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Risk of Stroke in Patients With Atrial Flutter

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Thromboembolism remains a major source of morbidity and mortality in patients with atrial arrhythmias. An increased incidence of stroke in patients with atrial flutter has only recently been reported.[1–3] Many patients with atrial flutter develop an episode of atrial fibrillation over time.[4–6] The development of an episode of atrial fibrillation in patients with atrial flutter complicates the overall assessment of the stroke risk in these patients. The issue of anticoagulation in such patients remains important because many patients with atrial flutter are currently cured by radiofrequency ablation of the atrial flutter isthmus. Several studies[7–10] have delineated a risk of 10% to 22% for the development of atrial fibrillation after "successful" atrial flutter isthmus ablation. Episodes of preablation atrial fibrillation and left ventricular dysfunction have been shown to be predictive of an episode of atrial fibrillation after atrial flutter isthmus ablation.[11–13] No clear strategy addressing anticoagulation before or after a successful atrial flutter isthmus ablation has emerged. Thus, knowledge of the future risk of atrial fibrillation in patients with atrial flutter would be important in developing such a strategy.

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We used the Medicare database to determine the long-term stroke risk to patients presenting with atrial flutter. In addition, we attempted to determine the incidence of atrial fibrillation after an initial hospitalization for atrial flutter in this population of patients.

The collection and structure of the Medicare data have been described elsewhere in detail.[14,15] Hospitalizations can be traced longitudinally.

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TABLE 1 Risk Ratio for Stroke in the Study Population (Cox proportional-hazards model)

Variable	Risk Ratio	95% Confidence Intervals	
		Lower	Upper
Age	1.031	1.030	1.032
Men	1.039	1.025	1.052
Race (black)	1.136	1.108	1.165
Acute MI	1.081	1.049	1.115
Congestive heart failure	1.198	1.179	1.218
Rheumatic heart disease	1.185	1.131	1.241
Systemic hypertension	1.587	1.566	1.607
Diabetes mellitus	1.507	1.485	1.529
Atrial fibrillation	1.642	1.620	1.664
Atrial flutter	1.406	1.352	1.463

MI = myocardial infarction.

Scanning the Medicare inpatient file, patients who were aged >65 years with a principal or a secondary diagnosis of atrial fibrillation or atrial flutter in 1984 were identified. A 5% random sample of other hospitalized patients was selected and constituted the control group. Patients were eliminated from the study for any one of the following reasons: (1) a diagnosis of stroke at admission, (2) subsequent development of atrial flutter in patients with atrial fibrillation (1.2%), or (3) development of atrial fibrillation or atrial flutter in the control cohort during the follow-up period (8.3%). The study population included 749,988 patients (atrial flutter [n = 17,413 patients], atrial fibrillation [n = 337,428 patients], and control [n = 395,147 patients]). Patients were followed for 8 years.

Based on the results of previous studies,[16,17] acute myocardial infarction, hypertension, congestive heart failure, rheumatic heart disease, and diabetes mellitus were considered as confounding factors. The vital status (dead or alive) of the study patients was determined using both the Medicare inpatient files (1984 to 1991) and the Social Security Master File (containing all death information up to June 30, 1995). Patients

