Efficacy and Safety of Different Antiplatelet Strategies in Survivors of Myocardial Infarction With Acute Coronary Syndrome

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ABSTRACT

Purpose: Many patients with acute coronary syndrome may experience recurrent myocardial infarction although they are receiving optional therapy, but they are still associated with poor clincial outcomes. The goal of this study was to assess different antiplatelet strategies in these patients.

Methods: This retrospective trial compared ticagrelor (180-mg loading dose, 90-mg BID maintenance dose) and clopidogrel (300- to 600-mg loading dose, 150-mg daily maintenance dose) for the prevention of cardiovascular events in 1083 patients with acute coronary syndrome and recurrent myocardial infarction admitted to the hospital undergoing percutaneous coronary intervention.

Findings: At the 24-month follow-up, a major adverse cardiovascular and cerebrovascular event (MACCE) occurred in 10.5% of patients receiving ticagrelor compared with 13.2% in the clopidogrel group ($P = 0.023$). Meanwhile, ticagrelor caused a higher rate of minor bleeding (18.1% vs 15.3%; $P = 0.008$). A survival analysis showed that ticagrelor decreased the incidence of MACCE (log-rank test, $P < 0.001$) and all-cause death (log-rank test, $P = 0.001$). The advantage of ticagrelor was also presented according to analysis of Seattle Angina Questionnaire scores.

Implications: In patients with recurrent myocardial infarction, the ticagrelor antiplatelet strategy significantly reduced the MACCE rate without increasing the risk of major bleeding, although patients did have a higher risk of minor bleeding. (*Clin Ther*. 2019;41:2090–2101)

Key words: acute coronary syndrome, clopidogrel, MACCE, recurrent, ticagrelor.

INTRODUCTION

Acute coronary syndrome (ACS) is one of the most severe cardiovascular diseases both worldwide and in China. Dual antiplatelet therapy has been the cornerstone strategy; this strategy involves the use of aspirin together with another antiplatelet agent with a different mechanism of action to enhance platelet inhibition.[1] Although treatment improvements in patients with ACS have been accomplished over the past decade, patients with previous ACS are at higher risk for recurrent cardiovascular events after the first event, with ~1%–9% of patients with ACS having subsequent cardiovascular events.[2–4] Gathering more details regarding patients with recurrent events can provide additional evidence for physicians and patients on how to best monitor patients' progress.

It is generally considered that patients with recurrent events are usually at high risk, antiplatelet strategy adjustment may play an important role in the process. Ticagrelor is an oral, direct-acting, reversible $P2Y_{12}$ inhibitor that provides more intense platelet inhibition with more rapid onset and offset

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compared with clopidogrel. In a study of 18,624 patients with ACS, ticagrelor and clopidogrel were compared for the prevention of cardiovascular events, and the results showed that ticagrelor significantly reduced the number of composite ischemic end point events, cardiac death, and myocardial infarction without an increased rate of major bleeding.[5]

There are limited data available regarding the antiplatelet strategies for recurrent cardiovascular events in China. The goal of this retrospective study was to explore if different antiplatelet agents could change the prognosis of recurrent events in patients with ACS in China.

PATIENTS AND METHODS

Study Design and Patients

Patients diagnosed with recurrent ACS who underwent a percutaneous coronary intervention (PCI) in our hospital were continuously enrolled. The study disposition and screening process are shown in the supplemental figure (given in the online version at https://doi.org/10.1016/j.clinthera.2019.08.007). In brief, a total of 13,206 patients from April 2012 to March 2016 post-PCI were enrolled; 1608 of these patients were identified with previous myocardial infarction according to their medical history records. After filtering by using the exclusion criteria and receipt of signed informed consent, 1242 patients were enrolled into 2 groups according to their antiplatelet strategies: the clopidogrel group (clopidogrel 75 mg daily plus aspirin 100 mg daily) and the ticagrelor group (ticagrelor 90 mg BID plus aspirin 100 mg daily). During the following 2-year follow-up period, 159 patients were lost to follow-up, and 1083 patients were ultimately included in the trial. The exclusion criteria included any history of surgical procedures within the past year (not including coronary artery bypass grafting), hematologic disorders, concomitant therapy with a strong cytochrome P-450 3A4 inhibitor or inducer, and pregnancy. The study was approved by the institutional ethics committee, and all participants provided written informed consent.

End Points

The primary efficacy end point was a composite of major adverse cardiovascular and cerebrovascular events (MACCE), a composite of all-cause death, myocardial infarction, target vessel revascularization, and stroke; other efficacy end points included stent thrombosis. The safety end point was bleeding complications that were classified according to the Thrombolysis In Myocardial Infarction (TIMI) criteria. Major life-threatening bleeding included the following: (1) fatal bleeding; (2) intracranial bleeding; (3) intrapericardial bleeding with cardiac tamponade; (4) hypovolemic shock or severe hypotension due to bleeding and requiring pressor drugs or surgery; and (5) a decline in the hemoglobin level of $\geq$5.0 g/dL. Minor bleeding was defined as any clinical signs or symptoms of bleeding, such as blood in urine, black stool, hemoptysis, petechiae, or ecchymosis.

