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Relationship Between Lesion Vessel Area and Myocardial Salvage Assessed by Myocardial Single Photon Emission Computed Tomography in Acute Myocardial Infarction With Stenting After Thrombectomy

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Abstract

Objectives. To study the relationship between lesion vessel area and myocardial salvage assessed by myocardial single photon emission computed tomography (SPECT) in acute myocardial infarction with stenting after thrombectomy.

Methods. This study included 71 patients who underwent stenting after thrombectomy for acute myocardial infarction. Intravascular ultrasound (IVUS) was performed after thrombectomy. Patients were classified into two groups: the High group with external elastic membrane cross-sectional area (EEM-CSA) of the lesion $\geq 18\,mm^2$ (34 patients) and the Low group with EEM-CSA $< 18\,mm^2$ (37 patients). Dual isotope myocardial SPECT imaging was undertaken by perfusion SPECT (^{201}Tl or ^{99m}Tc-MIBI) and ^{123}I-15-(*p*-iodophenyl)-3-(R,-S)-methylpentadecanoic acid (BMIPP). The image of the left ventricular myocardium was divided into 17 segments to calculate total defect score using a 5-grade assessment (0: normal−4: defect). Differences in total defect score of perfusion SPECT and ^{123}I-BMIPP was defined as mismatch.

Results. Culprit lesion morphology was assessed by IVUS. A higher incidence of lipid pool-like images (47% vs 5%, $p < 0.01$) was observed in the High group. The results of myocardial SPECT study revealed no difference in the total defect score of ^{123}I-BMIPP (18.3 ± 5.5 vs 17.3 ± 6.3 points) but the mismatch in total defect score of perfusion SPECT and ^{123}I-BMIPP was significantly lower in the High group (3.8 ± 3.9 vs 7.7 ± 4.2 points, $p < 0.05$).

Conclusions. Patients with a high culprit lesion vessel area show fewer beneficial effects in myocardial salvage compared with those with low vessel area as assessed by myocardial SPECT in acute myocardial infarction with stenting after thrombectomy.

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Key Words

■**Coronary heart disease** ■**Myocardial infarction, treatment (acute)**
■**Intravascular ultrasound** ■**Interventional cardiology (stent)**
■**Radionuclide imaging (SPECT)**

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INTRODUCTION

No reflow phenomenon is known to occur in reperfusion therapy by percutaneous transluminal coronary intervention (PCI) for acute myocardial infarction, and is a major issue for myocardial salvage in patients with acute myocardial infarction[1–3]. One mechanism for the occurrence of the no-reflow phenomenon in PCI is microvascular embolization caused by thrombus and plaque debris from the lesion site[4]. Thrombectomy devices and embolic protection devices are effective to prevent this occurrence[5–9]. However, several studies have noted patients with worsening of coronary flow after performing plain old balloon angioplasty or stent implantation following thrombectomy, suggesting that the preventive effects of thrombectomy devices against microvascular embolization may be insufficient in some patients[10,11].

Large lesion external elastic membrane cross-sectional area (EEM-CSA) as measured by intravascular ultrasound (IVUS) is an independent predictive factor of the no-reflow phenomenon in acute myocardial infarction[12]. However, no studies have investigated the effect of damage to the microcirculation in patients with a large lesion EEM-CSA if stenting is performed after thrombectomy.

This study investigated the relationship between culprit lesion vessel area, assessed by IVUS, and myocardial salvage, assessed by myocardial single photon emission computed tomography (SPECT), in patients with acute myocardial infarction who underwent stenting after thrombectomy.

SUBJECTS AND METHODS

Subjects

This study included 71 of 131 patients with initial myocardial infarction who underwent stenting from May 2003 to February 2005 at our institution within 12 hr of the onset of symptoms. These 71 patients underwent IVUS studies following thrombectomy. Patients with Thrombolysis in Myocardial Infarction (TIMI) flow grade[13] 3 in base line coronary angiography, target lesion in the left main coronary artery or left circumflex artery, or those using embolic protection devices were excluded from this study.

