Impact of Atrial Fibrillation on Mortality, Stroke, and Medical Costs

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**Background:** The impact of atrial fibrillation (AF) on mortality, stroke, and medical costs is unknown.

**Methods:** We conducted a prospective cohort study of hospitalized Medicare patients with AF and 1 other cardiovascular diagnosis (CVD) compared with a matched group without AF (n=26,753), randomly selected in 6 age-sex strata from 1989 MedPAR files of more than 1 million patients diagnosed as having AF. Stroke rates were also determined in another cohort free of CVD (n=14,267). Total medical costs after hospitalization were available from a 1991 cohort. Cumulative mortality, stroke rates, and costs following index admission were adjusted by multivariate and proportional hazard regression analyses.

**Results:** Mortality rates were high in individuals with CVD, ranging from 19.0% to 52.1% in 1 year. Adjusted relative mortality risk was approximately 20% higher in patients with AF in all age-sex strata during each of the 3 years studied (P<.05). Incidence of stroke was high in individuals with CVD, 6.2% to 15.4% in 1 year, with and without AF, and was at least 5-fold higher than in individuals without CVD. In those with CVD, stroke rates were approximately 25% higher in women with AF (P<.05) but only 10% higher in men. Adjusted total Medicare spending in 1 year was 8.6- to 22.6-fold greater in men, and 9.8- to 11.2-fold greater in women with AF (P<.05). Second- and third-year costs were increased as well.

**Conclusion:** Prevention of AF and treatment of patients with AF and associated CVD may yield benefits in reduced mortality and stroke as well as reducing health care costs.

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PATIENTS AND METHODS

SAMPLE AND DATA

Study patients were identified based on either principal or secondary inpatient diagnoses of AF (International Classification of Diseases, Ninth Revision, Clinical Modification\(^\text{10}\) [ICD-9-CM] code of 427.31) on 1989 Medicare hospital (MedPAR) records. To limit the study to newly incident cases of AF, we excluded all patients with AF on a previous admission during the preceding 2 years (1987-1988). A comparison group of patients without AF were identified who had no diagnosis of AF during the same period (1987-1989). The study sample was further restricted to those patients with at least 1 diagnosis of CVD (ICD-9-CM\(^\text{10}\) codes of 390-459, excluding 427.31). Thus, patients both with and without AF had documented CVD, not counting the diagnosis of AF itself. Another study sample of patients with and without AF, but free of CVD, was also chosen and was used as an index of the rates of stroke occurrence in men and women in these age groups.

The sample was drawn from the population of all hospitalized Medicare patients in the following 6 age-sex strata: men aged 65 to 74 years, 75 to 84 years, and 85 to 89 years, and women aged 65 to 74 years, 75 to 84 years, and 85 to 89 years. Power calculations were based on preliminary data of initial hospital costs and 90-day survival. For each stratum the sample sizes for the patients with and without AF were computed to attain 80% power with 2-sided tests (t tests for costs and log-rank test for survival) with a level of significance of .05. These calculations assumed the relative difference in hospital costs, i.e., the ratio of mean difference to the SD, would extend to 3 years for the total costs and the relative risk ratio of 90-day survival would extend to 3 years’ survival. We then selected 2 random samples (with and without AF) from each of these strata based on the terminal digits of their Medicare identification numbers. Sample sizes for patients with CVD are shown in

<table>
<thead>
<tr>
<th>Table 1</th>
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<tr>
<td>All Medicare hospital claims for these patients were then extracted from the date of index admission through 1992, permitting a full 3-year follow-up for each patient. Dates of death (if applicable) were obtained from the Health Care Financing Administration’s 1989 through 1992 eligibility files. Claims data for nonhospital services were not uniformly available until 1991. To compare total Medicare costs between patients with and without AF we selected a second sample of patients hospitalized in 1991, using the same sampling criteria described earlier. All Medicare claims for this second cohort of patients were extracted for a 12-month period beginning with the date of admission. Study results were found to be similar for both cohorts of patients; we choose to emphasize the 1989 cohort herein because of its longer follow-up period.</td>
</tr>
</tbody>
</table>

DEFINING OUTCOMES AND COSTS

Outcomes included mortality and stroke occurrence. Cumulative mortality rates were calculated for the 1-, 2-, and 3-year periods following hospital admission. Stroke occurrence was defined as an admission or readmission with a principal diagnosis of cerebral infarction (ICD-9-CM\(^\text{10}\) codes 434 or 436 on MedPAR records). Stroke occurrence was also determined for the cohort, from the 1989 MedPAR records, with and without AF and who had no CVD diagnoses. Stroke rates were calculated for the same time intervals as mortality. Costs were defined as Medicare payments plus any patient copayments and were calculated from the claims data associated with the index admission and any subsequent acute care hospitalizations. Costs for the 1991 cohort also included claims for long-term hospitals, skilled nursing facilities, home health care, hospital outpatient departments, and physicians. Cumulative medical spending equals the sum of all Medicare expenditures from date of admission through 1 year or until death, whichever comes first.

