Published in final edited form as:

Am Heart J. 2013 October ; 166(4): . doi:10.1016/j.ahj.2013.07.013.

Atrial fibrillation in myocardial infarction patients: impact on healthcare utilization

Alanna M. Chamberlain, PhD, MPH^a, Suzette J. Bielinski, PhD^a, Susan A. Weston, MS^a, Winslow Klaskala, MS PhD^b, Roger M. Mills, MD^b, Bernard J. Gersh, MB ChB DPhil^c, Alvaro Alonso, MD PhD^d, and Véronique L. Roger, MD, MPH^{a,c}

^aDepartment of Health Sciences Research, Mayo Clinic, Rochester, MN

^bJanssen Research and Development, LLC, Raritan, NJ

^cDivision of Cardiovascular Diseases, Mayo Clinic, Rochester, MN

^dDivision of Epidemiology and Community Health, School of Public Health, University of MN, Minneapolis, MN

Abstract

Background—Atrial fibrillation (AF) often complicates myocardial infarction (MI). While AF adversely impacts survival in MI patients, the impact of AF on healthcare utilization has not been studied.

Methods—The risk of hospitalizations, emergency department (ED) visits, and outpatient visits associated with prior, early-onset (<30 days post-MI) and late-onset (≥ 30 days post-MI) AF was assessed among incident MI patients from the Olmsted County, MN community.

Results—Of 1502 MI patients, 237 had prior AF, 163 developed new-onset AF, 113 developed late-onset AF, and 989 had no AF. Over a mean follow-up of 3.9 years, 3661 hospitalizations, 5559 ED visits, and 80,240 outpatient visits occurred. After adjustment, compared to patients without AF, those with prior and early-onset AF exhibited a 1.6-fold and 1.4-fold increased risk of hospitalization, respectively. In contrast, late-onset AF carried a 2.2-fold increased risk of hospitalization. The hazard ratios were 1.4, 1.2, and 1.8 for ED visits and 1.5, 1.2, and 1.7 for outpatient visits for prior, early-onset, and late-onset AF. Additional adjustment for time-dependent recurrent MI and heart failure attenuated the results slightly for hospitalizations and ED visits; however, patients with late-onset AF still exhibited more than a 50% increased risk for both utilization measures.

Conclusions—In MI patients, the risk of hospitalizations, ED visits, and outpatient visits differed by the timing of AF onset, with the greatest risk conferred by late-onset AF. AF imparts an adverse prognosis after MI underscoring the importance of its management in MI patients.

© 2013 Mosby, Inc. All rights reserved.

Address Correspondence To: Véronique L. Roger, MD, MPH. Department of Health Sciences Research, Mayo Clinic, 200 First St. SW, Rochester, MN 55905. roger.veronique@mayo.edu Phone: (507) 538-6916 Fax: (507) 284-1516.

Disclosures

Drs. Klaskala and Mills are employees of Janssen Research and Development, LLC. All other authors have no conflict of interest. All authors meet criteria for authorship, and have no financial or other relationships that could lead to a conflict of interest. The paper is original research that has not been published and is not under consideration elsewhere.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Introduction

Atrial fibrillation (AF), the most common cardiac arrhythmia in clinical practice, occurs frequently in myocardial infarction (MI) patients and is associated with an increased risk of stroke, heart failure (HF), and mortality.¹ The reported incidence of AF in MI ranges between 7% and 21%,² and in the setting of MI, AF increases the risk of mortality by approximately 40%.³ A recent systematic review and meta-analysis reported that the increased risk of death for these patients persisted for both those with AF prior to MI and those with new-onset AF, which was generally considered within the hospitalization for MI.³ In addition, a community-based study suggested the timing of AF as an important prognostic indicator in MI patients, with the highest risk of death observed among patients who developed AF more than 30 days after MI.⁴

Despite the evidence linking AF to poorer prognosis in MI patients, the impact of AF and, importantly, its timing in relation to MI onset on healthcare resource utilization, have not been investigated. Therefore, our aim was to determine whether MI patients with AF experienced a greater risk of subsequent hospitalizations, emergency department (ED) visits, and outpatient office visits compared with MI patients without AF, and whether the timing of AF in relation to MI differentially impacted the risk of these healthcare utilization measures in a community-based cohort of individuals with incident MI.

Methods

Study Population

This study was conducted in southeast Minnesota under the auspices of the Rochester Epidemiology Project (REP),⁵ a record linkage system that enables virtually complete capture of outcomes and healthcare utilization in Olmsted County. This study was approved by the Mayo Clinic and Olmsted Medical Center Institutional Review Boards.

