의학박사 학위논문

관상동맥중재술과 연관된 심근경색증의 정의

Clinically Relevant Myocardial Infarction Associated With Percutaneous Coronary Intervention

울 산 대 학 교 대 학 원

의 학 과

안 정 민

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지 도 교 수　김 영 학

이 논문을 의학박사 학위 논문으로 제출함

2018년 12월

울 산 대 학 교　대 학 원

의　학　과

안 정 민

안정민의 의학박사학위 논문을 인준함

심사위원 김 영 학 인

심사위원 이 승 환 인

심사위원 박 덕 우 인

심사위원 윤 성 철 인

심사위원 서 존 인

울 산 대 학 교 대 학 원

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Abstract

Background: The criteria for clinically relevant myocardial infarction (MI) associated with percutaneous coronary intervention (PCI) remains debatable. We aimed to determine the criteria of periprocedural MI associated with long-term mortality and with mortality rate similar to spontaneous MI.

Methods: From four prospective PCI registries, 17,190 patients with negative creatine kinase-MB (CK-MB) elevation at baseline who underwent drug-eluting stenting were included. Chest pain, cardiac enzyme, electrocardiographic changes, and angiographic mechanism were prospectively collected and independently adjudicated. Periprocedural MI was defined as post-PCI CK-MB elevation ≥3 times the upper reference limit (URL). Spontaneous MI was defined as spontaneous, non-PCI-related CK-MB elevation. The primary endpoint was all-cause mortality at a median follow-up of 4.5 years (interquartile range: 3.2, 5.2 years).

Results: The criteria of clinically relevant periprocedural MI associated with a higher risk of long-term mortality was CK-MB elevation ≥3 times the URL plus new-onset Q wave or angiographic major vessel complications or CK-MB elevation ≥10 times the URL (incidence, 2.9%; adjusted hazard ratio, 1.61; 95% confidence interval, 1.20-2.14; P=0.001). However, standardized mortality rate of periprocedural MI achieving new criteria was lower than that of spontaneous MI (2.28 per 100 person-year versus 6.14 per 100 person-year). CK-MB threshold for periprocedural MI with mortality similar to spontaneous MI was 58 times the URL.

Conclusions: This study provided criteria for periprocedural MI with a higher risk of long-term mortality based on the combination of cardiac enzyme elevation and supportive clinical features. Nevertheless, clinically relevant periprocedural MI showed lower mortality rate than spontaneous MI.

Keywords: periprocedural myocardial infarction, stent, cardiac enzyme, coronary artery disease

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Introduction

Percutaneous coronary intervention (PCI) is one of the most widely done medical procedures, with over 3 million performed worldwide each year (1-4). Depending on diagnostic criteria, practice pattern, and population characteristics, 5–19% of patients who underwent PCI are exposed to risks of myocardial infarction (MI) associated with PCI (5). However, clinical significance of periprocedural MI remained controversial (6). Different working groups suggested different definitions of periprocedural MI (7-11). Accordingly, this uncertainty leads to unnecessary medical test, increased cost, and longer hospital stay in clinical practice (12). Furthermore, clinical trials frequently counted periprocedural MI as MI events with spontaneous MI (13). This approach may obscure appropriate interpretation of trial results unless prognostic value of periprocedural and spontaneous MI was equivalent. Therefore, determining clinically relevant MI has clinically and academically important implication.

On the basis of a large contemporary PCI population with a broad spectrum of clinical characteristics and normal baseline cardiac biomarker, we aimed to determine the clinically relevant periprocedural MI criteria using the combination of cardiac enzyme, anginal symptom, electrocardiographic changes, and angiographic mechanism of post-PCI myonecrosis. Clinically relevant periprocedural MIs were evaluated in two steps: 1) those with a higher risk of mortality and 2) those with mortality similar to spontaneous MI.

Methods

Study Population

The study population that underwent drug-eluting stent was pooled from four prospective observational studies from 45 heart centers; the Interventional Cardiology Research Incorporation Cardiology Research Incorporation Society-Drug-Eluting Stents (IRIS-DES) registry, the ASAN Medical Center-Percutaneous Coronary Intervention (ASAN-PCI) registry, the ASAN Medical Center-Left Main (ASAN-MAIN) registry, the ASAN Medical Center-Multivessel Disease (ASAN-MV) registry. The study design and detailed entry criteria of each registry have been described previously (14-17), and the key features are summarized in Supplementary Table 1. Eligible patients were men and women without creatine kinase-MB (CK-MB) elevation before PCI and with serial CK-MB measurement after PCI. Patients with elevated CK-MB at baseline were excluded. The ethics committee of each participating center approved the study protocol, and all patients provided written, informed consent.

Procedures

PCI was performed using standard techniques (18,19). All patients undergoing PCI were prescribed aspirin plus clopidogrel before or during the coronary intervention. The standard anticoagulant during PCI was heparin. Use of intravascular ultrasound, adjunctive devices, or glycoprotein IIb/IIIa inhibitors was at the operator's discretion. After the procedure, aspirin was continued indefinitely, and clopidogrel was prescribed for at least 12 months.

Cardiac Enzyme Measurement

Routine CK-MB measurements, as measured by immunoassay, were obtained in all patients before PCI on admission in the department and after PCI, every 8 h for the first 24 h

and daily thereafter during hospitalization. CK-MB elevation was calculated as the ratio between the peak CK-MB and the upper reference limit (URL) for the participating laboratory of each study. All laboratory tests were performed by personnel unaware of patient information and study objectives.

Data Collection

Clinical, angiographic, procedural, and outcome data were prospectively recorded in a dedicated database by independent research personnel. Notably, these four registries used common standardized report form for MI including angina symptoms, electrocardiogram, serial cardiac enzyme measurement, and angiographic mechanisms of periprocedural MI. Chest pain was defined as the chest pain requiring electrocardiographic assessment and/or morphine injection. The 12-lead electrocardiograms were obtained before and after the PCI procedure, or if clinically indicated. After reviewing procedural angiography, the angiographic mechanism of periprocedural MI was recorded (20). Definitions of collecting variables are summarized in Supplementary Table 2. All data of interest were centrally collected, verified, and carefully adjudicated by an independent committee.

