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Association between Atrial Fibrillation and Costs after Myocardial Infarction: A Community Study

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Abstract

Objective—To estimate incremental economic impact of atrial fibrillation (AF) and the timing of its onset in myocardial infarction (MI) patients.

Patients and Methods—This retrospective cohort study included incident MI patients from Olmsted County, Minnesota, treated between 11/1/2002 and 12/31/2010. We compared inflation-adjusted standardized costs accumulated between incident MI and end of follow-up among 3 groups by AF status and its timing: no AF, new-onset AF (within 30 days after index MI), or prior AF. Multivariate adjustment of median costs accounted for right-censoring in costs.

Results—The final study cohort had 1,389 patients with 989 in no AF, 163 in new-onset AF, and 237 in prior AF categories. Median follow-up times were 3.98, 3.23, and 2.55 years, respectively. Mean age at index was 67 years, with significantly younger patients in no-AF group (64 years vs 76 and 77 years, respectively; $P<.001$). New-onset and prior AF patients had more comorbid conditions (hypertension, heart failure, and chronic obstructive pulmonary disease). After accounting for differences in baseline characteristics, we found adjusted median (95% CI) costs of $73,000 ($69,000–$76,000) for no AF; $85,000 ($81,000–$89,000) for new-onset AF; and $97,000 ($94,000–$100,000) for prior AF. Inpatient costs composed the largest share of total median costs (no AF, 82%; new-onset AF, 84%; and prior AF, 83%).

Conclusion—These findings indicate that AF frequently coexists with MI and imposes incremental costs, mainly attributable to inpatient care. AF timing matters as prior AF was found to be associated with higher costs than new-onset AF.

Keywords

cost; atrial fibrillation; myocardial infarction

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Disclosures

Dr. Mills is an employee of Janssen Research & Development LLC.

Introduction

Despite considerable improvements in therapy and outcome, myocardial infarction (MI) continues to impose substantial burden in terms of morbidity and mortality, which is further accentuated by post-MI complications including atrial fibrillation (AF), heart failure, and recurrent ischemia.[1–3] AF is a common arrhythmia in clinical practice that often complicates acute MI,[4, 5] and becomes increasingly more prevalent with advancing age.[6] The incidence of AF in the setting of MI varies according to how it is defined and the reported incidence of new-onset AF in patients hospitalized for MI ranges from 2% to 30%.[3, 7–9] AF in MI patients carries an increased risk of death, but there is uncertainty over whether this risk is independent of other comorbid conditions, and whether this risk varies with the timing of AF occurrence.[10–12] Although many investigators have assessed the economic burden of AF in general,[13–16] little is known about the incremental economic burden of AF after MI. Furthermore, although the timing of AF occurrence in MI patients has been found to confer differential mortality risks,[4] there is no evidence on whether AF timing differentially impacts costs. As such, the objective of this study was to estimate the incremental cost of AF in a well-defined community-based MI cohort and compare costs by the timing of AF in relation to MI.

Patients and Methods

Study Population

This study was conducted under the auspices of the Rochester Epidemiology Project, a unique research data infrastructure that provides validated capture of nearly all medical records of persons residing in Olmsted County, Minnesota for more than 40 years.[17–19] The record linkage of the Rochester Epidemiology Project is facilitated by the relative geographic isolation of Olmsted County, and that few health care providers cater to nearly all the health care needs of the community. The study was approved by Institutional Review Boards of both Mayo Clinic and the Olmsted Medical Center.

Identification of the Incident MI Cohort

To identify the incident MI cohort, we first identified all Olmsted County, Minnesota patients hospitalized at Mayo Clinic between 11/01/2002 and 12/31/2010, who presented with a troponin T value of ≥0.03 ng/mL.[20] Nurse coordinators approached these patients or their next of kin within 12 hours of the blood draw to request study participation.[21] Standardized criteria based on cardiac pain, biomarker levels, and Minnesota coding of electrocardiograms were used to determine MI status.[21–24] As per the new guidelines for using troponin T in the MI classification algorithm, a change in 2 troponin measurements was defined as a difference of at least 0.05 ng/mL.[25] Since troponin may remain elevated for up to 2 weeks after the onset of the precipitating event, the occurrence of any relevant comorbid condition was accounted for in the algorithm by downgrading biomarker results from abnormal to equivocal.[26] A significant change in troponin was considered diagnostic in renal failure which causes a chronic elevation in troponin, not a change.

