ORIGINAL ARTICLE

Relationship between an infarct-related artery, acute total coronary occlusion, and mortality in patients with ST-segment and non-ST-segment myocardial infarction

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KEY WORDS

angiography, coronary artery occlusion, mortality, non-ST--segment elevation myocardial infarction, ST-segment elevation myocardial infarction

ABSTRACT

INTRODUCTION The prevalence of total coronary occlusion of an infarct-related artery (IRA) and its impact on the outcome can differ between patients with non-ST-elevation myocardial infarction (NSTEMI) and those with ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI).

OBJECTIVES We evaluated the impact of IRA occlusion on the outcome of myocardial infarction according to the presence or absence of ST-segment elevation and the location of the culprit lesion.

PATIENTS AND METHODS We analyzed 4581 patients with STEMI and 2717 patients with NSTEMI who underwent PCI and were enrolled in the Polish Registry of Acute Coronary Syndromes. Patients were divided into 3 cohorts depending on the IRA: left anterior descending artery (LAD), left circumflex artery (LCx), or right coronary artery (RCA). Patients were further divided according to preprocedural Thrombolysis in Myocardial Infarction (TIMI) flow to either a subgroup with total occlusion (TO; TIMI flow grade, 0) or a subgroup with incomplete occlusion (nTO; TIMI flow grade ≥1).

RESULTS TO was observed in 2949 patients (64.4%) with STEMI and 723 patients (26.6%) with NSTEMI. The most common IRAs were the RCA (49.4%) and LCx (48.4%) in the STEMI and NSTEMI groups, respectively. STEMI patients with TO of the LAD showed higher mortality during the 36-month follow-up; mortality in the NSTEMI group was comparable between patients with TO and nTO. STEMI and NSTEMI groups with TO of the LCx showed higher in-hospital mortality. No differences were observed between patients with TO and nTO of the RCA.

CONCLUSIONS Totally occluded IRA (TIMI flow grade 0) on baseline angiogram was not associated with higher 36-month mortality rates after both NSTEMI and STEMI treated with PCI in comparison with patients with patent IRA except for totally occluded LAD in STEMI.

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INTRODUCTION Despite recent progress in cardiology, patients with myocardial infarction (MI) have shown only a slight decrease in the 12-month mortality rate.[1] Knowledge of coronary angiographic findings may help design more rational therapeutic strategies to improve clinical outcomes in these patients. Electrocardiography (ECG) remains the primary tool for identifying acute MI, and starting an emergent reperfusion strategy typically depends on the presence of ST--segment elevation in a surface 12-lead ECG.[2,3] However, it is well known that the sensitivity of ECG in the detection of total occlusion (TO) of the infarct-related artery (IRA) is suboptimal, particularly for posterolateral circulation.[4-8] Therefore, the incidence and clinical outcome of TO may differ depending on the coronary artery involved.

A lack of typical ECG presentation may delay prompt restoration of blood flow in the coronary artery and results in significant complications, including larger infarct sizes and higher mortality rates.[6] Conversely, electrocardiographic findings or clinical presentation on admission may be more predictive of the outcome than the presence or absence of TO. Accordingly, in the present study, we evaluated the impact of TO of the IRA on the outcome of MI, according to the presence or absence of ST-segment elevation and the location of the culprit lesion.

PATIENTS AND METHODS

Design of the registry

Data were obtained from the Polish Registry of Acute Coronary Syndromes (PL-ACS), the design of which has been described previously.[9] In brief, the PL-ACS registry is an ongoing, nationwide, multicenter, prospective, observational study of hospitalized patients, encompassing the entire spectrum of acute coronary syndromes (ACSs) in Poland. All Polish regions collect data for the registry. A detailed protocol with the inclusion and exclusion criteria, methods, logistics, and definitions of all fields in the registry dataset was prepared before the registry was started. The protocol was revised in May 2004 to comply with the Cardiology Audit and Registration Data Standards.[10] Patients with suspected ACS were screened for eligibility but were not enrolled until ACS was confirmed. If a patient was transferred to another hospital during the acute phase of MI, both hospitals were required to complete the case report form (CRF). Such dual hospitalizations were combined during data processing, and were subsequently analyzed as a single case.

Data collection CRFs, necessary for inclusion in the PL-ACS, were completed by attending physicians. CRFs included 125 fields pertaining to the demographic, clinical, and electrocardiographic characteristics of the patient; laboratory findings; diagnostic and treatment modalities; and in-hospital outcomes. In each hospital, an electronic version of the CRF was prepared, and initial edit checks were performed with dedicated software. Once a month, data were encoded and sent to the National Health Fund (in Polish, Narodowy Fundusz Zdrowia [NFZ]), a public health insurance institution, where they were compared with the standard CRF sent by the hospitals. After verification, data were sent to the central database. Follow-up data regarding posthospital mid- and long-term mortality rates were obtained from the NFZ. Because the NFZ insurance policy is obligatory for all Polish citizens, follow-up data were available for all patients.

Patients and definitions The study included patients with a confirmed ACS who were treated with percutaneous coronary intervention (PCI) between January and December 2008 and were registered in the PL-ACS. Patients with prior MI, PCI, coronary artery bypass grafting, or the left main coronary artery as the IRA were excluded from the analysis. Among the 7068 patients, 4581 presented with ST-segment elevation MI (STEMI) and 2717 presented with non-ST-segment elevation MI (NSTEMI).

Patients were divided into 3 cohorts according to the location of the culprit lesion: left anterior descending artery (LAD), left circumflex artery (LCx), or right coronary artery (RCA). Coronary flow prior to PCI was classified using the Thrombolysis in Myocardial Infarction (TIMI) flow grading system.[11] Each cohort was divided according to the TIMI flow grade assessed with angiography. A baseline TIMI flow grade of 0 was defined as TO, while a baseline TIMI flow grade of 1 or higher was defined as incomplete occlusion (nTO).

