

In-Hospital Bleeding Outcomes of Myocardial Infarction in the Era of Warfarin and Direct Oral Anticoagulants for Atrial Fibrillation in the United States: A Report From the National Cardiovascular Data Registry Acute Coronary Treatment and Intervention Outcomes Network Registry

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Background—We sought to examine patient characteristics, peri-infarction invasive and pharmacologic management, and in-hospital major bleeding in myocardial infarction patients with atrial fibrillation or flutter, based on home anticoagulant use.

Methods and Results—We stratified patients by home anticoagulant: (1) no anticoagulant, (2) warfarin, and (3) direct oral anticoagulants (DOACs) among ST-segment-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) patients with atrial fibrillation or flutter treated at 761 US hospitals in the ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry from January 2015 to December 2016. The primary outcome of our study was in-hospital major bleeding. Multivariable logistic regression was used to examine the independent association between home anticoagulant and in-hospital major bleeding. Among 6471 STEMI patients with atrial fibrillation or flutter, 15.7% were on warfarin and 13.0% on DOACs; among 19 954 NSTEMI patients, 22.8% were on warfarin and 15.4% on DOACs. In STEMI, door-to-balloon times were slightly higher in those on anticoagulant, with similar rates of angiography within 24 hours in the 3 groups. NSTEMI patients on anticoagulant were less likely to undergo angiography (49.3% no anticoagulant, 33.4% on warfarin, 36.4% on DOACs; $P<0.01$) or percutaneous coronary intervention within 24 hours (21.1% no anticoagulant, 14.3% on warfarin, 15.9% on DOACs; $P<0.01$). After multivariate adjustment, use of home warfarin (odds ratio: 1.00 [95% CI, 0.79–1.27] in STEMI and 1.13 [95% CI, 0.97–1.30] in NSTEMI) or DOAC (odds ratio: 0.93 [95% CI, 0.73–1.20] in STEMI and 0.97 [95% CI, 0.81–1.16] in NSTEMI) was not associated with increased in-hospital major bleeding compared with no anticoagulant.

Conclusions—In routine clinical practice, home warfarin or DOAC therapy is not associated with an increased risk of in-hospital bleeding compared with no anticoagulant. (*J Am Heart Assoc.* 2019;8:e011606. DOI: 10.1161/JAHA.118.011606.)

Key Words: atrial fibrillation • direct oral anticoagulant • myocardial infarction • novel oral anticoagulant • warfarin

Stroke prevention is among the primary therapeutic goals in managing atrial fibrillation or flutter (AF).^{1,2} Clinical guidelines for AF recommend the use of long-term anticoagulant therapy, as driven by individually predicted stroke risk.² Approximately 7% to 10% of myocardial infarction (MI) patients and 10% to 15% of patients undergoing percutaneous coronary intervention (PCI) have a history of AF.^{3,4} Dual

antiplatelet therapy (DAPT) is routine after PCI and has been shown to be superior to aspirin plus warfarin for the prevention of stent thrombosis.⁵ However, warfarin is more effective than DAPT for the prevention of stroke in AF.⁶

Since 2010, direct oral anticoagulants (DOACs) have been increasingly utilized for stroke prevention in AF given their advantages over warfarin. In patients with nonvalvular AF,

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Clinical Perspective

What Is New?

- ST-segment–elevation myocardial infarction (STEMI) patients on home warfarin or direct oral anticoagulants are managed similarly to those with no anticoagulant at presentation, without a clinically significant delay in primary percutaneous coronary intervention; non-STEMI patients on home warfarin or direct oral anticoagulants are less likely to undergo urgent angiography or percutaneous coronary intervention within 24 and 48 hours of admission compared with patients without home anticoagulant.
- Home warfarin or direct oral anticoagulant use is not associated with increased risk of in-hospital major bleeding compared with no home anticoagulant in both STEMI and non-STEMI cohorts.

What Are the Clinical Implications?

- In-hospital outcomes of STEMI and non-STEMI patients with atrial fibrillation or flutter are not negatively affected by home warfarin or direct oral anticoagulant therapy despite the perceived high bleeding risk; clinicians should not delay emergent or urgent percutaneous coronary intervention when needed in anticoagulated patients.

DOACs have been associated with similar efficacy for prevention of stroke and systemic embolism and rates of bleeding and intracranial hemorrhage similar to or lower than those with warfarin.^{7–10} At the same time, stronger P2Y₁₂ inhibitors (prasugrel and ticagrelor) have proven superior to clopidogrel in preventing ischemic events and stent thrombosis in patient with acute coronary syndrome (ACS).^{11,12} Peri-infarction management of AF patients might be affected by home anticoagulant status and requires careful weighing of risks of stent thrombosis, ischemic stroke, and bleeding, which are inherently higher in the peri-infarction and periprocedural periods.^{13–15} Prior studies have examined outcomes and bleeding rehospitalizations in AF patients with ACS who were treated in the era of clopidogrel and warfarin^{16,17}; however, relatively few data exist regarding contemporary management and in-hospital outcomes of MI in AF patients taking DOACs and new P2Y₁₂ inhibitors. Therefore, we sought to examine patient characteristics, peri-infarction management strategies, differences in periprocedural antithrombotic and antiplatelet therapies and in-hospital outcomes, particularly in-hospital major bleeding, in MI patients with AF stratified by home anticoagulant use in the NCDR (National Cardiovascular Data Registry) ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry database from January 2015 to December 2016.

Methods

ACTION Registry

The ACTION Registry is a US quality improvement initiative for patients with MI. Participating sites enroll consecutive, unselected patients with ST-segment–elevation MI (STEMI) and non-STEMI (NSTEMI), as previously described.¹⁸ This registry is part of a quality-improvement initiative sponsored by the American College of Cardiology (ACC) and American Heart Association (AHA) guidelines. The ACTION Registry includes data abstraction training, data quality thresholds for inclusion, site data-quality feedback reports, independent auditing, and data validation. Auditing of data has demonstrated chart review agreement of >93% of collected variables.¹⁹ At each participating site, the respective institutional review board approved registry participation. The requirement to obtain informed consent from the participants was waived.

Study Population

The starting analysis population (including the period when home DOAC data were collected by the ACTION Registry) comprised 293 197 MI patients from 781 US hospitals, who were cared for from January 2015 to December 2016 (Figure 1). STEMI and NSTEMI cohorts were analyzed separately. Patients were then stratified into 3 groups by home anticoagulant status: (1) no anticoagulant therapy, (2) warfarin therapy, or (3) DOAC therapy. Baseline patient demographics, medical history, presentation features, concomitant pharmacotherapies, and in-hospital outcomes were examined. Patients were excluded sequentially if they had no AF or were missing information regarding AF status (n=266 653), stayed in a non-ACTION hospital for >24 hours before transfer (n=3), were missing data regarding home DOAC status (n=76), or were listed as taking both warfarin and DOAC (n=40).

