รูปแบบการสั่งจ่ายยาและผลลัพธ์ทางคลินิกของการใช้ยาต้านเกล็ดเลือดในผู้ป่วยหัวใจขาดเลือดเฉียบพลันร่วมกับไตวายเรื้อรังระยะสุดท้าย
Prescription Patterns and Clinical Outcomes of Antiplatelet Therapy in Acute Coronary Syndrome with End-Stage Renal Disease

นิพนธ์ต้นฉบับ

Original Article

วรรณพัทธ เตไชยกุล[1], นริศรา บุญตัน[1], อรินทยา พรหมินธิกุล[2], มันตีวีร์ นิ่มวรพันธุ์[3] และ วรธิมา สีลวานิช[3]*

[1] ขณะทำการศึกษาเป็นนักศึกษาชั้นปีที่ 5 คณะเภสัชศาสตร์
[2] หน่วยวิชาระบบหัวใจและหลอดเลือด ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์
[3] ภาควิชาบริบาลเภสัชกรรม คณะเภสัชศาสตร์
[1-3] มหาวิทยาลัยเชียงใหม่ อ.เมืองเชียงใหม่ จ.เชียงใหม่ 50200
*** Corresponding author:** voratima.silavanich@gmail.com

วารสารไทยเภสัชศาสตร์และวิทยาการสุขภาพ 2563;15(3):163-168.

Wannapat Techaikool[1], Narisara Boontan[1], Arintaya Promintikul[2], Mantiwee Nimworapan[3] and Voratima Silavanich[3]*

[1] 5th year pharmacy student, Faculty of Pharmacy
[2] Division of Cardiology, Deparment of Internal Medicine, Faculty of Medicine
[3] Department of Pharmaceutical Care, Faculty of Pharmacy
[1-3] Chiang Mai University, Muang Chiang Mai, Chiang Mai 50200, Thailand
*** Corresponding author:** voratima.silavanich@gmail.com

Thai Pharmaceutical and Health Science Journal 2020;15(3):163-168.

บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาลักษณะการสั่งใช้ยาต้านเกล็ดเลือดในผู้ป่วยหัวใจขาดเลือดเฉียบพลันร่วมกับไตวายเรื้อรังระยะสุดท้าย และประเมินผลลัพธ์ทางคลินิก **วิธีการศึกษา:** การศึกษาเชิงพรรณนาย้อนหลังในผู้ป่วยหัวใจขาดเลือดเฉียบพลันที่มีไตวายเรื้อรังระยะสุดท้ายซึ่งได้รับยาต้านเกล็ดเลือดและมาติดตามการรักษาที่โรงพยาบาลมหาราชนครเชียงใหม่ ตั้งแต่วันที่ 1 มกราคม 2551 ถึง 1 มกราคม 2560 โดยติดตามผู้ป่วยเป็นเวลา 1 ปี **ผลการศึกษา:** กลุ่มตัวอย่าง 88 คน อายุเฉลี่ย 66.40 ปี ผู้ป่วยส่วนใหญ่ (ร้อยละ 86.63) มีภาวะหัวใจขาดเลือดเฉียบพลันชนิด non-ST-elevation myocardial infarction และไม่ได้รับการเปิดหลอดเลือดโดยได้รับการรักษาด้วยยา (ร้อยละ 63.64) ผู้ป่วยได้รับยาต้านเกล็ดเลือดสองชนิดร่วมกัน (dual antiplatelet therapy; DAPT) 73 คน (ร้อยละ 82.45) ได้แก่ aspirin กับ clopidogrel (ASA+CLP) 69 คน, aspirin กับ ticagrelor (ASAP+TCG) 3 คน และ aspirin กับ ticlopidine (ASA+TCP) 1 คน และได้รับยาต้านเกล็ดเลือดเดี่ยว 15 คน (ร้อยละ 17.05) พบผลลัพธ์หลัก 52 เหตุการณ์ ได้แก่ การกลับมาเป็นซ้ำของหัวใจขาดเลือด การกลับมารักษาที่โรงพยาบาล การเสียชีวิตจากสาเหตุอื่น และเกิดภาวะหลอดเลือดในสมอง โดยกลุ่มที่ได้รับยาต้านเกล็ดเลือดเดี่ยวเกิดผลลัพธ์หลักร้อยละ 80 สำหรับกลุ่มที่ได้รับยาต้านเกล็ดเลือดสองชนิดร่วมกัน พบว่ากลุ่ม ASA+CLP เกิดผลลัพธ์หลักร้อยละ 55.07 กลุ่ม ASA+TCG เกิดร้อยละ 33.33 ในขณะที่ผลลัพธ์รอง มีภาวะเลือดออก 13 เหตุการณ์ โดยพบมากที่สุดในกลุ่ม ASA+TCG (ร้อยละ 66.67) **สรุป:** ผู้ป่วยหัวใจขาดเลือดเฉียบพลันร่วมกับไตวายเรื้อรังระยะสุดท้ายส่วนใหญ่ได้รับยาต้านเกล็ดเลือดสองชนิดร่วมกัน ซึ่งยาชนิดหลัก คือ aspirin กับ clopidogrel โดยผู้ป่วยที่ได้รับยาต้านเกล็ดเลือดชนิดเดี่ยวเกิดผลลัพธ์หลักสูงกว่าการใช้ยาสองชนิดร่วมกัน พบว่ากลุ่มที่ได้รับ aspirin กับ clopidogrel เกิดผลลัพธ์หลักสูงกว่ากลุ่ม aspirin ร่วมกับ ticagrelor แต่พบภาวะเลือดออกสูงในกลุ่มที่ใช้ aspirin กับ ticagrelor