STEMI was diagnosed according to the presence of ST-segment elevation of 2 mm or higher in the adjacent chest leads, ST-segment elevation exceeding 1 mm in 2 or more standard leads, or a new left bundle branch block and positive cardiac markers. NSTEMI was defined as the absence of ST-elevation in the context of clinical and cardiac enzyme features that were indicative of a diagnosis of MI, specifically troponin values. A coronary artery was considered an IRA (culprit) on the basis of angiographic features (definite or suspected thrombus, ruptured or ulcerated plaque, or TIMI flow grade ≤2), ECG recordings, and echocardiographic findings.

In-hospital and long-term mortalities were defined on the basis of all-cause death (cardiac and noncardiac). Global Registry of Acute Coronary Events (GRACE) scores were calculated during data analysis using age, heart rate, systolic blood pressure, serum creatinine, Killip class at presentation, cardiac arrest on admission, elevated cardiac biomarkers, and ST deviation parameters. Diabetes, hypertension, or renal failure were diagnosed at the discretion of the attending physician, or were diagnosed and treated prior to presentation with ACS. Ejection fraction was assessed in the first echocardiography after hospital admission. MI symptoms (eg, typical chest pain, dyspnea) were determined by attending physicians. Enzymatic infarct size was evaluated using the maximum serum levels of creatine kinase MB isoenzyme (CK-MB) during hospitalization. Decisions related to treatment modalities (ie, stents, intraaortic balloon pumps, anti-GPIIb/IIIa antibodies, and methods of angioplasty) were at the discretion of the operators. Multivessel disease was defined as a stenosis of 70% or higher in at least 2 major epicardial coronary arteries, or of 50% or higher in the left main coronary artery.

Statistical analysis Numerical variables were presented as arithmetic mean values with SD for normal distribution or as median with interquartile range for nonnormal distributions. Normality was verified using the Kolmogorow–Smirnow test. The groups were compared using the 2-sample *t* test or the nonparametric

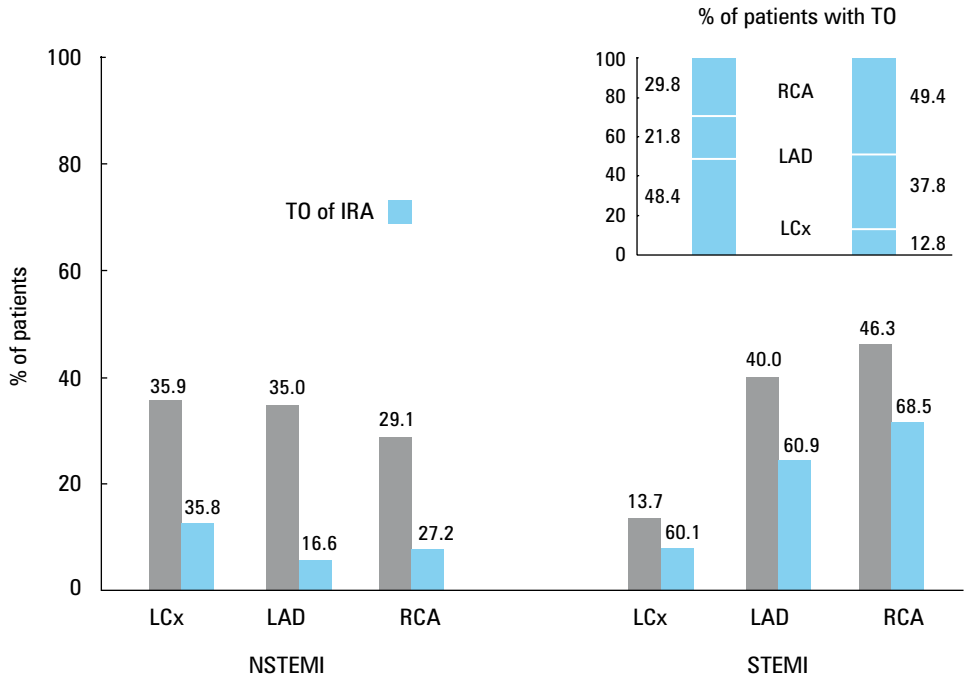

FIGURE 1 Distribution of infarct-related artery location and incidence of total occlusion depending on the type of myocardial infarction
Abbreviations: IRA, infarct-related artery; LAD, left anterior descending artery; LCx, left circumflex artery; NSTEMI, non-ST-segment elevation myocardial infarction; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction; TO, total occlusion

TABLE 1 Baseline clinical characteristics stratified by the type of myocardial infarction and preprocedural Thrombolysis in Myocardial Infarction Flow

Variable	NSTEMI (n = 2717)	STEMI (n = 4581)	TIMI 0 (n = 3672)	TIMI 1–3 (n = 3626)	*P* value	
					STEMI vs NSTEMI	TIMI 0 vs 1–3
Age, y, mean (SD)	64.4 (11.3)	62.4 (11.6)	62.5 (11.7)	63.8 (11.3)	<0.0001	0.04
Hypertension, n (%)	1943 (1.5)	2747 (60.0)	2241 (61.0)	2449 (67.5)	<0.0001	<0.0001
Diabetes mellitus, n(%)	668 (24.6)	889 (19.4)	734 (20.0)	823 (22.7)	<0.0001	0.005
Hyperlipidemia, n (%)	1116 (41.1)	1729 (37.7)	1383 (37.7)	1462 (40.3)	0.005	0.02
Current smokers, n (%)	736 (27.1)	1765 (38.5)	1371 (37.3)	1130 (31.2)	<0.0001	<0.0001
LVEF, %, mean (SD)	49.8 (9.7)	47.3 (9.4)	47.2 (9.5)	49.2 (9.6)	<0.0001	<0.0001
GRACE, points, mean (SD)	131.3 (32.8)	146.9 (32.2)	144.9 (34.0)	137.3 (32.1)	<0.0001	0.002
Max. CK-MB, mg/dl, median (IQR)	40 (21–89)	126 (52–241)	136 (55–256)	51.0 (25–125)	<0.0001	<0.0001
SBP, mmHg, mean (SD)	139.6 (24.5)	132.2 (26.3)	132.0 (26.2)	138.0 (25.2)	<0.0001	<0.0001
Time from symptoms to PCI, h, median (IQR)	14.3 (6.2–44.7)	4.95 (3.0–9.2)	5.6 (3.2–11.8)	8.2 (4.0–23.8)	<0.0001	0.001
Final TIMI flow grade 3, n (%)	2569 (94.6)	4235 (92.4)	3270 (89.1)	3534 (97.5)	0.0005	<0.0001
MVD, n (%)	1293 (47.6)	1853 (40.4)	1552 (42.3)	1594 (44.0)	<0.0001	0.14
Anti-GP IIb/IIIa, n (%)	156 (5.7)	1135 (24.8)	934 (25.4)	357 (9.8)	<0.0001	<0.0001