AF Case Ascertainment

Incident AF and its timing of onset were captured by electrocardiograms and *ICD-9-CM* (*International Classification of Diseases, Ninth Revision, Clinical Modification*) diagnosis codes 427.31 or 427.32 (primary or secondary diagnosis) during either a hospitalization or an outpatient visit. Manual review of medical records was undertaken when an electrocardiogram was not available or when the dates of the electrocardiogram and the diagnostic code did not match. The date of first ever (incident) AF event in the patient record was defined as the AF date.

AF Categories (Study Cohorts)

For each patient, the date of the incident MI was defined as the index date. Patients that had AF prior to the index date were in the *prior AF* group, whereas patients who developed AF on or within 30 days of the index MI date were included in the *new-onset AF* group. Patients who developed AF beyond 30 days of the index date were excluded from the study sample, and the remaining MI patients without an AF diagnosis constituted the *no-AF* group.

Baseline Characteristics of Patients

Baseline patient characteristics including age, sex, smoking status, and body mass index closest to the index date were collected from medical records. A standardized definition was used to calculate the estimated glomerular filtration rate.[27] Diagnoses in the medical records were used to capture baseline comorbid conditions, including hypertension, hyperlipidemia, heart failure, and chronic obstructive pulmonary disease. Diabetes mellitus was defined according to the criteria of the American Diabetes Association.[28] The Charlson comorbidity index (CCI) was also constructed for each patient to provide an overall disease severity measure.[29]

Characteristics of MI, including peak troponin (ng/mL), Killip class, and whether ST-segment elevation was present (STEMI), were recorded. Various treatments were also captured (eg, reperfusion/revascularization and discharge medications, including statins, aspirin, warfarin, β-blockers, and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers).

Study Outcome: Health Care Cost Measurement

Health care costs were captured from the Olmsted County Healthcare Expenditure and Utilization Database (OCHEUD), which provides the costs of health care services for Olmsted County, Minnesota, residents standardized at Medicare reimbursement rates.[19] OCHEUD is a standardization algorithm that uses an inflation adjuster and accounts for geographic wage differentials to convert health care costs to be nationally representative at constant dollars.[30] (See online supplement)

Costs that accumulated between index and end of follow-up were used for analyses. All cost outcomes were inflation adjusted to 2011. End of follow-up was defined as the earlier of death date, last clinic encounter, or study end date of 9/30/2011. Deaths were ascertained from death certificates filed in Olmsted County or from autopsy reports, obituary notices, or

electronic files of death certificates obtained from the Office of Vital Records in the Minnesota Department of Health.

The primary outcome of interest was total direct medical costs, which included costs of all inpatient and outpatient health care services between index date and end of follow-up. Secondary outcomes were components of the total medical cost: inpatient (hospitalization) and outpatient medical costs. Additionally, components of outpatient medical costs were analyzed separately, which included costs associated with 1) physician and office visits for evaluation and management; 2) outpatient procedures, imaging, diagnostic testing, and durable medical equipment; and 3) other outpatient or unclassified services.

Analytic Strategy

Descriptive statistics were used to report baseline patient characteristics, with mean and standard deviation (SD) for continuous covariates, and frequencies and percentages for categorical variables. Appropriate statistical tests were used for comparisons of patient characteristics among the 3 study groups, including the Kruskal-Wallis test for continuous covariates and the χ^2 tests for categorical covariates. Since the Kruskal-Wallis and χ^2 tests do not reveal whether a specific group differed from another group, we also conducted pairwise tests between the groups.

Complete cost accumulation was possible only for patients who died before the end of the study; thus, costs for the rest of the patients were censored. To account for censoring of costs, we conducted multivariable analyses of mean and median costs using methods proposed by Bang and Tsiatis.[31, 32] These methods extend the idea of propensity score weighted ordinary least squares estimation for mean costs and median regression for median costs.[33]

SAS statistical software, version 9.2 (SAS Institute Inc) was used for constructing the analytic data set, and Stata SE, version 11.2 (StataCorp LP) was used for statistical analyses.

