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Original article

Temporal pattern and costs of rehospitalization in atrial fibrillation/atrial flutter patients with one or more additional risk factors

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Atrial fibrillation – Cardiovascular disease – Cost – Hospitalization – Patient readmission – Risk factors

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Citation: J Med Econ 2012; 15:548–55**Abstract****Objectives:**

The ATHENA study showed that use of dronedarone reduced rates of first cardiovascular (CV) hospitalization in atrial fibrillation/flutter (AF/AFL) patients. AF is associated with high costs to payers, which are driven by high rates of hospitalization. This retrospective cohort study examined readmission patterns and costs to US payers in real-world AF/AFL patients with ≥ 1 additional risk factor (ARF).

Methods:

Patients hospitalized (January 2005–March 2008) with AF/AFL as primary diagnosis and having ≥ 1 year of health coverage, before and after their first (index) admission, were identified in the PharMetrics Patient-Centric database. As in the ATHENA study, patients had to be ≥ 75 years of age or ≥ 70 years, with ≥ 1 ARF. Rehospitalization patterns (all-cause, all CV-related [including AF/AFL] and AF/AFL-related alone) were examined over 1 year post-index, and costs of index vs later AF/AFL admissions compared.

Results:

The study included 3498 patients (mean 80 [SD 7.6] years; 42.4% men). Over 1 year, 1389 patients (39.7%) were rehospitalized for any cause (mean 1.7 [SD 1.3] events/patient), with 1223 patients (35.0%) undergoing CV-related (mean 1.6 [SD 1.0] events/patient) and 935 (26.7%) undergoing AF-related rehospitalization (mean 1.4 [SD 0.8] events/patient). Common causes of CV-related readmissions (primary diagnosis) were AF/AFL (47.5%), congestive heart failure (CHF) (9.9%), coronary artery disease (7.4%), and stroke/transient ischemic attack (6.2%). Readmission rates at 3 months were 16.2% (all-cause), 14.3% (all CV-related including AF/AFL), and 10.5% (AF/AFL-related alone). AF/AFL readmissions (primary diagnosis) were longer than initial hospitalizations (mean total 6.9 [SD 12.9] vs 4.3 [SD 5.1] days, $p < 0.0001$) and more costly (median \$1819 [25th percentile \$1066, 75th percentile \$5623] vs \$1707 [25th percentile \$1102, 75th percentile \$4749]).

Limitations:

This study excluded patients with pre-existing CHF, did not require electrocardiogram confirmation of AF/AFL diagnosis, and did not distinguish between paroxysmal, persistent, and permanent AF.

Conclusions:

AF/AFL patients with ≥ 1 ARF have high readmission rates. AF/AFL-related readmissions incur higher costs than the initial AF/AFL admissions.

Introduction

Atrial fibrillation (AF) and atrial flutter (AFL) affect ~ 3.3 million individuals in the US, and are associated with increased cardiovascular (CV) and cerebrovascular risk¹. Patients with AF and/or AFL are significantly more likely than

age-matched non-AF/AFL patients to have co-morbidities such as ischemic stroke, congestive heart failure (CHF), valvular heart disease, coronary artery disease, peripheral vascular disease, pulmonary disease, thyroid disease, diabetes mellitus, or hypertension¹. Moreover, the presence of AF and/or AFL puts patients at increased risk of hospitalization or death^{2,3}.

AF and AFL are associated with high healthcare costs, driven in particular by high rates of CV-related hospitalization⁴⁻⁸. For example, the incremental cost of AF in the US was projected to reach \$26.0 billion in 2010, of which \$16.4 billion (63%) represented inpatient costs⁸. A retrospective, cohort study of 4174 patients hospitalized with primary AF found that 12.5% and 10.1% of chronic AF and newly-diagnosed AF patients, respectively, were rehospitalized within 1 year of their index hospitalization with an AF-related diagnosis. The majority of these patients were readmitted within the first 6 months⁵.