Identification of the study cohort

Olmsted County, MN residents who presented to a Mayo Clinic facility between November 1, 2002 and December 31, 2010 with a troponin T value ≥ 0.03 ng/mL (the upper limit of normal for the assay, defined as the value at which the coefficient of variation for the assay is $\geq 10\%$)⁶ were identified within 12 hours of the blood draw and approached by nurse coordinators to enroll in our study.⁷

To determine MI status, we applied the epidemiologic criteria used by the World Health Organization^{8,9} and the Atherosclerosis Risk in Communities study,¹⁰ which define MI based on cardiac pain, biomarker levels, and Minnesota coding of the electrocardiogram. According to the new guidelines using Troponin T in the algorithm to classify MI events,¹¹ the presence or absence of a change (rise or fall) between any two troponin measurements is defined by a difference of at least 0.05 ng/mL, which is greater than the level of imprecision of the assay at all concentrations. As troponin can remain elevated for 2 weeks after events causing its rise, comorbid conditions were noted if they occurred within 2 weeks before the infarction and, when present, the biomarker results were downgraded from abnormal to equivocal in the algorithm.¹²

Myocardial infarction characteristics and treatments

The presence of ST segment elevation (STEMI) was determined using serial analysis of the ECG with the Minnesota codes as assigned by validated ECG software.¹³ The components of the Killip classification, including the presence or absence of a third heart sound, pulmonary rales, and the systolic blood pressure on the admission examination, were

grouped categorically defining Killip classes 1 to 4, with higher classes indicating a higher risk of mortality.¹⁴ Treatments for the MI during hospitalization, including percutaneous transluminal coronary angioplasty with or without stenting, coronary artery bypass grafting, or administration of thrombolytics, along with dismissal medications, were obtained from medical record review.

Ascertainment of atrial fibrillation

To provide as complete capture of AF events as possible, the first date of AF or atrial flutter as documented by an electrocardiogram (ECG) or an *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code of 427.31 or 427.32 during either a hospitalization or an outpatient visit identified possible incident AF events. The ECGs were electronically interpreted using Marquette codes, and as part of routine clinical practice, all ECGs were subsequently verified by a cardiologist. For events with a diagnostic code only or where the dates of the ECG and diagnostic code did not match, manual reviews of the medical records were undertaken to validate the event and to determine the incidence date of the AF.

For analyses, AF was divided into the following categories: *prior AF* (AF occurring prior to MI onset), *new-onset AF* (occurring on the same day or less than 30 days after MI onset), and *late-onset AF* (occurring 30 days or later after MI onset). Those patients who had no documented evidence of AF were categorized as *no AF*.

Clinical data collection

Patient characteristics including age, sex, and cigarette smoking status were obtained from review of patient medical records. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters) squared. Glomerular filtration rate (eGFR) was estimated using the closest serum creatinine value within 1 year of the index MI using the Modification of Diet in Renal Disease Study (MDRD) equation.¹⁵ Prevalent diabetes was defined by the American Diabetes Association criteria.¹⁶ Clinicians' diagnoses were used to identify hyperlipidemia, hypertension, history of HF, or chronic obstructive pulmonary disease (COPD) prior to the index MI. An overall comorbidity score for each patient was assigned using the Charlson comorbidity index.¹⁷

Ascertainment of healthcare utilization measures

Healthcare utilization was obtained from study enrollment through September 30, 2011. Hospitalizations, ED visits, and outpatient office visits were ascertained from the Olmsted County Healthcare Expenditure and Utilization Database, which contains healthcare utilization occurring in Olmsted County, MN from 1987 to present. Since all MI patients were hospitalized at study onset, only subsequent hospitalizations were identified. In-hospital transfers or transfers between Olmsted Medical Center and Mayo Clinic were analyzed as a single hospitalization. ED visits that resulted in a hospital admission were counted as both an ED visit and a hospitalization. Tests, imaging, or outpatient procedures were not considered as outpatient office visits and were not quantified.

Furthermore, the primary cause of each hospitalization was classified as cardiovascular (ICD-9 codes 390-459 and 745-747, ICD-10 codes I00-I99, Q20-Q28) or non-cardiovascular based on American Heart Association classifications.¹⁸ In addition, we identified hospitalizations which were due to a major bleeding event, whether cardiovascular related or not, using ICD-9 codes identified by Fosbol, et al as a guideline.¹⁹ Finally, ischemic strokes were identified using ICD-9 codes 433.x1, 434.x1 and 436.

