The Causes and Outcomes of Inadequate Implementation of Existing Guidelines for Antiplatelet Treatment in Patients With Acute Coronary Syndrome: The Experience From Taiwan Acute Coronary Syndrome Descriptive Registry (T-ACCORD Registry)

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ABSTRACT

Background: Benefits of antiplatelet agents in preventing future cardiovascular events have been well established. However, the prescription pattern of antiplatelet usage in patients with acute coronary syndrome (ACS) is rarely investigated. Hence, Taiwan ACute CORonary Syndrome Descriptive Registry (T-ACCORD Registry) aimed to evaluate medical practices in Taiwan in managing ACS patients.

Hypothesis: The guidelines of antiplatelet treatment is not properly implanted in the management of ACS patients.

Methods: This prospective observational study was performed between April 2004 and December 2006 in 27 hospitals in Taiwan. A total of 1331 patients with unstable angina or non–ST-elevation myocardial infarction (NSTEMI) discharged from hospitals was analyzed.

Results: The patients with older age, lower hemoglobin levels, or previous cardiovascular ischemic diseases were less likely to receive aspirin at discharge, whereas patients with NSTEMI were less likely to receive clopidogrel at discharge. The prescription of dual antiplatelet agents declined rapidly from 61.8% at discharge to 12.6% at 12 months. The most common reason for clopidogrel discontinuation was recorded as physician's judgment. Dual antiplatelet treatment for 9 months or longer was associated with lower 1-year mortality. Percutaneous coronary intervention (PCI) was the only factor leading to dual antiplatelet therapy for at least 9 months.

Conclusions: Our registry showed that underlying medical conditions may affect antiplatelet prescriptions at discharge. During the first year following an ACS episode, the prescription rate of dual antiplatelet therapy declined over time, mainly due to physician's judgment leading to the discontinuation of clopidogrel. Adherence to dual antiplatelet treatment was associated with lower total mortality at 1 year.

Introduction

Atherosclerotic cardiovascular disease is an important contributor to worldwide morbidity,[1] mortality,[2] and medical expenditures,[3,4] and acute coronary syndrome (ACS) is one of its major presentations.[5] Platelet activation is known to play a pivotal role in the pathophysiological mechanisms of ACS,[6,7] and several studies have demonstrated the benefit of antiplatelet agents—either aspirin, a cyclo-oxygenase (COX) inhibitor; or clopidogrel, an adenosine diphosphate (ADP) receptor antagonist—in both primary and secondary prevention of future cardiovascular

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events.[8–10] Antiplatelet agents are widely used as the standard treatment in ACS.[11–13]

Despite the strong evidence showing that guideline adherence with respect to antiplatelet usage is associated with decreased mortality in ACS patients,[14] the real-world registries have found inadequate achievement of guideline implementation.[15,16] Although underutilization of antiplatelet treatment in ACS patients has been described in the Can Rapid Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines (CRUSADE)[17] and Global Registry of Acute Coronary Events (GRACE)[15] registries, the prescription patterns of antiplatelet usage in ACS patients have never been investigated, and the factors associated with long-term antiplatelet treatment after ACS episodes have rarely been explored.

The Taiwan ACute CORonary Syndrome Descriptive Registry (T-ACCORD Registry) enrolled patients who had events of unstable angina or non–ST-elevation myocardial infarction (NSTEMI). The T-ACCORD Registry aimed to evaluate current clinical practice in managing ACS patients in relation to the usage of antiplatelet agents during the acute setting and after discharge.

Methods

Study Design and Outcome Measurements

The T-ACCORD Registry is a multicenter, prospective observational study. The registry was approved by the Institutional Review Board in each hospital, and all patients provided signed informed consents. Patients were eligible for screening if they met all the following criteria: at least 18 years of age; suspected ACS without ST-segment elevation; and clinical history consistent with new-onset, or worsening, angina pectoris. Patients were excluded from enrollment if they had any of the following criteria: current use of oral anticoagulants, long-term use of nonsteroidal anti-inflammatory drugs; active pathological bleeding; severe liver impairment; breast-feeding; or history of allergy, intolerance, or contraindication to clopidogrel or aspirin. Because the study was conducted between April 2004 and December 2006, the judgment of adequate implementation of antiplatelet treatment guidelines was based on 2002 American College of Cardiology/American Heart Association (ACC/AHA) treatment guidelines for unstable angina/NSTEMI[12] and the 2004 reimbursement guidelines of the Bureau of National Health Insurance (BNHI) in Taiwan. Adequate implementation of antiplatelet treatment guidelines was defined as indefinite use of aspirin along with clopidogrel loading dose of 300 mg followed by 75 mg daily for at least 9 months.

