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COMPARABLE EFFECTS OF TICAGRELOR AND CLOPIDOGREL BASED ON PLATELET AGGREGATION TEST IN PATIENTS WITH ACUTE CORONARY SYNDROME

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ABSTRACT
Ticagrelor and clopidogrel are $P2Y_{12}$ receptor inhibitors commonly administered as part of dual antiplatelet therapy in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). Although ticagrelor demonstrates a more rapid onset of action and stronger platelet inhibition than clopidogrel in pharmacodynamic studies, its superiority in routine clinical practice remains debated. This study aimed to compare the effects of ticagrelor and clopidogrel on platelet aggregation in ACS patients undergoing PCI. A cross-sectional comparative study was conducted involving 33 ACS patients who were consecutively recruited from patients undergoing PCI and receiving either ticagrelor or clopidogrel. Platelet aggregation was evaluated using light transmission aggregometry with adenosine diphosphate (ADP) as the agonist at concentrations of 1, 2, 5, and 10 µM. Differences in platelet aggregation between treatment groups were analyzed using the Mann–Whitney U test. No statistically significant differences in platelet aggregation were observed between the ticagrelor and clopidogrel groups at all ADP concentrations tested (all $p > 0.05$). These findings suggest comparable platelet inhibitory effects between both $P2Y_{12}$ inhibitors in ACS patients undergoing PCI. Ticagrelor and clopidogrel demonstrated similar platelet aggregation profiles, indicating comparable platelet reactivity under both treatment regimens in ACS patients undergoing PCI in real-world clinical settings.

Keywords: acute coronary syndrome; clopidogrel; platelet aggregation test; ticagrelor

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INTRODUCTION

Acute coronary syndrome (ACS) remains a major cause of morbidity and mortality worldwide and represents a significant burden on healthcare systems despite substantial advances in diagnostic and therapeutic strategies (Lindstrom et al., 2022). The condition encompasses a spectrum of clinical manifestations, including ST-segment elevation myocardial infarction, non–ST-segment elevation myocardial infarction, and unstable angina, all of which primarily result from acute disruption of atherosclerotic plaques followed by thrombus formation within the coronary arteries (Bergmark et al., 2022). Platelet activation plays a central role in the pathophysiology of ACS as well as in thrombotic complications following percutaneous coronary intervention (PCI), contributing to coronary occlusion, distal embolization, and recurrent ischemic events (Ibrahim & Kleiman, 2017;,Kottke-Marchant, 2009). Consequently, effective inhibition of platelet activation has become a fundamental therapeutic strategy in the management of ACS patients undergoing coronary revascularization.

Dual antiplatelet therapy (DAPT), consisting of aspirin combined with a $P2Y_{12}$ receptor inhibitor, remains the cornerstone of treatment for reducing the risk of stent thrombosis, myocardial infarction recurrence, and cardiovascular mortality following PCI. Current international and national guidelines recommend the routine use of DAPT in ACS patients unless contraindicated, emphasizing the importance of sustained platelet inhibition during both the acute and maintenance phases of treatment (Perhimpunan Dokter Spesialis Kardiovaskular Indonesia, 2024; Byrne et al., 2023; Gulati et al., 2021). The therapeutic effectiveness of DAPT largely depends on adequate inhibition of adenosine diphosphate (ADP)–mediated platelet activation through blockade of the platelet $P2Y_{12}$ receptor, which plays a crucial role in amplifying platelet aggregation and stabilizing thrombus formation (Gorog & Geisler, 2020).