Abbreviations: anti-GP IIb/IIIa, anti-glycoprotein IIb/IIIa antibodies; CK-MB, creatine kinase MB isoenzyme; IQR, interquartile range; LVEF, left ventricular ejection fraction; MVD, multivessel disease; SBP, systolic blood pressure; TIMI, Thrombolysis in Myocardial Infarction; others, see **FIGURE 1**

Mann–Whitney test, as appropriate. Categorical data were presented as absolute and relative frequencies. The differences in proportions between the groups were analyzed using the χ^2 test.

First, to determine possible predictors of 1- and 36-month mortality, variables were assessed in a univariate analysis. A multivariate logistic regression model was then developed using a directed stepwise approach. All variables with a *P* value of less than 0.1 were entered in the model. Correlated variables were not entered in the same multivariate model. Factors that met the significance criteria of less than 0.05 were retained in the final model. Hypotheses were verified at a significance level of *P* value of less than 0.05 with 2-sided testing. The statistical analysis was performed with SAS statistical package, version 9.2 (SAS Institute Inc., Cary, North Carolina, United States).

RESULTS Among the 7068 patients with MI, 4581 were diagnosed with STEMI and 2717 were diagnosed with NSTEMI. Of these patients, TO was identified in 2949 patients with STEMI (64.4%) and 723 patients with NSTEMI (26.6%). The most common IRAs in patients with TO were the RCA in the STEMI group (RCA, 49.4%; LAD, 37.8%; LCx, 12.8%) and the LCx in the NSTEMI group (LCx, 48.4%; LAD, 21.8%; RCA, 29.8%). Data are

TABLE 2 Clinical characteristics of patients with the left anterior descending artery as the infarct-related artery

Variable	NSTEMI (n = 949)			STEMI (n = 1831)			*P* value	
	TIMI 0 (n = 158)	TIMI 1–3 (n = 791)	*P* value	TIMI 0 (n = 1116)	TIMI 1–3 (n = 715)	*P* value	TO NSTEMI vs TO STEMI	NSTEMI vs STEMI
Sex, male, n (%)	97 (61.4)	506 (64.1)	0.53	726 (65.1)	497 (69.5)	0.04	0.37	0.09
Age, y, mean (SD)	64.0 (12.6)	65.7 (11.4)	0.11	62.7 (12.1)	62.4 (11.7)	0.62	0.19	<0.0001
Diabetes mellitus, n (%)	37 (23.4)	223 (28.2)	0.23	236 (21.1)	133 (18.6)	0.18	0.51	<0.0001
Hypertension, n (%)	120 (75.9)	580 (73.3)	0.49	664 (59.5)	424 (59.3)	0.93	<0.0001	<0.0001
Hyperlipidemia, n (%)	46 (29.1)	335 (42.3)	0.002	405 (36.3)	273 (38.2)	0.41	0.08	0.12
Current smokers, n (%)	30 (19.9)	175 (22.1)	0.38	392 (35.1)	260 (36.4)	0.59	<0.0001	<0.0001
Typical chest pain, n (%)	147 (93.0)	728 (92.0)	0.70	1071 (96.0)	684 (95.7)	0.75	0.09	<0.0001
Time from symptoms to PCI, h, median (IQR)	12.0 (5.7–30.0)	15.5 (6.3–53.6)	0.05	4.8 (2.9–9.0)	5.3 (3.2–10.3)	0.002	<0.0001	<0.0001
Killip class ≥III, n (%)	3 (1.9)	18 (2.3)	1.0	70 (6.3)	26 (3.6)	0.01	0.03	0.0002
GRACE score, points, mean (SD)	129.3 (31.4)	131.5 (32.0)	0.42	150.7 (34.6)	144.7 (29.6)	<0.0001	<0.0001	<0.0001
LVEF, %, mean (SD)	46.9 (10.7)	49.3 (9.8)	0.01	42.4 (9.7)	45.2 (9.7)	<0.0001	<0.0001	<0.0001
Postprocedural TIMI flow grade 3, n (%)	130 (82.3)	777 (98.2)	<0.0001	997 (89.3)	693 (96.6)	<0.0001	0.009	0.0010
Max. CK-MB, mg/dl, median (IQR)	59 (25–123)	29 (15–49)	<0.0001	165 (74–304)	84 (39–197)	<0.0001	<0.0001	<0.0001
Coronary stenting, n (%)	132 (83.5)	771 (97.5)	<0.0001	1049 (94.0)	686 (95.9)	0.07	<0.0001	0.66
DES, n (%)	5 (3.8)	68 (8.8)	0.0500	18 (1.7)	29 (4.2)	0.0016	0.1680	0.0004
Anti-GP IIb/IIIa, n (%)	15 (9.5)	35 (4.4)	0.009	369 (33.1)	128 (17.9)	<0.0001	<0.0001	<0.0001

Abbreviations: DES, drug-eluting stent; others, see TABLE 1 and FIGURE 1

presented in FIGURE 1. The baseline clinical characteristics of the study groups are shown in TABLE 1.