Until recently, anti-arrhythmic drug therapy had not been demonstrated to reduce the risk of hospitalization in AF or AFL. ATHENA (A placebo-controlled, double-blind, parallel arm Trial to assess the efficacy of dronedarone 400 mg bid for the prevention of cardiovascular Hospitalization or death from any cause in patiENTs with Atrial fibrillation/atrial flutter) was the first randomized controlled study to demonstrate that anti-arrhythmic drug therapy (dronedrone) could reduce the risk of CV-related hospitalization and death in AF/AFL patients. This study demonstrated significant reductions in the incidence of first CV hospitalization (−26%), CV death (−29%), and arrhythmic death (−45%) with use of dronedrone compared with placebo over a 12–30-month follow-up period⁹. However, the ATHENA study adopted the endpoint of first hospitalization, and did not examine subsequent rehospitalization events.

Hospital readmission has become the focus of much attention in the current healthcare debate in the US, with healthcare reformers proposing to cut spending and improve quality of care by penalizing institutions with high readmission rates. This has been prompted by the very high costs of unplanned rehospitalizations, with one estimate suggesting a cost of ~\$17.4 billion per year to Medicare alone¹⁰, of which ~\$12.0 billion for patients readmitted within 30 days is potentially preventable¹¹. The recent 'Hospital to Home' national quality improvement initiative of the American College of Cardiology and Institute for Healthcare Improvement aims to reduce all-cause readmission rates among patients hospitalized with heart failure and acute myocardial infarction. This initiative may be expanded to cover other CV conditions that are also characterized by high rates of hospital readmission.

An important question regarding chronic conditions associated with multiple hospitalizations, such as AF, is whether the patient's condition is worsening over time. One way of assessing this would be to compare the initial

hospitalization with subsequent readmissions: if each readmission requires a longer stay in hospital and a greater level of intervention, then this would suggest that the patient's condition was worsening. The aim of the present analysis was to determine the temporal pattern and cost of rehospitalization (relative to the initial hospitalization) among a cohort of hospitalized AF/AFL patients, with ≥ 1 additional risk factor (ARF), in the real-world setting.

Patients and methods

Study design

This was a retrospective cohort study using data from the PharMetrics Patient-Centric database (IMS Health, Danbury, CT) covering the period between January 1, 2004 and March 31, 2009. This database contains fully adjudicated medical and pharmaceutical claims from commercial health plan information collected from >94 different managed care organizations in addition to Medicare. The database includes information on outpatient pharmacy claims and medical hospitalization claims with discharge diagnoses as well as health plan costs from the third-party payer's perspective. Data from this database have been used in several previous health outcome studies¹²⁻¹⁶.

Patient selection

Adult patients hospitalized (index hospitalization identification period January 2005–March 2008) with AF/AFL as the primary diagnosis (International Classification of Diseases, ninth revision, Clinical Modification [ICD-9-CM] codes 427.31 and 427.32, respectively) were identified. In accordance with the published patient selection criteria of the ATHENA trial⁹, the AF/AFL patients included in this analyses (i.e., with ≥ 1 ARF) were required to be: (1) aged ≥ 75 years regardless of co-morbidities (as advanced age was considered an ARF); or (2) aged 70–74 years with ≥ 1 of the following additional CV risk factors: arterial hypertension, diabetes, arterial/pulmonary embolism, or stroke/transient ischemic attack (TIA). Patients were also required to have ≥ 12 months of continuous medical and prescription drug coverage both prior to and following their first hospitalization with a primary diagnosis of AF/AFL (the index event). As in the ATHENA study, patients were excluded from the analysis if they had a diagnosis of acute myocarditis or end-stage renal disease during the 12-month period preceding the index AF/AFL event. Patients in the ATHENA trial were not automatically excluded if they had a diagnosis of CHF. Patients with New York Heart Association (NYHA) Class I, II, and III CHF were included in the ATHENA trial and those with Class IV CHF were excluded. In our study, it was not

possible to identify NYHA CHF class; therefore we took the conservative approach of excluding all patients with CHF.