Endpoint, Definition, and Follow-up

The primary endpoint was defined as all-cause mortality, because it is the most robust and unbiased index, requiring no adjudication to avoid inaccurate or biased documentation and clinical assessments. Periprocedural MI was defined as CK-MB elevation ≥3 times the URL. Spontaneous MI was defined as any cardiac enzyme elevation with ischemic symptom and sign not related with the PCI procedure. Patients were clinically followed at 1, 6, and 12 months and annually thereafter via office visits or telephone call. Additional information was obtained as necessary from medical records from other hospitals.

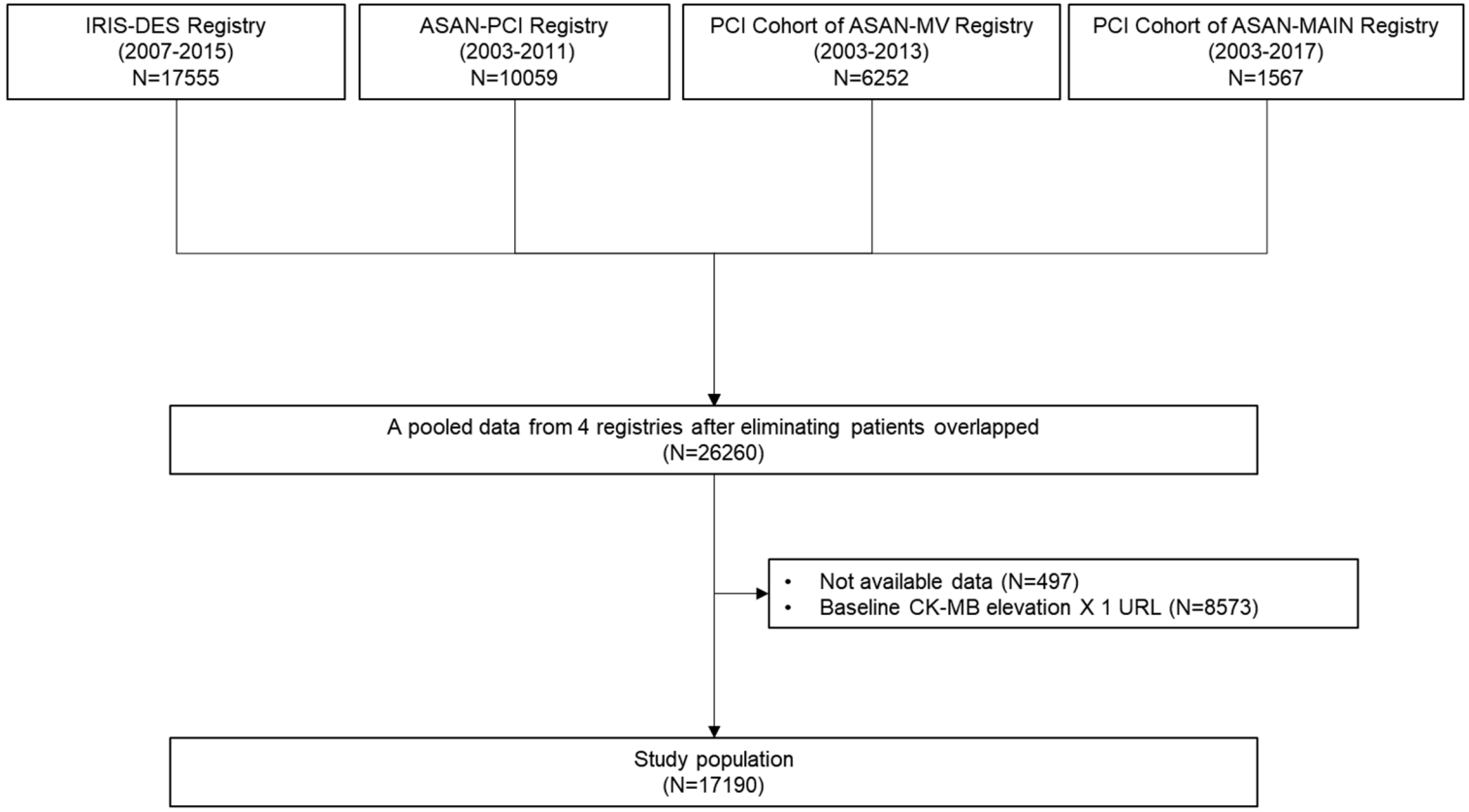
Statistical Analysis

Baseline characteristics were summarized for the patient groups as numbers (percentages) for categorical variables and as mean (standard deviation) for continuous variables. Differences in the parameters between the groups were compared using the Student's t-test for continuous variables and the chi-square test for categorical variables.

Stratified Cox proportional hazards models were used to estimate the adjusted association between various categories of periprocedural MI, spontaneous MI, and mortality. Clinically relevant variables (Table 1) were selected as potential risk-adjusting variables and entered into the multivariable model for estimating the adjusted treatment effect. In addition, to determine the criteria of periprocedural MI with mortality similar to spontaneous MI, we calculated the age-adjusted standardized mortality rates (SMRs) of periprocedural MI according to the CK-MB level. Standardized mortality rate was calculated as annualized mortality rate multiplied by a ratio of observed mortality to expected mortality in each category. Expected mortality was determined by applying indirect standardization method for age.

All reported P values were two sided, and a value of $P < 0.05$ was considered statistically significant. SAS software, version 9.1 (SAS Institute, Inc., Cary, NC), was used for all statistical analyses.