The baseline and follow-up visits were scheduled as following: visit 1, at discharge; visit 2, at 3 months; visit 3, at 6 months; visit 4, at 9 months; and visit 5, at 12 months. Patients discharged with a definite diagnosis of unstable angina or NSTEMI were included in further analysis based on the use of antiplatelet agents: Group 1, aspirin only; Group 2, clopidogrel only; and Group 3, aspirin combined with clopidogrel. This study assessed medical history and risk factors, previous atherothrombotic events, prior and concomitant medication, adverse events, adherence to antiplatelet treatment, reasons for discontinuation of antiplatelet treatment, and all-cause mortality at 1 year. Reasons for discontinuation of antiplatelet treatment were reported by participating physicians and included safety reasons, price issues, BNHI reimbursement guidelines, physician's judgment, and others. Safety reasons included concerns of bleeding complications and major surgery. Physician's judgment meant that a physician discontinued clopidogrel simply based on weighing benefit against risk, rather than safety reasons, price issues, or BNHI reimbursement guidelines. Reasons other than the above choices were attributed to others.

Statistical Analysis

Differences between groups were assessed by the χ^2 test for categorical variables and 1-way analysis of variance test or the Wilcoxon nonparametric test for continuous variables. The Scheffe test was used for post-hoc intergroup comparison of continuous variables. The tendencies of medication used in different groups from discharge to 12 months were tested by trend tests. Survival was estimated using the Kaplan-Meier method, and the log rank test was employed to test the null hypothesis of equality in overall survival among groups. The multivariate analysis model was employed to estimate the odds ratio (OR) for prescription of aspirin alone at discharge and dual antiplatelet agents at 9 months, respectively. A P value of <0.05 was considered statistically significant with a 95% confidence interval (CI). All statistical analyses were performed using SAS 9.1 for Windows.

Results

This study was conducted between April 2004 and December 2006. A total of 1406 patients were screened from 27 medical centers and regional hospitals in Taiwan. Due to lack of antiplatelet prescription at discharge or ST-segment elevation myocardial infarction (STEMI) as the final diagnosis, 75 patients were excluded from further analysis, leaving a total of 1331 patients in the study. Based on the antiplatelet therapy prescribed at discharge, the 1331 patients were classified into 3 groups: an aspirin-only group (Group 1, n = 255), a clopidogrel-only group (Group 2, n = 250), and a dual–antiplatelet agents group (Group 3, n = 856).

The baseline demographic data of the study subjects is displayed in Table 1. Among the 3 groups, patients in Group 2 were the oldest. More patients in Group 2 had renal insufficiency (serum creatinine >1.4 mg/dL), atrial

