**Research Journal of Life Science**
APRIL-2020 Volume 7 NO. 1 (19-28)
journal homepage: www.rjls.ub.ac.id

# Analysis of Platelet Function from Thromboelastography Examination in Patients with Single and Multiple Antiplatelet Therapy after Percutaneous Coronary Intervention at Dr. Saiful Anwar Malang

Sasmojo Widito*[1], Dadang Hendrawan[1], and Dedy Irawan[1]
[1]Department of Cardiology and Vascular Medicine, Faculty of Medicine, Brawijaya University, Dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia.

Email Address : sasmojowidito@gmail.com

**KEYWORDS**

Platelet
Thromboelastography
Percutaneous
Coronary Intervention
Heart disease

**Abstract** Each year, approximately 3 million people with coronary heart disease worldwide undergo percutaneous coronary intervention (PCI). Dual antiplatelet therapy (DAPT) with aspirin and P2Y12 inhibitors became the primary therapy for 6-12 months after PCI. DAPT can be continued > 12 months at a high risk of thrombosis. About 9-10% of patients with dual antiplatelet therapy still experience ischemia. The platelet function examination by thromboelastography (TEG). This research is an analytic observational study using a cross-sectional method. This study was conducted in Saiful Anwar General Hospital. Patients were divided into two groups: (1) on-single antiplatelet therapy; (2) on-dual antiplatelet therapy. The outcome measured result of the platelet function test was divided into standard, low platelet function, and platelet hypercoagulability. An analysis of the differences between single or multiple antiplatelet administration and the platelet function results was performed. There were 52 research subjects, each group of single and multiple antiplatelet therapies as many as 26 people, most of the subjects were male (82.6%) with a mean age of 57. The results of this study showed that there was no significant difference in the results of platelet function examinations between single and multiple antiplatelet therapies after 12 months of dual antiplatelet therapy.

## Introduction

Coronary Heart Disease (CHD) is the number one killer in the world. In 2010, coronary heart disease resulted in 13.1% of deaths in men. It is predicted that in 2020 it will be 14.3% and 14.9% in 2030. For women, deaths due to coronary heart disease in 2010 reached 13.6%, and it is predicted that in 2020 it will reach 13.9% and 14.1% in 2030 (Rilantono, 2012). Coronary heart disease is the leading cause of death in the United States, European countries, Japan, and Singapore (Cammerer *et al*., 2003; Kasotakis *et al*., 2009).

Percutaneous Coronary Intervention (IKP) with implantation of drug-eluting stents (DES) is the most frequently performed procedure in stable CHD and acute coronary syndrome. Every year about 3 million people around the world undergo IKP with the implantation of stents. Multiple antiplatelet therapies are given as standard therapy after IKP to prevent stent thrombosis, myocardial infarction, and stroke. In Europe, about 1.4 million patients per year receive dual antiplatelet therapy after IKP (Banerjee *et al*., 2017; Department of economic and social affairs, 2017).

The antiplatelet guidelines in the ESC 2017 state that it is recommended to administer multiple antiplatelets with a combination of aspirin and a P2Y12-ADP receptor inhibitor for at least 6-12 months after the IKP procedure, with class 1 recommendations. Multiple

**How to cite this article:** Widito, S., Hendrawan, D., Irawan, D. (2020). Analysis of Platelet Function from Thromboelastography Examination in Patients with Single and Multiple Antiplatelet Therapy after Percutaneous Coronary Intervention at Dr. Saiful Anwar Malang. Research Journal of Life Science, 7(1), 19-28. https://doi.org/10.21776/ub.rjls.2020.007.01.3

antiplatelet administration can be extended up to 30 months if there is a risk of thrombosis, which is high (Valgimigli *et al*., 2017).

The incidence of in-stent restenosis (ISR) has decreased drastically since the use of DES. However, DES is associated with an increased incidence of stent thrombosis, which is a dreaded complication of stent implantation because the mortality rate is quite high with the emergence of second-generation DES and P2Y12 inhibitor drugs, the incidence rate of thrombotic stents decreased by 50% compared to before (Berg *et al*., 2017).

About 20% of patients with myocardial infarction who did not experience cardiovascular events in the first year after stent insertion had a cardiovascular event 1-4 years after stent placement. Continuing multiple antiplatelet therapies for more than 12 months is expected to reduce cardiovascular events after stent placement. However, with an increased risk of bleeding, it is more appropriate to apply to high thrombosis risk patients with low bleeding risk (Kikkert and Damman, 2018).

