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Effect of a 180 mg ticagrelor loading dose on myocardial necrosis in patients undergoing elective percutaneous coronary intervention: A preliminary study

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Abstract

Background: *To examine whether a loading dose of ticagrelor on top of clopidogrel reduced post-percutaneous coronary intervention (PCI) myonecrosis.*

Methods: *Seventy seven coronary artery disease patients received a loading dose of 300 mg clopidogrel pre-PCI and were divided into three groups: group TT (n = 36): a loading dose of 180 mg ticagrelor pre-PCI, followed by ticagrelor 90 mg twice daily commencing one day post-PCI; group CT (n = 26): a maintenance dose of ticagrelor 90 mg twice daily; group CC (n = 15): clopidogrel 75 mg daily post-PCI. High sensitivity cardiac troponin T (hs-cTnT) and creatine kinase-MB (CK-MB) were measured pre-PCI and 0 h, 2 h or 24 h post-PCI. Platelet aggregation was measured in a separate cohort of 54 coronary artery disease patients (35 diabetic and 19 non-diabetic patients).*

Results: *There were no significant differences in hs-cTnT and CK-MB concentration among the three groups. In group TT, diabetic patients had significant higher Δhs-cTnT$_{2h-0h}$ than non-diabetic patients. In the second cohort, although baseline platelet aggregation was higher in diabetic than non-diabetic patients, platelet aggregation was comparable between diabetic and non-diabetic patients at 0 and 2 h post-PCI.*

Conclusions: *This study indicates that a loading dose of ticagrelor does not significantly reduce post-PCI myonecrosis. Diabetes is associated with more post-PCI myonecrosis. A loading dose of ticagrelor effectively reduces platelet aggregation in diabetic patients.* (Cardiol J 2017; 24, 1: 15–24)

Key words: coronary artery disease, ticagrelor, clopidogrel, myocardial necrosis, high sensitivity cardiac troponin T

Introduction

Dual antiplatelet therapy with aspirin and a P2Y12 inhibitor is the standard of care for acute coronary syndrome (ACS) [1, 2]. Clopidogrel, a thienopyridine, is a prodrug that undergoes hepatic conversion, therefore leading to a delayed onset of action and substantial variability between individuals in levels of platelet inhibition. Up to one third of patients are low responders to clopidogrel

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with inadequate platelet inhibition [3]. Ticagrelor, a reversible and direct-acting oral P2Y12-receptor antagonist, provides greater and more consistent platelet inhibition than clopidogrel, with more rapid onset and offset of action [4–6]. In the PLATelet inhibition and patient Outcomes (PLATO) trial, reversible long-term P2Y12 inhibition with ticagrelor was better than that with clopidogrel for the prevention of cardiovascular and total death, myocardial infarction (MI), and stent thrombosis, without an increase in the rates of major bleeding in a broad population of patients with ACS, who began treatment upon hospital admission [7, 8]. Although a loading dose of ticagrelor was used in PLATO trial [9], a recent study demonstrated that a loading dose of ticagrelor was not associated with a further platelet inhibition after switching from clopidogrel to ticagrelor for patients with ACS receiving ongoing clopidogrel treatment [10]. However, the above study only included clopidogrel responders [10]. It is known that a large number of patients with coronary artery disease (CAD) have diabetes and patients with diabetes had a higher number of clopidogrel non-responders, and increased platelet reactivity compared with nondiabetic subjects on combined aspirin and clopidogrel treatment [11]. Since ticagrelor has a higher potency of platelet inhibition [12], and stronger anti-inflammatory effect and vascular endothelial protection [13] compared to clopidogrel, it is herein hypothesized that an additional dose of ticagrelor might improve myonecrosis post-percutaneous coronary intervention (PCI). Therefore, in this observational study, the aim was to assess whether the administration of a loading dose of ticagrelor on top of clopidogrel reduces myocardial necrosis (measured by high sensitivity cardiac troponin T (hs-TnT) and creatine kinase-MB (CK-MB), after PCI in patients with stable CAD in relation to diabetic status.

