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Effect of multiple clinical factors on recurrent angina after percutaneous coronary intervention

A retrospective study from 398 ST-segment elevation myocardial infarction patients

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Abstract

Recurrent angina (RA) has an important influence on health status of patients after percutaneous coronary intervention (PCI). This study aimed to retrospectively investigate the effect of multiple clinical factors on both short-term and long-term development of RA.

A total of 398 ST-segment elevation myocardial infarction (STEMI) patients were studied for up to 12 months. The primary clinical outcome, RA, was assessed at 1-month and 12-month. In multivariate analyses, the effect of clinical factors, including baseline demographics, medical history, infarction-related arteries, procedural characteristics of PCI, and the use of medicines, was investigated in patients with and without RA.

The Logistic regression analysis showed that the patients with treatment through radial approach PCI (odds ratio [OR]: 0.42, 95% confidence interval [CI]: 0.18–0.96, $P < 0.05$) were less likely to have RA during 1-month assessment. During 12 months after PCI, male patients (OR: 0.53, 95% CI: 0.29–0.96, $P < 0.05$), and/or those treated with radial approach PCI (OR: 0.45, 95% CI: 0.21–0.97, $P < 0.05$) were less likely to have RA, whereas the patients with infarction related artery (IRA) in left anterior descending (LAD) (OR: 2.41, 95% CI: 1.20–4.84, $P < 0.01$) were more likely to have RA at follow-up. The Cox regression analysis further revealed that the patients with infarction of the LAD artery (hazard ratio [HR]: 2.08, 95% CI: 1.10–3.92, $P < 0.05$), but not with treatment through radial artery during PCI (HR: 0.42, 95% CI: 0.18–0.96, $P < 0.05$) had higher potential of development of RA during 12 months after PCI.

We studied the effects of multiple clinical factors on the development of RA after PCI. Our findings suggest that patients with infarction of the LAD artery, and/or treatment not through radial artery during PCI were associated with higher risk of RA and may require close follow-up.

Abbreviations: ACEI = angiotensin converting enzyme inhibitors, ACS = acute coronary syndrome, AMI = acute myocardial infarction, ARB = angiotensin receptor blockers, CCB = calcium channel blockers, CHD = coronary heart disease, CI = confidence interval, DBP = diastolic blood pressure, DM = diabetes mellitus, HC = hypercholesterolemia, HR = hazard ratio, HTG = hypertriglyceridemia, IABP = intra-aortic balloon pump, IRA = infarction related artery, LAD = left anterior descending, LCX = left circumflex, OR = odds ratio, PCI = percutaneous coronary intervention, RA = recurrent angina, RCA = right coronary artery, SBP = systolic blood pressure,, SD = standard deviation, STEMI = ST-segment elevation myocardial infarction, TP = temporary pacing.

Keywords: Acute coronary syndrome (ACS), Multiple clinical factor, Percutaneous coronary intervention (PCI), Recurrent angina (RA), Retrospective study, ST-segment elevation myocardial infarction (STEMI)

1. Introduction

Despite advances in therapeutic techniques, acute coronary syndrome (ACS) remains a major cause of morbidity and mortality worldwide.[1,2] Multiple risk factors for this disease have been identified,[3] including hypertension, hypercholesterolemia, obesity, diabetes, and genetic factors, for example, the polymorphisms of *G protein-coupled receptor kinases* (*GRKs*) gene,[4] *calcium/calmodulin-dependent kinase IV gene* (*CaMK4*),[5] and *platelet antigen 2* (*PlA2*) gene.[6,7] Percutaneous coronary intervention (PCI), one of the main treatment approaches for ACS, has effectively reduced both short-term and long-term mortality in patients with ST-segment elevation myocardial infarction (STEMI).[8]

Previous studies have investigated the effect of various clinical factors, such as sex,[9,10] blood pressure,[11] medical history,[12,13] infarction-related artery (IRA),[14–16] medications,[17] and PCI procedural characteristics[18,19] on the mortality of ACS patients. Such studies, however, have primarily focused on mortality and not on health outcomes of patients after PCI.