Health Status Measurement

The health status of all patients was assessed by using the Seattle Angina Questionnaire (SAQ). The SAQ is a 19-item questionnaire that measures 5 domains of health status related to coronary artery disease, including physical limitations (question 1), angina stability (question 2), angina frequency (questions 3 and 4), treatment satisfaction (questions 5−8), and quality of life (questions 9−11).[6,7] This questionnaire was translated into Chinese and assessed by 3 clinical physicians from different institutions. The questionnaire is scored by assigning each response an ordinal value, beginning with 1 for the response that implies the lowest level of functioning, and summing all items within each of the 5 scales. The scale scores are then transformed to a 0 to 100 range, with high scores indicating fewer symptoms and a better health status. According to previous studies,[8,9] SAQ angina frequency scores are categorized for descriptive purposes as follows: no angina, score = 100; monthly angina, score = 61 to 99; weekly angina, score = 31 to 60; and daily angina, score = 0 to 30. To improve the response rate, the SAQ is brief and self-administered, requiring <5 min to complete.

Data Collection and Follow-up

We collected data on patients' clinical characteristics and relevant risk factors such as hypertension, diabetes, previous myocardial infarction, and previous incidence of stroke or transient ischemic attack. Follow-up information was collected, according to a clinically designed questionnaire, every 3 months for 2 years after discharge. In addition, the presence of MACCE was

investigated. The SAQ was also completed by all patients.

Statistical Analysis

All continuous variables are presented as the mean (SD), and ANOVA was used to compare means between these 2 groups. Categorical variables are presented as frequencies or percentages and were compared by using the χ^2 test. The χ^2 test was used for the comparison of the primary end point. The absolute differences on MACCE between groups and the corresponding 95% CIs were reported. The Kaplan–Meier curve method was used to calculate time to clinical end points, and the log-rank test was used to compare the survival curves. The Cox proportional hazards model was further applied to estimate the potential factors involved in the interaction analysis. Statistical interactions between the clinical factors and antiplatelet strategies were tested by using multiple regression models. Data from all patients were censored at the date of the last available information. Unless otherwise specified, a 2-sided P value < 0.05 was considered to indicate statistical significance. Statistical analysis was performed by using STATA software version 12.0 (StataCorp, College Station, Texas).

RESULTS

We continuously recruited 1083 patients with ACS diagnosed with previous myocardial infarction undergoing PCI. Among 1083 patients with intact follow-up information, 560 were assigned to the clopidogrel group and 523 to the ticagrelor group. The baseline and procedural characteristics are shown in Table I.

Clinical Outcome

The primary end point of MACCE events at 24 months' post-PCI occurred in 74 patients (13.2%) in the clopidogrel group and in 55 patients in the ticagrelor group (10.5%) (Table II). The difference in the 24-month MACCE rates in the ticagrelor group was lower than that in the clopidogrel group (hazard ratio [HR], 1.252; 95% CI, 1.141–1.683; $P = 0.023$), indicating the superiority of the ticagrelor strategy over that of the clopidogrel strategy. Fig. 1 shows the cumulative Kaplan–Meier estimates of efficacy end points. Patients receiving ticagrelor therapy reported a lower cumulative risk of MAACE ($P < 0.001$) and all-cause death ($P = 0.001$); the risk of MI, target vessel revascularization, stent thrombosis, and stroke did not differ significantly between the 2 groups (Figure 1, Table III). There was no difference in risk of TIMI-defined major bleeding between the clopidogrel and ticagrelor groups (HR, 1.231; 95% CI, 0.586–1.896; $P = 0.14$), indicating that ticagrelor did not increase the risk of major bleeding. The risk of TIMI-defied minor bleeding was also higher compared with the clopidogrel group (HR, 0.654; 95% CI, 0.421–0.743; $P = 0.008$). Survival analysis indicated that clopidogrel contributed to lower major and minor bleeding rates ($P = 0.015$ and $P < 0.001$, respectively) (Fig. 2).

Subgroup Analysis of End Points

In the following analysis, we applied an interaction effect to determine the relation of various clinical factors to different antiplatelet strategies and the impact on efficacy and safety end points. For the efficacy end points, the potential clinical factors associated with MACCE were first identified by using a COX multivariate analysis, and the related factors are shown in Table III. Five factors, including age, diabetes, involvement of the left main artery, triple-vessel artery disease, and use of glycoprotein IIb/IIIa inhibitors, were found to be associated with MACCE. The stratified analyses revealed that participants aged >75 years had a lower ischemic rate in the ticagrelor group than those in the clopidogrel group (HR, 1.089; 95% CI, 1.008–1.363; $P = 0.042$). In addition, patients diagnosed with diabetes could also benefit from ticagrelor therapy (HR, 1.154; 95% CI, 1.092–1.367; $P < 0.001$). Similar results were also observed in patients with triple-vessel artery disease, involvement of the left main artery, and glycoprotein IIb/IIIa usage ($P = 0.003$, 0.028, and 0.011, respectively).