Patients who did not undergo IVUS were complicated by cardiogenic shock, had a target vessel < 2.5 mm from visual confirmation of coronary angiography findings, or in whom the IVUS catheter was unable to cross over the lesion were also excluded. The mean lesion EEM-CSA measured by IVUS was $18.4 \pm 4.3\,mm^2$ in patients exhibiting the no-reflow phenomenon during PCI for acute myocardial infarction[12]. Based on this result, the patients were classified into two groups according to lesion size: the High group with lesion EEM-CSA $\geq 18\,mm^2$ (34 patients, 34 lesions) and the Low group with EEM-CSA $< 18\,mm^2$ (37 patients, 37 lesions), for a comparative retrospective study of clinical outcomes.

Diagnosis and procedure

The diagnosis of acute myocardial infarction was made after $>$ 30 min of continuous chest pain, with ST segment elevation > 2.0 mm in at least two contiguous electrocardiogram leads, and a $>$ 3-fold increase in serum creatine kinase of the normal levels.

Baseline coronary angiography was conducted after 5,000 U of interarterial heparin was administered through a 6F or 7F sheath inserted in the radial or femoral artery. After performing angiography of the collateral artery and evaluating coronary flow by the Rentrop classification[14], angiography of the culprit artery was conducted with a guiding catheter to evaluate TIMI flow grade. The lesion was crossed by the guide wire and PCI was performed by inserting a 6F or 7F Thrombuster thrombectomy catheter (Kaneka Co. Ltd). Blood (20−50 m*l*) was manually aspirated while moving the thrombectomy catheter back and forth from the distal and proximal sites of the lesion.

After removal of the thrombectomy catheter, the Avanar IVUS catheter (Volcano Co. Ltd) was inserted distal to the lesion, and observations were conducted while pulling the catheter back to the coronary orifice using the auto pull back system (1 mm/sec). Plain old balloon angioplasty was performed after observations, followed by stent implantation. TIMI flow grade was assessed in the coronary angiography following PCI. The selection of type, size and length of stent to be used was left to the discretion of the operator. Dilation was achieved by inflation under a maximum inflation pressure of 10 atm or more.

In principle, oral administration of anti-platelet agent (aspirin 81 or 162 mg/day, ticlopidine 200 mg/day) was continued for at least 2 weeks following the procedure.

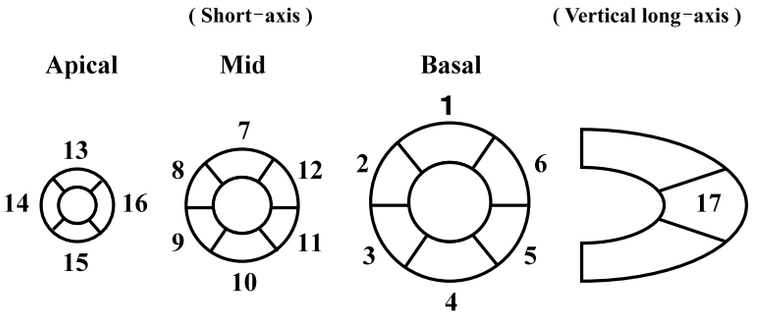

Fig. 1 Left ventricular myocardium was divided into 17 segments, and total defect score calculated using a 5-grade evaluation system
0: normal, 1: mildly reduced, 2: moderately reduced, 3: markedly reduced, 4: defect.

Angiographic analysis

Left ventricular angiography was performed on all patients in the acute phase (at the end of PCI) and the chronic phase (mean follow up 5.8 ± 1.1 months). CCIP-310 (Cathex Co. Ltd) was used for quantitative assessments of left ventricular angiography. For assessment of the left ventricular function, using the SD/chord on angiograms was calculated by the centerline method to obtain regional wall motion[15]. The differences in regional wall motion values from the acute to chronic phase were also calculated for study.

