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Article

Efficacy and Safety of Ticagrelor Monotherapy in Patients with Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention: A Retrospective Study

Dan Song[1,*], Ziwen Chen[1]

[1]Department of Pharmacy, The Central Hospital of Enshi Tujia and Miao Autonomous Prefecture, 445000 Enshi, Hubei, China
*Correspondence: 13317269666@163.com (Dan Song)

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Abstract

Background: Dual antiplatelet therapy (DAPT) is the standard treatment for percutaneous coronary intervention (PCI), but its optimal duration is controversial. Ticagrelor monotherapy has obvious advantages in reducing the bleeding risk, so this study investigated its efficacy and safety. **Objective**: The objective of this study was to explore the efficacy and safety of administering ticagrelor monotherapy to patients with acute coronary syndrome (ACS) undergoing PCI. **Methods**: This retrospective study chose 110 patients with ACS undergoing PCI from January 2022 to April 2024. In accordance with different antiplatelet therapy methods, 58 patients received DAPT of ticagrelor and aspirin, and 54 cases were included in the control group (CG) after excluding 4 cases. Meanwhile, 52 cases received ticagrelor monotherapy after 3 months of DAPT, and 49 cases were classified as the observation group (OG) after excluding 3 cases. The platelet inhibition rates, platelet aggregation functions, and adverse events before and after treatment were compared. **Results**: Intergroup comparison showed no significant difference in adenosine diphosphate-induced platelet inhibition rates 3 months (T1) and 6 months (T2) after operation (p = 0.129, 0.137), and the inhibition rate in OG was significantly lower than that in CG 12 months (T3) after operation ($p < 0.001$). At T1, T2, and T3, no significant difference in fibrinogen and prothrombin time was found (p = 0.112, 0.751, 0.590, 0.771, 0.109, 0.121). After 12-month follow-up, intergroup comparison revealed no significant difference in the incidence of ischemic events (OG vs. CG: 4.08% vs. 9.26%; p = 0.515) and a significantly lower incidence of bleeding events in OG than in CG (OG vs. CG: 4.08% vs. 18.52%; p = 0.023). **Conclusion**: Administering ticagrelor monotherapy after short-term DAPT (three months) to patients with ACS undergoing PCI effectively controlled the platelet inhibition rate, reduced bleeding events, and did not increase the risk of ischemic events.

Keywords

ticagrelor; acute coronary syndromes; percutaneous coronary intervention; platelet

Introduction

Dual antiplatelet therapy (DAPT) is the normative antithrombotic therapy after percutaneous coronary intervention (PCI) [1] and is suitable for the treatment of coronary artery diseases, but its optimal duration is still a controversial topic in the scientific community [2]. Prolonged durations of DAPT can reduce ischemic events, but it is associated with a high bleeding rate and possibly fatal outcomes [3]. Thus, long-term DAPT has a high bleeding risk. In the past decade, PCI has achieved extensive progress, and at present, the clinical understanding of bleeding after PCI has considerably improved. Exploring an optimized antiplatelet therapy strategy has become a top priority.

The use of $P2Y_{12}$ inhibitors for monotherapy after short-term DAPT has emerged as a new strategy to reduce bleeding. Ticagrelor is a novel oral antagonist of the $P2Y_{12}$-adenosine diphosphate (ADP) receptor and offers a strategy with rapid onset and obvious platelet inhibition in patients with acute coronary syndrome (ACS) [4]. The main active metabolite of ticagrelor, a reversible P2Y platelet inhibitor [5], is similar to that of the parent drug and shows antiplatelet activity [6]. Ticagrelor monotherapy after short-term DAPT provides the benefit of strong $P2Y_{12}$ inhibition, which is expected to reduce bleeding risks in patients with ACS. Studies on ticagrelor monotherapy in patients with ACS undergoing PCI are common, but their results are controversial. Hence, this study investigated the safety and efficacy of ticagrelor monotherapy after three-month DAPT in patients with ACS undergoing PCI.