Data from several large studies indicate that about 9-10% of patients receiving dual antiplatelet therapy still experience coronary thrombosis in the first 1 year after stent placement. Data is also obtained that about 2% of patient's experience bleeding events. Several scoring systems were developed to identify risks. Thrombosis and hemorrhage in patients on antiplatelet therapy. However, it has some drawbacks to its proper application (Fontana *et al*., 2020).

Individual-based therapy has developed recently in Europe and America where the use of platelet function tests to provide individual-based antiplatelet therapy is still being debated in the last 10 years. The American College of Cardiology / American Heart Association (ACC / AHA) issued a class IIb recommendation for the use of platelet function tests in patients with certain conditions receiving P2Y12 therapy. Inhibitor likewise, the European society of cardiology (ESC) issued a class IIb recommendation for the use of platelet function tests as a guide for lowering levels of P2Y12 inhibitor therapy. Thromboelastography (TEG) is a platelet function test method that can evaluate blood viscoelasticity and a picture of hemostatic function, including coagulation, platelet aggregation, and fibrinolysis. TEG can be used as a guide for administering individual-based antiplatelet therapy in CHD patients after undergoing IKP (Neumann *et al*., 2018; Fontana *et al*., 2020).

Based on the description above, the researchers felt the need to do a comparison examination to assess the therapeutic response between multiple antiplatelet and single antiplatelet administration with a TEG examination. It can be used to examine platelet function in CHD patients after undergoing IKP at Dr. Saiful Anwar Malang. The purpose of this study was to determine the differences in platelet function from the results of TEG examination in CHD patients who received multiple and single antiplatelet therapies after the IKP action at Dr. Saiful Anwar Malang and determining the correlation between platelet function from the results of TEG examination with multiple and single antiplatelet therapies.

**Materials and Methods**

This research was conducted at dr. Saiful Anwar Malang and started after getting approval and a research ethics commission. This research is an analytic observational study using a cross-sectional method. Sources of data used in this study are divided into primary data and secondary data. Primary data is obtained from the thromboelastography (TEG) examination in patients with coronary heart disease (CHD) after undergoing IKP action and receiving antiplatelet therapy. Secondary data were obtained from the patient's medical records to determine the sample to fit the inclusion and exclusion criteria.


**E-ISSN 2355-9926**

*Population and sample*

Populations

1) Target Population
   This study's target population was patients with coronary heart disease (CHD) undergoing percutaneous coronary intervention therapy (IKP).
2) Affordable Population
   This study's target population was patients with coronary heart disease (CHD) who underwent percutaneous coronary intervention therapy (IKP) treated at Dr. Saiful Anwar Malang.
3) Eligible subject
   Subjects that qualify for this study are affordable populations that meet predetermined inclusion and exclusion criteria.

*Sample Size*

The sample size in this study was obtained from the sample size formula for diagnostic test research as follows [26]:

The minimum sample size is based on the formula (Sastroasmoro, 2014).

$$N = \frac{Z\ \propto^2 P(1-P)}{d^2}$$

$$N = \frac{1.96^2 x 0.15\ (1-0.15)}{0.05^2}$$

N = 50

Zα : Standard variate Normal (P<0.05 = 1.96)
P : Proportion of expected based on literature
D : Absolute error decided by the researcher

The minimum number of subjects calculated based on this formula is 50 subjects taken using a non-random sampling technique, namely consecutive sampling. Subjects with a diagnosis of Coronary Heart Disease (CHD) who underwent IKP action at Dr. Saiful Anwar Malang, who met the inclusion and exclusion criteria in the study period, was taken as much as the number determined by the sample size formula.

*Research Variable*

This study was cross-sectional. The independent variable was multiple antiplatelet therapies and single antiplatelet therapy after 12 months of IKP action, and the dependent variable was platelet function obtained from thromboelastography (TEG).

