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Incidence and Predictors of Atrial Flutter in the General Population

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OBJECTIVES The goal of our study was to determine the incidence and predictors of atrial flutter in the general population.

BACKGROUND Although atrial flutter can now be cured, there are no reports on its epidemiology in unselected patients.

METHODS The Marshfield Epidemiological Study Area (MESA), a database that captures nearly all medical care among its 58,820 residents was used to ascertain all new cases of atrial flutter diagnosed from July 1, 1991 to June 30, 1995. To identify predisposing risk factors, we employed an age- and gender-matched case-control study design using eight additional variables.

RESULTS A total of 181 new cases of atrial flutter were diagnosed for an overall incidence of 88/100,000 person-years. Incidence rates ranged from 5/100,000 in those <50 years old to 587/100,000 in subjects older than 80. Atrial flutter was 2.5 times more common in men ($p < 0.001$). The risk of developing atrial flutter increased 3.5 times ($p < 0.001$) in subjects with heart failure and 1.9 times ($p < 0.001$) for subjects with chronic obstructive pulmonary disease. Among those with atrial flutter 16% were attributable to heart failure and 12% to chronic obstructive lung disease. Three subjects (1.7%) without identifiable predisposing risks were labeled as having "lone atrial flutter."

CONCLUSIONS This study, the first population-based investigation of atrial flutter, suggests this curable condition is much more common than previously appreciated. If our findings were applicable to the entire U.S. population, we estimate 200,000 new cases of atrial flutter in this country annually. At highest risk of developing atrial flutter are men, the elderly and individuals with preexisting heart failure or chronic obstructive lung disease. (J Am Coll Cardiol 2000;36: 2242–6) © 2000 by the American College of Cardiology

Atrial flutter is a condition in which, as has recently been shown, the contraction wave follows a circular and never ending path in the auricle, the circuits being completed at a rate of from 240 to 350 per minute in different subjects.

Sir Thomas Lewis, 1920 (1)

Recent technological advances have improved our understanding of the electrophysiologic substrate responsible for atrial flutter (2–8). Clinical application of this knowledge has made catheter-based radiofrequency ablation (RFA) a safe and effective therapeutic procedure (9–19).

Despite these technical developments, little is known about the epidemiology of atrial flutter in the general population (20). Our objectives were to determine its incidence and predisposing conditions.

METHODS

Marshfield Epidemiologic Study Area (MESA). Our institutional review board approved the study. Population-based epidemiologic research is feasible in central Wisconsin because the Marshfield Clinic and St. Joseph's Hospital provide almost all health care in this region. These institutions share a system of medical records including information on nearly all inpatient and outpatient encounters. The MESA has been established to conduct epidemiologic studies and population-based health research in a ZIP code-defined region that includes Marshfield and surrounding communities. Since most MESA residents (over 70%) have at least one health-related encounter every year and the health care status and the denominator of the population are updated daily, accurate longitudinal follow-up of individuals is possible. We have shown that over 95% of 58,820 area residents and virtually all health events are captured in the MESA database, including 99% of deaths, 94% of hospital discharges and 92% of medical outpatient visits (21).

Electrocardiographic definitions. Only patients with electrocardiographic (ECG) evidence of their first episode of atrial flutter (duration ≥5 s) were enrolled. Entry criteria required: a) standard 12-lead ECG or tracings obtained at the time of exercise stress test or b) ECG monitor or Holter strip recordings.

Atrial flutter was considered to be present if there were visible and highly regular "F" waves at a rate ≤350 beats/min. Highly regular "F" waves were defined as those in which the cycle to cycle atrial variability was ≤10 ms. Atrial flutter rate had to be greater than 190 beats/min among

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Abbreviations and Acronyms

AA = antiarrhythmic
COPD = chronic obstructive pulmonary disease
DM = diabetes mellitus
ECG = electrocardiogram or electrocardiographic
HF = heart failure
ICD = International Classification of Diseases
MESA = Marshfield Epidemiologic Study Area
PSVT = paroxysmal supraventricular tachycardia

patients receiving classes IA, IC or class III antiarrhythmic (AA) agents. In all others, the lowest acceptable atrial rate was 240 beats/min.