Materials and Methods

General Information

The clinical data of 110 patients with ACS who underwent PCI in our hospital from January 2022 to April 2024 were used for a retrospective analysis. In accordance with different antiplatelet therapy methods, 58 patients received DAPT of ticagrelor and aspirin, and 54 cases were included in the control group (CG) after excluding 4 cases. In the observation group (OG), 52 cases received ticagrelor monotherapy after 3 months of DAPT, and 49 cases were included after excluding 3 cases (Fig. 1).

This study is in line with the Declaration of Helsinki (2013) [7] and has been approved by the Ethical Committee of The Central Hospital of Enshi Tujia and Miao Autonomous Prefecture Hospital (approval no.: 2024-060-01). Informed consent was obtained from the patients.

Inclusion Criteria

(1) All patients received PCI for the first time in our hospital. (2) The New York Heart Association functional class of the patients was lower than Grade IV. (3) The platelet count was 100×10^9/L–450×10^9/L. (4) The patients had favorable compliance. (5) The patients had received only one antiplatelet therapy regimen.

Exclusion Criteria

(1) Patients with severe liver and kidney dysfunctions and malignant tumors; (2) patients with severe arrhythmia, severe cardiac insufficiency, acute and chronic pericarditis, uncontrolled hypertension, and diabetes mellitus; (3) patients with previous ischemic stroke within six months or hemorrhagic stroke; (4) patients who had undergone major surgery within three months; and (5) patients with coagulation dysfunction were excluded.

Methods

Control Group (CG)

Postoperative aspirin enteric-coated tablets (specification: 100 mg; NMPA approval no.: J20130078; manufacturer: Bayer HealthCare Manufacturing S.r.l.; (location: Via Delle Groane, Garbagnate Milanese MI, Italy) batch number: BJ88245) at an oral dose of 100 mg/d combined with ticagrelor (specification: 90 mg, NMPA approval no.: H20193252; manufacturer: Shanghai Huilun [Jiangsu] Pharmaceutical Co., Ltd.; Taizhou, Jiangsu, China; batch number: 2005341) at a maintenance dose of 90 mg were taken once every 12 h. The maintenance treatment lasted 12 months.

Observation Group (OG)

Three months after surgery, the patients received dual antithrombotic therapy of ticagrelor and aspirin enteric-coated tablets (the treatment standard referred to the method used in CG). Three months later, the patients received ticagrelor monotherapy at a maintenance dose of 90 mg once every 12 h for 12 months.

Observation Indicators

Basic Information

Basic data, including sex, age, body mass index, basic medical history, routine clinical indicators (blood lipid and blood pressure), ACS classification, number of lesions treated by PCI, and maximum stent length, were compared.

Platelet Inhibition Rate

The platelet inhibition rates of the two groups at postoperative 3 months (T1), 6 months (T2), and 12 months (T3) were compared. The ADP-induced platelet inhibition rate was determined through a thrombelastogram detected by a Teg Haemonetics analyzer (Haemonetics Company; 5000 type; NMPA (I): 20172406310; location: Boston, MA, USA; origin: MA, USA). Blood samples (3 mL) were collected using 3.8% sodium citrate and heparin anticoagulant tubes. Sample detection was completed within 2 h after blood collection, and the platelet inhibition rate was detected with ADP as an activator.

An ADP inhibition rate >90% was defined as high drug reactivity (bleeding risk), 75%–90% was defined as alert bleeding, 30%–75% indicated good efficacy, and <30% was defined as low drug reactivity (thrombosis risk).

Calculation formula:

ADP inhibition rate = [1 – (MAthrombin – MAfibbin)/MAADP – MAfibbin] × 100%, where MAADP, MAfibbin, and MAthrombin represent the maximum solidification strength under different conditions.

