuse a vasodilator, to render the wire sensitive to microvascular function. We hypothesize that the further decline in presssure ($\Delta FFR_{0.8}$) predicts MRI myocardial viability.

Methods—We studied 29 subjects with acute coronary syndrome including myocardial infarction. After successful culprit stenting, the resting coronary/aortic pressure was set to 0.8 using temporary balloon obstruction. $\Delta FFR_{0.8}$ was defined as 0.8-(distal coronary/aortic pressures) during adenosine-induced hyperemia. The average transmural extent of infarction was defined as the average area of MRI late gadolinium enhancement (after 2.8±1.5 days) divided by the corresponding full thickness of the gadolinium enhanced sector in short axis slices, and was compared with $\Delta FFR_{0.8}$.

Results—$\Delta FFR_{0.8}$ corresponded inversely and linearly with the average transmural extent of infarction (r^2=0.65, p<0.001). We found that a transmural extent of infarction of 0.50 corresponded to a $\Delta FFR_{0.8}$ threshold of 0.1, and had high sensitivity and specificity (100% and 94.4%, respectively).

Conclusions—Using only an upstream pressure-sensitive guidewire and a partially obstructing balloon during pharmacologic hyperemia, we were able to predict MRI myocardial viability with high accuracy after relief of epicardial stenosis. With further validation, this may prove a useful clinical prognostic tool after percutaneous intervention.

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Keywords

Coronary artery physiology; Microvascular resistance; Magnetic resonance imaging; Interventional cardiology; Intravascular diagnostics

Introduction

Pressure-wire based fractional flow reserve better predicts the physiological significance of epicardial coronary artery obstruction than does angiographic severity alone (1,2). However, fractional flow reserve alone does not necessarily predict preservation or recovery of contractile reserve in states of distal myocardial disease, whether infarct, myopathy, or hypertrophy (1). A test of distal microvascular integrity using only a pressure transducer would be a valuable tool.

Conventional pressure-wire measurements do not reflect microvascular function because the transducer is upstream of the subtended myocardium. Previous guidewire-based measurements of microvascular function therefor require an additional transducer element (often integrated into the same guidewire detector) to measure flow. We propose a simple invasive pressure-only test of microvascular function by imposing a calibrated resistance inside a coronary stent (a partially inflated balloon to achieve a specified pressure drop), followed by pressure measurement during vasodilator stress. In this test, resting P_d/P_{Ao} is set to 0.8 by the partially obstructing balloon, and downstream pressure drop during hyperemia (designated $\Delta FFR_{0.8}$) reflects microvascular integrity. We hypothesized that $\Delta FFR_{0.8}$ inversely corresponds to extent of infarction in the territory subtended by the lesion. We validate this simple test of risk area microvascular function against magnetic resonance late gadolinium enhancement in subjects undergoing stent treatment of acute coronary syndromes.

Materials and Methods

Human subjects

This trial was conducted according to the principles of the Declaration of Helsinki regarding investigation in humans, and was approved by the Institutional Review Board of Pusan National University Yangsan Hospital.

Subjects were recruited prospectively during the period Feb 2009 through March 2010. Candidates were eligible for inclusion if they were undergoing percutaneous coronary intervention for acute coronary syndromes, non-ST or ST-elevation myocardial infarction, if the culprit lesion was found in the proximal or middle segments of a major epicardial coronary artery with a reference vessel diameter between 2.75mm and 4.0mm, and if the culprit lesion was successfully treated with a coronary stent. Subjects were excluded if they had significant obstructive coronary artery lesion (>50%) in the target vessel distal to the culprit site, if they had a previous infarction other than in the culprit vessel, chronic kidney disease requiring renal replacement therapy, left ventricular hypertrophy with wall thickness > 12mm or hypertrophic cardiomyopathy on subsequent MRI or echocardiography, cardiogenic shock or requirement for catecholamine infusion, collateral flow to the target vessel more than angiographic grade 1, or excessive baseline variability (when the variation of FFR while obtaining data is greater than ± 0.01) of baseline distal coronary artery pressure during investigational balloon obstruction. All subjects consented in writing before participation.

Theory

The objective of this experiment is to assess the microvascular reactivity in the risk area subtended by a specific coronary lesion using a pressure-transducer coronary guidewire and pharmacologic vasodilation, and without Doppler ultrasound or thermodilution flow measurement. For the purpose of this experiment, microvascular integrity is considered directly related to myocardial viability.

A simplified coronary hydrodynamic model assumes two serial resistances in an atherosclerotic coronary artery, one in the obstructed epicardial coronary segment and a second in the distal microvasculature. Non-viable or dysfunctional myocardium has impaired distal microvascular flow reserve (1,3–6). Successful stent therapy of an isolated culprit conductance coronary artery stenosis essentially normalizes pressure-based fractional flow reserve (the ratio of distal coronary to aortic pressures during hyperemia), fixes the local cross sectional area despite pulsatile flow, and abates the pressure contribution of collateral arteries.

