JACC: CARDIOVASCULAR IMAGING VOL. 2, NO. 4, 2009

ISSN 1936-878X/09/$36.00
PUBLISHED BY ELSEVIER INC. DOI:10.1016/j.jcmg.2008.12.020

Impact of Plaque Composition on Cardiac Troponin Elevation After Percutaneous Coronary Intervention

An Ultrasound Analysis

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OBJECTIVES We used virtual histology–intravascular ultrasound (VH-IVUS) to study the relationship between pre-percutaneous coronary intervention (PCI) coronary plaque characteristics and post-PCI cardiac troponin I (cTnI) elevation.

BACKGROUND Percutaneous coronary intervention is often complicated by post-procedural myocardial necrosis as manifested by elevated cardiac markers.

METHODS Eighty consecutive patients (29 stable and 51 unstable angina) with normal pre-PCI cTnI levels were imaged before PCI using VH-IVUS. Patients were divided into 2 groups according to the presence (Group I, n = 38) or absence (Group II, n = 42) of post-PCI cTnI elevation ≥3× the upper limit of normal (0.08 ng/ml).

RESULTS The absolute and percent necrotic core volumes were significantly greater in Group I than in Group II (13.6 ± 6.4 mm^3 vs. 7.9 ± 4.4 mm^3, $p < 0.001$, and 19.8 ± 10.4% vs. 12.8 ± 8.4%, $p = 0.015$, respectively). The absolute and percent necrotic core areas were significantly greater in Group I than in Group II at the minimum lumen site (1.70 ± 0.91 mm^2 vs. 0.61 ± 0.39 mm^2, $p < 0.001$, and 22.9 ± 11.7% vs. 10.4 ± 6.6%, $p < 0.001$, respectively) and at the largest necrotic core site (2.00 ± 0.86 mm^2 vs. 0.81 ± 0.78 mm^2, $p < 0.001$, and 24.0 ± 11.7% vs. 12.9 ± 6.6%, $p < 0.001$, respectively). The ΔcTnI correlated with: 1) absolute and percent necrotic core area at the minimum lumen site and at the largest necrotic core site; 2) absolute necrotic core volume; 3) percent fibrofatty area at the minimum lumen site; and 4) lesion site plaque burden. In the multivariate analysis, absolute necrotic core area at the minimum lumen site was the only independent predictor of post-PCI cTnI elevation ≥3× the upper limit of normal (odds ratio: 1.318; 95% confidence interval: 1.090 to 1.594, $p = 0.004$).

CONCLUSIONS The VH-IVUS analysis shows that post-PCI cTnI elevation occurs in lesions with a large necrotic core area. The VH-IVUS may play an important role in detecting which lesions are high risks for myocardial necrosis after PCI. (J Am Coll Cardiol Img 2009;2:458–68) © 2009 by the American College of Cardiology Foundation

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Manuscript received June 13, 2008; revised manuscript received December 2, 2008, accepted December 19, 2008.

Cardiac troponin I (cTnI) is a sensitive and specific marker for detecting subtle degrees of myocardial damage (1–3). Elevated hospital admission troponin levels are associated with increased cardiac events in patients presenting with acute coronary syndromes (4–11). Percutaneous coronary intervention (PCI) may be complicated by myocardial necrosis as manifested by troponin elevation (12–17). In patients with normal admission cTnI levels, post-PCI cTnI elevation has been associated with increased short-term and mid-term cardiac events (16–18).

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Intravascular ultrasound (IVUS) is widely used to assess coronary artery morphometry. However, grayscale IVUS has significant limitations in assessing plaque composition (19,20). Spectral analysis of IVUS radiofrequency data (virtual histology [VH]-IVUS) may provide quantitative information on plaque composition; it has been validated in studies of explanted human coronary segments (21). A VH-IVUS characterizes atherosclerotic plaque as fibrotic, fibrofatty, dense calcium, and necrotic core (21,22).

So far, no studies have shown a relationship between plaque composition and post-PCI biomarker levels. Therefore, the purpose of the present study was to investigate the impact of pre-PCI coronary plaque compositions, as determined by VH-IVUS, on post-PCI cTnI elevation.

METHODS

Patient population. From our catheterization laboratory database, we retrospectively identified 80 patients (29 with stable angina and 51 with unstable angina) without cTnI elevation at admission who underwent pre-PCI VH-IVUS of a single, native, de novo coronary lesion. We excluded patients with acute ST-segment elevation myocardial infarction within 72 h, or elevated baseline pre-PCI cTnI, or patients who were treated with atheroablative devices or with poor-quality VH-IVUS. Overall, 90% of the patients received aspirin, and all patients received clopidogrel before PCI. Patients with acute myocardial infarction on admission, patients with multivessel or multilesion PCI, and patients who were treated with atheroablative or distal protection devices were excluded from this study. The protocol was approved by the institutional review board. Hospital records of patients were reviewed to obtain information on clinical demographics.

cTnI analysis. Venous blood samples were obtained within 1 h before PCI and within 24 h after PCI. The blood samples were centrifuged, and serum was removed and stored at −70°C until the assay could be performed. The cTnI levels were measured by a paramagnetic particle, chemiluminescent immunoenzymatic assay (Beckman Coulter Inc., Fullerton, California). The manufacturer's suggested upper normal cutoff value was 0.08 ng/ml. After PCI, there were 32 patients with no cTnI elevation, 7 patients with cTnI elevation <2× the upper limit of normal, 3 patients with cTnI elevation <3× the upper limit of normal, and 38 patients with cTnI elevation >3× the upper limit of normal. Patients were divided into 2 groups: post-PCI cTnI >3× the upper limit of normal (Group I) versus post-PCI cTnI <3× the upper limit of normal (Group II).