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Table 1. Demographic Data

Grouped by Anti-PLT Agent at Discharge	Total (n = 1331)	Group 1 (n = 225)	Group 2 (n = 250)	Group 3 (n = 856)	*P* Value
Age, y	65.4 ± 12.4	62.6 ± 12.9[a]	68.6 ± 11.4	65.3 ± 12.4[a,b]	<0.0001
Male (vs female)	929 (69.8%)	153 (68.0%)	162 (64.8%)	614 (71.7%)	0.0897
Height, cm	161.3 ± 8.1	160.9 ± 8.2[a]	159.9 ± 8.5	161.7 ± 8.0[a,b]	0.0091
Weight, kg	66.6 ± 12.1	66.0 ± 12.3[a]	64.8 ± 12.5	67.2 ± 11.8[a,b]	0.0196
BMI, kg/m^2	25.5 ± 3.8	25.3 ± 3.7	25.2 ± 4.2	25.7 ± 3.8	0.1541
Risk factors					
Current smoker	339 (25.5%)	66 (29.3%)	54 (21.6%)	219 (25.6%)	0.1534
Diabetes	538 (40.5%)	86 (38.2%)	118 (47.2%)	334 (39.1%)	0.0530
Hypertension	960 (72.2%)	160 (71.1%)	196 (78.4%)	604 (70.6%)	0.0510
Dyslipidemia	554 (41.7%)	85 (37.8%)	119 (47.6%)	350 (40.9%)	0.0739
Chronic renal failure[c]	331 (24.9%)	48 (21.3%)	80 (32.0%)	203 (23.7%)	0.0116
CHF	194 (14.6%)	24 (10.7%)	44 (17.6%)	126 (14.7%)	0.0996
LVEF < 40%	94 (7.1%)	14/225 (6.2%)	23/250 (9.2%)	57 (6.7%)	0.3337
Atrial fibrillation	68 (5.1%)	8 (3.6%)	22 (8.8%)	38 (4.4%)	0.0115
Hemoglobin (g/dL)	13.8 ± 9.6	15.7 ± 7.9[a]	12.3 ± 2.3	13.7 ± 7.5[a,b]	0.0007
History of ischemic condition	691 (52.0%)	117 (52.0%)	162 (64.8%)	412 (48.2%)	<0.0001
Ischemic heart disease					
Previous MI	232 (17.4%)	50 (22.2%)	59 (23.6%)	123 (14.4%)	0.0004
Previous angina	456 (34.3%)	69 (30.7%)	103 (41.2%)	284 (33.2%)	0.0295
Cerebrovascular diseases					
Stroke	109 (8.2%)	11 (4.9%)	37 (14.8%)	61 (7.1%)	<0.0001
TIA	7 (0.5%)	2 (0.9%)	3 (1.2%)	2 (0.2%)	0.1269
PAD	8 (0.6%)	1 (0.4%)	1 (0.4%)	6 (0.7%)	0.8161
Prior revascularization					
CABG	47 (3.5%)	5 (2.2%)	13 (5.2%)	29 (3.4%)	0.1997
PCI	349 (26.2%)	59 (26.2%)	84 (33.6%)	206 (24.1%)	0.0109
Carotid angioplasty	2 (0.2%)	0 (0.0%)	0 (0.0%)	2 (0.2%)	0.5733
Carotid endarterectomy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.0000

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; CHF, congestive heart failure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; PLT, platelet; TIA, transient ischemic attack.
[a] $P < 0.05$ as compared with group 2; based on Scheffe test.
[b] $P < 0.05$ as compared with group 1; based on Scheffe test.
[c] Serum creatinine >1.4 mg/dL.

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fibrillation, history of ischemia, and lower hemoglobin level. Approximately one-third of patients in Group 2 underwent percutaneous coronary intervention (PCI) prior to this event, which was a significantly higher percentage than in the other 2 groups.

Table 2 shows diagnosis, risk stratification, antiplatelet and anticoagulant treatment, and invasive procedures for each group of patients. Significantly more patients in Group 3 were diagnosed as NSTEMI. The GRACE risk score was significantly higher in Group 2 than in the other two groups. Anticoagulant therapy was used more frequently in Group 3 patients as compared with the other 2 groups. After grouping patients by antiplatelet treatment at discharge, it was noted that all groups tended to receive the same antiplatelet regimen as that before and during hospitalization.

We also analyzed the parameters associated with the lack of clopidogrel prescription at discharge using the multiple logistic regression model (Table 3). The patients who had NSTEMI were more likely than those with diagnosis of unstable angina to receive only aspirin at discharge. Furthermore, the patients with 2 or more CAD risk factors, a hemoglobin level <10.0 gm/dL, history of ischemic stroke, or prior use of clopidogrel before hospitalization were more likely to be associated with the prescription of clopidogrel at discharge.