Study end-points

Information was collected on gender, age, geographic region, health plan type, co-morbidities, Charlson co-morbidity index (CCI), and CHADS₂ index. The CCI was used as a composite measure of co-morbidity burden¹⁷, and the CHADS₂ score was used as a measure of stroke risk^{18,19}.

The temporal pattern of rehospitalization (categorized as all-cause, all CV-related [including AF/AFL], and AF/AFL-related alone) was assessed over the 12-month post-index period. CV-related rehospitalizations encompassed admissions with a primary or secondary diagnosis of circulatory system disease (ICD-9-CM codes 390–459.9) and included AF-related rehospitalizations, which were defined as admissions with a primary or secondary diagnosis of AF/AFL (ICD-9-CM codes 427.31 and 427.32, respectively). CV- and AF/AFL-related rehospitalizations were further sub-classified into those with a CV or AF/AFL primary diagnosis at hospital discharge. CV causes were further categorized based on the pre-specified main causes for CV hospitalization in the ATHENA study²⁰, which are as follows: AF/AFL, CHF, coronary atherosclerosis, TIA/stroke, blood pressure-related, acute myocardial infarction/intermediate coronary syndrome, ventricular arrhythmia, major bleeding, supraventricular rhythm disorder, venous thromboembolism, angina pectoris/chest pain, and other CV events.

Rehospitalization parameters included time to readmission (number of days between the index hospitalization and the first readmission during the 12-month post-index period), frequency of readmission, and reason for rehospitalization (e.g., all-cause, CV-associated [including AF/AFL-related], or AF/AFL-related alone). For the sub-set of AF/AFL patients with ≥ 1 ARF who underwent hospital readmission with AF/AFL as the primary discharge diagnosis, the cost of the first post-index rehospitalization (hospital and physician payments) was compared with the cost of the index AF/AFL hospitalization. The length of stay of the first post-index rehospitalization was also compared with that of the index hospitalization within this sub-set. These comparisons used the same patients for initial hospitalization and rehospitalization; therefore, demographics and co-morbidities were self-matched, with each patient serving as their own control.

Statistical analyses

Patient demographics, clinical characteristics, resource use, and cost data were summarized using

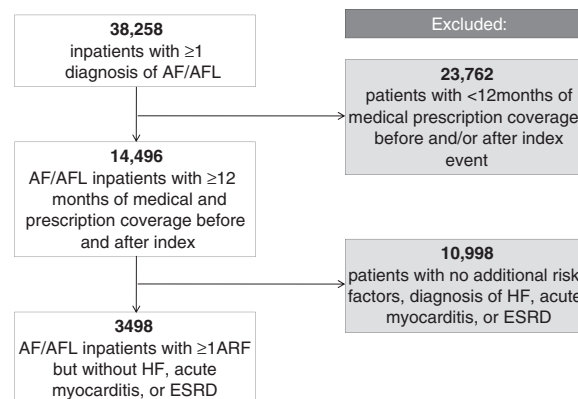


Figure 1. Patient identification and selection. AF, atrial fibrillation; AFL, atrial flutter; ARF, additional risk factor(s); ESRD, end-stage renal disease; HF, heart failure.

descriptive statistics. Comparisons of rehospitalization duration and costs between index AF/AFL hospitalizations and subsequent rehospitalizations for AF/AFL were performed using the Chi-square test for discrete variables and Student's *t*-test for continuous variables. Logistic regression analysis, with a maximum likelihood, binary response method, and Fisher scoring algorithm, was used to assess potential predictors of rehospitalization (age, gender, US Census Bureau region, healthplan type, and CCI). Odds ratio estimates with Wald 95% confidence limits were reported for each regression parameter. A separate analysis was performed to analyze cardiovascular-related co-morbidities (hypertension, stroke, diabetes, peripheral vascular disease, coronary artery diseases, thyroid diseases, pulmonary diseases, valvular heart disease, and cardiomyopathy) in concert with the predictors. Statistical significance was considered to be a *p*-value of ≤ 0.05 . All statistical analyses were performed using SAS 9.2.