The epicardial coronary artery distal to the stent is still upstream the microvascular circulation and contributes minimally to energy (pressure) loss during vasodilation. Partially inflating an angioplasty balloon inside the stent, calibrated to an arbitrary resting pressure, imposes a resistance proximal to the pressure-transducer. This resistance creates additional pressure loss only if pharmacologic vasodilatation augments blood flow, *ie* in a preserved myocardial territory. The pressure-transducer is thereby rendered sensitive to microvascular flow changes.

Equation 1 defines fractional flow reserve as the arteriovenous pressure drop beyond the stenotic coronary artery (P_d) divided by the arteriovenous pressure drop from the aorta (P_{Ao}), during a state of hyperemia. For convenience low myocardial venous (P_v) pressures are ignored.

$$FER=\frac{(P_d - P_v)}{(P_{Ao} - P_v)} \approx \frac{(P_d)}{(P_{Ao})} \quad \text{Equation (1)}$$

$$\Delta FFR_{0.8}=\left(\frac{P_{d(B)}}{P_{Ao(B)}}\right) - \left(\frac{P_{d(H)}}{P_{Ao(H)}}\right)=0.8 - \left(\frac{P_{d(H)}}{P_{Ao(H)}}\right) \quad \text{Equation (2)}$$

We define our measure of microvascular function ($\Delta FFR_{0.8}$) as the change in P_d/P_{Ao} between rest and pharmacological hyperemia when a partially obstructing balloon is inflated at rest to 80% of the inflow pressure (Figure 1A and B, and Equation 2). $P_{d(B)}$ and $P_{d(H)}$ indicate distal coronary artery pressure at baseline and during hyperemia, respectively. The first component $P_{d(B)}/P_{Ao(B)}$ is set to 0.8. This threshold was selected for patient tolerability and for convenience. This experiment assumes that venous pressures are negligible, that balloon-in-stent and other coronary segments are noncompressible, and that the non-target coronary artery is normal.

Measurement of $\Delta FFR_{0.8}$

After the culprit clinical lesion was successfully treated with a coronary stent, a 0.014” coronary guidewire incorporating a pressure transducer at the spring coil junction (PressureWire, Radi, St Jude Medical) was positioned 2–3cm distal to the implanted stent. An undersized balloon shorter (8–12mm length) and narrower (0.5mm less than the nominal stent delivery balloon diameter) was positioned inside the stent lumen. The undersized balloon was then inflated to achieve a mean distal coronary pressure 80% of the mean aortic

pressure at rest (Figure 1 A and B). Subjects (n=5) were excluded if Pd(B)/PAo(B) fluctuated more than ±0.01 at baseline. Coronary hyperemia was then induced using intravenous adenosine 140 mcg/kg/min infusion and ΔFFR0.8 calculated after two minutes, according to Equation 2.

Cardiac magnetic resonance imaging

All patients underwent cardiac magnetic resonance imaging after PCI with invasive hemodynamic assessment. Imaging was performed at 1.5T (*Avanto*, Siemens, Erlangen, Germany) with electrocardiographic gating and a standard torso phased array cardiac receiver coil. A balanced steady-state free precession pulse sequence during repeated breath-holds of approximately 10 seconds was used for cine images with multiple short axis views every 10 mm covering the entire left ventricle. Typical scan parameters were: voxels 1.8 × 1.8 × 6.0 mm^3; repetition time/ echo time, 2.8/1.4ms; flip angle 79°; matrix 192 × 156. Late gadolinium enhancement images were obtained approximately 15 minutes after (0.02 mmol/kg) intravenous administration of gadopentate-dimeglumine (*Magnevist*, Bayer-Schering, Berlin, Germany). The inversion time was set to null the signal of normal myocardium and ranged from 240 to 300 ms. Typical scan parameters were: repetition time/echo time, 8.1/3.1ms; flip angle 25°; triggering to every other heart beat; achieving voxels 1.8 × 1.3 × 8.0 mm^2. T2-based assessment of myocardial edema or risk area was not performed. Images were analyzed on a dedicated workstation (*Argus VF*, Siemens) by consensus of two independent observers, each with 7 years experience in cardiac MRI. Late gadolinium enhancement was defined as signal activity greater than two standard deviations from remote normal myocardium (7), summed from all slices. The risk segment area was defined as the transmural area extent bounded by the lateral margins of the late enhancement area (Figure 1C). Average transmural extent of infarction (TEI) is defined as the ratio of late gadolinium enhancement area to risk segment area, each summed from all slices(8).

Statistics

Continuous parameters were compared using a Student t-test (paired when appropriate) and their correlation measured using a Pearson product-moment correlation coefficient *r*. Categorical and ordinal parameters were compared using a Pearson chi square test. They are reported as mean ± standard deviation. The association between $\Delta FFR_{0.8}$ and other parameters was determined using univariate and multivariate logistic regression models (Generalized Linear Model, *SPSS* version 16, IBM). Receiver-operator analysis of the $\Delta FFR_{0.8}$ relationship with transmural extent of infarction was performed using MedCalc for Windows, version 10.0.0 (MedCalc Software, Mariakerke, Belgium).