In order to better understand the treatment pattern in addition to antiplatelet usage, the prescription rates of major cardiovascular medications at different time points were analyzed (Figure 1A). The prescription rates of β-blockers, angiotensin-converting enzyme inhibitors (ACEI), or angiotensin receptor blockers (ARB) (for patients who had a left ventricular ejection fraction (LVEF) <40%, heart failure, or diabetes), and lipid-lowering agents (for those with low-density lipoprotein (LDL) >100 mg/dL or total cholesterol >200 mg/dL) did not significantly vary during follow-up. However, the prescription rate of dual antiplatelet agents declined dramatically, from 61.8% at discharge to 12.6% at 12 months; whereas the prescription rate of aspirin as a single antiplatelet agent increased significantly, from 16.0% at discharge to 57.5% at 12 months. A subgroup analysis of group 3 patients who received dual antiplatelet treatment at discharge (Figure 1B and 1C) showed that only 26.9% and 24.4% of patients undergoing plain optimal balloon angioplasty (POBA) or coronary stenting, respectively, during hospitalization still received dual antiplatelet treatment at 9 months, indicating inadequate guideline implementation of antiplatelet treatment for ACS patients irrespective of coronary stenting.

Whether the duration of single or dual antiplatelet treatment is associated with long-term survival in ACS patients is an important issue to be investigated. Figure 2 displays the Kaplan-Meier survival estimates according to the duration of dual antiplatelet treatment. Compared with patients treated with dual antiplatelet therapy >9 months, patients not treated with dual antiplatelet therapy for such a period had a significantly higher mortality rate at 1 year (Figure 2A). When patients treated with dual antiplatelet therapy were further classified according to treatment durations of 0–3 months, 3–6 months, 6–9 months, and 9–12 months, the survival estimates did not significantly differ compared with those patients in whom dual antiplatelet therapy was prescribed for 9–12 months (Figure 2B).

We were also interested in understanding the parameters associated with dual antiplatelet therapy continued for at least 9 months in our patient population. In our multiple logistic regression model, PCI was the only significant parameter predicting dual antiplatelet therapy for at least 9 months (Table 3). The analysis of the reasons given for clopidogrel discontinuation before 9 months revealed that physician's judgment (53.4%) was the leading cause, followed by BNHI reimbursement guidelines (24.9%), price issues (13.1%), and safety concerns (4.9%).

Discussion

This study showed that there was inadequate guideline implementation of antiplatelet treatment during hospitalization and within the first year following an ACS event. A significant portion of patients received single antiplatelet treatment at discharge. Clopidogrel was discontinued over time in patients who had initially received dual antiplatelet treatment at discharge.

Comparison With Previous Surveys

In the CRUSADE Registry, clopidogrel was prescribed for 73% of unstable angina or NSTEMI patients at discharge,[17] and, similar to our investigation, patients who did not undergo PCI were less likely to receive clopidogrel at discharge. In the GRACE Registry,[15] 16.7% of the patients for whom PCI was performed did not receive clopidogrel, and only 38% of STEMI patients in that registry received clopidogrel. In our study, NSTEMI is associated with the lack of clopidogrel prescription at discharge. Global experiences have shown underutilization of dual antiplatelet agents in patients with ACS, especially in those who were diagnosed as having acute MI and those who did not undergo PCI.

Antiplatelet Treatment During Hospitalization

Compared with patients enrolled in randomized controlled trials, the patients in real-world registries usually exhibit a higher risk.[18] In our study, multivariate analysis showed that aspirin was less frequently prescribed in patients with older age, lower hemoglobin levels, two CAD risk factors or more, or previous ischemic stroke, implying dual antiplatelet treatment was underutilized in high-risk patients for whom aspirin was considered intolerable. Additionally, 34.8% of patients in Group 2 received aspirin

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Table 2. Indication for Admission, Risk Stratification, Antiplatelet and Anticoagulant Treatment, and Revascularization Procedures