Results

Of 1,700 incident MI patients, the final study sample included 1,389 cases (Figure). Of these patients, 989 had no AF, 237 had prior AF, and 163 had new-onset AF. Mean (SD) patient age was 67 (15) years, with significantly younger patients and a higher proportion of males in no-AF group than in prior and new-onset AF (Table 1). The 3 groups differed with regard to baseline smoking status, with significantly higher proportion of current smokers in the no-AF group. Patients with new-onset and prior AF had more severe comorbidity, with 39% and 60%, respectively, having CCI ≥3 compared with only 22% in no-AF group. Furthermore, the prevalence of the following baseline conditions exhibited an increasing prevalence from no-AF to new-onset AF to prior AF groups: hypertension, diabetes, heart failure and chronic obstructive pulmonary disease.

The characteristics of MI differed significantly between no-AF and prior AF: STEMI (23% vs 9%; $P<.001$), peak troponin (2 ng/mL vs 1 ng/mL; $P<.001$), and Killip class >1 (19% vs

38%; *P*<.001). Between new-onset AF and prior AF there were significant differences in STEMI (25% vs 9%; *P*<.001), and peak troponin (2 ng/mL vs 1 ng/mL; *P*=.001).

No-AF group had higher rates of reperfusion or revascularization than prior AF (64% vs 33%; *P*<.001) and new-onset (64% vs 45%; *P*<.001) groups. Compared with no-AF, both new-onset and prior AF groups had lower rates of prescriptions for statins, aspirin, and β-blockers and higher rates of warfarin at the time of discharge from the hospital.

Study patients were followed for a mean (SD) of 3.83 (2.53) years. Median total cost was significantly lower in no-AF group than new-onset AF ($44,159 vs $65,439; *P*=.001) and prior AF ($44,159 vs $72,636; *P*<.001; Table 2). Inpatient costs followed a similar pattern and constituted a substantial portion of total costs: 67% in no-AF group, 73% in prior AF group, and 80% in new-onset AF group. Median outpatient costs in no-AF group were significantly lower than in prior AF ($10,686 vs $13,784; *P*=.009). Components of outpatient costs, including those for evaluation and management, and for outpatient procedures, imaging, tests, and durable medical equipment, were not significantly different between the 3 study groups. Notably, costs associated with outpatient procedures, imaging, tests, and durable medical equipment constituted the largest share of outpatient costs (59%–63%).

Supplemental Tables 1 and 2 (Appendix) summarize the costs for complete and censored observations for each of the 3 study groups. In general, both mean and median total costs for the complete cases were higher for prior AF than no-AF, whereas for censored cases, mean and median total costs were higher for both prior AF and new-onset AF.

Multivariable Analyses

Table 3 displays adjusted median costs for the 3 study groups that adjusted for differences in patient baseline characteristics. The No-AF group had the lowest median cost at $72,752, followed by new-onset AF at $85,014 and prior AF at $96,892. Adjusted median inpatient cost followed a similar pattern with no-AF group having the smallest cost ($59,476), followed by new-onset AF ($71,357) and prior AF ($80,086). Adjusted median outpatient costs of approximately $11,000 were similar for each of the 3 groups. Supplemental Table 3 (Appendix) provides multivariable adjusted mean costs for the 3 groups. Unlike the adjusted median costs, the mean costs between the new-onset AF group and the prior AF group were not statistically different.

Discussion

The results of this community study of incident MI patients demonstrate that the presence of AF was associated with significant economic burden and the timing of occurrence had differential impacts on costs. The median total cost was lowest for the no-AF group and highest for the prior AF group. Notably, inpatient costs were the primary driver of total costs in this patient population, which ranged from 82% to 84% for the 3 groups.

It has been recently reported that the cost of patients with MI treated with percutaneous intervention had stabilized but were still higher than Medicare reimbursements.[34] The data

presented herein further document that comorbid conditions in general and AF in particular can be a substantial driver of incremental cost. Our finding that inpatient cost was the largest component of total cost was not surprising, because every patient in the study had at least 1 hospitalization during follow-up, and prior studies that assessed cost burden of AF in general have also found inpatient cost to be the largest component of total cost.[13, 15, 35] However, the finding that the median inpatient cost for the prior AF group was significantly higher than for the new-onset AF group was somewhat surprising, given the fact that patients who develop AF during admission have a worse prognosis than those who present with AF on admission.[6]