Coagulation Indexes

The coagulation indexes of the two groups were compared at T1, T2 and T3. Before surgery and at T1 and T3, elbow venous blood (2 mL) was collected to detect fibrinogen (FIB; normal range: 2–4 g/L) and prothrombin time (PT; normal range: 11–13 s) by using an automatic blood coagulation instrument (model: CL3000; Hunan Medical Products Administration Certification No.: 20222220378; Wuhan Easy Diagnosis Biomedicine Co., Ltd.; origin: Hubei, China).

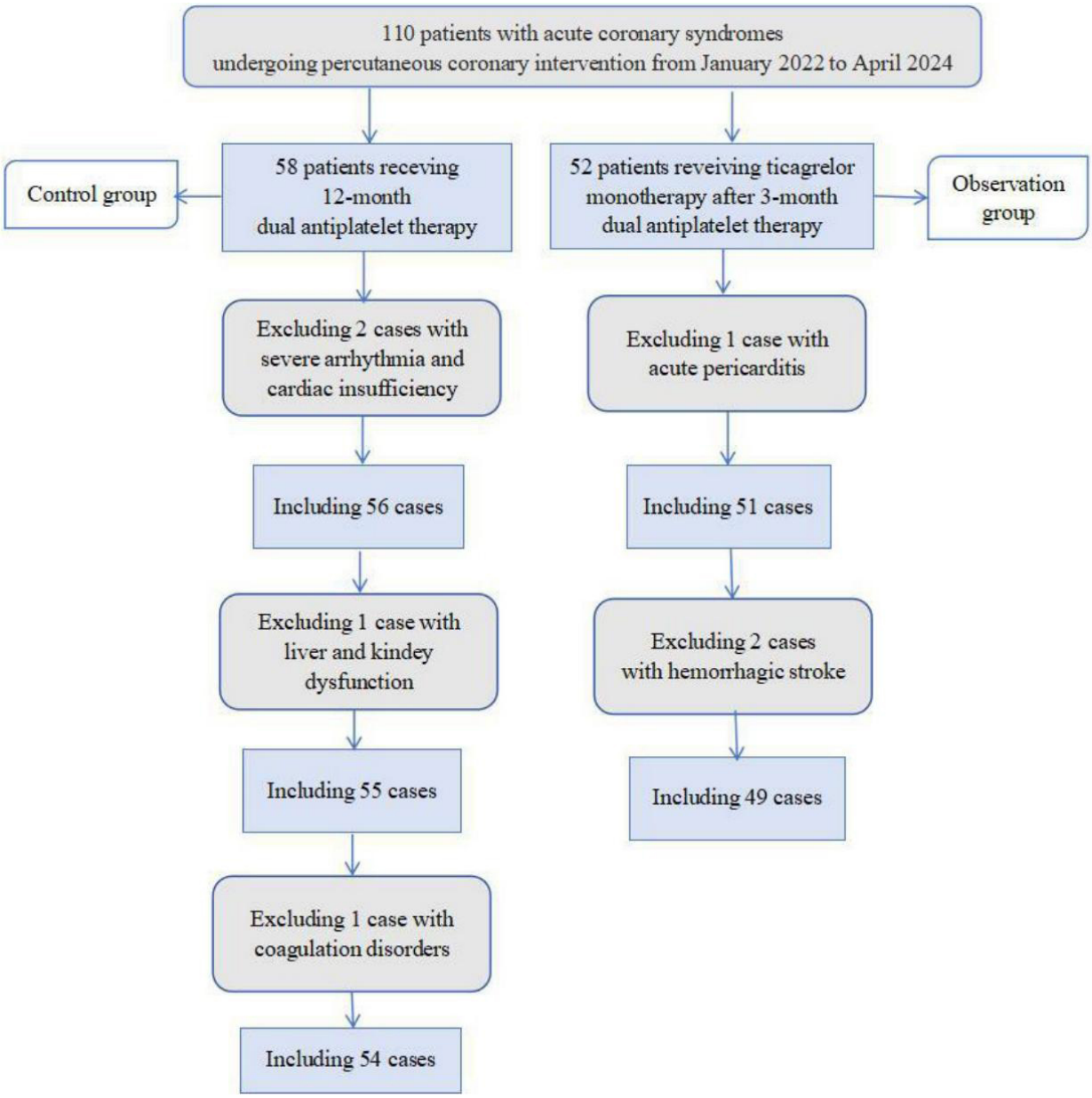

Fig. 1. Flow chart.

