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CLINICAL RESEARCH

Safety of prasugrel in real-world patients with ST-segment elevation myocardial infarction: 1-year results from a prospective observational study (Bleeding and Myocardial Infarction Study)

Sécurité du prasugrel chez des patients adressés pour un syndrome coronarien aigu avec sus-décalage du segment ST dans la « vraie vie » : résultats d'une étude observationnelle prospective sur 1 an (Bleeding and Myocardial Infarction Study)

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Summary

Background. — Antiplatelet therapies, including prasugrel, are a cornerstone in the treatment of ST-segment elevation myocardial infarction (STEMI), but are associated with a bleeding risk. This risk has been evaluated in randomized trials, but few data on real-world patients are available.

Aim. — To evaluate prasugrel safety in real-world patients with STEMI.

Methods. — Consecutive patients with STEMI were recruited over 1 year. Follow-up was done at 3 months and 1 year to evaluate prasugrel safety from hospital discharge to the STEMI anniversary date. The primary outcome was occurrence of any major bleeding according to the Bleeding Academic Research Consortium (BARC) 3 or 5 definitions, or minor bleeding according to the BARC 2 definition.

Results. — Overall, 1083 patients were recruited. Compared to patients treated with aspirin + clopidogrel, patients treated with aspirin + prasugrel had fewer BARC 3 or 5 bleedings (two [0.4%] patients vs. nine [1.8%] patients; $P = 0.04$), but more BARC 2 bleedings (45 [9.3%] patients vs. 20 [4.0%] patients; $P < 0.001$). The baseline characteristics of prasugrel- and clopidogrel-treated patients differed because the former were carefully selected (younger, higher body mass index, less frequent history of stroke). In the overall population, rates of in-hospital and out-of-hospital major bleeding were 2.6% ($n = 28$) and 1.3% ($n = 13$), respectively.

Conclusion. — The rate of major bleeding, particularly out-of-hospital bleeding, in patients treated with prasugrel is low within 1 year after a STEMI. Accurate selection of patient candidates for prasugrel is likely to have reduced the risk of bleeding.

Résumé

Contexte. — Les traitements antiplaquettaires, dont le prasugrel, sont un élément majeur dans le traitement du syndrome coronarien aigu avec sus-décalage du segment ST (SCA ST+) mais entraînent un sur-risque hémorragique. Ce risque a été évalué dans des essais cliniques randomisés mais il existe peu de données dans la « vraie vie ».

Objectif. — Évaluer la sécurité du prasugrel chez des patients adressés pour un syndrome coronarien aigu avec sus-décalage du segment ST dans la « vraie vie ».

Méthodes. — Les patients avec SCA ST+ ont été recrutés pendant un an et le suivi a été effectué, par téléphone, 3 mois et 1 an après le SCA ST+ afin d'évaluer la sécurité du prasugrel, en particulier pendant la période post-hospitalière. Le critère d'évènement principal était la survenue d'un évènement hémorragique majeur défini selon la classification Bleeding Academic Research Consortium (BARC) 3 ou 5 ou d'un évènement hémorragique mineur défini selon la classification BARC 2.

Résultats. — Mille quatre-vingt-trois patients ont été recrutés. Les patients traités par aspirine + clopidogrel avaient moins de saignements BARC 3 ou 5 que les patients traités par aspirine + prasugrel (9 patients, 1,8 % vs 2 patients, 0,4 % ; $p = 0,04$) mais ils avaient plus de saignements BARC 2 (20 patients, 4,0 % vs 45 patients, 9,3 % ; $p < 0,001$). Les caractéristiques des patients traités par prasugrel étaient différentes des patients traités par clopidogrel car la sélection était attentive : patients plus jeunes, indice de masse corporelle plus élevé, moins d'antécédent d'accident vasculaire cérébral. Les pourcentages de saignement intra-hospitalier

majeur et de saignement extra-hospitalier majeur étaient respectivement de 2,6 % ($n = 28$) et 1,3 % ($n = 13$).
Conclusion. — Les saignements majeurs, en particulier extra-hospitaliers, sont peu fréquents chez les patients traités par prasugrel dans l'année qui suit un SCA ST+. Une sélection attentive des patients pouvant bénéficier du prasugrel peut expliquer une diminution de ce risque.