Methods

Study patients

Patients with stable CAD who successfully underwent PCI at Xinhua Hospital, Shanghai, China were recruited between 1 January and 31 July 2014. Patients with class III/IV heart failure, abnormal liver or renal function, various inflammatory diseases or incorporative infection were excluded from the study. A total of 83 patients were included in the present study and all patients were given 300 mg clopidogrel loading dose before coronary angiography. Patients were divided into three groups: 1) group TT received additional 180 mg ticagrelor loading dose before PCI, and followed by a maintenance dose of 90 mg ticagrelor twice daily from the next day before and after PCI; 2) group CT received a maintenance dose of 90 mg ticagrelor twice daily before and after PCI; 3) group CC patients continued clopidogrel 75 mg daily therapy. Six patients were excluded due to acute myocardial ischemia caused by injury of side branch during PCI procedure. A total of 77 patients were finally included in this prospective study (group TT: n = 36, group CT: n = 26, and group CC: n = 15). All three groups were given 100 mg aspirin and 10 mg rosuvastatin daily. Baseline patient characteristics included age, sex and cardiovascular risk factors such as smoking, family history, hypertension and diabetes. The use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers, calcium channel blockers, beta-blockers and/or antidiabetic therapy (including insulin or oral medication) was decided on an individual basis by the attending physician.

In order to investigate the antiplatelet efficiency of a loading dose of ticagrelor in diabetic patients, another cohort of 54 patients with CAD were recruited and divided into diabetic group (n = 35) and non-diabetic group (n = 19) according to the global guideline for type 2 diabetes. Patients in both groups received 180 mg ticagrelor loading dose before PCI, and was followed by 90 mg ticagrelor twice daily before and after PCI. All patients were given 100 mg aspirin and 10 mg rosuvastatin daily. Baseline patient characteristics and medication details were recorded as above.

The present study complied with the Declaration of Helsinki and was registered in the Chinese Clinical Trial Registry (no. ChiCTR-TRC-14004377; http://www.chictr.org) and approved by the Ethics Committee of Experimental Research, Jiaotong University. All patients provided written informed consent.

Percutaneous coronary intervention

Percutaneous coronary intervention was performed via the radial artery according to standard clinical practice. The recorded coronary angiography films were analyzed with SYNTAX Score to evaluate the complexity of the coronary lesions by two experienced cardiologists blinded to the patient's clinical and laboratory data. Each coronary lesion producing a ≥ 50% luminal obstruction in vessels ≥ 1.5 mm was scored and collected to generate the SYNTAX score. The calculation was performed with the website-based SYNTAX calculator version 2.28 (www.syntaxscore.com). More-

over, the following PCI-related parameters were also collected including the number of diseased vessels and the number of stents implanted. More than 50% stenosis of the vessel was considered as a diseased vessel and culprit lesions with ≥ 75% stenosis were dilated and subsequently stented with drug-eluting stents. A vascular segment was considered to have been treated successfully when residual luminal narrowing in the dilated segment immediately after PCI was < 5%. The PCI procedure was considered successful when the target lesion was successfully treated without causing major complications (electrocardiographic or enzymatic evidence of new MI and or the need for bypass surgery during hospitalization or in-hospital death).

Biochemical analysis

Blood was taken the morning before coronary angiography and also before the loading dose of P2Y12 antagonists for baseline measurements. Serum samples were obtained by centrifuging the blood at 1600 g for 15 min at room temperature within 30 min of venipuncture and aliquots were stored immediately at –80°C for future analysis. Total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol and triglycerides were determined by enzymatic methods on the day of blood collection in the laboratories of the Xinhua Hospital. Fasting plasma glucose was measured by the hexokinase method. Serum hypersensitive C-reactive protein was detected by the particle-enhanced turbidimetric immunoassay. Serum aspartate aminotransferase, alanine aminotransferase, blood urea nitrogen and creatinine were detected using routine biochemical methods. All assays were performed in a blinded manner.

hs-cTnT and CK-MB measurements

Ten mL of blood samples for hs-cTnT and CK-MB testing were drawn into heparin tubes in each patient before PCI and 0 h, 2 h after PCI. Blood samples were centrifuged at 3,000 g for 10 min at room temperature and then plasma samples were stored at –80°C for future analysis. Plasma levels of hs-cTnT were analyzed using the new hs-cTnT quantitative electro chemiluminescence immunoassay (Roche Diagnostics, Mannheim, Germany). The lower detection limit is 0.01 μg/L with a recommended diagnostic threshold of 0.03 μg/L (hs-cTnT levels were detectable in all patients). Plasma levels of CK-MB were measured by enzyme linked immunosorbent assay (ELISA).

Platelet aggregation test

Blood samples were collected before PCI (also before admission of ticagrelor) and 0 h, 2 h after PCI. Platelet aggregation were determined by light transmission aggregometry (LBY-NJ4, PRECIL, Beijing, China) according to the guide of manufacturer in the central laboratory of the Xinhua Hospital.