According to previous studies,[10–12] age, diabetes, triple-vessel artery disease, and involvement of the left main artery are all important prognostic factors in the outcome of ACS. Results of logistic regression tests showed that age, diabetes, involvement of the left main artery, and triple-vessel occlusion were

Table I. Baseline characteristics of the study sample.

Characteristic	Clopidogrel 75 mg Daily (n = 560)	Ticagrelor 90 mg BID (n = 523)	*P*
Age, y*	66.69 (9.50)	65.56 (10.04)	0.058
Age ≥75 y, no/total no. (%)	92 (16.4)	87 (16.6)	0.927
Male sex, no/total no. (%)	290 (51.8)	308 (49.4)	0.420
BMI, kg/m^2,*	25.76 (2.50)	25.63 (2.33)	0.381
Cardiovascular risk factors, no. (%)			
Hypertension	301 (53.8)	267 (51.1)	0.374
Diabetes mellitus	313 (55.9)	275 (52.6)	0.274
Insulin-requiring	162 (28.9)	135 (25.8)	0.251
Dyslipidemia	357 (63)	355 (68)	0.153
Smoker	274 (48.9)	271 (51.8)	0.342
Previous vascular disease	162 (28.9)	160 (30.6)	0.549
Cardiogenic shock	21 (3.8)	17 (3.3)	0.655
Clinical presentation*			
Heart rate, beats/min	77.97 (14.56)	79.20 (15.07)	0.173
Systolic blood pressure, mm Hg	123.52 (20.42)	122.59 (17.90)	0.426
Diastolic blood pressure, mm Hg	68.94 (8.98)	69.12 (9.94)	0.752
Laboratory values*			
Hematocrit (%)	0.361 (0.063)	0.357 (0.061)	0.289
Hemoglobin (g/L)	135.04 (21.87)	136.61 (23.72)	0.258
PLT	196.83 (50.62)	193.86 (50.46)	0.338
eGFR (ml/min/1.73m^2)	85.53 (26.94)	87.70 (25.53)	0.162
GRACE scores	147.41 (32.38)	152.78 (34.86)	0.146
CRUSADE scores	39.87 (12.21)	40.11 (13.45)	0.056
Medical history, no. (%)			
ACE inhibitors/ARBs	476 (85)	423 (80.9)	0.071
β-Blockers	504 (90)	466 (89)	0.629
Tirofiban	398 (71)	366 (70)	0.694
LMWH	490 (87.5)	470 (90)	0.22
Statin	535 (95.5)	501 (95.8)	0.835
Killip classification, no. (%)			0.287
I	353 (63.0)	313 (59.8)	
II	129 (23.0)	116 (22.2)	
III	56 (10.0)	63 (12.0)	
IV	22 (3.9)	31 (5.9)	
PCI indication, no. (%)			0.179
STEMI, no. (%)	356 (63.6)	309 (59.1)	
Non-STEMI, no. (%)	145 (25.9)	162 (31.0)	
Unstable angina, no. (%)	59 (10.5)	52 (9.9)	
Total no. of stents*	1.72 (0.52)	1.78 (0.61)	0.067
TVD, no. (%)	102 (18.2)	99 (18.9)	0.762
Target vessel, no. (%)			0.986
LAD	235 (35.6)	215 (35.4)	
LCX	207 (31.4)	193 (31.8)	
RCA	218 (33.0)	199 (32.8)	

(*continued on next page*)

Table I. (*Continued*)

Characteristic	Clopidogrel 75 mg Daily (n = 560)	Ticagrelor 90 mg BID (n = 523)	*P*
LM involved	73 (12.8)	80 (15.3)	0.236
Radial artery access	453 (80.9)	424 (81.1)	0.941

ACE = angiotensin-converting enzyme; ARBs = angiotensin receptor blockers; BMI = body mass index; eGFR = effective glomerular filtration rate; LAD = left anterior descending branch; LCX = left circumflex artery; LM = left main artery; LMWH = low-molecular-weight heparin; MI = myocardial infarction; PCI = percutaneous coronary intervention; PLT = platelet; STEMI = ST-segment elevation myocardial infarction; TVD = triple vessel disease; RCA = right coronary artery; GRACE = global registry of acute coronary events; CRUSADE = Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes.
* Mean (SD).

associated with a negative correlation with ischemic end points (Fig. 4A).