Patient cohorts depending on the infarct-related artery

Left anterior descending artery In patients with STEMI with the LAD as the culprit artery, the TO subgroup had shorter time since admission to angioplasty, higher incidence of heart failure symptoms on admission, lower ejection fraction, greater enzymatic infarct size, higher mean GRACE risk score, lower incidence of the final TIMI flow grade 3, more frequent use of anti-IIb/IIIa antibodies, and a lower proportion of male patients than the nTO subgroup.

In patients with NSTEMI with the LAD as the culprit artery, the TO subgroup showed a lower incidence of hyperlipidemia, lower ejection fraction, greater enzymatic infarct size, lower frequency of the final TIMI flow grade 3 and coronary stenting, and more frequent use of glycoprotein IIb/IIIa inhibitors than the nTO subgroup. Clinical characteristics of the LAD cohort are presented in TABLE 2.

Left circumflex artery In patients with STEMI with the LCx as the culprit artery, the TO subgroup had a greater enzymatic infarct size, lower frequency of final TIMI flow grade 3 and coronary stenting, more frequent use of glycoprotein IIb/IIIa inhibitors, and higher proportion of current smokers than the nTO subgroup. In patients with NSTEMI with the LCx as the culprit artery, the TO subgroup had a lower mean age and incidence of hypertension, earlier angioplasty, higher incidence of heart failure symptoms on admission, greater enzymatic infarct size, lower frequency of final TIMI flow grade 3 and coronary stenting, more frequent use of anti-IIb/IIIa antibodies, and higher proportion of current smokers than the nTO subgroup. Clinical characteristics of the LCx cohort are presented in TABLE 3.

Right coronary artery In patients with STEMI with the RCA as the culprit artery, the TO subgroup had a lower ejection fraction, higher mean GRACE risk score, greater enzymatic infarct size, lower incidence of final TIMI flow grade 3 and coronary stenting, and more frequent use of glycoprotein IIb/IIIa inhibitors than the nTO subgroup. In patients with NSTEMI with the RCA as the culprit artery, the TO subgroup had a lower average age and incidence of both hypertension and diabetes mellitus, greater enzymatic infarct size, lower frequency of final TIMI flow grade 3 and coronary stenting, and higher frequency of anti-IIb/IIIa antibodies than the nTO subgroup. Clinical characteristics of the RCA cohort are presented in TABLE 4

TABLE 3 Clinical characteristics of patients with the left circumflex artery as the infarct-related artery

Variable	NSTEMI (n = 977)			STEMI (n = 627)			*P* value	
	TIMI 0 (n = 350)	TIMI 1–3 (n = 627)	*P* value	TIMI 0 (n = 377)	TIMI 1–3 (n = 250)	*P* value	TO NSTEMI vs TO STEMI	NSTEMI vs STEMI
Sex, male, n (%)	236 (67.6)	406 (64.9)	0.38	254 (67.4)	29 (73.2)	0.12	0.94	0.11
Age, y, mean (SD)	61.8 (11.3)	64.3 (10.9)	0.0008	61.9 (11.3)	61.8 (11.5)	0.92	0.93	0.007
Diabetes mellitus, n (%)	73 (20.9)	155 (24.7)	0.17	80 (21.2)	49 (19.6)	0.62	0.92	0.19
Hypertension, n (%)	223 (63.7)	452 (72.1)	0.005	230 (61.0)	161 (64.4)	0.39	0.47	0.005
Hyperlipidemia, n (%)	139 (39.7)	260 (41.5)	0.54	140 (37.1)	94 (37.6)	0.91	0.50	0.16
Current smokers, n (%)	118 (33.7)	172 (27.4)	0.03	174 (46.1)	92 (36.8)	0.02	0.0007	<0.0001
Typical chest pain, n (%)	335 (95.7)	584 (93.1)	0.1	369 (97.9)	241 (96.4)	0.26	0.09	0.003
Time from symptoms to PCI, h, median (IQR)	12.2 (5.9–27.0)	13.8 (6.2–44.8)	0.03	5.0 (3.0–8.5)	4.5 (3.0–7.7)	0.15	<0.0001	<0.0001
Killip class ≥ III, n (%)	15 (4.3)	13 (2.1)	0.04	22 (5.8)	11 (4.4)	0.43	0.35	0.01
GRACE score, points, mean (SD)	130.3 (35.4)	132.9 (31.7)	0.25	145.1 (33.2)	142.8 (30.0)	0.39	<0.0001	<0.0001
LVEF,%, mean (SD)	49.6 (9.1)	50.4 (10.2)	0.23	48.7 (8.3)	49.4 (8.4)	0.31	0.21	0.02
Postprocedural TIMI flow grade 3, n (%)	308 (88.0)	614 (98.1)	<0.0001	340 (90.2)	240 (96.0)	0.0068	0.40	0.09
Max. CK-MB, mg/dl, median (IQR)	121 (52–203)	45 (23–101)	<0.0001	191 (78–317)	99 (52–243)	<0.0001	<0.0001	<0.0001
Coronary stenting, n (%)	296 (84.6)	537 (95.2)	<0.0001	341 (90.4)	240 (96.0)	0.0091	0.02	0.4
DES, n (%)	1 (0.34)	20 (3.35)	0.0052	5 (1.5)	4 (1.7)	1.0000	0.2236	0.1869
Anti-GP IIb/IIIa, n (%)	33 (9.4)	29 (4.6)	0.0031	80 (21.2)	30 (12.0)	0.003	<0.0001	<0.0001

Abbreviations: see FIGURE 1 and TABLES 1 and 2

Clinical outcomes Patients with TO of the LAD showed higher mortality during the 36-month follow-up than patients with nTO; however, this relationship was only observed in the STEMI group. Mortality in the NSTEMI group was comparable between patients with TO and nTO (FIGURE 2). Patients with TO of the LCx had a higher in-hospital mortality rate in both the STEMI and NSTEMI groups; no further differences were observed during the follow-up. No differences were noted with respect to mortality between patients with TO and nTO of the RCA either in the STEMI or NSTEMI groups.