Statistical analysis

Baseline demographics of patients between groups were compared with the χ^2 test or Fisher's exact test for dichotomous variables and the one-way ANOVA test for continuous variables, as appropriate. Comparisons of concentrations of hs-cTnT or bleeding events between the three groups were achieved by one-way ANOVA test and Kruskal-Wallis H test, respectively. Spearman correlation analysis was performed to assess the correlations between log-transformed hs-cTnT at 2 h after PCI and baseline characteristics. Variables with $p < 0.15$ from spearman correlation analysis were included in multivariable linear regression analysis to evaluate independent predictors of hs-cTnT at 2 h after PCI. Continuous variables were expressed as mean ± standard deviation, if not stated otherwise. A two-sided p-value of < 0.05 was considered significant. All statistical analyses were performed with IBM SPSS statistics for Windows 19.0 (SPSS, Inc., Chicago, IL).

Results

Population characteristics

Baseline variables were comparable among group TT, CT and CC (Table 1) except that there were fewer men and fewer hypertensive patients in group TT. For the second cohort of 54 CAD patients recruited for investigation on the effects of ticagrelor on platelet aggregation in diabetes, baseline variables were comparable among diabetic (n = 35) and non-diabetic patients (n = 19) (Table 2).

Myocardial necrosis

No significant differences were observed among the three groups (TT, CT and CC) in serum hs-cTnT concentrations before PCI and at 0 h, or 2 h after PCI (Fig. 1A). hs-cTnT was slightly increased at 2 h after PCI in both group CT and group CC, however, they were slightly decreased in group TT when compared to 0 h after PCI, but this difference was not significant (Fig. 1C). Similarly, no significant differences were found in CK-MB levels before PCI, and at 0 h or 24 h among the three groups (Fig. 1B).

Table 1. Baseline characteristics — TT, CT and CC groups.

	Group TT (n = 36)	Group CT (n = 26)	Group CC (n = 15)	P
Demographics:				
Age [years]	66.1 ± 10.1	65.8 ± 10.4	66.9 ± 10.5	0.920
Male	20 (56%)	23 (88%)	12 (80%)	0.014
Medical history:				
Family history of CAD	3 (8%)	1 (4%)	2 (13%)	0.548
Hypertension	17 (47%)	18 (69%)	13 (87%)	0.021
Diabetes	11 (31%)	9 (35%)	5 (33%)	0.943
Prior myocardial infarction	7 (19%)	3 (12%)	3 (20%)	0.673
Smoking	13 (36%)	11 (42%)	6 (40%)	0.883
Baseline medications:				
Statin	35 (97%)	26 (100%)	15 (100%)	1.000
ACEI or ARB	16 (44%)	14 (54%)	11 (73%)	0.174
Beta-blocker	34 (97%)	25 (96%)	15 (100%)	0.985
Calcium-channel blocker	0 (0%)	4 (15%)	2 (13%)	0.058
Hypoglycemic agent	10 (28%)	9 (35%)	4 (27%)	0.810
Baseline laboratory data:				
HSCRP [mg/L]	2.57 ± 2.65	2.54 ± 3.54	2.50 ± 2.62	0.475
ALT [U/L]	22 ± 14	19 ± 7	36 ± 48	0.233
AST [U/L]	21 ± 8	18 ± 8	26 ± 18	0.052
Cholesterol [mmol/L]	4.04 ± 1.21	4.03 ±0.82	3.77 ± 0.69	0.646
Triglyceride [mmol/L]	1.83 ± 1.47	1.69 ± 1.17	1.33 ± 0.51	0.916
LDL [mmol/L]	2.35 ± 0.90	2.53 ± 0.69	2.48 ± 0.56	0.124
HDL [mmol/L]	1.32 ± 0.31	1.31 ± 0.26	1.49 ± 0.36	0.312
Glucose [mmol/L]	5.58 ± 1.35	6.17 ± 2.02	6.03 ±1.88	0.748
BUN [μmol/L]	5.34 ± 1.14	5.73 ± 1.24	5.57 ± 1.28	0.540
Creatinine [mmol/L]	65.9 ± 17.7	74.1± 16.7	69.7 ± 15.2	0.210
Coronary angiography details:				
SYNTAX Score	14.9 ± 1.7	11.3 ± 1.5	13.5 ± 2.4	0.338
Number of lesions	1.8 ± 0.9	1.5 ± 0.7	1.7 ± 0.8	0.441
Number of stents	1.5 ± 0.6	1.3 ± 0.5	1.2 ± 0.4	0.110

CAD — coronary artery disease; ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; HSCRP — hypersensitive C reactive protein; ALT — alanine transaminase; AST — aspartate transaminase; LDL — low-density lipoprotein; HDL — high-density lipoprotein; BUN — blood urea nitrogen

