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Relationship of Thrombus Characteristics to the Incidence of Angiographically Visible Distal Embolization in Patients With ST-Segment Elevation Myocardial Infarction Treated With Thrombus Aspiration

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Objectives This study sought to investigate the association between pathological characteristics of aspirated intracoronary thrombi and the incidence of angiographically visible distal embolization (AVDE) during primary percutaneous coronary intervention (p-PCI) in patients with ST-segment elevation myocardial infarction (STEMI) treated with thrombus aspiration.

Background AVDE of atherosclerotic and thrombotic material has been shown to impair myocardial perfusion and contribute to poor clinical outcome in patients with STEMI. Recent studies have shown that thrombus composition and size are associated with the incidence of AVDE.

Methods Aspirated thrombi from 164 STEMI patients within 12 h of symptom onset were investigated immunohistochemically using antibodies against platelets, erythrocytes, and inflammatory cells.

Results The angiographic results showed that AVDE during p-PCI occurred in 22 (13.4%) patients. Pathological analysis revealed that thrombi from patients with AVDE had a greater erythrocyte-positive area (60 ± 15% vs. 43 ± 21%, $p < 0.0005$) and more myeloperoxidase-positive cells (943 ± 324 cells/mm^2 vs. 592 ± 419 cells/mm^2, $p < 0.0005$) than those from patients without AVDE. Thrombus size, quantified as the thrombus surface area, was positively correlated with the erythrocyte component ($r = 0.362$, $p < 0.0001$). Moreover, multivariate logistic analysis demonstrated that erythrocyte-positive area in the thrombi, glucose levels on admission, larger vessel diameter (≥3.5 mm), and pre-balloon dilation were independent predictors of the incidence of AVDE.

Conclusions This study demonstrated that the erythrocyte-rich component of aspirated thrombi may be associated with the incidence of AVDE during p-PCI in patients with STEMI. (J Am Coll Cardiol Intv 2013;6:377–85) © 2013 by the American College of Cardiology Foundation

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Primary percutaneous coronary intervention (p-PCI) has significantly improved myocardial perfusion and survival after acute ST-segment elevation myocardial infarction (STEMI). However, despite the recent technical and mechanical improvements in percutaneous coronary intervention (PCI), a substantial number of STEMI patients treated with PCI show inadequate perfusion of the infarcted myocardium (1,2). During PCI, embolization of atherosclerotic and thrombotic material often occurs and can be visible on the coronary angiogram as a distal filling defect with abrupt cutoff in the distal vessel of the culprit lesion. This angiographically visible distal embolization (AVDE) of thrombus and plaque debris was found in 6% to 18% of patients with STEMI treated with PCI and was one of the major complications that could be closely associated with impairment of myocardial perfusion and poor clinical outcome (1–4).

Abbreviations and Acronyms

AVDE = angiographically visible distal embolization
CPK = creatine phosphokinase
DM = diabetes mellitus
GP = glycoprotein
IRA = infarct-related artery
MPO = myeloperoxidase
PCI = percutaneous coronary intervention
p-PCI = primary percutaneous coronary intervention
STEMI = ST-segment elevation myocardial infarction
TIMI = Thrombolysis In Myocardial Infarction

Previous studies have demonstrated that plaque volume and composition, especially necrotic core volume, is associated with AVDE in patients with STEMI (5). Moreover, the presence of an intracoronary thrombus at the lesion site has been shown to provide an increased risk of distal embolization (3,4). In fact, recent studies using thrombectomy or distal protection devices have demonstrated that the use of these devices significantly reduced the incidence of distal embolization and improved myocardial perfusion (2,6,7) and clinical outcome (8). A coronary thrombus consists mainly of platelets, erythrocytes, and fibrin, and often contains inflammatory cells. A recent study showed that thrombus composition and size were associated with AVDE after PCI, and the thrombi aspirated in patients with distal embolization were larger and contained more erythrocytes than thrombi aspirated in patients without distal embolization (4). Moreover, our recent study demonstrated that erythrocyte-rich thrombi were associated with poor myocardial perfusion, as assessed by ST-segment resolution and myocardial blush grade, after PCI in patients with STEMI (9). However, few data are available in detail on pathological characteristics of aspirated intracoronary thrombi in STEMI patients with and without AVDE.

Accordingly, the aim of the present study was to determine the association between pathological characteristics of aspirated intracoronary thrombi and the incidence of AVDE in patients with STEMI treated with thrombus aspiration. This study was a substudy of our previous report using aspirated intracoronary thrombi in STEMI patients (9).