Grouped by Anti-PLT Agent at Discharge	Total (n = 1331)	Group 1 (n = 225)	Group 2 (n = 250)	Group 3 (n = 856)	*P* Value
Diagnosis					0.0138
NSTEMI	426 (32.0%)	65 (28.9%)	64 (25.6%)	297 (34.7%)	N/A
Unstable angina	905 (68.0%)	160 (71.1%)	186 (74.4%)	559 (65.3%)	N/A
Presence of ST change	580 (43.6%)	81 (36.0%)	111 (44.4%)	388 (45.3%)	0.0410
GRACE score	99.0 (24–214)	95.5 (30–194)[a]	105.0 (40–214)	97.0 (24–207)[a]	<0.0001
Anticoagulant treatment	607 (45.6%)	88 (39.1%)	105 (42.0%)	414 (48.4%)[b]	0.0206
UFH	273/607 (45.0%)	40/88 (45.5%)	48/105 (45.7%)	185/414 (44.7%)	N/A
LMWH	291/607 (47.9%)	44/88 (50.0%)	53/105 (50.5%)	194/414 (46.9%)	N/A
Crossover between UFH & LMWH	43/607 (7.1%)	4/88 (4.5%)	4/105 (3.8%)	35/414 (8.5%)	N/A
GPIIb/IIIa inhibitor	51 (3.8%)	1 (0.4%)	9 (3.6%)[b]	41 (4.8%)[b]	0.0102
Antiplatelet treatment					
Before hospitalization					<0.0001
Aspirin only	483 (36.3%)	121 (53.8%)	51 (20.4%)	311 (36.3%)	N/A
Clopidogrel only	103 (7.7%)	1 (0.4%)	76 (30.4%)	26 (3.0%)	N/A
Clopidogrel + aspirin	134 (10.1%)	11 (4.9%)	9 (3.6%)	114 (13.3%)	N/A
During hospitalization					<0.001
Aspirin only	198 (14.9%)	162 (72.0%)	4 (1.6%)	32 (3.7%)	N/A
Clopidogrel only	164 (12.3%)	0 (0.0%)	156 (62.4%)	8 (0.9%)	N/A
Clopidogrel + aspirin	961 (72.2%)	61 (27.1%)	87 (34.8%)	813 (95.0%)	N/A
Periprocedural loading of clopidogrel	356/1071 (33.2%)	30/186 (16.1%)	59/184 (32.0%)[b]	267/701 (38.1%)[b]	<0.0001
Invasive vascularization procedures					
Cath	1071 (80.5%)	186 (82.7%)[a]	184 (73.6%)	701 (81.9%)[a]	0.0096
Time to cath, days	1 (0–63)	1 (0–11)	1 (0–17)	1 (0–63)	0.0770
Revascularization	951/1071 (88.8%)	104/186 (55.9%)	163/184 (88.6%)[b]	684/701 (97.6%)[b]	<0.0001
PCI only	921/951 (96.8%)	86/104 (82.7%)	154/163 (94.5%)	681/684 (99.6%)	<0.0001
CABG only	22/951 (2.3%)	14/104 (13.5%)	7/163 (4.3%)	1/684 (0.1%)	<0.0001
PCI + CABG	8/951 (0.8%)	4/104 (3.8%)	2/163 (1.2%)	2/684 (0.3%)	0.0010
POBA only in PCI	265/929 (28.5%)	62/90 (68.9%)	40/156 (25.6%)[b]	163/683 (23.9%)[b]	<0.0001
Stenting in PCI	664/929 (71.5%)	28/90 (31.1%)	116/156 (74.4%)[b]	520/683 (76.1%)[b]	<0.0001
Time to CABG days	6 (0–27)	3.5 (0–12)[a]	11 (6–27)[a,b]	6 (6–9)	0.0004

Abbreviations: CABG, coronary artery bypass grafting; cath, catheterization; GPIIb/IIIa inhibitor, glycoprotein IIb/IIIa inhibitor; GRACE, Global Registry of Acute Coronary Events study; LMWH, low-molecular-weight heparin; PCI, percutaneous coronary intervention; PLT, platelet; POBA, plain optimal balloon angioplasty; N/A, not applicable; NSTEMI, non–ST-segment elevation myocardial infarction; UFH, unfractionated heparin.

[a] $P < 0.05$ as compared with group 2; based on Scheffe test.

[b] $P < 0.05$ as compared with group 1; based on Scheffe test.

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Table 3. Multivariate Analysis of Parameters Associated with the Prescription of Antiplatelet Agents