Definitions and End Points

The primary outcome for our study was in-hospital major bleeding. Major bleeding was defined as any of the following criteria: (1) an absolute hemoglobin decrease ≥ 4 g/dL (baseline to nadir), (2) intracranial hemorrhage, (3) documented or suspected retroperitoneal bleed, (4) any red cell blood transfusion with baseline hemoglobin ≥ 9 g/dL, or (5) any red cell transfusion with hemoglobin < 9 g/dL and a suspected bleeding event. Given that most patients undergoing coronary artery bypass grafting (CABG) receive blood transfusions related to surgery, bleeding events were considered only if they occurred before CABG.¹⁹ Patients were considered to have AF if they had any history of such

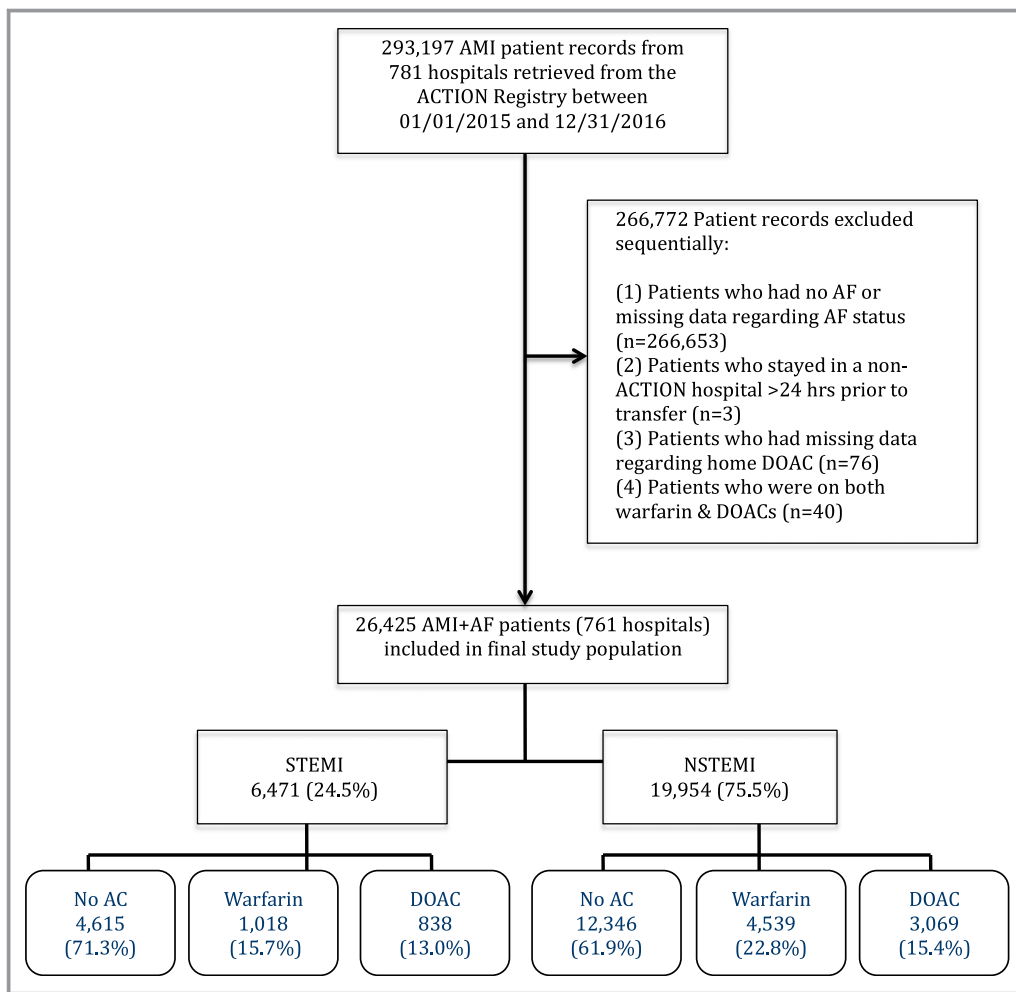


Figure 1. Study population. Flow chart of the patient records retrieved from the ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry database. AC indicates anticoagulation; AF, atrial fibrillation; AMI, acute myocardial infarction; DOACs, direct oral anticoagulants; NSTEMI, non-ST-segment-elevation myocardial infarction; STEMI, ST-segment-elevation myocardial infarction.

arrhythmias before hospital arrival. Patients were considered to be on home warfarin if they were taking warfarin routinely at home and within 2 weeks of hospitalization. Patients were considered to be on DOACs if they were on dabigatran, rivaroxaban, or apixaban routinely at home and within 2 weeks of hospitalization. Data on edoxaban use were not collected in the ACTION Registry. The CHA₂DS₂-VASc score (congestive heart failure, hypertension, age 65–74 years [with age ≥75 assigned 2 points], diabetes mellitus, previous stroke [2 points], presence of vascular disease, and female sex) ranged from 1 to 9.²⁰ All patients were automatically assigned 1 point for MI, which is delineated as vascular disease. P2Y₁₂ receptor inhibitors were defined as any of the following 3 medications: clopidogrel, prasugrel, or ticagrelor. DAPT was defined as aspirin plus ticlopidine, clopidogrel, prasugrel, or ticagrelor. An early invasive strategy was defined as cardiac catheterization within 48 hours of hospital arrival in NSTEMI

patients (excluding those with contraindications to cardiac catheterization). The conservative strategy was defined as no cardiac catheterization or cardiac catheterization >48 hours of hospital arrival in NSTEMI patients (excluding those with contraindications to cardiac catheterization). Initial creatinine clearance was estimated with the Cockcroft–Gault formula and was derived from data on admission, before any procedures.²¹

Statistical Analysis

Median values with 25th and 75th percentiles or mean values with standard deviations were used to describe continuous variables, and percentages were reported for categorical variables. Among 3 groups of patients (no anticoagulant, warfarin, and DOACs), categorical variables and continuous variables were compared using χ^2 and Kruskal–Wallis tests, respectively. For the in-hospital outcomes analyses, patients

who were transferred out of ACTION Registry hospitals (n=1324) were further excluded because their outcome status was no longer available. Furthermore, patients who had missing major bleeding data (n=146) were excluded from bleeding analyses; thus, the final analysis population consisted of 24 955 patients from 756 hospitals. To assess the relationship between home anticoagulant status and in-hospital outcomes, logistic generalized estimating equation regression with an exchangeable working correlation matrix (to account for within-hospital clustering of outcome) was used. This approach produces estimates that are similar to those from logistic regression with variances that are adjusted for the correlation of outcomes within a hospital.²² Covariates included in the models were based on the previously validated and published ACTION Registry in-hospital bleeding and mortality models^{23,24}: age, sex, race, weight, heart failure, cardiogenic shock and cardiac arrest on first medical contact, heart rate and systolic blood pressure on hospital admission, hypertension, diabetes mellitus, prior peripheral vascular disease, current or recent smoker, dyslipidemia, prior MI, prior PCI, prior CABG, prior heart failure, prior stroke, history of cancer, initial hemoglobin, initial serum creatinine, initial troponin ratio, and home medications (aspirin and P2Y₁₂ receptor inhibitors). In addition, the relationship between in-hospital outcomes and home anticoagulant status (home warfarin versus DOACs) among those who received home anticoagulants was investigated. Furthermore, using logistic generalized estimating equation regression, the interaction between home anticoagulant status and MI type (NSTEMI versus STEMI) was tested. Adjusted odds ratios and 95% CIs for in-hospital outcomes by home anticoagulant status were reported, for which patients with no anticoagulant were set as the reference group and patients with DOACs were set as the reference group for the analyses subset of those who received home anticoagulants. The percentage of missing data was low, <2% for most variables. For modeling, missing values of the continuous covariates were imputed to the MI type and sex-specific median of the nonmissing values. For categorical variables, missing values were imputed to the most frequent group. A $P<0.05$ was considered significant for all analyses. All statistical analyses were performed by the Duke Clinical Research Institute using SAS software (v9.4; SAS Institute).

Results

Overall Population

Of the analysis population of 26 425 acute MI patients with prior AF, 64.2% (16 961) presented with no home anticoagulant, 21.0% (5557) were on home warfarin, and 14.8% (3907) were on home DOACs (Figure 1). Of those on home DOACs,

44.3% were on apixaban, 38.7% on rivaroxaban, and 17.4% on dabigatran. Of the overall population, 6471 (24.5%) patients presented with STEMI, whereas 19 954 (75.5%) patients were admitted with NSTEMI.