The influence of diabetic status

The effects of a loading dose of ticagrelor on myocardial necrosis separately in diabetic and non-diabetic patients were noted (Fig. 2). Patients were stratified according to the presence of type 2 diabetes. Both hs-cTnT (Fig. 2A, B) and CK-MB (Fig. 2C, D) did not differ significantly among the three groups in either diabetic or non-diabetic patients. A comparison was made, hs-cTnT (Fig. 3A–C) and CK-MB (Fig. 3D–F) between diabetic and non-diabetic separately in groups TT, CT and CC. There were no significant differences in hs-cTnT and CK-MB at the different time points (above) between diabetic and non-diabetic patients in individual groups. We further compared Δhs-cTnT$_{2h-0h}$ between diabetic and non-diabetic patients in groups TT, CT and CC (Fig. 3G–I). In group TT, diabetic patients had significantly higher Δhs-cTnT$_{2h-0h}$ than non-diabetic patients (Fig. 3G). The difference in Δhs-cTnT$_{2h-0h}$ between diabetic and non-diabetic patients in group CT or CC was not significant (Fig. 3H, I).

Platelet aggregation

Attention was then turned as to whether higher Δhs-cTnT$_{2h-0h}$ levels after PCI in diabetic

Table 2. Baseline characteristics — diabetic and non-diabetic patients.

	DM (n = 35)	Non-DM (n = 19)	P
Demographics:			
Age [years]	70 ± 9	68 ± 15	0.793
Male	16 (46%)	12 (63%)	0.225
Medical history:			
Family history of CAD	22 (63%)	12 (63%)	0.983
Hypertension	32 (91%)	14 (74%)	0.082
Diabetes	35 (100%)	0 (0%)	0.000
Post PCI	12 (34%)	4 (21%)	0.314
Smoking	9 (26%)	7 (37%)	0.397
Baseline medications:			
ACE inhibitors/ARBs	23 (66%)	12 (63%)	0.852
Beta-blocker	33 (94%)	16 (84%)	0.227
Calcium-channel blocker	7 (20%)	2 (11%)	0.377
Hypoglycemic agent	21 (60%)	0 (0%)	0.000
Baseline laboratory data:			
HSCRP [mg/L]	2.33 ± 2.71	6.38 ± 23.20	0.321
ALT [U/L]	19 ± 8	23 ± 21	0.942
AST [U/L]	19 ± 5	25 ± 17	0.085
Cholesterol [mmol/L]	3.83 ± 1.01	4.26 ± 1.01	0.085
Triglyceride [mmol/L]	1.54 ± 0.86	1.68 ± 1.22	0.971
LDL [mmol/L]	2.18 ± 0.68	2.42 ± 0.60	0.133
HDL [mmol/L]	1.27 ± 0.29	1.37 ± 0.24	0.077
Glucose [mmol/L]	7.20 ± 2.47	5.20 ± 0.73	0.000
BUN [μmol/L]	6.15 ± 2.34	5.13 ± 1.36	0.147
Creatinine [mmol/L]	73.4 ± 16.2	74.0 ± 17.5	0.779

DM — diabetes mellitus; CAD — coronary artery disease; PCI — percutaneous coronary intervention; ACE — angiotensin-converting enzyme; ARBs — angiotensin II receptor blockers; HSCRP — hypersensitive C reactive protein; ALT — alanine transaminase; AST — aspartate transaminase; LDL — low-density lipoprotein; HDL — high-density lipoprotein. BUN — blood urea nitrogen

