Original Article

Presence of Severe Stenosis in Most Culprit Lesions of Patients with ST-segment Elevation Myocardial Infarction

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Abstract

Background: Previous studies revealed that culprit vessels of ST-segment elevation myocardial infarction (STEMI) were often related to mild or moderate stenosis. However, recent studies suggested that severe stenosis was primarily found in culprit lesions. The objective of this study was to analyze the stenosis severity of culprit lesions in STEMI patients and to clarify the paradoxical results.
Methods: A total of 489 consecutive STEMI patients who underwent primary percutaneous coronary intervention were retrospectively studied from January 2012 to December 2014. The patients were divided into three groups based on stenosis severity using quantitative coronary analysis: Group A, 314 cases, stenosis ≥70%; Group B, 127 cases, stenosis 50–70%; and Group C, 48 cases, stenosis ≤50%. The clinical, demographic, and angiographic data of all groups were analyzed.
Results: Patients in Group A exhibited a significantly higher prevalence of history of angina pectoris (95.9% vs. 62.5%, $P < 0.001$), multivessel disease (73.2% vs. 54.2%, $P = 0.007$), and lower cardiac ejection fraction (53.3 ± 8.6 vs. 56.8 ± 8.4, $P = 0.009$) than those in Group C. Multivariable analysis revealed that history of angina pectoris (odds ratio [*OR*]: 13.89, 95% confidence interval [*CI*]: 6.21–31.11) and multivessel disease (*OR*: 2.32, 95% *CI*: 1.25–4.31) were correlated with severe stenosis of the culprit lesion in Group A.
Conclusions: Most culprit lesions in STEMI patients were severe stenosis. These patients exhibited a higher prevalence of angina history and multivessel diseases.

Key words: Percutaneous Coronary Intervention; Quantitative Coronary Angiography; ST-segment Elevation Myocardial Infarction

Introduction

ST-segment elevation myocardial infarction (STEMI) often occurs because of plaque rupture or erosion, which is called vulnerable plaque. Vulnerable plaques were thought to represent a mild or moderate luminal stenosis in the past.[1,2] Previous studies indicated that mild or moderate coronary lesions exhibited a higher risk for acute myocardial infarction (AMI) than anatomically and physiologically severe lesions.[3,4] However, several recent studies suggested that severe stenosis of culprit lesions was found in most STEMI patients rather than mild or moderate stenosis,[5-9] but there were deficiencies in patient selection and study design. In this study, we analyzed stenosis severity of culprit lesions in STEMI patients retrospectively using quantitative coronary analysis (QCA) to clarify the paradoxical results in a larger population. Thrombus aspiration (TA) was performed in most cases before balloon predilation in our study.

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Methods

Patients

This study was a single-center retrospective study of 591 consecutive STEMI patients undergoing emergent percutaneous coronary intervention (PCI) from January 2012 to December 2014. STEMI diagnosis was based on chest pain lasting ≥30 min, elevated troponin I, and ST-segment elevation >1 mm in more than two adjacent leads in electrocardiography.[10] A total of 489 patients

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were eligible for QCA. Routine TA was performed effectively in 334 patients with thrombolysis in myocardial infarction (TIMI) flow Grade 0–1 or visible thrombus before primary PCI. One hundred and fifty-five patients with TIMI flow Grade 2 or 3 and no visible thrombus did not receive TA. One hundred and two patients were excluded: (1) 81 patients with predilation before TA (28 of these patients still had severe stenosis after dilation), (2) 16 patients with visible thrombus after TA, and (3) five patients with aspiration catheter or guidewire crossing failure. Clinical, demographic, and angiographic data were collected when the procedure was performed [Figure 1].