Quantitative coronary angiography (QCA) analysis. Quantitative analysis (CAAS II, Pie Medical, Maastricht, the Netherlands) was performed using standard protocols (23). With the outer diameter of the contrast-filled catheter as the calibration standard, the minimal lumen diameter, reference diameter, and lesion length were measured in diastolic frames from orthogonal projections. Films were recorded at 30 frames/s. The frame count was measured with a frame-counting cine viewer. Corrected Thrombolysis In Myocardial Infarction (TIMI) frame count was estimated as previously reported (24,25).

ABBREVIATIONS AND ACRONYMS

CSA = cross-sectional area
cTnI = cardiac troponin I
EEM = external elastic membrane
PCI = percutaneous coronary intervention
VH-IVUS = virtual histology–intravascular ultrasound

IVUS imaging and analysis. All pre-PCI VH-IVUS examinations were performed after intracoronary administration of 200 μg nitroglycerin. A 2-MHz, 2.9-F IVUS imaging catheter (Eagle Eye, Volcano Corp., Rancho Cordova, California) was advanced >10 mm beyond the lesion, and automated pullback was performed to a point >10 mm proximal to the lesion at a speed of 0.5 mm/s.

Quantitative volumetric grayscale and VH-IVUS analysis was performed across the entire lesion segment, and cross-sectional analysis was performed at the minimum lumen site and at the largest necrotic core site. Conventional quantitative volumetric grayscale IVUS analysis was performed according to the American College of Cardiology Clinical Expert Consensus Document on Standards for Acquisition, Measurement, and Reporting of Intravascular Ultrasound Studies (26). External elastic membrane (EEM) and lumen cross-sectional areas (CSAs) were measured. Plaque plus media CSA was calculated as EEM minus lumen CSA, and plaque burden was

Table 1. Baseline Characteristics According to the Presence/Absence of Post-PCI cTnI Elevation ≥3× the Upper Limit of Normal

	Group I (cTnI Elevation ≥3×) (n = 38)	Group II (cTnI Elevation <3×) (n = 42)	p Value
Age (yrs)	63 ± 13	65 ± 11	0.4
Male gender, n (%)	29 (76)	20 (48)	0.009
Clinical presentation, n (%)			0.4
Stable angina	12 (32)	17 (41)	
Unstable angina	26 (68)	25 (60)	
Diabetes mellitus, n (%)	12 (32)	10 (24)	0.4
Hypertension, n (%)	28 (74)	27 (64)	0.4
Smoking, n (%)	15 (40)	18 (43)	0.8
Pre-PCI aspirin use, n (%)	33 (89)	39 (93)	0.4
Pre-PCI clopidogrel use, n (%)	38 (100)	42 (100)	1.0
Clopidogrel loading, n (%)			0.012
None	7 (18)	1 (2)	
300 mg	12 (32)	8 (19)	
600 mg	19 (50)	33 (79)	
Bivalirudin use, n (%)	35 (92)	37 (88)	0.6
Glycoprotein IIb/IIIa inhibitor use, n (%)	4 (11)	6 (14)	0.6
Ejection fraction (%)	59 ± 6	59 ± 8	0.8
Total cholesterol (mg/dl)	178 ± 51	156 ± 40	0.041
Triglyceride (mg/dl)	123 ± 63	116 ± 60	0.6
LDL cholesterol (mg/dl)	107 ± 48	88 ± 34	0.063
HDL cholesterol (mg/dl)	46 ± 11	44 ± 11	0.3

Data are presented as the n (%) of patients or mean ± SD.
cTnI = cardiac troponin I; HDL = high-density lipoprotein; LDL = low-density lipoprotein; PCI = percutaneous coronary intervention.

calculated as plaque plus media divided by EEM CSA. Proximal and distal references were the single slices with the largest lumen and smallest plaque burden within 10 mm proximally and distally, but before any large side branch. Coronary artery remodeling was assessed by comparing the lesion site to the reference segment EEM CSA. Positive remodeling was defined as a remodeling index (lesion site EEM CSA divided by the average of the proximal and distal reference segment EEM CSA) >1.05, intermediate remodeling as a remodeling index between 0.95 and 1.05, and negative remodeling as a remodeling index <0.95 (27). The VH-IVUS analysis classified and color-coded tissue into 4 major components: green (fibrotic), yellow-green (fibrofatty), white (dense calcium), and red (necrotic core) (21,22). The VH-IVUS analysis was reported in absolute amounts and as a percentage of plaque area or volume.

