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Original Research Article

Effect of different doses of dual antiplatelet therapy in post-coronary stent patients: A prospective observational study from a clinical pharmacy perspective

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Abstract

Purpose: *To determine the effect of different dual antiplatelet therapy (DAPT) regimens on selected Indonesian population.*
Methods: *In a prospective study with a total to 70 patients at Dr. Soetomo General Academic Hospital in Indonesia, 3 different groups of patients with acute coronary syndrome (ACS) orally received 90 days of aspirin plus 75 mg clopidogrel (8 patients), or aspirin plus 2 x 90 mg ticagrelor (31 patients), or aspirin plus low-dose (3.75 mg) prasugrel (31 patients) after coronary stenting. The patients were followed up for 90 days. Regimen selection was based on the clinical judgement of cardiologists. The outcomes comprised major adverse cardiovascular events (MACEs) such as all-cause death, non-fatal myocardial infarction, definite or probable stent thrombosis, non-fatal stroke, and ischemia-driven revascularization, in addition to bleeding events using Bleeding Academic Research Consortium (BARC) criteria.*
Results: *Seventy patients completed follow-up. Patients in the aspirin plus clopidogrel group were generally older and potentially at higher bleeding risk. Polypharmacy was prevalent across all groups. Four MACEs occurred in two clopidogrel groups, one ticagrelor group, and one prasugrel group. No major bleeding occurred. However, minor bleeding appeared only in ticagrelor and prasugrel groups. Differences among the regimens were not statistically significant.*
Conclusion: *Short-term outcomes of aspirin plus clopidogrel, aspirin plus ticagrelor, and aspirin plus low-dose prasugrel were broadly comparable in the small, real-world Indonesian cohorts investigated. Notably, the study highlights how clinical pharmacists can strengthen cardiac care through individualized regimen selection, careful medication review in polypharmacy, and counseling to make patients adhere to regimens while safely navigating bleeding concerns. While supportive of national dosing recommendations, the findings should be interpreted cautiously, given the small sample size and non-randomized design used.*

Keywords: *Dual antiplatelet therapy, Acute coronary syndrome, Percutaneous coronary intervention, Bleeding, Clinical pharmacy*

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INTRODUCTION

Coronary artery disease (CAD) and acute coronary syndrome (ACS) remain leading causes of morbidity and mortality in Indonesia and worldwide [1]. Percutaneous coronary intervention (PCI), a minimally invasive procedure used to open narrowed or blocked coronary arteries caused by coronary artery disease, has become a cornerstone reperfusion strategy in ACS. However, the long-term success of PCI critically depends on effective prevention of stent thrombosis and recurrent ischemic events. Dual antiplatelet therapy (DAPT), typically consisting of aspirin and a P2Y12 inhibitor (a class of antiplatelet medications that prevent blood clots by blocking P2Y12 receptors on platelets), is the standard care after PCI, in order to reduce atherothrombotic risk [2].

Studies have shown that P2Y12 inhibitors such as ticagrelor and prasugrel demonstrated superior ischemic protection when compared with clopidogrel (another P2Y12 inhibitor), in large randomized trials [3-5]. However, these benefits were accompanied by increased bleeding risk, which may be particularly relevant in Asian populations. The so-called “East Asian paradox” describes the observation that East Asian patients tend to have a lower incidence of ischemic events but a higher susceptibility to bleeding when exposed to antithrombotic therapies. This has raised concerns about the direct extrapolation/application of Western trial doses to Asian patients [6].

The Indonesian Heart Association (IHA) recommends lower maintenance doses of prasugrel (3.75 mg once daily after a 20-mg loading dose), relative to the standard 10-mg dose used in Caucasian populations, with the aim of preserving antithrombotic efficacy while mitigating bleeding risk. Ticagrelor at a dose of 2 × 90 mg, and 75 mg clopidogrel are used as standard Caucasian doses [7]. However, clinical data on the comparative outcomes of these regimens in Indonesian ACS patients are scanty. In addition, real-world practice often involves elderly patients, multiple comorbidities, and polypharmacy, all of which further complicate DAPT optimization and underscore the role of clinical pharmacists [8].