คำสำคัญ: ยาต้านเกล็ดเลือด, โรคหัวใจขาดเลือดเฉียบพลัน, ภาวะไตวายเรื้อรังระยะสุดท้าย

Editorial note
Manuscript received in original form on January 23, 2020;
revised February 17, 2020;
and accepted in final form on February 18, 2020

Abstract

Objective: To explore the prescribing patterns of antiplatelets and to evaluate their clinical outcomes in acute coronary syndrome (ACS) patients with end-stage renal disease (ESRD). **Methods:** This retrospective study collected data from medical records of ACS patients with ESRD who visited Maharaj Nakorn Chiang Mai Hospital from January 1st 2008 to January 1st, 2017. The treatment information was reviewed for 1 year since antiplatelet therapy initiation or until discontinuation. **Results:** Of the 88 ACS patients with ESRD, their average age was 66.40 years old. Most patients (86.63%) had non-ST-elevation myocardial infarction. Medical therapies without revascularization were used in 63.64%. Seventy three patients (82.45%) were prescribed dual-antiplatelet therapy (DAPT), specifically 69 patients with aspirin plus clopidogrel (ASA+CLP), 3 with aspirin plus ticagrelor (ASA+TCG), 1 patient with aspirin plus ticlopidine (ASA+TCP) and 15 (17.05%) with single antiplatelet agent. Primary outcomes occurred in 52 events which included recurrent nonfatal myocardial infarction, hospitalization, death from other causes, and nonfatal stroke. Primary outcomes were mostly found in patients receiving single antiplatelet (80%). In the patients receiving DAPT, ASA+TCP had the most primary outcomes (100%), followed ASA+CLP (55.07%), and ASA+TCG (33.33%). Bleeding (secondary outcomes) was mostly found in ASA+TCG (66.67%). **Conclusion:** Most patients with ACS and ERSD were prescribed DAPT, especially with ASA+CLP. More cardiovascular events were found with single antiplatelet drug than DAPT. Patients taking ASA+CLP had higher cardiovascular events than those using ASA+TCG. Higher incidence of bleeding occurred in ASA+TCG.

Keywords: antiplatelet therapy, acute coronary syndrome, end-stage renal disease

Journal website: http://ejournals.swu.ac.th/index.php/pharm/index

Introduction

Ischemic heart disease (IHD) or coronary artery disease (CAD) is an ailment caused by narrowed arteries supplying blood to the heart muscle resulting in myocardial infarction. The clinical symptoms can be divided into two groups namely stable angina and acute coronary syndrome (ACS).[1] In Thailand, the mortality rate of the disease had continuously increased from 2012 to 2016. According to the Ministry of Public Health Annual Report of Thai population in 2014,[2] it was found that the male population lost 425,000 disability-adjusted life years (DALYs) because of IHD or 4.9% of other

diseases' DALYs; while the female counterpart lost 271,000 DALYs because of IHD or 4.3% of the other diseases' DALYs. Therefore, it can be seen that this disease is an important problem in Thailand. It has been found that 30 - 60% of ACS patients had required renal replacement therapy.[3-5] However, treating IHD with chronic kidney disease (CKD) is a clinical challenge.[6-7]