Recurrent angina (RA), defined as recurrence or persistence of chest pain or discomfort,[20] is a challenging condition and is one

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of the main reason for declining health and the quality of life for STEMI patients.[20,21] RA can be caused by structural factors (including in-stent thrombosis, restenosis, incomplete revascularization, or atherosclerotic disease progression),[22] or by functional factors (e.g., microvascular dysfunction, epicardial coronary spasm, or vasoconstriction at the stent edge).[23] It has been reported that up to one-third of patients treated with PCI might present with RA without clear obstructive structural lesions.[23]

2. Hypothesis

Our hypothesis is that the occurrence of RA is the result of multiple clinical factors. Therefore, this study aimed to retrospectively investigate both short-term and long-term effects of multiple clinical factors on the development of RA and attempt to identify predictors for increased likelihood of RA in STEMI patients after PCI, particularly in Northwest of China.

3. Methods

3.1. Patient population

A total of 416 STEMI patients who had undergone PCI at the Heart Center of the First Affiliated Hospital of Lanzhou University in China from 2009 to 2012 were enrolled in this study. The inclusion criteria were patients who had been diagnosed with STEMI following the ACC/AHA guidelines[24]; all patients who had undergone coronary angiography and successful reperfusion therapy to the IRA using the PCI procedure.

Eighteen patients were excluded because they had a history of any of the following: treatment with thrombolytic therapy or coronary artery bypass graft; cerebral hemorrhage less than 1 year or cerebral infarction <6 months; severe liver or kidney dysfunction; tumor patients; coagulopathy; contraindication of anti-platelet drug; and any patients who had the inadequate clinical notes or were unreachable via telephone follow-up. Therefore, 398 patients met the inclusion criteria and were analyzed in this study. The institutional review board at the First Affiliated Hospital of Lanzhou University granted a waiver of written informed consent and provided authorization for this study.

3.2. Treatment procedure

Each patient was given a dose of 300-mg aspirin and 300-mg clopidogrel before the PCI procedure. The PCI approach was performed through either radial or femoral artery. In addition, patients were implanted with the temporary pacing electrode if they had severe sinus bradycardia or II~III° atrioventricular block before operation. If cardiogenic shock or hemodynamic instability happened during operation, they were treated with intra-aortic balloon pump. Antiplatelet, antithrombin, statin, nitrates, ACEI/ARB, and other necessary medicine therapy were given to patients based on the ACC/AHA Guidelines during the treatment period.[24] After PCI, patients were given life-long aspirin 100 mg/day and clopidogrel 75 mg/day for at least 12 months.

3.3. Study clinical outcome

RA was the primary clinical outcome in this study. It was defined as angina recurrence or persistence, either stable or unstable after PCI,[20] without documented noncardiac causes of chest pain, such as gastrointestinal, pulmonary, musculoskeletal, or herpes zoster. Stable angina was defined as pain precipitated by exertion and relieved by rest and/or sublingual nitroglycerin, with no change in pattern or severity in the previous 6 weeks. Unstable angina was defined as either pain that presented at rest, or exertional pain of at least Canadian Cardiovascular Society class III that began or increased in severity at least I Canadian Cardiovascular Society class in the previous 2 months.[21] Patients who reported chest pain or discomfort were classified as having angina according to the validated Seattle Angina Questionnaire, which also included the severity, frequency, and stability subscales of the symptoms.[25]

The secondary clinical outcome in this study was all-cause death, allowing us to investigate factors associated with the incidence of death during the study period.