Clinical pharmacists are increasingly recognized as key members of the multidisciplinary cardiovascular care team, particularly for complex ACS patients who frequently present with multiple comorbidities and polypharmacy. The responsibilities of clinical pharmacists involve reconciliation of medications, identification and management of drug-drug interactions, optimization of antithrombotic regimens based on ischemic and bleeding risks, and structured patient counseling in order to improve medication adherence and early detection of bleeding symptoms [9]. In a resource-limited setting such as Indonesia, where physician workload is high and access to specialized cardiac care may not be regular, the contribution of clinical pharmacists to dual antiplatelet therapy (DAPT) optimization is potentially substantial but remains under-documented.

Against this background, a prospective observational pilot study was conducted to evaluate 90-day clinical outcomes with DAPT regimens using aspirin plus 75 mg clopidogrel, aspirin plus 2 x 90 mg ticagrelor, or aspirin plus low-dose 3.75 mg prasugrel, in Indonesian ACS patients undergoing PCI. From a clinical pharmacy perspective, the study was aimed not only at comparing short-term efficacy and safety but also at generating real-world data with potential to guide pharmacist-led decision-making, medication review, and patient counseling in routine practice.

METHODS

Study design and setting

This single-center, prospective observational pilot study was conducted at Integrated Heart Service Center, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (https://maps.app.goo.gl/pzNYV7HCiP58XDJY6). Patient recruitment and follow-up were performed between September 2023 and March 2024.

Participants and treatment groups

Seventy-seven (77) adult ACS patients (aged ≥ 18 years) who underwent PCI and received DAPT (aspirin plus a P2Y12 inhibitor) were screened for eligibility.

Inclusion criteria

Patients in the following categories were included: those who had undergone successful PCI with a drug-eluting stent implantation; patients who received aspirin plus one of the following P2Y12 inhibitors as part of DAPT immediately after PCI: 75 mg clopidogrel, 2x90 mg ticagrelor (standard dosing as per guidelines), or 3.75 mg prasugrel (low dose) for 90 days; and patients who provided written

informed consent and agreed to participate in the 90-day clinical follow-up.

Exclusion criteria

Patients who had platelet counts < 100,000/μL or > 500,000/μL, and those with active bleeding within the previous 3 months before enrolment, were excluded. In addition, patients with a history of hemorrhagic stroke and severe hepatic impairment, and those who were not likely to be able to complete 90-day follow-up, were excluded from the study.

Ethical approval and guidelines for the study

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee for Health Research at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, with approval no. 0657/KEPK/IV/2023. Written informed consent was obtained from each participant before enrollment.

Sources of drugs used

The aspirin used was a product of Phapros, while 75 mg clopidogrel, 90 mg ticagrelor, and 3.75 mg prasugrel were produced by Kimia Farma, Pratapa Nirmala (Fahrenheit), and Mitsubishi Tanabe Farma Indonesia, respectively. Assignment to clopidogrel, ticagrelor, or prasugrel was determined by the interventional cardiologist based on clinical judgment which was hinged on assessment of ischemic and bleeding risks, drug availability, and reimbursement considerations. No randomization or blinding procedure was applied.

Data collection and baseline variables

Demographic and clinical data were collected from medical records and direct interviews. The data collection covered age, sex, body weight and height, smoking status, ACS subtype ST-elevation myocardial infarction (STEMI) or non-STEMI)], renal function (estimated glomerular filtration rate, eGFR), and comorbidities such as hypertension, diabetes mellitus, CAD, stroke, dyslipidemia, and heart failure. The type of stent used (drug-eluting stent) and number of comorbidities were recorded.