It was found that the risk of IHD or CAD was increased with higher severity levels of CKD, especially among those with moderate-to-severe ones. Moreover, mortality rates and risks of bleeding were increased consistently.[8,9] According to the practice guidelines for management of IHD patients, it is recommended to use antiplatelet drugs in order to prevent cardiovascular and recurrent myocardial infarction. However, the evidences and data about treating and using antiplatelet drugs in patients with ESRD were somewhat limited.[10-12] It was also found that the impairment of kidney functions reduced the platelet inhibition of clopidogrel, therefore the risk of IHD was increased as compared to those with normal kidney functions.[13] ESRD patients also had a higher risk of stent thrombosis.[14]

Even though there is no clear suggestion about using antiplatelet drugs in ACS with ESRD patients, clopidogrel is an antiplatelet drug used with aspirin as dual antiplatelet therapy (DAPT) with the highest prescription in these patients. While prasugrel and ticagrelor are better than clopidogrel in terms of reduced incidence of cardiovascular death, IHD and stroke, they both are associated with increased bleeding risk. In these studies, the results were followed for one year. Nevertheless, the differences of the results were obvious after the first month of treatments.[15,16] These results might also be found in the patients with chronic kidney disease.[12,17] However, it was found that, the randomized controlled trials (large scale reliable study) was limited in patients with chronic renal failure, with only 4% of CKD patients.[15] Hence, it was difficult to apply the data to this group of patients. Additionally, the practice guidelines for treating patients with ACS indicated that the data about using antiplatelet drugs in ESRD patients were limited.[6,7] Thus, this study aimed to determine prescribing patterns of antiplatelet drugs in ACS patients with ESRD as well as clinical outcomes including cardiovascular events and safety regarding bleeding within a year or until discontinuation of any type of antiplatelet drugs.

Methods

This study used the retrospective descriptive design. The study was approved by the ethical committee of the Faculty of Medicine, Chiang Mai University (IRB No. 2561-05445).

The sample was all patients who visited the cardiovascular outpatient clinic at Maharaj Nakorn Chiang Mai from January 1st, 2008 to January 1st, 2017. The inclusion criteria were as follows: 1) patients who were diagnosed with acute coronary syndrome and end stage renal disease, 2) receiving at least 1 antiplatelet (aspirin and/or $P2Y_{12}$ inhibitors), and 3) age $\geq$ 18 years on the date of entry. The exclusion criteria were as follows: 1) patients whose medical record at the cardiovascular outpatient clinic at Maharaj Nakorn Chiang Mai Hospital could not be accessed, and 2) patients who were lost to follow-up at Maharaj Nakorn Chiang Mai Hospital. The details of sample selection are shown in Figure 1. There were a total of 88 patients who met the above criteria.

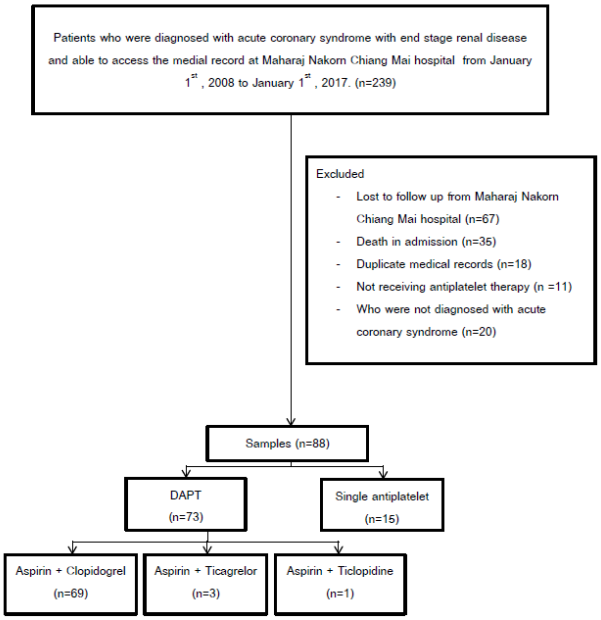

Figure 1 Study profile.