*Sample Inspection Procedure*

1. A 6 mL sample of fresh whole blood (fresh whole blood) from veins or arteries is placed in two citrate tubes (ratio of trisodium citrate 3.2%: blood is 1: 9).
2. TEG examination: as much as 1 mL of blood is taken from the citrate tube sample, mixed in the kaolin vial, and then shaken gently. A total of 0.34 ml of the blood was drawn with an automatic pipette and put in a TEG cuvette. To the cuvette, 20µL of 0.2 mol / L calcium was added to remove the citrate effect. Then the test is run without delay according to the manufacturer's instructions.

The TEG test parameter is a representation of hemostasis, which includes:

a. Reaction time (R) is the time from the beginning of the analysis until a clot is formed with a standard value of 5-10 minutes.
b. Coagulation time (K) is the time from the clot formation until the curve reaches an amplitude of 20 mm. Standard Value 1-3 Minutes
c. α-angle is the angle between the bases and the TEG curve intersection, which shows the clot formation speed with a reference value of 53°-72°.
d. Maximum Amplitude (MA) indicates clot strength with expected values of 50-70 mm.
e. Coagulation Index (CI) with reference values -3 to 3.


**E-ISSN 2355-9926**

f. Lysis at 30 minutes (LY30) is a value that shows the degree of fibrinolysis at 30 minutes with a reference value of 0% - 7.5%.

Hypercoagulability was indicated by shortening the R and K values, increasing α-angle, MA, CI, and LY30<0. Conversely, hypercoagulability was characterized by elongated R and K values, decreasing α-angle, MA, CI, and LY30>7.5%.

**Result and Discussion**

*Analysis of Basic Characteristics*

Patients who were the study sample were patients with coronary heart disease (CHD) who underwent percutaneous coronary intervention therapy (IKP) who received single or multiple antiplatelet therapies that were treated at Dr. Saiful Anwar Malang, who met the inclusion and exclusion criteria. Sample inclusion and exclusion criteria were determined through anamnesis, physical examination, laboratory examination, and medical record data. Subjects involved during the study period were 52 people. Of the 52 people, 26 were divided into 2 groups, 26 patients who received single antiplatelet therapy, and 26 patients who received dual antiplatelet therapy.

From the study results in the group of patients with single antiplatelet therapy, it was found that the number of men was more than that of women, namely men as many as 21 people (80.8%). Likewise, in the multiple antiplatelet groups, the number of men was greater than that of women, namely 22 people (84.6%).

The mean age did not differ significantly in patients receiving single antiplatelet therapy 58.7 ± 7.6 years, while patients receiving dual antiplatelet therapy were 56.6 ± 6.2 years. The mean body weight of patients receiving single antiplatelet therapy was 62.0 ± 4.8 kg, while in patients receiving dual antiplatelet therapy was 61.5 ± 4.7 kg.

There were 2 patients (7.7%) in the group of patients receiving dual antiplatelet therapy who had a history of bleeding while receiving antiplatelet therapy. The mean time from IKP to the patient underwent TEG examination was 13.6 ± 0.4 months in patients on single antiplatelet therapy and 13.3 ± 0.4 months in patients on dual antiplatelet therapy.

The risk factors obtained in patients who received single antiplatelet therapy included hypertension 16 patients (57%), DM 5 patients (19%), smoking 13 patients (50%), dyslipidemia 4 patients (15%), family history of heart disease 3 patients. (11%), history of MI in 1 patient (3.8%), CHF / EF <30% in 3 patients (11%), and 15 patients (57%) who had a previous history of IKP.

Whereas in patients who received multiple antiplatelet therapies, there were risk factors including hypertension in 12 patients (42%), DM 10 patients (38%), smoking 19 patients (73%), dyslipidemia in 6 patients (23%), family history of heart disease in 4 patients. (15%), history of MI in 14 patients (53%), CHF / EF <30% in 6 patients (23%), and 16 patients (61%) who had a previous history of IKP.

The 2 groups of patients' angiographic diagnosis results were mostly obtained with multivessel CAD, 17 patients (65%), and 22 patients (84%) who received multiple antiplatelet therapies. The most widely used type of stent was the first-generation DES stent, namely 21 patients (80%) in patients on single antiplatelet therapy and 20 patients (76%) in dual antiplatelet therapy patients. There was a stent diameter <3 mm in 10 patients (38%) of the patient group on single antiplatelet therapy and 9 patients (34.6%) in patients with dual antiplatelet therapy. We did not find patients with vein graft stents in either group of patients.