Concomitant medications were documented and categorized, with polypharmacy defined as the concurrent use of five or more drugs [10]. As part of routine pharmaceutical care, clinical pharmacists collected medication-related data such as use of antithrombotic agents, cardiovascular co-medications, and gastroprotective therapy. Pharmacists also participated in medication reconciliation at baseline and in follow-up contacts, which facilitated consistency in documentation of changes in drug therapy and potential drug-drug interactions. Data on educational levels, occupations, and places of residence of the patients were recorded as socio-demographic factors that may influence adherence to, and access to care.

Study endpoints

The primary efficacy endpoint was the occurrence of a major adverse cardiovascular event (MACE) within 90 days after PCI. This was defined as a composite of all-cause death, non-fatal myocardial infarction, definite or probable stent thrombosis, non-fatal stroke, or ischemia-driven revascularization.

The primary safety endpoint was the occurrence of bleeding events at days 15, 30, 45, and 90 following PCI, as classified according to the criteria of the Bleeding Academic Research Consortium (BARC) [11]. Minor bleeding was classified as BARC types 1-2, while major bleeding was classified as BARC types 3-5.

Follow-up

Patients were followed up clinically for 90 days after PCI, through scheduled visits and/or telephone contacts. The follow-up was primarily carried out by the pharmacists in collaboration with the cardiologist team. At each time point (days 15, 30, 45, and 90), information on MACEs and bleeding events was collected. Clinical pharmacists contributed to these follow-up assessments by verifying medication use, documenting self-reported adherence, and clarifying bleeding symptoms or adverse effects related to DAPT, whenever possible. Where necessary, additional data were retrieved from hospital records.

Statistical analysis

Data were analyzed using SPSS version 26 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean, standard deviation, or as median with interquartile range (IQR) where appropriate. Categorical variables are expressed as frequencies and percentages.

Baseline characteristics among the three treatment groups were compared using appropriate tests (e.g., analysis of variance or the Kruskal-Wallis test for continuous variables,

and the chi-square or Fisher's exact test for categorical variables). The number of patients who experienced MACEs or bleeding episodes in each group was compared using McNemar's test or the Friedman test, as applicable. Given the pilot nature of the study, analyses were primarily descriptive and exploratory: no formal sample size calculation was performed. Differences were assumed statistically significant at $p < 0.05$.

RESULTS

Baseline characteristics of included patients

Tables 1a & 1b show the demographic data of the participants. Post-PCI, 70 out of 77 ACS patients who were initially screened provided informed consent and completed the 90-day follow-up. These patients were categorized into three treatment groups based on the type of P2Y12 inhibitor received: clopidogrel (n = 8), ticagrelor (n = 31), and prasugrel 3.75 mg (n = 31).

Baseline demographic and clinical characteristics were largely comparable across groups. The clopidogrel group contained older patients (mean age: approximately mid-60s), relative to the prasugrel group (mean age: approximately 50 years). The majority of patients in all groups were male. All patients received drug-eluting stents. Hypertension and diabetes mellitus were the most common comorbidities seen. A significant proportion of patients in each group had multiple comorbid conditions. Patients with a smoking status were more frequent than those who never smoked. Most patients were on polypharmacy, with 5 or more concomitant medications in nearly all patients in each group, thereby reflecting the complexity of pharmacotherapy in this setting.