Statistical analysis. Statistical analysis was performed using SAS version 9.1 (SAS Institute Inc., Cary, North Carolina). Continuous variables were presented as the mean ± 1 SD; comparisons were conducted by Student *t* test or nonparametric Wilcoxon test if normality assumption was violated. Discrete variables were presented as percentages and relative frequencies; comparisons were conducted by chi-square statistics or Fisher exact test as appropriate. A Spearman correlation coefficient was used if the normality assumption was not satisfied. Multivariate logistic regression analysis was performed to identify independent predictors of post-PCI cTnI elevation >3× the upper limit of normal. Univariate analyses were first conducted to identify potential risk factors for post-PCI cTnI elevation >3× the upper limit of normal. The likelihood ratio test was used, and the variables with a value of $p < 0.2$ were included in the multivariate model. Finally, a step-down logistic regression was performed, with post-PCI cTnI elevation >3× the upper limit of normal and the covariates that remained significant in the previous analysis. The least significant variable was dropped at each step until only covariates with a value of $p < 0.05$ remained. Receiver-operator characteristics were generated from multiple sensitivity/specificity pairs. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics and angiographic and procedural results. The baseline characteristics are summarized in Table 1. There was a male predomi-

Table 2. Coronary Angiographic Findings and Procedural Results According to the Presence/Absence of Post-PCI cTnI Elevation ≥3× the Upper Limit of Normal

	Group I (cTnI Elevation ≥3×) (n = 38)	Group II (cTnI Elevation <3×) (n = 42)	p Value
Target vessel, n (%)			0.14
LAD	22 (58)	22 (52)	
LCX	7 (18)	3 (7)	
RCA	9 (23)	17 (41)	
Lesion location, n (%)			0.9
Ostium	3 (8)	2 (5)	
Proximal	11 (29)	12 (29)	
Middle	21 (55)	23 (55)	
Distal	3 (8)	5 (12)	
Pre-PCI TIMI flow grade 3	38 (100)	42 (100)	1.0
Bifurcation lesions, n (%)	12 (32)	10 (24)	0.4
Stent type, n (%)			0.4
Sirolimus-eluting stent	23 (61)	31 (74)	
Paclitaxel-eluting stent	10 (26)	7 (17)	
Bare-metal stent	5 (13)	4 (10)	
Stent diameter (mm)	3.22 ± 0.37	3.18 ± 0.42	0.7
Stent length (mm)	24 ± 10	22 ± 6	0.4
Reference diameter (mm)	3.34 ± 0.85	3.30 ± 0.75	0.3
Pre-MLD (mm)	1.04 ± 0.67	1.10 ± 0.53	0.2
Post-MLD (mm)	3.17 ± 0.66	3.12 ± 0.70	0.3
Lesion length (mm)	16 ± 8	14 ± 5	0.2
Side branch occlusion, n (%)	4 (11)	2 (5)	0.4
Post-PCI TIMI flow grade 0/1	4 (11)	0 (0)	0.047
Post-PCI corrected TIMI frame count	24 ± 10	20 ± 7	0.042

Data are presented as the n (%) of patients or mean ± SD.
LAD = left anterior descending artery; LCX = left circumflex artery; MLD = minimal lumen diameter; RCA = right coronary artery; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Table 1.

nance and higher total cholesterol level in Group I compared with Group II. Although there were no significant differences in the pre-PCI use of aspirin and clopidogrel between the 2 groups, more Group II patients received clopidogrel loading compared with Group I; and a higher loading dose of clopidogrel was used in Group II compared with Group I.

Angiographic findings and procedural results are summarized in Table 2. All lesions were treated with stent implantation: 54 lesions with sirolimus-eluting stents, 17 lesions with paclitaxel-eluting stents, and 9 lesions with bare-metal stents. There was no significant difference in the incidence of bifurcation lesion between both groups (11% in Group I vs. 5% in Group II, p = 0.4). Post-PCI TIMI flow grade 0/1 was observed more frequently in Group I compared with Group II (11% vs. 0%, p = 0.047), and post-PCI corrected TIMI frame count was significantly higher in Group I compared with Group II (24 ± 10 vs. 20 ± 7, p = 0.042). There was no edge dissection, which needs additional stent implantation, in both groups and there was no significant difference in the incidence of side branch occlusion between the 2 (post-PCI cTnI) groups.

Conventional IVUS and VH-IVUS results. An example of VH-IVUS is shown in Figure 1. Conventional IVUS findings are summarized in Table 3. There were strong trends for a smaller minimum lumen area and a larger plaque burden at the minimum lumen site and at the largest necrotic core site in Group I compared with Group II. Positive remodeling was more common and the remodeling index was significantly higher in Group I than in Group II.

The absolute and percent necrotic core volumes were significantly greater in Group I (those with significant increases in cTnI) than in Group II; conversely absolute and percent fibrofatty plaque volume were significantly smaller in Group I than in Group II (Fig. 2). The absolute and percent necrotic core areas were significantly greater in Group I than in Group II both at the