The multivariate analysis with logistic regression modeling (FIGURE 3) showed that TO was an independent predictor of 1-month (with increasing age) and 36-month (with increasing age and peripheral vascular disease) all-cause mortality in the LAD-related STEMI group. In the LAD-related NSTEMI group, TO did not predict short- or long-term mortality. TO was an independent predictor of 1-month mortality (with increasing age and heart and renal failure) in patients with STEMI and NSTEMI in the LCx cohort; however, no impact was observed on long-term mortality. In RCA-related STEMI and NSTEMI, TO did not predict short- or long-term mortality.

Patients with NSTEMI and TO of the LCx exhibited significantly higher mortality at 36 months when angioplasty was performed after more than 2 hours since hospital admission. No differences were noted with respect to mortality in patients with nTO in the LCx cohort (TABLE 5).

DISCUSSION

To the best of our knowledge, this is the first study describing the impact of total coronary occlusion on outcome depending both on the type of MI (STEMI vs NSTEMI) and on the culprit artery (LAD vs LCx vs RCA). The main findings can be summarized as follows: 1) acute total coronary artery occlusion occurred in 64.4% of the patients with STEMI and 26.6% of those with NSTEMI; 2) the RCA was identified as the culprit artery in approximately half of the patients with STEMI with TO, while the LCx was the culprit lesion in approximately half of the patients with NSTEMI with TO; 3) TO had an impact on mortality in patients with LAD-related STEMI throughout the entire follow-up, while it only worsened in-hospital mortality for patients with LCx-related STEMI and NSTEMI.

Following the redefinition of MI in 2000, acute MI has been classified as either STEMI or NSTEMI, depending on the appearance of the ECG.[12] According to the pathophysiological theory, STEMI is the result of acute occlusion of the culprit artery associated with transmural ischemia, whereas NSTEMI is typically the product of a transient or incomplete coronary occlusion resulting in nontransmural subendocardial ischemia.[13] However, while the occlusion of the culprit coronary artery is more frequently found in STEMI, it is also present in a significant number of patients with NSTEMI.[14] As confirmed by our study, the TO of the IRA was present in 64.4% of patients with STEMI and 26.6% of those with NSTEMI. The higher frequency of TO in patients

TABLE 4 Clinical characteristics of patients with the right coronary artery as the infarct-related artery

Variable	NSTEMI (n = 791)			STEMI (n = 2123)			*P* value	
	TIMI 0 (n = 215)	TIMI 1–3 (n = 576)	*P* value	TIMI 0 (n = 1456)	TIMI 1–3 (n = 667)	*P* value	TO NSTEMI vs TO STEMI	NSTEMI vs STEMI
Sex, male, n (%)	147 (68.7)	376 (65.3)	0.37	984 (67.6)	439 (65.8)	0.42	0.75	0.67
Age, y, mean (SD)	62.7 (11.9)	65.1 (10.9)	0.006	62.4 (11.4)	62.1 (11.0)	0.60	0.72	<0.0001
Diabetes mellitus, n (%)	37 (17.2)	143 (24.8)	0.02	271 (18.6)	120 (18.0)	0.73	0.64	0.008
Hypertension, n (%)	132 (61.4)	436 (75.7)	<0.0001	872 (59.9)	396 (59.4)	0.82	0.71	<0.0001
Hyperlipidemia, n (%)	91 (42.5)	245 (42.5)	0.90	562 (38.6)	255 (38.2)	0.87	0.33	0.05
Current smokers, n (%)	74 (34.4)	167 (29.0)	0.13	583 (40.4)	264 (39.6)	0.84	0.13	<0.0001
Typical chest pain,% (n)	202 (93.9)	532 (92.4)	0.45	1408 (96.7)	638 (95.7)	0.23	0.04	<0.0001
Time from symptoms to PCI, h, median (IQR)	15.4 (6.3–37.2)	14.5 (6.5–46.8)	0.78	5.0 (3.0–9.2)	4.8 (2.9–9.2)	0.51	<0.0001	<0.0001
Killip class ≥III, n (%)	4 (1.9)	13 (2.3)	1.0	62 (4.5)	32 (4.8)	0.78	0.07	0.002
GRACE score, points	132.0 (34.8)	130.2 (33.0)	0.53	147.4 (31.7)	144.2 (31.6)	0.03	<0.0001	<0.0001
LVEF, %, mean (SD)	49.4 (9.3)	50.8 (9.2)	0.1	49.6 (8.2)	50.8 (8.0)	0.003	0.76	0.30
Postprocedural TIMI 3 flow, n (%)	175 (81.4)	564 (97.9)	<0.0001	1320 (90.7)	645 (96.7)	<0.0001	<0.0001	0.42
Max. CK-MB, mg/dl, median (IQR)	41 (25–72)	33 (19–63)	0.04	129.5 (57–231)	84 (39–158)	<0.0001	<0.0001	<0.0001
Coronary stenting, n (%)	183 (85.1)	549 (95.3)	<0.0001	1361 (93.5)	642 (96.3)	0.01	<0.0001	0.07
DES, n (%)	3 (1.6)	18 (3.3)	0.2499	9 (0.66)	8 (1.25)	0.1830	0.1616	0.0167
Anti-GP IIb/IIIa, n (%)	24 (11.2)	20 (3.5)	<0.0001	413 (28.4)	115 (17.2)	<0.0001	<0.0001	<0.0001