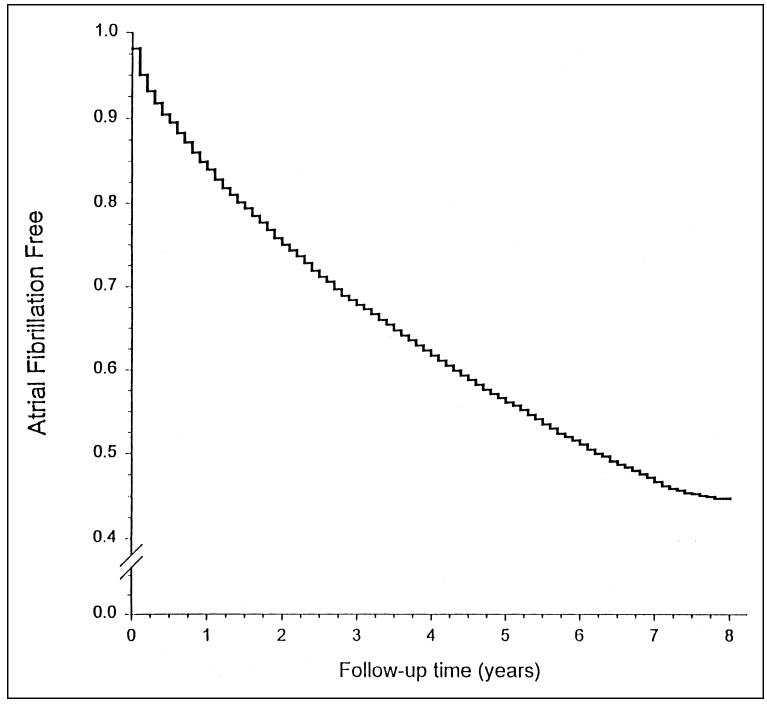

FIGURE 1. This figure uses a Kaplan-Meier analysis to display the incidence of the development of an episode of atrial fibrillation after the inception of the initial atrial flutter cohort.

TABLE 2 Risk Ratio for the Development of Atrial Fibrillation in the Atrial Flutter Cohort, n = 17,413 (Cox proportional-hazards model)

Variable	Risk Ratio	95% Confidence Intervals	
		Lower	Upper
Age	1.016	1.012	1.020*
Men	0.969	0.921	1.019†
Race (black)	0.916	0.834	1.005‡
Acute MI	0.800	0.718	0.891*
Congestive heart failure	1.243	1.174	1.316*
Rheumatic heart disease	1.464	1.250	1.715*
Systemic hypertension	1.333	1.267	1.402*
Diabetes mellitus	1.181	1.114	1.252*

*p = 0.0001; †p = 0.221; ‡p = 0.065.

were censored in the multivariable analysis if they died without developing the study outcome (stroke).

Kaplan-Meier product limit estimates were used to assess the cumulative incidence of stroke during the follow-up period, as well as the incidence of a transition from atrial flutter to an episode of atrial fibrillation. A Cox proportional-hazards model was used to determine the relative hazard of stroke occurrence for atrial fibrillation and atrial flutter compared with the control group, adjusting for patient demographics and other confounding variables. All statistical analyses were performed using the Statistical Analysis Software, Version 6.12 (SAS Inc., Cary, North Carolina).

The relative risks of stroke in the overall study population using demographic and discharge data are shown in Table 1. Hypertensive disease, congestive heart failure, diabetes, age, race, and sex contributed to the subsequent risk of stroke. The overall stroke risk in patients with atrial flutter was greater than the control group (RR = 1.406, $p < 0.0001$). However, the stroke risk was less than that in the cohort of patients with atrial fibrillation (RR = 1.642, $p < 0.0001$). The stroke risk for patients with atrial flutter fell between the control and the atrial fibrillation cohorts for the entire 8-year follow-up period.

Patients with atrial flutter developed an episode of atrial fibrillation over the 8-year period in a near-linear fashion. The incidence of the development of an episode of atrial fibrillation is displayed using a Kaplan-Meier analysis in Figure 1. In the cohort of patients with atrial flutter, the presence of the comorbid diagnoses of congestive heart failure, rheumatic heart disease, and hypertension predicted the development of an episode of atrial fibrillation. The relative risk that each comorbid variable conveyed to the development of an episode of atrial fibrillation is shown in Table 2.

Patients from the atrial flutter cohort were characterized as "isolated" atrial flutter (no hospitalization during the 8-year follow-up with a diagnosis of atrial fibrillation) or atrial flutter to atrial fibrillation (a subsequent hospitalization during the 8-year follow-up with an episode of atrial fibrillation). The risk of stroke in patients with atrial flutter was greatest in patients with a subsequent episode of atrial fibrillation. This effect is displayed in Figure 2 using a Kaplan-Meier analysis. Confidence intervals in patients in the atrial flutter group who subsequently developed atrial fibrillation ("atrial flutter to atrial fibrillation") and those in patients in the atrial fibrillation group overlap, so these risks are not significantly different. The confidence intervals of the isolated atrial flutter group and the control group do not overlap and are significantly different, but the absolute difference between these 2 groups is small.