Results

Human subjects

A total of 333 candidates were screened during the study period. Of 72 eligible candidates, 34 consented to participate. Of these, five were excluded because distal coronary pressure was unstable during partial balloon obstruction (0.8 ±0.03). Ultimately, 29 subjects with acute coronary syndrome or myocardial infarction were enrolled. Of these, more than half of patients (n= 18, 62%) were undergoing primary PCI for ST segment elevation myocardial infarction (STEMI). The left anterior descending artery was the culprit vessel in half (Table 1).

Predictors of ΔFFR0.8

Figure 2 shows a roughly linear inverse relationship between transmural extent of myocardial infarction, assessed by MRI late gadolinium enhancement, and $\Delta FFR_{0.8}$

(r^2=0.65, p<0.001). This remained largely unchanged after excluding the four subjects without evident late gadolinium enhancement on MRI (n=25, r^2=0.60, p<0.001).

A receiver-operator analysis was performed to determine a threshold $\Delta FFR_{0.8}$ value corresponding to an average transmural extent of infarction of 50%. A threshold $\Delta FFR_{0.8}$ value of 0.1 predicted a 50% transmural extent of myocardial infarction (Figure 3), with sensitivity 100%, specificity 94.4%, area under curve 0.997, positive predictive value 91.7%, and negative predictive value 100%. Excluding the four subjects without late gadolinium enhancement on MRI, the receiver-operator relationship was largely unchanged (sensitivity 100%, specificity 92.9%).

Clinical, laboratory, and MRI parameters were considered using this threshold $\Delta FFR_{0.8}$ greater and less than 0.1 (table 2). Six patients had evidence of microvascular obstruction on MRI, five of whom had $\Delta FFR_{0.8} < 0.1$. By univariate analysis, only overall myocardial ejection fraction, peak serum troponin value, MRI evidence of microvascular obstruction, TIMI angiographic myocardial blush score, and average transmural MRI extent of infarction were different between the high and low $\Delta FFR_{0.8}$ strata. By multivariate analysis (table 3-A), only average transmural extent of infarction predicted $\Delta FFR_{0.8}$.

When stratified according to average transmural extent of infarction as a marker of viability, the following parameters were found significant on univariate analysis (Table 3A): $\Delta FFR_{0.8}$, left ventricular ejection fraction, troponin I, MRI evidence of microvascular obstruction, and TIMI angiographic myocardial blush score. By multivariate analysis (Table 3B), $\Delta FFR_{0.8}$ and LV ejection fraction remained significant predictors of average transmural extent of infarction.

The subgroups ST-elevation versus non-ST-elevation myocardial infarction, or LAD versus non-LAD showed the same consistent relationship between $\Delta FFR_{0.8}$ and average transmural extent of infarction (Figure 4).

Discussion

We found that a pressure-wire-only measure of microvascular function, applied immediately after coronary artery stenting, predicts myocardial viability by MRI after acute coronary syndromes or myocardial infarction. We observed a linear relation between our index, $\Delta FFR_{0.8}$, and extent of viable myocardium subtended by the index coronary artery lesion. Traditionally, pressure-wire-only assessment of microvascular integrity is not possible in the absence of epicardial stenosis. Our calibrated in-stent balloon obstruction creates a temporary upstream resistance that allows downstream coronary artery pressure to fall during pharmacologic hyperemia. This renders the pressure-wire sensitive to alterations in microvascular function. Moreover, we identified a convenient threshold value of $\Delta FFR_{0.8}$=0.1 that corresponds to a transmural extent of infarction of 50%, which predicts recovery of myocardial contractile function after revascularization (9). These findings appeared consistent irrespective of coronary artery territory or clinical syndrome.

Invasive guidewire probes combining pressure transducers with Doppler ultrasound or thermistors have been used for combined assessment of resting and provoked pressure gradients as well as of velocities or cold-saline transit times (1). These allow combined invasive assessment of epicardial lesion severity and of microvascular function, applicable to the locally subtended myocardium. The Index of Microvascular Resistance (10–14) is a validated thermodilution measure that is independent of epicardial stenosis severity when corrected for collateral artery pressure (11). Indeed Aarnoudse and colleagues (11) used partially obstructive balloons inflated to different nominal cross-sectional areas inside coronary stents to simulate varying epicardial stenosis severity. The additional Doppler and

thermodilution transducer elements are subjectively more cumbersome to use but provide epicardial and microvascular indices attainable both before and after revascularization. Our alternative pressure-based measurement permits microvascular assessment and prognostication only after relief of the epicardial obstruction.

Why would $\Delta FFR_{0.8}$ correspond to the proportion of viable myocardium? We hypothesized that recruitable microvascular flow would relate linearly with the mass of subtended viable muscle (15). Absent epicardial stenosis, changes in our calibrated P_d/P_{Ao} during pharmacologic provocation reflect flow augmentation related only to recruited microvascular flow. Indeed we found the unitless measures $\Delta FFR_{0.8}$ to be inversely related to the transmural extent of infarction.

Kocaman *et al*(16) have reported clinical prognostic utility of an index they describe as "delta FFR," which is the magnitude in normalized pressure drop between resting and hyperemic conditions. This index is attractive because it is obtained before revascularization, and uses data otherwise routinely obtained during ordinary fractional flow reserve measurement. However, the epicardial component reflects a variable intrinsic baseline resistance (from the native lesion), compared with our calibrated epicardial coronary resistance, and therefore does not reflect purely on downstream microvascular integrity. Further comparison of the Kocaman "delta FFR" and our $\Delta FFR_{0.8}$ would be interesting. We did not obtain "delta FFR" in our study because of the large proportion of patients undergoing primary PCI for ST-elevation myocardial infarction.