Background

Cardiovascular diseases, including acute myocardial infarction, are currently one of the leading causes of death in Western countries. Medical therapies focus on anticoagulation and platelet inhibition to reduce the risk of thrombotic events and improve ischaemic outcomes in patients with ST-segment elevation myocardial infarction (STEMI). These therapies, coupled with early use of cardiac catheterization and revascularization, reduce the rate of death and reinfarction, but carry a bleeding risk. Indeed, bleeding is the most common non-cardiac complication of antithrombotic therapy in acute coronary syndromes (ACS), and has been associated with adverse outcomes, including myocardial infarction, stroke and death [1,2]. Thus, clinicians must balance antithrombotic treatment efficacy in preventing ischaemic events with the need to minimize the risk of serious bleeding complications. Bleeding is even more frequent when percutaneous coronary intervention (PCI) is performed in the context of acute STEMI, compared with bleeding complicating an elective procedure [3].

Several new antiplatelet therapies, including prasugrel, have been evaluated in randomized trials; they reduce the ischaemic risk but are associated with an increased risk of major bleeding. In patients with STEMI undergoing PCI, prasugrel is more effective than clopidogrel in the prevention of ischaemic events, without excess bleeding [4]. However, there are few data on the safety of new antiplatelet agents and bleeding risk within 1 year after STEMI in real-world patients [5—7]. The Bleeding and Myocardial Infarction (Bleed-MI) Study sought to evaluate the safety of prasugrel in real-world patients with STEMI, from hospital discharge to the anniversary date of the STEMI. Safety was assessed by analysing out-of-hospital bleeding.

Methods

Study patients

From 1st April 2011 to 31st March 2012, patients were included if they had a STEMI and were hospitalized in any of the nine primary percutaneous intervention centres in Brittany, France, within 24 hours after the onset of symptoms. There were no exclusion criteria. Data were recorded in the ORBI-registry, which was approved by the Commission nationale informatique et liberté. All patients were informed of the aims of the study and could request to be excluded. The follow-up interviews were conducted by telephone by research nurses at 3 months and 1 year. The follow-up questionnaire elicited key information about antiplatelet and anticoagulation therapies, medical treatment and occurrence of bleeding or ischaemic events. In case of bleeding or ischaemic events, the hospitalization reports and all medical examination results (e.g. blood tests, medical imaging, etc.) were recovered, so that all data were centralized. Patients for whom follow-up data were lacking were considered lost to follow-up.

Definitions

The Bleeding Academic Research Consortium (BARC) [8] was used to define bleeding events occurring within 1 year after a STEMI. BARC 3 or 5 bleedings were considered major bleedings; BARC 2 bleedings were considered minor bleedings. BARC 1 bleedings were not collected because they do not require treatment by a healthcare professional; thus, their collection would not have been exhaustive. Coronary artery bypass graft (CABG)-related bleedings (BARC 4 bleedings) were not analysed. Bleeding rates were also defined according to thrombolysis in myocardial infarction (TIMI) definitions [9]. Cardiovascular death was any death resulting from a new ACS, severe cardiac arrhythmia, refractory congestive heart failure, cardiogenic shock, stroke, sudden death or unwitnessed death. Acute myocardial infarction was defined in accordance with the universal definition of myocardial infarction proposed in 2012 [10]. Evaluation for stent thrombosis was performed according to the Academic Research Consortium criteria [11].

Study outcomes

The primary outcome was the occurrence of any minor or major bleeding between discharge and the end of follow-up at 1 year. A ''bleeding events'' committee validated, classified and located the site of each bleeding event, using telephone interviews, the hospitalization reports and the medical examination results. Prespecified secondary outcomes included in-hospital major bleeding and rates of premature discontinuation (transitory or not) of any antithrombotic treatment after a bleeding complication. The rates of major adverse cardiac events, including cardiovascular death, non-fatal STEMI, non-fatal stroke and stent thrombosis, were calculated.

Statistical methods

Data description started with displaying the number of patients with haemorrhage or who were censored with no event 12 months after myocardial infarction. Descriptive statistics included mean and standard deviation for normally distributed continuous variables, median and interquartile range otherwise, and number and percentage for categorical variables. Comparisons according to dual antiplatelet

regimen on discharge used the Chi-square test or Fisher's exact test for categorical variables and Student's *t* test or the Wilcoxon test for continuous variables. For the main outcome, a survival analysis was used. Only one event per subject could occur in the analysis.