3.4. Data collection, management, and patient follow-up

Patients included in the study were followed for 12 months after PCI to determine the reoccurrence of angina or if patients died during the study period from any cause. In-person or telephone interviews were conducted to determine RA. Among these 398 STEMI patients, 212 patients were followed up by face-to-face and 186 patients were followed up via telephone. During the interview, patients were asked if they had chest pain or discomfort (anginal symptoms) after PCI procedure, and to describe the severity and frequency of the symptoms, as relevant. Thus, patients were placed into 2 categories for analysis by presentation of RA or not, for both 1-month and 12-month follow-up assessment.

3.5. Statistical analysis

Continuous variables were presented as median (25^{th}, 75^{th} percentiles) or mean value ± SD, and were compared by unpaired t test or Mann–Whitney U test. For categorical variables, frequencies and the corresponding percentages were given, and were compared by χ^2 test with continuity correction or Fisher exact test.

Logistic regression was first performed to test the risk factors. The following covariates were analyzed: demographic characteristics, medical history (coronary heart disease family history, diabetes mellitus, hypertriglyceridemia, hypercholesterolemia and smoking history), IRA, use of medication, and PCI procedural characteristics. Univariate correlates of RA with a value of $P \leq 0.1$ were included in multivariate logistic regression analysis to further identify the potential risk factors for developing RA. The results were displayed as adjusted odds ratios (ORs) with 95% confidence intervals (CIs).

To further check our results, cox regression analysis was also performed. In the Cox regression model, the covariates were selected based upon univariate significance of P value ≤ 0.1. The results were reported as adjusted hazard ratios (HRs) with 95% CIs. In addition, a survival curve was also provided.

All analyses were performed using SPSS software version 22 (IBM Corp., Armonk, NY), and a P value of <0.05 was considered statistically significant.

4. Results

4.1. Baseline demographics

A total of 398 patients with STEMI and PCI met the inclusion criteria and were included in the study analyses. Table 1 describes the baseline demographics of the reserved patients. The median

Table 1

Basic demographics of the reserved 398 STEMI patients.

Variables	Value	95% CI
Sex	335 (M); 63 (F)	—
Age, y	59 (52–67)	58–60
SBP, mmHg	120 (106–136)	119–124
DBP, mmHg	75 (67–84)	74–77

Note: Data are presented as median (25^{th}–75^{th} percentiles). CI = confidence interval, DBP = diastolic blood pressure, SBP = systolic blood pressure.

age was 59 years (interquartile range: 15), 84% were male. Median systolic and diastolic blood pressures were 120 mmHg and 75 mmHg, respectively.

4.2. Comparison of baseline demographics and clinical characteristics

Table 2 shows the different baseline demographics and clinical characteristics between the patients with and without RA at 1-month and 12-month assessments, respectively. Among the total of 398 patients, 62 had RA at 1-month follow-up and 98 had RA at 12-month follow-up, which included all of the 62 patients who had RA at 1 month.

Sex was the only statistically significant demographic characteristic between the 2 groups, and males were less likely to experience RA (at 1-month assessment, 76% vs. 86%, $P < 0.05$; at 12-month assessment, 77% vs. 87%, $P < 0.05$).

There were multiple statistically significant clinical characteristics. At 1-month assessment, patients were more likely to experience RA if they had higher IRA of left anterior descending (LAD) (89% vs. 74%, $P < 0.05$); lower percentage of using statin (94% vs. 99%, $P < 0.05$), higher percentage of using ARB (39% vs. 24%, $P < 0.05$); and lower percentage of radial approach in PCI procedure (84% vs. 93%, $P < 0.05$).

At 12-month assessment, RA was observed more commonly in patients who had IRA in LAD (88% vs. 73%, $P < 0.01$); less IRA in right coronary artery (RCA) (46% vs. 61%, $P < 0.05$); a lower percentage of radial approach in PCI procedure (86% vs. 93%, $P < 0.05$); and less number of stent (1 vs. 2, $P < 0.05$). The significantly statistical difference observed with use of statin and ARB at 1 month was no longer evident following the assessent at 12 months.

Table 2

Comparison results of the baseline demographics and clinical characteristics between the patients with and without RA, separated by 1-month and 12-month follow-up.

