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Original article

Characteristics and clinical outcomes of patients with de-escalation from prasugrel to clopidogrel after acute myocardial infarction - Insights from the prospective Japan Acute Myocardial Infarction Registry (JAMIR) -

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ABSTRACT

Background: De-escalation of P2Y12 inhibitor may occur for various clinical reasons in patients with acute myocardial infarction (AMI). We aimed to assess the characteristics and outcomes of patients who underwent a de-escalation strategy in real-world clinical practice.

Methods and Results: We studied 2604 AMI patients initially treated with prasugrel using the Japan Acute Myocardial Infarction Registry (JAMIR) database. Of these, 110 (4%) were discharged on clopidogrel [de-escalation group; switching 4 days after admission (median)] and the remaining 2494 continued prasugrel at discharge (continuation group). The de-escalation group had higher incidence of heart failure or history of cerebrovascular disease, and were more likely to receive mechanical circulatory support, and oral anticoagulation than the continuation group. During mean follow-up of 309±133 days post-discharge, no significant differences were observed in ischemic events (2.2% vs. 2.8%, $p = 0.74$) or major bleeding (1.1% vs. 1.6%, $p = 0.72$) between the de-escalation and continuation groups.

Conclusions: Although, patients with de-escalation from prasugrel to clopidogrel had higher bleeding risk profile than those continued on prasugrel, post discharge ischemic and bleeding events were similar between patients with and without de-escalation. De-escalation strategy may be an option for AMI patients with high risk for bleeding.

Introduction

Antiplatelet therapy is a corner stone for reducing ischemic events following acute myocardial infarction (AMI). Potent P2Y12 inhibitors such as prasugrel and ticagrelor exhibit a strong and more consistent platelet inhibition and significantly reduce recurrent ischemic events in patients with acute coronary syndrome (ACS) when compared to clopidogrel [1,2]. However, this benefit is counterbalanced by higher bleeding risk, which is linearly related to the treatment potency and duration [3,4]. The selection of optimal antithrombotic agents in the acute and chronic phase after AMI, while balancing their benefits and risks, has been a

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matter of debate. Because the highest rate of ischemic events occurs in the first few days or weeks after AMI, a strategy of potent antiplatelet inhibition could be considered during the acute phase after the patient's presentation. Thereafter, de-escalation to a less potent regimen could offer a favorable balance of ischemic protection versus bleeding avoidance [5]. Recently, the TOPIC (timing of platelet inhibition after acute coronary syndrome) randomized study showed significant reduction of bleeding events without an increase in ischemic events when patients were switched from a regimen of aspirin plus prasugrel or ticagrelor to that of aspirin and clopidogrel after 1 month [6]. In addition, the TROPICAL-ACS (Testing Responsiveness To Platelet Inhibition On Chronic Antiplatelet Treatment For Acute Coronary Syndromes) study demonstrated the safety of a switching strategy based on platelet function testing results in those taking prasugrel for 2 weeks following percutaneous coronary intervention (PCI) [7]. In the current Japanese guideline, de-escalation strategy is mentioned as one method to reduce the risk of bleeding [8]. However, little is known about the characteristics and outcomes of patients who underwent P2Y12 inhibitor de-escalation strategy after AMI in real-world clinical practice. Therefore, the aim of this study was to examine the characteristics and outcomes of patients with AMI who underwent de-escalation of a P2Y12 inhibitor from prasugrel to clopidogrel in real-world clinical practice using a large-scale AMI database in Japan.

Methods

Study population

The Japan AMI Registry (JAMIR) is a multicenter, nationwide, prospective registry enrolling patients with AMI in Japan. The design and primary analysis of the JAMIR have been reported [9,10]. Briefly, consecutive patients presenting with spontaneous onset of AMI were enrolled between December 2015 and May 2017 at 50 institutions. Patient management including the choice and change of antiplatelet drugs was decided at the discretion of the treating physicians. This study was conducted in accordance with the ethical guidelines for medical research on humans laid out in the Declaration of Helsinki. This research protocol was approved by the Institutional Review Board of the National Cerebral and Cardiovascular Center (M26–150–5) and local ethics committees or local institutional review board at each study site. This study is registered with the Japanese UMIN Clinical Trials Registry (UMIN000019479).