Table 1a: Demographic data of coronary stent patients given aspirin plus DAPT

Parameter	Aspirin plus clopidogrel group	Aspirin plus ticagrelor group	Aspirin plus prasugrel group	*P-value*
Age (years)	63.9±10.3* 64#; IQR (70, 5; 59) 44 – 79**	55.0±9.9* 53#; IQR (64, 48) 34–79**	49.7±6.9* 50#; IQR (54, 43) 36–69**	0.096
Sex				
Male	6	24	25	0.975
Female	2	7	6	
Weight (kg)	59.4±10.6* 62#; IQR (68, 51) 40–70**	65.8±11.6* 65#; IQR (78, 60) 44–86**	67.9±10.4* 67#; IQR (75, 60) 48–90**	0.726
Height (cm)	159.0±7.9	163.0±7.6	164.0±6.2	0.080
Obesity status				
Underweight	1	2	0	0.515
Normal weight	6	17	16	
Overweight	1	9	12	
Obesity class 1	0	1	3	
Obesity class 2	0	2	0	
Diagnosis				
STEMI	8	27	29	0.351
Non-STEMI	0	4	2	
e-GFR				
>60%	4	20	25	0.867
≤60%	4	11	6	
Smoking habit				
Never	3	11	10	0.900
Active	5	20	21	
Type of stent (DES)	8	31	31	Constant
Comorbidities				
Hypertension	6	17	18	0.138
Diabetes mellitus	4	10	13	
CAD	1	11	3	
Stroke	2	2	3	
Dyslipidaemia	3	8	2	
Heart Failure	0	2	0	
Others	0	1	0	

*Mean±SD; #median; **range, ***includes homemakers, self-employed, and retirees

Table 1b: Demographic data of coronary stent patients given aspirin plus DAPT

Parameter	Aspirin plus clopidogrel group	Aspirin plus ticagrelor group	Aspirin plus prasugrel group	*P-value*
Number of comorbidities				
Nil	1	4	7	
1-2	3	19	22	0.583
≥3	4	8	2	
Polypharmacy				
Yes (≥5 drugs)	7	28	28	0.859
No (<5 drugs)	1	3	3	
Educational level				
Elementary	8	25	27	0.170
Higher education	0	6	4	
Jobs				
Unemployed	1	0	1	0.442
Government employee	0	0	2	
Private employee				
Other occupations***	2	11	19	
	5	20	9	
Residential area				0.597
Local	3	14	23	
Other cities	5	17	8	

Renal function, Estimated Glomerular Filtration Rate (eGFR), and other baseline variables did not differ significantly among the groups.

Efficacy outcomes regarding MACEs

Table 2 shows that over the 90-day follow-up, four patients experienced MACEs. Two events occurred in the clopidogrel group, while one event occurred in each of the ticagrelor and prasugrel groups. All-cause death was responsible for each of the recorded episodes of MACEs. There were no documented incidents of non-fatal myocardial infarction, stent thrombosis, non-fatal stroke, or ischemia-driven revascularization during the study period.

In terms of proportion, there was numerically a higher incidence of observed MACEs in the small clopidogrel cohort (2 out of 8 patients) than in the ticagrelor and prasugrel cohorts (1 out of 31 patients). However, given the small sample size and exploratory nature of the study, these differences did not reach statistical significance. Overall, 66 out of 70 patients (94.3%) remained free from MACE at 90 days.

Bleeding outcomes

Table 3 shows that no major bleeding events (BARC 3-5) were observed in any group during the 90-day follow-up. However, at various time points, minor bleeding (BARC 1-2) occurred only in the ticagrelor and prasugrel groups. In contrast, no bleeding episodes were recorded in patients who received clopidogrel.

The aspirin plus ticagrelor group had a few BARC 1-2 events on days 15, 30, 45, and 90, whereas the aspirin plus prasugrel group had isolated BARC 1-2 events at some follow-up points. Statistical analysis revealed no significant differences among the three treatment groups in terms of overall minor bleeding incidence over the 90 days.