First, univariate (marginal) Wald test statistics using the Cox model were performed for each covariate. Then, multivariable modelling was completed with a Cox proportional hazards model that contained all covariates significantly associated in the univariate analyses at the $P = 0.15$ level. We used a hand-made stepwise backward elimination process: following the fit of the multivariable model, we used the *P*-values from the Wald tests of the individual coefficients to identify covariates that might be deleted from the model. The linearity of the relationship between continuous covariates was not rejected except for haematocrit value when considering death; a cut-off at 37.4% was identified from martingale residuals analysis. In addition, the graphical and numerical methods derived from cumulative sums of martingale residuals over follow-up times or the covariate values of Lin et al. [12] were used for checking the proportional hazard assumption. For all statistical analyses, SAS software, version 9.3 (SAS Institute, Cary, NC, USA) was used.

Results

Study patients and in-hospital events

Overall, 1083 consecutive patients with STEMI from nine centres in Brittany were recruited from 1st April 2011 to 31st March 2012. No patient asked to be excluded. Follow-up occurred from 1st July 2011 to 31st March 2013. The baseline characteristics of the patients are summarized in Table 1. Coronary angiography was performed in 1060 (97.9%) patients, with radial access in 564 (53.2%) patients, and angioplasty was performed in 974 (89.9%) patients; 91.6% ($n = 892$) of stented patients received at least one stent, and 22.5% ($n = 219$) of stented patients had at least one drug-eluting stent. Glycoprotein IIb/IIIa inhibitors were used in 489 (45.2%) patients.

In-hospital BARC 3 bleeding was observed in 28 (2.6%) patients; there was no in-hospital BARC 5 bleeding (Table 2). Among these 28 patients, bleeding was attributed to a vascular access site in seven (25%) patients. In-hospital BARC 2 bleedings were not recorded. Switches from prasugrel to clopidogrel occurred in 48 (4.4%) patients, mainly for precaution of use.

Because of 51 (4.7%) in-hospital deaths, 1032 patients were analysed for follow-up. At discharge, 1021 (98.9%) patients were treated with aspirin, 513 (49.7%) with clopidogrel, 484 (46.9%) with prasugrel and 52 (5.0%) with a vitamin K antagonist (VKA). Overall, 956 (92.6%) patients were treated with dual antiplatelet therapy alone, and 32 (3.1%) were treated with triple antithrombotic therapy (aspirin + clopidogrel + a VKA or aspirin + prasugrel + a VKA). Twenty-three (2.2%) patients were treated with only one antiplatelet agent: aspirin ($n = 19$), clopidogrel ($n = 3$) and prasugrel ($n = 1$). Data were missing for 23 (2.2%) patients. A total of 26 (2.5%) patients were lost to follow-up at the end of the follow-up period (Fig. 1).

Table 1 Baseline characteristics of the patients and occurrence of bleeding events during the follow-up.
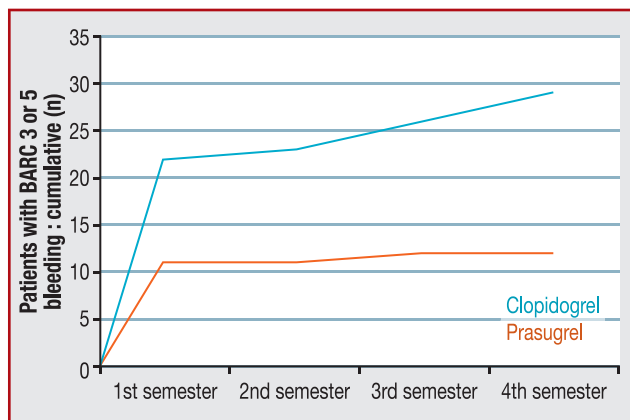
	Population ($n = 1083$)	Aspirin + clopidogrel ($n = 505$)	Aspirin + prasugrel ($n = 483$)	P
Age (years)	62.7 ± 14.0	67.3 ± 14.2	55.9 ± 10.2	<0.0001
Women	282 (26.0)	171 (33.9)	67 (13.9)	<0.0001
Body weight (kg)	75.5 ± 15.0	71.2 ± 14.7	80.7 ± 13.4	<0.0001
BMI (kg/m²)	26.3 ± 4.3	25.4 ± 4.3	27.2 ± 4.0	<0.0001
Cardiovascular risk factors				
Habitual smoker	439 (40.5)	159 (31.7)	254 (52.6)	<0.0001
Arterial hypertension	460 (42.5)	252 (49.9)	150 (31.1)	<0.0001
Diabetes mellitus	147 (13.6)	72 (14.3)	59 (12.2)	0.34
Other medical history				
Stroke/TIA	34 (3.1)	20 (4.0)	5 (1.0)	0.0034
Chronic renal disease	23 (2.1)	15 (3.0)	5 (1.0)	0.0309
Gastroduodenal ulcer	34 (3.1)	11 (2.2)	7 (1.4)	0.39
Initial use of glycoprotein IIb/IIIa inhibitors	489 (45.2)	233 (46.1)	233 (48.2)	0.51
Occurrence of bleeding events during follow-up				
Total		23 (4.6)	43 (8.9)	0.0110
BARC 2		15 (3.0)	42 (8.7)	0.0003
BARC 3		6 (1.2)	1 (0.2)	0.13
BARC 5		2 (0.4)	0 (0)	0.50
BARC 3 + 5		8 (1.6)	1 (0.2)	0.0389