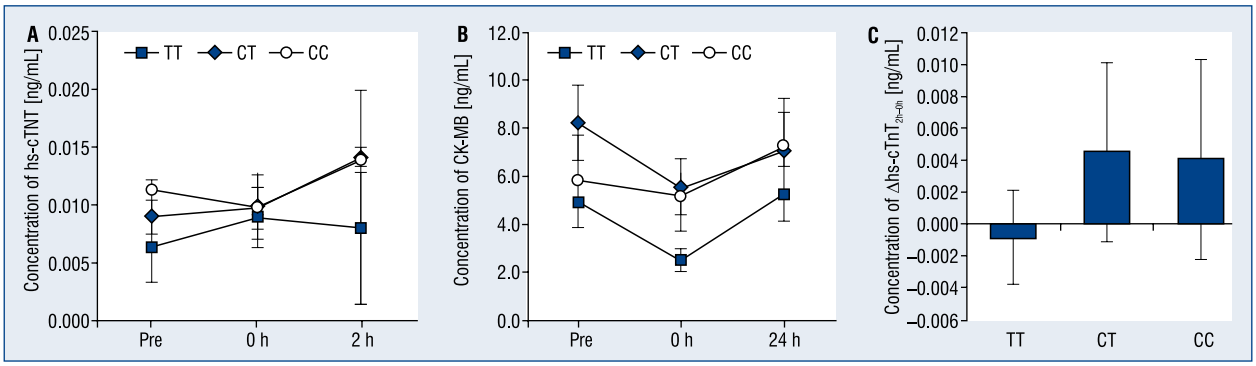

Figure 1. The effects of loading dose of ticagrelor on myocardial necrosis. All patients were given clopidogrel 300 mg loading dose before coronary angiography. Group TT (n = 36) received a loading dose of 180 mg ticagrelor pre percutaneous coronary intervention (PCI) and a maintenance dose of ticagrelor 90 mg twice per day commencing the day after PCI. Group CT (n = 26) received a maintenance dose of ticagrelor 90 mg twice pear day post PCI while group CC (n = 15) continued clopidogrel 75 mg daily. Concentrations of high sensitivity cardiac troponin T (hs-cTnT) (**A**) and creatine kinase-MB (CK-MB) (**B**) were measured before PCI and at 0 h and 2 h after PCI in these three groups; **C.** Delta change of hs-cTnT at 2 h relative to 0 h after PCI in groups TT, CT and CC; hs-cTnT = hs-cTnT$_{2h}$ – hs-cTnT$_{0h}$. Data are shown as mean ± SEM.

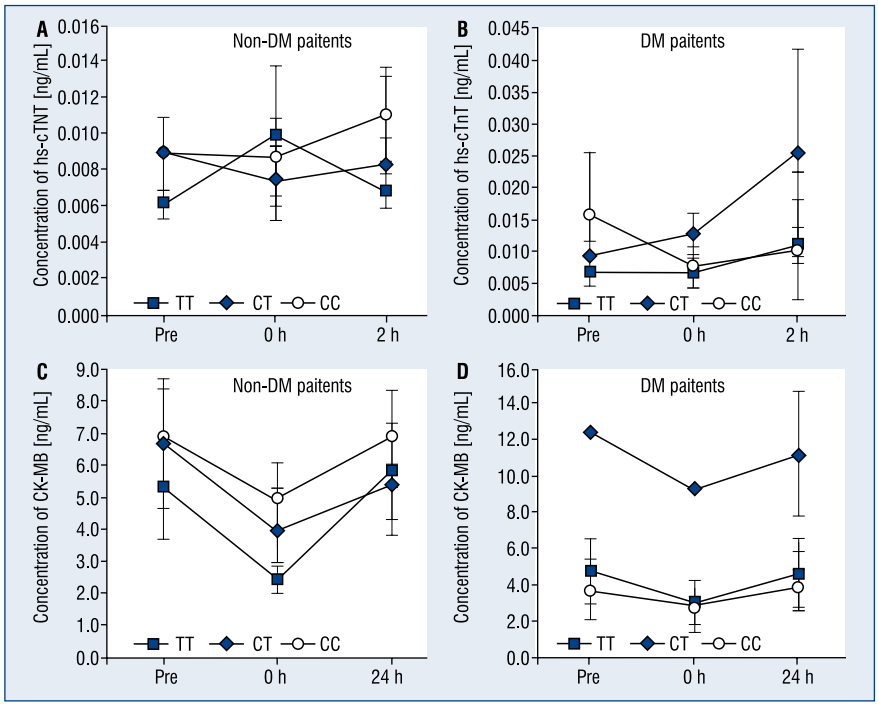

Figure 2. Concentrations of high sensitivity cardiac troponin T (hs-cTnT) and creatine kinase-MB (CK-MB) in diabetic and non-diabetic patients. All patients were given clopidogrel 300 mg loading dose before coronary angiography. Group TT (n = 36) received a loading dose of 180 mg ticagrelor pre percutaneous coronary intervention (PCI) and a maintenance dose of ticagrelor 90 mg twice per day commencing the day after PCI. Group CT (n = 26) received a maintenance dose of ticagrelor 90 mg twice per day post PCI while group CC (n = 15) continued clopidogrel 75 mg daily. hs-cTnT (**A**) or CK-MB (**C**) in non-diabetic patients in these three groups. hs-cTnT (**B**) or CK-MB (**D**) in diabetic patients in these three groups. Data are shown as mean ± SEM; DM — diabetes mellitus.

patients were associated with higher platelet aggregation in a separate cohort of CAD patients receiving a loading dose of 180 mg ticagrelor before PCI. Baseline platelet aggregation rate was significantly higher in diabetic patients compared to non-diabetic patients (Fig. 4A). Platelet aggregation was significantly reduced at 0 h and 2 h after PCI in both diabetic and non-diabetic patients due to the effect of a loading dose of ticagrelor (Fig. 4A). The reduction of platelet aggregation rate was greater in diabetic patients than non-diabetic patients at 0 h after PCI (Fig. 4B).