	Lack of Prescription of Clopidogrel at Discharge		Prescription of Clopidogrel and Aspirin ⩾ 9 months	
Parameter	Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value
Age, y	0.980 (0.968–0.993)	0.0025	0.994 (0.980–1.009)	0.4492
Male (vs female)	0.864 (0.627–1.191)	0.3719	0.920 (0.615–1.377)	0.6867
Atrial fibrillation	0.607 (0.330–1.114)	0.1068	1.223 (0.526–2.844)	0.6404
CAD risk factor ⩾ 2	0.630 (0.430–0.922)	0.0176	0.893 (0.609–1.308)	0.5603
Hemoglobin < 10 g/dL	0.504 (0.330–0.770)	0.0015	0.638 (0.321–1.267)	0.1993
Previous MI	0.776 (0.535–1.126)	0.1820	0.962 (0.592–1.561)	0.8745
Previous unstable angina	0.759 (0.534–1.079)	0.1248	1.063 (0.690–1.638)	0.7815
Previous stable angina	1.172 (0.735–1.871)	0.5048	1.004 (0.584–1.729)	0.9871
Ischemia stroke	0.514 (0.323–0.818)	0.0050	0.640 (0.300–1.364)	0.2474
TIA	0.481 (0.089–2.593)	0.3942	<0.001 (<0.001–<999.999)	0.9851
PAD	1.654 (0.191–14.351)	0.6481	3.114 (0.574–16.885)	0.1879
NSTEMI	1.467 (1.028–2.092)	0.0347	1.315 (0.903–1.915)	0.1532
PCI	1.090 (0.990–1.199)	0.0800	2.126 (1.364–3.314)	0.0009
Clopidogrel before hospitalization	0.369 (0.261–0.523)	<0.0001	0.677 (0.399–1.150)	0.1493

Abbreviations: CAD, coronary artery disease; CI, confidence interval; MI, myocardial infarction; NSTEMI: non–ST-segment elevation myocardial infarction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

as an "add-on therapy" to clopidogrel during hospitalization, but was discontinued at discharge according to the patient's clinical condition. The patients of Group 2 also had the highest GRACE risk score and lowest survival rate at 1 year. Underlying medical conditions may affect the prescription of antiplatelet agents, and a significant portion of the patients in our registry was considered unsuitable for dual-antiplatelet treatment because of aspirin intolerance.

Causes of Discontinuation

The percentage of dual antiplatelet treatment declined dramatically over time and was replaced by "aspirin-only" treatment. Although BNHI reimburses up to 9 months' treatment of dual antiplatelet agents for ACS patients, 24.9% of physicians claimed that the discontinuation of clopidogrel before 9 months was based on BNHI guidelines. Some physicians might subjectively adopt different BNHI guidelines in which clopidogrel is reimbursed for only 3 months after coronary stent implantation. Furthermore, in Taiwan, BNHI reimburses the entire expense of medications prescribed in the outpatient clinic, but a national global budget payment scheme restricts the expenditure of medical care in each hospital. In this registry, 13.1% of physicians discontinued clopidogrel

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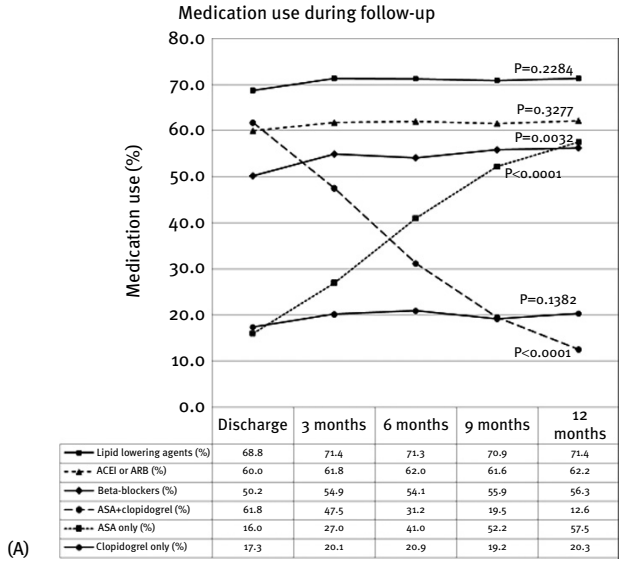
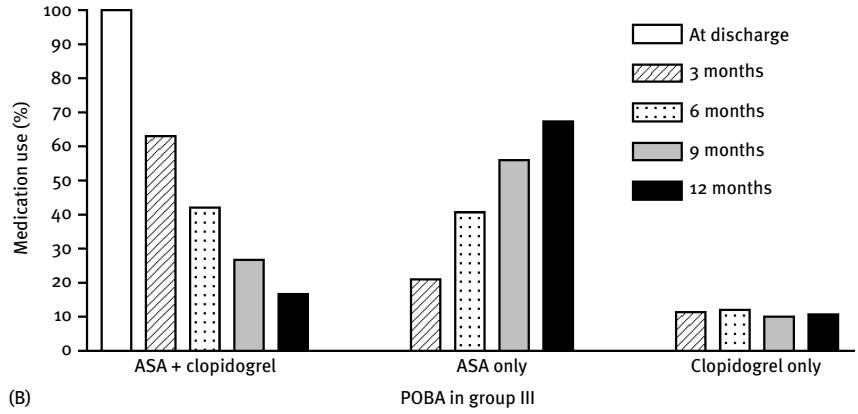