STATISTICAL METHODS

The primary statistical analysis compared costs and outcomes by AF status within 1, 2, and 3 years following the index hospitalization in 1989. Mortality and stroke occurrence were compared using \(\chi^2\) tests, and costs using t tests.

Multivariate analyses were performed to assess the impact of AF status on the outcomes variables while controlling for selected patient-level risk factors believed to be important outcome determinants. These risk factors include principal inpatient diagnoses of acute myocardial infarction, unstable angina, stable angina, or congestive heart failure; and secondary diagnoses of hypertension, diabetes, valvular disease, stroke, and chronic obstructive pulmonary disease. All analyses were performed at the strata level, i.e., among similar age and sex categories.

PROPORTIONAL HAZARD REGRESSION ANALYSIS

Proportional hazard regression was performed for the mortality and stroke analysis because of the proportional AF and non-AF survival patterns following patient identification.\(^\text{11}\) The dependent variables in these analyses, respectively, arc the number of days between the initial hospital admission date and the date of death, and the number of days between the initial hospital admission date and admission with a diagnosis of stroke. Patients were eliminated at death from the stroke regression analysis. The analysis focused on odds ratios generated from the proportional hazard regressions, which estimate the relative risk associated with the presence of AF.

ORDINARY LEAST-SQUARES REGRESSION ANALYSIS

Ordinary least-squares regression analysis was performed on cumulative Medicare acute care hospital payments at intervals of 1, 2, and 3 years following the initial hospitalization. The natural log of hospital payments is used because of the skewed nature of individual-level medical spending. The ordinary least-squares regression specification included the same diagnostic risk factor variables mentioned earlier, again with patients eliminated at death from analysis. The AF coefficients in these semilogarithmic regressions are interpreted as percentage increases in hospital payments associated with a diagnosis of AF during the index admission.\(^\text{12}\)
Patients with AF experienced significantly higher mortality rates than matched patients without AF (Table 2), a finding that persisted for each age-sex group during the 3-year study period (Figure). While the mortality differential narrowed over time, it remained substantial. Three years after the index admission, for example, male patients aged 65 to 74 years with AF were 28% more likely to have died, compared with their matched peers without AF. As expected, mortality rates rose with advancing age. The high mortality rates for patients both with and without AF reflect their relatively greater risk (by virtue of having been hospitalized), compared with the Medicare population generally.

Cardiac surgery rates were significantly greater in those with AF in all 6 sex-age strata. Cardiac surgery rates in men were twice that of women in cohorts both with and without AF. Rates were highest in the youngest group, intermediate in individuals aged 75 to 84 years, and lowest in individuals older than 85 years. Among men with AF aged 65 to 74 years, 18.9% had cardiac surgery compared with 12.4% in the cohort without AF (P < .05). At ages 75 to 84 years, rates were 8.2% in men and 4.6% in women with AF, compared with 6.2% and 2.8% in men and women without AF, respectively (P < .05 for both age groups). In the oldest stratum, patients aged 85 to 89 years, cardiac surgery rates were not significantly greater in men with AF (2.8%) than without AF (2.2%) but were in women with AF (1.7%) than without AF (1.1%) (P < .05).

STROKE

No differences in stroke occurrence were observed between male patients with and without AF (Table 3). However, female patients aged 75 to 89 years with AF were significantly more likely to be admitted with a stroke, compared with similarly aged women without AF. This elevated risk of stroke persisted during the follow-up period. At the 2- and 3-year follow-up points, women aged 65 to 74 years with AF were also significantly more likely to be hospitalized with a stroke (Table 3).

Compared with the age-sex strata of the cohort free of CVD (n = 14,267), the high stroke rates of the CVD cohort is apparent (Table 3). In the group without CVD, stroke rates were consistently higher, but not always significantly so, in patients with AF. However, stroke occurrence was many times higher in those with CVD, with stroke rates 5 to 10 times that of persons without CVD. For example, 1-year stroke occurrence was 7.9% in men aged 65 to 74 years with AF and CVD compared with 1.0% for men with AF but no CVD (Table 3). Similar wide differences were apparent in women and in the age-sex strata without AF.
We adjusted for this explicitly in the multivariate analyses later.