Adverse Events

The patients were followed up regularly for 12 months after discharge to record the occurrence of ischemic events, including ischemic stroke, cardiac death, acute myocardial infarction, and stent thrombosis, and bleeding events, such as mild (decrease in hemoglobin <3 g/dL with clinically visible bleeding), minor (reduction in hemoglobin within 3–5 g/dL with visible bleeding), and major bleeding (reduction in hemoglobin >5 g/dL and intracranial hemorrhage in the clinic or imaging) [8].

Statistical Methods

Statistical analysis was performed using SPSS 25.0 (Version : 25.0; Manufacturer: International Business Machines Corporation; location: Armonk, NY, USA).

The Shapiro–Wilk method was used to test the normal distribution of continuous variables. The data that conformed to the normal distribution were expressed as (mean $\pm$ SD), and *t* test was performed. The data that did not conform to the normal distribution were presented as M (P_{25}, P_{75}), and the Mann–Whitney U test was applied.

The measurement data were analyzed via Pearson's chi-square test or Fisher's exact test. $p < 0.05$ was considered statistically significant.

Table 1. Comparison of the baseline data of all patients.

Groups	OG (n = 49)	CG (n = 54)	z/t/χ^2	*p*
Sex (n, %)			0.196	0.658
Male	23 (46.94)	23 (42.59)		
Female	26 (53.06)	31 (57.41)		
Age (years old, (mean ± SD))	66.92 ± 12.95	62.87 ± 10.91	1.720	0.088
Body mass index (kg/m^2, (mean ± SD))	26.47 ± 3.33	26.84 ± 2.81	−0.611	0.543
Basic medical history (n, %)				
Hypertension	11 (22.45)	14 (25.93)	0.169	0.681
Hyperlipidemia	3 (6.12)	3 (5.56)	0.000	1.000
Diabetes mellitus	2 (4.08)	4 (7.41)	0.089	0.765
Total cholesterol (mmol/L, M (P_{25}, P_{75}))	4.30 (3.90, 5.00)	4.55 (4.00, 5.20)	−0.856	0.392
Triacylglycerol (mmol/L, M (P_{25}, P_{75}))	1.33 (0.89, 1.72)	1.32 (0.94, 1.76)	−0.310	0.756
Systolic pressure (mmHg, M (P_{25}, P_{75}))	110.00 (100.00, 122.00)	111.50 (103.00, 128.00)	−1.602	0.109
Diastolic pressure (mmHg, M (P_{25}, P_{75}))	72.00 (64.00, 82.00)	71.00 (65.00, 82.00)	−0.499	0.618
ACS classification (n, %)			0.101	0.951
Unstable angina	24 (48.98)	27 (50.00)		
ST-segment elevation myocardial infarction	11 (22.45)	13 (24.07)		
Non-ST-segment elevation myocardial infarction	14 (28.57)	14 (25.93)		
Number of lesions treated by PCI (n, %)			0.037	0.982
1	31 (63.27)	35 (64.81)		
2	13 (26.53)	14 (25.93)		
≥3	5 (10.20)	5 (9.26)		
Maximum stent length (mm, M (P_{25}, P_{75}))	22.10 (18.20, 26.60)	22.60 (18.80, 26.90)	−0.733	0.464
Minimum stent length (mm, (mean ± SD))	18.78 ± 2.46	19.07 ± 2.67	−0.573	0.568

The data that conformed to the normal distribution were expressed as (mean ± SD), and those that did not conform to the normal distribution were presented as M (P_{25}, P_{75}). OG, observation group; CG, control group; ACS, acute coronary syndrome; PCI, percutaneous coronary intervention.