(A)



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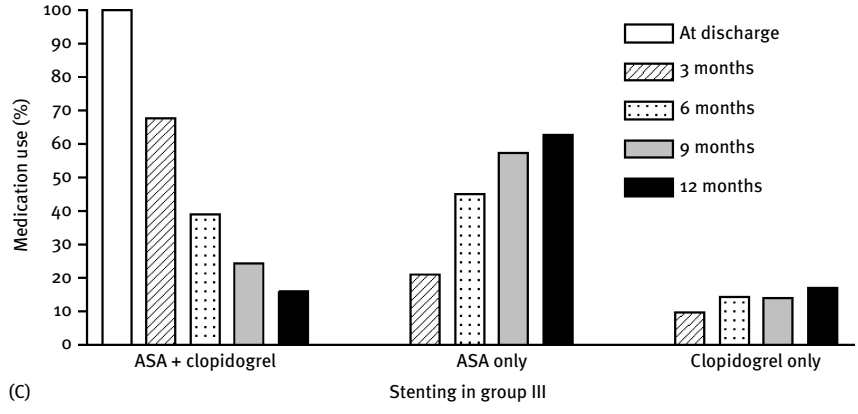

(C)

Figure 1. The prescription rates of major cardiovascular medications prescribed at different time points. The lines represent prescription rates of different cardiovascular medications at different time points, and the table at the bottom of the panel displays the percentages as indicated. *P* values following each line examine the trends of the variation of prescriptions (1A). The bar charts of the prescription rate of antiplatelet medications prescribed at different time points during follow-up for patients who received dual antiplatelet treatment at discharge (group 3) and POBA (1B) or coronary stenting (1C) during hospitalization. Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASA, aspirin; POBA, plain optimal balloon angioplasty.

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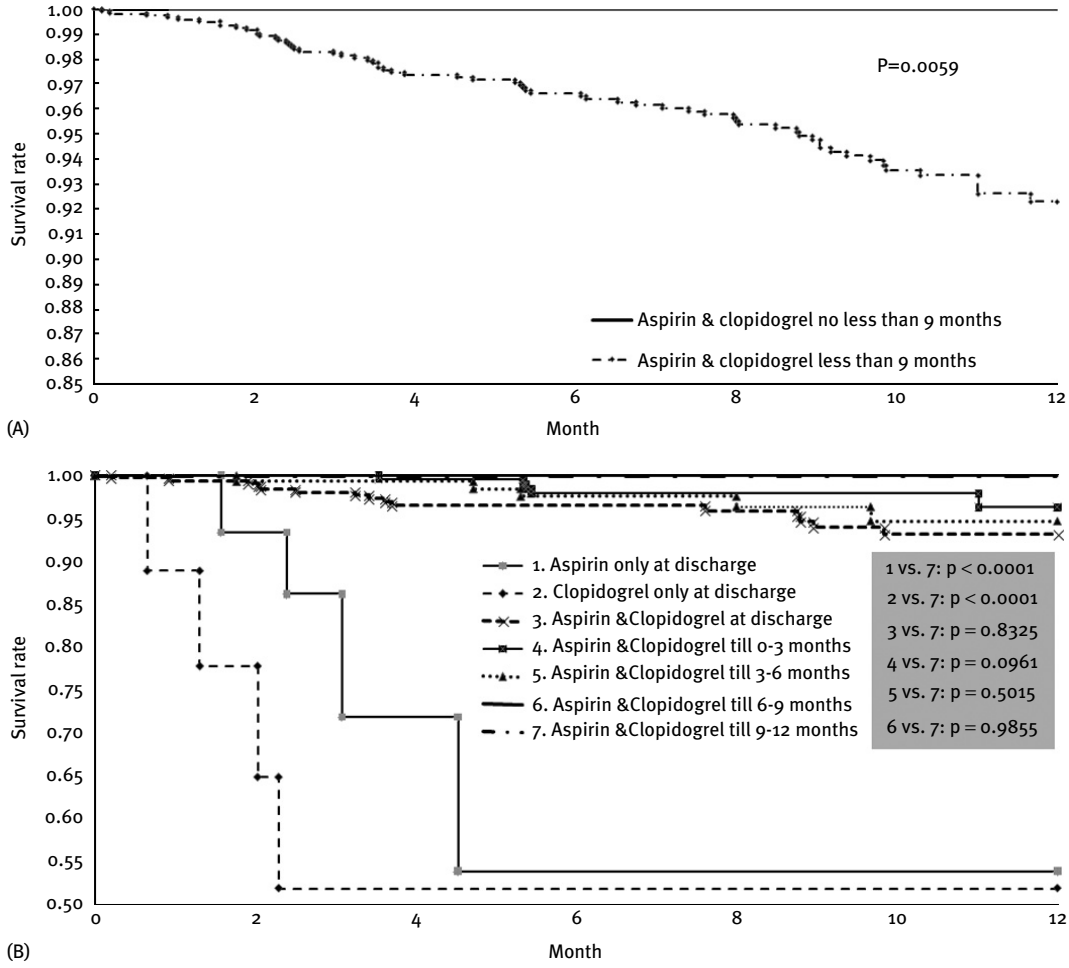