Table 5 displays the relative mortality and stroke risks for AF, adjusted for type of CVD and comorbid conditions, based on proportional hazards. Even after adjusting for these other patient characteristics, the presence of AF raises the risk of both death and stroke, significantly so in 4 of the 6 age-sex strata. Men aged 65 to 74 years and 85 to 89 years, and women aged 75 to 89 years were significantly more likely to die if they also had a diagnosis of AF, compared with otherwise similar patients without AF. Men aged 85 to 89 years and women in all age strata were significantly more likely to suffer a stroke if they had a diagnosis of AF. Stroke rates in the CVD strata, with and without AF, are remarkably high—approaching rates seen in high-risk patients with AF in observational and clinical trial series.3,5

Table 6 displays the relative cost impact associated with AF, expressed as the percentage difference in hospital costs compared with patients without AF, based on multivariate regression analysis results. The presence of AF raises hospital costs for all patients, and significantly so for all but the youngest stratum of females. Atrial fibrillation is particularly costly for men aged 65 to 74 years, increasing total hospital outlays by one third, compared with patients without AF. This cost differential persists during the 3-year period, even though we have adjusted for the higher mortality rates of patients with AF.

Analysis of the 1991 cohort (not shown) found 1-year mortality and stroke rates similar to those shown herein for the 1989 cohort. Table 7 presents 1-year costs for the 1991 cohort, in total and by the following categories: acute care hospitals, long-stay hospitals, skilled

COSTS

Table 4 compares the cumulative costs of acute hospital care for patients with and without AF. Patients with AF incurred significantly higher costs for the 12 months following index admission, compared with patients without AF of the same age and sex. The absolute difference (in dollar terms) was considerably larger for men aged 65 to 74 years. Examination of their MedPAR records found that these patients with AF were far more likely to undergo major cardiac surgery, compared with other patients (data not shown). Although patients with AF in all strata remain more costly throughout the study period, many of these differences lose statistical significance over time. In part this may be due to the truncation of their costs resulting from higher mortality rates.
nursing facilities, physicians and other service providers (eg, vendors of durable medical equipment or independent laboratories), hospital outpatient departments, and home health care. Total Medicare costs were significantly higher for patients with AF in all age-sex strata. Acute care hospital costs accounted for 50% to 60% of the total bill, and clearly drive the cost differential; there were few significant differences between patients with and without AF in other types of costs. The final column of Table 7 presents the percentage increase in total costs associated with AF (comparable with that shown in Table 6), based on multivariate regression analysis results. Significant increases in total Medicare spending associated with AF were found in all 6 strata.

We selected a sample of patients with a recent onset of AF, using the MedPAR databases for 1989 and 1991, stratified by age and sex, and matched them with similar age-

and sex-stratified patients without AF who also had CVD diagnoses. The use of this database provided a sizable population of patients with AF and controls matched for key variables of associated CVD diagnoses. We were thereby able to examine the net effect of AF after accounting for the powerful impact of the associated CVDs on mortality and stroke rates and on costs. We further adjusted for those principal and secondary cardiovascular inpatient diagnoses likely to be important contributors to these outcomes.

This patient sample had a high mortality rate, both with and without AF. For example, in the intermediate age category of 75 to 84 years, 47.1% of patients without AF and 53.9% of patients with AF were dead within 3 years (Table 2). Although high mortality rates were found in both sexes in these elderly Medicare patients, in each age-sex stratum mortality was significantly higher in patients with AF. After adjustment for associated primary and secondary diagnoses, the 3-year relative mortality rate in AF strata, compared with strata without AF, was 6% to 30% higher in men and 21% to 23% higher in women (Table 5).

The independent contribution of AF to risk of stroke observed in the prospective study of AF in the Framingham Study3,11 cohort of the same age was not seen in this data set. However, the use of MedPAR files for selection of patients with AF and CVD obviously yielded a population with extremely high stroke and mortality rates. Stroke rates of 5% to 12% annually have been seen in prospective observational data and in clinical trials of warfarin anticoagulation in AF.4,5 The magnitude of the risk factor–adjusted increased mortality in persons with AF in Framingham6 was 2-fold, considerably greater than the relative mortality risk of 7% to 22% seen herein (Table 5). This suggests a selection bias in this sample of Medicare applicants. It is likely that early overall mortality and stroke mortality in AF are not reflected in the Medicare data. However, the Medicare data reflect the actual morbidity, mortality, and costs incurred as a consequence of AF confronted by the government agency. The Framingham data also reflect, to some extent, an era when stroke

### Table 6. Added Acute Care Hospital Expenditures Associated With Atrial Fibrillation (AF) by Age and Sex

<table>
<thead>
<tr>
<th>Age, y</th>
<th>1 y % Increase</th>
<th>2 y % Increase</th>
<th>3 y % Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>35.2*</td>
<td>6.8</td>
<td></td>
</tr>
<tr>
<td>75-84</td>
<td>14.9*</td>
<td>16.3*</td>
<td>18.4*</td>
</tr>
<tr>
<td>85-89</td>
<td>10.5*</td>
<td>9.0*</td>
<td>8.0*</td>
</tr>
</tbody>
</table>

* Significant at P < .05. Adjusted for primary diagnoses of acute myocardial infarction, unstable angina, stable angina, and congestive heart failure; and secondary diagnoses of hypertension, diabetes, valvular disease, stroke, and chronic obstructive pulmonary disease. Patients were eliminated at death from analysis.