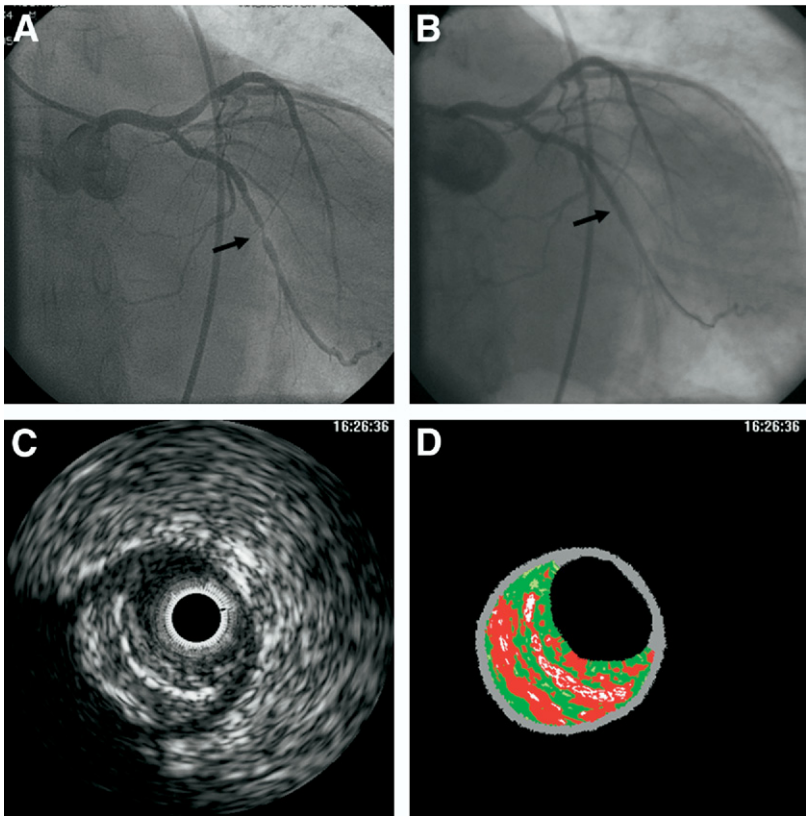

Figure 1. Pre-Interventional Imaging With Virtual Histology

(A) Pre-percutaneous coronary intervention (PCI) coronary angiogram (arrow indicates significant stenosis); **(B)** coronary angiogram after stent implantation (**arrow** indicates no residual stenosis); **(C)** pre-PCI grayscale intravascular ultrasound; and **(D)** pre-PCI virtual histology-intravascular ultrasound in the middle portion of the left circumflex artery.

minimum lumen site and at the largest necrotic core site. Absolute fibrotic area was significantly greater in Group I than in Group II at the minimum lumen site, and percent fibrofatty area was significantly smaller in Group I than in Group II at the minimum lumen site and at the largest necrotic core site (Fig. 3).

Correlations between ΔcTnI level and grayscale and VH-IVUS parameters. The ΔcTnI level correlated with: 1) absolute necrotic core area ($r = 0.419$, $p < 0.001$) and percent necrotic core area ($r = 0.310$, $p = 0.005$) at the minimum lumen site; 2) absolute necrotic core area ($r = 0.336$, $p = 0.002$) and percent necrotic core area ($r = 0.238$, $p = 0.034$) at the largest necrotic core site; 3) absolute necrotic core volume ($r = 0.347$, $p = 0.002$); 4) percent fibrofatty area at the minimum lumen site ($r = -0.270$, $p = 0.015$); and 5) lesion site plaque burden ($r = 0.248$, $p = 0.027$) (Fig. 4). There were no correlations between ΔcTnI level versus the other grayscale or VH-IVUS parameters.

Independent predictors of post-PCI cTnI elevation. Multiple logistic regression analysis was performed to determine independent predictors of post-PCI cTnI elevation >3× the upper limit of normal. All variables with $p < 0.2$ in univariate analysis were tested. Absolute necrotic core area at the minimum lumen site was the only independent predictor of post-PCI cTnI elevation >3× upper limit of normal (odds ratio: 1.318; 95% confidence interval: 1.090 to 1.594, $p = 0.004$). The area under the receiver-operator characteristic curve for absolute necrotic core area at the minimum lumen site predicting post-PCI cTnI elevation >3× upper limit of normal was 0.914 (Fig. 5).

DISCUSSION

The present VH-IVUS study showed a direct relationship between pre-PCI plaque composition and post-PCI myonecrosis. In particular, post-PCI

Table 3. Grayscale IVUS Findings According to the Presence/Absence of Post-PCI cTnI Elevation ≥3× the Upper Limit of Normal

	Group I (cTnI Elevation ≥3×) (n = 38)	Group II (cTnI Elevation <3×) (n = 42)	p Value
Reference			
EEM CSA (mm^2)	15.8 ± 4.7	15.4 ± 5.0	0.7
Lumen CSA (mm^2)	9.2 ± 3.0	9.2 ± 3.2	1.0
P&M CSA (mm^2)	6.6 ± 2.8	6.2 ± 2.6	0.6
Plaque burden (%)	41 ± 10	40 ± 9	0.6
Minimum lumen site			
EEM CSA (mm^2)	16.2 ± 4.4	15.2 ± 5.0	0.3
Lumen CSA (mm^2)	3.7 ± 0.8	4.0 ± 0.9	0.051
P&M CSA (mm^2)	12.5 ± 4.4	11.2 ± 4.4	0.19
Plaque burden (%)	77 ± 8	74 ± 7	0.065
Lesion length (mm)	18 ± 9	16 ± 7	0.4
Largest necrotic core site			
EEM CSA (mm^2)	16.4 ± 4.2	16.0 ± 5.0	0.7
Lumen CSA (mm^2)	4.8 ± 1.9	5.1 ± 2.2	0.068
P&M CSA (mm^2)	11.6 ± 3.5	10.9 ± 3.9	0.19
Plaque burden (%)	71 ± 9	68 ± 9	0.079
Volumetric analysis (mm^3)			
EEM volume	170.0 ± 102.8	160.7 ± 97.6	0.4
Lumen volume	59.8 ± 24.8	60.8 ± 22.3	0.8
P&M volume	110.2 ± 55.1	99.9 ± 48.5	0.3
Remodeling pattern, n (%)			0.046
Positive remodeling	20 (53)	11 (26)	
Intermediate remodeling	9 (24)	18 (43)	
Negative remodeling	9 (24)	13 (31)	
Remodeling index	1.03 ± 0.15	0.99 ± 0.12	0.038