Methods

Study patients. Between January 2004 and December 2008, 310 STEMI patients were admitted to our hospital, and of those, the study included 249 consecutive STEMI patients within 12 h of symptom onset who had undergone thrombus aspiration for de novo lesions. Sixty-one patients were excluded because 55 patients had symptoms for ≥12 h and/or had not had thrombus aspiration performed during PCI, and 6 patients developed stent restenosis/thrombosis. The AngioJet Thrombectomy catheter (Medrad, Warrendale, Pennsylvania) was not used nor were other thrombus disruption techniques performed during PCI. The inclusion and exclusion criteria were almost the same as our previous report (9), but we additionally excluded patients in whom a distal protection device was used during PCI in this study (n = 15). Other reasons for exclusion are as follows: ≥50% left main coronary artery stenosis (n = 6), thrombolytic therapy before PCI (n = 6), previous coronary bypass surgery (n = 2), renal dysfunction (serum creatinine levels ≥2.0 mg/dl; n = 10), concomitant inflammatory diseases or malignant tumors (n = 5), no material obtained by aspiration (n = 32), and not immunohistochemically classifiable due to a small tissue sample size (n = 9). Ultimately, 164 patients (126 men, mean age, 65 ± 12 years) were enrolled in the study. Ninety-six of the 164 patients were already reported in our previous study (9). All patients were taking aspirin and received 200 mg of ticlopidine or a 300-mg loading dose of clopidogrel before the procedure. Glycoprotein (GP) IIb/IIIa inhibitors were not used, because they had not been approved in Japan.

All the studies were approved by the ethics committee of Osaka City General Hospital, and written informed consent was obtained from all patients before the procedure.

Interventional procedure and angiographic outcomes. The infarct-related artery (IRA) was defined as a major coronary artery perfusing an area compatible with the distribution of ST-segment elevation in the 12-lead electrocardiogram. The patency of the IRA was assessed by angiography before PCI according to the Thrombolysis In Myocardial Infarction (TIMI) flow grade. Intracoronary thrombus at baseline was identified by angiography and assigned 1 of 5 scores according to the TIMI thrombus score (9). Subsequent PCI was performed for total occlusive lesions or lesions with >75% diameter stenosis, even with TIMI flow grade 3. All PCI procedures were performed using a femoral approach with a 7-F guiding catheter. After administration of 5,000 IU of heparin and conventional wire crossing, thrombus aspiration was performed using a single thrombectomy device (7-F Thrombuster catheter, Kaneka, Tokyo, Japan) through the target coronary segment ≥2 times until thrombi were angiographically invisible as determined by the operator's judgment. Intracoronary nitroglycerin (0.25 mg) was administered just before angiography both before

and after thrombus aspiration. Angiography was performed with each lesion viewed from ≥2 angles. Off-line quantitative coronary angiography was conducted using the view showing the greatest degree of stenosis. Left ventriculography was performed on admission, and the left ventricular ejection fraction was calculated. Angiographic analysis was performed by 2 independent cardiologists who were unaware of the patients' characteristics and histological classifications of aspirated intracoronary thrombi. In cases of disagreement, consensus was reached by further joint reading.

Definition of AVDE. AVDE was defined as a distal filling defect with abrupt cutoff in the distal vessel of the culprit lesion at any stage during PCI under conditions of all usable agents (dual antiplatelet agents and heparin infusion) without evidence of dissection, stenosis, or vasospasm. The evaluation of AVDE was conducted based on the coronary angiogram during the PCI procedure. The occurrence of no-reflow (TIMI flow grade 0 or 1) during PCI even with TIMI flow grade 2 or 3 by the initial angiogram was also classified as AVDE, but the occurrence of TIMI flow impairment without evidence of a distal filling defect at any stage of the procedure was not classified as AVDE.

Biochemical analysis. Venous blood samples from all patients were obtained from the forearm using standard venipuncture on admission to the hospital, before heparin administration. The concentration of high-sensitivity C-reactive protein was measured using the latex agglutination photometric immunoassay with an automated immunochemistry analyzer (LXz-6000, Eiken Chemical, Tokyo, Japan) with normal values <0.3 mg/dl.