Procedure

Patients were pretreated with aspirin (300 mg) and clopidogrel (300 mg) as early as possible prior to PCI. Coronary angiography was performed via a radial or femoral artery approach using a 6F or 7F sheath. Intravenous heparin boluses (60–100 U/kg) were administrated after sheath insertion. A glycoprotein IIb/IIIa inhibitor was used at the physician's discretion. An Export Aspiration Catheter (Medtronic Corporation, Minneapolis, USA) or Diver CE Aspiration Catheter (Invatec, Brescia, Italy) was used for manual aspiration. The aspiration catheter was advanced through the routine wire to the lesion, and suction was achieved via manual aspiration with a lockable 20 ml syringe and vacuum.[11]

Angiographic analysis

Two experienced operators independently reviewed the coronary angiograms. Coronary flow was graded using standard TIMI criteria. TIMI flow grade was defined as follows: TIMI 0 (no perfusion), the absence of any antegrade flow beyond a coronary occlusion; TIMI 1 (penetration without perfusion), faint antegrade coronary flow beyond the occlusion, with incomplete filling of the distal coronary bed; TIMI 2 (partial reperfusion), delayed or sluggish antegrade flow with complete filling of the distal territory; and TIMI 3, normal flow that fills the distal coronary bed completely.[12] Angiographic images were analyzed using a quantitative coronary angiogram analysis system (Medis QAngio XA 7.3, The Netherlands). The following parameters were measured using QCA: reference vessel diameter (RVD), averaged diameter of proximal and distal coronary segments without obvious narrowing; minimal luminal diameter (MLD), the smallest lumen diameter in the segment of a lesion; minimal lumen area; area stenosis (AS); lesion length (LL); and culprit lesion diameter stenosis (DS) ([RVD − MLD]/RVD × 100%).[9] The patients were divided into three groups according to the QCA results: Group A stenosis ≥70%, Group B stenosis 50–70%, and Group C stenosis ≤50%.

Statistical analysis

All data analysis was performed using the SPSS 19.0 (SPSS Inc., Chicago, IL, USA). All continuous variables were reported as a mean ± standard deviation (SD). Differences in baseline characteristics between the three groups were tested for significance using the Chi-square test or Fisher's exact test where appropriate. Logistic regression was used for the analysis of categorical variables where appropriate. The level of statistical significance was defined as $P < 0.05$ (two-sided). The difference between two groups was compared using Student–Newman–Keuls test.

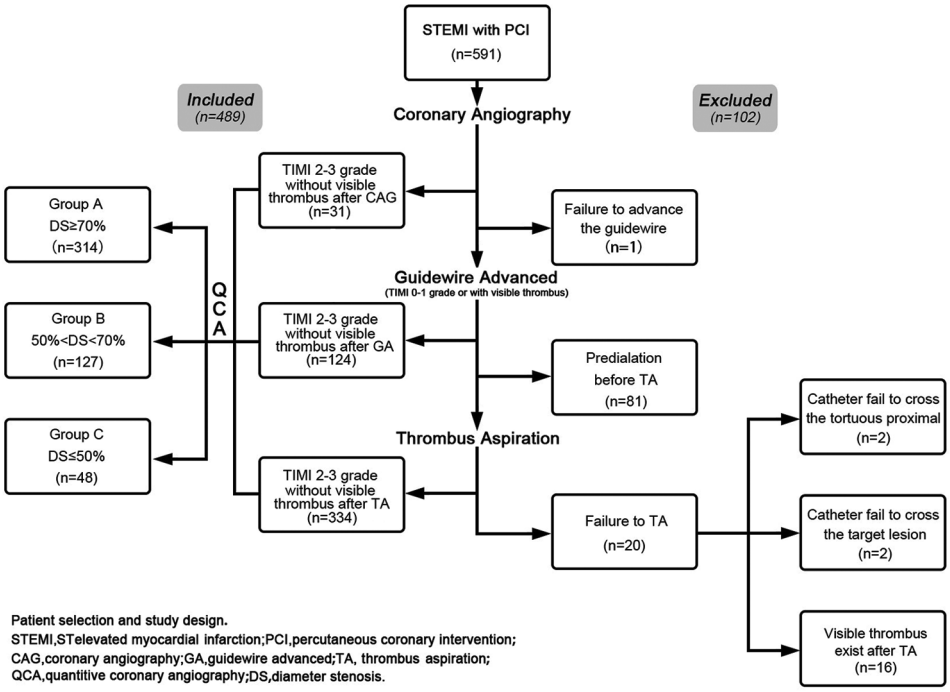

Figure 1: Study design with inclusion and exclusion criteria.