Factors	1-month follow-up			12-month follow-up		
	With RA	Without RA	*P*	With RA	Without RA	*P*
Demographic						
Patients number	62	336	—	98	300	—
Age, year	60 (53–68)	59 (52–67)	0.6	59 (51–68)	59 (53–67)	0.8
Male sex	47 (76)	288 (86)	<0.05	75 (77)	260 (87)	<0.05
SBP, mmHg	119 (100–137)	120 (106–136)	0.9	120 (108–136)	120 (106–137)	0.9
DBP, mmHg	79 (66–88)	75 (67–84)	0.3	76 (68–86)	75 (67–84)	0.3
Medical history						
CHD family history	3 (5)	15 (4)	0.8	5 (5)	13 (4)	0.8
Hypertension	27 (44)	142 (42)	0.9	41 (42)	128 (43)	0.9
DM	6 (10)	48 (14)	0.3	13 (13)	41 (14)	0.9
HTG	18 (29)	87 (26)	0.6	25 (26)	80 (27)	0.8
HC	7 (11)	27 (8)	0.4	12 (12)	22 (7)	0.1
Smoking history	37 (60)	187 (56)	0.6	57 (58)	167 (56)	0.7
IRA						
LAD	55 (89)	250 (74)	<0.05	86 (88)	219 (73)	<0.01
LCX	27 (44)	144 (43)	0.9	40 (41)	131 (44)	0.6
RCA	29 (47)	198 (59)	0.1	45 (46)	182 (61)	<0.05
Number of IRA						
Only one vessel	27 (44)	155 (46)	0.9	47 (48)	135 (45)	0.8
Two vessels	21 (34)	107 (32)		29 (30)	99 (33)	
Three vessels	14 (23)	74 (22)		22 (22)	66 (22)	
Use of medication						
β-blocker	43 (69)	194 (58)	0.1	62 (63)	175 (58)	0.4
Statin	58 (94)	332 (99)	<0.05	296 (99)	94 (96)	0.1
ACEI	32 (52)	166 (49)	0.7	53 (54)	145 (48)	0.3
ARB	24 (39)	81 (24)	<0.05	33 (34)	72 (24)	0.1
CCB	7 (11)	22 (7)	0.2	10 (10)	19 (6)	0.2
Nitrate	35 (56)	199 (59)	0.7	55 (56)	179 (60)	0.5
Procedural characteristics						
Radial approach	52 (84)	311 (93)	<0.05	84 (86)	279 (93)	<0.05
IABP	2 (3)	5 (1)	0.3	3 (3)	4 (1)	0.4
TP	6 (10)	46 (14)	0.4	11 (11)	41 (14)	0.5
Number of stent	1 (1–2)	2 (1–2)	0.1	1 (1–2)	2 (1–2)	<0.05

Note: Data are presented as number (%) or median (25^{th}–75^{th} percentiles).

ACEI = angiotensin converting enzyme inhibitors, ARB = angiotensin receptor blockers, CCB = calcium channel blockers, CHD = coronary heart disease, DBP = diastolic blood pressure, DM = diabetes mellitus, HC = hypercholesterolemia, HTG = hypertriglyceridemia, IABP = intra-aortic balloon pump, IRA = infarction-related artery, LAD = left anterior descending, LCX = left circumflex, RA = recurrent angina, RCA = right coronary artery, SBP = systolic blood pressure, TP = temporary pacing.

Table 3

Effects of all potential factors on the development of recurrent angina from the Logistic REGRESSION analysis.