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The risk of stroke in patients with atrial flutter delineated in this study is very similar to smaller but prospectively determined previously reported series.[1–3] The risk of stroke was higher in patients who developed an episode of atrial fibrillation at some point over the 8-year follow-up period. The patients with isolated atrial flutter had only a small increase in stroke risk when compared with the control group. This may be due to a misclassification in that some patients in the isolated atrial flutter group likely developed an episode of atrial fibrillation that did not require hospitalization. The absolute increase in stroke risk is small and may not be clinically relevant.

The occurrence of atrial fibrillation after a success-

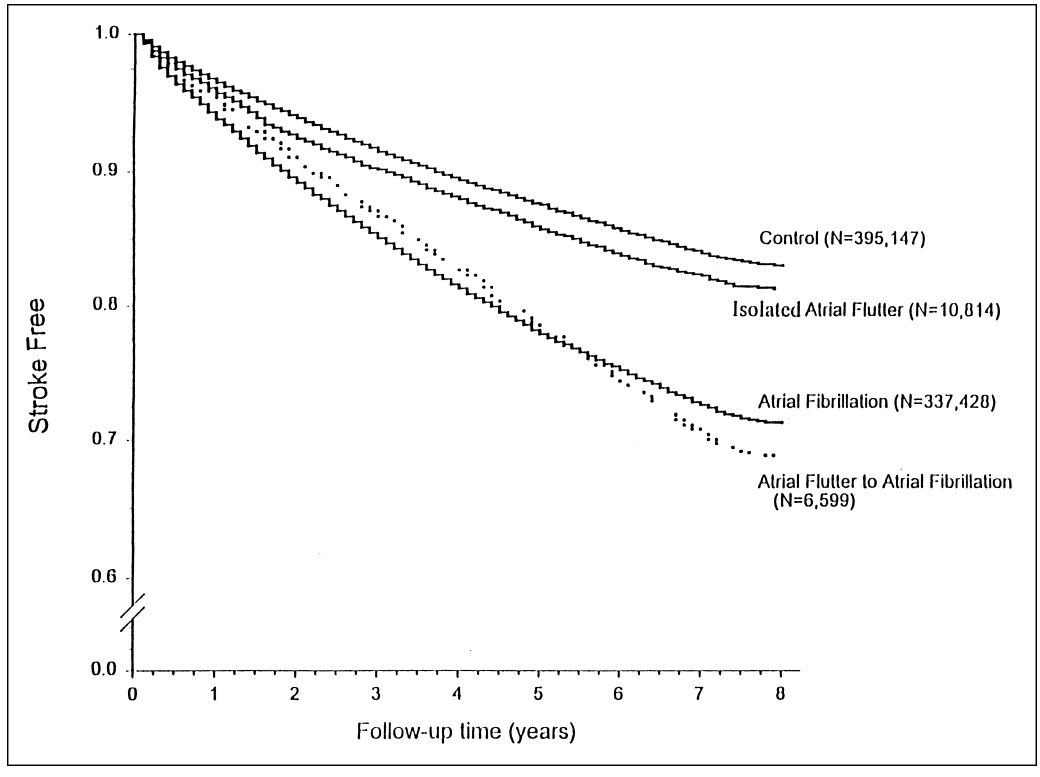

FIGURE 2. This figure uses a Kaplan-Meier analysis to display the incidence of stroke in the initial 3 cohorts. However, the atrial flutter cohort has been divided into patients who never had a subsequent episode of atrial fibrillation, "isolated" atrial flutter, and into patients with atrial flutter who then developed an episode of atrial fibrillation, "atrial flutter to atrial fibrillation."

ful atrial flutter isthmus ablation has been well recognized. Data presented here document an incidence of developing an episode of atrial fibrillation in patients presenting with atrial flutter that is quite similar to the incidence of developing an episode of atrial fibrillation after an atrial flutter isthmus ablation.[11–13]

The strengths and weaknesses of the Medicare database have been well documented.[18,19] Atypical rather than typical atrial flutter can be confused with atrial fibrillation. Miscoding atrial flutter as atrial fibrillation could lead to an overestimation of stroke risk. Conversely, if death occurred secondary to stroke outside the hospital more frequently in the atrial flutter group, stroke risk would be underestimated.