Associations between hs-cTnT levels and baseline characteristics

As shown in Figure 1, at 2 h after PCI hs-cTnT levels increased slightly in all groups compared to baseline levels. Since hs-cTnT was influenced by a lot of other factors [14], we intended to know whether baseline characteristics affected serum hs-cTnT concentrations at 2 h after PCI (Table 3). Only baseline hs-cTnT remained significantly correlated with hs-cTnT at 2 h after PCI in multivariable analysis. None of the baseline characteristics were independent factors affecting hs-cTnT at 2 h after PCI in stable CAD patients.

Bleeding events

A comparison was made of the total number of bleeding events among the three groups in diabetic and non-diabetic patients as well as the total number of bleeding events between diabetic and non-diabetic patients in groups TT, CT and CC (Table 4) over a 1 month period subsequent to PCI. No significant differences in bleeding events (whether major or minor bleeding) were found among groups independent of loading dose of ticagrelor or diabetic status.

Discussion

In stable CAD patients already receiving a loading dose of 300 mg clopidogrel, an additional loading dose of 180 mg ticagrelor did not significantly lower hs-cTnT or CK-MB concentration after PCI. After we stratified patients according

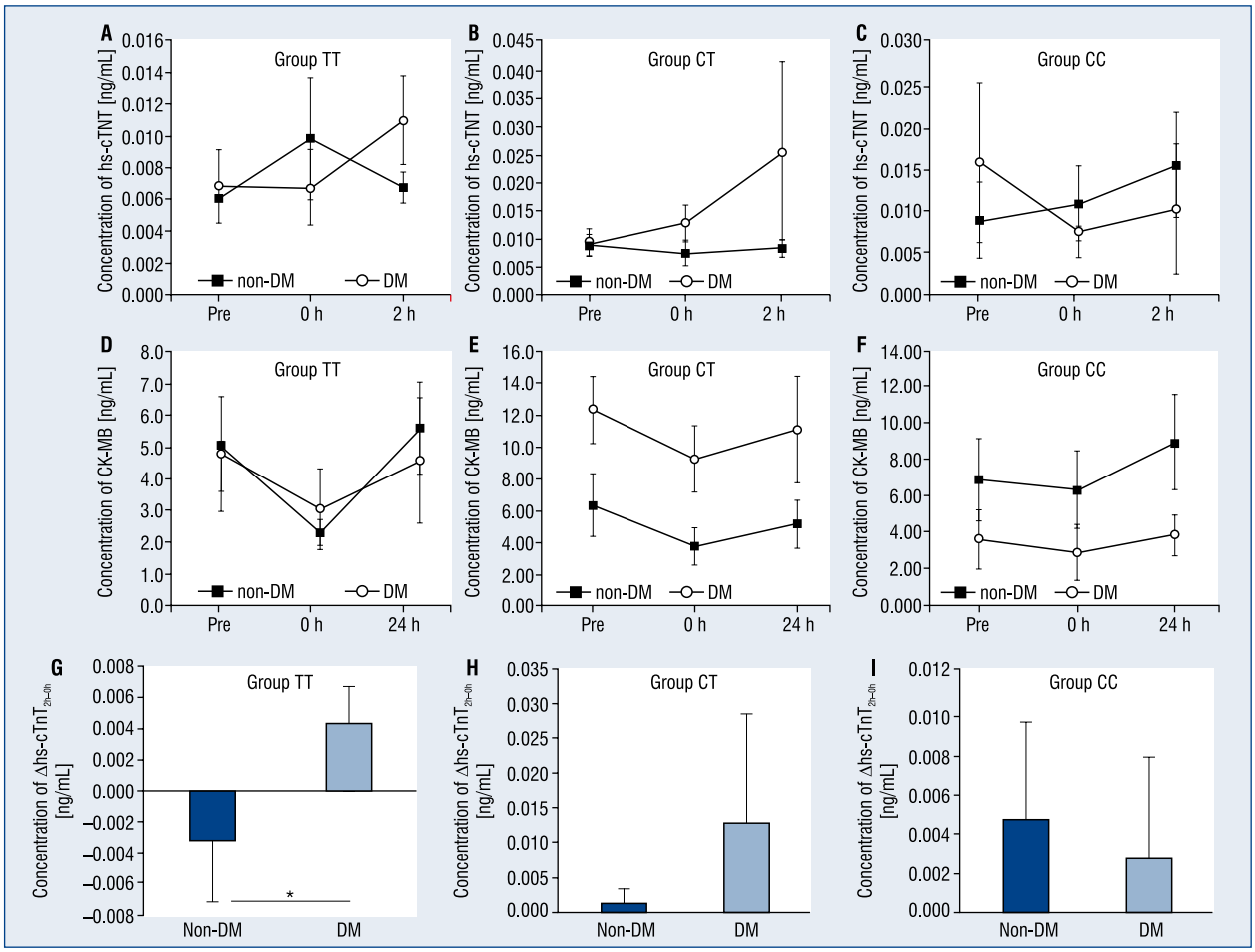

Figure 3. Concentrations of high sensitivity cardiac troponin T (hs-cTnT), creatine kinase-MB (CK-MB) and delta change of hs-cTnT in diabetic and non-diabetic patients. All patients were given clopidogrel 300 mg loading dose before coronary angiography. Group TT (n = 36) received a loading dose of 180 mg ticagrelor pre percutaneous coronary intervention (PCI) and a maintenance dose of ticagrelor 90 mg twice per day from the next day after PCI. Group CT (n = 26) received a maintenance dose of ticagrelor 90 mg twice per day post PCI while group CC (n = 15) continued clopidogrel 75 mg daily. Comparison in hs-cTnT between diabetic and non-diabetic patients in group TT (**A**), group CT (**B**) and group CC (**C**). Comparison in CK-MB between diabetic and non-diabetic patients in group TT (**D**), group CT (**E**) and group CC (**F**). Comparison in delta change of hs-cTnT between diabetic and non-diabetic patients in group TT (**G**), group CT (**H**), and group CC (**I**). Data are shown as mean ± SEM; DM — diabetes mellitus; *p < 0.05.