Patient selection criteria. To identify potential incident cases of atrial flutter, we used Marshfield Clinic's diagnostic database. Since 1979 this database has used the International Classification of Diseases (ICD) to track all diagnostic codes. To ensure complete ascertainment of all cases occurring from July 1, 1991 through June 30, 1995, we employed eight ICD, 9th revision, Clinical Modification (ICD-9-CM) codes in our initial screening. In addition to ICD 427.32 (atrial flutter), we used seven additional codes including 410 (acute myocardial infarction), 426.7 (Wolff-Parkinson-White syndrome), 427.0 (paroxysmal supraventricular tachycardia [PSVT]), 427.2 (paroxysmal tachycardia unspecified), 427.31 (atrial fibrillation), 427.81 (sinoatrial node dysfunction), 427.89 (other rhythm disorder, ectopic, nodal and wandering atrial pacemaker) and 427.9 (cardiac dysrhythmia, unspecified).

Since all patients diagnosed with these conditions were assessed for inclusion, approximately 2,000 potential incident cases of atrial flutter were screened. Final case inclusion required ECG confirmation atrial flutter by cardiac electrophysiologists. All eligible cases were enrolled. During 220,000 person-years of observation, approximately 29,000 ECG and rhythm strips, 1,100 Holter monitors and 500 ambulatory event recordings were obtained from MESA residents.

Selection of controls. Since age and gender are important predictors of disease and survival, each incident case was matched with a population-based control of the same age and sex. Controls were chosen randomly among MESA residents without previously documented atrial arrhythmias. Indications or complaints prompting health encounters among controls at the time of study entry were: a) a prescheduled office visit in 61% (including 36% with eye or dental appointments or cutaneous or musculoskeletal concerns), b) scheduled laboratory or other diagnostic tests in 35% and c) urgent evaluations in 4% (half of these or 2% due to potential cardiovascular complaints).

Data collection. Trained nurses undertook chart abstraction of risk factors. These were considered to be present if such condition was documented in the record before the diagnosis of atrial flutter. Information was mostly collected from typed physicians' notes. Quality assurance methods to ensure data integrity included reabstraction of every 10th medical record, double data entry of a random sample of 10% of collected information as well as range and edit checks on all collected data. All predetermined quality assurance parameters were exceeded.

Table 1. Clinical Characteristics: Atrial Flutter and Control Subjects

Characteristic	Patients (n = 181)	Controls (n = 181)	p Value
Heart failure (%)	22	8	0.001
Chronic pulmonary disease (%)	24	14	0.01
Diabetes mellitus (%)	16	10	0.07
Rheumatic heart disease (%)	2	1	0.18
Hyperlipidemia (%)	42	48	0.26
Myocardial infarction (%)	17	14	0.40
Hypertension (%)	47	52	0.60
Thyroid disease (%)	11	10	0.72
Mean age (yrs)	72	72	NS
Male gender (%)	62	62	NS

Statistical analysis. Incidence. The entire population of MESA, including persons of all ages, was considered at risk for developing atrial flutter. The number of verified incident cases was divided by the total number of person-years of observation of all MESA residents. Age- and gender-specific rates are presented as well as age-adjusted rates, calculated by using the 1990 U.S. census as standard.

Predisposing risk factors. To identify potential comorbidities associated with the development of atrial flutter, we used an age- and gender-matched case-control design in which atrial flutter was the outcome variable. Risk factors potentially predisposing a subject to the development of atrial flutter were chosen before data analysis. Selection of the 13 putative etiologic variables employed in the analysis was based on factors previously reported to predispose to atrial fibrillation (22–25). Table 1 shows baseline clinical diagnoses among cases and controls. For descriptive analyses we compared distributions for categorical variables using a chi-square test. We used Student *t* test to compare means for continuous variables.

RESULTS

Incidence of atrial flutter in the general population. Among 58,820 MESA residents, 181 new cases of atrial flutter were diagnosed during the four years of ascertainment (Table 2). Of these patients, 105 (58%) also had at least one episode of atrial fibrillation. The overall incidence of atrial flutter in the general population is 88/100,000. "Atrial flutter only" was 37/100,000 person-years. Adjusted for age, the incidence of atrial flutter in men (125/100,000, 95% confidence interval [CI] 102 to 149) was more than twice that of women (59/100,000, 95% CI, 44 to 73). As shown in Figure 1, the age-specific incidence of atrial flutter increased with age in both males and females.