Clopidogrel has historically been the most widely prescribed $P2Y_{12}$ receptor inhibitor due to its established clinical efficacy and favorable safety profile. However, clopidogrel is a prodrug requiring hepatic bioactivation through cytochrome P450 enzymes, particularly CYP2C19, to generate its active metabolite. Variability in enzymatic activity, influenced by genetic polymorphisms, drug–drug interactions, and clinical conditions, results in considerable interindividual differences in platelet inhibition. This phenomenon may lead to high on-treatment platelet reactivity (HTPR), which has been associated with an increased risk of thrombotic complications and adverse cardiovascular outcomes (Alvitigala et al., 2020 and Lodhi et al., 2024). Consequently, concerns regarding clopidogrel resistance have prompted the development and increasing use of newer $P2Y_{12}$ inhibitors with more predictable pharmacodynamic properties.

Ticagrelor, a direct-acting and reversibly binding $P2Y_{12}$ receptor antagonist, provides more rapid onset of action and stronger platelet inhibition independent of metabolic activation. Pharmacodynamic studies have demonstrated that ticagrelor achieves greater and more consistent suppression of platelet reactivity compared with clopidogrel. Large randomized clinical trials, most notably the Platelet Inhibition and Patient Outcomes (PLATO) trial, reported improved clinical outcomes among ACS patients treated with ticagrelor, including reduced rates of cardiovascular death and myocardial infarction without a significant increase in overall major bleeding (Herron & Bates, 2024). Based on these findings, contemporary clinical guidelines frequently recommend ticagrelor as a preferred $P2Y_{12}$ inhibitor in ACS management.

Nevertheless, evidence derived from real-world clinical practice has produced inconsistent results regarding the superiority of ticagrelor over clopidogrel. Observational studies and registry-based analyses have reported variable outcomes, particularly concerning major adverse cardiovascular events (MACE) and bleeding risk across different patient populations and healthcare settings (Almendro-Delia et al., 2022). Factors such as patient comorbidities, adherence, treatment accessibility, and ethnic or genetic variability may influence therapeutic response and partially explain discrepancies between randomized trials and routine clinical practice. These inconsistencies highlight the importance of evaluating antiplatelet efficacy not only through clinical endpoints but also through direct assessment of platelet function.

Most comparative investigations between clopidogrel and ticagrelor have primarily focused on clinical outcomes, whereas relatively few studies have explored their pharmacodynamic effects using laboratory-based platelet function testing (Kumar et al., 2024). Assessment of platelet aggregation provides mechanistic insight into the biological effectiveness of antiplatelet therapy and allows evaluation of individual variability in treatment response. Laboratory evaluation is particularly relevant in the era of personalized medicine, where tailoring antiplatelet therapy according to platelet reactivity may improve clinical outcomes while minimizing bleeding complications (Aluvilu & Ferro, 2022).

Light transmission aggregometry (LTA) remains the gold standard method for assessing platelet aggregation and evaluating response to $P2Y_{12}$ receptor inhibition. Using adenosine diphosphate (ADP) as an agonist, LTA measures changes in light transmission through platelet-rich plasma during platelet aggregation, thereby providing quantitative assessment of platelet reactivity. Despite the emergence of newer point-of-care assays, LTA continues to be widely utilized in research settings due to its high sensitivity and ability to characterize platelet function across varying agonist concentrations (Wadowski et al., 2021). Evaluation of platelet aggregation using multiple ADP concentrations may further enhance understanding of drug responsiveness under different levels of platelet stimulation.

Given the limited availability of pharmacodynamic data comparing ticagrelor and clopidogrel using platelet aggregation testing, particularly in real-world ACS populations, further investigation is warranted. Moreover, evidence from Southeast Asian populations remains scarce despite potential differences in genetic background and clinical characteristics that may influence response to antiplatelet therapy. Understanding laboratory-based platelet responses in these populations may provide additional insight into optimizing antiplatelet strategies in routine clinical practice. Therefore, this study aimed to compare platelet aggregation between ACS patients treated with ticagrelor and those treated with clopidogrel following PCI using light transmission aggregometry. By evaluating platelet reactivity under both treatment regimens, this study seeks to determine whether ticagrelor confers a measurable laboratory advantage over clopidogrel in platelet inhibition within real-world clinical conditions.