to the presence of type 2 diabetes, we found that in the patient group who received a loading dose of ticagrelor, diabetic patients had higher Δhs-cTnT$_{2h-0h}$ than non-diabetic patients. A loading dose of ticagrelor did not increase bleeding events in both diabetic and non-diabetic patients. Platelet aggregation was compared in a separate cohort of CAD patients who received a loading dose of 180 mg ticagrelor before PCI. Baseline platelet aggregation was higher in diabetic patients compared to non-diabetic patients, but platelet aggregation at 0 h and 2 h after PCI was similar for both diabetic and non-diabetic patients, suggesting that a loading dose of 180 mg ticagrelor before PCI effectively reduces platelet aggregation in diabetic patients to the comparable level in non-diabetic patients.

hs-cTnT assays have significantly improved the sensitivity for early diagnosis of acute MI as early as 2 h after patients are presented with chest pain [15–17]. Platelet aggregation is also significantly reduced 2 h after the first administration of ticagrelor [10]. So hs-cTnT was chosen at 2 h after PCI as a parameter to reflect whether a loading dose of ticagrelor could decrease post-PCI myocardial necrosis in stable CAD patients already receiving clopidogrel therapy. Myocardial necrosis,

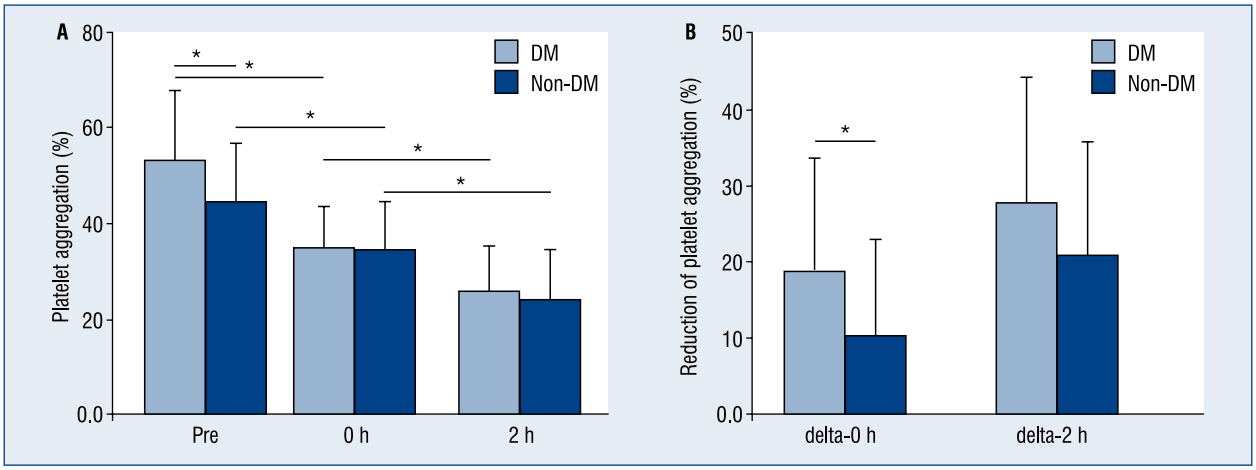

Figure 4. Residual platelet aggregation level in diabetic patients and non-diabetic patients with admission of 180 mg ticagrelor loading dose. Patients received 180 mg loading ticagrelor pre percutaneous coronary intervention (PCI), and followed by ticagrelor 90 mg twice per day commencing the day after PCI; **A.** Platelet aggregation in both diabetic (DM, n = 35) and non-diabetic (non-DM, n = 19) patients pre PCI, and 0 h and 2 h after PCI; **B.** The reduction of platelet aggregation at 0 h and 2 h after PCI relative to pre PCI value in both DM and non-DM groups. Data are shown as mean ± SEM; DM — diabetes mellitus; *p < 0.05.