Given the complications associated with co-occurrence of AF and MI, and the increased risk of all-cause mortality and stroke that AF imposes on MI patients,[3, 36] the management of this patient population can be challenging. Additionally, due to the lack of relevant randomized clinical trials, the available guidelines for managing AF in MI patients are based primarily on consensus (level C evidence),[37, 38] and therefore may not provide clinicians with objective guidance on how best to manage these patients in the real-world clinical practice setting. The lack of clear guidance and the associated uncertainty may result in higher health care utilization[39] in managing AF in MI patients, which in turn leads to higher costs. The significantly higher costs for MI patients with AF as shown in our study may reflect this possibility. Better management of this complex subgroup of patients also has public health implications, with the projected increase of AF prevalence to hit 15.9 million by 2050 from the current 2 to 3 million,[40, 41] thereby greatly increasing the current cost burden of $6.65 billion.[13]

Strengths and Limitations

The geographic setting of this study afforded several advantages. First, since the Rochester Epidemiology Project captures virtually all health care utilization within the community, it makes the findings less amenable to referral or selection bias. This is possible due to the relatively isolated geographic location of Olmsted County and the fact that out-of-county migration of MI patients is less than 8%.[4] Second, the study includes cases that were validated for both MI and AF, and the long-term follow-up enabled us to capture the incremental cost of AF in MI patients more accurately. Furthermore, substantial differences in costs between complete and censored cases (Appendix) imply that that a naive estimate of costs will significantly bias estimates, underscoring the need to account explicitly for the presence of censoring. The approach of Bang and Tsiatis[31, 32] for multivariate adjustment of median cost that we implemented accounted for right-censoring of health care costs.

The results of this study must be interpreted in view of the following limitations. AF can be asymptomatic or patients may not seek care for their symptoms. Thus, although we used both inpatient and outpatient ECGs and diagnostic codes to identify AF, there is a possibility of misclassification of patients with regard to the timing of AF, particularly between new-onset and prior AF groups, as some of the new-onset AF patients might have undiagnosed AF prior to their hospitalization for MI. Although differences in measurable comorbidities were adjusted for in our analyses, the comorbidities were captured only as binary covariates at baseline, which often fail to account for the severity or duration of the condition. Thus, as

in any observational study, the possibility of residual confounding cannot be ruled out. Finally, we did not capture prescriptions filled outside the inpatient setting. Although no prior estimate of the cost of outpatient medications for MI patients with concurrent AF is available, outpatient prescription drug costs for AF patients in general have been found to be 4% of the total cost,[13] which provides a rough estimate of the extent of underestimation of the total cost in our study.

Conclusion

In summary, our study offered a unique opportunity to evaluate the impact of AF on overall health care costs in a population-based, well-defined cohort of MI patients with long-term follow-up. Our findings showed that the median cost of medical care was significantly higher in MI patients with prior and new-onset AF than those without AF. Inpatient cost constituted 82% to 84% of the total cost in the 3 study groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AF	atrial fibrillation
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
MI	myocardial infarction
OCHEUD	Olmsted County Healthcare Expenditure and Utilization Database
STEMI	ST-segment elevation myocardial infarction

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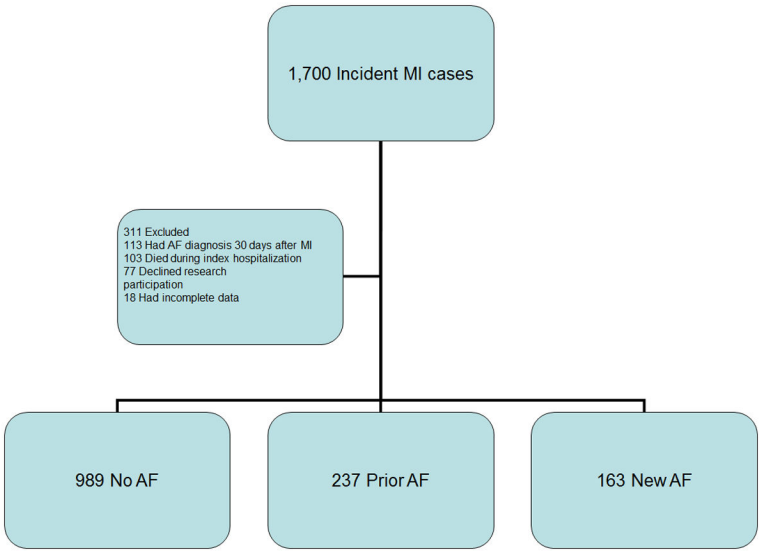

Figure.
Patient Flowchart.