For the safety end points (Table IV), 3 factors (age, tirofiban usage, and low-molecular-weight heparin usage) were identified as being related to bleeding events. Participants aged >75 years accounted for a lower bleeding rate in the clopidogrel group (HR, 0.622; 95% CI, 0.315−0.799; $P < 0.001$). In addition, patients receiving tirofiban and low-molecular-weight heparin reported a lower rate of bleeding risk in the clopidogrel group (HR, 0.708 [95% CI, 0.369−0.905; $P = 0.011$]; HR, 0.445 [95% CI, 0.321−0.809; $P = 0.029$]). Age, tirofiban, and low-molecular-weight heparin usage were all associated with increased likelihood of safety end points (Figure 4B).

SAQ Scores

Data regarding assessment of quality of life according to SAQ in the treatment subgroups are presented in Table V and .Fig. 3 There was abundant evidence of significant differences for patients with clopidogrel or ticagrelor usage throughout the entire follow-up process ($P < 0.05$). Regarding other

Table II. Primary end points at 24 months.

Variable	Clopidogrel Group	Ticagrelor Group	Hazard Ratio (95% CI)	*P*
Death from all cause	56/560	40/523	1.223 (1.015−1.698)	0.001
Cardiovascular death	36/560	22/523	1.366 (1.120−1.814)	0.014
MI	32/560	28/523	1.171 (0.556−1.409)	0.721
TVR	24/560	21/523	1.207 (0.776−1.784)	0.430
Stent thrombosis	19/560	18/523	1.036 (0.883−1.642)	0.367
Stroke	22/560	19/523	1.191 (0.654−1.329)	0.70
Overall MACCE	74/560	55/523	1.252 (1.141−1.683)	<0.001
Major bleeding	42/560	45/523	1.231 (0.586−1.896)	0342
Minor bleeding	86/560	95/523	0.654 (0.421−0.743)	<0.001

MACCE = major adverse cardiovascular and cerebrovascular events; MI = myocardial infarction; TVR = target-vessel revascularization.