Analysis of IVUS images

IVUS images were recorded on sVHS videotape and loaded into NETRA IVUS (ScImage, Ver. 2.04.00) for off-line analysis. The same investigator conducted all IVUS analyses. In IVUS assessment of culprit lesion morphology, fissure was defined as an abrupt, focal, superficial break in the linear continuity of the plaque, extending in a radial direction; dissection was defined as rupture of the vessel wall creating one or more neolumina; lipid pool-like image was defined as a pooling of low-echoic material or echolucent material covered with a high-echoic layer; and bright echoes deep in the vessel wall $>$ 90 degrees with acoustic shadowing were defined as superficial calcium[12]. NETRA IVUS was used to measure the EEM-CSA and lumen cross-sectional area (lumen-CSA) at the lesion site and at proximal and distal reference segments. Plaque cross-sectional area (plaque-CSA) was calculated as EEM-CSA minus lumen-CSA. Positive remodeling was defined when lesion EEM-CSA was larger than proximal reference EEM-CSA[16].

Myocardial SPECT analysis

Following the PCI procedure, all patients underwent dual isotope imaging by myocardial perfusion SPECT using ^{201}TlCl (^{201}Tl) or ^{99m}Tc-sestamibi (^{99m}Tc-MIBI) and myocardial fatty acid metabolic SPECT using ^{123}I-15-(*p*-iodophenyl)-3-(R, -S)-methylpentadecanoic acid (BMIPP)[17]. Myocardial perfusion SPECT was conducted at a mean 7.3 ± 4.7 days after the PCI procedure. Myocardial fatty acid metabolic SPECT was conducted at a mean 8.4 ± 2.1 days following the procedure.

The left ventricular myocardium was divided into 17 segments on short-axis and vertical long-axis tomograms (**Fig. 1**). Two physicians specializing in nuclear cardiology visually scored each segment into 5-grade (0: normal, 1: mildly reduced uptake, 2: moderately reduced uptake, 3: markedly reduced uptake, 4: defect of uptake). The sum of total scores was expressed as total defect score, and a difference between total defect score of the perfusion agent and fatty acid agent (fatty acid agent − perfusion agent) was classified as mismatch[18]. Scoring of myocardial SPECT was undertaken by investigators unaware of assignment of the High and Low groups.

Statistical analysis

Values are expressed as actual measurements, ratio (%) and mean ± standard deviation. Continuous variables were compared by the *t*-test, and group comparisons by the χ^2 test.

RESULTS

Patient characteristics

No differences existed between the groups in age, sex, coronary risk factors, onset to recanalization time, or drugs used following the procedure. The High group had a significantly higher post PCI peak creatine kinase-MB (High: 301 ± 157 IU/*l* vs Low: 221 ± 129 IU/*l*, $p < 0.05$; **Table 1**).

Table 1 Patient characteristics

	High group (n=34)	Low group (n=37)	p value
Age (yr)	64±12	67±12	NS
Male	29(85)	28(76)	NS
Risk factors			
Diabetes mellitus	11(32)	16(43)	NS
Hypertension	16(47)	20(54)	NS
Hyperlipidemia	15(44)	12(32)	NS
Smoking	16(47)	16(43)	NS
Onset to recanalization time (min)	234±186	264±216	NS
Creatine kinase (IU/*l*)	3,820±1,976	3,010±1,722	NS
Creatine kinase-MB (IU/*l*)	301±157	221±129	<0.05
Medications			
ACE or ARB	25(74)	29(78)	NS
Calcium blocker	12(35)	14(38)	NS
Beta-blocker	3(9)	3(8)	NS

Continuous values are mean±SD. ( ): %.
High group: With lesion external elastic membrane cross-sectional area≥18 mm². Low group: With lesion external elastic membrane cross-sectional area<18 mm².
ACE=angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker.

Angiographical characteristics and strategy for stenting

There were no differences between the groups in target vessel, number of lesion vessels, or TIMI flow grade and Rentrop classification in the baseline coronary angiography. Although the High group showed a lower incidence of TIMI 3 flow following PCI, this was not significant. Size of stent used (High: 3.9±0.4 vs Low: 3.2±0.3 mm, $p<0.01$) and maximum inflation pressure (High: 15.6±2.8 vs Low: 14.1±2.8 atm, $p<0.05$) were significantly higher in the High group (**Table 2**).