In this study, the data collection form was composed of 4 parts. Part 1 collected demographic data of the mother such as gender, age, weight, height, duration of illness as IHD and ESRD, and other comorbidities. Part 2 collected data related to drug usage, for example, the first date and stop date of antiplatelet usage, duration of antiplatelet usage, doses of antiplatelets, and other medication history. Part 3 collected results of laboratory tests, such as platelet counts, hematocrit,

hemoglobin, and serum creatinine. Part 4 collected clinical outcomes when receiving antiplatelet, for example, cardiovascular death, recurrent myocardial infarction and bleeding. Content validity of the data collection form was tested by three experts in cardiovascular disease, or having experience in taking care of patients with cardiovascular disease and CKD. The data collection form was revised based on their comments before data collection in the study.

In this study, clinical outcomes consisted of primary and secondary outcomes. Primary outcomes were the number of recurrent myocardial infarction, stroke, re-hospitalization, cardiovascular death, and death from any causes. The high number of primary outcomes indicated poor effectiveness of treatment.

Secondary outcome was the number of bleeding in various types. The high number of secondary outcome indicated high bleeding risk from treatment. The Thrombolysis in Myocardial Infarction (TIMI)-18 was used to classify the bleeding into 3 levels as follows. First, major bleeding included intracranial hemorrhage, blood loss with hemoglobin decline $\geq$ 5 gram/dL, or fetal bleeding that patients died within 7 days. Minor bleeding included blood loss with hemoglobin decline $\geq$ 3 gram/dL, but < 5 gram/dL. Patients had urgent need for medical treatment or surgery to stop bleeding, or temporarily or permanently stop antiplatelet treatment, dose adjustment, or longer hospitalization. Finally, minimal bleeding was bleeding that was not included in the above 2 levels.

Patients who were diagnosed with acute coronary syndrome and end stage renal disease were patients with ICD-10:I21 and ICD-10:N18.5, confirmed by diagnosis in the medical profile.

Data collection

Data were collected using ICD-10:I21 and ICD-10:N18.5 from electronic database at cardiovascular outpatient clinic of Maharaj Nakorn Chiang Mai Hospital. Demographic data, antiplatelet usage, and clinical outcomes, both primary and secondary, of patients who visited the clinic from January 1st, 2008 to January 1st, 2017, were collected. Patients were followed-up for their medical treatment for a year or until discontinuation of antiplatelet treatment that was recorded in their medical profile.

Data analysis

Data were analyzed using SPSS version 17.0. Descriptive statistics were used to analyze demographic data, antiplatelet usage, and clinical outcomes. The results were displayed in terms of frequency with percentage for discrete variables, mean with standard deviation continuous variables.

Results

Of the total of 88 patients, the majority received DAPT (73 patients or 82.95%), followed by aspirin with clopidogrel (69 or 78.41%), aspirin with ticagrelor (3 or 3.41%), and aspiring with ticlopidine (1 or 1.14%) (Table 1). Of the 15 patients taking single antiplatelets, the majority took aspirin (14 patients) and one took clopidogrel.

Table 1 Baseline characteristics and concomitant medication use.