STEMI Population

Of the STEMI cohort, 71.3% (4615) were not on any home anticoagulant, 15.7% (1018) were on warfarin, and 13.0% (838) were on DOACs (Table 1). Compared with those on no anticoagulant, patients on home warfarin or DOACs were older and had higher prevalence of diabetes mellitus, prior MI, prior heart failure, prior PCI or CABG, peripheral vascular disease, cerebrovascular disease, or prior stroke. The mean±SD CHA₂DS₂-VAsC score was higher in those on warfarin (4.8±1.5) and DOACs (4.5±1.5) compared with those with no anticoagulant (4.1±1.7). There was no significant difference among the 3 groups regarding symptom onset to arrival time (median ≈1.5 hours). Among patients on home warfarin, 55.2% had international normalized ratio (INR) values <2.0, 31.0% had INR values between 2.0 and 3.0, and 13.8% had INR values >3.0. Patients with no home anticoagulant were more likely to be on aspirin or DAPT at home compared with home warfarin or DOACs.

The frequency of primary PCI was higher in anticoagulant patients, whereas those with no home anticoagulant were more likely to receive thrombolytic therapy (Table 1, Figure 2). The rate of diagnostic angiography was similarly high (>98%) among the 3 anticoagulant groups, with ≈97% of patients undergoing diagnostic angiography within 24 hours. Among the primary PCI cohort, overall door-to-balloon times were slightly longer for those on warfarin or DOACs versus no home anticoagulant (median 59 or 58 minutes versus 56 minutes; $P<0.01$). Radial PCI was used in 26.1% of primary PCI, with higher frequency of radial PCI in those on home warfarin or DOACs (32.8% warfarin or 32.2% DOACs versus 23.5% with no anticoagulant; $P<0.01$). Bare metal stents were used more frequently in warfarin or DOACs patients compared with those with no anticoagulant.

Patients presenting with no home anticoagulant were more likely to receive unfractionated heparin, low-molecular-weight heparin, or glycoprotein IIb/IIIa agents during hospitalization (Figure 3). In the overall STEMI cohort, those on home warfarin or DOACs were less likely to receive prasugrel or ticagrelor within the first 24 hours compared with those with no home anticoagulant. Among those receiving primary PCI, 98% received aspirin and 93% received one of the P2Y₁₂ inhibitors within 24 hours of hospitalization, with similar rates of aspirin and P2Y₁₂ administration among the 3 groups; however, similar to the overall STEMI cohort, primary PCI patients on warfarin or DOACs were less likely to receive prasugrel or ticagrelor (Table S1).

Table 1. Baseline Characteristics and Concomitant Therapies by Home Anticoagulant Agent: STEMI Patients

Patient Characteristics	STEMI (n=6471)	No Anticoagulant (n=4615; 71.3%)	Warfarin (n=1018; 15.7%)	DOACs (n=838; 13.0%)	P Value
Baseline characteristics					
Age, y	73.0 (64.0–82.0)	72.0 (63.0–82.0)	76.0 (68.0–83.0)	74.0 (66.0–81.0)	<0.01
Female	35.9	36.0	37.1	33.9	0.34
Race/Ethnicity					0.44
White	87.1	86.9	86.2	89.3	
Black	6.7	6.8	7.5	5.6	
Asian	1.2	1.3	1.1	0.8	
Hispanic	4.0	3.9	4.4	3.5	
Body mass index, kg/m ²	28.0 (24.4–32.5)	27.7 (24.3–32.1)	28.3 (24.9–33.2)	28.8 (25.3–33.4)	<0.01
Hemoglobin, g/dL	13.8 (12.2–15.1)	13.9 (12.3–15.2)	13.5 (11.9–14.9)	13.6 (12.2–15.0)	<0.01
eGFR, mL/min/1.73 m ² †	65.2 (44.7–90.9)	66.0 (44.6–92.1)	60.2 (43.7–85.6)	68.0 (47.3–91.3)	<0.01
CHA ₂ DS ₂ -VASC score	4.3±1.7	4.1±1.7	4.8±1.5	4.5±1.5	<0.01
Medical comorbidities					
Current/recent smoker	20.6	22.6	14.8	16.2	<0.01
Hypertension	81.1	79.0	86.2	86.8	<0.01
Dyslipidemia	63.9	61.8	70.0	67.8	<0.01
Prior MI	23.5	22.6	26.3	24.7	0.03
Prior HF	19.4	16.4	27.8	25.3	<0.01
Prior PCI	26.0	23.9	30.7	31.6	<0.01
Prior CABG	11.3	10.2	13.9	14.1	<0.01
Prior stroke	12.4	10.9	16.7	15.5	<0.01
Currently on dialysis	2.5	2.6	3.4	1.2	0.01
Cerebrovascular disease	18.9	16.7	25.6	23.0	<0.01
Peripheral vascular disease	10.1	9.6	12.7	10.1	0.01
Diabetes mellitus	32.3	30.6	37.3	35.1	<0.01
Presentation characteristics					
Symptom onset to arrival, h*	1.5 (0.9–2.8)	1.5 (0.9–2.8)	1.4 (0.9–2.9)	1.5 (0.9–2.8)	0.92
HF	13.9	13.2	16.9	13.8	<0.01
Shock	13.3	13.7	13.3	11.5	0.22
Cardiac arrest	12.3	13.1	10.7	10.4	0.02
Home medications					
Aspirin	44.8	48.8	34.0	35.8	<0.01
Clopidogrel	9.8	10.3	9.7	7.5	0.05
Prasugrel	0.6	0.6	0.2	0.7	0.21
Ticagrelor	0.6	0.7	0.4	0.8	0.47
P2Y ₁₂ inhibitors	11.0	11.5	10.3	8.9	0.07
DAPT	7.5	8.5	5.3	4.7	<0.01
Procedural and reperfusion characteristics					
Diagnostic angiography†	98.5	98.4	99.1	98.5	0.29
Diagnostic angiography within 24 h†	96.6	96.7	96.4	96.4	0.81

Continued

Table 1. Continued

Patient Characteristics	STEMI (n=6471)	No Anticoagulant (n=4615; 71.3%)	Warfarin (n=1018; 15.7%)	DOACs (n=838; 13.0%)	P Value
CAD distribution					0.17
1 vessel	38.8	37.9	40.6	41.6	
2 vessels	28.7	29.1	28.0	27.6	
3 vessels	29.1	29.9	27.7	26.6	
None	3.2	3.0	3.5	3.8	
No reperfusion	17.8	17.8	19.1	16.7	0.41
Thrombolytic therapy only	4.5	5.3	2.8	2.6	<0.01
Primary PCI only	77.5	76.8	78.1	80.5	0.05
Radial PCI	26.1	23.5	32.8	32.2	<0.01
Bare metal stent	27.3	25.0	36.1	30.0	<0.01
Drug-eluting stent	73.1	75.6	64.0	70.2	<0.01
Door-to-balloon, min*	57.0 (44.0–72.0)	56.0 (43.0–71.0)	59.0 (46.0–73.0)	58.0 (46.0–73.0)	<0.01
CABG	3.7	4.0	3.0	2.5	0.05
Medications within 24 h					
Aspirin	97.2	97.4	96.6	96.7	0.38
Clopidogrel	50.4	48.2	56.0	55.6	<0.01
Prasugrel	7.7	9.1	4.7	3.9	<0.01
Ticagrelor	31.3	32.4	27.1	30.2	<0.01
P2Y ₁₂ inhibitors	83.6	83.8	82.6	84.3	0.62

Data are presented as median (interquartile range), mean±SD, or %. CAD indicates coronary artery disease; CABG, coronary artery bypass grafting; DAPT, dual antiplatelet therapy; DOACs, direct oral anticoagulants; eGFR, estimated glomerular filtration rate; HF, heart failure; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment-elevation myocardial infarction.

*Among nontransfer patients.

†Patients with contraindications for catheterization were excluded.

‡eGFR was determined with the Cockcroft-Gault formula; dialysis patients excluded from calculations.