Study endpoints

The primary end point of the study was the composite of cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke. Major safety end points included type 3 or 5 bleeding based on the Bleeding Academic Research Consortium (BARC) criteria or major bleeding based on the Thrombolysis in Myocardial Infarction (TIMI) criteria [11,12].

Secondary end points included net adverse clinical event (NACE) defined as the composite of cardiovascular death, non-fatal myocardial infarction, non-fatal cerebral infarction, and BARC type 3 or 5 bleeding; individual components of ischemic events; all-cause death; stent thrombosis; major and minor bleeding based on the TIMI criteria; and type 2, 3, or 5 bleeding based on the BARC criteria. Stent thrombosis was defined as definite or probable according to the Academic Research Consortium definition [13].

Statistical analysis

Continuous variables are presented as means ± standard deviation (SD) or medians and interquartile range (IQR), depending on the distribution of the data. Categorical variables are presented as number and percentages. The *t*-test and the Mann-Whitney U test were used to compare continuous variables, and the chi-square test was used to compare dichotomous variables. Univariate and multivariate logistic regression models were used to calculate odds ratios (ORs) and 95% confidence intervals (CI) for de-escalation from prasugrel to clopidogrel. The adjusted odds ratios and 95%CI were estimated after adjustment for covariates based on their potential to be associated with de-escalation using stepwise-backward selection with probability to remove the effect of regression at $p>0.2$.

Cumulative incidence rates of post-discharge outcomes were estimated by the Kaplan-Meier method and compared by the log-rank test in patients who underwent de-escalation from prasugrel to clopidogrel versus those continued on prasugrel. Adjusted survival curves were constructed using the inverse probability of treatment weighting (IPTW). The propensity scores were estimated by multiple logistic-regression analysis, adjusted for age (≥75 years), sex, body weight (≤50 kg), clinical presentation, use of anticoagulants, history of cerebrovascular disease, use of primary PCI, transradial approach, Killip class ≥2, estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2, history of previous myocardial infarction or PCI, history of malignancy, and duration of dual antiplatelet therapy (DAPT). Furthermore, we examined the impact of a de-escalation strategy on the post-discharge outcomes for primary and safety end points among patients with high-bleeding risk based on major criteria in the Academic Research Consortium for High Bleeding Risk (ARC–HBR) [14]. Some of the major criteria in the ARC–HBR were not available or needed to be modified due to data availability in the registry. Accordingly, in the present study, patients were considered to be at high-bleeding risk if at least one of the following criteria were met: concomitant use of oral anticoagulants, hemoglobin level <11 mg/dL, periprocedural bleeding events (BARC type 3 or 5 bleeding events within 48 h after PCI procedure), history of malignancy, or eGFR<30 ml/min/1.73m^2. Cumulative incidence rates were obtained using the Kaplan-Meier approach.

Throughout the present study, the levels of significance were set as $p<0.05$. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Baseline patient characteristics

A total of 3411 patients were registered in the JAMIR from the 50 institutions. The current study excluded the following subjects: 61 patients who did not have data regarding the use of antiplatelet therapy; 601 patients who were not initially treated with prasugrel; 20 patients who underwent triple antiplatelet therapy (aspirin, prasugrel, and clopidogrel); 10 patients who underwent switching from clopidogrel to prasugrel during hospitalization; and 115 patients who died during hospitalization. Finally, 2604 patients were included in the current analysis (Fig. 1). Most patients (n = 2516, 97%) received 3.75 mg prasugrel as maintenance dose, while only 3 patients (0.1%) received 2.5 mg prasugrel. Among the study population, 110 (4%) underwent switching from prasugrel to clopidogrel by the time of discharge. The median time of switching from prasugrel to clopidogrel after admission was 4 days [IQR 2 to 12 days]. The patient characteristics are summarized in Table 1. Patients who underwent de-escalation from prasugrel to clopidogrel were more likely to have heart failure on admission (Killip class ≥2), previous history of coronary artery bypass grafting and cerebrovascular disease and had higher peak creatine kinase level than those continued on prasugrel. In terms of medication, use of oral anticoagulants was more frequent in patients with de-escalation