Abbreviations: see FIGURE 1 and TABLES 1 and 2

TABLE 5 Mortality according to preprocedural Thrombolysis in Myocardial Infarction flow and time from admission to percutaneous coronary intervention with non-ST-segment elevation myocardial infarction with the left circumflex artery as the infarct-related artery

Mortality, n (%)	TIMI 0 (n = 350; 35.8%)			TIMI 1–3 (n = 627; 64.2%)		
	Time from dmission to PCI ≤2 h (n = 205; 58.6%)	Time from dmission to PCI >2 h (n = 145; 41.4%)	*P* value	Time from dmission to PCI ≤2 hours (n = 346; 55.2%)	Time from dmission to PCI >2 hours (n = 281; 44.8%)	*P* value
30-day	12 (5.8)	12 (8.3)	0.38	13 (3.8)	11 (3.9)	0.92
6-month	14 (6.8)	17 (11.7)	0.11	27 (7.8)	22 (7.8)	0.99
12-month	18 (8.8)	20 (13.8)	0.14	29 (8.4)	32 (11.4)	0.21
36-month	24 (11.7)	29 (20.0)	0.03	50 (14.4)	47 (16.7)	0.43

Abbreviations: PCI, percutaneous coronary intervention; others, see TABLE 1

with STEMI might be explained by differences in culprit lesion morphology between patients with STEMI and NSTEMI, as described in optical coherence tomography study.[15] This study has reported that plaque rupture (70% vs 47%), thin cap atheromas (78% vs 49%), and red thrombi (78% vs 27%) are typically more common in patients with STEMI than in those with NSTEMI. Interestingly, the area of the ruptured cavity appears to be significantly greater in the STEMI population. The size of the underlying lipid pool or necrotic core affects post-plaque rupture thrombus formation and, therefore, may be an important determinant of coronary artery occlusion.[15]

Patients with STEMI, irrespective of the occlusion status, showed a greater infarct size, as assessed by serum CK-MB levels, than patients with NSTEMI (with the exception of those presenting with TO of the LCx). It is possible that ST-segment elevation itself is indicative of the infarct size. It has previously been reported that patients with nonspecific changes on ECG typically have smaller infarctions than those presenting with features of an ischemic ECG.[16,17] Furthermore, in other cardiac magnetic resonance studies, the infarct size has been shown to be greater in patients with STEMI as compared with those with NSTEMI.[18-21] Sarafoff et al[18] performed a multivariate analysis according to the presence of ST-segment elevation, infarct size, and extent of transmural necrosis, and demonstrated that the univariate association between ST-segment