Results

Patient population

A total of 38,258 hospitalized AF/AFL patients were identified in the database, of whom 3,498 met the study inclusion criteria and were classified as having ≥ 1 ARF (Figure 1). The AF/AFL patients with ≥ 1 ARF had a mean age of 80.0 years (SD = 7.6 years), 42.4% were male, and they had high levels of co-morbidity and stroke risk (mean baseline CCI 1.7 [SD 1.8] and CHADS₂ score 2.2 [SD 1.0]) (Table 1).

Pattern of rehospitalization

In total, 1,389 (39.7%) of the 3,498 AF/AFL patients with ≥ 1 ARF were rehospitalized (all causes) over the 12-month post-index period (mean 1.7 [SD 1.3]

Table 1. Baseline demographic and clinical characteristics of AF/AFL patients with ≥ 1 ARF.

	AF/AFL patients with ≥ 1 ARF (n = 3498)
Male, n (%)	1484 (42.4)
Age, years, mean (SD)	80.0 (7.6)
Age group, n (%)	
70–74 years	889 (25.4)
75–79 years	1075 (30.7)
≥ 80 years	1534 (43.9)
Region, n (%)	
East	800 (22.9)
Midwest	1462 (41.8)
South	345 (9.9)
West	891 (25.5)
CV co-morbidities, n (%)	
Hypertension	3119 (89.2)
Stroke/TIA	546 (15.6)
Diabetes	839 (24.0)
PVD	324 (9.3)
CAD	1212 (34.6)
Thyroid diseases	610 (17.4)
Pulmonary diseases	544 (15.6)
VHD	592 (16.9)
Cardiomyopathy	148 (4.2)
CCI, mean (SD)	1.7 (1.8)
CCI scores, n (%)	
0	1008 (28.8)
1–2	1587 (45.4)
3–4	672 (19.2)
5–6	231 (6.6)
CHADS, mean (SD)	2.2 (1.0)
CHADS scores, n (%)	
0	1 (0.03)
1–2	2530 (72.3)
3–4	878 (25.1)
5–6	89 (2.5)

AF, atrial fibrillation; AFL, atrial flutter; ARF, additional risk factor(s); CCI, Charlson co-morbidity index; CHADS, CHADS₂ index (Congestive heart failure, history of Hypertension, Age ≥ 75 years, Diabetes mellitus, and past history of Stroke or TIA); CAD, coronary artery disease; PVD, peripheral vascular disease; SD, standard deviation; TIA, transient ischemic attack; VHD, valvular heart disease.

readmissions per rehospitalized patient) (Figures 2 and 3). Of these, 1223 patients (35.0% of the study cohort) underwent a CV-related rehospitalization (mean 1.6 [SD 1.0] readmissions per rehospitalized patient), which included AF/AFL-related readmissions. When AF/AFL-related rehospitalizations were assessed alone, 935 patients (26.7% of the study cohort) were rehospitalized (mean 1.4 [SD 0.8] readmissions per rehospitalized patient). Rehospitalization with a CV or AF/AFL primary diagnosis occurred in 804 (23.0%) patients (mean 1.4 [SD 0.7] readmissions per rehospitalized patient) and 426 (12.2%) patients (mean 1.2 [SD 0.5] readmissions per rehospitalized patient), respectively. The most frequent causes of readmission with a CV primary diagnosis were AF/AFL (521/1097 total primary CV readmissions, 47.5%), CHF (109/1097, 9.9%), coronary artery disease (81/1097, 7.4%), and stroke/TIA (68/1097, 6.2%) (Table 2).