Table 1

Baseline Characteristics of Patients with Myocardial Infarction and No Atrial Fibrillation, Prior Atrial Fibrillation, or New-Onset Atrial Fibrillation*

Variable	Total (N=1,389)	No AF (n=989)	Prior AF (n=237)	New-Onset AF (n=163)	*P* Value	*P* Value (No AF vs Prior AF)	*P* Value (No AF vs New-Onset AF)	*P* Value (New-Onset AF vs Prior AF)
Demographics								
Age at MI, mean (SD), y	67.2 (15.2)	63.5 (14.8)	76.6 (10.8)	75.6 (13.0)	<.001†	<.001§	<.001§	.91§
Male sex	810 (58.3)	612 (61.9)	118 (49.8)	80 (49.1)	.001≠	.001≠	.002≠	.89≠
CV risk factors								
BMI, mean (SD)	28.8 (6.4)	28.9 (6.4)	28.5 (6.9)	28.6 (6.0)	.32§	.13§	.89§	.34§
Smoking status					<.001≠	.001≠	<.003≠	.51≠
Never	558 (40.2)	385 (38.9)	105 (44.3)	68 (41.7)				
Former	545 (39.2)	361 (36.5)	110 (46.4)	74 (45.4)				
Current	286 (20.6)	243 (24.6)	22 (9.3)	21 (12.9)				
Comorbidities at index								
Hypertension	962 (69.3)	636 (64.3)	201 (84.8)	125 (76.7)	<.001≠	<.001≠	.002≠	.04≠
Hyperlipidemia	903 (65.0)	626 (63.3)	163 (68.8)	114 (69.9)	.11≠	.11≠	.10≠	.81≠
Diabetes mellitus	300 (21.6)	200 (20.2)	66 (27.8)	34 (20.9)	.04≠	.01≠	.85≠	.11≠
Heart failure	198 (14.3)	77 (7.8)	101 (42.6)	20 (12.3)	<.001≠	<.001≠	.06≠	<.001≠
COPD	230 (16.6)	120 (12.1)	79 (33.3)	31 (19.0)	<.001≠	<.001≠	.02≠	.002≠
Charlson Comorbidity Index					<.001≠	<.001≠	<.001≠	<.001≠
0	504 (36.3)	433 (43.8)	25 (10.5)	46 (28.2)				
1–2	460 (33.1)	335 (33.9)	71 (30.0)	54 (33.1)				
≥3	425 (30.6)	221 (22.3)	141 (59.5)	63 (38.7)				
eGFR, mL/min per 1.73 m^2					<.001≠	<.001≠	<.001≠	.10≠
≥90	116 (8.4)	95 (9.6)	13 (5.5)	8 (4.9)				
60 to <90	602 (43.3)	488 (49.3)	61 (25.7)	53 (32.5)				
30 to <60	556 (40.0)	356 (36.0)	116 (48.9)	84 (51.5)				
<30	115 (8.3)	50 (5.1)	47 (19.8)	18 (11.0)				
MI characteristics								

Variable	Total (N=1,389)	No AF (n=989)	Prior AF (n=237)	New-Onset AF (n=163)	*P* Value	*P* Value (No AF vs Prior AF)	*P* Value (No AF vs New-Onset AF)	*P* Value (New-Onset AF vs Prior AF)
STEMI	292 (21.0)	230 (23.3)	22 (9.3)	40 (24.5)	<.001[≠]	<.001[≠]	.72[≠]	<.001[≠]
Peak troponin T, mean (SD), ng/mL	1.8 (3.2)	1.9 (3.2)	1.0 (2.4)	2.1 (4.0)	<.001[†]	<.001[§]	.20[§]	.001[§]
Killip class >1	321 (23.1)	185 (18.7)	89 (37.6)	47 (28.8)	<.001[≠]	<.001[≠]	.04[≠]	.29[≠]
Treatments								
Reperfusion or revascularization	781 (56.2)	630 (63.7)	78 (32.9)	73 (44.8)	<.001[≠]	<.001[≠]	<.001[≠]	.02[≠]
Statins at discharge	1,033 (74.4)	789 (79.8)	137 (57.8)	107 (65.6)	<.001[≠]	<.001[≠]	<.001[≠]	.1[≠]
Aspirin at discharge	1,178 (84.8)	868 (87.8)	178 (75.1)	132 (81.0)	<.001[≠]	<.001[≠]	.02[≠]	.17[≠]
β-Blockers at discharge	1,141 (82.1)	837 (84.6)	177 (74.7)	127 (77.9)	<.001[≠]	<.001[≠]	.03[≠]	.46[≠]
ACEI or ARB at discharge	819 (59.0)	597 (60.4)	135 (57.0)	87 (53.4)	.19[≠]	.34[≠]	.09[≠]	.48[≠]
Warfarin at discharge	169 (12.2)	44 (4.5)	89 (37.6)	36 (22.1)	<.001[≠]	<.001[≠]	<.001[≠]	001[≠]