Statistical analysis

Statistical analyses were performed using SAS statistical software, version 9.2 (SAS Institute Inc., Cary, NC). Means and proportions of participant characteristics by AF category were presented. Follow-up time was calculated from the index date of MI until death, last follow-up, or September 30, 2011, whichever came first.

Andersen-Gill modeling, which allows for modeling of multiple outcome events, was used to calculate hazard ratios (HRs) of hospitalizations and ED visits by category of AF. For each outcome, unadjusted and age- and sex-adjusted Andersen-Gill models were modeled with an indicator for prior AF and both new-onset AF and late-onset AF modeled as time-dependent variables. Fully-adjusted Andersen-Gill models included the following covariates at the time of MI: age, sex, BMI, ever smoking, eGFR, STEMI, Killip class, peak troponin, and prevalent comorbidities, including hypertension, hyperlipidemia, diabetes, HF, and COPD. Additional adjustment for recurrent MI and HF as time-dependent variables was also modeled. Finally, we categorized each hospitalization according to the principal diagnosis as cardiovascular or non-cardiovascular and analyses were performed separately for each category.

Since outpatient office visits during follow-up may cluster together (e.g. multiple outpatient visits on a given day or within a span of several days as part of the diagnostic process or for yearly physical examinations), we modeled the outpatient visits using 2 approaches. The first approach used an Andersen-Gill model counting every visit (in the case where multiple visits occurred on a single day, the follow-up time during that day was split to account for the multiple visits). In a second approach, we considered outpatient visits occurring on the same day or consecutive days as a single encounter and used the Andersen-Gill method modeling outpatient encounters. Since results did not differ between the two approaches, we report the HRs for the model counting all visits.

Sensitivity analyses, including additional adjustments for dismissal medications (aspirin, statins, beta blockers, and angiotensin converting enzyme inhibitors/angiotensin receptor blockers) and reperfusion/revascularization were conducted for all healthcare utilization measures. Interactions of AF group with sex for all outcomes were also tested. Finally, the association of AF category with the risk of recurrent MI was modeled using Cox proportional hazards regression.

Results

Between November 2002 and December 2010, we identified 4957 patients without prior MI who presented to a Mayo Clinic facility with elevated troponin T (Figure 1). Research authorization was available on 4856 (98%) patients, of which 1700 (35%) met the criteria for incident MI. Of these 1700 validated incident MI patients, we excluded those who died in the hospital (n=103), those who did not provide research authorization for capture of utilization measures (n=77), and those with incomplete information on covariates (n=18). Of the 1502 remaining patients in our cohort, 57.7% were men and the mean age was 67.6 ± 15 years. There were 237 (15.8%) patients who had AF prior to their incident MI, 163 (10.9%) who developed new-onset AF, 113 (7.5%) who developed late-onset AF, and 989 (65.8%) with no AF. Patients with AF were older at the index MI and had a greater number of comorbidities; in particular, those with AF prior to MI had worse renal function and were more likely to have prevalent HF and COPD than those who developed AF after MI or those without AF (Table I).

Over a mean follow-up of 3.9 years, 3661 hospitalizations, 5559 ED visits, and 80,240 outpatient office visits occurred. Fifty-one percent of ED visits were followed by a

hospitalization within 48 hours, while 78% of hospitalizations were preceded by an ED visit. Of the hospitalizations, 1209 (33%) were for cardiovascular causes and 2452 (67%) were non-cardiovascular. In addition, 98 (3%) of the hospitalizations were for major bleeding episodes and 41 (1%) were due to ischemic strokes.

The timing of AF in relation to MI differentially impacted the risk of subsequent hospitalizations (Table II). In fully-adjusted models, those with prior AF exhibited a 1.6-fold increased risk of hospitalizations (HR 1.57, 95% CI 1.29-1.91) and those with new-onset AF exhibited a 1.3-fold increased risk (HR 1.34, 95% CI 1.11-1.63), whereas late-onset AF was associated with more than a 2-fold increased risk (HR 2.18, 95% CI 1.67-2.83) compared to those without AF. Further adjustment for HF and recurrent MI as time-dependent variables attenuated the HRs, particularly in the late-onset AF group, but the largest risk of hospitalizations was still observed among those with late-onset AF.