Data are presented as the n (%) of patients or mean ± SD.
CSA = cross-sectional area; EEM = external elastic membrane; IVUS = intravascular ultrasound; P&M = plaque plus media; other abbreviations as in Table 1.

cTnI elevation >3× normal was predicted by a larger necrotic core area at the minimum lumen site.

The marker cTnI is sensitive and specific for detecting subtle myocardial damage (1–3). In patients with non–ST-segment elevation acute coronary syndrome, increased pre-PCI cTnI and cardiac troponin T levels have been associated with increased short-term and intermediate-term cardiac events (4–11). Post-PCI cTnI elevation has been associated with increased short-term and intermediate-term adverse cardiac events in patients without elevation of pre-PCI cTnI levels (16–18). The pathophysiology of myocardial necrosis during PCI has been related to development of no-reflow, side branch occlusion, abrupt vessel closure, and atherothrombotic or platelet embolization (28–30). Kotani et al. (31) reported that no-reflow during PCI in patients with acute coronary syndromes is attributable not just to the thrombus burden, but also to plaque components of the atheromatous lesions. They concluded that no-reflow may be caused by "gruel" embolized from an atheroma attributable to mechanical plaque disruption during intervention, suggesting that pre-PCI plaque composition may have an impact on myonecrosis during intervention.

However, there are few published data regarding the relationship between pre-PCI lesion subsets and post-PCI biomarker levels. Kini et al. (32) reported that pre-PCI angiographic predictors of creatine kinase-MB elevation were diffuse coronary disease, type C lesion according to the American College of Cardiology/American Heart Association classification, and multivessel disease. Fujii et al. (33) compared creatine kinase-MB release after stent implantation in 62 patients with IVUS-detected ruptured plaques with 62 matched control patients; patients with ruptured plaques had higher creatine kinase-MB release rates than control patients, and independent predictors of post-PCI creatine kinase-MB elevation were presence of ruptured plaque and unstable angina. Prati et al. (34) reported that a marked post-stenting reduction in plaque volume, which was significantly greater in

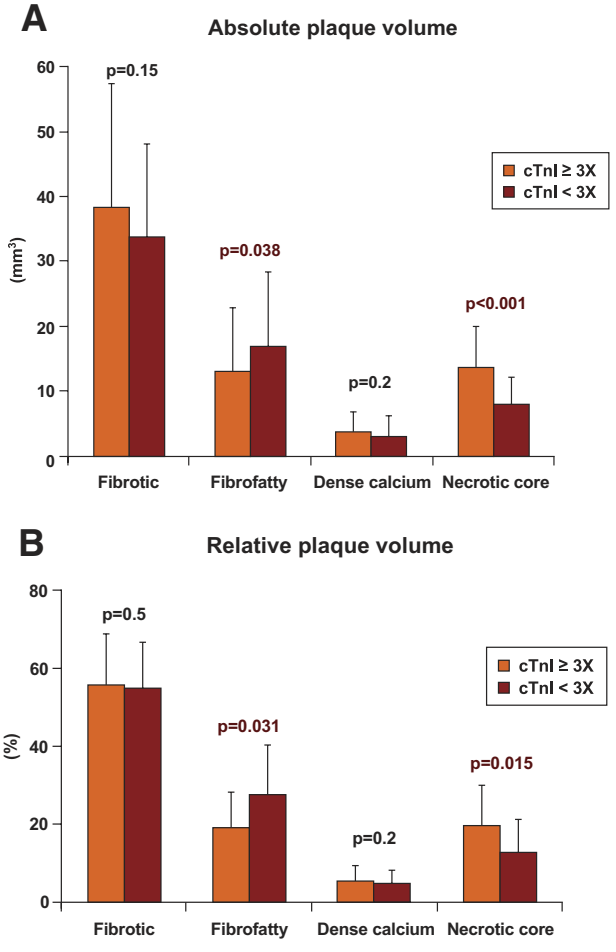

Figure 2. Volumetric Virtual Histology Plaque Component Analysis

Volumetric virtual histology plaque component analysis according to the presence or absence of post-percutaneous coronary intervention cardiac troponin I (cTnI) elevation ≥3× normal. Results are shown for **(A)** absolute and **(B)** relative quantifications. The absolute and percent necrotic core volume was significantly greater (13.6 ± 6.4 mm^3 vs. 7.9 ± 4.4 mm^3, 19.8 ± 10.4% vs. 12.8 ± 8.4%); conversely absolute and percent fibrofatty plaque volume was significantly smaller (13.1 ± 9.9 mm^3 vs. 16.9 ± 11.6 mm^3, 19.0 ± 9.3% vs. 27.5 ± 13.0%) in patients with cTnI elevation ≥3× the upper limit of normal.

unstable angina lesions than in stable angina lesions, was associated with post-procedural creatine kinase-MB release. Mehran et al. (35) studied 2,256 consecutive patients who underwent PCI of 2,780 native coronary lesions and had pre-PCI IVUS imaging; both a greater lesion and reference segment plaque burden were associated with post-PCI creatine kinase-MB elevation.