Data are expressed as mean ± standard deviation or number (%). BARC: Bleeding Academic Research Consortium; BMI: body mass index; TIA: transient ischaemic attack.

Table 2 Chronology of in-hospital and out-of-hospital bleeding.

	In-hospital bleeding (n = 1083)	Out-of-hospital bleeding (n = 1006)
BARC definition		
BARC 2 bleeding	Not collected	66 (6.6)
BARC 3 bleeding	28 (2.6)	11 (1.1)
BARC 3a	17 (1.6)	6 (0.6)
BARC 3b	9 (0.8)	3 (0.3)
BARC 3c	2 (0.2)	2 (0.2)
BARC 5 bleeding	0 (0)	2 (0.2)
BARC 5a	0 (0)	2 (0.2)
BARC 5b	0 (0)	0 (0)
BARC 3 or 5 bleeding	28 (2.6)	13 (1.3)
TIMI definition		
TIMI major bleeding	10 (0.9)	6 (0.6)
TIMI major or minor bleeding	22 (2.0)	13 (1.3)

Data are expressed as number (%). BARC: Bleeding Academic Research Consortium; TIMI: thrombolysis in myocardial infarction.

Out-of-hospital bleeding

Out-of-hospital major bleeding according to BARC 3 or 5 definitions occurred in 13 of 1006 (1.3%) patients (Table 2). Out-of-hospital major bleeding according to the
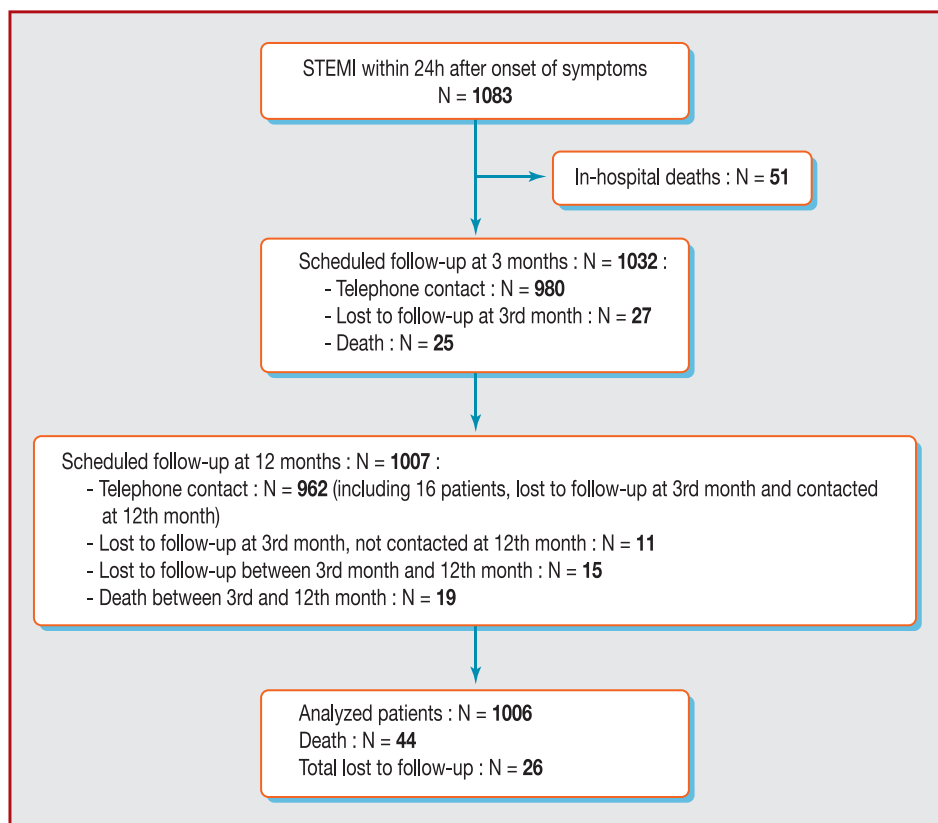

Figure 2. Patients with Bleeding Academic Research Consortium 3 or 5 bleeding during the follow-up period.

