

Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study

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KEYWORDS

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Aims We aimed to investigate the prevalence and incidence of atrial fibrillation (AF) in a large European population-based study.

Methods and results The study is part of the Rotterdam study, a population-based prospective cohort study among subjects aged 55 years and above. The prevalence at baseline was assessed in 6808 participants. Incidence of AF was investigated during a mean follow-up period of 6.9 years in 6432 persons. We identified 376 prevalent and 437 incident cases. Overall prevalence was 5.5%, rising from 0.7% in the age group 55–59 years to 17.8% in those aged 85 years and above. The overall incidence rate was 9.9/1000 person-years. The incidence rate in the age group 55–59 years was 1.1/1000 person-years, rose to 20.7/1000 person-years in the age group 80–84 years and stabilized in those aged 85 years and above. Prevalence and incidence were higher in men than in women. The lifetime risk to develop AF at the age of 55 years was 23.8% in men and 22.2% in women.

Conclusion In this prospective study in a European population, the prevalence and incidence of AF increased with age and were higher in men than in women. The high lifetime risk to develop AF was similar to North American epidemiological data.

Introduction

Atrial fibrillation (AF) is associated with substantial mortality and morbidity from thrombo-embolism, heart failure, and impaired cognitive function.^{1–5} With populations aging, AF is likely to become a greater public health burden, and thus reliable prevalence and incidence figures are needed both for clinicians and policy-makers.⁶

The prevalence of AF has been investigated in several countries, but many epidemiological uncertainties still remain, in particular as to why the prevalence figures differ widely between studies.^{7–17} Prevalence rates in the elderly are scarce. Incidence data on AF are also limited. Only two American population-based studies have presented data on incidence.^{18,19} A Canadian study presented incidence figures in men only and one British population study presented the incidence of AF, based mainly on hospitalizations.^{20,21} In this analysis, from the Rotterdam Study, we report the prevalence and incidence of AF, the prevalence of AF at three moments during follow-up and the lifetime risk of AF, in a large population-based epidemiological study.

Methods

Study population

The Rotterdam Study is a population-based prospective cohort study, which started in 1990 in Ommoord, a suburb of Rotterdam. The study design has been described in detail elsewhere.²² In short, all inhabitants of this area aged 55 and above ($n = 10\,275$) were invited to participate and 78% ($n = 7983$) entered the study. They were interviewed at home and most ($n = 7151$) were examined at the research centre to enable the collection of baseline data (1990–93), including a 10-s 12-lead resting ECG. Those who did not visit the research centre were in general dependent or lived in nursing homes. The participants were re-examined in two follow-up rounds. The first examination round was performed between July 1993 and December 1994. The second follow-up round started in April 1997 and ended in December 1999. The Medical Ethics Committee of Erasmus University approved the study and participants gave informed consent.

Evaluation of AF

Three methods were used to assess cases of AF or atrial flutter:^{23,24} (i) At baseline and during follow-up examinations, 10-s 12-lead ECGs were recorded at the research centre with an ACTA Gnosis IV ECG recorder (EsaOte, Florence, Italy), stored digitally and analysed with the Modular ECG Analysis System (MEANS).^{25,26} MEANS is

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characterized by a high sensitivity (96.6%) and a high specificity (99.5%) in coding arrhythmias.²⁷ To verify the diagnosis of AF, all ECGs with a diagnosis of AF or atrial flutter or any other rhythm disorder were recorded independently by two physicians who were blinded to the MEANS diagnosis. The judgement of a cardiologist was asked and taken as decisive in case of persistent disagreement. (ii) General practitioners participating in the Rotterdam study sent computerized information on AF, based on their own records and on hospital discharge letters, to the researchers of the Rotterdam study. Specially trained follow-up assistants verified this information. A senior physician examined all the information and coded the events according to the International Classification of Diseases (code I48 of the 10th revision). For a diagnosis of AF or atrial flutter, we required an ECG that verified the diagnosis. (iii) Hospital discharge diagnoses were also obtained from the LMR system (de Landelijke Medische Registratie). This national registration accumulates all hospital discharge diagnoses of Dutch inhabitants.