A similar pattern was observed for both ED visits and outpatient visits, although with slightly smaller HRs. The HRs for ED visits were 1.42 (95% CI 1.16-1.73), 1.17 (95% CI 0.96-1.42), and 1.78 (95% CI 1.39-2.29) for prior, new-onset, and late-onset AF, respectively, compared to those without AF in the fully-adjusted model. The corresponding adjusted HRs for outpatient visits were 1.46 (95% CI 1.30-1.64), 1.23 (95% CI 1.08-1.41), and 1.72 (95% CI 1.47-2.02). Further adjustment for recurrent MI and HF as time-dependent variables minimally attenuated the results for ED visits and outpatient visits.

In ancillary analyses, we identified the primary causes of each hospitalization as cardiovascular or non-cardiovascular. The associations of AF status with hospitalization were higher for cardiovascular hospitalizations compared to non-cardiovascular hospitalizations for all AF groups (Figure 2).

Sensitivity analyses additionally adjusting for dismissal medications, including aspirin, statins, beta blockers, and angiotensin converting enzyme inhibitors/angiotensin receptor blockers, as well as reperfusion/revascularization were conducted for all healthcare utilization measures, and results did not differ (data not shown). Furthermore, the associations of AF group with healthcare utilization did not differ by sex ($p > 0.30$ for all healthcare utilization outcomes). Finally, 170 patients experienced a recurrent MI. The risk of recurrent MI differed by AF timing, with the largest increased risk observed in those with late-onset AF (fully-adjusted HRs (95% CI): 1.46 (0.92-2.31), 1.70 (1.04-2.78), and 2.51 (1.61-3.93) for prior, new-onset, and late-onset AF, respectively).

Discussion

In this community cohort of individuals with incident MI, the risk of subsequent healthcare resource utilization differed markedly by the presence and timing of AF in relation to MI. Patients developing late-onset AF (< 30 days after MI onset) exhibited a nearly 2-fold increased risk of hospitalizations, ED visits, and outpatient visits compared to those without AF.

Atrial fibrillation complicating myocardial infarction is associated with adverse outcomes and poor prognosis

The concurrence of AF with MI is associated with increased morbidity and mortality. An increased risk of stroke and transient ischemic attack has been reported in both clinical trial populations and convenience samples of consecutive hospitalized patients. In the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-I) trial, MI patients with AF experienced higher rates of in-hospital stroke (3.1%) compared to those without AF (1.3%).²⁰ Among MI patients with clinical signs of

HF or left ventricular dysfunction enrolled in the Optimal Trial in Myocardial Infarction with the Angiotensin II Antagonist Losartan (OPTIMAAL) trial, those with either AF at baseline or new-onset AF during follow-up exhibited an approximately 2-fold greater risk of subsequent stroke compared with those with no AF.²¹ In addition, the risk of future stroke or transient ischemic attack during 1 year of follow-up was more than 3-fold greater in MI patients with transient AF occurring during the hospitalization for MI compared to those without AF in two different studies enrolling consecutive hospitalized patients.^{22, 23} However, in another convenience sample of MI patients, while the incidence of ischemic stroke was much higher in the first year of follow-up in patients with AF than those without AF during hospitalization for MI, the odds of developing ischemic stroke over a mean of 7 years was no different between those with and without AF.²⁴

In addition to the evidence implicating AF as a risk factor for subsequent stroke in MI patients, many studies have investigated the association of AF with both short-term (in-hospital and/or 30-day) and long-term mortality after MI. Although some of the data are conflicting, the majority of studies have shown an increased risk of mortality among MI patients with AF. These studies have been summarized in a recent systematic review and meta-analysis, which reported a pooled odds ratio (OR) for mortality of 1.46 (95% CI, 1.35-1.58) for the 23 out of 43 studies identified that reported estimates adjusted for confounding factors.³ In subgroup analyses stratified by the timing of AF in relation to MI, those with AF prior to MI exhibited a 1.3-fold increase in the odds of death and those with new-onset AF, which was generally considered within the hospitalization for MI, exhibited a 1.4-fold increase in the odds of death compared to those without AF. Finally, a recent community-based study identified the timing of AF as an important prognostic indicator in MI, with the highest risk of death observed among patients who developed AF more than 30 days after MI (2.5-fold increased risk compared to no AF).⁴ Our study, which is the first to assess the impact of the timing of AF on healthcare utilization in MI patients, shows a similar pattern whereby those with late-onset AF exhibited the greatest risk of subsequent hospitalizations, ED visits, and outpatient visits.