	1-month follow-up						12-month follow-up					
	Univariate			Multivariate			Univariate			Multivariate		
Factors	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Demographics												
Age	1.01	0.98–1.04	0.58				1.00	0.97–1.02	0.76			
Male sex	0.52	0.27–1.01	<0.05*	0.57	0.29–1.14	0.11	0.50	0.28–0.89	<0.05*	0.53	0.29–0.96	<0.05
SBP	1.00	0.99–1.01	0.83				1.00	0.99–1.01	0.98			
DBP	1.01	0.99–1.03	0.32				1.01	0.99–1.03	0.32			
Medical history												
CHD family history	1.09	0.31–3.88	0.90				1.19	0.41–3.42	0.75			
Hypertension	1.05	0.61–1.82	0.85				0.97	0.61–1.53	0.89			
DM	0.64	0.26–1.57	0.33				0.97	0.50–1.89	0.92			
HTG	1.17	0.64–2.13	0.61				0.94	0.56–1.59	0.82			
HC	1.46	0.61–3.51	0.40				1.76	0.84–3.71	0.14			
Smoking history	1.18	0.68–2.05	0.56				1.11	0.70–1.76	0.67			
IRA												
LAD	2.70	1.19–6.16	<0.05*	2.32	0.96–5.62	0.06	2.65	1.38–5.11	<0.01*	2.41	1.20–4.84	<0.01
LCX	1.03	0.60–1.78	0.92				0.89	0.56–1.41	0.62			
RCA	0.61	0.36–1.06	0.08*	0.75	0.42–1.36	0.34	0.55	0.35–0.87	<0.01*	0.72	0.43–1.21	0.22
Number of IRA												
Single												
Double	1.13	0.61–2.10	0.71				0.84	0.50–1.43	0.52			
Triple	1.09	0.54–2.19	0.82				0.96	0.53–1.72	0.88			
Use of medication												
β-blocker	1.66	0.93–2.96	0.09*	1.61	0.87–2.98	0.13	1.23	0.77–1.97	0.39			
Statin	0.18	0.04–0.72	<0.05*	0.23	0.05–1.08	0.06	0.32	0.08–1.30	0.11			
ACEI	1.09	0.64–1.88	0.75				1.26	0.80–1.99	0.32			
ARB	1.99	1.13–3.51	<0.05*	1.79	0.98–3.28	0.06	1.61	0.98–2.64	0.06*	1.61	0.96–2.69	0.07
CCB	1.82	0.74–4.46	0.19				1.68	0.75–3.75	0.21			
Nitrate	0.89	0.52–1.54	0.68				0.87	0.55–1.37	0.54			
Procedural characteristics												
Radial approach	0.42	0.19–0.92	<0.05*	0.42	0.18–0.96	<0.05	0.45	0.22–0.93	<0.05*	0.45	0.21–0.97	<0.05
IABP	2.21	0.42–11.64	0.35				2.34	0.51–10.63	0.27			
TP	0.68	0.28–1.66	0.39				0.80	0.39–1.62	0.53			
Number of stent	0.85	0.63–1.16	0.30				0.80	0.61–1.03	0.08*	0.83	0.63–1.11	0.21

ACEI = angiotensin converting enzyme inhibitors, ARB = angiotensin receptor blockers, CCB = calcium channel blockers, CHD = coronary heart disease, CI = confidence interval, DBP = diastolic blood pressure, DM = diabetes mellitus, HC = hypercholesterolemia, HTG = hypertriglyceridemia, IABP = intra-aortic balloon pump, IRA = infarction-related artery, LAD = left anterior descending, LCX = left circumflex, OR = odds ratio, RCA = right coronary artery, SBP = systolic blood pressure, TP = temporary pacing. Data are presented as n (%) or median (25th–75th percentile).

* Means the univariate features ($P \leq 0.1$) included in multivariate regression analysis.

Neither medical history nor the number of diseased vessels showed any statistical significant differences in the occurrence of RA (all $P \geq 0.05$) at 1-month or 12-month assessment.

4.3. Risk factors for the development of RA from logistic regression analysis

Table 3 summarizes the effect of all potential factors on the development of RA using logistic regression analysis. The key risk factors at the 2 independent time points (1-month and 12-month follow-up) have been identified from the univariate and multivariate regression analysis.