Figure 2. Kaplan-Meier survival estimates of patients grouped by different antiplatelet treatment at discharge. Kaplan-Meier survival estimates of patients with or without dual antiplatelet treatment for at least 9 months (A) and patients grouped by different durations of dual antiplatelet therapy (B) are plotted according to their antiplatelet treatment as indicated. *P* values examine the significance of differences between the groups by log rank test.

because of price issues. Whether this discrepancy in guideline implementation is due to global budget policy and subsequently influences clinical outcomes of patients deserves further investigation.

Duration of Dual Antiplatelet Treatment and Outcomes

Although no deaths were observed in those receiving dual antiplatelet treatment for at least 6 months, our registry data failed to demonstrate whether longer duration of dual antiplatelet treatment was associated with lower 1-year mortality rates. The Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) study has demonstrated long-term efficacy of dual antiplatelet treatment in ACS patients,[19] and the benefit of dual antiplatelet treatment could be observed as early as 30 days and was sustained for up to 12 months. Nevertheless, other studies examining patients with STEMI[20,21] or patients undergoing PCI[22] have shown a progressively greater difference in outcomes between dual antiplatelet treatment and aspirin-only treatment. In one study[23] investigating the optimal duration of dual antiplatelet treatment after successful bare metal stent placement, patients treated with 6 months of clopidogrel and aspirin had a trend toward fewer adverse events compared with those treated for 30 days. The extended use of clopidogrel to 1 year in patients implanted with a drug-eluting stent (DES) also was associated with a significantly reduced risk of death or MI by landmark analysis in one registry.[24] Importantly, dual antiplatelet treatment for at least 1 year is recommended for patients receiving DES in 2007 ACC/AHA guidelines for unstable angina/NSTEMI.[25] Further investigations are

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warranted to verify the optimal treatment duration of dual antiplatelet agents in different subpopulations.

Study Limitations

The primary limitation of this study is its nonrandomized and observational nature, which limits the analysis of clinical outcomes among different treatment groups. Secondly, all-cause mortality was the only recorded clinical endpoint. Nevertheless, the results generated from this registry can still reflect current practices in the management of ACS patients in a real-world setting.

Conclusion

The results of our study showed that underlying medical conditions may affect the prescription of antiplatelet treatment in ACS patients. During the first year following an ACS episode, the prescription rate of dual antiplatelet agents declined over time, mainly due to physician's judgment leading to the discontinuation of clopidogrel. Compared with aspirin or clopidogrel alone, adherence to dual antiplatelet therapy for at least 9 months was associated with lower total mortality at 1 year.

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