Table 2. Comparison of the platelet inhibition rates of the two groups (%, M (P_{25}, P_{75})).

Groups	OG (n = 49)	CG (n = 54)	z	*p*
T1	59.00 (53.00, 64.00)	57.50 (52.00, 63.00)	−1.519	0.129
T2	66.00 (60.00, 71.00)	68.50 (62.00, 74.00)	−1.488	0.137
T3	53.00 (46.00, 62.00)	62.00 (56.00, 74.00)	−4.050	<0.001

Results

Baseline Data

Table 1 shows no significant difference in preoperative baseline data, such as sex, age, body mass index, and basic medical history, between both groups ($p > 0.05$).

Platelet Inhibition Rate

Table 2 shows no significant difference in platelet inhibition rates induced by ADP between the two groups at T1 and T2 ($p = 0.129, 0.137$) and a significantly lower platelet inhibition rate in OG compared with CG at T3 ($p < 0.001$).

Coagulation Indexes

Table 3 shows no significant difference in FIB and PT between the two groups at T1, T2, and T3 ($p = 0.112, 0.751, 0.590, 0.771, 0.109, 0.121$).

Adverse Events

After 12-month follow-up, intergroup comparison revealed no significant difference in the incidence of ischemic events between the two groups (OG *vs.* CG: 4.08% *vs.* 9.26%; $p = 0.515$) and a significantly lower incidence of bleeding events in OG compared with that in CG (OG *vs.* CG: 4.08% *vs.* 18.52%; $p = 0.023$), as shown in detail in Table 4.

Table 3. Comparison of the coagulation indexes of the two groups (M (P_{25}, P_{75})).

Groups		OG (n = 49)	CG (n = 54)	z	*p*
FIB (g/L)	T1	4.53 (4.06, 5.16)	4.93 (4.11, 5.38)	−1.588	0.112
	T2	4.57 (4.31, 5.23)	4.75 (4.22, 5.37)	−0.317	0.751
	T3	4.86 (4.37, 5.37)	4.94 (4.42, 5.55)	−0.538	0.590
PT (s)	T1	13.09 (12.18, 14.46)	13.10 (12.14, 14.15)	−0.291	0.771
	T2	16.38 (14.37, 17.86)	15.55 (13.94, 17.35)	−1.605	0.109
	T3	14.52 (13.33, 15.79)	15.17 (13.25, 16.89)	−1.549	0.121

FIB, fibrinogen; PT, prothrombin time.

Table 4. Comparison of adverse events in both groups (n, %).

Groups	OG (n = 49)	CG (n = 54)	χ^2	*p*
Ischemic events	2 (4.08)	5 (9.26)	0.423	0.515
Ischemic stroke	1 (2.04)	1 (1.85)		
Cardiac death	0 (0.00)	1 (1.85)		
Acute myocardial infarction	0 (0.00)	1 (1.85)		
Stent thrombosis	1 (2.04)	2 (3.70)		
Bleeding events	2 (4.08)	10 (18.52)	5.202	0.023
Mild bleeding	1 (2.04)	3 (5.56)		
Minor bleeding	1 (2.04)	4 (7.41)		
Major bleeding	0 (0.00)	3 (5.56)		

Discussion

DAPT is the key to preventing recurrent ischemic events after PCI, but it increases the risk of bleeding complications [9]. Relevant guidelines recommend 12-month DAPT as the classic strategy for preventing long-term recurrent events and stent thrombosis [10]. In recent years, because of the increased bleeding risk caused by DAPT, multiple clinical studies have probed the efficacy and safety of discontinuing aspirin and giving ticagrelor monotherapy to patients receiving DAPT after PCI [11,12]. Ticagrelor is the first reversible ADP $P2Y_{12}$ receptor antagonist approved for treating ACS [13], and it exerts direct action rather than being activated by liver metabolism.