At 1-month assessment, univariate analysis identified sec, LAD, RCA, β-Blocker, statin, ARB, and radial approach as the potential impact factors ($P \leq 0.1$) for the development of RA. However, multivariable regression model only revealed that radial approach (OR: 0.42, 95% CI: 0.18–0.96, $P < 0.05$) decreased the probability of RA.

At 12-month assessment, univariate analysis identified sex, LAD, RCA, ARB, radial approach, and number of stent as the potential impact fators ($P \leq 0.1$) for the development of RA. Meanwhile, multivariable regression model revealed that the IRA in LAD increased while male patients and radial approach decreased the probability of RA independent from confounding factors (OR: 2.41, 95% CI: 1.20–4.84, $P < 0.01$ for LAD; OR: 0.53, 95% CI: 0.29–0.96, $P < 0.05$ for male sex; OR: 0.45, 95% CI: 0.21–0.97, $P < 0.05$ for radial approach).

4.4. Risk factors for the development of RA from Cox regression

Table 4 summarizes the effects of potential factors on the development of RA using Cox regression analysis. The key risk factors have been identified. At 12-month assessment, univariate analysis identified sex, LAD, RCA, statin, ARB, and radial approach as the potential impact factors ($P \leq 0.1$) for the development of RA. However, multivariable regression model only revealed that LAD (HR: 2.08, 95% CI: 1.10–3.92, $P < 0.05$) and radial approach (HR: 0.42, 95% CI: 0.18–0.96, $P < 0.05$) were statistically significant.

Figure 1 shows the cumulative rate curve of RA for the 5 statistical time points (1, 3, 6, 9, and 12 months after PCI) and the cumulative rates of RA were 14.1%, 18.9%, 20.7%, 23.0%, and 23.2%, respectively.

Table 4

Effects of all potential factors on the development of recurrent angina from the Cox regression analysis (12-month follow-up).

	Univariate			Multivariate		
Factors	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
Demographics						
Age	1.00	0.98–1.02	0.81			
Male sex	0.59	0.37–0.94	<0.05*	0.63	0.39–1.01	0.06
SBP	1.11	0.68–1.84	0.67			
DBP	0.90	0.53–1.51	0.68			
Medical history						
CHD family history	1.16	0.47–2.84	0.75			
Hypertension	0.97	0.65–1.46	0.90			
DM	0.96	0.53–1.72	0.96			
HTG	0.96	0.61–1.51	0.86			
HC	1.54	0.84–2.83	0.16			
Smoking history	1.09	0.73–1.63	0.67			
IRA						
LAD	2.31	1.26–4.22	<0.01*	2.08	1.10–3.92	<0.05
LCX	0.91	0.61–1.36	0.65			
RCA	0.62	0.42–0.92	<0.05*	0.76	0.49–1.18	0.23
Number of IRA						
Single						
Double	0.88	0.55–1.39	0.58			
Triple	0.97	0.58–1.61	0.91			
Use of medication						
β-blocker	1.20	0.79–1.81	0.39			
Statin	0.41	0.15–1.12	0.08*	0.63	0.22–1.80	0.39
ACEI	1.20	0.81–1.79	0.36			
ARB	1.49	0.98–2.26	0.06*	1.42	0.92–2.19	0.12
CCB	1.51	0.78–2.90	0.22			
Nitrate	0.89	0.60–1.32	0.56			
Procedural characteristics						
Radial approach	0.54	0.30–0.94	<0.05*	0.42	0.18–0.96	<0.05
IABP	1.89	0.60–5.96	0.28			
TP	0.68	0.44–1.54	0.55			
Number of stent	0.82	0.65–1.04	0.10*	0.87	0.68–1.12	0.29

ACEI = angiotensin converting enzyme inhibitors, ARB = angiotensin receptor blockers, CCB = calcium channel blockers, CI = confidence interval, CHD = coronary heart disease, DBP = diastolic blood pressure, DM = diabetes mellitus, HC = hypercholesterolemia, HR = hazard ratio, HTG = hypertriglyceridemia, IABP = intra-aortic balloon pump, IRA = infarction-related artery, LAD = left anterior descending, LCX = left circumflex, RCA = right coronary artery; SBP = systolic blood pressure, TP = temporary pacing.