IVUS findings

Comparison of culprit lesion morphology found a higher incidence of fissure or dissection (High: 56% vs Low: 11%, $p<0.01$), lipid pool-like image (High: 47% vs Low: 5%, $p<0.01$), and positive remodeling (High: 47% vs Low: 5%, $p<0.01$) in the High group. IVUS measurements showed EEM-CSA (High: 25.0±6.2 vs Low: 14.7±3.0 mm², $p<0.01$) and plaque-CSA (High: 21.1±5.8 vs Low: 11.3±2.0 mm², $p<0.01$) at the lesion site were significantly higher in the High group, but no significant difference was observed for lumen-CSA (**Table 3**).

Myocardial SPECT findings

^{201}TlCl or ^{99m}Tc-MIBI total defect score (High: 14.5±6.6 vs Low: 9.9±5.3 points, $p<0.05$) was significantly higher in the High group. There was no difference in ^{123}I-BMIPP total defect score (High: 18.3±5.5 vs Low: 17.3±6.3 points). On the other hand, mismatch of total defect score (High: 3.8±3.9 vs Low: 7.7±4.2 points, $p<0.05$) was significantly lower in the High group (**Table 4**).

Regional wall motion finding and incidence of Q-wave in electrocardiogram 2 months after the onset of acute myocardial infarction

The difference in regional wall motion (SD/chord) from the acute to chronic phase (High: 0.20±0.31 vs Low: 0.38±0.33 SD/chord, $p<0.05$) was significantly lower in the High group. The High group had a significantly higher incidence of patients (High: 68% vs Low: 43%, $p<0.05$) with Q-wave in the electrocardiogram 2 months after the onset of acute myocardial infarction (**Table 5**).

DISCUSSION

Achievement of TIMI 3 flow in reperfusion therapy by PCI for acute myocardial infarction is an important factor for prognosis[19]. However,

Table 2 Angiographical characteristics and strategy for stenting

	High group (n=34)	Low group (n=37)	p value
Target vessel			
Left anterior descending artery	18(53)	22(59)	NS
Right coronary artery	16(47)	15(41)	NS
Extent of coronary artery disease			
One-vessel disease	22(65)	25(68)	NS
Two-vessel disease	7(20)	7(19)	NS
Three-vessel disease	5(15)	5(13)	NS
Collateral flow grade at baseline coronary angiography			
Grade 0	19(56)	21(57)	NS
Grade 1	13(38)	15(40)	NS
Grade 2	2(6)	1(3)	NS
Grade 3	0	0	NS
TIMI flow grade at baseline coronary angiography			
TIMI 0	21(62)	22(59)	NS
TIMI 1	4(12)	7(19)	
TIMI 2	9(26)	8(22)	
TIMI 3	0	0	
TIMI flow grade at final coronary angiography			
TIMI 0	0	0	NS
TIMI 1	0	0	
TIMI 2	4(12)	1(3)	
TIMI 3	30(88)	36(97)	
Ejection fraction at acute phase(%)	53.7±12.7	53.5±12.4	NS
Strategy for stenting			
Stent size(mm)	3.9±0.4	3.2±0.3	<0.01
Stent length(mm)	18.4±4.0	18.9±4.7	NS
Maximum inflation pressure(atm)	15.6±2.8	14.1±2.8	<0.05

Continuous values are mean±SD. ( ): %.
Explanation of the groups as in Table1.
TIMI=Thrombolysis in Myocardial Infarction.

although the current achievement rate of TIMI 3 flow in coronary angiography after PCI is about 80−90%, the achievement of good flow on the microcirculation level is only 20−30%[20,21]. Therefore, new methods to replace TIMI flow grade in the assessment of myocardial reperfusion are currently under study. The myocardial blush grade[22] and TIMI myocardial perfusion grade[23] are being used in coronary angiography.

Myocardial scintigraphy is an effective method to assess damage of the microcirculation[24]. In this study, the mismatch between fatty acid metabolic agents and perfusion agents in myocardial SPECT was used to assess myocardial salvage by PCI. This mismatch is distinctly observed in the acute to subacute period following reperfusion therapy in patients with myocardial infarction. The mismatch area reflects the area of myocardial salvage achieved through reperfusion therapy[25,26]. The myocardial infarct size(risk area)at the time of the onset of infarct can be estimated indirectly from the defect area of fatty acid metabolic agents in the subacute phase[27,28].