### Table 7. Cumulative Medicare Spending Within 1 Year of Hospital Admission by Stratum Pair and Type of Spending, 1991 Cohort

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Total Payments</th>
<th>Acute Care Hospital</th>
<th>Long-term Hospital and Skilled Nursing Facilities</th>
<th>Physician/Outpatient</th>
<th>Hospital Outpatient</th>
<th>Home Health Care</th>
<th>Adjusted Total AF Added Costs, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With AF</td>
<td>Without AF</td>
<td>With AF</td>
<td>Without AF</td>
<td>With AF</td>
<td>Without AF</td>
<td>With AF</td>
</tr>
<tr>
<td></td>
<td>75-84</td>
<td>18.718</td>
<td>16.634</td>
<td>15.107</td>
<td>9.816</td>
<td>959</td>
<td>972</td>
</tr>
<tr>
<td></td>
<td>85-89</td>
<td>15.726</td>
<td>15.096</td>
<td>14.691</td>
<td>8.892</td>
<td>1194</td>
<td>1057</td>
</tr>
</tbody>
</table>

* With atrial fibrillation (AF) and without AF means differ significantly at .05 level of confidence. Adjusted for primary diagnoses of acute myocardial infarction, unstable angina, stable angina, and congestive heart failure; and secondary diagnoses of hypertension, diabetes, valvular disease, stroke, and chronic obstructive pulmonary disease. Patients were eliminated at death from analysis.

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was more severe and had a higher case-fatality rate than the recent period during which the Medicare data were collected. There may also have been a failure to designate the AF along with the underlying cardiovascular condition in a substantial number of Medicare claims that resulted in early death leading to misclassification, and an underestimate of the influence of AF on mortality and stroke occurrence.

Stroke rates were highest in the first year with a much lower incidence of stroke in years 2 and 3. Although the basis for the lower rates in the subsequent years is unknown, the competing high mortality experienced by these patients with associated CVD may have played a role. In addition, these Medicare patients represented “incident” AF with no diagnosis of AF during the 2 prior years. In the Framingham Study, stroke rates were higher in the first year (and particularly in the first 6 months after the onset of AF) and then leveled off.

Also, in the Framingham data, most of the patients with AF did not receive anticoagulant therapy (which has been demonstrated to reduce stroke and death) which has been used with increasing frequency in recent years. Although we did not determine the accuracy of hospital discharge diagnoses for identifying stroke, a comprehensive comparison of the diagnoses from the MedPAR files determined that if the codes for cerebral infarction were used, ICD-9-CM code 434 or 436, 85% and 86% of incident or recurrent stroke events were identified. In this study these diagnostic rubrics were successful in identifying the large majority of stroke events.

Acute care hospital payments and total medical payments were high with and without AF but were clearly greater in those with AF. Costs were highest in the youngest stratum, aged 65 to 74 years, and decreased successively with increasing age. A good deal of these payments were for surgery, principally coronary artery bypass grafting, which was most frequently performed in this youngest group. Nevertheless, across the array of Medicare spending, those with AF incurred higher costs than those without this arrhythmia (Tables 6 and 7).

A major strength of this study design is the use of a large database of physician-designated acute care hospital diagnoses with actual spending figures from a recent period in the United States. It is representative of Medicare recipients who account for the majority of the US elderly population. In addition, the MedPAR files permit the patients to be followed up for disease outcomes and death longitudinally over the years.

Limitations include the absence of patients younger than 65 years and the lack of information concerning non-hospitalized patients. There were little data available on the duration, intermittency, or chronicity of AF and none on the drugs for anticoagulation or arrhythmia. Patients with more severe disease, a greater number of CVD diagnoses, and those who underwent cardiac surgery are more likely to develop AF as well as the outcomes studied—death and stroke. They will also require more extensive medical care that is therefore likely to be more costly. The MedPAR data set does not allow us to precisely match patients with CVD with AF to patients with CVD without AF. We have attempted to take into account the presence of certain comorbid conditions, eg, acute myocardial infarction and congestive heart failure, which might be expected to have an adverse influence on outcome. Additional studies focusing on clinical and echocardiographic measures of comorbid disease duration and severity are needed to more accurately classify patients in this manner.

It may be possible to prevent AF through treatment of hypertension and diabetes and prevention of congestive heart failure and valve disease. At present, improved clinical management, including better control of ventricular rate or reversion to sinus rhythm and warfarin anticoagulation, would seem to offer the greatest promise for reducing the morbidity, mortality, and hospital costs associated with AF.

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REFERENCES