METHOD

Study Design and Populations

This cross-sectional comparative study was conducted to evaluate platelet aggregation profiles among patients diagnosed with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). The study was performed between May and July 2025 at the cardiology center of H. Adam Malik General Hospital, a tertiary referral hospital in Indonesia. Eligible participants consisted of adult patients diagnosed with ACS, including ST-segment elevation myocardial infarction, non–ST-segment elevation myocardial infarction, or unstable angina, who underwent PCI and received dual antiplatelet therapy (DAPT).

Patients were treated according to standard clinical practice with DAPT consisting of aspirin combined with either ticagrelor or clopidogrel as the $P2Y_{12}$ receptor inhibitor. Selection of antiplatelet agents was determined by the attending cardiologist based on clinical indications and routine therapeutic considerations. Patients were included consecutively during the study period to minimize selection bias. Exclusion criteria included known hematologic disorders affecting platelet function, active infection or inflammatory disease, severe hepatic impairment, recent blood transfusion, use of additional anticoagulant or antiplatelet agents other than standard DAPT, or inadequate blood sample quality for platelet function testing. A total of 33 eligible patients fulfilling the inclusion criteria were consecutively recruited using a consecutive sampling technique.

Blood Sampling Procedure (Pre-analytical Phase)

Blood sampling was performed after PCI once patients had received maintenance doses of their respective $P2Y_{12}$ inhibitor to ensure adequate pharmacologic exposure. Samples were obtained within 48 hours following PCI during stable clinical conditions. Venous blood was collected by trained personnel using atraumatic venipuncture techniques to minimize artificial platelet activation. Blood was drawn into 2.0 mL tubes containing 3.2% sodium citrate anticoagulant at a blood-to-anticoagulant ratio of 9:1. Tourniquet application was minimized and released immediately after venous access was established. Samples exhibiting clot formation, hemolysis, or delayed processing were excluded from analysis. Following collection, specimens were transported at room temperature and processed promptly. All platelet function testing procedures were completed within

three hours after sampling to preserve platelet viability and functional integrity.

Platelet Aggregation Measurement (Analytical Phase)
Platelet aggregation was assessed using light transmission aggregometry (LTA), which remains the reference standard method for evaluating platelet function. Measurements were performed using the AggRAM™ aggregometry system (Helena Laboratories, USA) according to standardized laboratory procedures. Platelet-rich plasma (PRP) was prepared by centrifuging citrated whole blood at low speed (approximately 150–200 × g for 10 minutes) to obtain platelet-containing supernatant plasma. Subsequently, platelet-poor plasma (PPP) was obtained through high-speed centrifugation of residual blood samples and was used as a reference for baseline light transmission calibration.

Aggregation testing was performed by stimulating PRP with adenosine diphosphate (ADP) as the agonist at final concentrations of 1, 2, 5, and 10 μM to evaluate platelet responsiveness across varying degrees of stimulation. Changes in optical density were continuously recorded, and maximal platelet aggregation was expressed as the percentage increase in light transmission relative to PPP, which was defined as 100% aggregation. Instrument calibration and internal quality control procedures were performed daily according to manufacturer recommendations to ensure analytical accuracy and reproducibility. All analyses were conducted by trained laboratory personnel blinded to patients' antiplatelet treatment groups to reduce measurement bias.

Data Processing and Statistical Analysis (Post-Analytical Phase)
Platelet aggregation results were recorded as continuous variables and summarized according to treatment groups. Distribution of numerical data was evaluated prior to comparative analysis. Due to the non-normal distribution of aggregation values, nonparametric statistical testing was applied. Comparisons of platelet aggregation between ticagrelor and clopidogrel groups at each ADP concentration were analyzed using the Mann–Whitney U test. Statistical analyses were performed using SPSS software version 31.0 (IBM Corp., Armonk, NY, USA). All statistical tests were two-tailed, and a p value < 0.05 was considered statistically significant.