NSTEMI Population

Of the NSTEMI cohort, 61.9% (12 346) were not on any home anticoagulant, 22.8% (4539) were on warfarin, and 15.4% (3069) were on DOACs (Table 2). Patients on home warfarin or DOACs had a higher prevalence of cardiac comorbidities. The mean±SD CHA₂DS₂-VASc score was higher in those on warfarin (5.2±1.5) or DOACs (5.0±1.5) compared with those with no anticoagulant (4.8±1.6). There was not a significant difference among the 3 groups regarding symptom onset to arrival time (median ≈2.3 hours). Among NSTEMI patients on home warfarin, 42.5% had INR values <2.0, 41.7% had INR values between 2.0 and 3.0 and 15.8% had INR values >3.0. Patients with no home anticoagulant were more likely to be on home aspirin, one of the P2Y₁₂ inhibitors, or DAPT compared with patients on home anticoagulants. Few patients (<1%) were on home prasugrel or ticagrelor.

Patients on home warfarin or DOACs had longer arrival to coronary angiography times and were less likely to undergo urgent coronary angiography compared with those with no home anticoagulant, with lower rates of angiography within

24 and 48 hours. PCI was performed in 39.7% and CABG in 6.8% of NSTEMI patients. PCI rates were lower in those on home warfarin or DOACs than those not on home anticoagulant (PCI within 24 hours: 14.3% warfarin, 15.9% DOACs, 21.1% no anticoagulant; *P*<0.01; PCI within 48 hours: 24.5% warfarin, 28.3% DOACs, 30.9% no anticoagulant; *P*<0.01; Figure 2). Overall, 32% of PCIs were performed radially, with greater frequency of radial PCI in those admitted on warfarin or DOACs than those not on home anticoagulant (33.9% warfarin, 36.0% DOACs, 30.6% no anticoagulant; *P*<0.01).

Patients with no home anticoagulant were more likely to be treated with unfractionated or low-molecular-weight heparin during hospitalization (Figure 4). Utilization of glycoprotein IIb/IIIa agents was low overall (5%), with less utilization by those on home warfarin or DOACs. In the NSTEMI cohort, clopidogrel was used in 33.2%, prasugrel in 1.9% and ticagrelor in 6.9% of patients within the first 24 hours (Table 2). Among the NSTEMI cohort undergoing an invasive strategy, aspirin, clopidogrel, prasugrel, and ticagrelor were administered more often within the first 24 hours in those

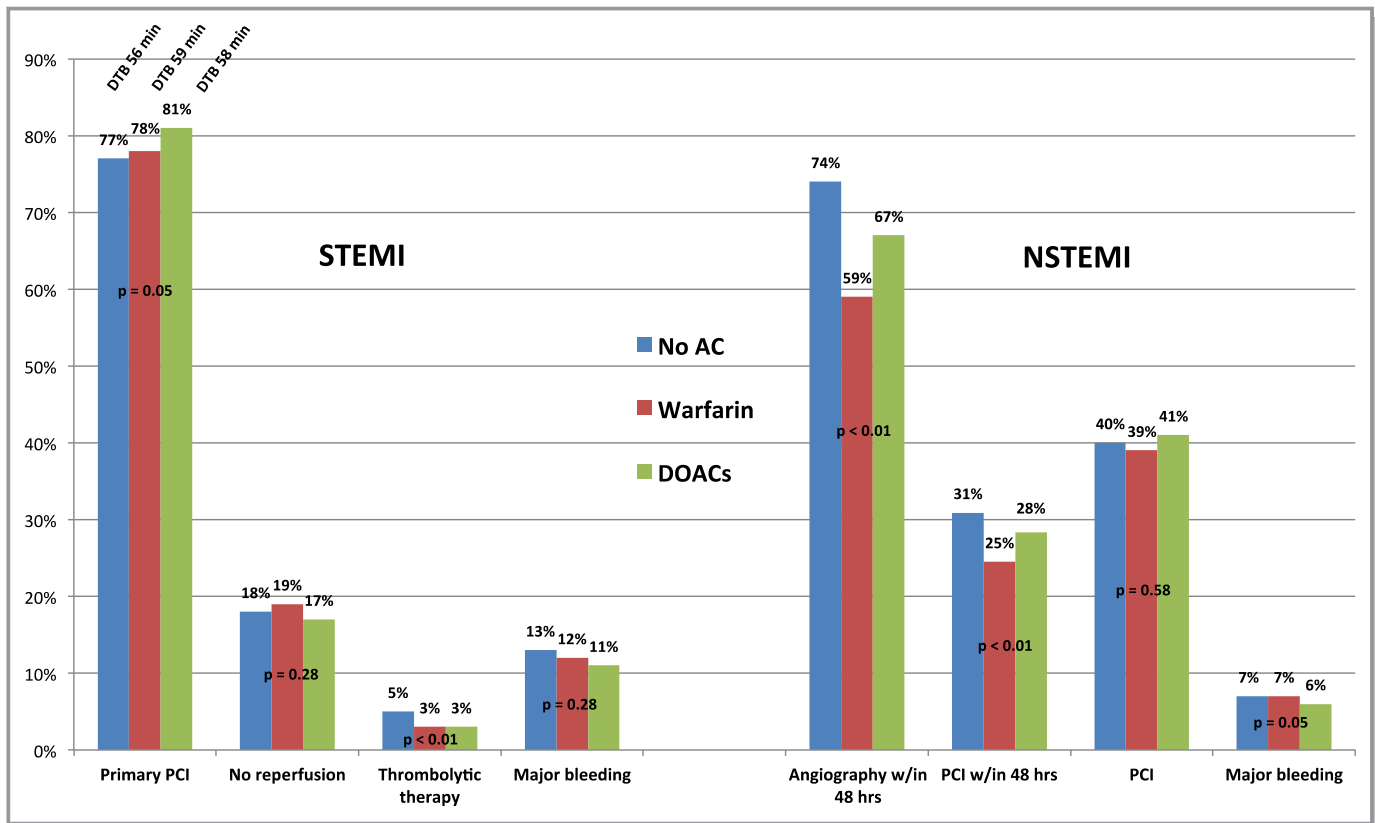


Figure 2. Therapeutic strategy and major bleeding according to home anticoagulant status in STEMI and NSTEMI. AC indicates anticoagulation; DOACs, direct oral anticoagulants; DTB, door-to-balloon time; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction.

with no home anticoagulant compared with those on home anticoagulants (Table S2).

In-Hospital Bleeding

In the STEMI cohort, 12.8% experienced major bleeding, and there were no significant differences in in-hospital major bleeding rates among the 3 groups (13.2% no anticoagulant, 12.4% warfarin, 11.2% DOACs; $P=0.28$; Figure 2). Similarly, there were no differences in major bleeding rates among patients undergoing primary PCI (13.2% no anticoagulant, 13.0% warfarin, 11.6% DOACs; $P=0.57$) or those receiving thrombolytic therapy (18.8% no anticoagulant, 14.8% warfarin, 14.3% DOACs, $P=0.78$). Among STEMI patients on warfarin, bleeding rates were 11.2% for INR <2.0 , 14.1% for INR 2.0 to 3.0, and 15.7% for INR >3.0 . After multivariate adjustment (Table 3), no statistically significant association remained between in-hospital bleeding and home anticoagulant status in the STEMI cohort. Among patients on home anticoagulants, there were no differences between home warfarin and home DOACs with regard to bleeding (Table S3).

In the NSTEMI cohort, major bleeding occurred in 6.6% of patients, and there was a trend toward less major bleeding in those on home DOACs (6.7% no anticoagulant, 7.0% warfarin,

5.6% DOACs; $P=0.05$; Figure 2). In the NSTEMI cohort treated with an invasive strategy, there was a statistically significant difference in bleeding rates (6.0% no anticoagulant, 6.6% warfarin, 3.8% DOACs; $P<0.01$), whereas in the patients treated with a conservative strategy, there was a trend toward fewer bleeding events in the DOAC group (9.2% no anticoagulant, 8.0% warfarin, 6.6% DOACs; $P=0.07$). No differences in overall red cell transfusion or non-CABG red cell transfusion rates were observed among the 3 groups. Among NSTEMI patients on warfarin, bleeding rates were 6.4% for INR <2.0 , 6.2% for INR 2.0 to 3.0, and 10.3% for INR >3.0 . After multivariate adjustment for baseline differences, there was no statistically significant association between major bleeding and home anticoagulant status in the NSTEMI cohort (Table 3). Bleeding rates were overall higher with femoral versus radial access, without significant differences in bleeding between no home anticoagulant, warfarin or DOACs within each access stratum in STEMI and NSTEMI (Table S4).