In patients with multiple antiplatelet therapies, 14 patients (53.8%) were found to


**E-ISSN 2355-9926**

have a DAPT score <2. Meanwhile, in patients with multiple antiplatelet therapies, 22 patients (84%) had a DAPT score ≥ 2.

The results of the examination of platelet function with TEG examination obtained a mean MA value of 52.6 ± 9.5 in patients with single antiplatelet therapy and 49.6 ± 9.9 in patients with multiple antiplatelet therapies.

Based on the data above, it was found that patients who received single antiplatelet therapy with normal platelet function TEG results were 10 patients (38%), 16 patients (61%) had low platelet function. There were no patients with platelet hypercoagulability results. Patients who received therapy. Multiple antiplatelet with normal platelet function TEG results in 8 patients (30%), 18 patients (69%) low platelet function, and no patients with platelet hypercoagulability were found.

**Table 1. The results of the examination of platelet function with TEG examination**

| Parameters | Single Antiplatelet (n = 26) | Multiple Antiplatelet (n=26) | P-Value |
|---|---|---|---|
| **Gender** | | | |
| **Male (n,%)** | 21 (80.8 %) | 22 (84.6 %) | 1.000 |
| **Female (n, %)** | 5 (19.2 %) | 4 (15.4 %) | |
| **Age (Years) (mean±SD)** | 58.7 ± 7.6 | 56.6 ± 6.2 | 0.289 |
| **Weight (Kg) (mean±SD)** | 62.0 ± 4.8 | 61.5 ± 4.7 | 0.729 |
| **Time from IKP (Month) (mean±SD)** | 13.6 ± 0.4 | 13.3 ± 0.4 | 0.920 |
| **Bleeding History (n, %)** | 0 (0 %) | 2 (7.7%) | 0.471 |
| **Risk Factors** | | | |
| **Hypertension (n, %)** | 16 (57.1 %) | 12 (42.9 %) | 0.404 |
| **DM (n, %)** | 5 (19.2 %) | 10 (38.5 %) | 0.221 |
| **Smoke (n, %)** | 13 (50.0 %) | 19(73.1 %) | 0.154 |
| **Dyslipidemia (n, %)** | 4 (15.4 %) | 6 (23.1 %) | 0.491 |
| **Family History (n, %)** | 3 (11.5 %) | 4 (15.4 %) | 0.692 |
| **History of MI (n, %)** | 1 (3.8 %) | 14 (53.8 %) | 0.000 |
| **CHF/EF < 30 % (n, %)** | 3 (11.5 %) | 6 (23.1 %) | 0.281 |
| **Previous PCI History (n, %)** | 15 (57.7 %) | 16 (61.6 %) | 0.783 |
| **Diagnosis of Angiography** | | | |
| **CAD Single Vessel (n, %)** | 9 (34.6 %) | 4 (15.4 %) | 0.200 |
| **CAD Multivessel (n, %)** | 17 (65.4 %) | 22 (84.6 %) | |
| **Type of Stent** | | | |
| **Stent 1$^{St}$ DES (n, %)** | 21 (80.8 %) | 20 (76.9%) | 1.000 |
| **Stent 2$^{nd}$ DES (n, %)** | 5 (19.2 %) | 6 (23.1 %) | |
| **Diameter of stent < 3 mm (n, %)** | 10 (38.5 %) | 9 (34.6 %) | 0.779 |
| **Vein graft stent (n, %)** | 0 (0 %) | 0 (0 %) | |
| **DAPT Score** | | | |


**E-ISSN 2355-9926**

| Parameters | Single Antiplatelet (n = 26) | Multiple Antiplatelet (n=26) | P-Value |
|---|---|---|---|
| **< 2 (n, %)** | 14 (53.8 %) | 4 (15.4 %) | 0.009 |
| **≥ 2 (n, %)** | 12 (46.2 %) | 22 (84.6 %) | |
| **Result of TEG** | | | |
| **Maximum Amplitude (MA) (Second) (mean±SD)** | 52.6 ± 9.5 | 49.6 ± 9.9 | 0.267 |
| **Low Platelet Function (n, %)** | 16 (61.5 %) | 18 (69.2 %) | 0.771 |
| **Normal Platelet Function (n, %)** | 10 (38.5 %) | 8 (30.8 %) | |
| **Platelet Hypercoagulability (n, %)** | 0 (%) | 0 (%) | |

*Results of Bivariate Test Analysis*

To determine the relationship between variables, we conducted a bivariate test analysis. The results of the analysis showed that there was no significant difference (p> 0.05) between the groups of patients who received single antiplatelet therapy and those who received multiple antiplatelet therapies in the study parameters including gender, body weight, time of IKP, bleeding history, risk factors for hypertension, DM, smoking, dyslipidemia, family history of heart disease, CHF / EF <30%, previous history of IKP, diagnosis of angiography, type of stent, stent diameter and vein graft stent.