Ethical Considerations
This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Health Research Ethics Committee of Universitas Sumatera Utara (No. 310/KEPK/USU/2025). Institutional research permission was also granted by the Research Working Team of H. Adam Malik General Hospital (No. DP.04.03/D.XXVIII.2.2.3/536/2025). All participants received comprehensive information regarding the objectives, procedures, potential risks, and expected benefits of the study prior to enrollment. Written informed consent was obtained from all participants before blood sampling and data collection were performed.

RESULT
A total of 33 patients diagnosed with acute coronary syndrome (ACS) who underwent percutaneous coronary intervention (PCI) were included in the analysis. The mean age of the study population was 54.3 ± 11.6 years, reflecting a relatively young cohort of patients presenting with coronary artery disease. The majority of participants were male (90.9%), consistent with the known predominance of ACS among men in middle-aged populations. Regarding clinical presentation, most patients were diagnosed with ST-segment elevation myocardial infarction (STEMI) (75.8%), while the remaining patients presented with non–ST-segment elevation myocardial infarction or unstable angina (NSTEMI/UAP). Cardiovascular risk factors were highly prevalent among study participants. A substantial proportion of patients were active smokers (78.8%), while diabetes mellitus, hypertension, and dyslipidemia were identified in 66.7%, 72.7%, and 84.8% of patients,

respectively. Obesity was observed in 45.4% of subjects. Detailed demographic and clinical characteristics are summarized in Table 1.

Table 1.
Baseline characteristics

Patients characteristics	Result
Age (mean ± SD)	54,30 ± 11,6*
Age group (years)	
26-35	1 (3,0%)
36-45	5 15,2%)
46-55	13 (39,4%)
56-65	8 (24,2%)
>65	6 (18,2%)
Sex	
Male	30 (90,9%)
Female	3 (9,1%)
Diagnosis	
STEMI	25 (75,8%)
NSTEMI/UAP	8 (24,2%)
Smoking	26 (78,8%)
Diabetes mellitus	22 (66,7%)
Hypertension	24 (72,7%)
Obesity	15 (45,4%)
Dyslipidemia	28 (84,8%)

Baseline hematologic profiles were analyzed to ensure comparability between clinical and treatment subgroups prior to platelet aggregation assessment (Table 2). No statistically significant differences were observed in platelet-related indices between patients classified according to ACS subtype (STEMI vs. NSTEMI/UAP) or according to antiplatelet regimen (ticagrelor vs. clopidogrel). Measured platelet parameters included platelet count, mean platelet volume (MPV), immature platelet fraction (IPF), plateletcrit (PCT), platelet distribution width (PDW), and platelet large cell ratio (P-LCR). All indices demonstrated comparable values across study groups (all $p > 0.05$), indicating similar baseline platelet production, size distribution, and turnover status. These findings suggest that subsequent differences in platelet aggregation responses were unlikely to be influenced by baseline hematologic variability.

Table 2.
Baseline platelet indices

Platelet indices	Diagnosis		*p*
	STEMI	NSTEMI/ UAP	
Platelet count	241.000 (148.000 – 365.000)	244.000 (163.000 – 328.000)	0,966
MPV	9,5 (8,6 – 10,8)	9,55 (8,4 – 10,6)	0,866
IPF	2,7 (1,2 – 7,5)	2,8 (2,2 – 6,2)	0,833
PCT	0,23 (0,13 – 0,30)	0,22 (0,16 – 0,26)	0,689
PDW	9,9 (8,4 – 12,4)	9,7 (8,3 – 10,7)	0,474
P-LCR	20,4 (13,5 – 31,3)	21,8 (12,5 – 27,4)	0,887
Platelet indices	Drug		*P*
	Ticagrelor	Clopidogrel	
Platelet count	240.000 (148.000 – 321.000)	258.000 (176.000 – 365.000)	0,294
MPV	9,45 (8,6 – 10,7)	9,5 (8,4 – 10,8)	0,870
IPF	2,65 (1,2 – 7,5)	2,9 (1,3 – 6,2)	0,842
PCT	0,225 (0,13 – 0,30)	0,22 (0,20 – 0,30)	0,384
PDW	9,74 (8,7 – 12,1)	9,9 (8,3 – 12,4)	0,986
P-LCR	20,4 (13,5 – 29,3)	21,8 (12,5 – 31,3)	0,810