Clinical features at initial diagnosis. Baseline characteristics of the 181 patients with atrial flutter and their matched controls are shown in Table 1. For both groups the

Table 2. Incidence of Atrial Flutter in the General Population

	Men			Women			Total		
	Person/Yr	Cases	Rate	Person/Yr	Cases	Rate	Person/Yr	Cases	Rate
0–49 yrs	84,915	6	0.07	82,250	2	0.02	167,165	8	0.05
50–59 yrs	8,715	15	1.72	8,643	4	0.46	17,358	19	1.09
60–69 yrs	7,223	29	4.02	7,982	20	2.51	15,204	49	3.22
70–79 yrs	5,943	36	6.06	7,918	21	2.65	13,862	57	4.11
80+ yrs	2,837	26	9.16	5,337	22	4.12	8,174	48	5.87
Total	109,634	112	1.02	112,129	69	0.62	221,763	181	0.82
Total-age adjusted*			1.25			0.59			0.88
(95% CI)			(1.02, 1.49)			(0.44, 0.73)			(0.75, 1.01)

*Age-adjusted using the 1990 U.S. total white population census.

mean age was 72 ± 12 (mean ± standard deviation) years, and 112 (62%) were men. The diagnosis was made by multichannel ECG recording in 104 patients (57%) and by 12-lead ECG in 77 patients (43%). Type I atrial flutter was diagnosed in 90% of the patients. In three cases (1.7%) there were neither identifiable recent predisposing events nor chronic preexisting comorbidities. These patients were labeled as having "lone atrial flutter." The other 178 patients (98.3%) had either definite documentation of a potentially predisposing condition or proven structural heart disease. In 108 cases (59.7%) atrial flutter occurred for the first time ever within 30 days of a likely predisposing event (such as major surgical procedure, pneumonia, etc). Of these, 42 (23% of the total 181) had their initial episode within four weeks of coronary artery bypass or valve replacement surgery. In the remaining 70 cases (38.7%), atrial flutter was associated with chronic comorbidities such as hypertension, diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), etc. At the time of initial diagnosis of atrial flutter, none had undergone RFA, and five patients (2.8%) were currently receiving AA drugs. Of these, four were taking type IA drugs, and one was taking a class III agent. None were on type IC AA agents.

Factors predisposing the development of atrial flutter. Individuals with a history of heart failure (HF), (RR 3.5, 95% CI, 1.7 to 7.1) or COPD (RR 1.9, 95% CI l, 1.1 to 3.4) were at increased risk of developing atrial flutter. Differences among cases and controls regarding the other eight preselected variables are shown in Table 3. Because of the strength of association, the population-attributable risk for developing atrial flutter was calculated. It was estimated that 15.8% and 11.6% atrial flutter cases in this cohort could be attributed to HF and COPD, respectively. Antiarrhythmic drugs did not predispose a subject to the development of atrial flutter.

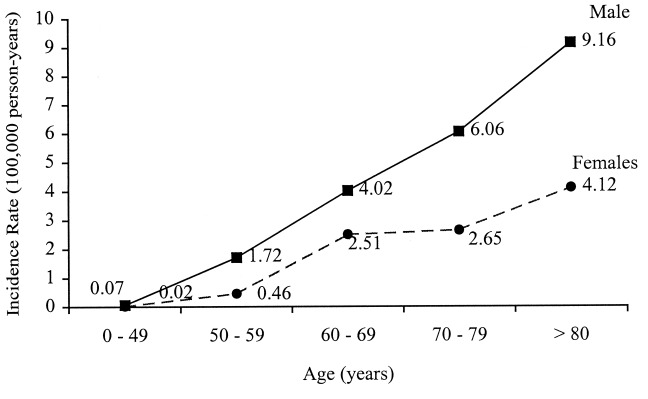

Figure 1. Incidence rates of atrial flutter by age and gender (100,000 person-years). **Black squares** = males; **black circles** = females.

DISCUSSION

Our current knowledge of atrial flutter has been largely derived from the published clinical experience of patients referred to tertiary care centers (9–19). Recent technological advances by these institutions have enhanced our understanding of the electrophysiologic mechanisms responsible for its initiation and maintenance (2–8). Practical application of this information has resulted in the widespread use of catheter-based RFA as a safe and curative procedure in these individuals. Despite these great technological achievements, little is known regarding the magnitude of this problem or how to prevent atrial flutter in the population at large (20). In fact, there are no previous reports on the epidemiology of atrial flutter in the general population. Framingham, the only population-based study that enrolled patients with atrial flutter, used a working definition of "atrial fibrillation" that included cases with either "atrial fibrillation or atrial flutter on ECG." Our data show that atrial flutter is much more common than previously appreciated.