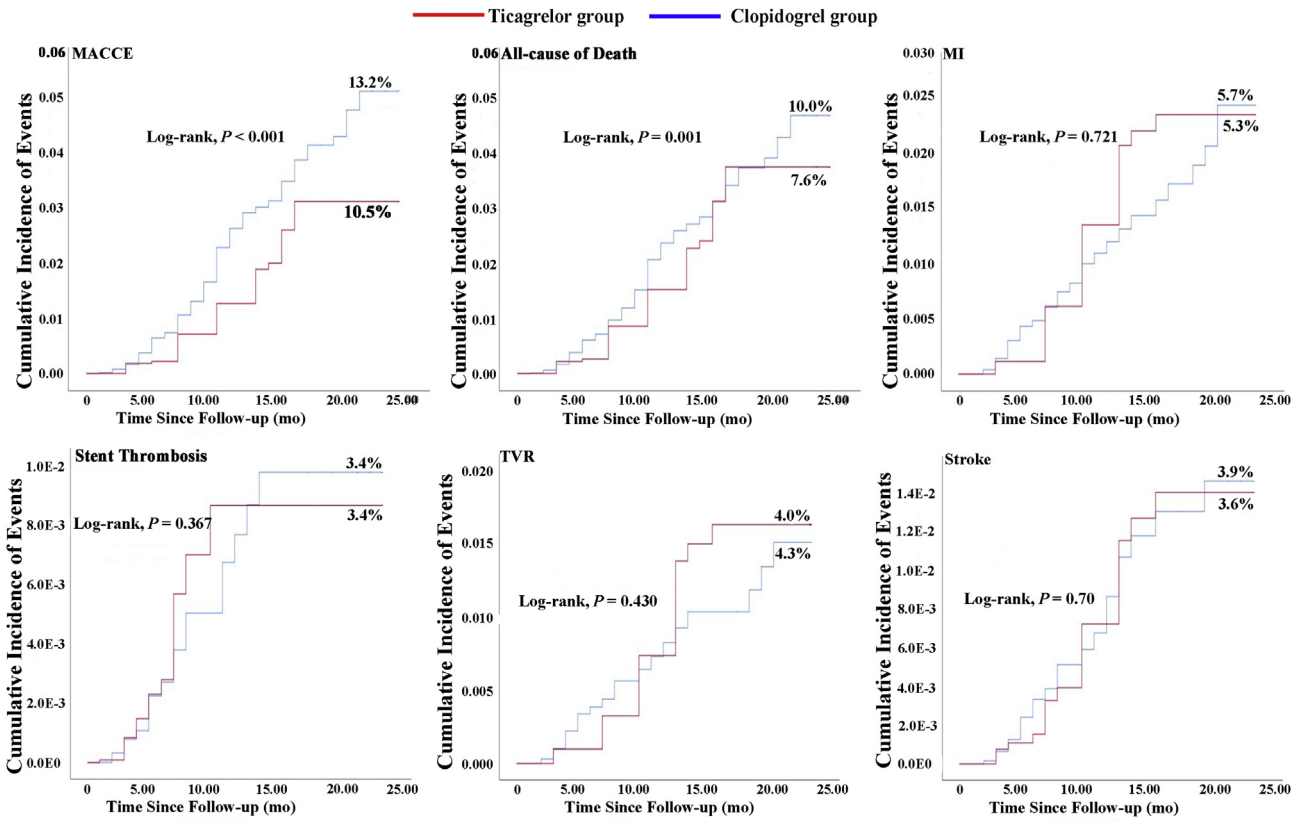

Figure 1. Cumulative efficacy events incidence after 24-month follow-up. MACCE = major adverse cardiovascular and cerebrovascular event; MI = myocardial infarction; TVR = target-vessel revascularization.

subscales of this questionnaire, no differences were found in the first half-year, but we did observe gradual differences in the following observation period.

DISCUSSION

The present study showed that, compared with clopidogrel, the use of ticagrelor in patients with ACS and previous myocardial infarction could significantly reduce the rate of MACCE, a composite of all-cause death, myocardial infarction, target vessel revascularization, and stroke. However, although the beneficial effects of the ticagrelor strategy were achieved without a significantly increased risk of major bleeding, ticagrelor indeed contributed to a higher risk of minor bleeding. Subgroup analysis indicated that patients aged >75 years and use of tirofiban and low-molecular-weight heparin may comprise the major portion with higher minor bleeding risk. Age is an important clinical factor related to ischemic and bleeding risk.[11,13] Tirofiban reportedly reduces death and myocardial infarction in patients with ACS, with the most marked benefit for patients with high ischemic risk, while also causing bleeding events. For multivessel PCI and younger patients, tirofiban may contribute a lower rate of primary end points but higher bleeding risk for elderly patients, which was consistent with Shimada et al.[14]

Our findings differ from those of a previous study in 2008,[15] which showed that ticagrelor is associated with significantly higher rates of clinically

Table III. Association between antiplatelet strategies and efficacy end points according to baseline characteristics.

Subgroup	Clopidogrel Group	Ticagrelor Group	Hazard Ratio (95% CI)	*P*	*P* for Interaction
Age					0.002
>75 y	92/560	87/436	1.089 (1.008–1.363)	0.042	
<75 y	468/560	436/523	1.134 (0.855–1.526)	0.376	
Sex					0.441
Male	290/560	308/523	1.152 (0.659–1.287)	0.131	
Female	270/560	215/523	1.278 (0.632–1.877)	0.366	
DM					0.017
No	247/560	248/523	1.444 (0.895–1.634)	0.32	
Yes	313/560	275/523	1.154 (1.092–1.367)	<0.001	
Angiopathy					0.532
No	398/560	363/523	0.590 (0.401–0.809)	0.384	
Yes	162/560	160/523	1.029 (0.876–1.138)	0.701	
Diagnosis					0.736
STEMI	356/560	309/523	0.704 (0.660–1.032)	0.255	
Non-STEMI	145/560	162/523	1.082 (0.493–1.207)	0.392	
UA	59/560	52/523	0.699 (0.421–1.408)	0.696	
LM involved					<0.001
No	487/560	443/523	1.130 (0.802–1.403)	0.104	
Yes	73/560	80/523	1.203 (1.011–1.587)	0.028	
Triple-vessel artery					<0.001
No	458/560	424/523	1.092 (0.761–1.422)	0.214	
Yes	102/560	99/523	1.209 (1.121–1.503)	0.003	
β-Blocker					0.897
No	56/560	57/523	0.882 (0.561–1.302)	0.656	
Yes	504/560	466/523	0.286 (0.089–0.732)	0.771	
Tirofiban					0.024
No	162/560	157/523	1.057 (0.973–1.402)	0.316	
Yes	398/560	366/523	1.226 (1.152–1.590)	0.011	

DM = diabetes mellitus; LM = left main artery; STEMI = ST-segment elevation myocardial infarction; UA = unstable angina.

relevant hemorrhagic complications and increased thromboembolic and ischemic cardiac events among triple therapy–treated patients. We reviewed our patient information and found that race may be an important contributor to this finding. Andreou et al[15] included PIONEER AF-PCI (Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI), RE-DUAL PCI (Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation), and GEMINI-ACS-1 (A Study to Compare the Safety of Rivaroxaban Versus Acetylsalicylic Acid in Addition to Either Clopidogrel or Ticagrelor Therapy in Participants with Acute Coronary Syndrome) in their analysis, which enrolled few Asian patients.

Actually, in our previous study, we found that ticagrelor may cause a higher rate of minor bleeding.[16] In the future, physicians should make more detailed treatment strategies for patients with these features.