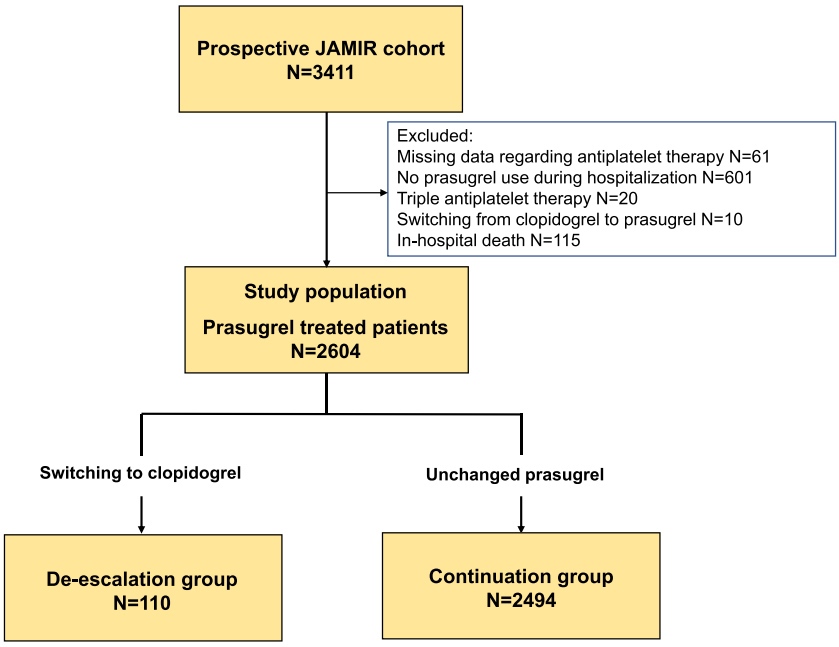

Fig. 1. Study flowchart. JAMIR, Japan Acute Myocardial Infarction Registry.

Table 1
Patient characteristics.

	Overall $n = 2604$	De-escalation $n = 110$	Continuation $n = 2494$	p-value
Age (years)	66.8 ± 13.0	68.0 ± 12.7	66.8 ± 13.0	0.35
Female	21.7	20.9	21.7	0.84
BMI (kg/m^2)	24.0 ± 4.0	23.8 ± 4.1	24.0 ± 4.0	0.60
Use of ambulance	82.1	90.0	81.8	0.03
Time from onset to admission (min)	132 [63, 305]	214 [74, 510]	130 [63, 300]	0.004
STEMI	80.7	85.5	80.5	0.20
Killip class ≥2	19.4	30.9	18.9	0.002
Hypertension	71.9	73.6	71.9	0.68
Diabetes	34.2	36.4	34.1	0.63
Dyslipidemia	71.1	63.6	71.4	0.08
Previous myocardial infarction	7.8	8.2	7.8	0.88
Previous PCI	9.3	11.8	9.1	0.34
Previous CABG	1.6	4.6	1.5	0.01
Previous cerebrovascular disease	7.0	13.6	6.7	0.005
Peripheral artery disease	2.3	0.9	2.4	0.32
Malignancy	6.8	6.4	6.8	0.87
Atrial fibrillation	5.5	10.0	5.3	0.03
Current smoking	43.2	49.1	42.9	0.43
eGFR (ml/min/1.73m^2)	67.5 ± 23.2	62.9 ± 23.4	67.7 ± 23.2	0.04
Hemoglobin (g/dL)	14.1 ± 2.1	13.9 ± 1.9	14.1 ± 2.1	0.33
ARC–HBR major criteria (%)*	25.9	44.6	25.1	<0.001
Peak CK (IU/L)	2416 ± 2485	3128 ± 3203	2384 ± 2444	0.02
Peak CK-MB (IU/L)	230 ± 237	290 ± 324	227 ± 231	0.05
LVEF (%)	52.6 ± 11.8	47.1 ± 12.8	52.9 ± 11.7	<0.001
Medication during hospitalization				
Aspirin	99.8	99.1	99.8	0.08
ACE inhibitors	54.2	61.8	53.8	0.10
ARBs	28.0	24.6	28.1	0.42
Beta-blockers	66.9	73.6	66.6	0.13
Statins	92.6	90.9	92.7	0.49
Oral anticoagulants	11.5	26.4	10.9	<0.001
Proton pump inhibitors	93.1	94.6	93.0	0.54