The platelet inhibition rate measured by thrombelastogram in this study revealed the antiplatelet effect on patients after PCI. An extremely high or low inhibition rate has adverse effects on patients, so the inhibition rate needs to be controlled in an appropriate range. The intergroup comparison showed no significant difference in ADP-induced platelet inhibition rates at T1 and T2 ($p > 0.05$) and a significantly lower ADP-induced platelet inhibition rate in OG compared with that in CG at T3 ($p < 0.001$). The inhibition rate ranged from 30% to 75%, indicating that ticagrelor monotherapy after 3 months of DAPT effectively controlled the platelet inhibition rate, thereby reducing the bleeding risk to a certain extent. Kim *et al.* [14] studied patients with ACS undergoing drug-eluting stent treatment and found that in comparison with ticagrelor-based 12-month DAPT, ticagrelor monotherapy after 3-month DAPT exhibits a statistically apparent reduction in the composite outcome of major bleeding and cardiovascular events within 1 year. Gragnano *et al.* [15] discovered that regardless of PCI complexity, compared with standard DAPT, P2Y inhibitor monotherapy after 1–3 months of DAPT results in semblable mortality and ischemic events and a reduced risk of major bleeding; these results are similar to those obtained in the present study. After 12-month follow-up, no significant difference in the incidence of ischemic events was found between OG and CG (4.08% *vs.* 9.26%; $p > 0.05$), and OG had a significantly lower incidence of bleeding events than CG (4.08% *vs.* 18.52%; $p < 0.05$), indicating that antiplatelet therapy with ticagrelor monotherapy after 3-month DAPT reduces bleeding events. Ticagrelor can affect the expression of molecules involved in inflammatory regression [16]. It is an antagonist of equilibrative nucleoside transporter-1 [17]. Adenosine receptor antagonism suppresses the activation of threonine kinase and the mammalian target of rapamycin [18]. Additionally, ticagrelor restrains the equilibrative nucleoside transporter-1 adenosine transporter protein, resulting in an elevated adenosine concentration in the blood. This action enhances the biological efficacy of ticagrelor in anticoagulation and anti-inflammation effects [19]. Therefore, in theory, ticagrelor has antiplatelet and anti-inflammatory effects, and it can replace the combination therapy of DAPT as a single drug treatment.

This study found no significant difference in FIB and PT in both groups at T1, T2, and T3 ($p > 0.05$). The comparison of the coagulation function indexes revealed no difference in the effects of the two treatment methods on the coagulation indexes. The antiplatelet therapy with ticagrelor monotherapy and DAPT for 12 months had the

same effects on stabilizing the coagulation function. The GLOBAL LEADERS study published in 2018 is a representative study [20], and it demonstrated that ticagrelor monotherapy after short-term DAPT may be reasonable.

This study has some limitations. For instance, the small sample size and single sample range resulted in biased research data. In addition, as a retrospective research, this study lacked data on the therapeutic effect and adverse reactions of ticagrelor monotherapy. Large-scale evidence that can explain the differences in individual responses to ticagrelor in different populations remains lacking.

Conclusion

Administering ticagrelor monotherapy after short-term DAPT to patients with ACS undergoing PCI can effectively control the platelet inhibition rate and reduce bleeding events, and it does not increase the risk of ischemic events. An appropriate antiplatelet therapy should be selected for different individuals in clinical practice.

Availability of Data and Materials

The datasets used and/or analyzed during the current study were available from the corresponding author on reasonable request.

Author Contributions

DS designed the study; both authors conducted the study; ZWC collected and analyzed the data. DS and ZWC participated in drafting the manuscript, and both authors contributed to critical revision of the manuscript for important intellectual content. Both authors gave final approval of the version to be published. Both authors participated fully in the work, take public responsibility for appropriate portions of the content, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

This study has been approved by the Medical Ethics Committee of the Central Hospital of Enshi Tujia and Miao Autonomous Prefecture (Approval No.:2024-060-01). This study has obtained the informed consent of patients.

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Conflict of Interest

The authors declare no conflict of interest.

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