Figure 1. Study Flow



ASAN MAIN, ASAN Medical Center-Left Main; ASAN MV, ASAN Medical Center-Multivessel Disease; ASAN PCI, ASAN Medical Center-Percutaneous Coronary Intervention; IRIS-DES, Interventional Cardiology Research Incorporation Cardiology Research Incorporation Society-Drug-Eluting Stents

Results

Baseline Characteristics

Between July 2003 and September 2017, of the 17,190 eligible patients who received drug-eluting stent implantation, 1,594 patients (9.3%) have CK-MB elevation ≥3 times the URL (Figure 1). The distribution of CK-MB elevation is demonstrated in Supplementary Figure 1. Of those, 48.1% had chest pain requiring electrocardiographic assessment and/or morphine injection, 14.4% had electrocardiographic changes, and 70.3% had identifiable angiographic causes. The relationship between chest pain, electrocardiographic change, angiographic mechanism, and CK-MB elevation is shown in Figure 2. Patients with periprocedural MI were older, predominantly female, had unstable angina, lower body mass index, and were more frequently associated with complex coronary artery disease (Table 1).

Periprocedural MI Associated with a Higher Risk of Long-Term Mortality

During the median follow-up of 4.5 years (interquartile range: 3.2 to 5.2 years), 1167 deaths from any causes occurred. CK-MB elevation ≥3 times the URL was not associated with a higher risk of long-term mortality.

Figure 3 summarizes the adjusted risk of long-term mortality in various subgroups of periprocedural MI (CK-MB elevation ≥3 times the URL). Chest pain was not associated with mortality. Among electrocardiographic changes, newly developed Q wave was significantly associated with an increased long-term risk of mortality. New-onset left bundle branch block (LBBB) developed in four patients. Due to its rarity, statistical significance was not achieved. T-wave inversion was the most frequent change after PCI but was not associated with mortality. In addition, ST segment elevation or depression was clinically irrelevant. Procedural coronary angiograms of 1,367 patients with periprocedural MI were centrally collected and adjudicated

Table 1. Baseline Characteristics of Patients

	Total Cohort (N=17109)	PMI (N=1594)	SMI (N=189)	P Value*	P Value†
Age – yr	63.2 ±10.1	65.6 ±9.7	63.3 ±10.5	<0.001	0.91
Male sex – no. (%)	11664 (68.2)	1012 (63.5)	135 (71.4)	<0.001	0.38
Unstable angina – no. (%)	6837 (40.0)	702 (44.0)	101 (53.4)	0.001	<0.001
Body mass index‡	25.0 ±3.1	24.7 ±3.0	25.1 ±3.3	0.001	0.57
Hypertension – no. (%)	10719 (62.7)	1071 (67.2)	131 (69.3)	<0.001	0.07
Medically treated diabetes – no. (%)	5665 (33.1)	498 (31.2)	75 (39.7)	0.10	0.06
Current smoker – no. (%)	4108 (24.0)	345 (21.6)	54 (28.6)	0.022	0.16
Hyperlipidemia – no. (%)	7297 (42.7)	668 (41.9)	76 (40.2)	0.55	0.54
Previous bypass surgery – no. (%)	397 (2.3)	32 (2.0)	6 (3.2)	0.43	0.59
Previous myocardial infarction – no. (%)	1241 (7.3)	110 (6.9)	20 (10.6)	0.60	0.10
Previous PCI – no. (%)	2698 (15.8)	231 (14.5)	46 (24.3)	0.15	0.002
Previous heart failure – no. (%)	297 (1.7)	42 (2.6)	7 (3.7)	0.005	0.07
Previous stroke – no. (%)	1221 (7.1)	132 (8.3)	18 (9.5)	0.07	0.25
Peripheral vascular disease – no. (%)	380 (2.2)	51 (3.2)	7 (3.7)	0.007	0.25
Chronic renal failure – no. (%)	486 (2.8)	69 (4.3)	24 (12.7)	<0.001	<0.001
Chronic lung disease – no. (%)	318 (1.9)	32 (2.0)	5 (2.6)	0.72	0.59
Ejection fraction				<0.001	0.04
>50%	15717 (91.9)	1414 (88.7)	164 (86.8)		
40-50%	944 (5.5)	119 (7.5)	17 (9.0)		
<40%	448 (2.6)	61 (3.8)	8 (4.2)		
Left main disease – no. (%)	1332 (7.8)	177 (11.1)	15 (7.9)	<0.001	>0.99
Multivessel disease – no. (%)	9492 (55.5)	1202 (75.4)	130 (68.8)	<0.001	<0.001
Location of target vessel – no. (%)					
Left main	1694 (9.9)	224 (14.1)	19 (10.1)	<0.001	>0.99
Left anterior descending artery	11758 (68.7)	1243 (78.0)	129 (68.3)	<0.001	0.95
Left circumflex artery	4810 (28.1)	609 (38.2)	61 (32.3)	<0.001	0.23
Right coronary artery	5918 (34.6)	651 (40.8)	72 (38.1)	<0.001	0.35
Number of stent	1.8 ±1.1	2.5 ±1.4	2.0 ±1.1	<0.001	0.02

*P for the comparison between patients with or without periprocedural myocardial infarction.
†P for the comparison between patients with or without spontaneous myocardial infarction.
‡The body mass index is the weight in kilograms divided by the square of the height in meters. PCI, percutaneous coronary intervention; PMI, periprocedural myocardial infarction; SMI, spontaneous myocardial infarction

according to the prespecified definition of angiographic mechanisms. Side-branch occlusion was the most frequent cause of myocardial necrosis but was not significantly associated with mortality. In addition, the occlusion of large side branch ≥2 mm (70 patients) did not affect the long-term mortality risk (adjusted hazard ratio [aHR], 1.04; 95% confidence interval [CI], 0.43–2.53; P = 0.93). Main vessel complications including coronary artery perforation, distal embolization, no reflow, thrombus, and flow limiting dissection were significantly associated with the long-term mortality risk. Within subgroups of the main vessel complications, the increased mortality was observed in patients with perforation (aHR, 7.92; 95% CI, 1.96–32.0; P = 0.004) and distal embolization (aHR, 2.78; 95% CI, 1.47–5.23; P = 0.002). No reflow was associated with the increased tendency of mortality (aHR, 2.26; 95% CI, 0.93–5.47; P = 0.07) (Supplementary Figure 2). In a categorical analysis of CK-MB elevation, its elevations of 10–20 times the URL and of ≥20 times the URL were significantly associated with mortality.