Table 3. Association between high sensitivity cardiac troponin T (hs-cTnT) levels and population characteristics.

Characteristic	Univariable		Multivariable	
	Spearman correlation	P	β	P
Sex	–0.183	0.111		
Prior MI	0.187	0.103		
hs-cTnT	0.283	0.013	12.279	0.014
Creatinine	0.244	0.033	0.005	0.058

MI — myocardial infarction

Table 4. Bleeding events in 1 month after percutaneous coronary intervention.

	Non-diabetes mellitus patients				Diabetes mellitus patients			
	Group TT (n = 25)	Group CT (n = 17)	Group CC (n = 10)	P	Group TT (n = 11)	Group CT (n = 9)	Group CC (n = 5)	P
Bleeding events	3 (12%)	2 (12%)	0 (0%)	0.524	1 (9%)	0 (0%)	0 (0%)	0.529

which can range from a minor elevation of cardiac enzymes to a large infarct, is the most common complication following PCI. Microembolization of plague debris during PCI procedure has been proposed as the most likely cause of myocardial necrosis [18], and myocardial necrosis could also be associated with ischemia and reperfusion injury after stent implantation and sudden blood supply of ischemic myocardial tissues [19]. Cardiac troponins are a more sensitive marker than CK-MB in detecting minor degrees of myocardial necrosis following PCI [20, 21]. Previous studies have suggested that elevation of troponins after PCI is predictive of future cardiac events [22, 23]. In the present study, we did not observe that a loading dose of ticagrelor significantly decreased hs-cTnT or CK-MB after PCI. It has been reported that the increase in hs-cTnT concentration could be due to

other non-ischemic factors such as heart failure, diabetes mellitus and ventricular hypertrophy [14, 24]. Correlation analysis was done between hs-cTnT$_{2h}$ after PCI and baseline characteristics of patients, and it was found that hs-cTnT$_{2h}$ after PCI was strongly associated only with baseline hs-cTnT level, but not with other factors, suggesting that hs-cTnT levels at 2 h after PCI in our patients is not significantly affected by other factors.

Patients were then stratified according to the presence of type 2 diabetes mellitus. There were no significant differences in patients' characteristics at baseline between diabetic and non-diabetic patients in each group, but diabetic patients had a tendency of more previous MI and higher fasting blood glucose levels (data not shown). We found that in the group receiving additional loading dose of ticagrelor, diabetic patients had higher Δhs-cTnT$_{2h–0h}$ than non-diabetic patients. It was then examined as to whether higher Δhs-cTnT$_{2h–0h}$ after PCI in diabetic patients were associated with higher platelet aggregation in a separate cohort of CAD patients receiving 180 mg loading dose of ticagrelor before PCI. Baseline platelet aggregation rate was higher in diabetic when compared to non-diabetic patients, as seen in the another study [11], but a loading dose of ticagrelor lowered platelet aggregation level in diabetic patients to a comparable level in non-diabetic patients at 0 h and 2 h after PCI. So, Δhs-cTnT$_{2h–0h}$ was higher after PCI in diabetic when compared to non-diabetic patients but a comparable platelet aggregation rate between diabetic and non-diabetic patients indicate that other factors such as inflammation, blood glucose, microenvironment or vascular abnormality may have contributed to myocardial necrosis following PCI [25].

Limitations of the study

The present study has several limitations. First, it was a single center design study with a relatively small sample size. Second, this study used hs-cTnT concentration instead of periprocedural MI as an endpoint. So, larger-scale studies with periprocedural MI as an endpoint are needed for further research.

Conclusions

In conclusion, our study indicates that administration of a loading dose of ticagrelor does not significantly impact post-PCI myonecrosis in CAD patients. Diabetes is associated with higher Δhs-cTnT$_{2h–0h}$ after PCI in patients receiving a loading dose of ticagrelor, which evidently is not due to a higher platelet aggregation in diabetic patients. A loading dose of ticagrelor effectively reduces platelet aggregation in diabetic patients to a comparable level in non-diabetic patients.

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Conflict of interest: None declared

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