* Means the univariate features ($P \leq 0.1$) included in multivariate regression analysis.

4.5. Risk factors for the incidence of death

Table 5 lists the risk factors for the incidence of death for both two follow-up periods: 5 patients died in 1-month follow-up (1.3% in all patients) and 9 patients died in 12-month follow-up (2.3% in all patients).

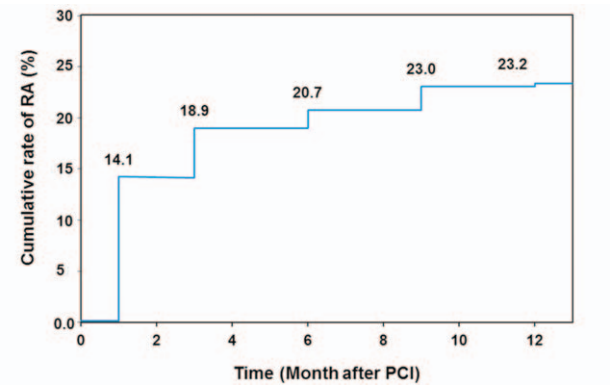

Figure 1. Cumulative rate curve of recurrent angina (RA) at the 5 statistical time points: 1, 3, 6, 9, and 12 months after percutaneous coronary intervention (PCI).

At 1-month assessment, among the 5 death cases, 4 were male (80%). Four of them had an IRA of LAD and also had an IRA of RCA. Moreover, 2 dead patients used β-blocker and 2 used ARB. At 12-month assessment, among the 9 dead cases, 6 were male (66.7%). Eight dead patients had an IRA of LAD and 7 had an IRA of RCA. Moreover, 4 dead patients used β-blocker and 3 used ARB. Most importantly, no matter in 1-month follow-up or 12-month follow-up, all of dead patients had radial approach when performed PCI procedure, as well as were given statin during the whole treatment.

5. Discussion

7835968976Management of RA after PCI among STEMI patients remains a clinical challenge. This study retrospectively investigated both short-term (1 month) and long-term (12-month) effects of multiple clinical factors, including baseline demographics, medical history, infarction-related artery, use of medication and procedural characteristics of PCI on the development of RA after PCI for 398 STEMI patients.

We found that female STEMI patients were more likely to experience RA. Some previous researches that studied cronary diease and/or acute myocardial infarction (AMI) have also shown that women had a higher short-term[20,26,27] and long-term[28]

Table 5

Risk factors for the incidence of death.

Factors	Number of total patients with the factor	1-month follow-up		12-month follow-up	
		Number of dead patients	% in dead patients	Number of dead patients	% in dead patients
Male sex	335	4	80	6	66.7
LAD	305	4	80	8	88.9
RCA	227	4	80	7	77.8
β-blocker	237	2	40	4	44.4
ARB	105	2	40	3	33.3
Statin	390	5	100	9	100
Radial approach	363	5	100	9	100

ARB = angiotensin receptor blockers, LAD = left anterior descending, RCA = right coronary artery.

risk than men for developing RA. Similar to other studies,[28] this association is not statistically significant after we controlled for clinical factors such as medical history, IRA, medications, and PCI procedural characteristics. In addition, we found that being female is not associated with statistically significant reduction in mortality after PCI. In this study, 3 female patients died during the 12-month follow-up period (1 before 1-month assessment and 2 before the 12-month assessment). It is possible that our analysis in mortality may be hampered by small sample size(only 63 females in total 398 patients) of STEMI patients from the Northwest of China.