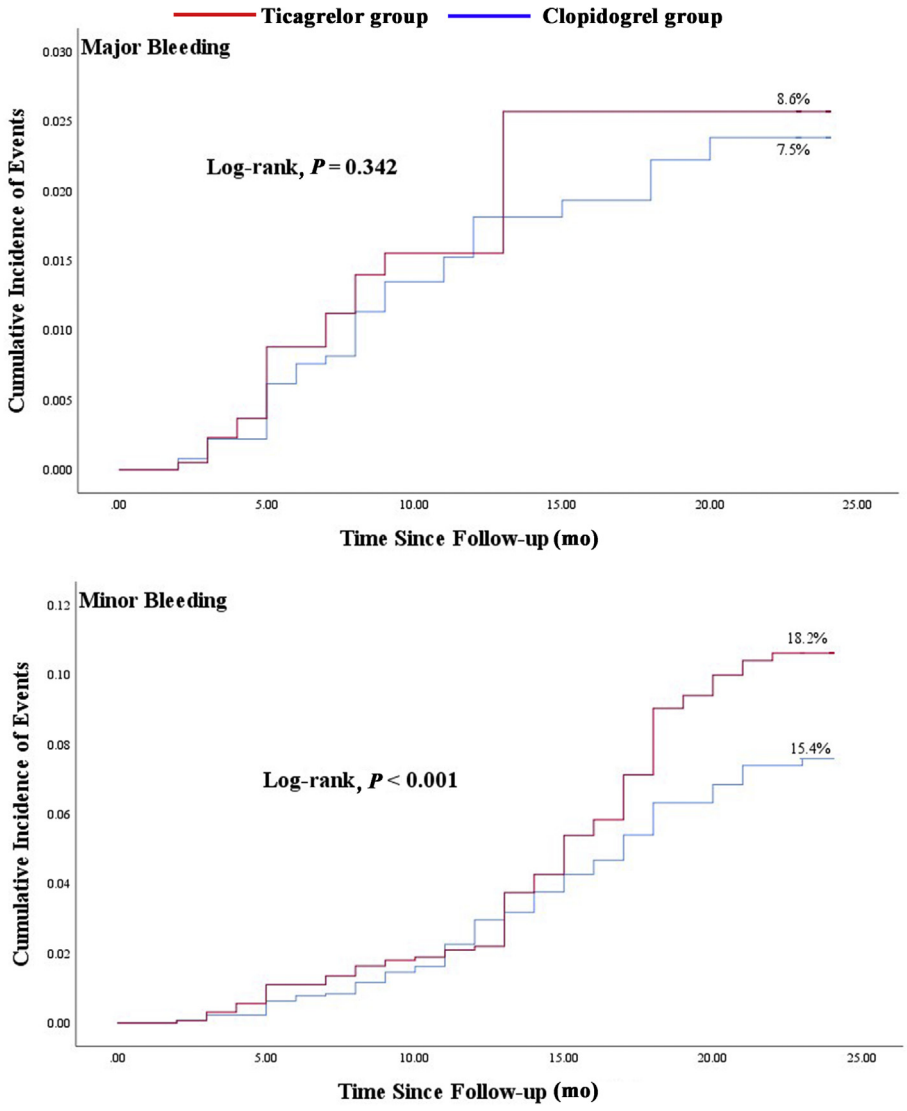

Figure 2. Cumulative safety events incidence after 24-month follow-up.

Antiplatelet treatment has been the milestone for patients diagnosed with ACS, recently, more and more studies have been largely focused on reducing ischemic event occurrence meanwhile the bleeding events. Many patients may experience recurrent myocardial infarction although receiving optional therapy and is associated with poor clinical outcomes.[17,18] The CHARISMA (Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance) study examined a group of patients with a history of atherothrombotic disease or risk factors for atherothrombotic events; 9478 patients with a history of myocardial infarction, ischemic stroke, or documented peripheral arterial disease were enrolled, and the rate of a composite of death, myocardial infarction, or stroke was lower in those receiving aspirin and clopidogrel than in those treated with aspirin alone.[19] Another clinical trial published in 2015[20] also reported