On the basis of the above findings, the new criteria of clinically relevant periprocedural MI was defined as newly developed Q wave or main vessel complications with CK-MB elevation ≥3 times the URL or CK-MB elevation ≥10 times the URL. The incidence of the new criteria was 2.9% and was significantly associated with long-term mortality (aHR, 1.61; 95% CI, 1.20–2.14; P < 0.001). In addition, we evaluated the prognostic value of periprocedural MI defined by different working groups (Supplementary Table 3). The incidence of periprocedural MI according to the second and third universal definitions and the definition of the Society for Cardiovascular Angiography and Interventions (SCAI) consensus was 9.3%, 4.2%, and 2.4%, respectively. The increased mortality was associated with the third universal and SCAI definitions (Table 2).

Periprocedural MI with Long-Term Mortality Rate Similar to Spontaneous MI

Figure 2. Symptom and Sign of Periprocedural Myocardial Infarction

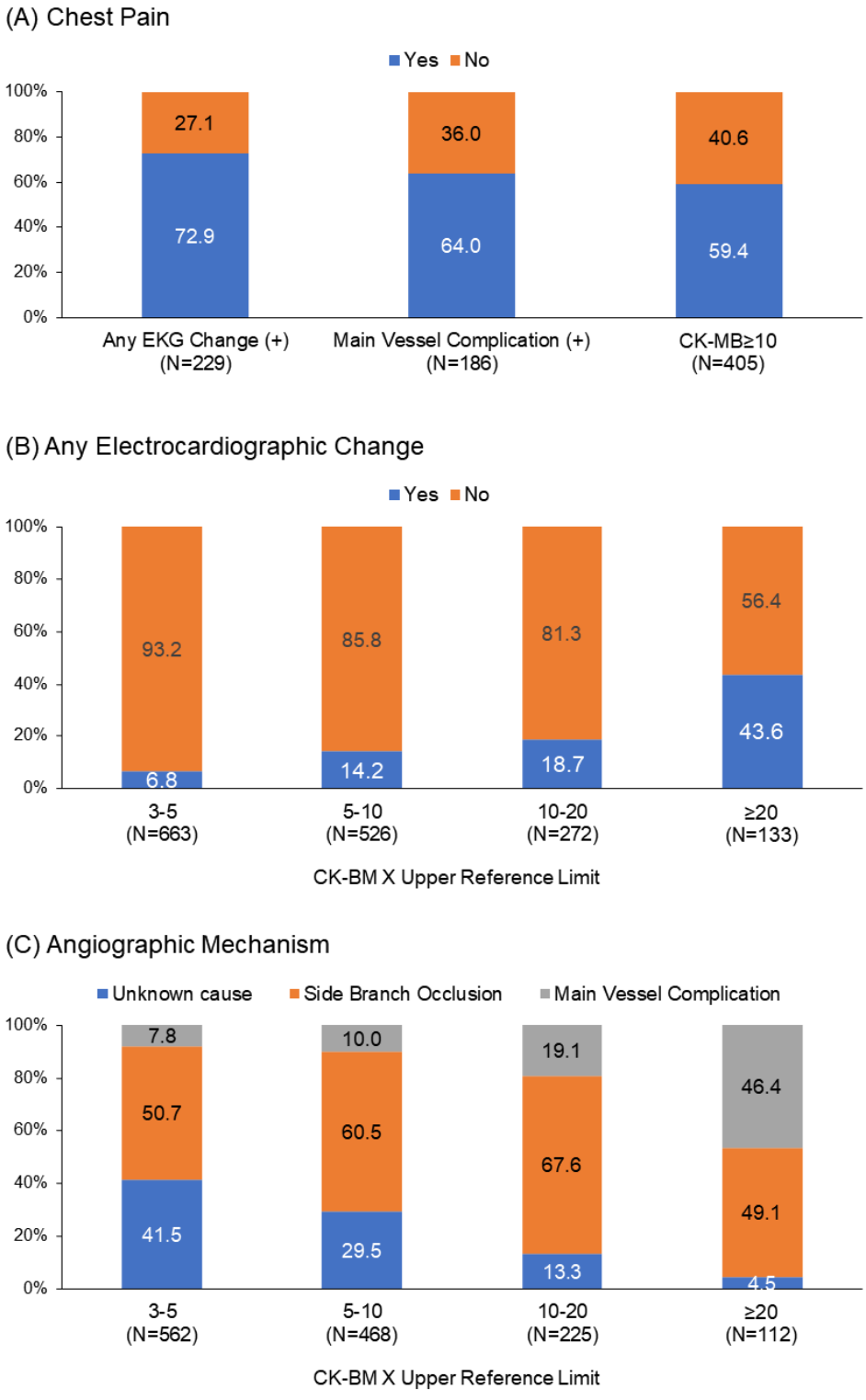
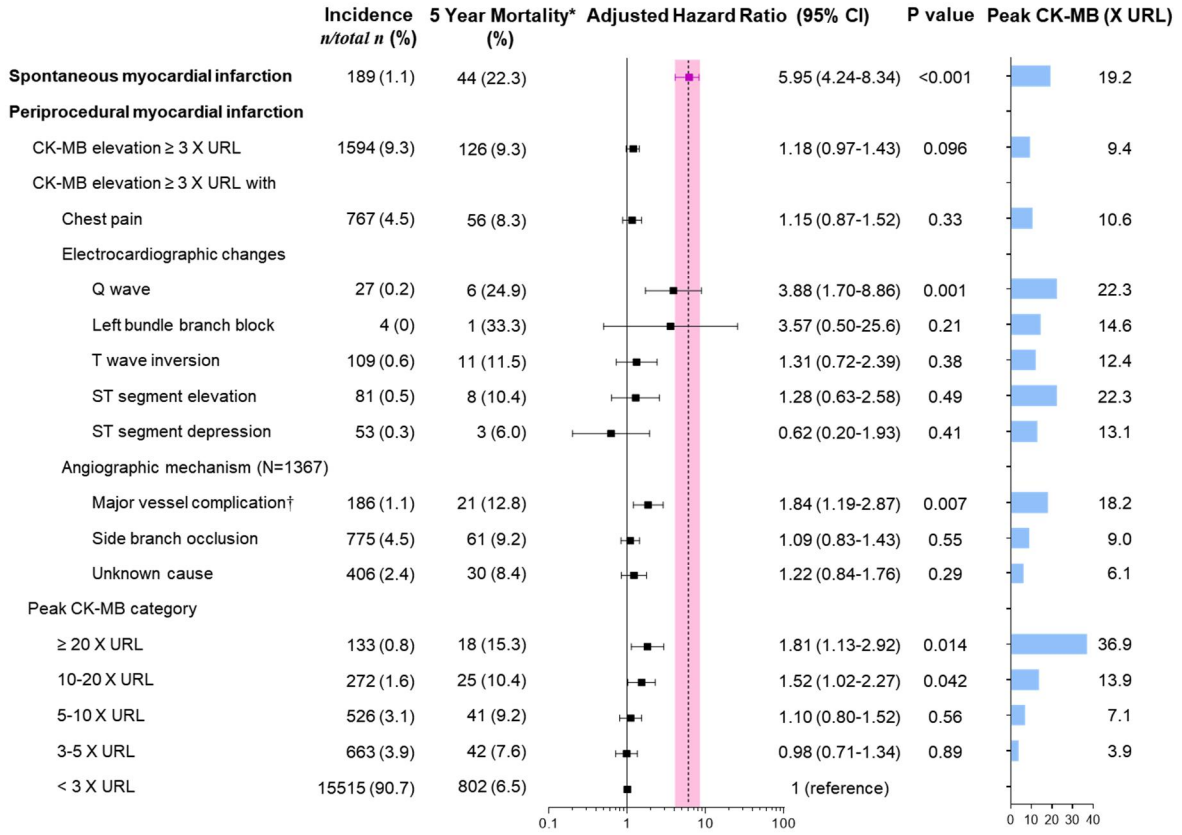