Pressure-derived coronary flow reserve measurements are similar attempts to assess combined epicardial and microvascular function in the presence of coronary stenoses. Akasaka and colleagues (17) found pressure-derived coronary flow reserve corresponded to Doppler and flow-meter measurements in animals. MacCarthy and colleagues (18) measured pressure-derived coronary flow reserve after stenting using partially-obstructive balloons similar to our approach. They found their measurement underestimated thermodilution-based coronary flow reserve and was insufficient to estimate coronary flow reserve in purely microvascular dysfunction.

We assessed infarcted area using a patient- and vessel-specific index different from standard American Society of Echocardiography segmentation (19). Instead we measured infarct area by MRI late gadolinium enhancement. At the time of our study we were technically unable to use more advanced T2-weighted measures of myocardial edema (20) to determine risk area. Instead we determined the "average transmural extent of infarction" using surrounding healthy myocardial segments, based on O'Regan and colleagues' (8) evidence that lateral infarct margins approximate the ischemic bed in both partial thickness and transmural infarcts.

Other limitations of this study include our failure to obtain baseline and hyperemic pressure gradients and matching thermodilution transit time measurements, for comparative "delta FFR" and Index of Microvascular Resistance measurements. Our local ethics board did not favor obtaining these comparative measurements in the subject population undergoing primary angioplasty for acute myocardial infarction, because of concerns about prolonged research procedures. Our incidence of slow-flow or no-reflow was low but MRI microvascular obstruction appreciable, reflecting our community reperfusion intervals; conceivably the relationship between $\Delta FFR_{0.8}$ and transmural extent of infarction would differ after late reperfusion (21–23). Only 29 of 333 candidate subjects are reported, although 45% of eligible subjects were enrolled. Our approach is unsuitable for patients not undergoing PCI. We used an undersized balloon for the purpose of this research procedure, however the clinical post-dilatation or stent delivery balloons also may be employed.

We conclude that $\Delta FFR_{0.8}$ is a simple candidate predictor of downstream myocardial viability immediately after percutaneous stenting of acute coronary syndrome and myocardial infarction. A $\Delta FFR_{0.8}$ value of 0.1 corresponds to a transmural extent of infarction of 50%, which predicts recovery of contractile function after revascularization. The test is attractive in its simplicity but applicable only after revascularization. Further consideration of this test might establish its value in a wider range of conditions, especially after later reperfusion of myocardial infarction, and in comparison with the related "delta FFR" before revascularization and the thermodilution-based "index of microvascular resistance (IMR)."

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Acronyms and Abbreviations

FFR	fractional flow reserve
Δ $FFR_{0.8}$	0.8 - hyperemic P_d/P_{Ao}
MRI	magnetic resonance imaging
P_d/P_{Ao}	Ratio of distal to aortic pressure
PCI	Percutaneous coronary intervention
TEI	Transmural extent of myocardial infarction

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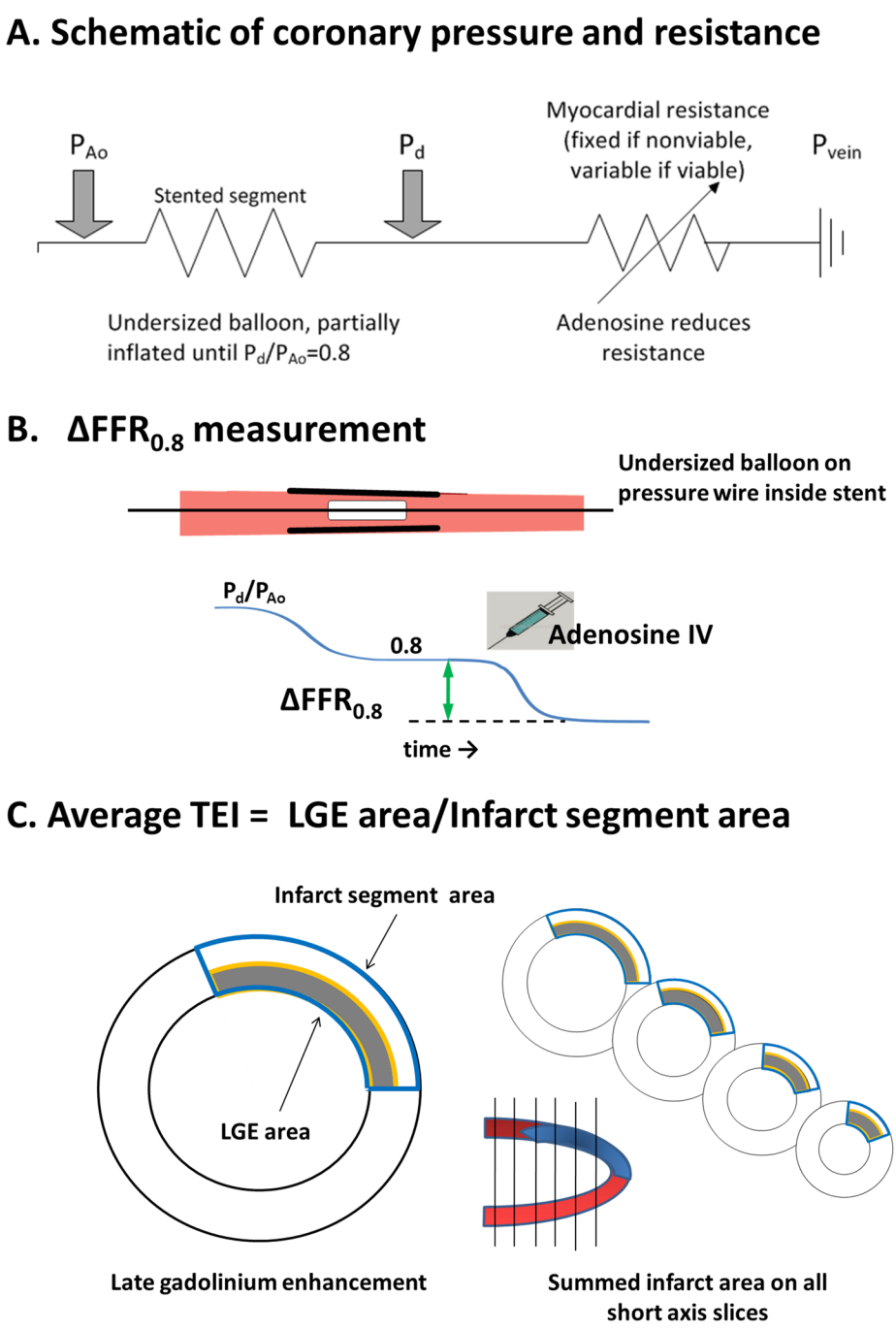