Analysis of aspirated samples. The retrieval of the thrombus was done via aspiration through the catheter lumen, and collected from the device filter. Collected thrombi were immediately washed with saline, snap-frozen, and then stored at −80°C. Frozen samples of aspirated thrombi were serially sectioned to produce 5-μm-thick sections and then fixed in acetone. Each first and second section was stained with hematoxylin-eosin, and the cellular components were analyzed using monoclonal antibodies against a protein specific to erythrocyte membranes (glycophorin-A, Dako, Glostrup, Denmark), platelet GP IIb/IIIa (CD41, Dako), activated platelets (P-selectin [CD62P, Dako]), smooth muscle cell actin (1A4, Dako), macrophages (HAM56, Dako), neutrophils (CD66b [80H3, Beckman Coulter, Fullerton, California]), and myeloperoxidase (MPO) (MPO-7, Dako). Sections were incubated at 4°C overnight or for 1 h at room temperature and then subjected to a 3-step staining procedure using the streptavidin-biotin complex method for detection. Peroxidase activity was visualized with 3-amino-9-ethyl-carbazole (Sigma-Aldrich Co. LLC, St. Louis, Missouri) (10 min, room temperature), and the sections were faintly counterstained with hematoxylin. The tissue areas that were stained positive for erythrocytes (glycophorin-A) and P-selectin–positive platelets were quantified using computer-aided planimetry and expressed as a percentage of the total thrombus surface area. The numbers of MPO-positive cells were counted in all the tissue sections, and expressed as the number of cells per mm^2 of tissue. Morphometric analysis was performed by a single investigator who was blinded to the patient and angiographic characteristics.

Statistical analysis. The results for normally distributed continuous variables are expressed as mean ± SD, and continuous variables that did not follow a normal distribution are presented as median (interquartile range). The Mann–Whitney *U* test was used to compare the groups of patients with and without AVDE. Categorical variables were compared using a chi-square test or Fisher exact test. Pearson correlation coefficients were calculated to assess the relationships between thrombus size, quantified as the thrombus surface area, and the erythrocyte- or platelet-positive areas and the number of MPO-positive cells. Univariate and multivariate logistic regression analysis was performed to identify the independent factors associated with the incidence of AVDE. Univariate analysis included baseline patient characteristics, previously reported factors associated with AVDE, and other conceivable parameters, and multivariate analysis included significant ($p < 0.05$) factors in univariate analysis. All analyses used 2-sided tests with a significance level of $p < 0.05$. Data were analyzed using SPSS version 16.0 for Windows (SPSS, Chicago, Illinois).

Results

Clinical presentation, biochemical analysis, and angiographic findings. The angiographic results showed that AVDE during p-PCI occurred in 22 (13.4%) patients. The baseline characteristics and biochemical analysis in patients with and without AVDE are shown in Table 1. In patients with AVDE, diabetes mellitus (DM) tended to be more prevalent ($p = 0.06$), and on-admission glucose levels were significantly higher ($p = 0.035$) than in patients without AVDE. Moreover, serum maximum creatine phosphokinase (CPK) and CPK-myocardial band (CPK-MB) levels were significantly higher in patients with than without AVDE (CPK, $p = 0.04$; CPK-MB, $p = 0.01$).

Angiographic findings and acute procedural results are presented in Table 2. The baseline angiogram revealed a higher rate of occlusion in the IRA ($p = 0.08$) and higher (flow grade ≥3) TIMI thrombus score ($p = 0.08$) in patients with AVDE, but the differences did not reach significance. Furthermore, there was a larger vessel diameter ($p = 0.02$) and a longer stent length ($p = 0.01$) in patients with AVDE, and more patients with AVDE used pre-balloon dilation ($p = 0.01$) and required the use of an

Table 1. Baseline Clinical Characteristics Between Patients With and Without AVDE