TIMI definition occurred in 6 of 1006 (0.6%) patients. In total, BARC 3 or 5 bleeding, including in-hospital bleeding, was observed in 41 (3.8%) patients, and occurred during the first trimester in 33 patients (80.5% of major bleedings; Fig. 2). The most frequent out-of-hospital BARC 3 or 5 bleeding sites were gastrointestinal (n = 6) and cerebral (n = 4). The most frequent out-of-hospital BARC 2 bleeding sites were ear, nose and throat (n = 26), cutaneous (n = 14) and gastrointestinal (n = 12; Table 3).

Patients treated with aspirin + prasugrel compared with patients treated with aspirin + clopidogrel had statistically significantly less BARC 3 or 5 bleeding (0.4% vs. 1.8%, respectively; $P = 0.04$), but more BARC 2 bleeding (9.3% vs. 4.0%,

Figure 1. Flow-chart.

Table 3   Location of out-of-hospital bleeding and vascular access.1.

Location of bleeding	BARC classification			Radial access
	BARC 2	BARC 3	BARC 5	
Cutaneous	14	1	0	5 (33)
Gastrointestinal	12	6	0	13 (72)
Cerebral	0	2	2	0 (0)
Ear, nose and throat	26	0	0	15 (57)
Respiratory tract	5	0	0	2 (40)
Urinary tract	5	0	0	4 (80)
Other	4	2	0	3 (50)
Total	66	11	2	42 (53)

Data are expressed as number or number (%). BARC: Bleeding Academic Research Consortium.

respectively; $P < 0.001$). Among the 988 patients treated with dual antiplatelet therapy, the baseline characteristics of patients treated with prasugrel were different to those of patients treated with clopidogrel (Table 1). Patients treated with aspirin + prasugrel were more often male, younger, with a higher body mass index and less frequent history of arterial hypertension, stroke or transient ischaemic attack. Patients treated with prasugrel were carefully selected: eight (1.7%) prasugrel-treated patients were aged ≥75 years, while 193 (37.6%) clopidogrel-treated patients were aged ≥75 years. Thirteen (2.7%) prasugrel-treated patients weighed <60 kg, whereas 107 (20.8%) clopidogrel-treated patients weighed <60 kg. Five (1.0%) prasugrel-treated patients had a history of stroke or transient ischaemic attack compared with 19 (3.7%) clopidogrel-treated patients. In the Bleed-MI Study, the rate of major out-of-hospital bleeding was low, so it reduced the statistical power for detecting any clinical and biological predictors of bleeding events.

Antithrombotic agents

Among the 79 patients with out-of-hospital BARC 2, 3 or 5 bleeding, 25 patients were treated with aspirin + clopidogrel (5.2% of patients using this combination), 45 with aspirin + prasugrel (9.5% of patients using this combination), two with aspirin + a VKA (14.3% of patients using this combination), four with aspirin + clopidogrel + a VKA (16% of patients using this combination), two with aspirin + prasugrel + a VKA (28.6% of patients using this combination) and one with aspirin alone (5.3% of patients using aspirin alone). Hence, 7.3% of patients (70/956) treated with two antiplatelet agents experienced out-of-hospital bleeding, and 18.7% of patients (6/32) treated with three antithrombotic agents experienced out-of-hospital bleeding. Moreover, 0.9% of patients (9/956) treated with dual antiplatelet therapy alone experienced BARC 3 or 5 out-of-hospital bleeding, and 7.7% (4/52) of patients treated with a VKA experienced BARC 3 or 5 out-of-hospital bleeding. Anticoagulant agents therefore had an important role in the occurrence of major bleeding events.