Significance of atrial fibrillation developing late after myocardial infarction

The differential association observed for healthcare utilization and mortality by timing of AF in MI patients may reflect different pathophysiologic mechanisms. For example, late-onset AF may be a marker of worsening cardiac function, including elevated filling pressures, atrial volume overload, left ventricular systolic dysfunction, and advanced HF. In particular, lower left ventricular ejection fraction was associated with AF developing during hospitalization after MI in the GUSTO-I trial²⁰ and studies of consecutive hospitalized MI patients, including the TRAndolapril Cardiac Evaluation (TRACE) registry of 27 centers in Denmark²⁵ and a study including 3 hospitals in Italy.²⁶ Furthermore, HF occurring as a complication during hospitalization for MI was predictive of subsequent AF during hospitalization in the TRACE registry²⁷ and a population-based cohort of MI patients in the Worcester, MA metropolitan area.²⁸ In addition, HF is one of the strongest predictors of subsequent AF during the hospitalization for MI, even after multivariable adjustment.²⁹⁻³¹ Rathore and colleagues identified advanced HF as the most significant predictor of the development of AF (OR 1.58, 95% CI 1.45-1.73) among almost 107,000 Medicare patients hospitalized for MI in the Cooperative Cardiovascular Project.³⁰ In a study of 320 patients who developed AF after MI and 330 without AF, HF occurring as a complication after MI was also the most important predictor of AF (OR 3.03, 95% CI 2.08-4.43).²⁹ Finally, when the timing of AF and HF during hospitalization was considered, 84% of AF events followed the development of HF.

Although these aforementioned studies predict the development of new AF during the hospital course, worsening cardiac function may also be involved in the excess risk of

healthcare utilization among those developing later AF. In particular, we found that after the additional adjustment for time-dependent HF and recurrent MI, the risk of hospitalizations and ED visits was somewhat attenuated, lending evidence that some of the excess risk in the late-onset group was due to the subsequent development of HF and recurrent MI after AF. However, since our results were still significant even after adjustment for time-dependent HF and recurrent MI, AF itself may partially be responsible for the increased risk of hospitalizations and ED visits in the late-onset AF group.

Limitations and strengths

Several limitations should be acknowledged. First, although we employed a rigorous approach to validate the AF events in our cohort, because AF can be asymptomatic and transient in nature, some misclassification in AF status may have occurred. Second, we do not have information on duration of AF and thus cannot categorize the AF events as paroxysmal, persistent, or permanent AF, eliminating the ability to adjust our models for type of AF. Third, information on treatments for AF were not uniformly available; thus, we were unable to adjust for AF treatment in our models nor provide results stratified by treatment. Fourth, we did not assess healthcare utilization occurring outside of Olmsted County; however, since Olmsted County is relatively isolated from other urban centers and the majority of health care for local residents is provided by the few medical centers within Olmsted County, we expect any missing resource utilization to have been sufficiently infrequent so as not to have impacted the results. Finally, because the Olmsted County population consists mainly of whites, our results may not be generalizable to more ethnically diverse populations.

Our study brings important new knowledge to the field. Key strengths of our study include the ascertainment and validation of incident MI using rigorous epidemiologic criteria and our ability to assess the timing of AF in relation to MI, particularly including AF developing late after the MI. In addition, while we cannot exclude the possibility of some residual confounding due to unmeasured variables affecting our estimates, we had access to an average of almost 40 years of information on comorbidities from patients' medical records prior to the MI, as well as the ability to identify recurrent MI and HF developing after the MI. These comprehensive data allowed us to make extensive adjustments for confounders in our models. Finally, our study was conducted in a community-based cohort of incident MI; accordingly, our findings are representative of real-world MI patients and are less affected by selection bias than clinical trial populations.³²

Conclusion

In this community-based cohort of incident MI patients, we observed marked differences in healthcare resource utilization by the timing of AF in relation to MI, with the greatest risk of subsequent hospitalizations and ED visits occurring among those with AF that developed more than 30 days after MI onset. Our data also confirm that AF is an important prognostic indicator in MI patients. However, the evidence base for management of patients with co-existing MI and AF is limited, and additional trials are needed to improve evidence-based management strategies for these individuals.

Acknowledgments

We thank Susan Stotz, RN, Ruoxiang Jiang, and Deborah Russell for their study support.

Funding Sources

This work was supported by grants from the National Institutes of Health (R01 HL59205), the National Institute on Aging (R01 AG034676), and Janssen Scientific Affairs, LLC. Dr. Roger is an Established Investigator of the

American Heart Association. The funding sources played no role in the design, conduct, or reporting of this study. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents.

The final manuscript has been read and approved by all authors. Drs. Klaskala and Mills are employees of Janssen Research and Development, LLC.