Data are given as mean ± standard deviation, median [interquartile range] or percent.
BMI, body mass index; STEMI, ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; ARC–HBR, Academic Research Consortium for High Bleeding Risk; CK, creatinine kinase; LVEF, left ventricular ejection fraction; ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers.
* Patients with at least one of following criteria: concomitant use of oral anticoagulants, hemoglobin level <11 mg/dL, periprocedural bleeding events (Bleeding Academic Research Consortium type 3 or 5 bleeding events within 48 h after PCI procedure), history of malignancy, or eGFR<30 ml/min.

Table 2
Angiographic and interventional characteristics.

	Overall $n = 2604$	De-escalation $n = 110$	Continuation $n = 2494$	p-value
Emergent CAG	99.2	100	99.2	0.35
Puncture site				0.02
Radial	67.5	56.4	68.0	
Femoral	30.9	40.0	30.5	
Brachial	1.6	3.6	1.5	
Culprit lesion				
Left main coronary artery	1.2	1.8	1.1	0.50
Left anterior descending artery	47.7	49.1	47.6	0.76
Left circumflex artery	14.6	16.4	14.5	0.59
Right coronary artery	37.4	36.4	37.5	0.81
None	0.5	0	0.5	0.45
Number of diseased vessels				0.39
0	1.0	0.9	1.0	
1	58.8	53.6	59.0	
2	25.1	24.6	25.1	
3	15.2	20.9	14.9	
Mean number of diseased vessels	1.5 ± 0.8	1.7 ± 0.8	1.5 ± 0.8	0.12
Thrombolysis	0.6	0	0.6	0.41
Primary PCI	96.9	97.3	96.9	0.80
Door to balloon time, (min)	67 [50, 97]	65[50, 104]	67 [50, 97]	0.76
Stent use *	93.4	91.6	93.5	0.44
DES use*	98.0	98.1	98.0	0.90
Final TIMI flow				0.01
0	1.6	2.7	1.6	
1	1.3	0.9	1.3	
2	5.3	11.8	5.1	
3	91.7	84.6	92.0	
Concomitant PCI in non-culprit lesion	5.2	7.3	5.1	0.30
Use of IABP	10.5	18.2	10.1	0.01
Use of VA ECMO	0.7	3.6	0.5	<0.001
CABG during hospitalization	1.3	2.7	1.3	0.20

Data are given as median [interquartile range] or percent.
CAG, coronary angiography; PCI, percutaneous coronary intervention; DES, drug-eluting stent; TIMI, Thrombolysis in Myocardial Infarction; IABP, intra-aortic balloon pumping; VA-ECMO, venoarterial extra-corporeal membrane oxygenation; CABG, coronary artery bypass grafting.
* Among patients treated with primary PCI.

than those continued on prasugrel. In addition, the prevalence of patients with high-bleeding risk according to the ARC–HBR major criteria was significantly higher in patients with de-escalation than in those continued on prasugrel. Table 2 shows angiographic and interventional characteristics. Use of mechanical circulatory support including intra-aortic balloon pumping and venoarterial extra-corporeal membrane oxygenation was more frequent in patients with de-escalation than those continued on prasugrel. In contrast, patients continued on prasugrel were more likely to undergo a procedure via the radial access than those with de-escalation.