	AVDE (+) (n = 22)	AVDE (−) (n = 142)	p Value
Age, yrs	63.5 ± 9.6	65.0 ± 11.9	0.37
Men	21 (95)	105 (74)	0.11
Body mass index, kg/m^2	23.7 ± 3.5	24.2 ± 3.3	0.60
Hypertension	13 (59)	84 (59)	0.96
Diabetes mellitus	12 (55)	43 (30)	0.06
Smoking	17 (77)	80 (56)	0.11
Total cholesterol, mg/dl	195 ± 47	202 ± 51	0.81
HDL cholesterol, mg/dl	46 ± 14	51 ± 13	0.13
LDL cholesterol, mg/dl	129 ± 44	131 ± 44	0.54
Triglycerides, mg/dl	114 ± 64	103 ± 64	0.40
Glucose, mg/dl	221 ± 134	182 ± 68	0.035
HbA_{1c}, %	6.6 ± 1.3	6.3 ± 1.6	0.32
OMI	3 (14)	18 (13)	0.98
Previous AP	4 (18)	50 (35)	0.20
Elevated TnT >0.1 ng/ml	13 (59)	71 (50)	0.46
Max CPK, U/l	6,052 ± 6,106	3,429 ± 2,993	0.04
Max CPK-MB, U/l	670 ± 635	338 ± 285	0.01
Killip class ≥2	5 (23)	30 (21)	0.90
Reperfusion time, min	349 ± 224	309 ± 179	0.52
Medications at hospital admission			
Aspirin	8 (36)	31 (22)	0.27
ACE inhibitors/ARB	5 (23)	34 (24)	0.93
Beta-blockers	1 (5)	13 (9)	0.73
Calcium antagonists	9 (41)	50 (35)	0.63
Nitrates	2 (9)	12 (8)	0.96
Statins	2 (9)	17 (12)	0.83
Leukocyte count, mm^{-3}	10,896 ± 3,722	10,707 ± 3,811	0.81
Neutrophil count, mm^{-3}	8,417 ± 3,964	7,900 ± 3,689	0.63
Hs-CRP, mg/dl	0.33 (0.13–0.89)	0.24 (0.08–0.44)	0.08

Values are mean ± SD, n (%), or median (interquartile range).

+ = positive; − = negative; ACE = angiotensin-converting enzyme; AP = angina pectoris; ARB = angiotensin II type 1 receptor blocker; AVDE = angiographically visible distal embolization; CPK = creatine phosphokinase; CPK-MB = creatine phosphokinase myocardial band; HbA_{1c} = glycosylated hemoglobin; HDL = high-density lipoprotein; Hs-CRP = high-sensitivity C-reactive protein; LDL = low-density lipoprotein; OMI = old myocardial infarction; TnT = troponin T.

intra-aortic balloon pump for cardiogenic shock or no-reflow ($p < 0.005$).

Histological findings in aspirated samples. In aspirated samples, histopathological analysis revealed only thrombus components in 118 patients (72%), and both thrombus and plaque fragments, which contained macrophage-derived foam cells and occasional smooth muscle cells, in 46 patients (28%). Representative micrographs of an aspirated thrombi in a patient with AVDE are shown in Figure 1. In patients with AVDE, the glycophorin-A–positive erythrocytes area was usually large (Figs. 1A and 1B), whereas the P-selectin–positive platelets area, which was the inverse of the erythrocyte-positive area, was usually small (Fig. 1C). Regarding inflammatory cells, the thrombi were infiltrated with abundant MPO-positive cells (Fig. 1D). Results of the morphometric analysis are shown in Figure 2. The erythrocyte-positive area was significantly greater in patients with than without AVDE (60 ± 15% vs. 43 ± 21%, respectively, $p < 0.0005$). By contrast, the percentage of P-selectin–positive platelets was significantly less in patients with than without AVDE (26 ± 17% vs. 46 ± 21%, respectively, $p < 0.0001$). Furthermore, patients with AVDE had more MPO-positive cells (943 ± 324 cells/mm^2 vs. 592 ± 419 cells/mm^2, $p < 0.0005$).

With regard to thrombus size, the thrombus surface area was significantly greater in patients with than without AVDE (7.20 ± 6.94 mm^2 vs. 3.32 ± 4.97 mm^2, $p < 0.0005$) (Fig. 3A). As shown in Figures 3B to 3D, thrombus surface area was positively associated with the erythrocyte-positive area ($r = 0.362$, $p < 0.0001$) (Fig. 3B) and negatively associated with the platelet-positive area ($r = -0.239$, $p < 0.005$) (Fig. 3C). Moreover, thrombus surface area was positively associated with the number of MPO-positive cells ($r = 0.443$, $p < 0.0001$) (Fig. 3D).