Results

Baseline characteristics

Table 1 lists the baseline characteristics of the three groups. A total of 314 (64.2%) of the 489 patients with ≥70% stenosis of the culprit lesion in Group A exhibited a significantly higher frequency of angina pectoris history (95.9% vs. 62.5%, $P < 0.001$) and lower ejection fraction (EF) values (53.3 ± 8.6 vs. 56.8 ± 8.4, $P = 0.009$) than patients in Group C. There was no significant difference in age, sex, smoking history, hypertension, blood lipids, heart rate, renal function, onset-to-hospital, vascular disease, and Killip class >1 between the three groups. Multivariable analysis revealed that the history of angina pectoris (odds ratio [*OR*]: 13.89, 95% confidence interval [*CI*]: 6.21–31.11) was correlated with severe stenosis of the culprit lesion in Group A [Figure 2].

Angiographic findings and stenosis severity analysis

Table 2 lists the angiographic characteristics. 64.2% of the STEMI patients were assigned to Group A, 25.9% to Group B, and 9.8% to Group C. No difference in the location of the culprit lesion between the three groups was found in our study. 73.2% of the patients in Group A exhibited more complex lesions and multiple vessel disease, and patients in Group C had a tendency of thrombus burden. Coronary flow as measured by TIMI flow grade was similar among the three groups. Collaterals were present in 49 patients in the entire study population. Multivariable analysis revealed that multivessel disease was correlated with severe stenosis of the culprit lesion in Group A (*OR*: 2.32, 95% *CI*: 1.25–4.31) [Figure 2]. Among patients with TIMI flow Grade 2 or 3 without visible thrombus after TA, 61% exhibited severe stenosis in the culprit lesion and 72% of the patients without thrombus after CAG exhibited severe stenosis in the culprit lesion [Figure 3].

Table 3 shows the results of QCA analyses. There were significant differences between the three groups in DS (77.64 ± 6.60 vs. 59.60 ± 5.45 vs. 40.42 ± 8.58, $P < 0.001$), MLD (0.71 ± 0.27 vs. 1.24 ± 0.27 vs. 1.83 ± 0.52, $P < 0.001$), AS (94.60 ± 2.71 vs. 83.63 ± 4.35 vs. 66.78 ± 7.11, $P < 0.001$), and LL (20.18 ± 9.94 vs. 16.75 ± 8.42 vs. 13.48 ± 6.47, $P < 0.05$), but no significant differences in RVD (3.18 ± 0.65 vs. 3.12 ± 0.56 vs. 3.21 ± 0.89, $P > 0.05$).

Clinical outcomes

Eight patients in Group A and six patients in Group B and Group C had a combined clinical end point of reinfarction and in-hospital death. There was no statistical significance between the three groups, but a tendency of higher occurrence was observed in Group A.

Discussion

Atherosclerotic plaque and thrombus burden contribute to the occurrence of STEMI.[1,2] The cause of AMI was previously recognized as a rupture of the plaque, which was associated with mild or moderate coronary stenosis.[1-4] Little *et al*.[3] observed 42 consecutive patients who had undergone coronary angiography before and up to 1 month after AMI onset. The time intervals between the previous and second angiography ranged from 6 weeks to 11 years. They concluded that AMI occurred in most patients with <50% stenosis, but the infarction did not occur with previous significant stenosis. Ambrose *et al*.[4] also revealed that AMI was caused by the occlusion of an artery with severe stenosis in only one-third of patients. However, several recent studies disputed these results