Platelet aggregation analysis using light transmission aggregometry (LTA) demonstrated aggregation patterns typically observed among patients receiving dual antiplatelet therapy. Aggregation curves in most subjects showed an initial increase in light transmission reaching a peak aggregation level followed by a gradual decline exceeding 10%, reflecting reversible platelet aggregation in response to adenosine diphosphate (ADP) stimulation (Figure 1). This pattern indicates partial suppression of ADP-mediated platelet activation consistent with effective $P2Y_{12}$ receptor inhibition. Overall, hypoaggregation was observed in the majority of patients (90.9%), supporting adequate pharmacodynamic response to antiplatelet therapy following PCI. A small proportion of patients demonstrated normoaggregation (6.1%), while hyperaggregation was identified in only one subject (3.0%). These findings highlight the presence of interindividual variability in platelet responsiveness despite standardized treatment with dual antiplatelet therapy.

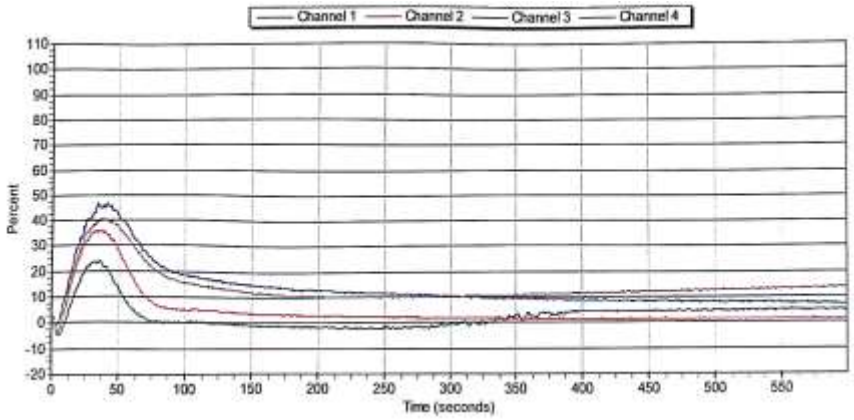


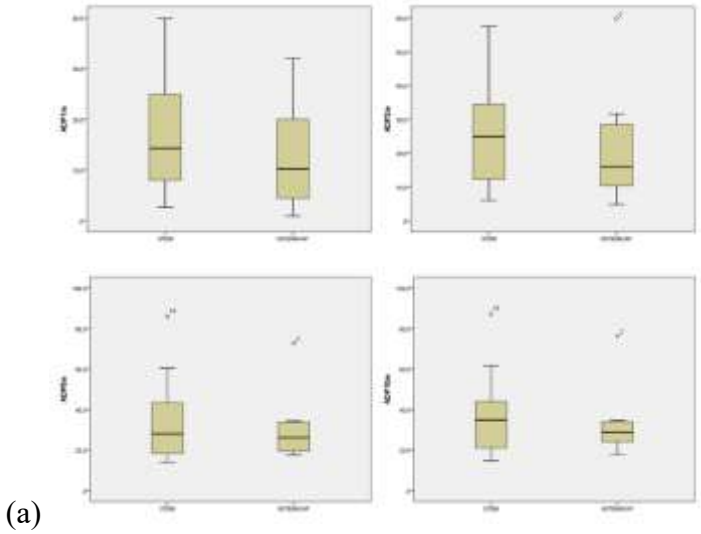
Figure 1. Representative LTA curve showing the typical rise-to-peak and gradual decline pattern in patients receiving $P2Y_{12}$ receptor inhibitors