Atrial flutter in the general population. Adjusted for the U.S. population, the overall incidence of atrial flutter is 88/100,000 person-years. While in clinical practice atrial flutter appears to be less common than PSVT, our data show that in the general population, atrial flutter is diagnosed for the first time more than twice as often (26). If our results were extrapolated to the entire U.S. population, we estimate there would be 200,000 new cases of atrial flutter in the U.S. annually. Approximately 80,000 of these would be cases of "atrial flutter only." Adjusted for age, the incidence of atrial flutter in men (125/100,000) is more than 2.5 times that of women (59/100,000). The age-specific incidence of atrial flutter increases exponentially with age (Fig. 1) from 5/100,000 person-years in those <50 years old to 587/

Table 3. Odds Ratio, Association Between Atrial Flutter and Clinical Variables

Variables	Matched-Pair Status (Patients/Controls)*				Odds Ratio	(95% Confidence Interval)	p Value
	+/+	+/−	−/+	−/−			
Heart failure	5	35	10	131	3.5	(1.7–7.1)	0.001
Chronic pulmonary disease	6	37	19	119	1.9	(1.1–3.4)	0.02
Diabetes mellitus	5	24	13	139	1.8	(0.9–3.6)	0.07
Rheumatic heart disease	0	4	1	176	4.0	(0.4–36)	0.21
Hyperlipidemia	34	42	53	52	0.8	(0.5–1.2)	0.26
Myocardial infarction	3	28	22	128	1.3	(0.7–2.2)	0.40
Hypertension	46	43	48	44	0.9	(0.6–1.4)	0.60
Thyroid disease	3	17	15	146	1.1	(0.6–2.3)	0.72

*Patients and their respective age– and gender–matched controls are shown according to their positive (+) or negative (−) status for each of the clinical variables listed above.

100,000 person-year among individuals ≥80 years, an increase of more than a hundred fold in the elderly. At the time of initial diagnosis, nearly all new cases (173 of 181, 96%) were >50 years of age. The incidence rate of atrial flutter in this large subset of our patients is an astonishing 317/100,000 person-years, a figure that approaches that reported for atrial fibrillation (27).

Clinical risk factors associated with atrial flutter. In addition to advancing age and male gender, at highest risk of developing atrial flutter were MESA residents with HF and COPD. A weaker association was also noted for those with DM ($p = 0.07$). The risk of developing atrial flutter increased 3.5 times in HF ($p < 0.001$) and 1.9 times ($p < 0.001$) in those with COPD. Sixteen percent of atrial flutter cases were attributable to HF and 12% to COPD. While we may have found previously unidentified risk factors for developing atrial flutter, only a small portion of the new cases can be explained by these predisposing conditions alone. The contribution of HF, COPD, DM and other conditions may have been underestimated due to potentially incomplete ascertainment of mild cases.

At the time of the initial diagnosis, only four of 181 (2.2%) patients were taking AA drugs. It is unlikely, therefore, that the conversion of atrial fibrillation into atrial flutter is a likely etiology of atrial flutter in the general population.

We have recently reported a kindred study with an autosomal dominant dilated cardiomyopathy in which atrial flutter is an early expression of the disease (28). Their genetically based cardiomyopathy was caused by a missense mutation in the rod domain of a lamin gene. Since one of the affected families was from MESA, we evaluated whether familial clustering on that basis was contributing to our findings. A comparison of the surnames of all 181 atrial flutter cases in this epidemiologic study with the 13 last names in the two affected families failed to identify any evidence among study patients. These observations do not exclude a potentially genetic contribution to the development of atrial flutter.

Further research is needed to determine whether aggressive efforts targeting earlier identification of individuals at risk as well as primary prevention and innovative treatments of the treatable predisposing conditions can impact the occurrence of atrial flutter and its associated complications.

Study limitations. We minimized selection bias by identifying practically all cases occurring in the entire population of a defined region. Although ICD-9-CM coding of medical conditions may not be completely accurate, we used a large set of codes in an attempt to identify all cases. It is unlikely that we missed many, if any, incident cases of clinically significant atrial flutter. Given its intermittent and often asymptomatic nature and the existing technological limitations, complete ascertainment of atrial flutter in any population would require life long continuous monitoring of all individuals in the area, a study not likely to ever be feasible or ethical. To identify risk factors for developing atrial flutter, we used an age- and gender-matched case-control design in which atrial flutter was the outcome variable. Unlike studies of volunteer cohorts screened over time, MESA represents an unselected sample representative of an entire population. The MESA population is predominantly white and rural. Though we are not aware of studies establishing racial, ethnic or residential predisposition to atrial flutter, our results should be used cautiously to project to other population groups.

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