Recently, several studies have shown the relationship between VH-IVUS findings and post-PCI distal embolization (36,37). Kawaguchi et al. (36) investigated high-risk plaque of distal embolization after stent deployment in patients with acute ST-segment elevation myocardial infarction with VH-IVUS, and they showed that necrotic core volume clearly predicted ST-segment re-elevation, which was used to evaluate distal embolization in this study after stent deployment as compared with fibrous, fibro-lipid, dense calcium, and total plaque volumes. Kawamoto et al. (37) investigated the relationship between coronary plaque components and small embolic particles during stenting and examined the influence on the coronary microcirculation using VH-IVUS, and they showed that the necrotic core component identified with VH-IVUS was related to liberation of small embolic particles during coronary stenting, which resulted in the poorer recovery of coronary flow velocity reserve.

In the present study, post-PCI myocardial injury occurred in lesions with a large necrotic core area [this result is consistent with previous VH-IVUS studies by Kawaguchi et al. (36) and by Kawamoto et al. (37)], especially in lesions with a large absolute necrotic core area at the minimum lumen site. The derived effect size (using the Cohen *d* approximation) of the difference in absolute necrotic core area at the minimum lumen site between the 2 (post-PCI cTnI) groups would equal 1.71 (95% confidence interval: 1.42 to 1.83). Different people offer different advice regarding how to interpret the resultant effect size, but the most accepted opinion is that of Cohen, in which 0.2 is indicative of a small effect, 0.5 a medium, and 0.8 a large effect. Therefore, this effect size of 1.71 in the present study is very large and suggests that there is a consistent difference in the absolute necrotic core area at the minimum lumen site, on average, between the 2 (post-PCI cTnI) groups.

Selvanayagam et al. (38) showed 2 types of myocardial injury after PCI using magnetic resonance imaging. They investigated the quantitative relationship between irreversible injury and cTnI release, and they showed that patients demonstrating post-procedural elevation in cTnI have evidence of new irreversible myocardial injury on delayed-enhancement magnetic resonance imaging and the magnitude of this injury correlates directly with the extent of cTnI elevation. They indicated that there are 2 distinct sites of new hyperenhancement; the majority of patients showed new irreversible injury in a previously normal area in the apical myocardium, which likely represents new myocardial necrosis resulting from distal embolization of particulate matter during balloon inflation and stenting, and in the remaining patients with new hyperenhancement, it was located in the basal or mid-ventricular myocardium, adjacent to the inserted stent, which might be attributable to side branch