Table 1: Baseline clinical and demographic characteristics in three groups

Baseline clinical and demographic characteristics	Group A DS ≥70% ($n = 314$)	Group B 50%< DS <70% ($n = 127$)	Group C DS ≤50% ($n = 48$)	P_{ac}	P_{ab}	P_{bc}
Age, mean ± SD, years	60.3 ± 10.8	60.3 ± 10.7	56.3 ± 11.3	0.018	0.965	0.034
Male, *n* (%)	211 (67.2)	82 (64.6)	27 (56.2)	0.137	0.596	0.311
Diabetes, *n* (%)	60 (19.1)	34 (26.8)	18 (37.5)	0.004	0.075	0.166
Hypertension, *n* (%)	141 (44.9)	51 (40.2)	21 (43.8)	0.881	0.363	0.667
Smoking, *n* (%)	198 (63.1)	76 (59.8)	30 (62.5)	0.941	0.529	0.748
LDL, mean ± SD, mmol/L	1.95 ± 1.40	1.92 ± 1.11	1.89 ± 0.96	0.775	0.829	0.869
LVEF, mean ± SD, %	53.3 ± 8.6	54.5 ± 7.5	56.8 ± 8.4	0.009	0.174	0.082
Heart rate, mean ± SD, bpm	74.95 ± 17.12	74.36 ± 17.48	76.20 ± 17.00	0.638	0.745	0.613
Renal function, mean ± SD, μmol/L	72.96 ± 26.68	75.71 ± 23.84	69.98 ± 19.30	0.457	0.313	0.138
WBC, mean ± SD, $\times 10^9$/L	10.61 ± 3.39	11.60 ± 5.93	10.19 ± 4.65	0.450	0.028	0.140
Onset-to-hospital, mean ± SD, h	6.50 ± 6.34	6.14 ± 5.54	6.74 ± 6.02	0.806	0.576	0.533
Angina pectoris, *n* (%)	301 (95.9)	110 (86.6)	30 (62.5)	<0.001	<0.001	<0.001
Cerebrovascular and peripheral events, *n* (%)	46 (14.6)	14 (11.0)	5 (10.4)	0.432	0.315	0.908
Killips class >1, *n* (%)	17 (5.4)	7 (5.5)	3 (6.2)	0.813	0.967	0.851
In-hospital clinical-outcome						
MI, *n* (%)	3 (1.0)	1 (0.8)	3 (6.2)	0.866	0.007	0.766
Death, *n* (%)	5 (1.6)	3 (2.4)	0	0.616	0.379	0.613
MACE, *n* (%)	8 (2.6)	3 (2.4)	3 (6.2)	0.910	0.164	0.872

DS: Diameter stenosis; SD: Standard deviation; LDL: Low-density lipoprotein; LVEF: Left ventricular ejection fraction; WBC: White blood cell; MI: Myocardial infarction; MACE: Major adverse cardiac event; P_{ac}: *P* value from the comparison of Group A and Group C; P_{ab}: *P* value from the comparison of Group A and Group B; P_{bc}: *P* value from the comparison of Group B and Group C.