Table 2. Baseline Angiographic Data and Procedural Results Between Patients With and Without AVDE

	AVDE (+) (n = 22)	AVDE (−) (n = 142)	p Value
Infarct-related artery			0.91
LAD/RCA/LCX	8/13/1 (36/59/5)	61/68/13 (43/48/9)	
Initial TIMI flow grade			0.08
0/1–2/3	19/2/1 (86/9/5)	89/33/20 (63/23/14)	
Multivessel disease	7 (32)	43 (30)	0.87
Rentrop collateral grading ≥2	4 (18)	20 (14)	0.76
TIMI thrombus score ≥3	21 (95)	104 (73)	0.08
Pre-balloon dilation	18 (82)	75 (53)	0.01
Post-stent dilation	4 (18)	40 (28)	0.33
IABP use	9 (41)	1 (1)	<0.005
Stent implantation	20 (91)	136 (96)	0.72
Stents per lesion	1.22 ± 1.17	1.09 ± 0.43	0.97
Stent size, mm	3.62 ± 0.34	3.40 ± 0.40	0.07
Stent length, mm	29.5 ± 26.3	20.3 ± 8.2	0.01
QCA analysis, baseline			
Reference diameter, mm	3.68 ± 0.72	3.29 ± 0.51	0.02
MLD, mm	0.10 ± 0.21	0.11 ± 0.23	0.91
% DS	97.2 ± 5.6	96.5 ± 7.0	0.57
QCA analysis (after PCI)			
MLD, mm	3.07 ± 0.93	2.87 ± 0.52	0.03
Acute gain, mm	2.96 ± 0.92	2.76 ± 0.59	0.06
%DS	15.9 ± 23.7	12.4 ± 13.4	0.92
Ejection fraction, %	44.3 ± 12.1	47.8 ± 10.4	0.19

Values are n (%), n/n/n (N/N/N), or mean ± SD.

DS = diameter stenosis; IABP = intra-aortic balloon pump; LAD = left anterior descending coronary artery; LCX = left circumflex artery; MLD = minimal lumen diameter; QCA = quantitative coronary angiography; RCA = right coronary artery; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Table 1.

Erythrocyte component of thrombi and AVDE. The results of univariate and multivariate analyses of factors associated with AVDE are listed in Table 3. Multivariate analysis revealed that the independent factors associated with the incidence of AVDE were on-admission glucose levels (adjusted odds ratio [95% confidence interval]: 1.008 [1.001 to 1.014]; p = 0.0258), larger vessel diameter (3.964 [1.238 to 12.692]; p = 0.0203), pre-balloon dilation (7.561 [1.944 to 29.408]; p = 0.0035), and erythrocyte-positive area (1.055 [1.020 to 1.091]; p = 0.0018).

Discussion

In several previous studies, histopathological analysis was performed to determine the components of intracoronary thrombi aspirated from STEMI patients (10–12). However, these studies were based on thrombus materials fixed in formalin, and they did not evaluate platelets and erythrocytes using immunohistochemical methods with specific antibodies. Our study used frozen thrombus samples, because monoclonal antibodies against P-selectin and GP IIb/IIIa work well only on frozen sections. To the best of our knowledge, the present study is the first to pathologically demonstrate that the erythrocyte-rich component in aspirated coronary thrombi is closely associated with thrombus size and the incidence of AVDE during p-PCI in STEMI patients.

Previous studies evaluated factors that increase the risk of distal embolization. Treatment of right coronary artery or vein grafts, low TIMI flow grade before PCI, higher TIMI thrombus score, longer target lesion, and larger vessel diameter have all been shown to be associated with the risk of distal embolization (3,4,13). These findings suggest that distal embolization occurs more frequently during PCI in lesions with high thrombus or high plaque burden. However, previous studies did not fully evaluate the association between histopathological characteristics of intracoronary thrombus components and distal embolization. Our study clearly demonstrates that the erythrocyte component is significantly associated with a high thrombus burden that increases the risk of distal embolization. These results may reflect the mechanism of thrombosis whereby an initial platelet-rich thrombus, aggregated and formed at the site of plaque disruption or erosion, grows with an increase in the fibrin component, trapping large numbers of erythrocytes and inflammatory cells to form an erythrocyte-rich thrombus (14–18).

The important finding of the present study is that inflammatory cells, such as MPO-positive cells, in the