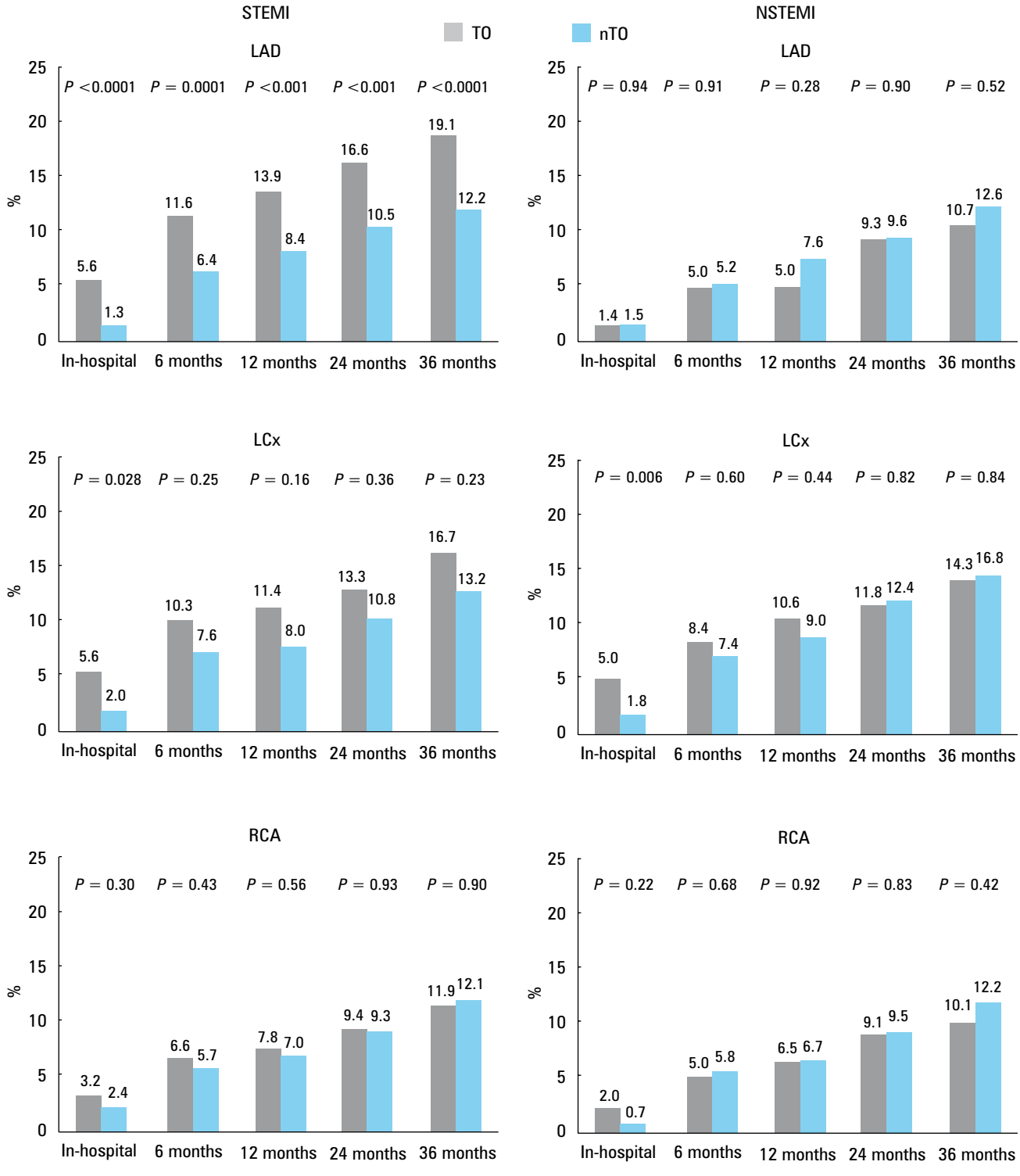

FIGURE 2 Mortality rates depending on infarct-related artery location in patients with ST-segment elevation myocardial infarction (left-hand panels) and non-ST-segment elevation myocardial infarction (right-hand panels)
Abbreviations: nTO, incomplete occlusion; others see **FIGURE 1**

elevation and full-thickness necrosis/damage is relatively weak, with the infarct size as the only significant parameter.[18] It is likely that the lack of ST-segment elevation in patients with NSTEMI with acute TO of the LAD and RCA was therefore reflective of the comparatively smaller infarct size. These patients, when compared with those with STEMI with TO of the LAD and RCA, had a 3-fold smaller peak CK-MB level. Unfortunately, however, our registry does not record data regarding the culprit vessel diameter and collateral circulation, both of which have been documented to be predictive of infarct size, clinical outcome, and ECG presentation.[22-24]

Among patients in the NSTEMI group, those with TO of the LCx had a nearly 2-fold greater enzymatic increase than those with TO of the LAD, and nearly a 3-fold greater increase than those

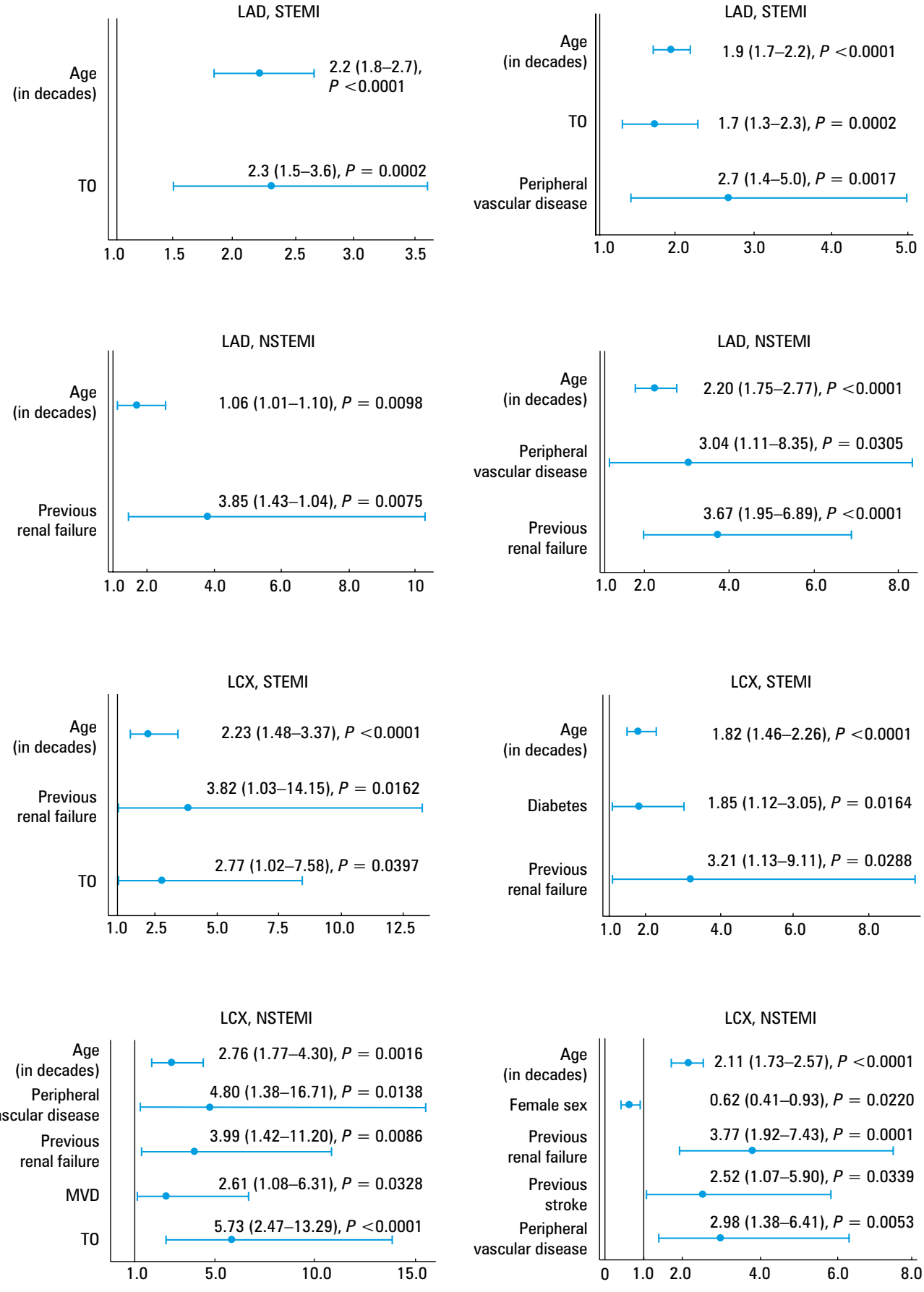

FIGURE 3 Independent predictors of mortality at 1 month (left-hand panels) and 36 months (right-hand panels). Data are presented as odds ratios with 95% CIs. Abbreviations: see **FIGURE 1** and **TABLE 1**