Figure 3. Risk of Long-Term Mortality in Subgroup of Periprocedural Myocardial Infarction and Spontaneous Myocardial Infarction



*Event rate was derived from Kaplan–Meier estimate. †Major vessel complication included coronary perforation, distal embolization, no reflow, thrombus, flow limiting dissection, and others. CI, confidence interval; URL, upper reference limit

Table 2. Criteria of Clinically Relevant Periprocedural Myocardial Infarction*

Criteria	Incidence	5-year mortality†	Adjusted HR (95% CI)	P value	Standardized mortality rate (95% CI)
Spontaneous myocardial infarction	1.1%	22.3%	5.95 (4.24-8.34)	<0.001	6.14 per 100 person-year (95% CI, 3.51-9.97)
Periprocedural myocardial infarction					
Second universal definition	9.3%	9.3%	1.18 (0.97-1.43)	0.098	1.68 per 100 person-year (95% CI, 1.17-2.34)
Third universal definition	4.2%	11.5%	1.48 (1.15-1.89)	0.002	1.96 per 100 person-year (95% CI, 1.17-3.08)
SCAI consensus document	2.4%	12.2%	1.61 (1.18-2.20)	0.002	2.31per 100 person-year (95% CI, 1.19-4.06)
New criteria‡	2.9%	11.6%	1.61 (1.20-2.14)	0.001	2.28 per 100 person-year (95% CI, 1.25-3.80)

*Definitions are summarized in Supplementary Table 3.

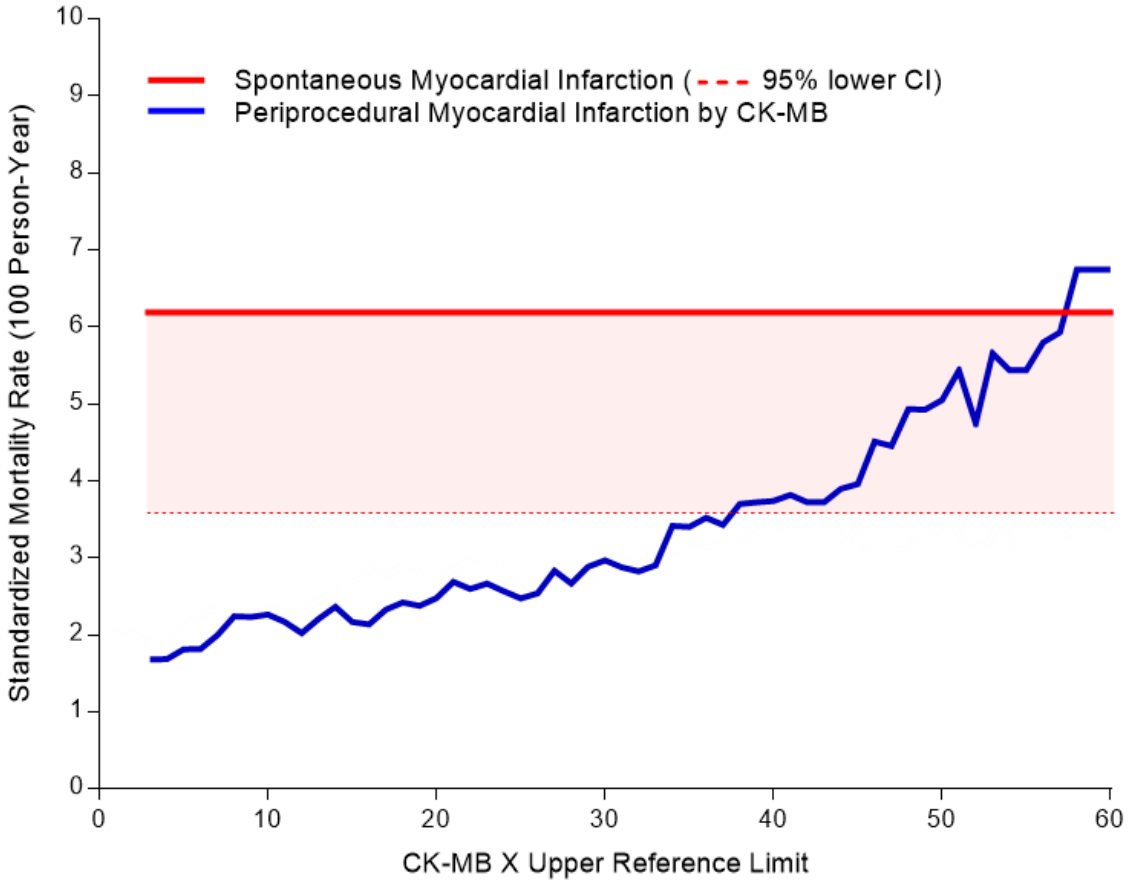
†Event rate was derived from Kaplan–Meier estimate.