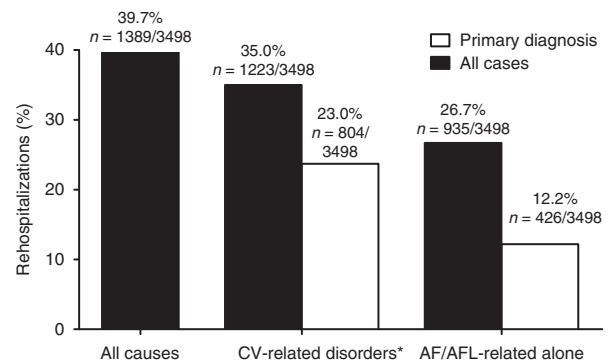


Figure 2. Rehospitalization rates (percentage of patients) for all-cause rehospitalizations, among all AF/AFL patients with ≥ 1 ARF (n = 3498). AF, atrial fibrillation; AFL, atrial flutter; CV, cardiovascular. *Includes AF/AFL-related rehospitalizations.

Cumulative readmission rates over the 12-month post-index follow-up period are summarized graphically (Figure 4). Cumulative all-cause rehospitalization rates at 1, 3, and 6 months' follow-up were 9.0%, 16.2%, and 25.9%, respectively. Cumulative rehospitalization rates with a CV (including AF/AFL) or AF/AFL primary diagnosis alone, respectively, were 5.1% and 3.3% at 1 month, 9.5% and 5.6% at 3 months, and 15.4% and 8.4% at 6 months. For those AF/AFL patients with ≥ 1 ARF who were readmitted with a primary diagnosis of AF/AFL (n = 426), 26.8%, 45.5%, and 68.5% of all such readmissions recorded over the 12-month follow-up period occurred within 1, 3, and 6 months, respectively, of the index event. Corresponding figures for readmissions with a CV primary diagnosis (n = 804) at 1, 3, and 6 months were 22.3%, 41.4%, and 66.8%, respectively.

Predictors of rehospitalization

Linear regression analysis indicated that co-morbidity identified by a CCI score of ≥ 5 (vs a CCI score of 0)—and specifically hypertension, peripheral vascular disease, coronary artery disease and valvular heart disease—were significant predictors of all-cause and CV rehospitalization. Age over 80 years vs age 70–74 years and female gender compared with male gender were also significant predictors of all-cause and CV rehospitalization. This analysis also identified some geographic variation in the risk of rehospitalization.

Rehospitalization costs and resource utilization

For the sub-set of AF/AFL patients with ≥ 1 ARF who underwent an AF/AFL-related rehospitalization, the cost of the first rehospitalization with a primary diagnosis of AF/AFL was significantly higher than the cost of the corresponding index hospitalization (mean US\$4418 [SD

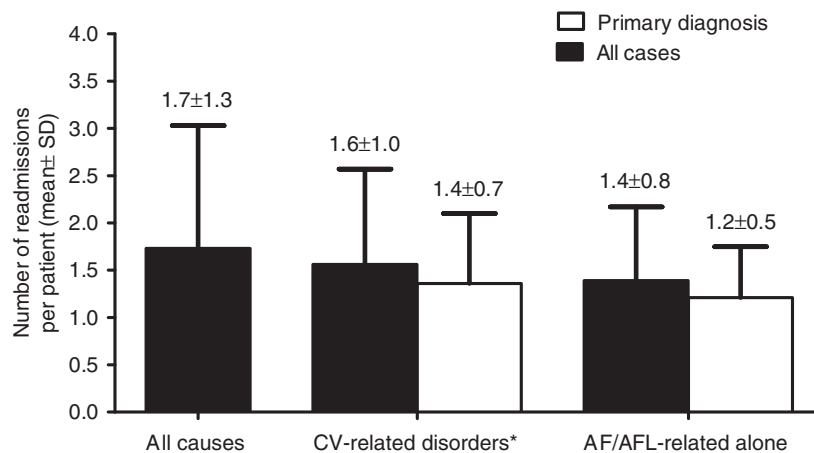


Figure 3. Mean (\pm SD) number of readmissions per patient among the sub-group of rehospitalized AF/AFL patients with ≥ 1 ARF ($n = 1389$). AF, atrial fibrillation; AFL, atrial flutter; CV, cardiovascular. *Includes AF/AFL-related rehospitalizations.