with TO of the RCA. The primary reason underpinning such observations could be the relatively poor sensitivity of ECG in detecting acute occlusion in the posterolateral circulation, due to the lack of the corresponding leads. A 12-lead ECG detects acute occlusion of the LAD and RCA in 70% to 92% of the cases; however, this drops to a range of 32% to 48% in cases where the IRA is the LCx.[4,5,25,26] In our study, the LCx constituted approximately 50% of all cases with TO in the NSTEMI group. Conversely, in the STEMI group, the LCx was the least common IRA, with only 13% of the patients presenting with such lesions. This proportion is in accordance with the results of randomized clinical trials involving patients with STEMI undergoing PCI.[27-29] Such findings could not be explained by variations in the likelihood of LCx plaque rupture, as it has been suggested that the lateral wall is equally prone to MI as the other 2 coronary territories, when imaged using cardiac magnetic resonance.[30] Furthermore, an intravascular imaging study has demonstrated that plaque rupture can occur along the entire LCx artery.[31] These findings suggest that within the group of patients with LCx-related NSTEMI there is a large subset of patients with complete occlusion, who should perhaps be considered as a "STEMI equivalent" group, in whom these findings are missed by standard ECG. In the present analysis, patients in the STEMI and NSTEMI groups with TO of the LCx had a 2-fold higher in-hospital mortality rate than their nTO counterparts. This increase in mortality was comparable between patients with STEMI and NSTEMI. Acute TO, along with increasing age and heart and renal failure, was an independent predictor of higher mortality at 1 month among patients with LCx-related MI.

The LAD supplies 40% to 50% of the left ventricular myocardium; therefore, acute TO of the LAD could result in ischemia of a large proportion of the myocardium.[32,33] A pathological study reported a mean infarct size of 40% of the left ventricle for lesions located in the LAD, compared with 18% for lesions in the RCA and 20% for those in the LCx.[34] In the present study, among patients with LAD-related STEMI, the presence of TO was associated with greater impairment of baseline left ventricular ejection fraction, higher incidence of heart failure symptoms on admission, and higher mortality during the entire 36-month follow-up, when compared with the nTO group. Moreover, the multivariate analysis revealed that TO was an independent predictor of 1- and 36-month mortality in patients with LAD-related STEMI.

In the group with the RCA as the IRA, the presence of TO did not have an impact on mortality either in the STEMI or NSTEMI group. One possible explanation is that TO of the RCA was associated with a smaller enzymatic infarct size, when compared with LAD- and LCx-related MI. Furthermore, in the STEMI group, TO of the RCA was not associated with a higher incidence of pulmonary edema or cardiogenic shock than the equivalent nTO condition. This is a significant finding given the observations suggesting that cardiogenic shock at presentation is highly predictive of mortality.[35-37]

The median time from symptoms to angioplasty in patients with STEMI with TO of the IRA was significantly shorter than that in patients with NSTEMI. Whether the outcome may have been improved with earlier intervention in patients with NSTEMI with TO is difficult to assess. Current clinical guidelines for NSTEMI do not recommend early routine invasive intervention, as clinical trials have failed to show benefits for such an approach.[2] However, data in patients with NSTEMI and TO are lacking. In our study, more than a quarter of all patients with NSTEMI, and a third of those with the LCx as the IRA, exhibited TO. Patients with NSTEMI and TO of the LCx had a significantly higher 36-month mortality rate when the PCI was performed more than 2 hours after admission to the hospital.

It is difficult to compare patients with STEMI and NSTEMI who present with TO, given the heterogeneity of the groups. First, patients with NSTEMI are thought to have a different etiopathogenic mechanism, characterized by a greater severity of coronary disease, diffuse arteriosclerosis, and an atheromatous plaque whose rupture can affect the smallest vessels.[38,39] Secondly, the NSTEMI population itself encompasses a number of heterogeneous patient subgroups. The primary subgroup is that of patients who present with incomplete occlusion of the IRA and subendocardial ischemia only.[13] Another subgroup includes patients with disease progressing to TO and who typically have well-developed collaterals that prevent transmural ischemia and ST-segment elevation on ECG.[40] There are also patients with acute TO of the LCx, which is not detected by ECG.[25,26] Furthermore, the sensitivity of ECG in detecting IRA occlusion may be weakened by several other factors, including prior MI, bypass surgery, or variation in coronary anatomy.[41]

Limitations of the study Our study has several limitations. First, the culprit artery was determined by cardiologists in catheterization laboratories (using ECG, angiographic, and echocardiographic findings), and identification of the IRA in patients with multivessel disease may have differed between operators. Second, it was impossible to compare the enzymatic infarct size between the study groups using troponin values due to variability in troponin type (troponin T or troponin I) and cut-off values used among hospitals participating in the PL-ACS. Patients with previous MI, PCI, or coronary artery bypass grafting were excluded from the study, as the culprit vessel in these subjects might have been incorrectly identified due to chronic TO. Furthermore, there were no data regarding detailed angiographic features, such as the presence or absence of collateral circulation in coronary angiograms.

Conclusions In conclusion, patients with STEMI with TO of the LAD showed higher mortality rates during the 36-month follow-up. TO was also associated with increased in-hospital mortality of patients with STEMI and NSTEMI with the LCx as the IRA. The LCx constituted approximately one-half of all cases with TO in the NSTEMI group, mainly due to suboptimal sensitivity of ST-segment elevation for detection of TO in this artery. Greater efforts must be made to early detect acute LCx occlusion. Patients with NSTEMI and TO of the LCx exhibited significantly higher mortality at 36 months when the PCI was performed with more than 2-hour delay after hospital admission.

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Contribution statement JK was responsible for the concept, design, and execution of the study, interpretation of the data, and composition of the manuscript. MG, LP, and MG were responsible for execution of the study and interpretation of the data. MB, JC, IK, and HS were responsible for the concept, design, and execution of the study, as well as interpretation of the data.

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