‡New criteria from this study including variables only significantly associated with a higher risk of long-term mortality: newly developed Q wave or main vessel complications in patients with CK-MB elevation ≥3 times the upper reference limit or CK-MB elevation >10 times the upper reference limit.

CI, confidence interval; SCAI, Society for Cardiovascular Angiography and Interventions

During follow-up, 189 patients (1.1%) experienced spontaneous MI. The SMR of spontaneous MI was 6.14 per 100 person-year (95% CI, 3.51–9.97). The SMR of the new criteria of periprocedural MI was 2.28 per 100 person-year (95% CI, 1.25–3.80). The SMRs of third and SCAI definitions were 1.96 per 100 person-year (95% CI, 1.17–3.08) and 2.31 per 100 person-year (95% CI, 1.19–4.06), respectively (Table 2). Figure 4 depicts the SMR of periprocedural MI according to the CK-MB elevation. The SMR curve of periprocedural MI crossed the 95% lower CI of spontaneous MI at 36 times the URL of CK-MB elevation. The CK-MB threshold for periprocedural MI that achieved the same prognosis as spontaneous MI was 58 times the URL. In addition, the SMR of the newly developed Q wave and main vessel complications were 4.0 per 100 person-year (95% CI, 0.29–17.1) and 2.45 per 100 person-year (95% CI, 0.87–5.44), respectively.

Figure 4. Cardiac Enzyme Threshold of Periprocedural Myocardial Infarction Compared With Spontaneous Myocardial Infarction



Discussion

This large, prospective observational study is the first to systematically demonstrate the criteria of clinically relevant periprocedural MI based on cardiac enzyme and supportive clinical features in patients without CK-MB elevation before PCI. The criteria of periprocedural MI significantly associated with a higher risk of mortality was newly developed Q wave or main vessel complications with CK-MB elevation ≥3 times the URL or CK-MB elevation >10 times the URL. Nevertheless, clinically relevant periprocedural MI showed a lower mortality rate compared with spontaneous MI. The peak CK-MB cutoff value for periprocedural MI that achieved the same prognosis as spontaneous MI was 58 times the URL. This study provided valuable information for redefining the criteria of clinically relevant periprocedural MI. In addition, the finding of the inequivalent prognostic value between periprocedural MI and spontaneous MI should be considered in daily practice and in appropriate interpretation and design of clinical trials.

This study showed that only large periprocedural MI (CK-MB >10 times the URL or Q wave) was significantly associated with a risk of long-term mortality. Previous studies have conflicting results regarding cardiac enzyme elevation. Some studies showed no relationship between periprocedural cardiac enzyme elevation and mortality. Others showed significant relationship, but the threshold value was different. However, previous studies were limited by the lack of appropriate adjudication and categorical analysis (3–5, 5–10, and >10) (6). In this study, we performed vigorous adjustment using various potential confounders and categorical analysis and showed that the mortality started to increase at CK-BM elevation >10 times the URL. A low degree of CK-MB elevation was not associated with long-term mortality.

The newly developed Q wave is a traditional marker of MI. In a previous study, the incidence of Q wave after PCI was 0.6% and associated with about 10-fold risk of long-term mortality (21). Similarly, in this study, Q wave was rare (0.2%), but was associated with about

four-fold increased risk of long-term mortality. The new-onset LBBB could be an important criterion of clinically relevant periprocedural MI. However, due to its rarity, statistical significance was not achieved. Other ischemic changes in electrocardiogram did not have significant prognostic value. Interestingly, ST elevation was associated with high peak CK-BM level but was not associated with a risk of long-term mortality. This could be explained by early surge of CK-MB caused by transient myocardial damage.

Side-branch occlusion was the most frequent angiographic mechanism, accounting for 56.7% of periprocedural MI. However, even large side-branch (>2 mm) occlusion was not associated with a higher risk of mortality, probably due to the relatively small supplying myocardial territory and less severe myonecrosis. Conversely, main vessel complications increased the long-term risk of mortality because of the large myocardial damage supported by high CK-MB elevation. Operators should focus more on preventing major vascular complication in the main coronary arteries. Moreover, about 30% of patients with periprocedural MI had no identifiable angiographic mechanisms, as explained by functional or structural microvascular obstruction, which was not associated with worse survival (20).