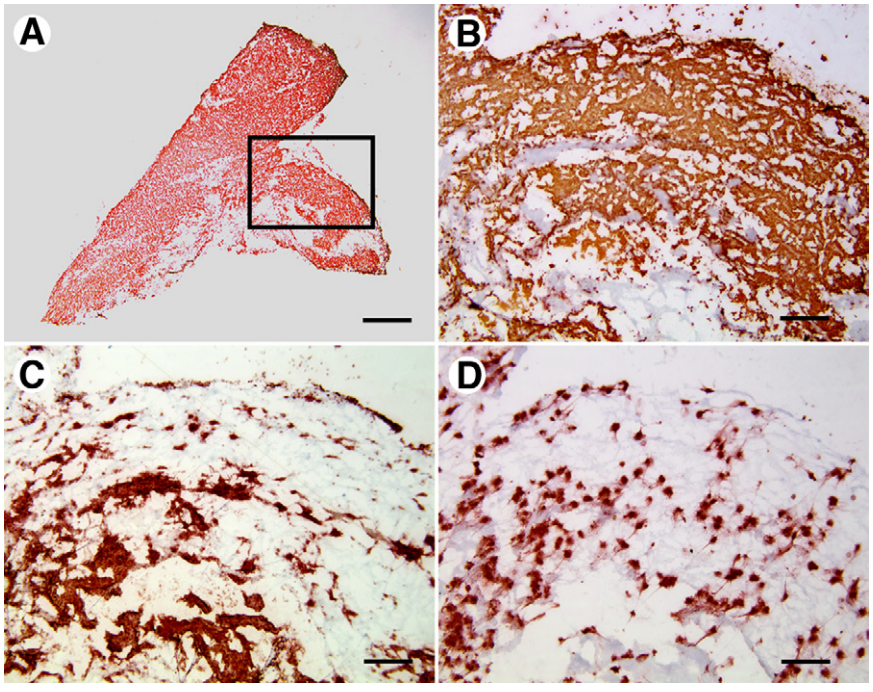

Figure 1. Representative Micrographs of an Aspirated Thrombus From a Patient With AVDE

(A) Immunostaining for erythrocytes (glycophorin-A). The **boxed area** is enlarged in **B to D**. **(B)** Immunostaining for erythrocytes (glycophorin-A). **(C)** Immunostaining for platelets (P-selectin). **(D)** Immunostaining for myeloperoxidase (MPO-7). Scale bar: **(A)** 500 μm; **(B to D)** 100 μm. AVDE = angiographicly visible distal embolization.

thrombi specimens were greater in patients with than without AVDE. Moreover, the number of MPO-positive cells in the thrombus specimens was significantly associated with thrombus size. Previously, we reported that the vast majority of MPO-positive cells were neutrophils, whereas only occasional MPO-positive cells were macrophages,

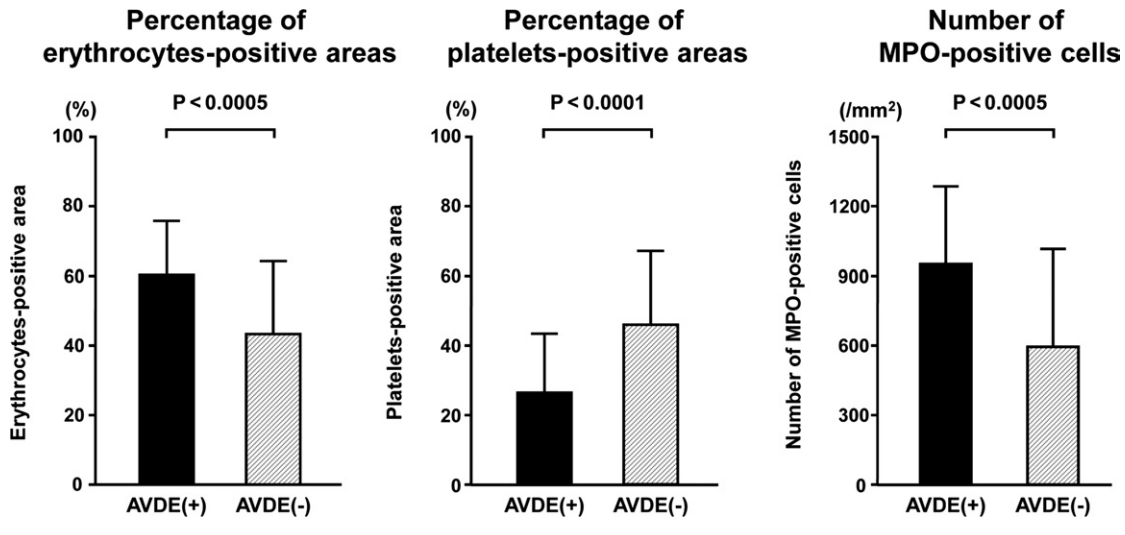

Figure 2. Morphometric Analysis of Aspirated Thrombi in Patients With and Without AVDE

Graphs showing glycophorin-A– and P-selectin–positive areas expressed as percentages of the total thrombus surface area and the number of myeloperoxidase (MPO)-positive cells expressed per mm^2 of tissue in patients with and without AVDE. **Solid bars** = AVDE (+) group; **shaded bars** = AVDE (−) group. + = positive; − = negative; other abbreviations as in Figure 1.