Independent determinants of de-escalation from prasugrel to clopidogrel after acute myocardial infarction

We assessed factors associated with de-escalation from prasugrel to clopidogrel during hospitalization. In multivariable analysis, independent determinants of de-escalation from prasugrel to clopidogrel were history of cerebrovascular disease (OR 2.26, 95%CI 1.15–4.13), use of anticoagulants (OR 2.40, 95%CI 1.42–3.92), and periprocedural major bleeding events (BARC type 3 or 5 bleeding within 48 h after PCI) (OR 14.92, 95%CI 4.87–44.68) (Table 3).

Table 3
Independent determinants of de-escalation from prasugrel to clopidogrel after acute myocardial infarction.

	OR	95% CI	p-value
Age ≥75 years	0.96	0.58 - 1.57	0.88
Male sex	1.18	0.66 - 2.20	0.59
Body weight ≤50kg	1.25	0.63 - 2.37	0.52
ST-elevation myocardial infarction	1.12	0.61 - 2.16	0.73
Prior cerebrovascular disease	2.26	1.15 - 4.13	0.01
Use of anticoagulants	2.40	1.42 - 3.92	0.001
Use of ambulance	1.98	0.99 - 4.54	0.08
Higher peak CK (CK >1688 U/L)	1.47	0.93 - 2.34	0.10
Number of diseased vessels	1.26	0.96 - 1.64	0.09
Periprocedural major bleeding event*	14.92	4.87 - 44.68	<0.001

OR, odds ratio; CI, confidence interval; CK, creatinine kinase.
* Bleeding Academic Research Consortium type 3 or 5 bleeding events within 48 h after percutaneous coronary intervention procedure.

Association of switching with post-discharge outcomes

The mean follow-up period was 309±133 days after discharge. The median duration of DAPT was shorter in patients with de-escalation than those continued on prasugrel (267 vs. 306 days, $p = 0.001$), which was mainly associated with earlier discontinuation of aspirin in the de-escalation group (290 vs. 351 days, $p<0.001$). The detail of antiplatelet therapy after DAPT is shown in **Online** Fig. 1. In the de-escalation group, 59% of patients continued DAPT by the end of follow-up. Among the rest of 41%, 15% received aspirin, 25% received P2Y12 inhibitor as single antiplatelet therapy, while 1% discontinued antiplatelet therapy after DAPT. In the continuation group, 67% of patients continued DAPT by the end of follow-up. Among the rest of 33%, 25% received aspirin, 4% received P2Y12 inhibitor, while 4% discontinued antiplatelet therapy after DAPT.

Table 4 shows the incidence of primary outcome and major bleeding events after discharge. Unadjusted Kaplan-Meier curves

Table 4
Clinical outcomes after discharge.

	De-escalation $n = 110$	Continuation $n = 2494$	p-value
Cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke (primary endpoint)	1.8	2.8	0.55
BARC type 3 or 5 bleeding	1.8	1.7	0.94
TIMI major bleeding	0	0.6	0.40
NACE (primary endpoint+BARC type 3 or 5 bleeding)	3.6	4.4	0.71
All-cause death	3.6	1.8	0.15
Myocardial infarction	0.9	2.0	0.43
Stroke	0	0.5	0.45
Stent thrombosis	0.9	0.2	0.13
BARC type 2, 3, or 5 bleeding	1.8	2.7	0.59
TIMI major or minor bleeding	0.9	1.0	0.89
Fatal bleeding	0	0.1	0.72
Intracranial bleeding	0	0.3	0.58
Blood transfusion due to bleeding event	0.9	1.0	0.89

Data are given as percent.
BARC, Bleeding Academic Research Consortium; TIMI, Thrombolysis in Myocardial Infarction; NACE, net adverse clinical event.