The chest discomfort longer than 20 min was considered the sign of prolonged ischemia in the universal definition (8). Instead of non-specific definition, we applied more strict criteria: chest pain requiring electrocardiographic evaluation and/or morphine injection. However, predefined severe chest pain was not significantly associated with mortality. In addition, about 27.1% and 40.6% of asymptomatic patients had electrocardiographic changes and CK-MB elevation >10 times the URL. Therefore, chest pain did not appear to be a gatekeeper for detecting significant periprocedural MI. Routine cardiac enzyme measurement or electrocardiography assessment should be considered post-PCI periods even in asymptomatic patients.

The higher long-term mortality of spontaneous MI than periprocedural MI could be

explained by different pathophysiology and patient characteristics. Spontaneous MI occurred because of plaque rupture or supply–demand mismatch in case of severe coronary artery disease and was diagnosed only in selected patients at risk with concerning symptom and sign who sought medical care (6,22). Periprocedural MI is related with procedural complications, whose detrimental effect would be attenuated by restoring antegrade flow by PCI. In addition, as immediate attempt to correct flow limitation was carried out in most cases, periprocedural MI may have much shorter ischemic time and smaller amount of myocardial damage compared with spontaneous MI (6,22). Yet, it is noteworthy that periprocedural MI with very high elevated CK-MB showed prognostic equivalence.

In clinical trials, spontaneous and periprocedural MI were frequently considered as the same MI events using equal weighting based on the assumption that they are of similar clinical relevance (13,23). However, the risk difference between two types of MI shown in our study and others (22-24) is strongly against those approaches because it carried the risk that the effect of rare but more clinically important spontaneous MI could be diluted by more common but less prognostically relevant procedural MI (13,23). Moreover, our findings support the recommendation of separately reporting spontaneous and periprocedural MI and of reporting infarct size using area under the curve or peak cardiac enzyme level (7,8,13).

This study has several limitations. First, we did not have serial measurement of cardiac troponins because of government insurance policy. Although cardiac troponins have become the key diagnostic test in patients with suspected spontaneous MI, the relationship between cardiac troponins and mortality in patients with periprocedural MI was less evident, and it is too sensitive to detect myocardial necrosis associated with PCI (9,25,26). Accordingly, recent criteria of academic research consortium-2 and fourth universal definition (10,11) could not be evaluated in this study. Second, serial myocardial image or echocardiography to assess for new loss of viable myocardium due to periprocedural MI was not performed in this registry because

in clinical practice, it is not standard care unless patients had serious complication during PCI (8,10). However, adding to other criteria, the incidence and prognostic value of new loss of viable myocardium in periprocedural MI should be evaluated in future studies. Third, we studied only patients without cardiac enzyme elevation prior to PCI. Clinically relevant criteria of patients with baseline cardiac enzyme elevation will be studied in other studies. Fourth, outcomes other than mortality including angina scale, heart failure, exercise performance, quality of life, and rehospitalization were not evaluated (12). Finally, as an observational analysis, unmeasured residual confounders related to myonecrosis and mortality or selection bias cannot be completely excluded although numerous clinical, angiographic, and procedural factors associated with mortality were adjusted.

Conclusion

Increased mortality was associated only with large infarct size evidenced by highly elevated cardiac enzyme or newly developed Q wave or with angiographic complications in patients with periprocedural MI. Nevertheless, clinically relevant periprocedural MI showed a lower mortality risk than spontaneous MI. Future research should address the criteria of clinically relevant periprocedural MI in patients with elevated cardiac enzyme at baseline. In addition, cardiac enzyme threshold using cardiac specific troponin test should be evaluated.

References

1. Benjamin EJ, Blaha MJ, Chiuve SE et al. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. Circulation 2017;135:e146-e603.
2. Barbato E, Dudek D, Baumbach A, Windecker S, Haude M. Current trends in coronary interventions: an overview from the EAPCI registries. EuroIntervention 2017;13:Z8-Z10.
3. Li J, Dharmarajan K, Li X et al. Protocol for the China PEACE (Patient-centered Evaluative Assessment of Cardiac Events) retrospective study of coronary catheterisation and percutaneous coronary intervention. BMJ open 2014;4:e004595.
4. Jang JS, Han KR, Moon KW et al. The Current Status of Percutaneous Coronary Intervention in Korea: Based on Year 2014 Cohort of Korean Percutaneous Coronary Intervention (K-PCI) Registry. Korean Circ J 2017;47:328-340.
5. Cho MS, Ahn JM, Lee CH et al. Differential Rates and Clinical Significance of Periprocedural Myocardial Infarction After Stenting or Bypass Surgery for Multivessel Coronary Disease According to Various Definitions. JACC Cardiovasc Interv 2017;10:1498-1507.
6. Prasad A, Herrmann J. Myocardial infarction due to percutaneous coronary intervention. N Engl J Med 2011;364:453-64.
7. Thygesen K, Alpert JS, White HD et al. Universal definition of myocardial infarction. J Am Coll Cardiol 2007;50:2173-95.
8. Thygesen K, Alpert JS, Jaffe AS et al. Third Universal Definition of Myocardial Infarction. J Am Coll Cardiol 2012;60:1581-1598.
9. Moussa ID, Klein LW, Shah B et al. Consideration of a new definition of clinically relevant myocardial infarction after coronary revascularization: an expert consensus

document from the Society for Cardiovascular Angiography and Interventions (SCAI). J Am Coll Cardiol 2013;62:1563-70.

10. Garcia-Garcia HM, McFadden EP, Farb A et al. Standardized End Point Definitions for Coronary Intervention Trials: The Academic Research Consortium-2 Consensus Document. Circulation 2018;137:2635-2650.

11. Thygesen K AJ, Jaffe AS et al. Fourth Universal Definition of Myocardial Infarction (2018). Circulation 2018 (in press).