Variables	Number (%)				
	Total (N = 88)	Clopidogrel with aspirin (n = 69)	Ticagrelor with aspirin (n = 3)	Ticlopidine with aspirin (n = 1)	Single antiplatelet (n = 15)
Age (years) (mean ± SD)	66.40 ± 11.57	66.74 ± 10.92	70.67 ± 5.69	77 ± 0	63.27 ± 15.00
Female	51 (57.95)	39 (56.52)	1 (33.33)	1 (100)	10 (66.67)
Smoking status					
Current smokers	3 (3.41)	2 (2.90)	0 (0)	1 (100)	0 (0)
Former smokers	18 (20.45)	11 (15.94)	2 (66.67)	0 (0)	5 (33.33)
Never smokers	57 (76.14)	56 (81.16)	1 (33.33)	0 (0)	0 (0)
Types of acute coronary syndrome					
NSTEMI	76 (86.36)	61 (88.41)	3 (100)	0 (0)	12 (80)
STEMI	11 (12.50)	8 (11.59)	0 (0)	1 (100)	2 (13.33)
UA	1 (1.14)	0 (0)	0 (0)	0 (0)	1 (6.67)
Types of revascularization					
Non-invasive procedures (medication therapy)	56 (63.64)	43 (62.32)	0 (0)	0 (0)	13 (86.67)
Invasive procedures	32 (36.36)	26 (37.68)	3 (100.00)	1 (100.00)	2 (13.33)
Bare PCI	6 (6.82)	4 (5.80)	1 (33.33)	1 (100.00)	0 (0)
DES PCI	21 (23.86)	19 (27.53)	2 (66.67)	0 (0)	0 (0)
CABG	5 (5.68)	3 (4.35)	0 (0)	0 (0)	2 (13.33)
Types of end stage renal disease					
GFR < 15 ml/min	23 (26.14)	18 (26.09)	1 (33.33)	1 (100)	3 (20)
Hemodialysis	53 (60.23)	40 (57.97)	2 (66.67)	0 (0)	11 (73.33)
Peritoneal dialysis	10 (11.36)	10 (14.49)	0 (0)	0 (0)	0 (0)
Kidney transplantation	2 (2.27)	1 (1.45)	0 (0)	0 (0)	1 (6.67)
Comorbidities					
Hypertension	81 (92.05)	64 (92.75)	2 (66.67)	1 (100)	14 (93.33)
Diabetes mellitus	47 (53.41)	37 (53.62)	1 (33.33)	0 (0)	9 (60.00)
Dyslipidemia	55 (62.50)	45 (65.22)	1 (33.33)	1 (100)	8 (53.33)
Chronic heart failure	18 (20.45)	17 (24.64)	0 (0)	1 (100)	0 (0)
Anemia	11 (12.50)	7 (10.14)	1 (33.33)	1 (100)	2 (13.33)
Gastrointestinal bleeding	4 (4.55)	2 (2.90)	0 (0)	0 (0)	2 (13.33)
Gastric ulcer	2 (2.27)	2 (2.90)	0 (0)	0 (0)	0 (0)
Ischemic stroke	12 (13.64)	10 (14.49)	0 (0)	0 (0)	2 (13.33)
Others	35 (39.77)	27 (39.13)	1 (33.33)	0 (0)	7 (46.67)
Duration of DAPT (months) (median ± IQR)	7.5 ± 11	11 ± 9	2 ± 12	3 ± 0	0
Aspirin					
0-81 mg	80 (90.91)	65 (94.20)	3 (100)	0 (0)	12 (80.0)
82-162 mg	1 (1.14)	1 (1.45)	0 (0)	0 (0)	0 (0)
163-325 mg	6 (6.81)	3 (4.35)	0 (0)	1 (100)	2 (13.33)
No aspirin	1 (1.14)	0 (0)	0 (0)	0 (0)	1 (6.67)
Medications					
Statins	81 (92.05)	62 (89.86)	3 (100)	1 (100)	15 (100)
Beta blockers	79 (89.77)	64 (92.75)	3 (100)	1 (100)	11 (73.33)
PPIs	60 (68.18)	47 (68.12)	1 (33.33)	1 (100)	11 (73.33)
ACEIs/ARBs	16 (18.18)	14 (20.29)	1 (33.33)	0 (0)	1(6.67)

Abbreviations: DAPT, dual antiplatelet therapy; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina; PCI, percutaneous coronary intervention; DES, drug eluting stent; GER, glomerular infiltration rate; ACEIs, angiotensin converting enzyme inhibitors; ARBs, angiotensin receptor blockers; PPIs, proton pump inhibitors.

Of the total of 88 patients, their average age was 66.40 ± 11.57 years (Table 1). About three quarters never smoked (76.14%). In terms of ACS, the majority had NSTEMI (86.63%) and did not have revascularization meaning that they were treated with medication only (63.64%). Almost two-thirds had hemodialysis (60.23%).

The most frequently found c-morbidities were hypertension, hyperlipidemia and diabetes (92.05%, 62.50% and 53.41%, respectively). Median duration of DAPT was 7.5 ± 11 months with the longest duration among those using clopidogrel in the DAPT (11 ± 9 months). Among patients receiving clopidogrel, most received aspirin at a dose of not more than 81 mg (94.20%); while all patients receiving ticagrelor (100%) did so. Most patients received statins (92.05%) and beta blockers (89.77%).

Clinical outcomes

A total of 52 primary outcomes occurred including recurrent myocardial infarction, stroke, re-hospitalization, cardiovascular death, and death from any causes.