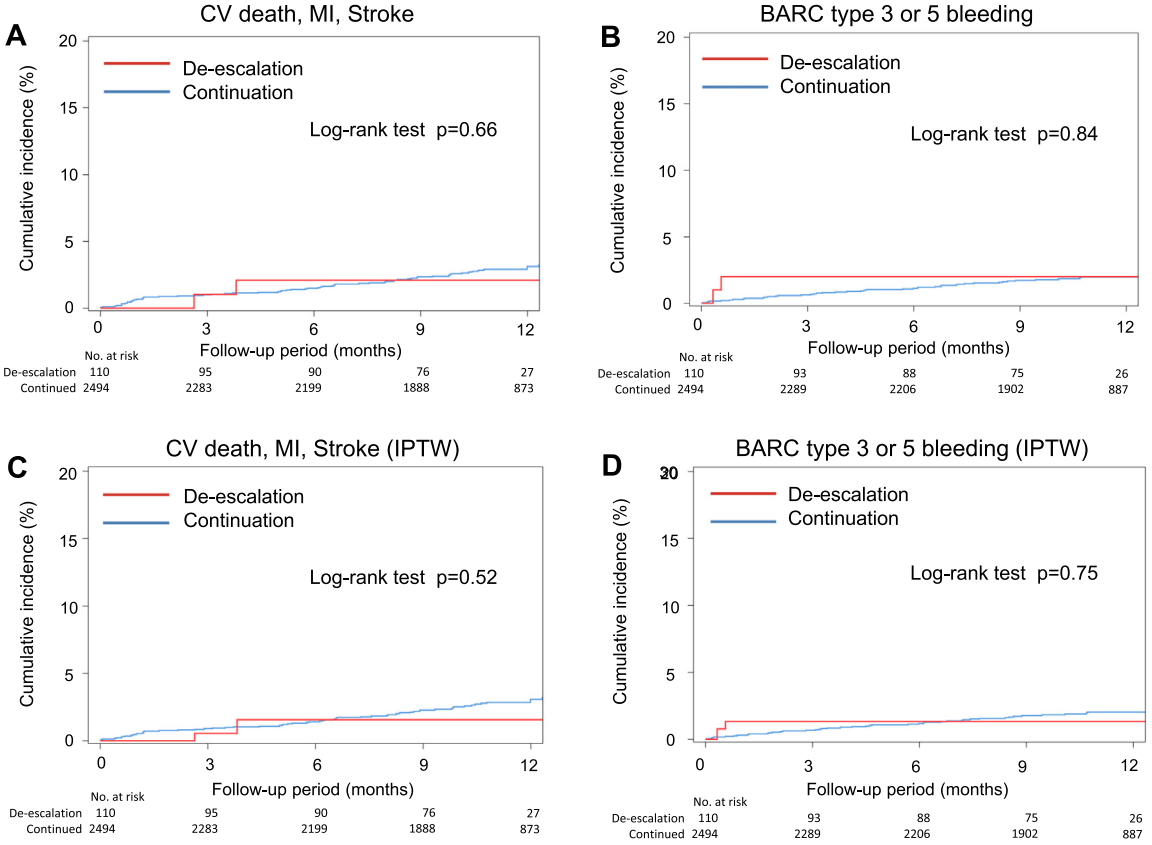

Fig. 2. Unadjusted and adjusted Kaplan-Meier curves for post-discharge outcomes between patients with and without de-escalation.(A) cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke. (B) BARC type 3 or 5 bleeding. (C) cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke after adjustment by IPTW method. (D) BARC type 3 or 5 bleeding after adjustment by IPTW method. CV, cardiovascular; MI, myocardial infarction; BARC, Bleeding Academic Research Consortium; IPTW, inverse probability of treatment weighting.

are presented in Fig. 2**A and B**. The incidence of primary outcome was 1.8% in patients with de-escalation and 2.8% in those continued on prasugrel (log-rank test, $p = 0.66$). The incidence of major bleeding was comparable between the groups (BARC type 3 or 5 bleeding; 1.8% vs. 1.7%, log-rank test, $p = 0.81$). Propensity analysis using IPTW noted similar results (Fig. 2**C, D**). There were no significant differences in the risks of primary outcome (log-rank test, $p = 0.52$) and BARC type 3 or 5 bleeding between patients with de-escalation and those continued on prasugrel (log-rank test $p = 0.75$).