Table 2. Specific causes of readmission with a CV-related primary diagnosis among AF/AFL patients with ≥ 1 ARF.

CV cause	Readmissions, <i>n</i>	Percentage
AF/AFL	521	47.5%
CHF	109	9.9%
Coronary atherosclerosis	81	7.4%
TIA/stroke	68	6.2%
Blood pressure-related	47	4.3%
AMI/ICS	35	3.2%
Ventricular arrhythmia	5	0.5%
Major bleeding	9	0.8%
Supraventricular rhythm disorder	3	0.3%
Venous thromboembolism	2	0.2%
Angina pectoris/chest pain	2	0.2%
Other CV events	215	19.6%
Total	1097	100%

AF, atrial fibrillation; AFL, atrial flutter; AMI, acute myocardial infarction; ARF, additional risk factor(s); CHF, congestive heart failure; CV, cardiovascular; ICS, intermediate coronary syndrome; TIA, transient ischemic attack.

\$6294] vs \$3589 [SD \$4194], $p = 0.0036$) (Figure 5a). The median costs of rehospitalization compared with index hospitalization were \$1819 [25th percentile \$1066, 75th percentile \$5623] vs \$1707 [25th percentile \$1102, 75th percentile \$4749]). In addition, the duration of hospital stay was on average 2.6 days longer on readmission compared with the index event (mean 6.9 [SD 12.9] vs 4.3 [SD 5.1 days], $p < 0.0001$) (Figure 5b).

Discussion

According to this analysis of the PharMetrics Patient-Centric database, almost two out of five (39.7%) AF/AFL patients with ≥ 1 ARF were rehospitalized (all causes) during the 12-month period following their initial

(index) AF/AFL-related hospitalization. Each of these patients underwent, on average, 1.7 rehospitalizations (all-cause) over this 12-month follow-up period. In the great majority of cases (88%), the cause of readmission was a CV-related disorder (including AF/AFL) and, more specifically, an AF/AFL-related disorder alone (67.3%). AF/AFL accounted for nearly half (47.5%) of all rehospitalizations with a CV-related primary diagnosis among AF/AFL patients with ≥ 1 ARF, making it the most common reason for readmission in these patients. As may be anticipated, clinical characteristics and demographics found to significantly predict CV and all-cause rehospitalization included advanced age and increased co-morbidity.

In this cohort of AF/AFL patients with ≥ 1 ARF, the rate of readmission with AF/AFL as the primary discharge diagnosis (12.2% over 12 months) was similar to that reported in an earlier retrospective cohort analysis, using the Integrated Health Care Information Services, Inc. (IHCIS) National Managed Care Benchmark database, of 4174 patients with newly diagnosed and chronic AF (10.1% and 12.5%, respectively, over 12 months)⁵. In addition, the temporal patterns of readmission were similar in the two analyses. For example, in the present study, 26.8%, 45.5%, and 68.5% of first readmissions with primary AF/AFL occurred within 1, 3, and 6 months, respectively, of the index event compared with 17.6%, 43.4%, and 65.8% (chronic AF patients), and 22.7%, 44.5%, and 67.2% (newly diagnosed AF patients) of corresponding first readmissions in the earlier study⁵. However, in comparison with the former study, patients in the present analysis were older (mean age 80.0 vs 62.4–64.0 years) and had higher baseline levels of co-morbidity (mean CCI score 1.7 vs 0.8–1.0). This might explain why a higher percentage of AF/AFL readmissions occurred within 1 month in the AF/AFL patients identified in this study, with ≥ 1 ARF,