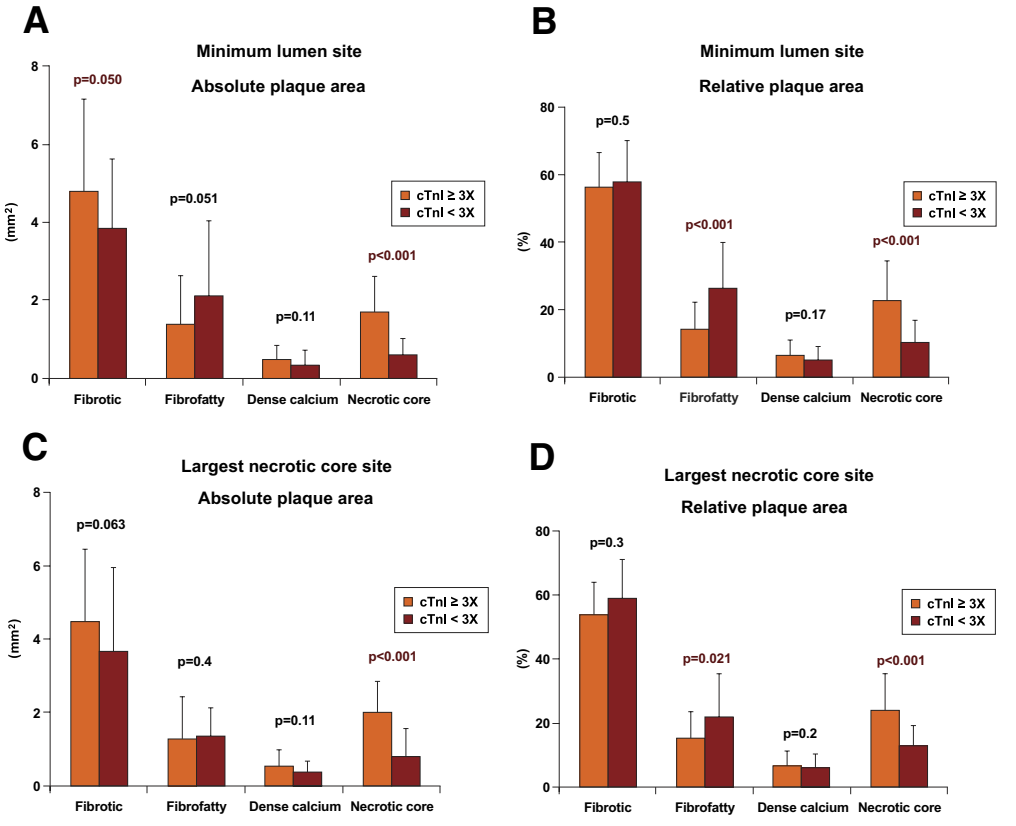

Figure 3. Cross-Sectional Virtual Histology Plaque Component Analysis

Cross-sectional virtual histology plaque component analysis at the minimum lumen site **(A, B)** and at the largest necrotic core site **(C, D)** according to the presence or absence of post-percutaneous coronary intervention cTnI elevation ≥3× the upper limit of normal. Results are shown for **(A, C)** absolute and **(B, D)** relative quantifications. At the minimum lumen site, **(A)** the absolute necrotic core and fibrotic area were significantly greater (1.70 ± 0.91 mm^2 vs. 0.61 ± 0.39 mm^2, 4.79 ± 2.39 mm^2 vs. 3.84 ± 1.80 mm^2); **(B)** percent necrotic core area was significantly greater (22.9 ± 11.7% vs. 10.4 ± 6.6%), and percent fibrofatty area was significantly smaller (14.2 ± 8.3% vs. 26.5 ± 13.6%) in patients with cTnI elevation ≥3× normal. At the largest necrotic core site, **(C)** absolute necrotic core area was significantly greater (2.00 ± 0.86 mm^2 vs. 0.81 ± 0.78 mm^2); **(D)** percent necrotic core area was significantly greater (24.0 ± 11.7% vs. 12.9 ± 6.6%), and percent fibrofatty area was significantly smaller (15.4 ± 8.3% vs. 22.0 ± 13.6%) in patients with cTnI elevation ≥3× the upper limit of normal. Abbreviations as in Figure 2.

flow impairment/occlusion. In the present study, post-PCI TIMI flow grade 0/1 was observed more frequently and post-PCI corrected TIMI frame count was significantly higher in patients with post-PCI cTnI elevation; however, there was no difference in the incidence of side branch occlusion between the 2 (post-PCI cTnI) groups.

In the present study, there was also a strong relationship between a larger lesion site plaque burden and post-PCI cTnI elevation. However, the lesion site plaque burden was not an independent predictor of post-PCI cTnI elevation once plaque composition was considered. The size of the necrotic core may be the link between plaque burden and post-PCI myonecrosis. In fact, in the current analysis, the absolute necrotic core area correlated with the plaque burden at the minimum lumen site ($r = 0.286$, $p = 0.010$).

Kotani et al. (31) compared the aspirated materials between the lesions with no-reflow to those without no-reflow using a thrombectomy device. In their study, all aspirates after PCI contained platelet aggregates or fibrin–platelet complexes, suggesting that glycoprotein IIb/IIIa inhibitors may attenuate the complications during PCI for acute coronary syndrome patients. Therefore, if a large necrotic core at the minimum lumen site is observed before PCI, one may consider using glycoprotein IIb/IIIa inhibitors during PCI to potentially reduce the post-PCI myocardial injury.

Study limitations. First, this study is based on a small number of patients, raising the possibility