The two groups in this study showed no difference in the total defect score of fatty acid metabolic agents in the subacute phase, suggesting that no significant difference was present in the risk area. On the other hand, the mismatch in total defect score of the fatty acid metabolic agent and perfusion agent was significantly lower in patients with

Table 3 Intravascular ultrasound findings

	High group (n=34)	Low group (n=37)	p value
Intravascular ultrasound lesion morphology			
Fissure/dissection	19(56)	4(11)	<0.01
Lipid pool-like image	16(47)	2(5)	<0.01
Superficial calcium	13(38)	18(49)	NS
Positive remodeling	16(47)	2(5)	<0.01
Intravascular ultrasound measurements			
Reference proximal site			
EEM-CSA(mm^2)	22.5±5.8	16.6±3.2	<0.01
Lumen-CSA(mm^2)	11.2±3.4	8.3±2.3	<0.01
Plaque-CSA(mm^2)	11.2±4.2	8.2±1.6	<0.01
Lesion site			
EEM-CSA(mm^2)	25.0±6.2	14.7±3.0	<0.01
Lumen-CSA(mm^2)	3.9±1.2	3.4±0.9	NS
Plaque-CSA(mm^2)	21.1±5.8	11.3±2.0	<0.01
Reference distal site			
EEM-CSA(mm^2)	17.5±4.4	12.2±3.3	<0.01
Lumen-CSA(mm^2)	8.6±2.7	5.9±2.0	<0.01
Plaque-CSA(mm^2)	8.9±3.2	6.3±2.4	<0.01

Continuous values are mean±SD. ( ): %.
Explanation of the groups as in Table 1.
EEM=external elastic membrane; CSA=cross-sectional area.

Table 4 Myocardial single photon emission computed tomography findings

	High group (n=34)	Low group (n=37)	p value
Total defect score of ^{201}TICI or ^{99m}Tc-MIBI (point)	14.5±6.6	9.9±5.3	<0.05
Total defect score of ^{123}I-BMIPP(point)	18.3±5.5	17.3±6.3	NS
Mismatch of total defect score(point)	3.8±3.9	7.7±4.2	<0.05

Values are mean±SD.
Explanation of the groups as in Table 1.
^{99m}Tc-MIBI=^{99m}Tc-sestamibi; ^{123}I-BMIPP=^{123}I-15-(*p*-iodophenyl)-3-(R, -S)-methylpentadecanoic acid.

Table 5 Regional wall motion finding in left ventriculography and incidence of Q-wave in electrocardiogram 2 months after the onset of acute myocardial infarction

	High group (n=34)	Low group (n=37)	p value
Regional wall motion(SD/chord)			
Acute phase	−1.65±0.55	−1.79±0.46	NS
Chronic phase	−1.45±0.45	−1.41±0.39	NS
Difference in regional wall motion(SD/chord)	0.20±0.31	0.38±0.33	<0.05
Q-wave in electrocardiogram 2 months after onset	23(68%)	16(43%)	<0.05

Difference of regional wall motion was calculated as regional wall motion at chronic phase minus regional wall motion in the acute phase.
Continuous values are mean±SD.
Explanation of the groups as in Table 1.

high lesion EEM-CSA. Therefore, we infer that in stenting after thrombectomy, there is less reperfusion on the microcirculation level in patients with high EEM-CSA.

In addition, the high lesion EEM-CSA group of patients had a lower degree of improvement of local wall motion in the infarct area from the acute to chronic phases compared to the low group and also had a high ratio of Q-wave myocardial infarction in 2 month after the onset. The area of mismatch reflects stunned myocardium and shows an improvement over time in wall motion[18,29]. There were no significant differences between the two groups in SPECT observed risk area, onset to recanalization time, TIMI flow grade and collateral grade at baseline coronary angiography, or pharmacologic agents used after the procedure. This leads us to believe that the difference in myocardial salvage effects by PCI was reflected in the degree of improvement in wall motion in the chronic phase.