In-Hospital Mortality

The overall in-hospital mortality in STEMI was 14.4%. There was a significant difference in all-cause mortality among the 3 home anticoagulant groups (14.9% no anticoagulant, 14.7% warfarin, 10.8% DOACs; $P<0.01$). After multivariate adjustment, there

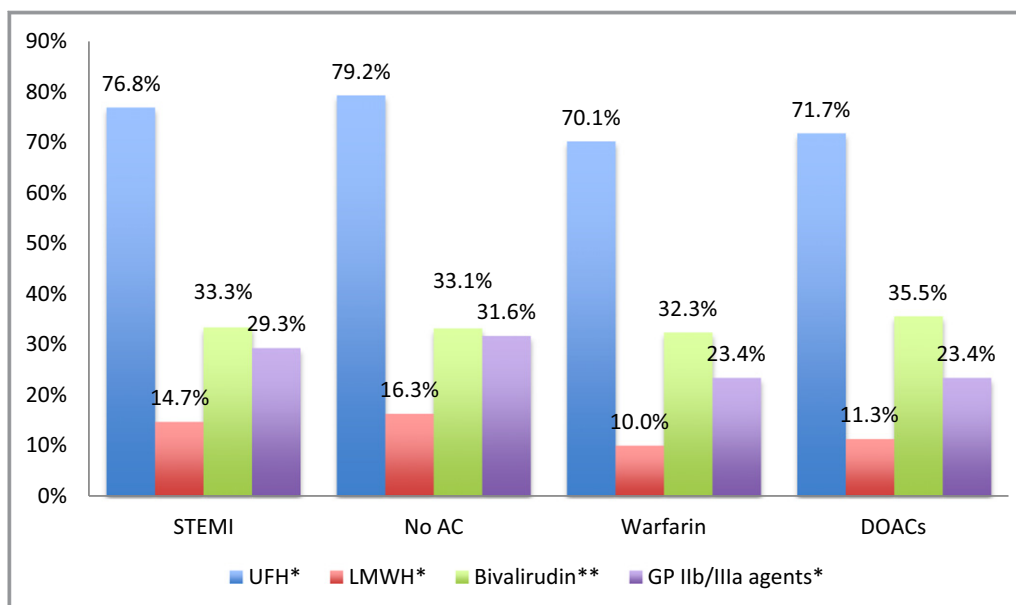


Figure 3. Anticoagulant use during hospitalization according to home anticoagulant status in STEMI. * $P<0.01$; ** $P=0.32$. AC indicates anticoagulation; DOACs, direct oral anticoagulants; GP, glycoprotein; LMWH, low-molecular-weight heparin; STEMI, ST-segment-elevation myocardial infarction; UFH, unfractionated heparin.

remained a significant difference between in-hospital mortality in STEMI, with lower mortality in the home warfarin group versus no anticoagulant and lower mortality in the DOAC group versus no anticoagulant (Table 3). However, there were no differences between home warfarin and home DOACs regarding mortality after adjusting for patient characteristics (Table S3).

The observed overall in-hospital mortality with NSTEMI was 5.6%, and there was a significant difference in all-cause mortality among the 3 home anticoagulant groups (6.1% no anticoagulant, 5.5% warfarin, 3.7% DOACs; $P<0.01$). After multivariate adjustment, there remained a significant difference between in-hospital mortality and home anticoagulant status in NSTEMI, with lower mortality in the home warfarin group versus no anticoagulant and lower mortality in the home DOAC group versus no anticoagulant (Table 3). There was a trend toward lower mortality favoring DOACs over warfarin after adjusting for patient characteristics (odds ratio: 0.79; 95% CI, 0.62–1.01; Table S3).

Other In-Hospital Outcomes

In the STEMI cohort, the rate of stroke was similar in the 3 groups (1.8% no anticoagulant, 1.2% warfarin, 1.6% DOACs; $P=0.45$). The mean length of stay was slightly longer in patients on home warfarin (mean: 5.0 ± 5.6 days with no anticoagulant, 5.4 ± 5.9 days with warfarin, 5.0 ± 5.0 days with DOACs; $P=0.02$). In the NSTEMI cohort, the rate of in-hospital stroke was lower in those on home warfarin or DOACs (0.6% warfarin, 0.7% DOACs, 1.0% no anticoagulant;

$P=0.03$) than those with no home anticoagulant. The length of stay was slightly longer in patients on home warfarin (mean: 5.3 ± 5.6 days with no anticoagulant, 5.6 ± 4.7 days with warfarin, 5.1 ± 4.7 days with DOACs; $P<0.01$).

Discussion

Several important and novel findings resulted from this large contemporary observational study of a national multicenter MI registry. First, 9% of patients presenting with MI have a reported history of prior AF, with the majority (>64%) not treated with home anticoagulant. Approximately 15% of AF patients presenting with MI were on one of 3 DOACs between 2015 and 2016. Second, 78% of STEMI patients are treated with primary PCI, and those on home warfarin or DOACs are managed similarly to those with no anticoagulant at presentation, without a clinically significant delay in primary PCI. In contrast, NSTEMI patients on home warfarin or DOACs are less likely to undergo urgent angiography or PCI within 24 to 48 hours of admission compared with patients without home anticoagulant. Third, home warfarin or DOAC use was not associated with increased risk of in-hospital major bleeding compared with no home anticoagulant in both STEMI and NSTEMI cohorts. Finally, home anticoagulant with warfarin and particularly with home DOAC therapy is associated with a reduced risk of in-hospital death compared with no home anticoagulant.

Unlike the STEMI cohort, the NSTEMI patients on warfarin or DOACs experienced a delay in coronary angiography or PCI and had lower utilization of angiography and PCI within 24 and

Table 2. Baseline Characteristics and Concomitant Therapies by Home Anticoagulant Agent: NSTEMI Patients

Patient Characteristics	NSTEMI (n=19 954)	No Anticoagulant (n=12 346; 61.9%)	Warfarin (n=4539; 22.8%)	DOACs (n=3069; 15.4%)	P Value
Baseline characteristics					
Age, y	76.0 (67.0–83.0)	75.0 (67.0–83.0)	78.0 (70.0–84.0)	75.0 (68.0–82.0)	<0.01
Female	38.6	39.3	36.9	38.4	0.02
Race/Ethnicity					<0.01
White	86.6	85.6	88.6	87.4	
Black	7.5	8.2	6.0	7.2	
Asian	1.2	1.3	1.0	1.2	
Hispanic	3.6	3.8	3.1	3.4	
Body mass index, kg/m ²	28.2 (24.6–32.9)	28.0 (24.3–32.6)	28.5 (24.8–33.3)	28.7 (25.2–33.5)	<0.01
Hemoglobin, g/dL	13.0 (11.5–14.5)	13.1 (11.5–14.6)	12.9 (11.3–14.3)	13.0 (11.5–14.4)	<0.01
eGFR, mL/min/1.73 m ² †	59.0 (40.5–83.8)	59.8 (40.1–85.4)	55.2 (39.1–78.0)	62.1 (43.7–86.9)	<0.01
CHA ₂ DS ₂ -VASc score	4.9±1.6	4.8±1.6	5.2±1.5	5.0±1.5	<0.01
Medical comorbidities					
Current/recent smoker	14.8	16.9	10.3	12.9	<0.01
Hypertension	89.4	88.0	91.5	91.9	<0.01
Dyslipidemia	73.6	71.5	77.3	77.0	<0.01
Prior MI	33.0	32.5	35.0	32.5	<0.01
Prior HF	35.8	32.0	44.5	37.9	<0.01
Prior PCI	33.5	32.2	35.3	35.9	<0.01
Prior CABG	25.7	24.2	30.0	25.0	<0.01
Prior stroke	15.9	14.3	19.4	17.0	<0.01
Currently on dialysis	5.2	5.7	6.1	2.0	<0.01
Cerebrovascular disease	25.4	23.3	29.6	27.7	<0.01
Peripheral vascular disease	15.9	15.2	17.7	15.8	<0.01
Diabetes mellitus	43.2	41.3	46.6	45.5	<0.01
Presentation characteristics					
Symptom onset to arrival, h*	2.3 (1.2–5.2)	2.3 (1.2–5.1)	2.4 (1.2–5.4)	2.3 1.3–5.2)	0.26
HF	26.5	25.6	29.7	25.1	<0.01
Shock	2.2	2.5	2.1	1.3	<0.01
Cardiac arrest	2.4	2.6	2.2	1.8	0.03
Home medications					
Aspirin	56.0	62.5	46.6	43.8	<0.01
Clopidogrel	16.7	19.8	12.4	11.0	<0.01
Prasugrel	0.6	0.7	0.3	0.5	<0.01
Ticagrelor	0.7	0.9	0.4	0.7	<0.01
P2Y ₁₂ inhibitors	18.0	21.3	13.0	12.1	<0.01
DAPT	12.6	16.3	6.9	5.9	<0.01
In-hospital procedural characteristics					
Arrival to diagnostic angiography, h	28.2 (16.0–52.2)	25.0 (14.1–46.5)	41.0 (20.2–68.3)	33.2 (19.5–54.8)	<0.01
Diagnostic angiography†	93.6	94.0	92.9	93.2	0.05
Diagnostic angiography within 24 h†	43.7	49.3	33.4	36.4	<0.01

Continued

Table 2. Continued

Patient Characteristics	NSTEMI (n=19 954)	No Anticoagulant (n=12 346; 61.9%)	Warfarin (n=4539; 22.8%)	DOACs (n=3069; 15.4%)	P Value
Invasive strategy (angiography within 48 h) [†]	69.5	74.1	58.7	67.0	<0.01
CAD distribution					0.01
1 vessel	23.7	23.7	22.6	25.5	
2 vessels	24.5	24.5	24.5	24.2	
3 vessels	41.1	41.4	42.3	38.2	
None	10.6	10.3	10.6	12.0	
PCI	39.7	39.6	39.4	40.5	0.58
Radial PCI	32.2	30.6	33.9	36.0	<0.01
Bare metal stent	18.9	16.3	24.0	21.6	<0.01
Drug-eluting stent	81.6	84.3	76.4	78.6	<0.01
CABG	6.8	7.4	5.3	6.4	<0.01
Medications within 24 h					
Aspirin	96.2	96.9	95.1	95.1	<0.01
Clopidogrel	33.2	36.4	28.3	27.3	<0.01
Prasugrel	1.9	2.3	0.8	1.5	<0.01
Ticagrelor	6.9	7.8	4.9	6.1	<0.01
P2Y ₁₂ inhibitors	40.4	44.8	32.8	33.9	<0.01

Data are presented as median (interquartile range), mean±SD, or %. CAD indicates coronary artery disease; CABG, coronary artery bypass grafting; DAPT, dual antiplatelet therapy; DOACs, direct oral anticoagulants; eGFR, estimated glomerular filtration rate; HF, heart failure; MI, myocardial infarction; NSTEMI, non-ST-segment-elevation myocardial infarction; PCI, percutaneous coronary intervention.

*Among nontransfer patients.

[†]Patients with contraindications for catheterization were excluded.

[‡]eGFR was determined with Cockcroft-Gault formula; dialysis patients excluded from calculations.

48 hours. A delay in coronary angiography might be reasonable for low-risk ACS patients, whereas high-risk patients might benefit from more urgent revascularization.²⁵ Furthermore, the lack of difference in bleeding outcomes in studies of fully anticoagulated patients^{26,27} and in our STEMI cohort suggests that urgent revascularization in fully anticoagulated NSTEMI patients on warfarin or DOACs could be safely performed.

Utilization of Anticoagulation and DOACs

DOACs have been increasingly adopted in clinical practice^{28–30} because they overcome many of the limitations of warfarin therapy, including warfarin's narrow therapeutic range, drug–drug and drug–food interactions, need for frequent monitoring, delayed onset/offset, and higher bleeding risk. Clinical trials of the 4 available DOACs have demonstrated efficacy similar to warfarin (rivaroxaban or edoxaban) or improved (dabigatran or apixaban) for stroke and systemic embolism prevention and have been associated with similar (dabigatran, rivaroxaban) or lower (apixaban, edoxaban) rates of major bleeding and lower rates of intracranial hemorrhage than warfarin in patients with

nonvalvular AF.^{7–10,31} Given the improved safety profile of DOACs, replacing warfarin with DOACs seems reasonable, particularly in patients requiring concomitant antiplatelet therapy. In a recent meta-analysis, DOACs were more effective in reducing stroke or systemic embolism and safer with respect to the reduction of intracranial hemorrhage in nonvalvular AF patients treated with concomitant aspirin.³² Despite this accruing evidence, our data show that DOAC utilization in the community is low in patients presenting with MI (15% of AF patients), although it is approaching that of warfarin (21% of AF patients). In fact, the majority of AF patients in this study were not on any oral anticoagulant, despite high CHA₂DS₂-VASC scores (mean: 4.7±1.6). Underutilization of oral anticoagulants and leveling off of warfarin and DOACs in the community might explain a lack of decline in AF-related strokes between 2000 and 2010 seen in population studies.³³ More recent US studies have shown a promising but slow increase in anticoagulant rates since the introduction of DOACs.^{28,29} It is alarming that ≈65% of patients presenting with MI, despite high CHA₂DS₂-VASC scores, are currently not being anticoagulated in the community. Further efforts to identify AF patients, to guide

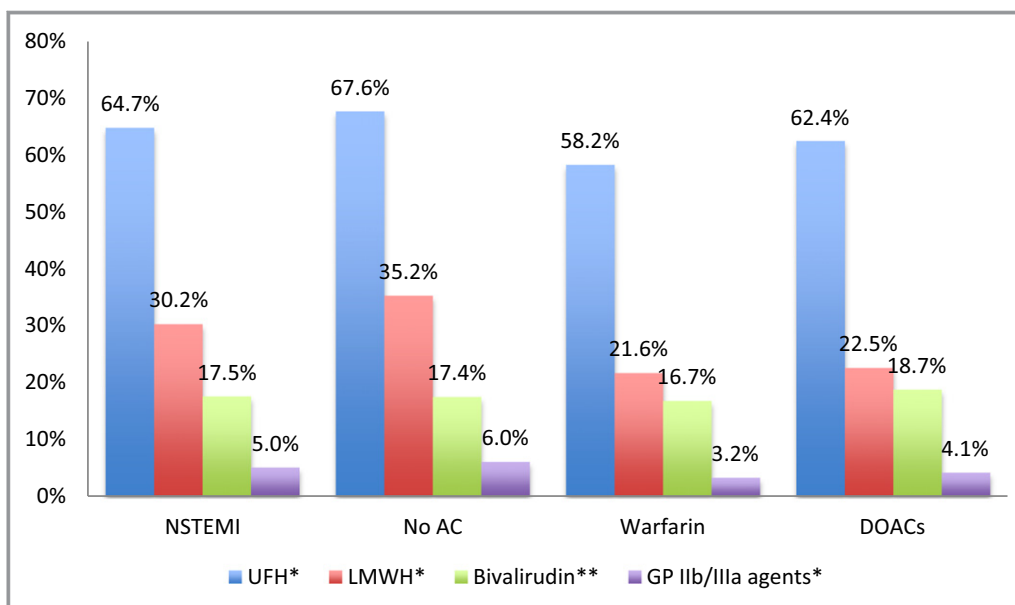


Figure 4. Anticoagulant use during hospitalization according to home anticoagulant status in NSTEMI. * $P < 0.01$; ** $P = 0.09$. AC indicates anticoagulation; DOACs, direct oral anticoagulants; GP, glycoprotein; LMWH, low-molecular-weight heparin; NSTEMI, non-ST-segment-elevation myocardial infarction; UFH, unfractionated heparin.

proper patient selection for anticoagulants, and to expand the utilization of anticoagulants for AF are needed.

In-Hospital Bleeding

Clinical guidelines for management of MI are based on randomized trials that have largely excluded patients on chronic warfarin or DOAC therapy.³⁴ The clinical dilemma for

AF patients requiring urgent or emergent PCI includes how to choose between acute antithrombotic therapies while carefully balancing the risks of bleeding and ischemic events. A higher risk of bleeding has been described early after MI and PCI in patients with AF on warfarin,^{17,19} whereas such data in the era of DOACs are lacking. One of our key findings is that patients with STEMI on warfarin or DOACs receive reperfusion therapy without clinically significant delay in door-to-balloon times and, importantly, without increase in in-hospital bleeding. Similarly, prior analysis of the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA Guidelines) registry suggested that in patients with non-ST-segment-elevation ACS on home warfarin, the adjusted risk of major bleeding was similar to that of nonanticoagulated patients (odds ratio: 1.02; 95% CI, 0.93–1.11).³⁵ A meta-analysis of primarily observational studies suggests that coronary angiography and PCI can be safely performed on uninterrupted anticoagulation with warfarin.²⁶ However, prior studies of MI patients with AF lack data on frequency of subtherapeutic INR levels.³⁵ Notably in our study, 55% of STEMI and 43% of NSTEMI patients presenting on warfarin had INR values < 2.0 , which is consistent with subtherapeutic INR levels in population studies of patients on warfarin presenting to emergency departments.²⁷ Importantly, our data provide further insight regarding acute hemorrhagic risks in vulnerable MI patients, with novel evidence for those on home DOACs. Given the underlying concerns about

Table 3. Adjusted Association Between Home Anticoagulation Status and In-Hospital Major Bleeding and Mortality (No Home Anticoagulation as Reference)

Outcome	Anticoagulation Status	Adjusted OR	
		OR (95% CI)	Global P Value
Major bleeding (STEMI)*	Warfarin	1.00 (0.79–1.27)	0.87
	DOACs	0.93 (0.73–1.20)	
Major bleeding (NSTEMI)*	Warfarin	1.13 (0.97–1.30)	0.21
	DOACs	0.97 (0.81–1.16)	
Mortality (STEMI)†	Warfarin	0.78 (0.61–1.00)	< 0.01
	DOACs	0.61 (0.46–0.81)	
Mortality (NSTEMI)†	Warfarin	0.82 (0.68–0.97)	< 0.01
	DOACs	0.67 (0.54–0.83)	

DOACs indicates direct oral anticoagulants; MI, myocardial infarction; NSTEMI, non-ST-segment-elevation myocardial infarction; OR, odds ratio; STEMI, ST-segment-elevation myocardial infarction.

*Adjusted $P = 0.68$ for interaction between home anticoagulant and MI type.

†Adjusted $P = 0.95$ for interaction between home anticoagulant and MI type.

performing procedures on fully anticoagulated patients, it is reassuring to demonstrate a lack of increased bleeding with uninterrupted DOACs. Recent data suggest that performing other invasive cardiovascular procedures in AF patients might also be safer with uninterrupted DOAC therapy. In patients undergoing AF ablation in the RE-CIRCUIT (Randomized Evaluation of Dabigatran Etxilate Compared to Warfarin in Pulmonary Vein Ablation: Assessment of an Uninterrupted Periprocedural Anticoagulation Strategy) trial, anticoagulation with uninterrupted dabigatran was associated with fewer bleeding complications than uninterrupted warfarin.³⁶

In-Hospital Mortality

The finding of lower in-hospital mortality in MI patients with AF on home warfarin or DOACs is intriguing and might be related to early and effective inhibition of thrombin formation with anticoagulation. In the setting of ACS, AF patients have been shown to have poorer reperfusion of the infarct-related artery compared with those without AF, potentially contributing to higher mortality among AF patients.³⁷ Consequently, direct and selective inhibition of factor Xa with DOACs, which target the final common pathway of the coagulation cascade as well as platelet activation, could potentially contribute to early mortality benefits. However, the observed findings of improved mortality might be secondary to anticoagulant selection bias, as well as differences in presenting characteristics (eg, frailty) and patient-specific modifications in management of fully anticoagulated patients. Among NSTEMI patients, for instance, those without home anticoagulants were more likely to present with cardiogenic shock or cardiac arrest compared with those on home anticoagulants, factors known to be associated with poor survival. In contrast, anticoagulated patients were more likely to have PCI performed via the radial access and receive fewer glycoprotein IIb/IIIa agents, factors that lead to lower in-hospital bleeding and have an impact on short-term mortality.^{38,39} Interestingly, in the non-ST-segment-elevation ACS cohort of the CRUSADE registry, anticoagulated patients had a trend toward lower adjusted odds of in-hospital mortality (odds ratio: 0.90; 95% CI, 0.80–1.02) compared with nonanticoagulated patients.³⁵ Recent randomized trials of AF and PCI have not demonstrated a clear short-term mortality advantage of DOACs versus warfarin therapy.^{40–42} The ATLAS ACS 2–TIMI 51 (Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome–Thrombolysis in Myocardial Infarction 51) trial has shown a long-term mortality difference in favor of a low dose of rivaroxaban plus DAPT,⁴⁰ whereas other randomized clinical trials have not demonstrated any mortality advantage of DOAC therapy.^{41,42} Further studies would be needed to demonstrate whether significant differences exist

in in-hospital outcomes in fully anticoagulated patients on warfarin or DOACs undergoing urgent invasive procedures.

Transradial Versus Transfemoral Access

As expected, clinicians modify their approach to management of anticoagulated AF patients with MI. This was noted in a recent analysis of the NCDR ACTION Registry, in which patients with AF meeting indications for anticoagulation were more likely to receive bare metal stents than drug-eluting stents—presumably because of the shorter duration of P2Y₁₂ inhibition required after bare metal stent.⁴³ Similarly, in our analysis, anticoagulated patients were more likely to receive bare metal stents and less likely to receive glycoprotein IIb/IIIa inhibitors. Furthermore, despite persistent underutilization of the transradial approach to PCI in the United States (only 30% of patients in this analysis), it is apparent that interventionalists are more amenable to performing transradial primary PCI in AF patients on oral anticoagulants than in those with no anticoagulation (24% with no anticoagulant versus 33% on warfarin or 32% on DOACs). Transradial access for STEMI has steadily increased in the United States, from 2% to 23% between 2009 and 2015⁴⁴; however, utilization of the transradial approach still lags substantially behind that of other developed countries, where transradial PCI is used in >50% of STEMI cases.⁴⁵ Multiple studies have demonstrated that the greatest benefit of transradial PCI, in terms of reduction in bleeding and vascular complications, has been observed in high-risk patients with ACS, for which, paradoxically, its utilization has been the lowest.⁴⁶ Interestingly, the lowest bleeding rates in our study were seen in those on home DOACs undergoing procedures through transradial access. The transradial approach to primary PCI in STEMI has been associated with a decrease in mortality compared with transfemoral PCI in both observational and randomized studies.³⁹ Prevention of access-site bleeding has been postulated to be an important mechanism through which transradial PCI reduces mortality. Wider adoption of transradial PCI in interventional practice, particularly in STEMI patients on warfarin or DOACs, presents an opportunity to potentially improve overall PCI safety and lower bleeding rates.

Limitations

Several limitations of this study should be recognized. First, data regarding provider rationale for AF treatment choices (eg, timing, type, or duration of AF; patient bleeding risk; fall risk) were lacking. Furthermore, data regarding in-hospital anticoagulant management (eg, whether warfarin or DOACs were stopped or interrupted periprocedurally) were not recorded in the database. Second, selection bias for home anticoagulant strategy and residual confounding cannot be ruled out as an explanation for some observed outcomes, particularly

in-hospital mortality. Although we attempted to address this by adjusting for a broad range of patient-level clinical factors, the possibility of confounding by unmeasured covariates remains. Third, the ACTION Registry collects data from ≈70% of hospitals in the United States; therefore, this report might not be representative of all hospitals in the United States. In addition, only a proportion of the collected data are audited, raising the potential for inaccurate data collection. However, we would expect such data to be distributed equally among the groups. Finally, the study did not have an adequate sample size to compare different DOACs or different combinations of oral anticoagulants and antiplatelet regimens.

Conclusions

This analysis of the largest contemporary US multicenter MI registry shows that the majority of MI patients with prior AF are not on home oral anticoagulants, whereas 15% present on DOACs. STEMI patients on home warfarin or DOACs undergo primary PCI without a clinically significant delay. Conversely, NSTEMI patients on home warfarin or DOACs are less likely to undergo urgent angiography or PCI within 24 and 48 hours of admission compared with patients without home anticoagulant. In patients presenting with MI and prior history of AF, home warfarin or DOAC therapy is not associated with an increased risk of in-hospital bleeding and might be associated with a reduced risk of death compared with no anticoagulant. These data suggest that in-hospital outcomes of STEMI and NSTEMI patients with AF are not negatively affected by home warfarin or DOAC therapy despite the perceived high bleeding risk.

Author Contributions

Dr Feldman had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study Concept and design: Feldman, Madias; Acquisition of Data: Chen; Statistical Analysis: Chen; Analysis and interpretation of data: Feldman, Madias; Drafting of the article: Feldman, Wang, Chen, Swaminathan, Madias; Critical revision of the article for important intellectual content: Feldman, Wang, Chen, Swaminathan, Kim, Wong, Minutello, Bergman, Singh, Madias; Study Supervision: Feldman, Madias.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. Medications Administered Within 24 Hours by Home Anticoagulant Agent and Reperfusion Strategy: STEMI patients.

Patient Characteristics*	STEMI	No AC	Warfarin	DOACs	p Value
<i>Primary PCI</i> (n=5,013)					
Aspirin	97.8	98.0	97.3	97.4	0.46
Clopidogrel	52.9	50.0	60.2	60.0	<0.01
Prasugrel	9.4	11.2	5.8	4.5	<0.01
Ticagrelor	37.0	38.6	31.7	34.8	<0.01
P2Y ₁₂ inhibitors	92.7	92.7	92.2	93.1	0.84
Unfractionated heparin	77.2	79.3	71.2	73.0	<0.01
Low molecular weight heparin	13.7	15.3	9.2	10.6	<0.01
Bivalirudin	39.5	39.3	38.6	41.7	0.43
GP IIb/IIIa inhibitor	35.1	38.3	28.1	26.9	<0.01
<i>Thrombolytic therapy</i> (n=294)					
Aspirin	97.2	97.1	96.2	100.0	0.69
Clopidogrel	66.0	63.2	88.9	68.2	0.03
Prasugrel	4.1	4.6	3.7	0.0	0.58
Ticagrelor	16.9	18.3	11.1	9.1	0.38
P2Y ₁₂ inhibitors	82.4	81.3	96.3	77.3	0.12
Unfractionated heparin	89.7	90.5	85.7	86.4	0.63
Low molecular weight heparin	18.2	19.4	14.3	9.1	0.41
Bivalirudin	22.6	24.0	17.9	13.6	0.44
GP IIb/IIIa inhibitor	16.0	16.3	14.8	14.3	0.95

* Data are presented as %.

AC=anticoagulation; DOACs=direct oral anticoagulants; GP=glycoprotein; PCI=percutaneous coronary intervention; and STEMI=ST-segment elevation myocardial infarction.

Table S2. Medications Administered Within 24 Hours by Home Anticoagulant Agent and Treatment Strategy: NSTEMI patients.

Patient Characteristics*	NSTEMI	No AC	Warfarin	DOACs	p Value
<i>Invasive strategy</i> <i>(n=10,938)</i>					
Aspirin	97.5	98.1	96.3	96.5	<0.01
Clopidogrel	38.9	40.5	37.5	33.7	<0.01
Prasugrel	3.0	3.6	1.5	2.4	<0.01
Ticagrelor	10.7	11.5	9.0	9.2	<0.01
P2Y ₁₂ inhibitors	50.5	53.3	46.0	44.0	<0.01
Unfractionated heparin	73.2	74.5	70.0	71.7	<0.01
Low molecular weight heparin	29.5	33.6	21.8	21.2	<0.01
Bivalirudin	23.9	24.1	22.5	24.5	0.23
GP IIb/IIIa inhibitor	8.5	9.5	6.6	6.9	<0.01
<i>Conservative strategy</i> <i>(n=4,758)</i>					
Aspirin	94.4	94.8	94.4	92.7	0.09
Clopidogrel	25.7	29.9	21.5	20.3	<0.01
Prasugrel	0.6	0.9	0.4	0.5	0.14
Ticagrelor	2.5	3.0	1.5	2.7	0.02
P2Y ₁₂ inhibitors	28.3	33.2	22.9	23.1	<0.01
Unfractionated heparin	61.4	64.0	58.2	59.1	<0.01
Low molecular weight heparin	32.0	38.8	23.0	26.4	<0.01
Bivalirudin	17.0	15.4	19.0	18.4	<0.01
GP IIb/IIIa inhibitor	1.0	1.5	0.3	0.9	<0.01

*Data are presented as %.

AC=anticoagulation; DOACs=direct oral anticoagulants; GP=glycoprotein; PCI=percutaneous coronary intervention; and NSTEMI = non-ST-segment elevation myocardial infarction.

Table S3. Adjusted Association Between Home Anticoagulation Status and In-Hospital Major Bleeding and Mortality among Patients Received Home Anticoagulation (Warfarin as Reference).

Outcome	Anticoagulation Status	Adjusted Odds Ratio	
		OR (95% CI)	p Value
Major bleeding (STEMI)*	DOACs	0.95 (0.68-1.33)	0.77
Major bleeding (NSTEMI)*	DOACs	0.86 (0.70-1.06)	0.17
Mortality (STEMI)**	DOACs	0.77 (0.56-1.06)	0.11
Mortality (NSTEMI)**	DOACs	0.79 (0.62-1.01)	0.06

* Adjusted p-values (interaction between homeACs and MI type) = 0.65

** Adjusted p-values (interaction between homeACs and MI type) = 0.83

CI = confidence interval; DOACs = direct oral anticoagulants; NSTEMI = non-ST-segment elevation myocardial infarction; OR = odds ratio; and STEMI = ST-segment elevation myocardial infarction.

Table S4. In-Hospital Major Bleeding Rates Stratified by Access Site (Radial versus Femoral).

Major Bleeding	STEMI	No AC	Warfarin	DOACs	p Value
Radial access (%)	9.7	10.6	8.4	7.7	0.32
Femoral access (%)	14.8	14.9	15.7	13.7	0.67
Major Bleeding	NSTEMI	No AC	Warfarin	DOACs	p Value
Radial access (%)	5.3	5.3	6.5	3.6	0.11
Femoral access (%)	8.9	8.9	10.0	7.0	0.07

AC=anticoagulation; DOACs=direct oral anticoagulants; NSTEMI = non-ST-segment elevation myocardial infarction; and STEMI=ST-segment elevation myocardial infarction.