12. Stone GW. Periprocedural Myocardial Infarction: The "SCAI" Is the Limit. JACC Cardiovasc Interv 2016;9:2229-2231.

13. Leonardi S, Armstrong PW, Schulte PJ, Ohman EM, Newby LK. Implementation of standardized assessment and reporting of myocardial infarction in contemporary randomized controlled trials: a systematic review. Eur Heart J 2013;34:894-902d.

14. Park DW, Kim YH, Song HG et al. Outcomes after unrestricted use of everolimus-eluting and sirolimus-eluting stents in routine clinical practice: a multicenter, prospective cohort study. Circ Cardiovasc Interv 2012;5:365-71.

15. Park DW, Kim YH, Song HG et al. Long-term comparison of drug-eluting stents and coronary artery bypass grafting for multivessel coronary revascularization: 5-year outcomes from the Asan Medical Center-Multivessel Revascularization Registry. J Am Coll Cardiol 2011;57:128-37.

16. Park DW, Kim YH, Yun SC et al. Long-term outcomes after stenting versus coronary artery bypass grafting for unprotected left main coronary artery disease: 10-year results of bare-metal stents and 5-year results of drug-eluting stents from the ASAN-MAIN (ASAN Medical Center-Left MAIN Revascularization) Registry. J Am Coll Cardiol 2010;56:1366-75.

17. Park SJ, Ahn JM, Park GM et al. Trends in the outcomes of percutaneous coronary

intervention with the routine incorporation of fractional flow reserve in real practice. Eur Heart J 2013;34:3353-61.

18. Park SJ, Kim YH, Park DW et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease. N Engl J Med 2011;364:1718-27.

19. Park SJ, Ahn JM, Kim YH et al. Trial of everolimus-eluting stents or bypass surgery for coronary disease. N Engl J Med 2015;372:1204-12.

20. Park DW, Kim YH, Yun SC et al. Impact of the angiographic mechanisms underlying periprocedural myocardial infarction after drug-eluting stent implantation. Am J Cardiol 2014;113:1105-10.

21. Stone GW, Mehran R, Dangas G, Lansky AJ, Kornowski R, Leon MB. Differential impact on survival of electrocardiographic Q-wave versus enzymatic myocardial infarction after percutaneous intervention: a device-specific analysis of 7147 patients. Circulation 2001;104:642-7.

22. Bangalore S, Pencina MJ, Kleiman NS, Cohen DJ. Prognostic implications of procedural vs spontaneous myocardial infarction: results from the Evaluation of Drug Eluting Stents and Ischemic Events (EVENT) registry. Am Heart J 2013;166:1027-34.

23. Leonardi S, Thomas L, Neely ML et al. Comparison of the prognosis of spontaneous and percutaneous coronary intervention-related myocardial infarction. J Am Coll Cardiol 2012;60:2296-304.

24. Prasad A, Gersh BJ, Bertrand ME et al. Prognostic significance of periprocedural versus spontaneously occurring myocardial infarction after percutaneous coronary intervention in patients with acute coronary syndromes: an analysis from the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial. J Am Coll Cardiol 2009;54:477-86.

25. Cockburn J, Behan M, de Belder A et al. Use of troponin to diagnose periprocedural

myocardial infarction: effect on composite endpoints in the British Bifurcation Coronary Study (BBC ONE). Heart 2012;98:1431-5.

26. Lim CC, van Gaal WJ, Testa L et al. With the "universal definition," measurement of creatine kinase-myocardial band rather than troponin allows more accurate diagnosis of periprocedural necrosis and infarction after coronary intervention. J Am Coll Cardiol 2011;57:653-61.

국문 요약

목적: 경피적 관상동맥 중재술과 관련된 임상적으로 의미 있는 심근경색증의 기준은 논쟁의 여지가 있어, 장기 사망률의 증가 및 자발성 심근경색증과 유사한 장기 사망률을 보이는 경피적 관상동맥 중재술 관련 심근경색증의 기준을 결정하고자 하였다.

방법: 4 개의 대규모 경피적 관상동맥 중재술 레지스트리를 바탕으로 하여, 약물 방출 스텐트 삽입술을 시행받은 환자 중, 시술 전 심근효소치가 정상인 17,190 명의 환자를 분석하였다. 흉통의 양상, 심근효소치, 심전도 변화 및 시술 합병증을 전향적으로 수집하여 등록하였다. 일차 평가 변수는 평균 추적 관찰 기간 동안 (4.5 년; 사분위 범위, 3.2–5.2 년) 발생한 모든 사망으로 하였다.

결과: 장기 사망률의 증가와 관련 있는 심근경색증은 심근효소치가 기준보다 3 배이상 상승하면서, 심전도에서 새롭게 발생하는 Q 파가 관찰되거나, 혹은 혈관조영술에서 관찰되는 주혈관 합병증의 발생 혹은 심근효소치의 10 배이상의 상승으로 정의 할 수 있었다. (incidence, 2.9%; adjusted hazard ratio, 1.61; 95% confidence interval, 1.20-2.14; P=0.001). 그러나, 새로운 진단기준을 적용하여도, 장기 사망률은 자발적 심근경색증보다 통계적으로 의미있게 낮았다 (2.28 per 100 person-year versus 6.14 per 100 person-year). 자발적 심근경색증과 유사한 사망률을 가진 관상동맥 중재술 관련 심근경색증의 심근효소의 상승은 정상의 58 배였다.

결론: 본 연구는 심근효소 상승 및 임상적 특징의 조합에 기초하여 장기 사망률이 높은 관상동맥 중재술 관련 심근경색증의 기준을 제시하였다는데 학문적 의의가 있다. 그럼에도 불구하고, 임상적으로 의미 있는 관상동맥 중재술 관련 심근경색증은 자발성 심근경색증 보다 낮은 사망률을 보였다.

중심단어: 심근경색증, 관상동맥중재술, 스텐트