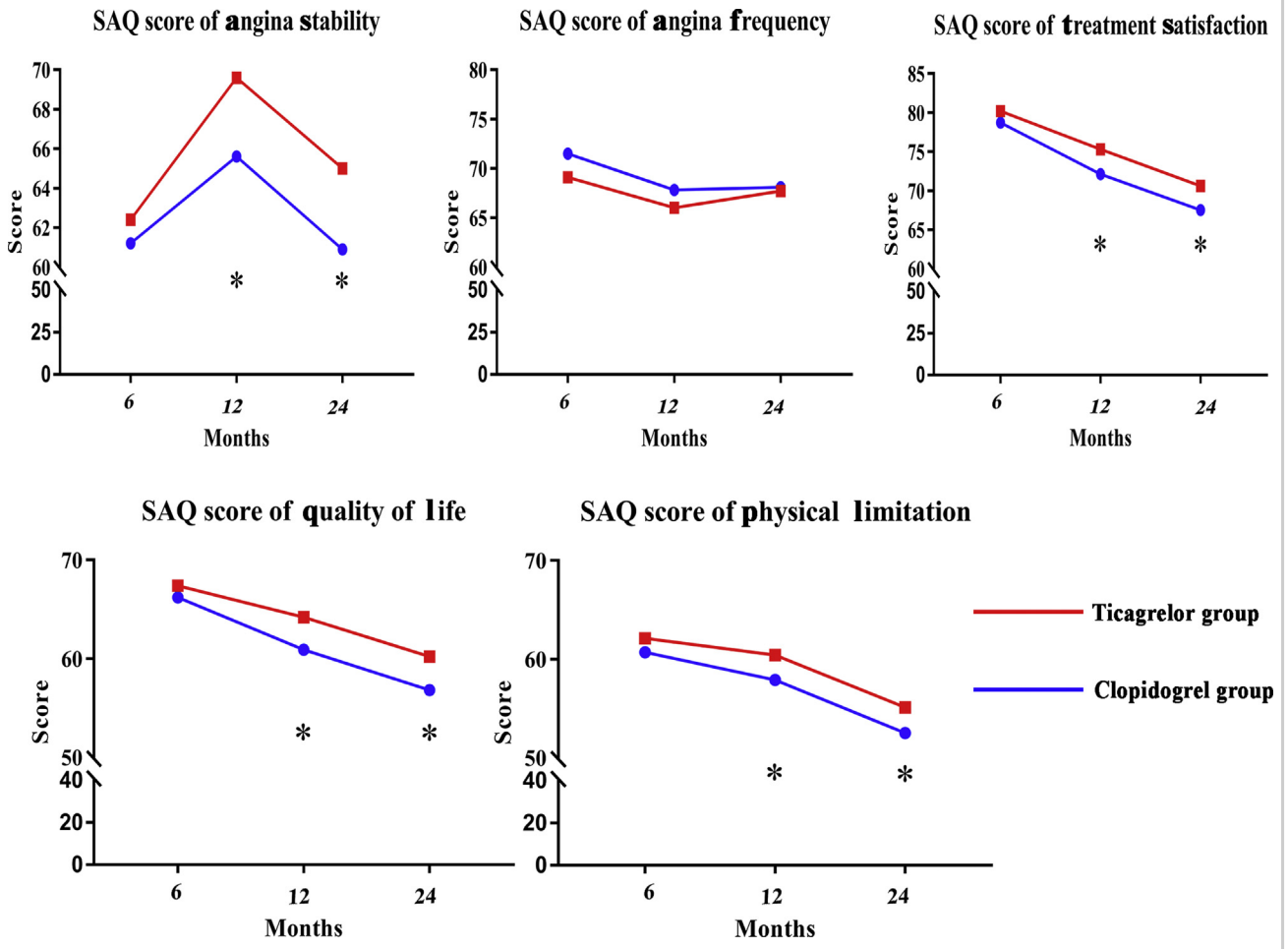

Figure 3. Analysis of Seattle Angina Questionnaire (SAS) scores after 24-month follow-up.

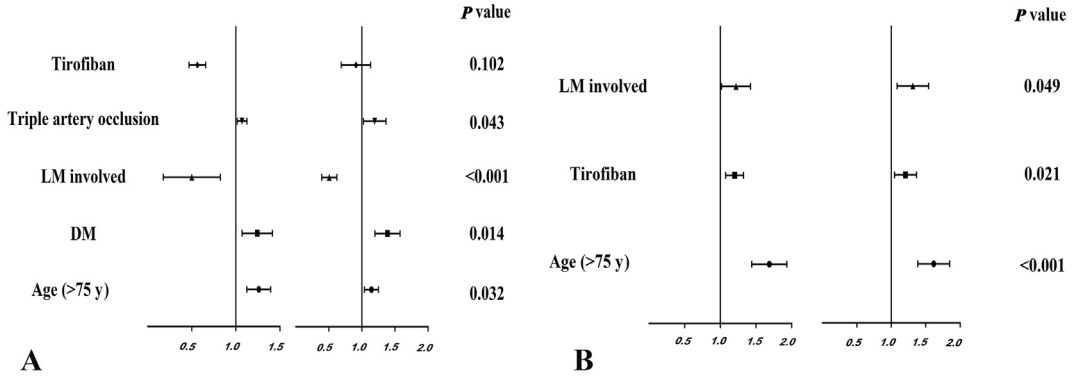

Figure 4. Logistic regression analysis of risk factors. DM = diabetes mellitus; LM = left main artery.

Table IV. Association between antiplatelet strategies and safety end points according to baseline characteristics.