Table 2: Documented MACE during the 90-day use of aspirin plus DAPT

Group	90 days of MACE observation		Total	*P*-McNemar
	Without MACE	*All-cause death*		
Aspirin-Ticagrelor	30	1	31	1.000
	0	0	0	
Aspirin-Prasugrel	30	1	31	1.000
	0	0	0	
Aspirin-Clopidogrel	6	2	8	0.500
	0	0	0	
Total	**66**	**4**	**70**	

P > 0.05 (not statistically significant)

Table 3: Bleeding events during 90 days post-PCI among the three DAPT groups

Group	H15			H30			H45			H90			*P* - Friedman
	No bleeding	BARC 1	BARC 2	No bleeding	BARC 1	BARC 2	No bleeding	BARC 1	BARC 2	No bleeding	BARC 1	BARC 2	
Aspirin-ticagrelor	27	3	1	28	3	0	28	2	0	27	2	1	0.849
Aspirin-prasugrel	31	0	0	30	0	1	29	1	1	29	1	0	0.572
Aspirin-clopidogrel	7	0	0	7	0	0	6	0	0	6	0	0	-

P > 0.05 (not statistically significant); H15, H30, H45 and H90 correspond to days when bleeding was monitored

DISCUSSION

In the present observational pilot study of Indonesian ACS patients undergoing PCI, DAPT regimens incorporating aspirin plus either clopidogrel, ticagrelor, or low-dose prasugrel (3.75 mg) were associated with low rates of 90-day MACEs and no major bleeding incidents. Only four MACEs due to all-cause death occurred in the 70 patients studied, while minor BARC 1-2 bleeding was confined to patients given aspirin plus ticagrelor or prasugrel. There were no statistically significant differences in efficacy or safety outcomes among the three P2Y12 inhibitor regimens.

From a clinical pharmacy perspective, these findings suggest that IHA-recommended low-dose prasugrel (3.75 mg) appears feasible in real-world Indonesian practice, with short-term ischemic and bleeding outcomes that were comparable to those of clopidogrel and ticagrelor, within the limitations of the small cohort studied. This adds local evidence to the broader literature, which suggests that dose adjustments of potent P2Y12 inhibitors may be appropriate in East Asian populations with higher vulnerability to bleeding. Several reports have documented increased bleeding events in Asians when DAPT is used. Asian ethnicity was identified as an independent predictor of moderate bleeding complications in the CHARISMA study. Moreover, prolonged DAPT was a significant predictor of bleeding complications only in the East Asian population [6,12-14].

However, the results must be interpreted cautiously. The higher numerical proportion of MACEs in the clopidogrel group may reflect combined influences of the small sample size and selection bias rather than a true difference in drug efficacy. Clinicians may preferentially prescribe clopidogrel to older or more fragile patients perceived to have a higher bleeding risk, as suggested by the older age distribution and possible higher bleeding risk features in this group. Such confounding by indication is an inherent limitation of non-randomized observational designs and an indication that the present study cannot be used to establish comparative effectiveness. Overall, despite suggestions for additional randomized controlled trials of DAPT in the elderly, clopidogrel is comparable to ticagrelor or prasugrel in effectiveness in preventing major adverse cardiovascular events, with the lowest number of bleeding events in elderly patients [15,16].

In the ticagrelor and prasugrel groups, bleeding outcomes were reassuring, with no major bleeding incidents recorded, apart from only minor BARC 1-2 episodes. While this aligns with the intent of dose reduction strategies for prasugrel in East Asian populations, the short 90-day follow-up and relatively small sample size limit the ability to detect rare but clinically important bleeding events [13]. Furthermore, the study did not formally evaluate decreases in hemoglobin levels, transfusion requirements, and hospitalizations as a result of bleeding, all of which are highly relevant from a clinical pharmacy standpoint.

Implications for clinical pharmacy practice

The high prevalence of polypharmacy and multiple comorbidities across all three DAPT regimens underscores the need for systematic involvement of clinical pharmacy in ACS care [17]. In such patients, clinical pharmacists are uniquely positioned to perform comprehensive medication review, identify overlapping antithrombotic effects, and mitigate drug-drug interactions involving anticoagulants, non-steroidal anti-inflammatory drugs, proton pump inhibitors, or traditional/herbal medicines. The present pilot data have demonstrated that short-term DAPT outcomes were generally favorable when guideline-recommended regimens were used within a structured tertiary care environment, suggesting that pharmacist-supported implementation of national dosing recommendations is both feasible and safe [7].