Table 2: Angiographic characteristics in three groups

Variables	Group A DS ≥70% (n = 314)	Group B 50%<DS <70% (n = 127)	Group C DS ≤50% (n = 48)	P_{ac}	P_{ab}	P_{bc}
Angiographic characteristics, *n* (%)						
Left dominance	40 (12.7)	12 (9.4)	10 (20.8)	0.140	0.311	0.043
Right dominance	274 (87.3)	115 (90.6)	38 (79.2)	0.130	0.332	0.043
Multivessel disease	230 (73.2)	90 (70.9)	26 (54.2)	0.007	0.612	0.037
Left main	3 (1.0)	3 (2.4)	0 (0.00)	0.498	0.245	0.283
LAD	180 (57.3)	57 (44.9)	27 (56.2)	0.889	0.018	0.179
LCX	38 (12.1)	12 (9.4)	3 (6.2)	0.233	0.426	0.584
RCA	93 (29.6)	55 (43.3)	18 (37.5)	0.270	0.006	0.487
Base TIMI flow grade, *n* (%)						
0, 1	236 (75.2)	86 (67.7)	36 (75.0)	0.981	0.111	0.350
2	16 (5.1)	4 (3.2)	3 (6.2)	0.738	0.374	0.350
3	62 (19.8)	37 (29.1)	9 (18.8)	0.872	0.032	0.164
Thrombus burden grade, *n* (%)						
0	104 (33.1)	33 (26.0)	9 (18.7)	0.045	0.143	0.317
1–2	12 (3.8)	6 (4.7)	1 (0.2)	0.547	0.664	0.426
3–4	47 (15.3)	39 (30.7)	17 (35.4)	<0.001	<0.001	0.551
5	151 (48.1)	49 (38.6)	21 (43.8)	0.575	0.069	0.534

DS: Diameter stenosis; P_{ac}: P value from the comparison of Group A and Group C; P_{ab}: P value from the comparison of Group A and Group B; P_{bc}: P value from the comparison of Group B and Group C; LAD: Left anterior descending; LCX: Left circumflex; RCA: Right coronary artery; TIMI: Thrombolysis in myocardial infarction.

Table 3: QCA characteristics in three groups

QCA characteristics	Group A DS ≥70% (n = 314)	Group B 50%< DS <70% (n = 127)	Group C DS ≤50% (n = 48)	P_{ac}	P_{ab}	P_{bc}
RVD (mm)	3.18 ± 0.65	3.12 ± 0.56	3.21 ± 0.89	0.018	0.362	0.426
MLD (mm)	0.71 ± 0.27	1.24 ± 0.27	1.83 ± 0.52	<0.001	<0.001	<0.001
AS (%)	94.60 ± 2.71	83.63 ± 4.35	66.78 ± 7.11	<0.001	<0.001	<0.001
DS (%)	77.64 ± 6.60	59.60 ± 5.45	40.42 ± 8.58	<0.001	<0.001	<0.001
LL (mm)	20.18 ± 9.94	16.75 ± 8.42	13.48 ± 6.47	<0.001	0.0007	0.016

Values were shown as mean ± SD. AS: Area stenosis; DS: Diameter stenosis; LL: Lesion length; MLD: Minimal lumen diameter; P_{ac}: P value from the comparison of Group A and Group C; P_{ab}: P value from the comparison of Group A and Group B; P_{bc}: P value from the comparison of Group B and Group C; RVD: Reference vessel diameter; SD: Standard deviation; QCA: Quantitative coronary analysis.

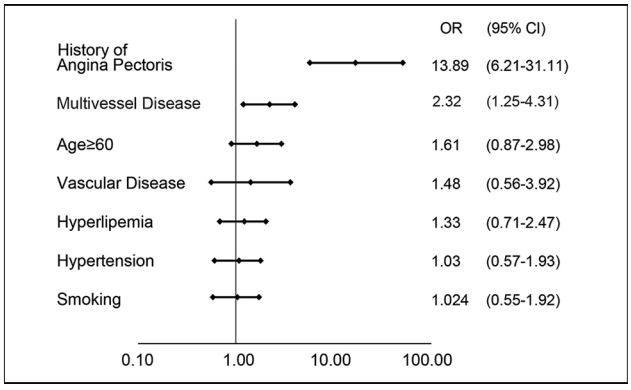

Figure 2: Multivariable analysis showed that both histories of angina pectoris and multivessel disease were correlated with severe stenosis of the culprit lesion in Group A.