Association of switching with post-discharge outcomes in patients with high-bleeding risk (ARC–HBR major criteria)

We examined association of switching with post-discharge outcomes in patients with high-bleeding risk according to the ARC–HBR major criteria. Among patients who have characteristics indicating high risk of bleeding ($n = 674$, 26% of overall study population), the frequency of BARC type 3 or 5 bleeding after discharge in patients with de-escalation was zero, and numerically lower than that of patients continued on prasugrel (0% vs. 4.2%), although

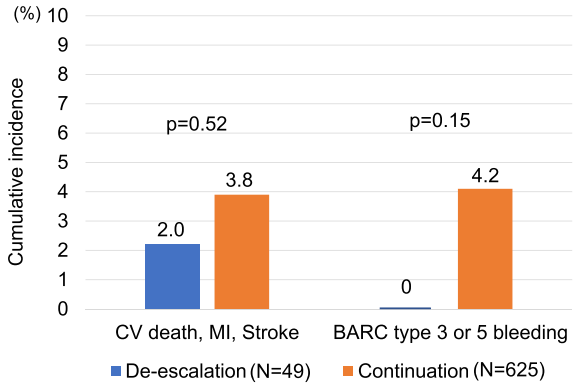

Fig. 3. Post-discharge outcomes in patients with high-bleeding risk according to the ARC–HBR major criteria. ARC–HBR, Academic Research Consortium for High Bleeding Risk; CV, cardiovascular; MI, myocardial infarction; BARC, Bleeding Academic Research Consortium.

the difference did not meet statistical significance ($p = 0.15$). There was no significant difference in primary outcome between patients with de-escalation and those continued on prasugrel (2.0% vs. 3.8%, $p = 0.52$) (Fig. 3).

Impact of high-bleeding risk (ARC–HBR major criteria) on post-discharge outcomes in patients continued on prasugrel

We also examined the association between the presence of high-bleeding risk and clinical outcomes in patients continued on prasugrel ($n = 2494$). In the continuation group, 625 patients (25%) had high-bleeding risk according to the ARC–HBR major criteria. The frequency of BARC type 3 or 5 bleeding was significantly higher in patients with high-bleeding risk than those without (4.2% vs. 0.9, $p<0.001$) while there was no significant difference in the primary outcome between the groups (3.8% vs. 2.4%, $p = 0.06$).

Discussion

In this analysis of a nationwide prospective registry in Japan, the principal findings were as follows. 1) Among patients treated initially with prasugrel, approximately 4% underwent de-escalation to clopidogrel by the time of discharge. 2) Patients with de-escalation were more likely to have characteristics indicating increased risk of bleeding than those continued on prasugrel. 3) However, no significant differences were observed in ischemic events or major bleeding between patients with de-escalation and those continued on prasugrel.

Our study showed that 4% of patients underwent switching from prasugrel to clopidogrel in the early phase following AMI. Similarly, previous observational data demonstrated that up to 14% of ACS patients experienced de-escalation of P2Y12 inhibitor [15-20]. Consistent with the current study, previous studies have shown that de-escalation of P2Y12 inhibitors was associated with prior bleeding events or factors related to bleeding risk such as prior stroke or transient ischemic attack, and discharge on oral anticoagulants [15,16,18]. These data indicate the need for the evaluation of efficacy and safety of the de-escalation strategy in real-world clinical practice.