Figure 1.

A. The circuit diagram schematizes the hemodynamic measurement. Upstream resistance is created by a partially inflated balloon in the epicardial coronary artery. The pressure transducer guidewire is distal to this artificial resistance, and measures the pressure drop created between the aorta and the coronary artery. The microvascular bed serves as a downstream variable resistance sensitive to adenosine.

B. How $\Delta FFR_{0.8}$ is measured. A balloon dilatation catheter is positioned into a schematic stented coronary artery segment and inflated until the resting P_d/P_{Ao}

value is 0.8. Thereafter intravenous adenosine is administered to induce maximal coronary hyperemia and $\Delta FFR_{0.8}$ is measured as the further drop in P_d/P_{Ao} from 0.8.

C. How the average transmural extent of infarction (TEI) is measured. The area of late gadolinium enhancement is measured in a stack of six late gadolinium enhancement MRI images. The risk area is measured as the corresponding full thickness area of myocardium. The average transmural extent of infarction is the ratio of the two.

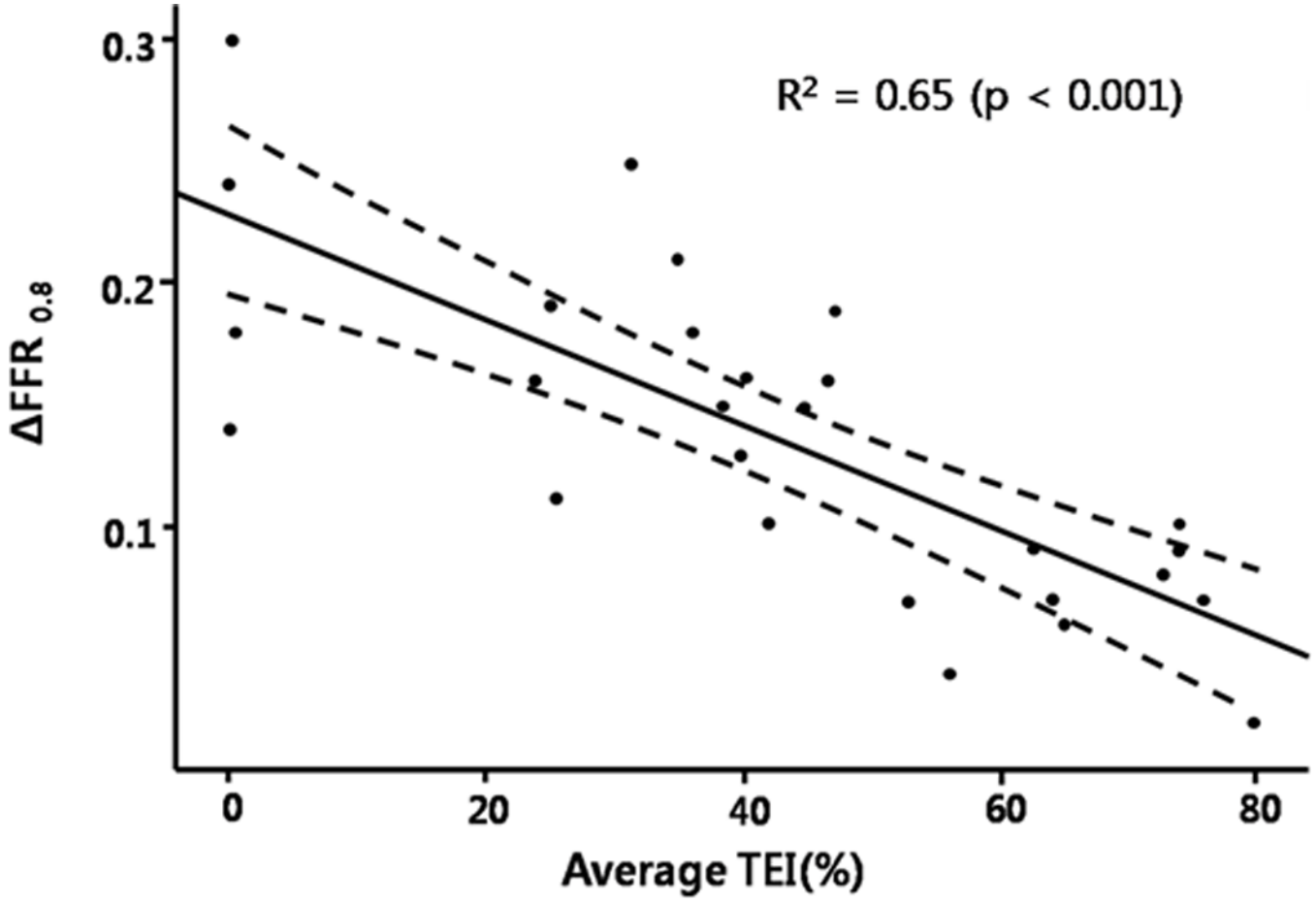

Figure 2.
The relationship between $\Delta FFR_{0.8}$ and average transmural extent of infarction (TEI).

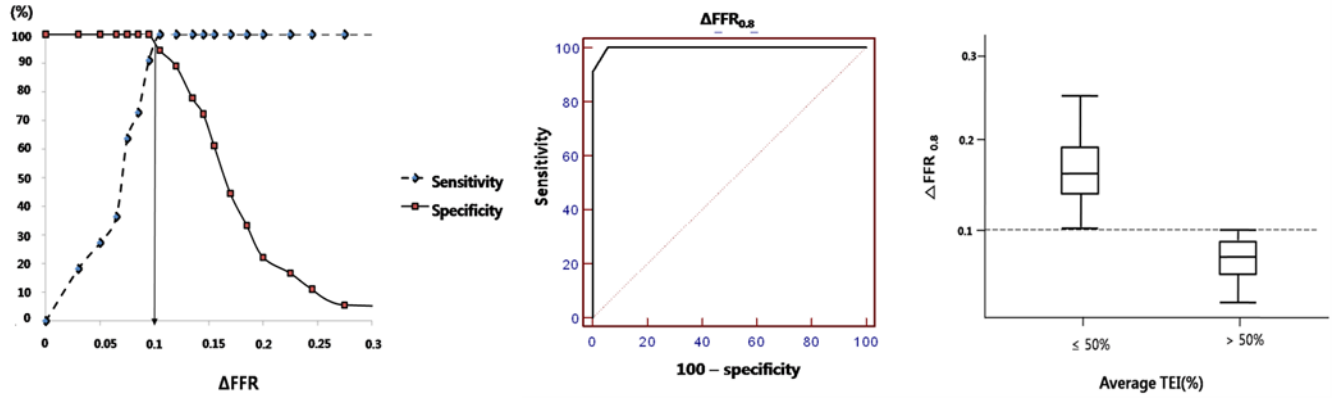

Figure 3.

Receiver-operator characteristics of $\Delta FFR_{0.8}$. The threshold $\Delta FFR_{0.8}$ =0.1 corresponds to 50% average transmural extent of infarction (TEI).