Minor bleeding events, although not life-threatening, have essential implications for adherence. In the absence of adequate counseling, patients may down-titrate or discontinue DAPT without informing the physicians in charge [18]. A clinical pharmacist can bridge this gap by providing targeted education on the expected side effects of DAPT, by distinguishing nuisance bleeding from warning signs of major hemorrhage, and re-emphasizing the risks associated with premature discontinuation [19]. In the Dr. Soetomo Hospital setting, pharmacist involvement in follow-up facilitated consistent documentation of bleeding symptoms and medication changes, which are crucial for interpreting real-world safety profiles.

In addition, the choice among clopidogrel, ticagrelor, and low-dose 3.75 mg prasugrel in routine practice is often influenced by a combination of clinical factors, reimbursement policies, and patient preferences. Clinical pharmacists can support cardiologists by integrating risk scores, renal function, age, and

co-prescribed drugs into individualized DAPT recommendations, while also considering affordability and accessibility. The present study, although exploratory, provides locally relevant outcome data with potential to inform pharmacists' shared decision-making while advocating for structured pharmacy services in cardiac units. Finally, this study has several important strengths. It provides prospective, real-world data on IHA-recommended P2Y12 inhibitor doses in Indonesian ACS patients, incorporates standardized bleeding definitions (BARC), and focuses on a clinically meaningful 90-day window after PCI when both ischemic and bleeding risks are high. A further strength of this work is the integration of clinical pharmacy services in data collection and follow-up, which reflects real-world multidisciplinary practice and highlights the feasibility of embedding pharmacist-led medication management within ACS care pathways.

Limitations of the study

Nevertheless, key limitations must be acknowledged, such as a small sample size and the pilot nature of the study (only 70 patients). These constraints limit the capacity of the study to detect modest differences in relatively infrequent clinical endpoints such as MACE and major bleeding. Moreover, the study was based on a non-randomized design. Treatment allocation by physicians introduces confounding by indication: elderly or high-bleeding risk patients were more likely to receive clopidogrel. The study was done in a single-center setting. Therefore, the findings may not be generalizable to other hospitals or healthcare systems. Additionally, the follow-up period was short: the 90-day time frame may not be long enough for detecting longer-term variations in ischemic or bleeding risk associated with different DAPT strategies.

Therefore, future studies should be multicentered, with larger samples, and ideally should involve the use of randomized or properly score–adjusted designs to reduce confounding. In addition, incorporating genetic testing for clopidogrel metabolism and structured pharmacy interventions (medication review and adherence clinics) would further strengthen the evidence base and highlight the added value of clinical pharmacists in optimizing DAPT.

CONCLUSION

From a clinical pharmacy perspective, the present study underscores the importance of pharmacist-led medication review in polypharmacy, individualized DAPT selection based on ischemic and bleeding risks, and structured patient counseling to maintain adherence in the presence of minor bleeding or other adverse effects. Expanding and formalizing clinical pharmacy services in cardiac units may enhance the safe implementation of DAPT guidelines and improve long-term cardiovascular outcomes in Indonesian and other Asian populations. However, there is a need for larger, multicenter studies to confirm these preliminary observations and to more precisely define the added value of clinical pharmacists in optimizing DAPT.

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Conflict of interest

The authors declare that they have no conflicts of interest related to this study.

Contributions of authors

The authors declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Additionally, the authors declare that all authors contributed equally to the conception and design of the study, data collection, analysis, interpretation of data, and writing of the manuscript. All authors have read and approved the manuscript for publication. In addition, all authors agree to be accountable for all aspects of this study.

Availability of data and materials

The data used during the study are available from the corresponding author on reasonable request.

Use of Artificial Intelligence/research reporting tool

The authors did not use artificial intelligence or a research reporting tool for writing this manuscript.

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