The results of the chi-square test showed that the proportion of patients with a history of MI who received multiple antiplatelets was significantly higher than those who received single antiplatelet (53.8% versus 3.8% respectively, with p-value = 0.000)

The chi-square test results showed that the proportion of patients with a DAPT score> 2 who received multiple antiplatelets was significantly higher than those who received a single antiplatelet (84.6% versus 46.2% respectively, p = 0.009).

The bivariate analysis results using the chi-square test showed no significant difference in the low platelet function examination results between patients on single and multiple antiplatelet therapies (61.5% compared to 69.2%, respectively (p-value = 0.771).

**Discussion**

This study involved 52 patients, 83% of whom were men, the mean age of the patients was 57.6 ±6.9 years, and the mean weight was 61.7 ± 4.7 kg. 59.6% of the patients had undergone PCI. 78% of patients diagnosed with CAD multivessel disease angiography using 1st Generation DES were 78%, and about 36% of patients used stents <3 mm in diameter. Following previous studies that the Population was suffering from coronary heart disease, most of them are male. We assume that the proportion of men who experience CHD is more than women.

Anthropometric baseline data also obtained results that were not statistically significant, indicating that the two groups' distribution had the same anthropometric characteristics.

Based on the results of bivariate data analysis using the chi-square test, it was found that there was a significantly higher difference in the history of MI in patients who received multiple antiplatelet therapies compared to single antiplatelet therapy. It is following the theory of Yeh *et al*., 2016 where in patients with risk factors for DM, smoking, history of MI, previous history of IKP, stent diameter <3 mm,


**E-ISSN 2355-9926**

use of paclitaxel stents, CHF / EF <30% and patients with vein stent-grafts ischemic risk are more significant than those who do not have the risk factors above (Yeh *et al*., 2016).

Based on the bivariate data analysis results using the chi-square test, it was found that there was a significantly higher difference in the DAPT score >2 in patients who received multiple antiplatelet therapies compared to single antiplatelet therapy, according to studies from the DAPT trial. The results of the calculation of DAPT score >2 are a group of patients with a higher ischemic risk, so it is recommended that long-term dual antiplatelet therapy for up to 30 months can reduce the incidence of stent thrombosis, MI, stroke, and death. However, it must be watched out for this long-term administration of multiple antiplatelet to increase bleeding risk (Yeh *et al*., 2016).

Data analysis results with the chi-square test showed no significant difference in platelet function examinations between patients who received single antiplatelet therapy and those who received multiple antiplatelet therapies. Most of the patient groups who received dual antiplatelet therapy (69%) and single antiplatelet therapy (61%) able to achieved pharmacological targets. However, about 30% of patients received multiple antiplatelet therapies, and 38% received single antiplatelet therapy, unable to achieve the target. The expected pharmacology is the MA value <50 seconds (Low platelet function). Some studies stated that the individual response to antiplatelet varies widely. Resistance or nonresponsive to antiplatelet means a condition in which the antiplatelet drug cannot reach its pharmacological target. The measurement of platelet function determines this. Recently, laboratory measurement methods have been developed to diagnose antiplatelet resistance. However, none have been accepted as standard tools due to the variability between individuals and the poor correlation between these devices. The antiplatelet resistance mechanism is not fully understood; it is multifactorial, involving dynamic pharmacology, kinetic drug pharmacology, and genetic polymorphisms (Bonello *et al*., 2010; Hidayati *et al*., 2017; Li et al., 2019).

The results of this study indicate that single and multiple antiplatelet administration are equally beneficial for preventing thrombosis in CHD patients undergoing percutaneous coronary intervention (IKP) procedures, but also have a risk of bleeding that must be watched out.