IVUS of the culprit lesion morphology found higher incidence of fissure or dissection and lipid pool-like images in patients with high lesion EEM-CSA. Other than thrombus, the significant factor for microvascular embolization in patients with acute myocardial infarction is the plaque constituents that accompany plaque rupture[30−32]. In addition, culprit lesions in large vessels that have lipid pool-like images or ruptured plaque contain a large lipid core and plaque gruel at the lesion site. Thus, severe microvascular embolization occurs in many patients caused by the large amounts of plaque crushed during the PCI procedure[12,33−35]. Therefore, regardless of aspiration of thrombus by thrombectomy, subsequent PCI would cause more serious microvascular embolization of plaque debris, leading to less benefit for myocardial salvage in patients with high lesion EEM-CSA.

The use of embolic protection devices has been considered as a method to prevent microvascular embolization by plaque debris or thrombus. In Japan, the Guardwire Plus™ (Medtronic Co. Ltd) can be used as an embolic protection device, but the efficacy was not demonstrated in the Enhanced Myocardial Efficacy and Recovery by Aspiration of Liberated Debris (EMERALD) trial, a prospective randomized controlled trial for patients with acute myocardial infarction[36]. However, the Guardwire Plus™ is effective, for saphenous vein grafts and for acute myocardial infarction culprit lesions identified by angioscopy as ruptured plaque with large amounts of plaque debris at the lesion site[35,37]. As culprit lesions in large vessels have similar lesion characteristics, we believe that the Guardwire Plus™ can contribute to the achievement of good reperfusion in such patients by effectively preventing distal embolization.

Study limitations

This study was a non-randomized retrospective single-center trial, with subjects limited to those who underwent IVUS. A larger prospective multicenter investigation is necessary.

CONCLUSIONS

Patients with stenting after thrombectomy for acute myocardial infarction and a high culprit lesion vessel area show less benefit in myocardial salvage assessed by myocardial single photon emission computed tomography. The adjunctive use of embolic protection devices for culprit lesions in large vessels should be assessed to achieve optimal reperfusion on the microcirculation level.

要　約

急性心筋梗塞に対する血栓吸引術後ステント植え込み術における病変部位の血管面積と心筋 Single Photon Emission Computed Tomography からみた心筋サルベージ効果の関係

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目　的: 急性心筋梗塞に対する血栓吸引術後ステント植え込み術における病変部位の血管面積と心筋 single photon emission computed tomography (SPECT) からみた心筋サルベージ効果の関係を検討する.

方　法: 急性心筋梗塞と診断され血栓吸引術後ステント植え込み術を施行した症例のうち，吸引術後血管内心エコー法(IVUS)を施行しえた71症例を対象とした．さらに病変部位external elastic membrane cross-sectional area(EEM-CSA)≧18 mm^2の高値群(34例)とEEM-CSA＜18 mm^2の低値群(37例)の2群に分け比較検討した．心筋SPECTは血流SPECT(^{201}Tlまたは^{99m}Tc-MIBI)と^{123}I-BMIPPの2核種を撮像した．さらに撮像画像の左室心筋を17分割し，5段階評価(0: 正常から4: 欠損)を用いて総欠損スコアを算出した．また，血流SPECTと^{123}I-BMIPPの総欠損スコアの差を集積乖離と定義した．

結　果: IVUSからみた病変血管形態の比較において脂質プール様イメージング(47% vs 5%，p＜0.01)は高値群に高率に認められた．心筋SPECTの検討結果において^{123}I-BMIPPの総欠損スコアに差はなかったが(18.3±5.5 vs 17.3±6.3 point)，血流シンチグラフィーと^{123}I-BMIPPとの総欠損スコアの集積乖離はEEM-CSA高値群が有意に低値を示した(3.8±3.9 vs 7.7±4.2 point，p＜0.05)．

結　論: 急性心筋梗塞に対する血栓吸引術後ステント植え込み術においてIVUSからみた病変血管面積の高値例は，低値例に比べ心筋SPECTからみた心筋サルベージ効果が劣る．

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