Because our findings encompass a Medicare population, extrapolations to a younger population should be made cautiously. The overall treatment of heart disease has changed dramatically over the past 15 years, and thus caution should be used in using these data in the current treatment era.

Only a randomized study would define the excess stroke risk in patients with atrial flutter. Given the logistical and ethical difficulties of such a trial, the present study sheds reasonable insights into the risk of stroke in patients with atrial flutter.

Patients with atrial flutter are at an increased risk of stroke, and this risk is greatest in patients who develop an episode of atrial fibrillation. Therapy with warfarin should be considered based on these presented data; if not, patients with atrial flutter should be followed closely for the development of atrial fibrillation.

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Lethal Ventricular Arrhythmias Following One-Step Pacemaker Reprogramming for Rapid Tracking of Atrial Tachyarrhythmias

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Rapid ventricular rates induce electrophysiologic remodeling that can promote arrhythmogenesis on abrupt slowing. Polymorphic ventricular tachycardia can occur during pacing at "usual" rates after atrioventricular (AV) junction ablation for rapidly conducting atrial tachyarrhythmias. The risk of programming abrupt decreases in the ventricular rate for pacemaker-dependent patients with rapid tracking of atrial tachyarrhythmias has not been reported.

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The computerized records of all outpatient and inpatient dual-chamber pacemaker evaluations performed by the arrhythmia device clinic staff at Rush-Presbyterian-St. Luke's Medical Center between 1996 and 1999 were reviewed. Approximately 600 patients with dual-chamber pacemakers were actively followed up at our clinic during that period. All instances in which the pacing mode was changed from a tracking mode (VDD[R], DDD[R]) to a nontracking mode (DDI[R], VVI[R]) were identified. Patients were included in the analysis if they presented with tracking of a supraventricular rhythm at or close to the upper rate limit and if they were pacemaker dependent (i.e., there were no intrinsically conducted beats after reprogramming to the nontracking mode). Patients in whom pharmacologic or electrical cardioversion of the supraventricular tachyarrhythmia and reprogramming were performed in the same setting were excluded from analysis. Clinical characteristics of the patients, programmed pacemaker settings, and short-term outcome were recorded.

The clinical characteristics of the 5 study patients are presented in Table 1. There were 3 men and 2 women (age 62 ± 21 years), all with structural heart disease (left ventricular ejection fraction 30 ± 14%). Tracked tachyarrhythmias were atrial flutter in 2 patients, atrial fibrillation in 2, and atrial tachycardia in 1. The presenting rate was 109 ± 19 beats/min. Mode switching was not available in 4 generators and not enabled in 1. Symptoms included dyspnea in 4 patients and palpitation in 1. Pacemakers were reprogrammed to DDI(R) in 3 patients or VVI(R) mode in 2 patients, at a lower rate of 65 ± 5 beats/min. Reprogramming was performed in the pacemaker clinic in 4 patients and during hospitalization in 1. The reprogrammed pacing mode and rate were selected by the attending cardiologist. A rapid reduction in symptoms secondary to the rapid pacing rates was the therapeutic goal.

Two outpatients (40%) developed polymorphic ventricular arrhythmias. These were the 2 patients with largest reductions in pacing rate after mode reprogramming. Patient 4 had mitral valve replacement, severe cardiomyopathy, and unsuspected hypokalemia. His pacing rate was decreased from 110 to 60 beats/min. He collapsed upon leaving the clinic and was found in ventricular fibrillation. After defibrillation, the pacing rate was increased to 90 beats/min without recurrences. Patient 5 was a woman with persistent humoral rejection of a cardiac transplant whose pacing rate was decreased from 140 to 70 beats/min. She had several syncopal episodes later that day. Polymorphic ventricular tachycardia and ventricular fibrillation were documented after hospitalization. Despite multiple defibrillations, she died shortly thereafter in electromechanical dissociation.

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During the last decade, the arrhythmogenic potential of an abrupt slowing of the ventricular rate in patients with supraventricular tachyarrhythmias has been increasingly recognized. Several investigators have reported the development of polymorphic ventricular tachycardia or fibrillation after programming of what would otherwise be considered a normal pac-

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