It is following the theory of Valmigli et al., (2018) where after the IKP procedure, the patient received antiplatelet therapy. Multiple antiplatelet therapies are required to reduce the risk of thrombotic stents. The antiplatelets given were aspirin and P2Y12 inhibitors (Clopidogrel, prasugrel, and ticagrelor). The treatment duration is at least 6 months - 1 year according to the patient's clinical condition. After that, it was continued with single antiplatelet administration, but in a patient with a high risk of thrombosis calculated based on the DAPT score, multiple antiplatelet administration could be continued for up to 24-30 months (Levine *et al*., 2016; Valgimigli *et al*., 2017).

TEG can evaluate blood viscoelasticity and provide an overall picture of hemostatic function, including coagulation, platelet function, platelet-fibrinogen interactions, and fibrinolysis. The results of this examination can be used to predict the bleeding situation, hypercoagulation, and fibrinolysis. In patients undergoing antiplatelet therapy, the examination of platelet function with TEG is useful for monitoring antiplatelet therapy's effectiveness and determining the choice of antiplatelet drugs to be given to each patient (Swallow *et al*., 2006; Zhao *et al*., 2016).


**E-ISSN 2355-9926**

Given the nature of CHD as a chronic disease and the high risk for CHD patients to experience cardiovascular events

**Conclusion**

Based on the results of statistical tests that have been carried out, it can be concluded that there is no significant difference in platelet function in post-percutaneous coronary heart disease patients who receive single antiplatelet therapy with multiple antiplatelet after 12 months of receiving multiple antiplatelet therapies (hypothesis is accepted). The measuring instrument used to assess platelet function in this study is TEG. The TEG results can be used to determine the status of platelet function in CHD patients receiving antiplatelet therapy.

**References**

Banerjee, S., Angiolillo, D. J., Boden, W. E., Murphy, J. G., Khalili, H., Hasan, A. A., Harrington, R. A., & Rao, S. V. (2017). Use of Antiplatelet Therapy/DAPT for Post-PCI Patients Undergoing Noncardiac Surgery. Journal of the American College of Cardiology, 69(14), 1861–1870. https://doi.org/10.1016/j.jacc.2017.02.012

Berg, J. M., Zwart, B., van 't Hof, A. W. J., Liem, A., Waltenberger, J., de Winter, R. J., & Jukema, J. W. (2017). Optimal duration of dual antiplatelet therapy after percutaneous coronary intervention or after acute coronary syndrome. *Netherlands Heart Journal*, *25*(12), 655–663. https://doi.org/10.1007/s12471-017-1023-y

Bonello, L., Tantry, U. S., Marcucci, R., Blindt, R., Angiolillo, D. J., Becker, R., Bhatt, D. L., Cattaneo, M., Collet, J. P., Cuisset, T., Gachet, C., Montalescot, G., Jennings, L. K., Kereiakes, D., Sibbing, D., Trenk, D., Van Werkum, J. W., Paganelli, F., Price, M. J., … Gurbel, P. A. (2010). Consensus and Future Directions on the Definition of High On-Treatment Platelet Reactivity to Adenosine Diphosphate. *Journal of the American College of Cardiology*, *56*(12), 919–933. https://doi.org/10.1016/j.jacc.2010.04.047

Cammerer, U., Dietrich, W., Rampf, T., Braun, S. L., & Richter, J. A. (2003). The Predictive Value of Modified Computerized Thromboelastography and Platelet Function Analysis for Postoperative Blood Loss in Routine Cardiac Surgery. *Anesthesia & Analgesia*, *96*(1), 51–57. https://doi.org/10.1097/00000539-200301000-00011

Fontana, P., Roffi, M., & Reny, J. L. (2020). Platelet Function Test Use for Patients with Coronary Artery Disease in the Early 2020s. *Journal of clinical medicine*, *9*(1), 194. https://doi.org/10.3390/jcm9010194

Hidayati, F., Irawan, B., & Mumpuni, H. (2017). Aspirin and Clopidogrel Resistance in Coronary Artery Disease. *ACI (Acta Cardiologia Indonesiana)*, *3*(1), 33. https://doi.org/10.22146/aci.29683

Kasotakis, G., Pipinos, I. I., & Lynch, T. G. (2009). Current evidence and clinical implications of aspirin resistance. *Journal of vascular surgery*, *50*(6), 1500–1510. https://doi.org/10.1016/j.jvs.2009.06.023