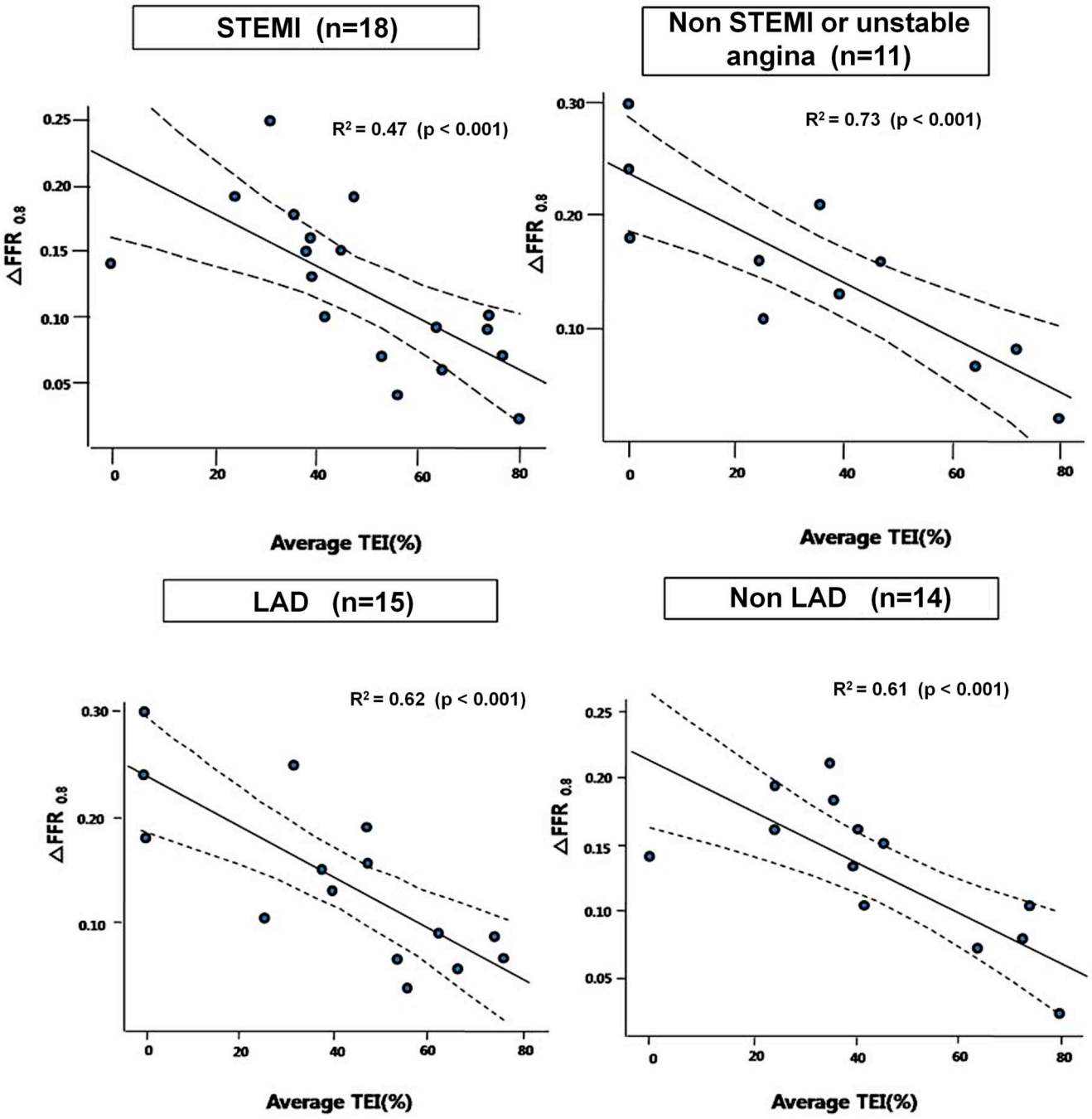

Figure 4.
The relationship between $\Delta FFR_{0.8}$ and average transmural extent of infarction (TEI) according to subgroups. In the lower right panel (non-LAD lesions), the rightmost circle represents two overlapping data points.

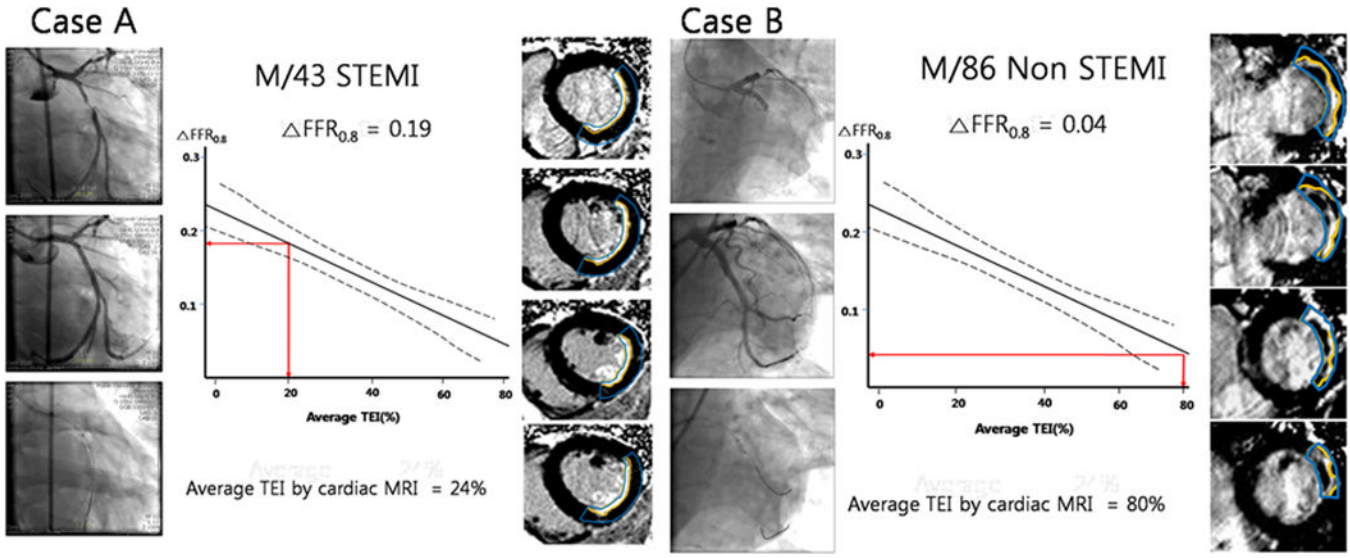

Figure 5.