References

1. Kannel WB, Benjamin EJ. Current perceptions of the epidemiology of atrial fibrillation. *Cardiol Clin.* 2009; 27:13–24. vii. [PubMed: 19111760]
2. Schmitt J, Duray G, Gersh BJ, et al. Atrial fibrillation in acute myocardial infarction: a systematic review of the incidence, clinical features and prognostic implications. *Eur Heart J.* 2009; 30:1038–45. [PubMed: 19109347]
3. Jabre P, Roger VL, Murad MH, et al. Mortality associated with atrial fibrillation in patients with myocardial infarction: a systematic review and meta-analysis. *Circulation.* 2011; 123:1587–93. [PubMed: 21464054]
4. Jabre P, Jouven X, Adnet F, et al. Atrial fibrillation and death after myocardial infarction: a community study. *Circulation.* 2011; 123:2094–100. [PubMed: 21536994]
5. St. Sauver JL, Grossardt BR, Yawn BP, et al. Use of a medical records linkage system to enumerate a dynamic population over time: the Rochester Epidemiology Project. *Am J Epidemiol.* 2011; 173:1059–68. [PubMed: 21430193]
6. Apple FS, Wu AHB, Jaffe AS. European Society of Cardiology and American College of Cardiology guidelines for redefinition of myocardial infarction: how to use existing assays clinically and for clinical trials. *Am Heart J.* 2002; 144:981–86. [PubMed: 12486421]
7. Roger VL, Killian JM, Weston SA, et al. Redefinition of myocardial infarction: prospective evaluation in the community. *Circulation.* 2006; 114:790–97. [PubMed: 16908764]
8. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, et al. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation.* 1994; 90:583–612. [PubMed: 8026046]
9. Tunstall-Pedoe H, Kuulasmaa K, Mahonen M, et al. Contribution of trends in survival and coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA project populations. Monitoring trends and determinants in cardiovascular disease. *Lancet.* 1999; 353:1547–57. [PubMed: 10334252]
10. White AD, Folsom AR, Chambless LE, et al. Community surveillance of coronary heart disease in the Atherosclerosis Risk in Communities (ARIC) Study: methods and initial two years' experience. *J Clin Epidemiol.* 1996; 49:223–33. [PubMed: 8606324]
11. Alpert JS, Thygesen K, Antman E, et al. Myocardial infarction redefined--a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol.* 2000; 36:959–69. [PubMed: 10987628]
12. Jaffe AS. Elevations in cardiac troponin measurements: false false-positives: the real truth. *Cardiovasc Toxicol.* 2001; 1:87–92. [PubMed: 12213978]
13. Kors JA, Crow RS, Hannan PJ, et al. Comparison of computer-assigned Minnesota Codes with the visual standard method for new coronary heart disease events. *Am J Epidemiol.* 2000; 151:790–7. [PubMed: 10965976]
14. Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience of 250 patients. *Am J Cardiol.* 1967; 20:457–63. [PubMed: 6059183]
15. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate. *Ann Intern Med.* 2006; 145(4):247–54. [PubMed: 16908915]
16. Standards of medical care in diabetes--2006. *Diabetes Care.* 2006; 29(Suppl 1):S4–42. [PubMed: 16373931]

17. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987; 40:373–83. [PubMed: 3558716]
18. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. *Circulation.* 2012; 125:e2–e220. [PubMed: 22179539]
19. Fosbol EL, Wang TY, Li S, et al. Safety and effectiveness of antithrombotic strategies in older adult patients with atrial fibrillation and non-ST elevation myocardial infarction. *Am Heart J.* 2012; 163:720–8. [PubMed: 22520540]
20. Crenshaw BS, Ward SR, Granger CB, et al. Atrial fibrillation in the setting of acute myocardial infarction: the GUSTO-I experience. *J Am Coll Cardiol.* 1997; 30:406–13. [PubMed: 9247512]
21. Lehto M, Snapinn S, Dickstein K, et al. Prognostic risk of atrial fibrillation in acute myocardial infarction complicated by left ventricular dysfunction: the OPTIMAAL experience. *Eur Heart J.* 2005; 26:350–6. [PubMed: 15618041]
22. Bishara R, Telman G, Bahouth F, et al. Transient atrial fibrillation and risk of stroke after acute myocardial infarction. *Thromb Haemost.* 2011; 106:877–84. [PubMed: 21866303]
23. Siu C-W, Jim M-H, Ho H-H, et al. Transient atrial fibrillation complicating acute inferior myocardial infarction: implications for future risk of ischemic stroke. *Chest.* 2007; 132:44–9. [PubMed: 17400657]
24. Milika AR, Zorana VM, Mihailo MD, et al. The long-term risk of stroke in patients with acute myocardial infarction complicated with new-onset atrial fibrillation. *Clin Cardiol.* 2009; 32:467–70. [PubMed: 19685521]
25. Pedersen OD, Abildstrom SZ, Ottesen MM, et al. Increased risk of sudden and non-sudden cardiovascular death in patients with atrial fibrillation/flutter following acute myocardial infarction. *Eur Heart J.* 2006; 27:290–5. [PubMed: 16267070]
26. Berton G, Cordiano R, Cucchini F, et al. Atrial fibrillation during acute myocardial infarction: association with all-cause mortality and sudden death after 7-year of follow-up. *Int J Clin Pract.* 2009; 63:712–21. [PubMed: 19392921]
27. Pedersen OD, Bagger H, Kober L, et al. The occurrence and prognostic significance of atrial fibrillation/-flutter following acute myocardial infarction. *Eur Heart J.* 1999; 20:748–54. [PubMed: 10329066]
28. Saczynski JS, McManus D, Zhou Z, et al. Trends in atrial fibrillation complicating acute myocardial infarction. *Am J Cardiol.* 2009; 104:169–74. [PubMed: 19576341]
29. Asanin M, Perunicic J, Mrdovic I, et al. Prognostic significance of new atrial fibrillation and its relation to heart failure following acute myocardial infarction. *Eur J Heart Fail.* 2005; 7:671–6. [PubMed: 15921810]
30. Rathore SS, Berger AK, Weinfurt KP, et al. Acute myocardial infarction complicated by atrial fibrillation in the elderly: prevalence and outcomes. *Circulation.* 2000; 101:969–74. [PubMed: 10704162]
31. Wong C-K, White HD, Wilcox RG, et al. Significance of atrial fibrillation during acute myocardial infarction, and its current management: insights from the GUSTO-3 trial. *Card Electrophysiol Rev.* 2003; 7:201–7. [PubMed: 14739713]
32. Steg PG, Lopez-Sendon J, Lopez De Sa E, et al. External validity of clinical trials in acute myocardial infarction. *Arch Intern Med.* 2007; 167(1):68–73. [PubMed: 17210880]

Clinical Summary

- The timing of atrial fibrillation (AF) in relation to myocardial infarction (MI) differentially impacts healthcare utilization.
- MI patients who developed AF 30 days or more after MI experienced the highest rates of healthcare utilization, with a 2-fold increased risk of hospitalizations, emergency department visits, and outpatient visits compared to those without AF.
- Patients with prior and new-onset AF also exhibited increased healthcare utilization, but associations were modest for new-onset AF

Figure 1. Ascertainment of incident myocardial infarction in Olmsted County, MN, 2002-2010
MI, myocardial infarction.

Figure 2. Cause-specific hazard ratios (95% CI) for hospitalizations by atrial fibrillation category

Hazard ratios are adjusted for age, sex, body mass index, ever smoking, estimated glomerular filtration rate, ST elevation MI, Killip class, peak troponin, hypertension, hyperlipidemia, diabetes, heart failure, and chronic obstructive pulmonary disease. CV, cardiovascular.