To ascertain AF at baseline, we used ECGs as described earlier. In addition, the general practitioner files of all participants were screened for the presence of AF at or before baseline.

We did not consider a person as having AF if: (i) AF occurred during the process of dying and was not the cause of death; or (ii) if transient AF occurred during a myocardial infarction or a cardiac operative procedure.

Information on vital status was obtained on a regular basis from the central registry of the Municipality of Rotterdam, from collaborating general practitioners and by obtaining information during follow-up rounds. For those participants whose information on vital status remained missing, the Central Registry of Genealogy of the Netherlands was consulted. This national institute receives population registry records of those inhabitants of the Netherlands who have died.

All participants were followed from the date of entry into the Rotterdam study (1990–93) to the date of onset of AF, the date of death or to 1 January 2000, whichever came first. The date of onset of AF was defined as the midpoint between the date of the follow-up round at which AF was detected and the date of the previous round at which AF had not yet been detected. If also or only information of a diagnosis of AF was available from either the general practitioner files and/or the LMR registry, this date was taken as the date of onset. Follow-up by 1 January 2000 was complete for 99.1% of the total study population.

General baseline measurements

Information on current health status, medical history, and smoking was obtained using a computerized questionnaire. Participants were classified as current or non-smokers. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Blood pressure was measured twice at the right upper arm with a random zero mercury sphygmomanometer in the sitting position. Systolic and diastolic blood pressures were calculated as the average of the two consecutive measurements. Hypertension was defined as a systolic blood pressure of 160 mmHg or over or a diastolic blood pressure of 100 mmHg or over, or the use of blood pressure lowering drugs prescribed for hypertension.²⁸ A history of myocardial infarction was defined as a self-reported myocardial infarction with hospital admission or the presence of a myocardial infarction on the ECG. A positive report of myocardial infarction was confirmed by reviewing the medical records of general practitioners and specialists for the presence of myocardial infarction. Left ventricular hypertrophy was diagnosed by the MEANS program with an algorithm that takes into account QRS voltages, with an age-dependent correction, and repolarization changes. Diabetes was defined as the use of anti-diabetic medication or a random or post-load serum glucose level of 11.1 mmol/L or more. Heart failure at baseline was assessed as described previously.^{29,30} In short, diagnosis of heart failure

was based on a score of heart failure symptoms, on medication prescribed with the indication of heart failure, on hospital discharge diagnoses, and on the information available in general practitioner files. Blood samples were drawn by venapuncture, and serum total cholesterol and HDL cholesterol were measured with an automated enzymatic method.

Population for analysis

For this study, an ECG was not available for analysis of AF at baseline in 343 participants because of logistic reasons. The population for analysis consisted of 6808 participants for whom at baseline an ECG was available. In this population, prevalence at baseline and at three consecutive moments during follow-up was measured. After exclusion of 376 participants with AF at baseline, the incidence, and lifetime risk of AF were calculated in 6432 persons.

Statistical analysis

Prevalence of AF at baseline was calculated as the proportion of those who had AF in the study population at the time of the baseline measurements. Wilson's score method for a binomial proportion was used to calculate 95% CI. Prevalence estimates were calculated for the total study population, for men and women separately, and for different age categories. Crude incidence rates for AF were calculated by dividing the number of incident cases of AF by the number of person-years accumulated in the population without AF at baseline. The 95% CI were calculated based on the Poisson distribution. Incidence rates were calculated for men and women separately and for 5-year age categories. To evaluate whether the prevalence became higher during follow-up, we calculated prevalence figures at three moments during follow-up: at the end of the baseline measurements (1 July 1993), at the end of the first follow-up round (1 January 1995), and at the end of the second follow-up round (1 January 2000). A logistic regression model was used to evaluate differences between the prevalence at 1 July 1993 and at 1 January 2000. In this analysis, observation 1 (1 July 1993) and observation 2 (1 January 2000) were considered as two independent observations. The lifetime risk of AF with 95% CI was calculated using a SAS macro from the Framingham Study.³¹ This macro takes into account competing risk of death.³² The risks of AF were calculated for men and women separately at the ages of 55, 60, 65, 70, 75, 80, and 85 years onwards. SPSS 11 for Windows (SPSS Inc., Chicago, IL, USA) and SAS 8.2 (SAS Institute Inc., Cary, NC, USA) were used for data analyses.