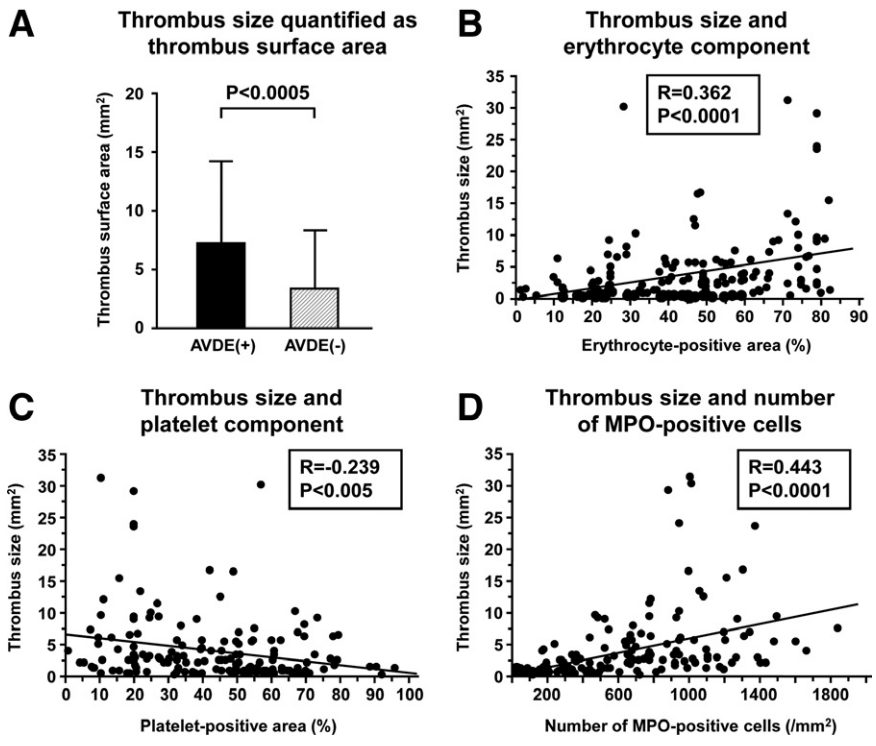

Figure 3. Relationships Between Thrombus Size and Components

(A) Graph showing total thrombus surface area (thrombus size) in patients with and without AVDE. **Solid bar** = AVDE (+) group; **shaded bar** = AVDE (−) group. **(B to D)** Correlations between thrombus surface area and the erythrocyte-positive areas **(B)**, platelet-positive areas **(C)**, and the number of MPO-positive cells **(D)**. Abbreviations as in Figures 1 and 2.

based on double-immunostaining techniques (19). Our study and others have also shown that high neutrophil aggregates that stain positive for MPO and CD66b in an aspirated thrombus are associated with impaired coronary microcirculation, as assessed by ST-segment resolution and myocardial blush grade, in patients with STEMI (9,12). MPO is a strong pro-oxidant heme protein released mainly from activated neutrophils in vascular lesions. It has been reported that activated neutrophils can induce alterations of erythrocyte properties, which result in hyperaggregability (20), and increase the expression of tissue factor activity, leading to a thrombotic state (21). Hence, our present observations and these previous data suggest that activated neutrophils present at the site of disrupted plaques or thrombi may affect thrombus composition and growth, which could lead to poor procedural outcome during PCI in patients with STEMI.

In our study, multivariate analysis revealed that plasma glucose levels on admission were an independent factor associated with AVDE. The underlying mechanism responsible for the adverse effects of hyperglycemia may have several explanations. Hyperglycemia has been shown to increase the expression of proinflammatory cytokines, resulting in plugging of leukocytes in the capillaries that may impair myocardial perfusion (22,23). Moreover, hyperglycemia may also augment thrombus formation (24), and erythrocyte aggregation is reported to be increased in DM patients (25). In fact, previous studies have demonstrated a positive relationship between acute hyperglycemia and no-reflow in patients with STEMI (26,27). Additionally, DM has been shown to be associated with impaired myocardial perfusion after primary angioplasty in patients with STEMI (28). These findings are of considerable interest, because they suggest that plasma glucose concentration may influence blood properties and contribute to the evolution of thrombus formation and growth.