Although recent randomized trials have demonstrated the safety of the de-escalation strategy [6,7], conflicting results exist in real-world clinical practice. Registry data from Greece showed that de-escalation from prasugrel or ticagrelor to clopidogrel was observed in 1.8% of ACS patients undergoing PCI, and was associated with higher incidence of major adverse cardiovascular events and bleeding events than those without de-escalation during a mean follow-up period of 42±11 days [17]. In a large multicenter, longitudinal registry which enrolled 12,365 AMI patients in US, there was no significant difference in six-month major cardiovascular events or bleeding events between patients undergoing in-hospital switching from potent P2Y12 inhibitors to clopidogrel and those continued on potent P2Y12 inhibitors [16]. However, these observational studies had limitations because clinical outcomes in these studies included ischemic and bleeding events before the switching of P2Y12 inhibitors, making it difficult to assess the safety of the de-escalation strategy. Furthermore, the follow-up periods in these studies were relatively short (up to six months). By contrast, the present study evaluated post-discharge outcomes, allowing the evaluation of ischemic and bleeding events after the switching of P2Y12 inhibitor, with a longer-follow up period (309±133 days after discharge). Notably, the incidence of bleeding events after discharge was comparable between patients with de-escalation and those continued on prasugrel even though patients who underwent de-escalation had characteristics indicating increased bleeding risk compared with those continued on prasugrel. In addition, de-escalation of P2Y12 inhibitor was not associated with excess risk of post- discharge ischemic events. Although the duration of DAPT was shorter in patients with de-escalation than those continued on prasugrel, these results were consistent even after adjusting for potential confounders including duration of DAPT in the propensity analysis (IPTW).

It is important to identify patients who may benefit from switching from a potent to a moderate P2Y12 inhibitor following AMI. Bleeding risk should be the priority in determining the use of antithrombotic drugs including their switching. Recently, the ARC–HBR defined new criteria for patients at high-bleeding risk undergoing PCI [14]. In the present study, 26% of AMI patients initially treated with prasugrel met the definition of high-bleeding risk according to the ARC–HBR major criteria. Among them, there was a trend toward lower incidence of bleeding events in the de-escalation group, although the difference did not reach statistical significance. In addition, the presence of high-bleeding risk was associated with higher incidence of major bleeding in patients continued on prasugrel. Taken together, these results suggest that de-escalation strategy may be an acceptable choice for patients with high-bleeding risk. Further large-scale studies are required to examine the potential benefit of the use of risk prediction tools in de-escalation strategy following AMI.

A number of caveats should be noted. First, the present study was an observational study and switching from prasugrel to clopidogrel was not randomized, which was inherent bias. Indeed, the prevalence of patients with high-bleeding risk according to the ARC–HBR major criteria was significantly higher in patients with de-escalation than in those continued on prasugrel. Second, the present study might be underpowered to assess significant differences in clinical events. Therefore, the current results should be viewed as hypothesis generating. Third, a variety of factors might have contributed to the decision to switch, including the clinical setting, patient characteristics, concomitant therapies, development of side effects, medication adherence, and patient/physician preference. Fourth, none of the patients was treated with ticagrelor in the present study because ticagrelor was not available until March 2017, which was only a few months before the end of patient enrollment. Fifth, data were not available for some ARC–HBR criteria, and we used only major criteria of the ARC–HBR for the definition of patients with high-bleeding risk. Therefore, we should be cautious in interpreting the results of subgroup analysis. Sixth, the usual dose of prasugrel (loading dose 20 mg, maintenance dose 3.75 mg) is different from that of other countries. Finally, because of the small number of patients treated with 2.5 mg prasugrel ($n = 3$) the present study could not assess the impact of 2.5 mg dose of prasugrel. The previous study reported that 2.5 mg dose of

prasugrel may be one option for patients with high bleeding risk (e.g. elderly, low body weight) [21].

Conclusion

Patients with de-escalation from prasugrel to clopidogrel before discharge had a higher bleeding risk profile than those continued on prasugrel. However, there were no significant differences in ischemic events or bleeding events after discharge between patients with de-escalation and those without, which suggest that de-escalation strategy may be an option for AMI patients with high-risk for bleeding. Given the observational nature and relatively small sample size of the current study, further studies are required.

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Declaration of Competing Interest

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Supplementary materials

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