Kikkert, W. J., & Damman, P. (2018). Optimal duration of dual antiplatelet therapy for coronary artery disease. *Netherlands heart journal : monthly journal of the*


**E-ISSN 2355-9926**

*Netherlands Society of Cardiology and the Netherlands Heart Foundation*, *26*(6), 321–333. https://doi.org/10.1007/s12471-018-1113-5

Levine G. N., Bates, E. R., Bittl, J. A., Brindis, R. G., Fihn, S. D., Fleisher, L. A., Granger, C. B., Lange, R. A., Mack, M. J., Mauri, L., Mehran, R., Mukherjee, D., Newby, L. K., O'Gara, P. T., Sabatine, M. S., Smith, P. K., Smith, S. C. Jr. (2016). 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery. Circulation, 134(10), e123-55. doi: 10.1161/CIR.0000000000000404. Epub 2016 Mar 29. Erratum in: Circulation, 134(10), e192-4. PMID: 27026020.

Li, Y., Chang, H., Ni, L., Xue, P., Li, C., Yuan, L., Cui, H., & Yu, C. (2019). Analysis of thrombelastogram-guided medication in patients with coronary heart disease after percutaneous coronary intervention. *Experimental and Therapeutic Medicine*, 3047–3052. https://doi.org/10.3892/etm.2019.7294

Neumann, F. -J., Sousa-Uva, M., Ahlsson, A., Alfonso, F., Banning, A. P., Benedetto, U., Byrne, R. A., Collet, J.-P., Falk, V., Head, S. J., Jüni, P., Kastrati, A., Koller, A., Kristensen, S. D., Niebauer, J., Richter, D. J., Seferović, P. M., Sibbing, D., Stefanini, G. G., … Henderson, R. (2018). 2018 ESC/EACTS Guidelines on myocardial revascularization. *European Heart Journal*, *40*(2), 87–165. https://doi.org/10.1093/eurheartj/ehy394.

Rilantono, L. I., Rahajoe, A. U., & Santoso, K. (2018). Penyakit kardiovaskular (PKV) : 5 rahasia (1st ed., V). Jakarta: Fakultas Kedokteran Universitas Indonesia.

Sastroasmoro, S. (2014). *Dasar-dasar metodologi penelitian klinis* (5th ed.). Bagian Ilmu Kesehatan Anak, Fakultas Kedokteran, Universitas Indonesia.

Swallow, R. A., Agarwala, R. A., Dawkins, K. D., & Curzen, N. P. (2006). Thromboelastography: potential bedside tool to assess the effects of antiplatelet therapy?. Platelets, 17(6), 385–392. https://doi.org/10.1080/09537100600757521.

Valgimigli, M., Bueno, H., Byrne, R. A., Collet, J. P., Costa, F., Jeppsson, A., Jüni, P., Kastrati, A., Kolh, P., Mauri, L., Montalescot, G., Neumann, F. J., Petricevic, M., Roffi, M., Steg, P. G., Windecker, S., Zamorano, J. L., Levine, G. N., ESC Scientific Document Group, ESC Committee for Practice Guidelines (CPG), … ESC National Cardiac Societies (2018). 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration


**E-ISSN 2355-9926**

with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *European heart* journal, 39(3), 213–260. https://doi.org/10.1093/eurheartj/ehx419.

Yeh, R. W., Secemsky, E. A., Kereiakes, D. J., Normand, S. L., Gershlick, A. H., Cohen, D. J., Spertus, J. A., Steg, P. G., Cutlip, D. E., Rinaldi, M. J., Camenzind, E., Wijns, W., Apruzzese, P. K., Song, Y., Massaro, J. M., Mauri, L., & DAPT Study Investigators (2016). Development and Validation of a Prediction Rule for Benefit and Harm of Dual Antiplatelet Therapy Beyond 1 Year After Percutaneous Coronary Intervention. *JAMA*, *315*(16), 1735–1749. https://doi.org/10.1001/jama.2016.3775.

Zhao, S. W., Wang, Y. P., Xu, L. D., & Gang, W. (2016). The application of thromboelastogram in detection of indexes of antiplatelet therapy for coronary heart disease. Journal of thoracic disease, 8(12), 3515–3520. https://doi.org/10.21037/jtd.2016.12.77


**E-ISSN 2355-9926**