Comparative analysis based on clinical diagnosis revealed no statistically significant differences in platelet aggregation between patients with STEMI and those with NSTEMI/UAP across all tested ADP concentrations (1, 2, 5, and 10 µM; all $p > 0.05$) (Table 3). Median aggregation values tended to be numerically higher among STEMI patients; however, these differences did not reach statistical significance. The absence of significant variation suggests that platelet reactivity following PCI and antiplatelet therapy was comparable regardless of ACS subtype. These findings indicate that disease presentation alone may not substantially influence pharmacodynamic response to $P2Y_{12}$ inhibition during the early post-intervention period.

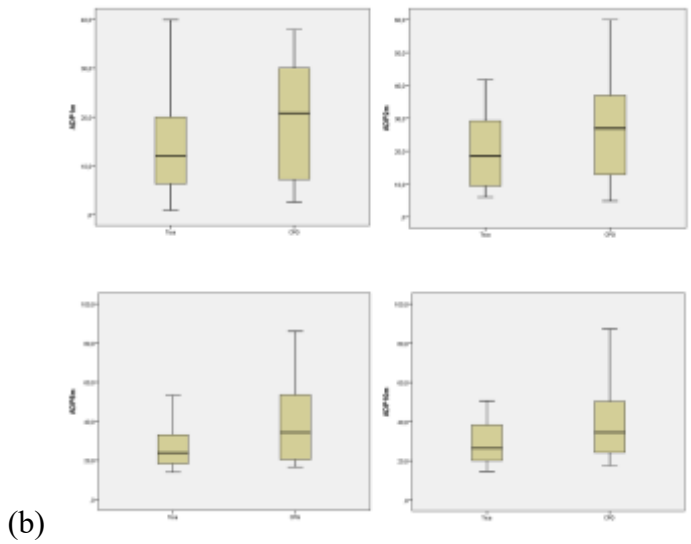
The primary analysis comparing platelet aggregation responses between ticagrelor and clopidogrel treatment groups demonstrated no statistically significant differences across all ADP concentrations tested (1, 2, 5, and 10 µM; all $p > 0.05$). Although patients receiving ticagrelor consistently exhibited slightly lower median aggregation values compared with those receiving clopidogrel, the observed differences were small and did not achieve statistical significance. These results indicate that both $P2Y_{12}$ receptor inhibitors produced comparable inhibition of platelet aggregation in ACS patients undergoing PCI under real-world clinical conditions. The similarity in aggregation responses suggests equivalent platelet reactivity between treatment regimens within the studied population.

Table 3.
Platelet aggregation test result based on diagnosis and therapy

Platelet aggregation test	Diagnosis		*p*
	STEMI	NSTEMI/ UAP	
ADP 1 µM	14,3 (2,6-39,9)	10,2 (0,9-32,0)	0,294
ADP 2 µM	24,9 (6,0-57,5)	16,0 (4,8-59,9)	0,450
ADP 5 µM	28,1 (14,0-86,0)	26,1 (17,4-72,8)	0,801
ADP 10 µM	34,9 (14,7-87,2)	28,8 (17,6-76,3)	0,644
Platelet aggregation test	Drug		*p*
	Ticagrelor	Clopidogrel	
ADP 1 µM	12,05 (0,9-39,9)	20,80 (2,6-37,9)	0,199
ADP 2 µM	18,5 (6,0-41,7)	26,9 (4,8-59,9)	0,193
ADP 5 µM	23,9 (14,0-53,2)	34,3 (16,6-86,0)	0,116
ADP 10 µM	26,4 (14,7-50,6)	34,5 (17,6-87,2)	0,120



(a)



(b)

Figure 2. Boxplots showing platelet aggregation responses (ADP 1–10 µM) according to (a) clinical diagnosis and (b) $P2Y_{12}$ inhibitor used (Tica: ticagrelor; CPG: clopidogrel). No significant intergroup differences were observed (all $p > 0.05$)

DISCUSSION

This study demonstrated no significant difference in ADP-induced platelet aggregation between ticagrelor and clopidogrel among patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). Although ticagrelor is theoretically more potent due to its

direct, rapid, and reversible inhibition of the $P2Y_{12}$ receptor, our findings align with a growing body of recent evidence indicating that ticagrelor's superiority is not universally observed in clinical or pharmacodynamic outcomes.