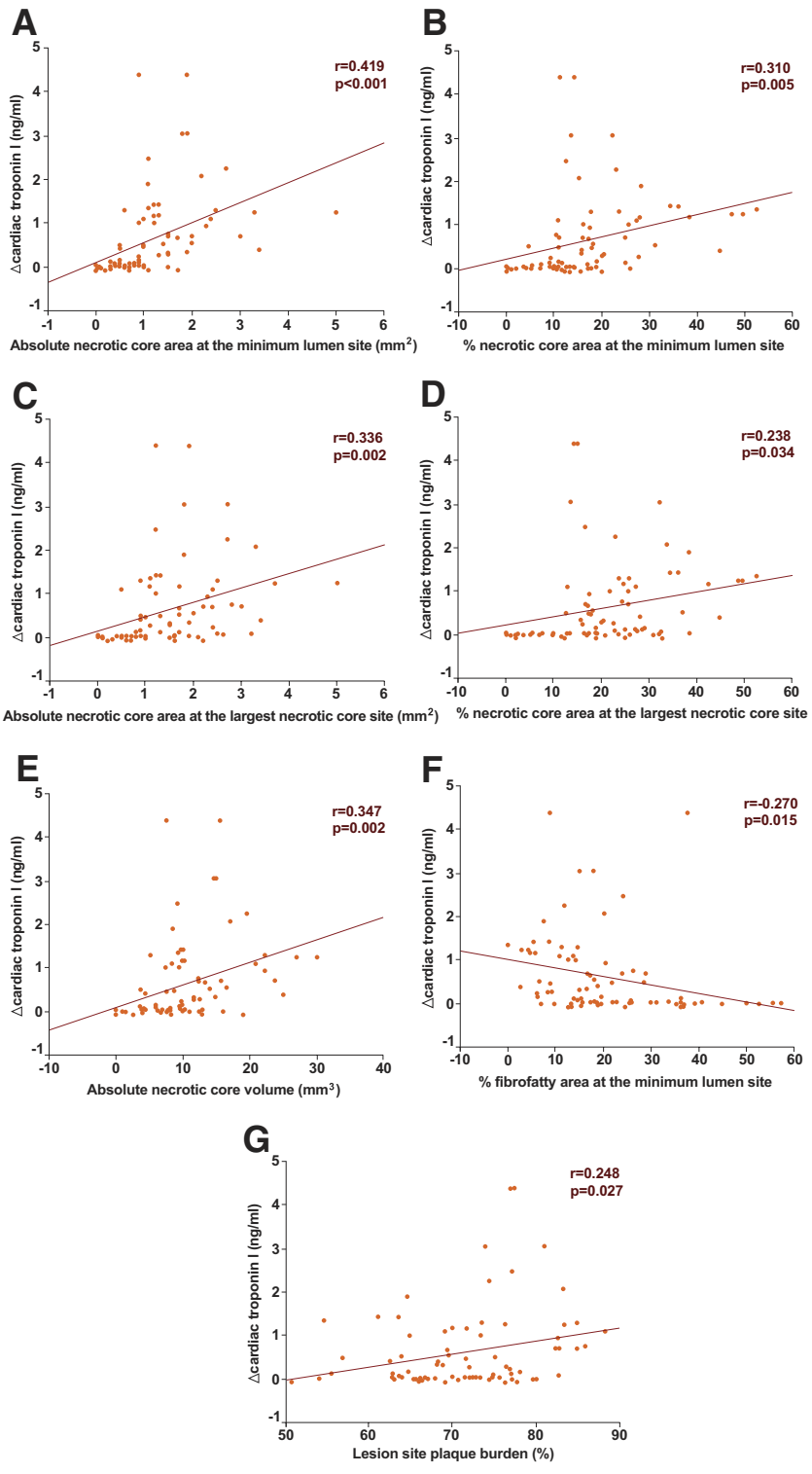

Figure 4. Correlations to Cardiac Troponin Level

Correlations of Δcardiac troponin I level and **(A)** absolute necrotic core area at the minimum lumen site, **(B)** percent necrotic core area at the minimum lumen site, **(C)** absolute necrotic core area at the largest necrotic core site, **(D)** percent necrotic core area at the largest necrotic core site, **(E)** absolute necrotic core volume, **(F)** percent fibrofatty area at the minimum lumen site, and **(G)** lesion site plaque burden.

of selection bias. Second, this was a retrospective single-center study. The results of this study should be verified by further prospective investigation. Third, although patients with post-PCI cTnI elevation received lower use of the high loading dose of clopidogrel, the fact remains that a higher dose of clopidogrel loading was not a significant predictor of post-PCI cTnI elevation by multivariate analysis. This is inconsistent with the results of the ARMYDA-2 (Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty) study (39), which showed that pre-treatment with a 600-mg loading dose of clopidogrel 4 to 8 h before the procedure was safe and, as compared with the conventional 300-mg dose, significantly reduced periprocedural myocardial infarction in patients undergoing PCI. The difference between the results of the ARMYDA study and those of the present study may be attributable to the possible selection bias and the small study size in the present study. Fourth, the cTnI level was not measured serially after stent implantation, and we did not measure the cTnI level at the same time after stent implantation in all patients. Fifth, we did not attempt to differentiate between atherosclerotic plaque and thrombus because VH-IVUS could not determine the presence of thrombus.

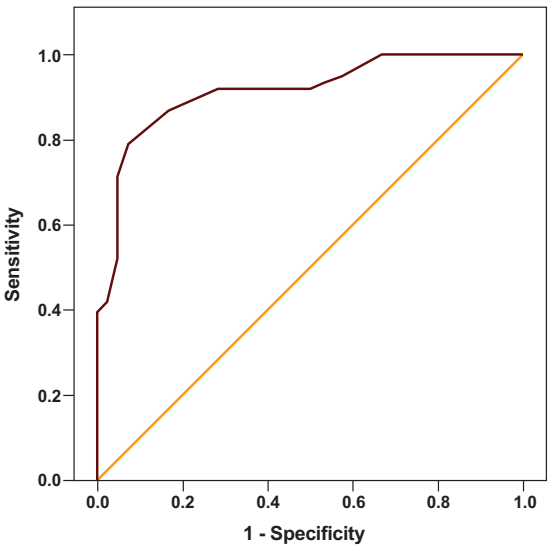

Figure 5. Receiver-Operator Characteristic Curve for Necrotic Core Area Predicting Troponin Level

Receiver-operator characteristic curves for absolute necrotic core area at the minimum lumen site predicting post-PCI cTnI elevation >3× the upper limit of normal. The area under the receiver-operator characteristic curve for absolute necrotic core area at the minimum lumen site predicting post-PCI cTnI elevation >3× the upper limit of normal was 0.914. Abbreviations as in Figures 1 and 2.

CONCLUSIONS

The present VH-IVUS study showed that post-PCI cTnI elevation occurred in lesions with a larger necrotic core. The VH-IVUS analysis may be a useful modality for detecting lesions at risk for myocardial necrosis during PCI.

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Key Words: coronary disease ■ troponin ■ stents ■ plaque ■ intravascular ultrasound.