The previous studies have shown a link between smoking and angina in AMI patients.[26,29] However, our study did not find an association between smoking and occurrence of RA, which is consistent with some previous research.[28] In addition, although another published study has reported that ACS patients with diabetes had a higher rate of RA after PCI,[30] our study also did not find significant association between the medical history (diabetes, hypertension, and hypercholesterolemia) and outcome of RA.

A potentially important finding of our study was that the LAD-related infarcts seem to be related to RA in post-PCI patients. Our results suggest that STEMI patients with RA after PCI had significantly higher percentage of IRA in LAD during both 1-month and 12-month assessments. In the literature, many studies have shown that LAD-related infarcts in patients treated with PCI have worse prognosis and lower left ventricular ejection fraction when compared with non-LAD-related infarcts.[31,32] This is thought to be mainly because of the increased muscle mass at risk and a lower likelihood of achieving normal myocardial perfusion despite restored epicardial flow, resulting in a large amount of damaged myocardium.[33] However, to the best of our knowledge, there is no study that reported that the LAD-related infarcts were related to RA in post-PCI patients.

Santulli et al has reported that lymphocyte G protein-coupled receptor kinase 2 (GRK2) levels, which is related to worse cardiac function, increased quickly after STEMI and some patients showed reduced GRK2 levels in response to β-blocker therapy, suggesting that it is important to give STEMI patients β-blocker therapy in the early stage.[34,35] Another prospective study investigated the predictor factors of RA in patients with ACS use of a population data of China and they found use of β-blocker was an independent predictive factor for RA.[17] Some studies have also shown the use of statin reduced the incidence of RA after PCI in coronary artery disease patients with normal cholesterol levels.[36,37] However, neither β-blocker nor statin has been identified as the risk factor for the development of RA in this study, which only focused on STEMI patients with PCI. Our study has shown that this finding might be related to observations.

Radial approach has been recommended by EAPI/ESC as preferred access in primary PCI,[38] which allows early ambulation, shorter hospital stay, more reduction in bleeding and access site complications, and superior net clinical benefit compared with the femoral approach.[39–42] A strong association between radial approach PCI and a reduction in adverse cardiovascular events in patients with ACS has also been reported by some randomized controlled studies.[18,19,43] Furthermore, a meta-analysis of 12 randomized trials comparing radial and femoral approach for primary PCI in STEMI patients has demonstrated that mortality was significantly reduced with the radial approach.[44] However, to the best of our knowledge, there is no study reported that the radial approach PCI was associated with decreased RA. Our results found that a decreased percentage of radial approach is associated with a significant increase the probability for developing RA in STEMI patients during both 1-month and 12-month assessments. Future randomized trials will be useful to confirm these findings.

6. Limitations

This study has several limitations. First, the study had a relatively small number of patients from a single center; therefore, the results may not be generalizable to other population. However, this study focused on the STEMI patients from the northwest of China only and provided useful insights regarding the occurrence of RA in the targeted population. Second, this is an observational study. It is possible that certain unobserved factors such as genetic background,[3] precise mechanism, and pathophysiology[35] of STEMI may also influence the likelihood of RA after controlling most RA-associated risk factors in our model. Therefore, we examined the robustness and sensitivity of our results by employing different models. Overall, our results are very robust to different model specification. Finally, the content, extent, and severity description of symptoms were self-reported, hence are subjected to recall bias. Based on these limitations, future large-scale clinical studies are needed.

7. Conclusion

This retrospective study of 398 STEMI patients explored the effect of multiple demographic and clinical factors on the development of RA after PCI. Our results suggest that patients with infarction of left anterior descending artery were associated with higher risk of RA during the follow-up. Compared with femoral approach, patients experienced the treatment through radial artery during PCI are related to lower risks of RA for up to 1 year after the procedure. Further research, with a nationally representative sample and a prospective study design or longer-term follow-up

could provide additional insights into reoccurring angina in patients who undergo PCI.

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