The 2025 TC4 pragmatic randomized controlled trial found no meaningful superiority of ticagrelor over clopidogrel in preventing major cardiovascular events in ACS patients, even when analyzed with Bayesian informed priors, suggesting substantial uncertainty regarding ticagrelor's routine benefit in real-world practice (Kutcher et al., 2025). Likewise, the 2025 Ticagrelor Paradox systematic review concluded that many post-PLATO studies failed to replicate ticagrelor's reported advantages, implying that earlier trial benefits may have been overstated or population-specific (Watanabe et al., 2025; Doshi, 2024) These contemporary data collectively support the neutral pharmacodynamic results found in the present study.

A particularly interesting finding in our study was the observation that patients with ST-segment elevation myocardial infarction (STEMI) exhibited higher median platelet aggregation than those with NSTEMI/unstable angina, despite most STEMI patients receiving ticagrelor. Although statistically non-significant, this paradox is biologically plausible. STEMI is characterized by abrupt total coronary occlusion, massive thrombin generation, enhanced ADP release, and accelerated inflammatory responses—all contributing to significantly heightened baseline platelet reactivity. Prior research by Sulianty and Aman has similarly demonstrated higher platelet aggregation in STEMI compared with NSTEMI patients (Sulianty & Aman, 2011).

Moreover, urgent PCI in STEMI necessitates rapid loading of antiplatelet therapy; thus, blood sampling often occurs before ticagrelor achieves maximal receptor occupancy. In contrast, NSTEMI patients typically receive antiplatelet therapy earlier during risk stratification, allowing more complete pharmacodynamic effect at the time of platelet testing. Importantly, the interpretation of platelet function results must also consider the timing between drug administration, blood sampling, and assay processing. Rollini et al. demonstrated that pharmacodynamic measurements can fluctuate significantly depending on how many hours have passed from blood sampling to testing, particularly when using assays such as VerifyNow or LTA. In their prospective study, $P2Y_{12}$ reaction units decreased significantly at 30 minutes and 2 hours post-dose before rising again at 4 hours, indicating that platelet reactivity is dynamic rather than static during the early phase of therapy. LTA showed a similar time-dependent decline, whereas VASP remained stable regardless of sampling time. This finding suggests that early post-PCI measurements—especially in STEMI patients who are sampled soon after urgent loading doses—may underestimate the maximal pharmacodynamic effect of ticagrelor simply because steady-state inhibition has not been reached (Rollini et al., 2016). These results further support the higher median aggregation seen in STEMI patients in our study despite more frequent ticagrelor use, reinforcing the critical role of timing in interpreting laboratory platelet reactivity.

Additional PCI-related mechanical stimulation—especially prominent in complex STEMI interventions—may further activate platelets and obscure in vitro inhibition. Interindividual variability in ticagrelor absorption and distribution, influenced by hemodynamic instability, hepatic perfusion, or metabolic factors, may also contribute to higher residual aggregation levels in STEMI despite use of a potent agent (Sanderson et al., 2021; He et al., 2023)