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; BMI, body mass index (weight in kilograms divided by height in meters squared [kg/m^2]); COPD, chronic obstructive pulmonary disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; STEMI, ST segment elevation myocardial infarction.

[*] Values are number (percentage) unless specified otherwise.

[†] By the Kruskal-Wallis test.

[≠] By the χ^2 test.

[§] By the Mann-Whitney test.

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Table 2

Univariate Analyses of Cost Outcomes

Variable	Total (N=1,389)	No AF (n=989)	Prior AF (n=237)	New-Onset AF (n=163)	*P* Value	*P* Value No AF vs Prior AF	*P* Value No AF vs New-onset AF	*P* Value New AF vs Prior AF
Total medical cost					<.001*			
Mean (SD)	76,515 (84,961)	65,874 (73,202)	109,736 (113,337)	92,773 (88,776)		<.001†	<.001†	.20†
Median	49,589	44,159	72,636	65,439		<.001≠	.001≠	.54≠
Inpatient					<.001*			
Mean (SD)	57,363 (69,831)	47,995 (59,574)	84,702 (93,338)	74,454 (74,301)		<.001†	<.001†	.48†
Median	35,390	29,904	52,723	52,422		<. 001≠	<.001≠	>.99≠
Outpatient					.33*			
Mean (SD)	19,152 (28,871)	17,880 (24,891)	25,034 (42,924)	18,319 (24,860)		.23†	.45†	.20†
Median	11,467	10,686	13,784	11,007		.009≠	.87≠	.22≠
Outpatient evaluation and management					.46*			
Mean (SD)	4,252 (4,349)	4,147 (4,029)	4,821 (5,579)	4,059 (4,136)		.56†	.28†	.30†
Median	3,102	3,057	3,490	2,954		.08≠	.74≠	.22≠
Outpatient procedure, imaging, test, and durable medical equipment					.42*			
Mean (SD)	12,855 (22,254)	12,089 (19,164)	16,858 (33,737)	11,684 (17,797)		.72†	.22†	.28†
Median	6,866	6,737	8,157	6,470		.31≠	.87≠	.31≠
Outpatient other/unclassified					.57*			
Mean (SD)	2,045 (6,055)	1,643 (4,332)	3,355 (8,544)	2,576 (9,460)		.41†	.63†	.28†
Median	350	324	525	412		.65≠	.24≠	.56≠

Abbreviation: AF, atrial fibrillation.

*By the Kruskal-Wallis test.

†By the Mann-Whitney test.

≠By the Mood Median Test.

Table 3

Adjusted Median Cost Outcomes*

Variable	No AF (n=989)	New-Onset AF (n=237)	Prior AF (n=163)
Total medical cost	72,752 (69,371–76,134)	85,014 (81,431–88,597)	96,892 (93,510–100,273)
Inpatient	59,476 (56,940–62,013)	71,357 (68,647–74,068)	80,086 (77,549–82,622)
Outpatient	10,795 (10,226–11,364)	10,686 (10,120–11,253)	10,996 (10,427–10,427)
Outpatient evaluation and management	2,347 (2,209–2,484)	2,109 (1,976–2,242)	2,615 (2,478–2,753)
Outpatient procedure, imaging, tests, and durable medical equipment	6,379 (6,007–6,752)	5,693 (5,321–6,065)	5,618 (5,246–5,990)
Outpatient other unclassified	422 (388–456)	519 (485–554)	500 (466–534)

Abbreviation: AF, atrial fibrillation.

*Values are median dollars (95% CI dollars), adjusted for age, sex, body mass index (weight in kilograms divided by height in meters squared [kg/m^2]), smoking status, hypertension, hyperlipidemia, diabetes mellitus, heart failure, chronic obstructive pulmonary disease, eGFR (elevated glomerular filtration rate), peak troponin, and STEMI (ST segment elevation myocardial infarction).

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