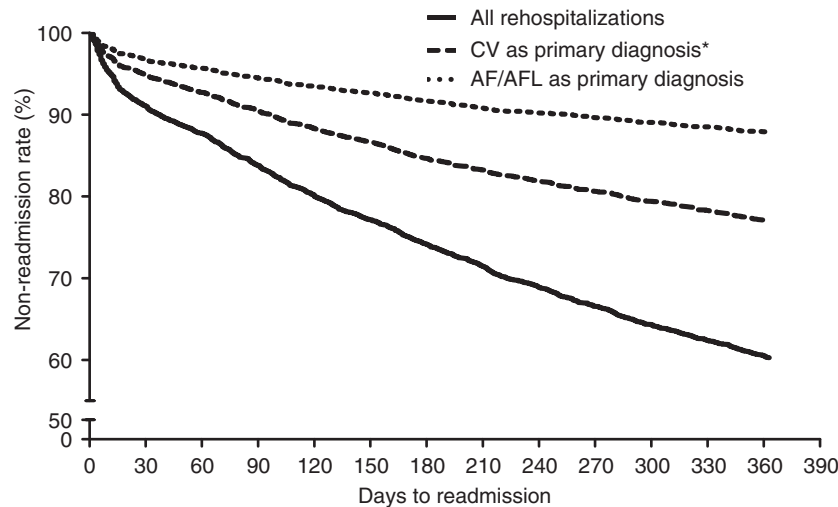


Figure 4. Cumulative percentage of AF/AFL patients with ≥ 1 ARF who were not readmitted during the post-index follow-up period. AF, atrial fibrillation; AFL, atrial flutter; CV, cardiovascular. *Includes AF/AFL-related rehospitalizations.

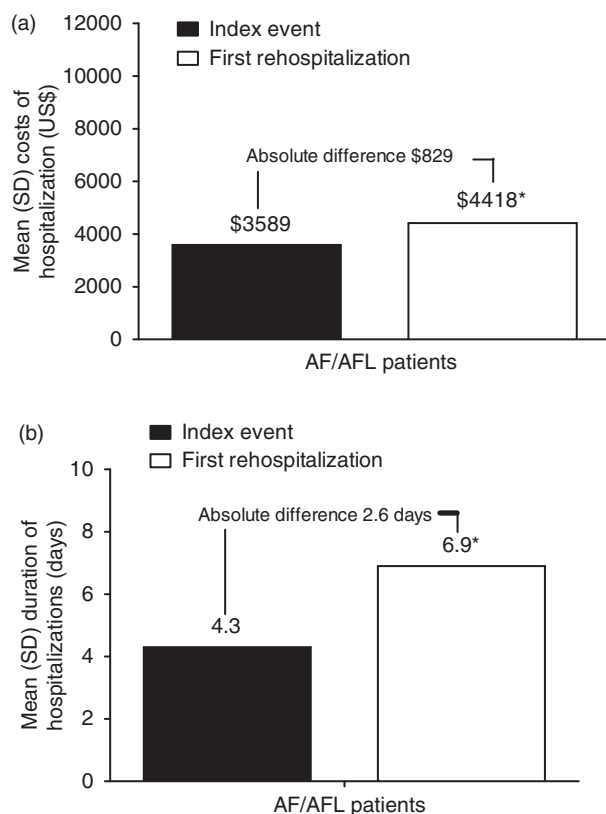


Figure 5. (a) Mean \pm SD costs in US dollars and (b) days of hospitalization, for the first readmission during the post-index period vs the index event. AF, atrial fibrillation; AFL, atrial flutter; US, United States. * $p < 0.0001$ vs index event.

as compared with a wider AF patient population assessed in the earlier study.