Recent literature reinforces that ticagrelor's benefit is highly context dependent. A 2025 multicenter registry of STEMI complicated by cardiogenic shock reported no significant difference in mortality or major bleeding between ticagrelor and clopidogrel, suggesting that the extreme thrombotic and inflammatory burden in STEMI may diminish the clinical distinction between agents (Zhou et al., 2025). A 2024 systematic review in STEMI likewise found no statistically significant differences in

mortality, recurrent myocardial infarction, stroke, or TIMI flow between ticagrelor and clopidogrel (Geravandi et al., 2024). Additionally, a 2025 pharmacogenomic analysis showed that ticagrelor's clinical benefit is restricted to patients with high ABCD-GENE risk scores, while lower-risk groups derive no advantage and may experience increased bleeding (Xu et al., 2025). These findings underscore that biologic heterogeneity, gene–drug interactions, and clinical state all influence the net effect of $P2Y_{12}$ inhibition.

The need to balance antithrombotic efficacy with bleeding risk further complicates therapy selection. A 2025 cohort study noted higher rates of dyspnea and a trend toward increased major bleeding with ticagrelor compared to clopidogrel, highlighting the importance of individualized therapy (Rauf et al., 2025). Meanwhile, a 2025 target-trial emulation in older adults showed modest reductions in major adverse cardiovascular events without significantly increasing major bleeding, though confidence intervals remained wide, creating uncertainty regarding net clinical benefit (Marxer et al., 2025). Meta-analytic data from chronic coronary syndrome populations further demonstrate that ticagrelor reduces stent thrombosis but offers no statistically significant reduction in mortality, MI, or overall MACE compared with clopidogrel (Khan et al., 2025). Taken together, these results highlight that ticagrelor's pharmacologic potency does not necessarily translate into superior clinical outcomes or greater platelet suppression in all settings.

Overall, this study adds to emerging evidence that ticagrelor's superiority is not absolute but instead determined by timing, baseline thrombotic activity, genetic background, hemodynamic status, and clinical phenotype. In real-world ACS, these factors may attenuate pharmacodynamic differences, resulting in comparable platelet aggregation between ticagrelor and clopidogrel, despite pharmacologic expectations.

A key strength of this study is the direct pharmacodynamic comparison between ticagrelor and clopidogrel using light transmission aggregometry (LTA), which remains the reference method for assessing platelet function. The use of multiple ADP concentrations (1–10 μM) allowed a comprehensive evaluation of platelet responsiveness across a range of stimulation intensities, providing a more detailed characterization of $P2Y_{12}$ inhibitor effects. Additionally, blood sampling was conducted within a controlled timeframe following PCI, and preanalytical procedures were standardized to minimize variability in platelet activation.

However, several limitations should be acknowledged. First, the relatively small sample size (n=33) reduces statistical power and may limit the ability to detect subtle differences between the two treatment groups. Second, CYP2C19 genotyping was not performed, preventing identification of clopidogrel non-responders—a factor that may influence observed pharmacodynamic variability. Third, the cross-sectional design captures platelet inhibition at a single time point, which may not represent full steady-state pharmacodynamics for either drug. Fourth, the use of LTA alone without complementary assays (e.g., VerifyNow $P2Y_{12}$, VASP-PRI) may not fully reflect the complexity of $P2Y_{12}$ signaling and platelet behavior in vivo. Finally, this was a single-center study conducted in a population with high prevalence of metabolic comorbidities, which may limit generalizability to broader ACS cohorts.

CONCLUSION

This study found no significant difference in ADP-induced platelet aggregation between ticagrelor and clopidogrel in ACS patients undergoing PCI. The higher median aggregation observed in STEMI patients, despite more frequent ticagrelor use, likely reflects greater baseline thrombotic activation and the influence of sampling timing and clinical instability rather than reduced drug potency. These findings align with recent evidence showing that ticagrelor's pharmacodynamic advantage is context-dependent and may not be uniformly observed across all ACS presentations. Clinicians should interpret platelet function results within the clinical context, recognizing that

timing of measurement, disease severity, and patient-specific factors can affect pharmacodynamic responses. Standardized sampling intervals and consideration of complementary platelet assays may improve assessment accuracy.

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