Discontinuation of medication

Bleeding (BARC 2, 3 or 5) led to temporary or definitive discontinuation of at least one antithrombotic agent in 27 of 79 patients who had bleeding. Among these patients, five had prasugrel replaced by clopidogrel. The discontinuation was definitive for 20 patients (74% of patients with discontinuation of treatment): aspirin in two patients, clopidogrel in eight patients, prasugrel in eight patients, a VKA in one patient and prasugrel + a VKA in one patient. The discontinuation was temporary for seven patients: aspirin in three patients, clopidogrel in one patient, aspirin + clopidogrel in one patient and a VKA in two patients. The mean duration of antithrombotic agent discontinuation was 6.5 months (± 4.5 months). Antithrombotic agents were interrupted before month 6 in 13 (48.1%) patients, after month 6 in 14 (51.9%) patients and beyond month 9 in 11 (40.7%) patients.

The most frequent bleeding sites leading to treatment discontinuation were gastrointestinal (25.9%), ear, nose and throat (25.9%) and cutaneous (25.9%). Interestingly, bleeding that led to discontinuation of medications was not major in most cases; in fact, 74.1% of those bleeds were BARC 2, 14.8% were BARC 3a, 3.7% were BARC 3b and 7.4% were BARC 3c. No ischaemic event was observed after discontinuation of antithrombotic medications. No relationship was found between bleeding occurrence and increased risk of ischaemic event.

Factors predictive of death

Forty-four (4.4%) patients died from any cause during follow-up. From the multivariable analysis, the factors independently associated with death included age (hazard ratio [HR]: 2.2, 95% confidence interval [CI]: 1.6—3.0; $P < 0.001$), signs of congestive heart failure on presentation (HR: 4.1, 95% CI: 2.1—8.1; $P < 0.001$) and baseline haematocrit ≤37.4% (HR: 0.3, 95% CI: 0.2—0.6; $P < 0.001$). Although any BARC 3 or 5 bleeding predicted death in the univariate analysis, these factors did not remain independent predictors of death after adjustment for other covariates. This was also true for sex, weight, body mass index, history of hypertension, prior coronary heart disease, prior chronic renal disease, baseline creatinine and duration of hospitalization.

Out-of-hospital ischaemic events

The rate of out-of-hospital major adverse cardiac events among patients with BARC 2, 3 or 5 bleeding was 7.6% ($n = 6$). There was no statistically significant difference compared

with the entire population. Among all patients, the rate of out-of-hospital major adverse cardiac events was 6.1% ($n = 61$): death from cardiovascular causes occurred in 24 (2.4%) patients, non-fatal myocardial infarction in 10 (1.0%) patients, non-fatal non-STEMI in seven (0.7%) patients, non-fatal stroke in five (0.5%) patients, fatal stent thrombosis in eight (0.8%) patients and non-fatal stent thrombosis in seven (0.7%) patients. The rate of stent thrombosis was 1.5%: five patients had a definite stent thrombosis, five patients had a probable stent thrombosis and five patients had a possible stent thrombosis.

Discussion

The Bleed-MI Study allowed evaluation of the safety of prasugrel in non-selected STEMI patients in a real-world setting, according to bleeding risk. This knowledge is crucial for the clinician, who must choose the best antithrombotic treatment and its optimal duration according to the ischaemic and bleeding risks. The final decision concerning an individual patient must be made by the physician responsible, taking into account the benefit/risk balance, as stated in the latest European Society of Cardiology guidelines for the management of STEMI [3].

In the TRial to assess Improvement in Therapeutic Outcomes by optimizing platelet inhibitioN with prasugrel-TIMI (TRITON-TIMI 38) [13], patients aged ≥75 years gained no net benefit from prasugrel, and there were no statistically significant higher rates of non-CABG-related TIMI major bleeding in the prasugrel group versus the clopidogrel group (4.3% vs. 3.3%; $P = 0.10$). In the Bleed-MI Study, patients treated with prasugrel had more BARC 2 bleeding events compared with patients treated with clopidogrel, but fewer BARC 3 or 5 bleedings. This low risk of major bleeding in prasugrel-treated patients in this real-life registry, despite frequent use, is reassuring, and can be explained by the selection of patient candidates for prasugrel (i.e. those with a lower bleeding risk). This means that the contraindications and precautions for use of prasugrel are relevant. Moreover, it means that physicians are using the drug in appropriate candidates. Nevertheless, 33 patients (6.81% of patients treated with prasugrel) with contraindications or precautions for use of prasugrel received prasugrel in the study: five patients with a history of stroke or transient ischaemic attack, eight patients aged ≥75 years, 13 patients weighing <60 kg and seven patients with concomitant use of a VKA.