Subgroup	Clopidogrel Group	Ticagrelor Group	Hazard Ratio (95% CI)	*P*	*P* for Interaction
Age					0.012
>75 y	92/560	87/523	0.622 (0.315−0.799)	<0.001	
≤75 y	468/560	436/523	1.021 (0.878−1.322)	0.084	
Angiopathy					0.443
No	398/560	363/523	0.466 (0.239−1.080)	0.401	
Yes	162/560	160/523	1.210 (0.913−1.304)	0.309	
Diagnosis					0.153
STEMI	356/560	309/523	0.934 (0.552−1.074)	0.069	
Non-STEMI	145/560	162/523	1.142 (0.886−1.333)	0.101	
UA	59/560	52/523	0.884 (0.609−1.222)	0.280	
Tirofiban					0.048
No	162/560	157/523	1.032 (0.826−1.135)	0.109	
Yes	398/560	366/523	0.708 (0.369−0.905)	0.011	
LWMH					0.033
No	70/560	53/523	0.726 (0.550−1.086)	0.20	
Yes	490/560	470/523	0.445 (0.321−0.809)	0.029	

LMWH = low-molecular-weight heparin; STEMI = ST-segment elevation myocardial infarction; UA = unstable angina.

Table V. Seattle Angina Questionnaire scores (mean [SD]).

Domain	Clopidogrel Group	Ticagrelor Group	*P*
Angina stability			
6-mo	61.2 (20.5)	62.4 (18.7)	0.12
12-mo	65.6 (19.9)	69.6 (21.1)	<0.001
24-mo	60.9 (24.5)	65.0 (23.8)	0.002
Angina frequency			
6-mo	71.5 (24.1)	69.1 (23.3)	0.285
12-mo	67.8 (20.2)	66 (20.7)	0.476
24-mo	68.1 (23.9)	67.7 (22.5)	0.331
Treatment satisfaction			
6-mo	78.7 (19.1)	80.2 (20.3)	0.17
12-mo	72.1 (18.4)	75.3 (17.2)	<0.001
24-mo	67.5 (21.5)	70.6 (21.4)	<0.001
Quality of life			
6-mo	66.2 (22.3)	67.4 (21.8)	0.38
12-mo	60.9 (24.6)	64.2 (23.9)	<0.001
24-mo	56.8 (24.2)	60.2 (25.5)	<0.001
Physical limitation			
6-mo	60.7 (20.8)	62.1 (21.6)	0.089
12-mo	57.9 (23.6)	60.4 (23.8)	0.018
24-mo	52.5 (25.1)	55.1 (24.6)	0.021

that continuation of dual antiplatelet therapy beyond 1 year is indicated to prevent recurrent infarction in patients tolerating the treatment. These 2 studies focused on the duration of antiplatelet therapy. The focus of the present study was more on a comparison of different strategies for prevention.

Survivors of ACSs have a high risk of recurrent events,[21] and these patients to some extent are at high ischemic risk; ticagrelor, as a stronger potent antiplatelet agent, may benefit patients. In our analysis, patients with the 5 clinical factors discussed in the Results benefited from ticagrelor. Li et al[22] reported that in pre–myocardial infarction patients, diabetes was a significant and independent predictor of all-cause death and composite end points. We also found that patients with diabetes may benefit more from ticagrelor, a result of the relatively high ischemic risk.

Some limitations of the present study should be taken into consideration. First, this was a retrospective analysis of a consecutive cohort of patients treated with primary angioplasty from a single center in China, and the data may not reflect the general population of ACS patients. A retrospective study does not have the same value as a prospective one, and a nonrandomized study also cannot be compared with a randomized controlled trial. However, retrospective studies have their own advantages. There are many "interesting findings" we may learn from our patients, such as the issue in our study, although usually physicians do not know whether these findings can promote the improvement of treatment strategies. Randomized controlled trials or prospective studies require more financial and time supports, which may not ultimately yield any useful information. In these situations, retrospective studies could offer some evidence-based predictions. Second, in this trial, the percentage of patients who underwent a platelet function test and genotype test was low; Man et al reported that the Asian population has almost twice the prevalence of the CYP2C19 loss-of-function genotype compared with that of the white population, thus contributing to the high prevalence of low clopidogrel responsiveness in Asian subjects.[23] Finally, some patients enrolled in our study may switch from clopidogrel to ticagrelor or vice versa. We did not take this factor into consideration.

CONCLUSIONS

This novel study investigated the relation between antiplatelet strategies and nonfatal recurrent myocardial infarction in patients with ACS who were treated with PCI. Generally, ticagrelor could reduce the risk of MACCE with an increase in the risk of minor bleeding but no increased risk of major bleeding. Age, use of tirofiban, and use of low-molecular-weight heparin were the 3 key factors responsible for the bleeding end points.

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DISCLOSURES

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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APPENDIX A. SUPPLEMENTARY DATA

The following is the Supplementary data to this article: