University of Massachusetts Medical School eScholarship@UMMS

Population and Quantitative Health Sciences Publications

Population and Quantitative Health Sciences

2018-02-28

Recent Trends in Oral Anticoagulant Use and Post-Discharge Complications Among Atrial Fibrillation Patients with Acute Myocardial Infarction

Amartya Kundu University of Massachusetts Medical School

Et al.

Let us know how access to this document benefits you.

Follow this and additional works at: https://escholarship.umassmed.edu/qhs_pp

Commons, Epidemiology Commons, Cardiovascular Diseases Commons, Clinical Epidemiology Commons, Epidemiology Commons, and the Health Services Administration Commons

Repository Citation

Kundu A, Day KO, Lessard DM, Gore JM, Yu H, Akhter MW, Fisher DZ, Hayward RM, Henninger N, Kapoor A, Yarzebski JL, Goldberg RJ, McManus DD. (2018). Recent Trends in Oral Anticoagulant Use and Post-Discharge Complications Among Atrial Fibrillation Patients with Acute Myocardial Infarction. Population and Quantitative Health Sciences Publications. https://doi.org/10.4022/jafib.1749. Retrieved from https://escholarship.umassmed.edu/qhs_pp/1212

This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in Population and Quantitative Health Sciences Publications by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.



Original Research

Journal of Atrial Fibrillation



www. jafib.com

Recent Trends In Oral Anticoagulant Use and Post-Discharge Complications Among Atrial Fibrillation Patients With Acute Myocardial Infarction

Amartya Kundu¹, Kevin O'Day², Darleen M. Lessard³, Joel M. Gore¹, Steven A. Lubitz⁴, Hong Yu³, Mohammed W. Akhter¹ Daniel Z. Fisher¹, Robert M. Hayward Jr.¹, Nils Henninger⁵, Jane S. Saczynski⁶, Allan J. Walkey⁷, Alok Kapoor², Jorge Yarzebski³, Robert J. Goldberg³, David D. McManus¹

¹Department of Cardiology, University of Massachusetts Medical School, Worcester, MA, USA.

²Department of Medicine, University of Massachusetts Medical School, Worcester, MA, USA.

³Department of Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, MA, USA.

⁴Cardiac Arrhythmia Service, Massachusetts General Hospital, Boston, MA, USA.

⁵Department of Neurology, University of Massachusetts Medical School, Worcester, MA, USA

⁶Department of Pharmacy and Health System Sciences, Northeastern University, Boston, MA, USA.

⁷Department of Medicine, Boston University School of Medicine, Boston, MA, USA.

Abstract

Background: Atrial fibrillation (AF) is a common complication of acute myocardial infarction (AMI). The CHA₂DS₂VASc and CHADS₂risk scores are used to identify patients with AF at risk for stroke and to guide oral anticoagulants (OAC) use, including patients with AMI. However, the epidemiology of AF, further stratified according to patients' risk of stroke, has not been well characterized among those hospitalized for AMI.

Methods: We examined trends in the frequency of AF, rates of discharge OAC use, and post-discharge outcomes among 6,627 residents of the Worcester, Massachusetts area who survived hospitalization for AMI at 11 medical centers between 1997 and 2011.

Results: A total of 1,050AMI patients had AF (16%) and the majority (91%) had a CHA_2DS_2VASc score >2.AF rates were highest among patients in the highest stroke risk group. In comparison to patients without AF, patients with AMI and AF in the highest stroke risk category had higher rates of post-discharge complications, including higher 30-day re-hospitalization [27 % vs. 17 %], 30-day post-discharge death [10 % vs. 5%], and 1-year post-discharge death [46 % vs. 18 %] (p<0.001 for all). Notably, fewer than half of guideline-eligible AF patients received an OAC prescription at discharge. Usage rates for other evidence-based therapies such as statins and beta-blockers, lagged in comparison to AMI patients free from AF.

Conclusion: Our findings highlight the need to enhance efforts towards stroke prevention among AMI survivors with AF.

Introduction

Atrial fibrillation (AF) is a cardiac arrhythmia that affects thousands of hospitalized Americans, with an increasing prevalence in the United States^{[1],[2]}. Atrial fibrillation is frequently observed as a complication of acute myocardial infarction (AMI), affecting 5-13% of all patients suffering an AMI^{[3]-[7]}. New-onset and prevalent AF is not only associated with higher rates of in-hospital complications such as heart failure, stroke, and death^{[7]-[10]}, but also a higher likelihood of re-hospitalization among hospital survivors of an AMI^[7].

The CHADS₂ and CHA₂DS₂VASc scoring systems are used to stratify patients with AF at risk for developing stroke and identify patients who may benefit from oral anticoagulation (OAC), including patients with AMI^{[8],[11],[12]}. Although antiplatelet drugs prevent thromboembolic complications in patients with AMI, particularly

Key Words

Atrial fibrillation, Anticoagulation, Outcomes, Epidemiology.

Corresponding Author

Amartya Kundu, Department of Cardiology, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA, USA those receiving percutaneous interventions (PCI), these agents have minimal impact on stroke risk in patients with AF^[11].

Therefore,prescription of OAC in addition to antiplatelet therapy is recommended for AMI patients with AF consistently in the ESC and ACC/AHA/HRS guidelines^{[11],[13]}.However, practice patterns vary widely, particularly when dual antiplatelet therapy is prescribed among AMI patients,largely due to concerns about the bleeding risk from "triple therapy", but also because many providers view newonset AF following AMI as being associated with lower risk for stroke^[14]. Observational studies have lent credibility to these concerns by showing an elevated bleeding risk among patients treated with dual antiplatelet agents and OAC^[15].

Few investigations have described the epidemiology of AF among patients with AMI, further stratified according to stroke risk, or trends in OAC prescription and post-discharge complications among guideline-eligible AF patients with AMI. Therefore, we analyzed data from the multi-hospital, population-based, Worcester Heart Attack Study (WHAS)^{[7],[8],[16],[17]}.

 Demographic and Clinical Characteristics of Hospital Survivors of

 Table 1:
 Acute Myocardial Infarction (AMI), further stratified according to

 Atrial Fibrillation (AF) Status

Characteristics	No AF [n=5577]	AF- A ₂ DS ₂ VASc =1-2 [n=96]	AF- 2VASc=3- 6 [n=798]	AF- 2VASc=7- 9 [n=156]	p-value
Age (mean, years)[SD]	67.9	58.4 [8.6]	78.3 [9.78]	81.8 [6.1]	<.001
Years[SD]	[14.3]				
Age <65 y (%)	39.2	68.7	8.1	1.3	<.001
Age 65-74	21.3	16.6	21.5	8.3	<. 001
Age 75-84	24.1	0	37.8	53.2	<.001
Age >= 85 y	15.3	14.6	32.4	37.2	<. 001
Sex, % Men	57.7	87.5	52.7	32.7	<.001
White Race	89.4	89.6	92.5	94.2	0.01
АҒ Туре					
Incident	0	87.5	58.4	48.1	<. 001
Prevalent	0	12.5	41.6	51.9	<. 001
Medical History (%)					
Angina Pectoris	16.2	10.4	16.8	21.1	0.15
Hypertension	69.1	26.1	77.9	96.1	<. 001
Heart Failure	20.9	5.2	29.8	64.1	<. 001
Stroke	10.6	0	7.0	64.1	<. 001
Diabetes	32.9	6.2	30.9	67.3	<. 001
Hyperlipidemia	54.9	44.8	51.2	56.4	0.06
COPD	15.9	17.7	22.7	19.2	<. 001
Prior bleeding	22.4	19.8	33.4	28.8	<. 001
СКD	16.2	13.5	22.9	35.9	<. 001
STEMI	36.6	57.3	28.8	27.5	<. 001
NSTEMI	63.4	42.7	71.2	72.5	<. 001
Initial AMI	65.0	82.3	62.4	58.3	<. 001
Creatinine in mg/dl	1.3 [1.0]	1.2 [0.7]	1.5[1.1]	1.6 [0.8]	<. 001
- Mean [SD]					
Troponin I Peak in	16.7	16.6 [49.6]	20.7 [57.9]	24.9 [75.6]	.029
ng/mL - Mean [SD]	[65.5]				
Mean HASBLED	1.6 [1.0]	0.7 [0.8]	2.0 [0.8]	3.0 [0.7]	<.001
score [SD]					
Mean CHADS ₂ VASc	3.8 [1.9]	1.6 [0.4]	4.5 [1.0]	7.4[0.6]	<.001
in - H o s p i t a l C om p lication s (%)					
Complicated AMI*	32.6	39.6	58.3	64.7	<.001
Cardiogenic Shock	2.1	9.3	7.7	2.5	<. 001
Heart Failure	30.3	33.3	54.2	60.9	<.001
Stroke	1.1	1.1	2.5	5.8	<.001
Heart Block	1.2	6.3	3.1	2.5	<.001
Recurrent AMI	0.7	0	0.5	0	0.5
Hospital Procedures (%)					
Cardiac	59.2	71.9	43.7	30.8	<.001
Catheterization					
PCI	42.8	63.5	31.2	18.6	<. 001

* Complicated AMI included the development of cardiogenic shock, heart failure, stroke, recurrent AMI, or heart block.

Methods

The WHAS is an ongoing, population-based, observational study of patients hospitalized at all 11 medical centers in central



Massachusetts, documenting long-term trends in the incidence, morbidity, mortality, and complications of AMI^{[7],[8],[1],[17]}. Our analyses focused on patients who were hospitalized with a discharge diagnosis of AMI at all Worcester Standard Metropolitan Statistical Area (SMSA) hospitals during 8 biennial years between 1997 and 2011. We selected these study years based on the availability of data on AF status, CHADS, and CHA,DS,VASc scores, and systematic

Post-Discharge Outcomes* among Hospital Survivors of Acute Myocardial Infarction (AMI), further stratifiedaccording to Atrial Fibrillation (AF) Status								
Outco	me	No AF	AF- CHA ₂ DS ₂ VASc 1-2	AF- CHA ₂ DS ₂ VASc 3-6	AF- CHA ₂ DS ₂ VASc 7-9			
30 - day R	e-	17.1	16.2 %	27.1 %	27 %			
hospitaliza	ation**		OR 0.9 (0.5-1.7)	OR 1.5 (1.2-1.8)	1.2 (0.7-1.7)			
30-day Mo	ortality	4.9	7.3 % OR 1.5 (0.7-3.4)	8.8 % OR 1.3 (1-1.7)	10.3 % OR 1.3 (0.7-2.3)			
1- year Mo	ortality	18	14.6 % OR 0.8 (0.4-1.5)	33.9 % OR 1.7 (1.4-2.1)	46.1 % OR 2.2 (1.6-3.2)			

collection of OAC prescription rates and post-discharge outcomes. Since this study primarily focused on post-discharge outcomes and OAC prescription, patients who died during hospitalization were excluded. Medical records of patients admitted for possible AMI at all metropolitan Worcester medical centers were reviewed and validated. Diagnosis of AMI was confirmed using pre-established criteria^[18]. The methods used for the identification of patients hospitalized



Figure 2: Trends in the Rates of AF by CHADS₂ Score between 1997 and 2011.

 Discharge Medication Prescription (%) among Hospital Survivors

 Table 3:
 of Acute Myocardial Infarction with Atrial Fibrillation (AF), further

 stratified according to CHA2DS2VASc Score

Medication	No AF	AF-	AF-	AF-	p-value
		CHA ₂ DS ₂ VASc 1-2	CHA ₂ DS ₂ VASc 3-6	CHA ₂ DS ₂ VASc 7-9	
Warfarin*	7.5	31.1	34.6	37.9	< .001
Dual Antiplatelet Therapy	44.7	43.7	26.5	25	< .001
Aspirin only	86.4	88.5	80.7	78.2	< .001
Clopidogrel only	50.1	58.3	38.8	33.9	< .001
Beta Blockers	83.9	79.1	77.9	80.7	< .001
ACE/ARB	59.5	62.5	58	64.7	0.9
Lipid Lowering Agents	63.8	65.6	55.3	62.1	< .001
Triple Therapy *	4.4	19.7	15.2	10.3	< .001

* Data on Warfarin and Triple Therapy Rates collected from 2003-2011 only. n=3910.

with AMI and various comorbidities and complications have been described in prior publications^{[7],[8],[16],[17]}. The data collected included patients' age, gender, race, comorbidities (hypertension, heart failure, stroke, hyperlipidemia, chronic obstructive pulmonary disease [COPD], chronic kidney disease [CKD], diabetes), type of AMI,physiologic parameters (admission heart rate, blood pressure,



the study due to the different mechanisms and natural historyof surgical patients with AF^[19].

Patients with confirmed AMI were further stratified according to their CHA₂DS₂VAScscore based on documentation of risk factors in the medical record [age, sex, history of heart failure, hypertension, diabetes mellitus, stroke or transient ischemic attack, vascular disease (including myocardial infarction and peripheral artery disease)]

CHADS₂≤1 CHADS₂≥2	,					
Infarction (AMI) and Atrial Fibrillation (AF), further stratified by CHADS ₂ Scores						
Post-Discharge Prescription Rates of Warfarin, Antiplatelet Agents and Triple Therapy from 2003-2011 in Patients with Ac						

Year	Warfarin (%)	Aspirin Alone (%)	Clopidogrel Alone (%)	DAPT (%)	Triple Therapy (%)	Warfarin (%)	Aspirin Alone (%)	Clopidogrel Alone (%)	DAPT (%)	Triple Therapy (%)
2003	35.3	29.4	5.9	51.0	17.7	32.5	40.8	3.2	36.3	7.6
2005	21.2	12.1	3.0	66.7	6.1	37.0	38.7	3.4	47.9	16.0
2007	30.6	38.9	2.8	50.0	16.7	38.8	38.8	0.0	50.5	14.6
2009	39.1	30.4	8.7	56.5	17.4	39.7	33.3	1.6	58.7	25.4
2011	36.4	30.3	0.0	60.6	24.2	32.8	27.7	3.1	54.7	15.6

* DAPT/Dual Antiplatelet Therapy = Aspirin + Clopidogrel

respiratory rate, serum creatinine and peak troponin), in-hospital and discharge medications, in-hospital complications and postdischarge outcomes. Rates of warfarin, aspirin, and clopidogrel prescription were determined based on the discharge medication list. Rates of direct oral anticoagulant prescription were not examined in this study, as these agents were not approved for use in the US until 2010, nor collected in this study until after 2011. Rigorous methods have been used to identify deaths and cases of read mission to area hospitals^[7]. Patient's AF status was determined based on available clinical data^{[7],[16]}. A review of ambulance transport records, emergency admission notes, progress notes, and in-hospital 12-lead ECGs was conducted to identify patients with AF. The classification of prevalent AF was assigned if a patient had prior AF noted in their hospital admission note or any progress note. A case of incident, or newly diagnosed, AF was defined according to the following criteria: No documentation of pre-existing AF anda) AF on any 12-lead ECG obtained during the index hospitalization^{[8],[17]}, or b) new-onset AF documented in any clinical note during the index hospitalization. For purposes of focusing on post-discharge outcomes and discharge prescription practices, we included hospital survivors with both incident and prevalent AF. Patients who under went coronary artery bypass grafting (CABG) during hospitalizationwere excluded from

^{[11],[13]}. Patients were grouped into 3 categories according to their CHA₂DS₂VASc score (Group 1 =CHA₂DS₂VASc score 1-2, Group 2 = CHA₂DS₂VASc 3-6, Group 3 = CHA₂DS₂VASc 7-9) to distinguish between those at lower, high, and very high risk of thromboembolism²⁰⁻²³. Although use of the CHA₂DS₂VASc stroke risk score was introduced in 2009, the CHADS₂ scoring system was in use for most of the period under study. Therefore, we also stratified

Yearly Trends in Discharge Anticoagulation Prescription (%) in Table 5: Patients with Acute Myocardial Infarction (AMI) and Atrial Fibrillation (AF), further stratified by CHA ₂ DS ₂ VASc scores									
Medication	AF Status	2003	2005	2007	2009	2011			
Warfarin	No AF	6.2	6.6	8.3	8	9.1			
	AF-CHA2DS2VASc 1-2	29.4	9.1	28.6	70	25			
	AF- CHA2DS2VASc 3-6	33.7	38.2	33	31.8	35.8			
	AF- CHA2DS2VASc 7-9	32.3	23.1	51.7	53.8	35.7			
Triple Therapy	No AF	2.3	4.4	5.5	5.5	4.9			
	AF- CHA2DS2VASc 1-2	17.6	0	28.6	40	18.8			
	AF- CHA2DS2VASc 3-6	10.9	16.5	12.6	20.6	22.4			
	AF- CHA2DS2VASc 7-9	2.9	7.7	20.7	23.1	0			

Table 6:

Discharge Medication Prescription (%) among Hospital Survivors of Acute Myocardial Infarction (AMI) with Atrial Fibrillation (AF), further stratified according to Risk of Bleeding

Medication	Overall N=1050		AF-CHADS ₂ VASc 1-2 N=96			AF-CHADS ₂ VASc >2 N=954	p- value
	Low HASBL ED	High HASBL ED	Low HASBL ED	High HASBL D	Low HASBL ED	High HASBL D	
Warfarin*	36.4	32	31.6	25	37.1	32.1	0.2
DAPT	28.7	25.9	43.4	50	26.6	25.6	0.3
Aspirin only	82.2	78.2	89.1	75	81.2	78.2	0.1
Clopidogrel only	41.3	36.5	58.7	50	38.8	36.3	0.1
Triple Therapy *	17.5	9.7	21	0	17	9.8	0.005

* DAPT/Dual Antiplatelet Therapy = Aspirin + Clopidogrel

the cohort according to CHADS₂score (congestive heart failure, hypertension, age, diabetes, and stroke)using similar methods,but divided the population into two groups – those with CHADS₂ score less than two and those with a CHADS₂ score of two or more, in order to identify the proportion of the population eligible for OAC prescription based on contemporary guidelines^{[11],[13]}.

We examined differences in the frequency and outcomes of patients with AF compared to those without AF through the use of chisquare tests and one-way analysis of variance (ANOVA) for discrete and continuous variables, respectively. We examined differences in the characteristics and use of different evidence-based AMI and AF therapies according to stroke risk classifications through the Cochran-Armitage test for trends. Differences in post-discharge complications, including hospital re-admission and mortality, as well as the associated crude and multivariable adjusted odds ratios (OR) with 95% confidence intervals (CI), were assessed. The odds of developing these complications were adjusted for confounding demographic and clinical factors.

We restricted our analyses on post-discharge prescription rates of OAC to the study years 2003-2011 because data on OAC was not collected in this study until 2003. HAS-BLED scores were calculated to characterize participant's risk of bleeding on OAC using the following factors documented in the medical record age, hypertension, abnormal renal/liver function, stroke, bleeding history, drugs or alcohol use (1 pointeach)^{[11],[21]}. Since INRs prior to admission were not abstracted as part of this population-based study, we were not able to determine time in therapeutic range over the preceding 4 weeks among individuals treated with vitamin K antagonists. Hospital re-admission data was collected at only 3 of the major Worcester hospitals, and was reported for the years 1999-2011. All analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC).

Results

The baseline characteristics of 6,627 patients discharged from all participating medical centers in central Massachusetts with an independently confirmed AMI during the years under study are shown in [Table 1]. The mean age of this population sample was 69 years, 40% were women, and approximately two-thirds presented with an initial AMI. A total of 1,050patients (16%) had AF. Of these, the majority were at a high (76%) or very high risk (15%) for stroke according to their CHA,DS,VASc score. Patients in the "lower" stroke risk category were more likely to have new-onset AF compared to prevalent AF, whereas patients with AF in the highest stroke risk group were older, more likely to be male, have higher serum troponin levels, have a history of CKD, and have higher average HAS-BLED scores. Patients with AF and higher CHA₂DS₂VASc scores were also more likely to have their AMI hospitalization complicated by development of heart failure or stroke. We also observed that in patients with AMI and AF, bleeding risk (based on HAS-BLED score) tracked closely with stroke risk [Table 1].

Rates of AF increased significantly between 1997 and 2003, after which time AF rates remained relatively stable, and patterns did not appear to differ significantly according to CHA_2DS_2VASc stroke risk category[Figure 1]. Rates were highest among patients with AF in the highest stroke risk group, but the relative proportion of individuals in the lowest stroke risk category appeared to increase during the most recent study years. Similar results were seen in AF rates stratified by $CHADS_2$ scores, with higher rates observed among patients with AF and a $CHADS_2$ score>2 [Figure 2].

In comparison to AMI patients who remained free from AF during their hospitalization, individuals with AF in the highest stroke risk category had significantly higher rates of post-discharge complications, including higher 30-day re-hospitalization rates [27 % vs. 17 %], 30-day post-discharge death rates [10 % vs. 5%], and 1-year post-discharge death rates [46 % vs. 18%] (p<0.001 for all). Notably, we observed a direct relationship between CHA₂DS₂VASc category and rates of readmission or death within 30 days, as well as death rates at 1-year [Table 2]. Furthermore, after adjustment for several demographic factors, comorbid conditions, and AMIassociated characteristics, AF patients in the highest stroke risk group had 2-fold higher odds of dying at 1-year after discharge, compared to patients free from AF. However, adjustment for the same set of key covariates attenuated crude associations observed between stroke risk and readmission, as well as mortality 30-days after discharge [Table 2].

We also examined the use of evidence-based medications for AMI or AF at discharge, further stratified by stroke risk. Rates of OAC use were highest among patients with highest CHA₂DS₂VASc scores (38% in the very high stroke risk, 35% in the high stroke risk, and 31% in the lowest stroke risk), but less than half of patients at high or very-high stroke risk received an OAC prescription at discharge.

Interestingly, aspirin and clopidogrel use were also lower among AMI patients with AF at highest stroke risk, compared to those at lower risk (88.5 % and 58.3% among those with AF in the lowest stroke risk category vs. 78.2 % and 33.9% among those with AF highest stroke risk, respectively). In contrast, prescription of beta-blockers and lipid-lowering agents did not vary among AF patients based on stroke risk [Table 3].

Notably, only 1 in 4 AMI patients with AF and a high or very high stroke risk score received dual antiplatelet therapy at hospital discharge. Low rates of OAC prescription at discharge were also observed when stratifying the patients based on their CHADS₂ score[Table 4]. We did not observe any significant change in the rates of OAC prescription over time among individuals with AF [Table 5]. Lastly, in AF patients at elevated stroke risk, we observed no significant relations between bleeding risk and rates of OAC prescription at discharge [Table 6].

Discussion

The CHA₂DS₂VASc scoring system is a well-validated stroke risk stratification tool for patients with non-valvular AF^[24]. Components of the CHA₂DS₂VASc score are readily available prognostic risk factors for outcomes of is chemic heart disease^[25]. The CHA₂DS₂VASc score has been shown to successfully estimate the risk of adverse events in patients with AMI^[24] and also identify post-STEMI patients at high risk of developing new onset AF and stroke^[26].

There are limited studies that have evaluated the prognostic utility of stroke risk classification schemes in predicting the risk of adverse outcomes in patients with concomitant AMI and AF.In a study of more than 15,000 patients admitted with AMI to hospitals in Korea, the investigators assessed the utility of CHA2DS2VASc scores in predicting the risk of dying and/or recurrent MI in patients with and without AF. They found that higher CHA2DS2VASc scores were associated with an increased risk of adverse cardiovascular outcomes in AMI patients at 1,6,12, and 24 months, irrespective of the presence of AF^[27]. In our community-wide study involving almost 7,000 hospital survivors, patients with AF and a higher CHA2DS2VASc scores were at greater risk for both short- and long- term adverse events than both AF patients with lower CHA2DS2VASc scores, and patients without AF. In particular, we observed a direct relationship between increasing CHA2DS2VASc scores and odds of dying at 1-year after discharge in patients with AF, compared to patients free from AF. This was not seen in AF patients with a low CHA2DS2VASc score [Figure 3]. Our findings expand on the results of the previous Korean study (27), and suggest that the CHA2DS2VASc system can be used as a tool to predict survival among patients with AMI and AF.

Current AF and AMI management guidelines support the use of dual antiplatelet therapy plus OAC when independent indications for AMI and AF exist^{[28],[29]}. However, institution of "triple therapy" poses risks for bleeding. Inasmuch, alternative strategies have been proposed for patients with AMI and AF, such as discontinuing antiplatelet drugs among patients who are greater than 12 months out from undergoing a PCI^[30]. In clinical practice, there is significant individualization of treatment with respect to balancing the risks of stroke and bleeding.In our study, approximately 90% of patients with AMI and AF had a high or very high risk for thromboembolism based on having a CHA₂DS₂VASc score>2. However, only 1 out of 4 AMI patients with AF received dual antiplatelet therapy at the time of hospital discharge and less than half received OAC at discharge, suggesting thata treatment gap between guideline and real-world rates of prescription exists.

Reasons for the low rates of OAC usage among AMI patients with AF at hospital discharge may include lack of awareness of guidelines, provider or patient concerns over risk for bleeding with the use of OAC and antiplatelet drugs, or under-estimation of stroke risk from AF complicating AMI. Since the FDA approved the first target specific OAC agent, dabigatran, for use in 2010 and our study ended in 2011, we do not believe that the low rates of OAC seen in our study relate to the use of vitamin-K antagonist alternatives. Furthermore, we have generally observed high rates of adherence to AMI-specific guideline recommendations for effective patient management in this community-wide study, with the majority of eligible patients having been treated with aspirin, statins, beta-blockers and prompt percutaneous revascularization for STEMI^[31]. This was corroborated in our analysis as the vast majority of AMI patients with AF received guideline-directed antiplatelet, lipid-lowering agents, and betablocker therapies [Table 3]. Therefore, we do not believe that the low rate of observed OAC prescription reflects a general disregard among providers at participating hospitals for guideline recommendations. An alternative explanation for our findings is that, despite evidence to the contrary(7), hospital providers may consider AF complicating an AMIto be of lesser clinical significance than AF in the community, irrespective of their CHADS₂ or CHA₂DS₂VASc scores.

Neither treatment nor outcomes of A Fare mandated publically reported quality metrics. It has not been until recently that the American Heart Association created and distributed a 'Get with the Guidelines' for AF, a mechanism to enhance adherence to guidelinerecommendations for AF treatment, including use of OAC for patients at intermediate and high stroke risk^[32]. It is certainly possible that clinicians managing patients with AMI during the period under study may not have been aware of the importance of stroke risk estimation and OAC prescription for at-risk patients. It is our hope that, through increased public and clinician AF awareness, adherence to guideline recommendations for OAC among eligible AMI patients with AF will increase.

Strengths of the present study include the population-based design involving all patients hospitalized with AMI across central Massachusetts. Inclusion of all regional hospitals in Worcester, the large number of patients hospitalized with AMI and AF, and the use of standardized criteria for diagnosing AMI and AF were additional strengths. We were also able to control for a variety of potential confounding variables outside of the CHA₂DS₂VASc scoring system that could have contributed to post-discharge outcomes.

Limitations

Limitations of this study include the lack of data on type of AF (paroxysmal, persistent, or permanent) and the inability to determine the time in therapeutic INR range among patients with AF prior to admission. Our study population likely included a number of patients at high risk for bleeding, and we did not systematically assess

components of frailty, such as falls, weight loss, or grip strength, which may influence decisions to with hold OAC. We also did not assess for patient-level factors, such as patient's attitudes about OAC, allergies or prior adverse reactions that may have led to the with holding of OAC's at the time of hospital discharge. Data on prescription rates of anti arrhythmic medications in patients with AF was not collected. Since this study was conducted in a single geographic region, there was potential for under-estimation of re-hospitalization rates, as patients may have presented outside of the hospital network for subsequent hospitalizations. Moreover, hospital re-admission data was reported at only 3 of the major Worcester hospitals, although these comprise the majority of all AMI admissions in this population. Data on the etiology of death after hospital discharge was not available.

Conclusions

We observed that a large proportion of patients hospitalized for AMI over a 14-year period had AF,and that the proportion of AF patients at high risk for stroke remained elevated throughout the study. Another interesting finding was that less than half the patients with a high CHA₂DS₂VASc were discharged on anticoagulation therapy. Our findings suggest significant deviation from guidelinebased AF management practices in the context of AMI, and that patients with higher CHA₂DS₂VASc scores may benefit from greater monitoring and/or more aggressive treatment in the peri-discharge period. Future studies are needed to see if the CHA₂DS₂VASc score can truly be validated as tool for not only predicting stroke risk, but also post-discharge outcomes (including mortality) in patients with AMI and AF.

References

- Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna WP, Seward JB, Tsang TS. Secular Trends in Incidence of Atrial Fibrillation in Olmsted County, Minnesota, 1980 to 2000, and Implications on the Projections for Future Prevalence. Circulation 2006; 114:119-125.
- Poli D, Antonucci E. Epidemiology, Diagnosis, and Management of Atrial Fibrillation in Women. Int J Womens Health 2015; 7:605-614.
- Lopes RD, Elliott LE, White HD, Hochman JS, Van de Werf F, Ardissino D, Nielsen TT, Weaver WD, Widimsky P, Armstrong W, Granger CB. Antithrombotic therapy and outcomes of patients with atrial fibrillation following primary percutaneous coronary intervention: results from the APEX-AMI trial. Eur Heart J 2009; 30:2019–2028.
- Crenshaw B, Granger C, Stebbins A, Topol E, Califf R. Atrial fibrillation in the setting of acute myocardial infarction: the GUSTO-I experience. Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries. J Am Coll Cardiol 1997; 30:406–413.
- Pizzetti F, Turazza FM, Franzosi MG, Barlera S, Ledda A, Maggioni AP, Santoro L, Tognoni G. Incidence and prognostic significance of atrial fibrillation in acute myocardial infarction: the GISSI-3 data. Heart 2001; 86:527–532.
- Wong CK, White HD, Wilcox RG, Criger DA, Califf RM, Topol EJ, Ohman EM. New atrial fibrillation after acute myocardial infarction independently predicts death: the GUSTO-III experience. Am Heart J 2000; 140:878–885.
- Kundu A, O'Day K, Shaikh AY, Lessard DM, Saczynski JS, Yarzebski J, Darling C, Thabet R, Akhter MW, Floyd KC, Goldberg RJ, McManus DD. Relation of Atrial Fibrillation in Acute Myocardial Infarction to In-Hospital Complications and Early Hospital Readmission. Am J Cardiol. 2016;117:1213-1218.
- 8. Goldberg RJ, Yarzebski J, Lessard D, Wu J, Gore JM. Recent trends in the incidence rates of and death rates from atrial fibrillation complicating initial acute

myocardial infarction: a communitywide perspective. Am Heart J 2002; 143:519 –527.

- Rathore SS, Berger AK, Weinfurt KP, Schulman KA, Oetgen WJ, Gersh BJ, Solomon AJ. Acute Myocardial Infarction Complicated by Atrial Fibrillation in the Elderly: Prevalence and Outcomes. Circulation 2000; 101:969-974.
- Zusman O, Amit G, Gilutz H, Zahger D. The Significance of New Onset Atrial Fibrillation Complicating Acute Myocardial Infarction. Clin Res Cardiol 2011; 101:17-22.
- 11. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M,Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016 Oct 7;37(38):2893-2962. Epub 2016 Aug 27.
- 12. Stenestrand U, Lindbäck J, Wallentin L; RIKS-HIA Registry. Anticoagulation therapy in atrial fibrillation in combination with acute myocardial infarction influences long-term outcome: a prospective cohort study from the Register of Information and Knowledge About Swedish Heart Intensive Care Admissions (RIKS-HIA). Circulation 2005; 112:3225-3231.
- 13. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT. 2014 AHA/ACC/ HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2014;64:2246-2280.
- Lubitz SA, Yin X, Rienstra M, Schnabel RB, Walkey AJ, Magnani JW, Rahman F, McManus DD, Tadros TM, Levy D, Vasan RS, Larson MG, Ellinor PT, Benjamin EJ.. Long-term outcomes of secondary atrial fibrillation in the community: the Framingham Heart Study. Circulation. 2015;131:1648-1655.
- 15. Lamberts M, Olesen JB, Ruwald MH, Hansen CM, Karasoy D, Kristensen SL, Køber L, Torp-Pedersen C, Gislason GH, Hansen ML. Bleeding after initiation of multiple antithrombotic drugs, including triple therapy, in atrial fibrillation patients following myocardial infarction and coronary intervention: a nationwide cohort study. Circulation 2012;126:1185-1193.
- Goldberg RJ, Gore JM, Alpert JS, Dalen JE. Recent changes in attack and survival rates of acute myocardial infarction (1975 through 1981). The Worcester Heart Attack Study. JAMA 1986; 255:2774 –2779.
- Goldberg RJ, Yarzebski J, Lessard D, Gore JM. A two-decades (1975 to 1995) long experience in the incidence, in-hospital and long-term case-fatality rates of acute myocardial infarction: a community-wide perspective. J Am Coll Cardiol 1999; 33:1533–1539.
- Floyd KC, Yarzebski J, Spencer FA, Lessard D, Dalen JE, Alpert JS, Gore JM, Goldberg RJ. A 30-year perspective (1975-2005) into the changing landscape of patients hospitalized with initial acute myocardial infarction: Worcester Heart Attack Study. Circ Cardiovasc Qual Outcomes 2009; 2:88-95.
- Maesen B, Nijs J, Maessen J, Allessie M, Schotten U. Post-operative atrial fibrillation: a maze of mechanisms. Europace 2012; 14:159-174.
- 20. Olesen JB, Torp-Pedersen C, Hansen ML, Lip G. The Value of the CHA₂DS₂-VASc Score for Refining Stroke Risk Stratification in Patients with Atrial Fibrillation with a CHADS2 Score 0–1: A Nationwide Cohort Study. Thromb Haemost Thrombosis and Haemostasis 2012; 107: 1172-1179.
- Lane DA, Lip GY. Use of the CHA(2)DS(2)-VASc and HAS-BLED scores to aid decision making for thromboprophylaxis in nonvalvular atrial fibrillation. Circulation. 2012;126:860-5
- Saczynski JS, McManus D, Zhou Z, Spencer F, Yarzebski J, Lessard D, Gore JM, Goldberg RJ. Trends in atrial fibrillation complicating acute myocardial infarction. Am J Cardiol 2009; 104:169-174.
- 23. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, Hochman JS, Krumholz HM, Kushner FG, Lamas GA, Mullany CJ, Ornato JP, Pearle DL,

Sloan MA, Smith SC Jr, Alpert JS, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Gregoratos G, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK, Ornato JP. ACC/ AHA guidelines for the management of patients with ST-elevation myocardial infarction; A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction) J Am Coll Cardiol 2004;44:E1–E211.

- 24. Chua SK, Lo HM, Chiu CZ, Shyu KG. Use of CHADS₂ and CHA₂DS₂-VASc Scores to Predict Subsequent Myocardial Infarction, Stroke, and Death in Patients with Acute Coronary Syndrome: Data from Taiwan Acute Coronary Syndrome Full Spectrum Registry. PloS one. 2014;9:e111167.
- 25. Avezum A, Makdisse M, Spencer F, Gore JM, Fox KA, Montalescot G, Eagle KA, White K, Mehta RH, Knobel E, Collet JP; GRACE Investigators. Impact of age on management and outcome of acute coronary syndrome: observations from the Global Registry of Acute Coronary Events (GRACE). Am Heart J 2005; 149:67-73.
- 26. Lau KK, Chan PH, Yiu KH, Chan YH, Liu S, Chan KH, Yeung CY, Li SW, Tse HF, Siu CW. Roles of the CHADS₂ and CHA₂DS₂-VASc scores in postmyocardial infarction patients: Risk of new occurrence of atrial fibrillation and ischemic stroke. Cardiol J 2014; 21:474-483.
- 27. Kim KH, Kim W, Hwang SH, Kang WY, Cho SC, Kim W, Jeong MH; Other Korean Working Group in Myocardial Infarction Registry Investigators. The CHA2DS2VASc score can be used to stratify the prognosis of acute myocardial infarction patients irrespective of presence of atrial fibrillation. J Cardiol. 2015 ;65(2):121-127.
- 28. Faxon DP, Eikelboom JW, Berger PB, Holmes DR Jr, Bhatt DL, Moliterno DJ, Becker RC, Angiolillo DJ. Antithrombotic therapy in patients with atrial fibrillation undergoing coronary stenting: a North American perspective: executive summary. Circ Cardiovasc Interv 2011; 4:522–534.
- 29. Rubboli A, Halperin JL, Airaksinen KE, Buerke M, Eeckhout E, Freedman SB, Gershlick AH, Schlitt A, Tse HF, Verheugt FW, Lip GY. Antithrombotic therapy in patients treated with oral anticoagulation undergoing coronary artery stenting. An expert consensus document with focus on atrial fibrillation. Ann Med 2008;40:428–436.
- 30. Capodanno D, Angiolillo DJ. Management of antiplatelet and anticoagulant therapy in patients with atrial fibrillation in the setting of acute coronary syndromes or percutaneous coronary interventions. Circ Cardiovasc Interv. 2014;7:113-124.
- Fornasini M, Yarzebski J, Chiriboga D, Lessard D, Spencer FA, Aurigemma P, Gore JM, Goldberg RJ. Contemporary trends in evidence-based treatment for acute myocardial infarction. Am J Med 2010;123:166-172.
- 32. http://www.heart.org/HEARTORG/Professional/GetWithTheGuidelines/ GetWithTheGuidelines-AFIB/Get-With-The-Guidelines-AFIB_ UCM_448881_SubHomePage.jsp. Date accessed: 13 July 2017.