In comparison with the initial (index) hospitalization for primary AF/AFL, each subsequent rehospitalization for

primary AF/AFL proved to be more protracted (mean 6.9 vs 4.5 days) and more costly (mean \$4418 vs \$3589; median costs \$1819 vs \$1707). The increased length of stay and cost of rehospitalization for primary AF/AFL may possibly be a reflection of disease progression and the need for more intensive inpatient care. It should be noted that regression analyses were not used to adjust for co-morbidity within resource utilization and costs associated with rehospitalization for primary AF/AFL, since this comparison was conducted within the same group of patients. Proportionately, the increase in mean hospital costs (23%) was substantially less than the increase in length of hospital stay (53%). This may be due to the use of a diagnosis-related group (DRG) or modified DRG payment system whereby hospital reimbursement might be capped or limited, regardless of the length of hospital stay. In this case, rehospitalization is likely to impose a financial burden on the hospital in addition to the payer. Based on the reported study average of 1.2 primary AF/AFL readmissions per rehospitalized patient, the estimated mean costs of the primary hospitalization and subsequent primary AF/AFL rehospitalizations over the 12-month post-index period amount to \$8935 (\$3589 + [1.2 \times \$4418]) per patient; based on median costs this value is \$3890 (\$1707 + [1.2 \times \$1819]). It should be emphasized, however, that these costs are applicable only to the small minority (12.2%) of the study population undergoing rehospitalization for primary AF during the post-index period. The costs for patients requiring rehospitalization due to other causes were not determined in this study.

Set against the background of the recent 'Hospital to Home' national quality improvement initiative and studies that have demonstrated the high cost burden of unscheduled hospital readmissions^{10,11}, the high rate of

rehospitalization among AF/AFL patients highlights the need for renewed efforts to reduce hospitalizations and improve post-discharge transition of care across the spectrum of CV disease.

This study has several limitations. First, in contrast to the ATHENA study, which included patients with mild-to-moderate CHF (NYHA class II–III; who accounted for ~20% of the study population) and excluded those with severe CHF (NYHA class IV), the present study excluded all patients with pre-existing CHF, since the claims data did not allow determination of CHF severity. Accordingly, this study is likely to have under-estimated the actual readmission rate among the real-world AF/AFL population with ≥ 1 ARF. Secondly, in contrast to the ATHENA study, which was confined to patients with paroxysmal or persistent AF, this analysis may have included patients with permanent AF, since the ICD-9-CM diagnostic codes do not differentiate between AF sub-types. Furthermore, in the present study, the diagnosis of AF/AFL was not required to be confirmed by electrocardiogram and the use of ICD-9-CM diagnostic codes on non-diagnostic claims introduces the potential for coding error. Another limitation is that the PharMetrics Patient-Centric database may be under-represented in certain geographic regions in the US (e.g., the West) and, therefore, these findings may not be fully representative of AF/AFL patients with ≥ 1 ARF nationwide.

Conclusion

In the real-world setting, AF/AFL patients with ≥ 1 ARF experience a high rate of rehospitalization after their initial admission. Subsequent AF/AFL-related readmissions incur higher medical costs to payers and longer inpatient stays compared with the initial AF/AFL admission. This increased resource utilization represents an economic burden on the healthcare system and is also likely to have a negative impact on patient wellbeing.

Transparency

Declaration of funding

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Declaration of financial/other relationships

The authors received no financial support or other form of compensation related to the development of this paper. ANA has received funding for research and speaking from Sanofi-Aventis Inc. and Boehringer Ingelheim. MJ is an employee of Sanofi-Aventis Inc. JL is an employee of Novosys Health, which has a research consulting agreement with Sanofi-Aventis Inc.

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Previous presentation

This study was presented as an oral presentation at the Heart Rhythm Society 32nd Annual Scientific Sessions, San Francisco, CA, USA, May 5, 2011 and the abstract was published in *Heart Rhythm* 2011;8 (5, Supplement):S212–213.

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