Unlike many studies, we included non-selected patients, which makes our results useful in real-world practice. Most studies have included selected patients (patients undergoing PCI for STEMI, for example). In the Bleed-MI Study, coronary angiography was not performed in 22 (2%) patients and no angioplasty was performed in 109 (10.1%) patients; these patients are rarely studied in randomized trials. Moreover, we focused on out-of-hospital events: in-hospital bleeding, often related to procedural bleeding complications (PCI or CABG), should be differentiated from out-of-hospital bleeding. The rate of out-of-hospital major bleeding within 1 year after a STEMI was low at 1.3% according to the BARC definition and at 0.6% according to the TIMI definition. The rate of major out-of-hospital bleeding was particularly low

in patients treated with prasugrel because of the accurate selection of patients.

The chronology of major bleeding is important because of its effect on the duration of combination antithrombotic treatment in patients with a high bleeding risk. Bleeding can lead to transitory or permanent discontinuation of one or more antithrombotic treatments, with the risk of stent thrombosis in stented patients and ischaemic complications in all patients. In total, 68.3% of major bleedings occurred during the initial hospitalization. In a study published by Collet et al. [14] in 2004, 5.4% patients admitted for a suspected ACS had recently had antiplatelet agents withdrawn, which was found to be an independent predictor of mortality and bleeding at 30 days. In the Bleed-MI Study, out-of-hospital bleeding (BARC 2, 3 or 5) led to early discontinuation of any thrombotic agent (before 6 months) in only 13 patients (16.5% of out-of-hospital bleedings). Moreover, there was no ischaemic event among the 27 patients who discontinued their treatment. Bleeding (including minor bleeding) must not be underestimated, and should be systematically sought during the medical follow-up of patients after an ACS, as this would promote treatment compliance.

The reported rates of major bleedings at 9—12 months' follow-up after an ACS vary from 2 to 6% [7,15—17]. In the Bleed-MI Study, in-hospital and out-of-hospital major bleeding occurred in 3.8% according to the BARC definition and in 1.5% according to the TIMI definition. In TRITON-TIMI 38 [13], the rate of non-CABG-related TIMI major bleeding at 15 months in the entire population was 2%. Considering only patients undergoing PCI for STEMI [4], the risk of non-CABG major bleeding was lower, at 1.1%, which is close to our rate of 1.5%. In the PLATO study [17], the rate of non-CABG-related TIMI major bleedings at 12 months among patients with a STEMI was 2.2%. Considering the location of bleedings in our study, the most frequent out-of-hospital major bleeding sites were gastrointestinal, but the most frequent out-of-hospital minor bleeding sites were ear, nose and throat and cutaneous, while the most severe out-of-hospital bleeding sites were cerebral. In the Global Registry of Acute Coronary Events [18], the most common life-threatening in-hospital bleeding complications were also gastrointestinal.

Study limitations

As in any registry, this observational study has some limitations. For instance, 26 patients (2.5%) were lost to follow-up. The follow-up was made by telephone contact at 3 months and at 1 year, but data collection was done by qualified hospital staff with directed questionnaires, which limits the loss of data. Moreover, BARC 1 bleedings were not collected because their collection would not have been exhaustive, as a result of the declaratory nature of data collection, and premature treatment cessation because of BARC 1 bleedings could not have been analysed.

No patient was treated with ticagrelor, because this treatment was not yet available in Brittany during the study.

According to an analysis from the TRITON-TIMI 38 study [19], independent predictors of non-CABG-related serious bleeding throughout 15 months were female sex, use of a glycoprotein IIb/IIIa inhibitor, duration of intervention, age, assignment to prasugrel versus clopidogrel, STEMI, femoral access, creatinine clearance, hypercholesterolaemia and

hypertension. In the Bleed-MI Study, the low rate of major out-of-hospital bleedings reduced the statistical power for detecting clinical and biological predictors of bleeding events. Any usual predictors of bleeding events could not be found, and no statistical association between the occurrence of major bleeding and mortality was demonstrated.

Conclusion

Within 1 year after a STEMI, the major bleeding rate in patients treated with prasugrel is low when patients are carefully selected. The question remains of extending the prescription of new antiplatelet agents to a broader population of patients, but with the risk of modifying the benefit-risk balance that we have documented in real-world selected patients.

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Disclosure of interest

The authors declare that they have no competing interest.

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