Two case examples showing the relationship between $\Delta FFR_{0.8}$ and average transmural extent of infarction (TEI). In cases A and B, the left panels show representative pre-PCI coronary angiograms. The middle panels show the aggregate relationship of transmural extent of infarction to $\Delta FFR_{0.8}$, with the patient-specific findings indicated in red. The right panels show the corresponding gadolinium contrast-enhanced enhancement MR images, with the late gadolinium enhancement areas outlined in yellow and risk area outlined in blue.

Table 1

Baseline clinical and angiographic characteristics

Clinical Characteristics (n=29)	
Age	61±12
Sex, (M/F)	24/5
Coronary risk factors, n (%)	
Diabetes	6 (20)
Hypertension	9 (31)
Smoking	14 (48)
Hypercholesterolemia	5 (17)
STEMI/NSTEMI/UAP, n (%)	18 (62) / 8 (28) / 3 (10)
LV ejection fraction (%)	55±9
Time interval between PCI and MRI (days)	2.8±1.5
Angiographic Data (n=29)	
Culprit Vessel, n (%)	
LAD	15 (51)
LCx	5 (17)
RCA	9 (32)
Location of lesion, n(%)	
Proximal	15 (51)
Mid	14 (49)
Infarct related artery diameter stenosis (%)	95±6
Reference vessel size (mm)	3.27±0.30
Stent length (mm)	25.6±5.8
Thrombolysis in Myocardial Infarction flow after PCI, n (%)	
Grade 2	1 (3)
Grade 3	28 (97)
Thrombolysis in Myocardial Infarction angiographic myocardial blush grade after PCI, n (%)	
Grade 0 or 1	4 (14)
Grade 2	3 (10)
Grade 3	22 (76)

Table 2

Clinical and laboratory parameters according to ΔFFR 0.8 threshold of 0.1.

	$\Delta FFR_{0.8} > 0.1$ (n=17)	**$\Delta FFR_{0.8} \leq 0.1$ (n=12)**	***p***
Age	59±13	65±12	0.746
Sex, Male	14 (82.4)	10 (83.3)	0.671
Coronary risk factors, n			
Diabetes	4 (23.5)	2 (16.7)	0.513
Hypertension	9 (52.9)	2 (16.7)	0.053
Dyslipidemia	2 (11.8)	2 (16.7)	0.556
Smoking	8 (47.1)	6 (50)	0.587
Clinical diagnosis			0.437
STEMI / NSTEMI / UAP	9/5/3	9/3/0	
LV EF (%)	59.5±8.4	49.8±7.6	0.004 *
Peak Troponin I	36.2±58.6	121.1±106	0.024 *
Time to reperfusion time in STEMI	4.8±2.3	6.6±5.4	0.011 *
Time interval of MRI and PCI (days after PCI)	2.7±1.3	3.0±1.8	0.651
Culprit vessel, n			0.108
LAD / LCX / RCA	9/1/7	6/4/2	
Location of lesion			0.254
Proximal / Mid	8/9	8/4	
Infarct related artery diameter stenosis	0.94±0.07	0.97±0.03	0.275
Reference Vessel Size (mm)	3.32±0.30	3.20±0.31	0.560
Stent length (mm)	26.8±5.3	23.9±6.3	0.532
Thrombolysis in Myocardial Infarction flow grade before PCI, n			0.812
Grade 0/1/2/3	8/0/3/6	7/0/2/3	
Average transmural extent of infarction (TEI) by MRI (%)	27.8±17.3	66.6±11.7	<0.001 *
Microvascular obstruction by MRI (n,%)	1 (8.3%)	5 (29.4%)	0.054
Thrombolysis in Myocardial Infarction angiographic myocardial blush grade after PCI			0.037 *
Grade 0 or 1 (n, %)	0 (0)	4 (33.3)	
Grade 2 (n,%)	2 (11.8)	1 (8.3)	
Grade 3 (n,%)	15 (88.2)	7 (58.3)	

Parameters marked with an asterisk have $p<0.05$ on univariate analysis.

Table 3

A. Regression analysis of ΔFFR 0.8

		Average transmural extent of infarction (TEI)	LV ejection fraction	Late gadolinium enhancement area	Infarct segment area	Troponin I	MRI Microvascular obstruction	Time-to perfusion	LAD vs non LAD	TIMI myocardial blush score
	r^2	0.65	0.29	0.23	0.00	0.35		0.10		
Univariate analysis	*p*	<0.001	0.002	0.010	0.985	0.001	0.016	0.208	0.701	0.016
Multivariate analysis	*p*	0.005	0.380	0.099		0.344	0.964			0.922

B. Regression analysis of average transmural extent of infarction (TEI)

		Δ $FFR_{0.8}$	LV ejection fraction	Troponin I	MRI Microvascular obstruction	Time-to perfusion	LAD vs non LAD	TIMI myocardial blush score
	r^2	0.65	0.44	0.46		0.17		
Univariate analysis	*p*	<0.001	<0.001	<0.001	0.006	0.100	0.750	0.007
Multivariate analysis	*p*	0.008	0.024	0.092	0.774			0.932