Table 1

Baseline participant characteristics by atrial fibrillation category

	No AF (N=989)	Prior AF (N=237)	New-onset AF (N=163)	Late-onset AF (N=113)
Demographics				
Age (years)	63.5 (14.8)	76.6 (10.8)	75.6 (13.0)	72.6 (11.6)
Male	612 (61.9)	118 (49.8)	80 (49.1)	57 (50.4)
Cardiovascular risk factors				
Body mass index (kg/m ²)	28.9 (6.4)	28.5 (6.9)	28.5 (6.0)	28.5 (5.6)
Smoking status				
Never	385 (38.9)	105 (44.3)	68 (41.7)	42 (37.2)
Former	361 (36.5)	110 (46.4)	74 (45.4)	56 (49.6)
Current	243 (24.6)	22 (9.3)	21 (12.9)	15 (13.3)
Hypertension	636 (64.3)	201 (84.8)	125 (76.7)	90 (79.6)
Hyperlipidemia	626 (63.3)	163 (68.8)	114 (69.9)	75 (66.4)
Diabetes	200 (20.2)	66 (27.8)	34 (20.9)	30 (26.5)
Comorbidities at index				
Heart failure	77 (7.8)	101 (42.6)	20 (12.3)	19 (16.8)
COPD	120 (12.1)	79 (33.3)	31 (19.0)	23 (20.4)
Charlson comorbidity index				
0	433 (43.8)	25 (10.5)	46 (28.2)	23 (20.4)
1-2	335 (33.9)	71 (30.0)	54 (33.1)	48 (42.5)
3	221 (22.3)	141 (59.5)	63 (38.7)	42 (37.2)
eGFR (mL/min per 1.73 m ²)				
90	95 (9.6)	13 (5.5)	8 (4.9)	6 (5.3)
60 to <90	488 (49.3)	61 (25.7)	53 (32.5)	41 (36.3)
30 to <60	356 (36.0)	116 (48.9)	84 (51.5)	53 (46.9)
<30	50 (5.1)	47 (19.8)	18 (11.0)	13 (11.5)
MI characteristics				
ST elevation MI	230 (23.3)	22 (9.3)	40 (24.5)	15 (13.3)
Peak troponin (ng/mL)	0.65 (0.22,2.01)	0.24 (0.10,0.85)	0.48 (0.15,2.34)	0.48 (0.15,1.49)
Killip class >1	185 (19.1)	89 (38.2)	47 (28.8)	35 (32.1)
MI treatments				
Reperfusion / revascularization	630 (63.7)	78 (32.9)	73 (44.8)	56 (49.6)
Statins at dismissal	789 (79.9)	137 (57.8)	107 (65.6)	88 (77.9)
Aspirin at dismissal	868 (87.9)	178 (75.1)	132 (81.0)	97 (85.8)
Beta blockers at dismissal	837 (84.7)	178 (75.1)	126 (77.3)	95 (84.1)
ACEI/ARBs at dismissal	597 (60.4)	135 (57.0)	87 (53.4)	73 (64.6)

Values are expressed as mean (SD) for normally distributed continuous variables, median (25th, 75th percentile) for non-normally distributed continuous variables, and N (%) for categorical variables. MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; ACEI/ARB, angiotensin converting enzyme inhibitors/angiotensin receptor blockers

Table 2

Hazard ratios (95% CI) for healthcare utilization measures by atrial fibrillation category

	No AF	Prior AF	New-onset AF	Late-onset AF
Hospitalizations				
Crude	1.00 (ref)	2.51 (2.10-3.00)	1.56 (1.28-1.91)	2.72 (2.03-3.65)
Age-and sex-adjusted	1.00 (ref)	2.14 (1.78-2.58)	1.35 (1.10-1.65)	2.41 (1.79-3.24)
Fully-adjusted *	1.00 (ref)	1.57 (1.29-1.91)	1.34 (1.11-1.63)	2.18 (1.67-2.83)
Fully-adjusted †	1.00 (ref)	1.50 (1.25-1.81)	1.24 (1.02-1.50)	1.79 (1.35-2.38)
Emergency department visits				
Crude	1.00 (ref)	1.99 (1.66-2.37)	1.30 (1.05-1.60)	2.06 (1.59-2.68)
Age-and sex-adjusted	1.00 (ref)	1.78 (1.49-2.13)	1.18 (0.96-1.45)	1.89 (1.46-2.45)
Fully-adjusted *	1.00 (ref)	1.42 (1.16-1.74)	1.18 (0.96-1.44)	1.79 (1.40-2.30)
Fully-adjusted †	1.00 (ref)	1.39 (1.15-1.69)	1.11 (0.90-1.36)	1.56 (1.20-2.01)
Outpatient office visits				
Crude	1.00 (ref)	1.59 (1.42-1.78)	1.33 (1.17-1.52)	1.78 (1.53-2.08)
Age-and sex-adjusted	1.00 (ref)	1.50 (1.34-1.68)	1.27 (1.10-1.45)	1.70 (1.46-1.98)
Fully-adjusted *	1.00 (ref)	1.42 (1.26-1.61)	1.24 (1.08-1.42)	1.68 (1.44-1.97)
Fully-adjusted †	1.00 (ref)	1.39 (1.24-1.57)	1.20 (1.04-1.38)	1.58 (1.35-1.85)

* Adjusted for age, sex, body mass index, ever smoking, estimated glomerular filtration rate, ST elevation MI, Killip class, peak troponin, hypertension, hyperlipidemia, diabetes, heart failure, and chronic obstructive pulmonary disease.

† Adjusted for age, sex, body mass index, ever smoking, estimated glomerular filtration rate, ST elevation MI, Killip class, peak troponin, hypertension, hyperlipidemia, diabetes, heart failure, chronic obstructive pulmonary disease, recurrent MI and HF post MI.