On the basis of our study, an erythrocyte-rich component often reflects high thrombus burden, which increases the risk of AVDE. Therefore, the evaluation of thrombus burden or color using, not only coronary angiography, but also intravascular imaging modalities, such as ultrasound, angioscopy, or optical coherence tomography, may provide important information about the amount of thrombus that should be aspirated or if distal protection devices should be used during PCI.

Study limitations. First, this study was a nonrandomized, relatively small study, and included only patients who had

Table 3. Univariate and Multivariate Logistic Analysis for Predicting the Incidence of AVDE

Variables	Univariate	p Value	Multivariate	p Value
Age, yrs	0.989 (0.950–1.029)	0.59		
Men	7.400 (0.961–56.966)	0.0546		
Hypertension	1.027 (0.412–2.559)	0.95		
Hypercholesterolemia	0.457 (0.169–1.236)	0.12		
Diabetes mellitus	2.857 (1.146–7.122)	0.0243	2.329 (0.750–7.232)	0.14
Glucose levels on admission	1.005 (1.000–1.010)	0.0445	1.008 (1.001–1.014)	0.0258
Elevated TnT >0.1 ng/ml	1.527 (0.580–4.018)	0.39		
Pre-infarction angina	0.409 (0.131–1.275)	0.12		
Inferior myocardial infarction	1.572 (0.632–3.911)	0.33		
OMI	1.022 (0.276–3.789)	0.97		
Killip class ≥2	1.098 (0.375–3.219)	0.86		
Time to reperfusion ≥6 h	2.258 (0.891–5.723)	0.09		
Multivessel coronary disease	1.111 (0.423–2.922)	0.83		
Rentrop collateral grading ≥2	0.739 (0.203–2.690)	0.65		
Baseline TIMI flow grade 0	3.772 (1.065–13.354)	0.0396	1.519 (0.299–7.728)	0.61
TIMI thrombus score ≥3	7.951 (1.034–61.142)	0.0463	4.193 (0.337–52.193)	0.27
Lesion length ≥20 mm	1.445 (0.576–3.625)	0.43		
Vessel diameter ≥3.5 mm	3.390 (1.300–8.841)	0.0126	3.964 (1.238–12.692)	0.0203
Pre-balloon dilation	4.020 (1.295–12.476)	0.016	7.561 (1.944–29.408)	0.0035
Ejection fraction <35%	2.145 (0.701–6.566)	0.18		
Percentage of erythrocyte area	1.043 (1.018–1.070)	0.0009	1.055 (1.020–1.091)	0.0018

Values are odds ratios (95% confidence intervals).
Abbreviations as in Tables 1 and 2.

thrombus aspiration performed during p-PCI. In addition, our study excluded patients with no thrombus material or very small, unanalyzable material obtained by aspiration. Therefore, a degree of patient selection bias may have occurred. Second, we could not perform a contemporary assessment of plaque morphology or volume. Because plaque volume and composition have been shown to be associated with distal embolization, further studies using ultrasound or optical coherence tomography are needed to assess the relationship between thrombus characteristics and plaque morphology. Third, we were unable to assess whether retrieval of the thrombus was complete or whether the thrombus we analyzed was head or tail, surface or center. Because measurement of the actual amount of thrombus present in the vessel was difficult in the use of coronary angiography, and potential distortion of the samples might have occurred by aspiration through the catheter lumen, there is a possibility that the thrombus was misclassified if only part of the thrombus was aspirated. Therefore, a sampling bias must be considered in studies based on the examination of these specimens. Finally, the antithrombotic regimen used in this study was relatively dated because GP IIb/IIIa inhibitors and other novel thrombolytic therapies have not been approved for patients with STEMI in Japan. Thus, dual antiplatelet therapy and heparin use were common treatments for STEMI. However, recent studies using GP IIb/IIIa inhibitors for STEMI demonstrated that early treatment with GP IIb/IIIa inhibitors resulted in improvement of pre- and post-procedural TIMI flow grades and less distal embolization during p-PCI (29). Therefore, more aggressive antithrombotic treatment might have an impact on thrombus characteristics and procedural outcome.

Conclusions

The present study demonstrated that an erythrocyte-rich component in aspirated coronary thrombi and plasma glucose levels on admission were closely associated with the incidence of AVDE during p-PCI in patients with STEMI treated with thrombus aspiration. These findings suggest that interaction among thrombus size, thrombus components, and some factors influencing blood properties and/or inflammation could be associated with procedural outcome during PCI in patients with STEMI.

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Key Words: distal embolization ■ erythrocyte ■ intracoronary thrombus ■ myocardial infarction.