In was found that the patients receiving aspirin and ticlopidine had the highest percentage of primary outcomes (1 event in 1 patient, or 100 %) followed by patients receiving single antiplatelet drugs (12 events in 15 patients, or 80 %), those receiving aspirin and clopidogrel (38 events in 69 patients, or 55.07 %) and those receiving aspirin and ticagrelor (1 event in 3 patients, or 33.33 %), respectively.

The most found primary outcomes were recurrent myocardial infarction 29 events, followed by re-hospitalization 20 events, death from any causes 5 events and ischemic stroke 3 events. However, no deaths from cardiovascular disease were found (Table 2).

Table 2 Clinical outcomes of DAPT in ACS with ESRD.

Clinical outcomes	Total events (events)	Clopidogrel with aspirin (n = 69)	Ticagrelor with aspirin (n = 3)	Ticlopidine with aspirin (n = 1)	Single antiplatelet (n = 15)
Primary outcome*	**52**	**38 (55.07)**	**1 (33.33)**	**1 (100)**	**12 (80.0)**
Recurrent MI	29	23 (33.33)	0 (0)	1 (100)	5 (33.33)
Ischemic stroke	3	3 (4.35)	0 (0)	0 (0)	0 (0)
Hospitalization from cardiovascular cause	20	13 (18.84)	1 (33.33)	0 (0)	6 (40.0)
Death from cardiovascular disease	0	0 (0)	0 (0)	0 (0)	0 (0)
Death from other causes	5	4 (5.80)	0 (0)	0 (0)	1 (6.67)
Secondary outcomes	**13**	**11 (15.94)**	**2 (66.67)**	**0 (0)**	**0 (0)**
Major TIMI Bleeding	1	1 (1.45)	0 (0)	0 (0)	0 (0)
Minor TIMI Bleeding	11	10 (14.49)	1 (33.33)	0 (0)	0 (0)
Minimal TIMI Bleeding	1	0 (0)	1 (33.33)	0 (0)	0 (0)

* A given patient could experience more than one event.

Note: High proportion of primary outcomes means poor treatment efficacy; high proportion of secondary outcomes: high bleeding risk

Regarding secondary outcomes, 13 of 88 patients (14.77 %) had events considered as the secondary outcomes including major, minor and minimal TIMI bleedings. Among various antiplatelet regimens, the patients receiving DAPT with aspirin and ticagrelor had the highest percentage of bleeding (2 events in 3 patients, or 66.67%). Of these two events, one was minor, and the other was minimal TIMI bleeding. The second most regimen was aspirin with clopidogrel (11 events in 69 patients, or 15.94 %). No bleedings in patients receiving aspirin with ticlopidine or those taking single antiplatelet drugs were found (Table 2).

Discussions and Conclusion

This study was retrospective in design with all diagnosed patients with ACS and ESRD who received services at the outpatient cardiology clinic of Maharaj Nakorn Chiang Mai Hospital. The data of clinic visits from 1st January 2008 to 1st January 2017 were collected. There were 88 patients receiving antiplatelet drugs. It was also found that most patients received DAPT (73 patients or 82.95 %), and 15 patients (17.05%) received single antiplatelet drugs. The most $P2Y_{12}$ inhibitor used with aspirin was clopidogrel (78.41%). This was consistent with the findings of Rymer et al who studied the safety of antiplatelet drugs being used by the patients with CKD after having IHD.[19] They found that the patients with advanced chronic kidney disease (high severity level) were usually prescribed clopidogrel more frequently than ticagrelor and prasugrel to be used with aspirin.[19] This prescribing pattern was consistent with the literature review by Summaria and et al who collected data on antiplatelet drugs use in patients with ESRD and found that the collected data were limited in this group of patients. Generally, the data were not from randomized controlled studies, but from drug use in clinical experiences. It was found that the most frequently used antiplatelet drug with aspirin was clopidogrel.[20] The primary clinical outcomes in aspirin with clopidogrel group shown in our study including recurrent myocardial infarction, stroke, re-hospitalization, cardiovascular death, and death from any causes were approximately 55% of the cases. In PLATO study, such primary outcomes were found about 12%.[15] This could be possibly due to the fact that all patients in our present study had ESRD; while only 4% of the patients in PLATO had CKD (eGFR < 60 mil/min/1.73m^2, in PLATO study). The CKD increased the risks of death, cardiovascular events and readmission.[21] Nonetheless, when considering the

primary outcomes it was found that the patients receiving clopidogrel with aspirin had 23 events of recurrent myocardial infarction (33%). On the other hand, patients receiving ticagrelor with aspirin had no recurrent myocardial infarction.