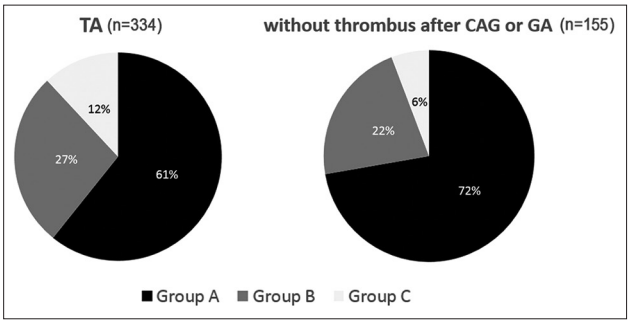

Figure 3: Proportion of severe stenosis in patients with or without thrombus aspiration.

and reconsidered the importance of stenosis severity in the culprit lesion.[5-9] Frøbert *et al*.[6] examined 156 AMI patients and found that the underlying stenosis was over 50% in 151 of these patients (96%) and >70% in 103 (66%) patients. The majority of AMI occurred in culprit lesions severely stenotic, contrary to past beliefs. Manoharan *et al*.[7] also reported that the underlying residual stenosis was significant in most STEMI patients. In this study, 317 acute coronary syndrome patients were investigated, and only 102 patients were STEMI. Another single-center registry study investigated 483 consecutive patients with STEMI undergoing PCI, but only 172 patients who underwent TA were eligible. A total of 119 patients had residual stenosis ≥50%.[9]

The reason for two different results of the severity degree of culprit lesions in STEMI patients is unknown. The following reasons may explain this paradox: (1) previous studies that support nonsignificant stenosis underlying STEMI enrolled a limited number of PCI patients because of technological deficiency, but recent studies that support significant stenosis underlying STEMI included more PCI patients, which better reflects the real world, (2) the mean time interval between the initial coronary angiogram to AMI onset was a long period of time (25 months in average, ranged from 18 to 40 months) in previous studies.[13,14] The PROSPECT study has demonstrated that there was progression from a mild DS at baseline to a severe stenosis at the time of AMI onset during a median 3.4-year follow-up,[15] (3) recent imaging studies have found that vulnerable plaque had larger plaque volume and necrotic core size with greater positive remodeling, which contributed to misconception of the mild vulnerable plaque,[13] and (4) the lack of a TA device may have given the false impression that a stenosis appeared more severe than it was prior to rupture.

In our study, 591 consecutive patients were investigated, and 102 patients were excluded. In the finally enrolled 489 patients, 334 with TIMI flow Grade 0–1 or with visible thrombus before PCI were analyzed using QCA following routine TA (about 61% patients with severe stenosis in culprit lesions). QCA was performed directly without TA in the remaining 155 patients with TIMI flow Grade 2 or 3 and no visible thrombus (about 72% patients with severe stenosis in culprit lesions). 64.29% of the patients exhibited severe stenosis in culprit lesions. Our study indicated that patients in Group A had more complex lesions and multiple vessel disease, and patients in Group C had a tendency to greater thrombus burden. Thrombus burden may overestimate the stenosis of culprit lesions. Previous studies did not use a TA device during the PCI process. Results from these studies were questioned. TA was used in over 60% of enrolled patients in our study, and most of the thrombus burden was removed. However, most significant stenosis remained in the culprit lesion after TA. We also observed that patients with significant stenosis had a lower thrombus burden, and patients with nonsignificant stenosis exhibited a greater thrombus burden. Therefore, nonsignificant stenosis may have more thrombus external to the plaque, and severe stenosis may possess thrombus deep into internal plaques and cause injury.

Our study had some advantages compared to other studies: (1) a large population was investigated for 3 years, (2) the proportion of excluded patients were relatively low (only 17%), and (3) the removal of thrombus burden via the routine use of a TA catheter allowed for a more precise stenosis assessment.

However, this study was a single-center, retrospective study of STEMI patients only. Intravenous ultrasound and optical coherence tomography were not performed, and the smaller thrombus burden may interfere with the assessment of culprit lesions in patients with STEMI.

In conclusion, most of the culprit lesions in this study were severe stenosis in STEMI patients. Patients with ≥70% stenosis in culprit lesions had a higher prevalence of angina history, multiple vessel disease, and lower EF.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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