In terms of secondary outcomes, it was found that patients receiving ticagrelor with aspirin had two events of bleeding (66.67%) compared with 11 events of clopidogrel with aspirin (15.94%). This was consistent with PLATO study[15] which found that patients receiving clopidogrel with aspirin had more primary outcomes than those receiving ticagrelor with aspirin (11.7% and 9.8%, respectively). In contrast, the events of bleeding were not different between the two groups (11.6% and 11.2%, respectively, *P*-value 0.43).

Our results were consistent with the PEGASUS-TIMI 54 study which analyzed the efficacy and safety of ticagrelor use in patients with myocardial infarction and chronic renal failure (GFR < 60 ml/ min/ 1.73m^2) who did not receive renal replacement therapy.[22] In PEGASUS-TIMI 54 study, it was found that using ticagrelor with aspirin could reduce the major adverse cardiovascular events (MACE) as compared to using only aspirin, but the risk of bleeding was increased.[22] Furthermore, there were meta-analysis studies and systematic review which found 4,518 cardiovascular events and 1,962 deaths among 27,773 CKD patients.[23] The use of antiplatelet drugs reduced the risk of the cardiovascular events by 15% (OR = 0.85; 95% CI = 0.74 - 0.94). However, antiplatelet drugs did not reduce overall deaths (OR = 0.87; 95% CI = 0.71 - 1.01) or incidence of renal failure (OR = 0.87; 95% CI = 0.32 - 1.55).[23] They also found significantly undesirable symptoms in patients receiving antiplatelet drugs either primary bleeding (OR = 1.33; 95% CI = 1.11 - 1.59) or secondary bleeding (OR, 1.66; 95% CI, 1.27-2.05). It was concluded that using antiplatelet drugs in 1,000 chronic kidney disease patients for 12 months could prevent 23 cardiovascular events, and 9 bleeding events may occur while using the medicine. Hence, antiplatelet drugs have the benefit of preventing cardiovascular events beyond the risk of bleeding.[23]

For the duration of using DAPT in the patients with ACS, the practice guideline suggested that both antiplatelet drugs have to be used for at least 12 months.[6,7] However, there are guidelines for specific patients with a high risk of bleeding, which may reduce the duration of combined antiplatelet drugs to 3 to 6 months if evaluated using the PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy (PRECISE-DAPT). The PRECISE-DAPT scores of 25 points or higher were not associated with further decrease in MI but more risk of bleeding. The considered factors were hemoglobin, white blood cells, age, kidney functions (creatinine), and prior bleeding.[24] Hence, the factors of bleeding might be the factors used for considering and reducing the medication duration of both antiplatelet drugs in the patients with ESRD in this study. In our study, the medication duration of both antiplatelet drugs had the median of 7.5 $\pm$ 11 months. It was found that the group using the $P2Y_{12}$ inhibitor which was clopidogrel had the longest duration of DAPT (11 $\pm$ 9 months), while the group receiving ticagrelor had the shortest duration of DAPT (2 $\pm$ 12 months). This is consistent with the findings of Rymer et al that the rate of discontinuation of the potent antiplatelet group was higher especially in the group with the CKD stage 2 or higher (GFR of 60 to 89 ml/min/1.73 m^2).[19]

This present study had certain limitations. With the retrospective nature of the study, minimal TIMI bleeding could be underreported since such minimal bleeding incidences were not commonly recorded in the medical profile. In addition, since data were collected in only one hospital, the total number of patients included was relatively small. As result, power of analysis was low and generalization to the study population could be limited. Future studies with a larger sample size from many hospitals should be conducted.

In conclusion, among ACS patients with ESRD, the most used DAPT was clopidogrel with aspirin. As expected, the use of single antiplatelet drugs was inferior to DAPT since more ischemia related events (primary outcomes) were found with single drugs. Among DAPT, as in accordance with recommendations, aspirin with ticagrelor was superior to aspirin with clopidogrel as fewer ischemia-related events were found in the ticagrelor combination. However, more bleeding was found in aspirin plus ticagrelor.

Acknowledgement

The authors would like to thank all personnel at the Medical Records and Statistics section of the Maharaj Nakorn Chiang Mai Hospital for their kind assistance. Our great gratitude is also extended to those who provided information and assistance in obtaining patient information.

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