Results

Baseline characteristics of our study population are presented in *Table 1*. In the study population, 209 cases had AF on the ECG at baseline. Investigation of general practitioner files identified another 167 participants who had no AF at the baseline examination, but had been diagnosed with AF in an earlier period. They were also included as AF cases. The total number of prevalent cases was therefore 376, including 169 men (44.9%) and 207 women (55.1%).

The overall prevalence of AF was 5.5%, 6.0% in men and 5.1% in women. The prevalence in the age stratum 55–60 years was 0.7% and increased with each successive stratum. In the stratum of 85 years and above, the prevalence was 17.8%. Prevalence in each age stratum was higher in men than in women (*Table 2*).

After exclusion of the prevalent AF cases, 437 participants developed new AF (198 men and 239 women) during a follow-up of 44 175 person-years (mean 6.9 years); the overall incidence was 9.9/1000 person-years. There was a steep increase in the incidence with age, with the exception

of those who were older than 85 years. The incidence was 1.1/1000 person-years at ages 55–60, rose to 20.7/1000 person-years in the age group 80–85 but stabilized (18.2/1000 person-years) in those who were 85 years and above (Table 3). The incidence was higher in men than in women across all age groups.

Prevalence figures during follow-up were calculated based on the prevalence at baseline, on the incidence figures of AF,

and on the mortality figures of the study population. The prevalence at 1 July 1993 was 6.1% (men, 6.8%; women, 5.5%). The prevalence increased to 6.7% (men, 7.9%; women, 5.9%) on 1 January 1995 and to 8.3% (men, 9.5%; women, 7.5%) on 1 January 2000. This increase, although substantial (OR, 1.40; 95% CI, 1.22–1.62) was not significant after adjustment for age at the date of the measurement of the concerning prevalence figures (OR, 1.05; CI, 0.91–1.22, prevalence at 1 January 2000 when compared with the prevalence at 1 July 1993). Further adjustment for gender only minimally changed the age-adjusted point estimate.

Period risk and lifetime risk at different ages for men and women separately are shown in Table 4. At the age of 55 years, the lifetime risk of AF was 23.8% for men and 22.2% for women. Lifetime risks remained almost the same across age categories until the age of 75 years. After that, lifetime risks decreased in a pattern that was the same for men and women. Women and men did not differ substantially in lifetime risks. However, men constantly had a higher risk for future AF than women if limited time periods were considered, independent of the age group.

Discussion

In this large population-based study, the prevalence of AF increased with age and was higher in men than in women in each age group. The incidence of AF was also higher in each successive age group, except for those who were older than 85 at baseline. The incidence rate was higher in

Table 1 Baseline characteristics of the study population. The Rotterdam Study 1990–93 ($n = 6808$)

Characteristic	
Age (years)	69.3 ± 9.1
Gender (% women)	59.5
BMI (kg/m ²)	26.3 ± 3.7
Hypertension (%)	21.4
Systolic blood pressure (mmHg)	139.3 ± 22.5
Diastolic blood pressure (mmHg)	73.6 ± 11.7
Total cholesterol (mmol/L)	6.6 ± 1.2
HDL cholesterol (mmol/L)	1.35 ± 0.36
Current smoking (%)	22.8
Diabetes mellitus (%)	10.5
History of myocardial infarction (%)	12.8
Left ventricular hypertrophy (%)	5
Heart failure (%)	2.5

Numbers are mean ± SD for continuous variables and percentages for dichotomous variables.

Table 2 Prevalence with 95% CI of AF at baseline by gender and age. The Rotterdam Study 1990–93 ($n = 6808$)

Age group (years)	All			Men			Women		
	<i>n</i>	Cases	Cases/ <i>n</i> ^a	<i>n</i>	Cases	Cases/ <i>n</i> ^a	<i>n</i>	Cases	Cases/ <i>n</i> ^a
55–59	1161	8	0.7 (0.4–1.4)	485	4	0.8 (0.3–2.1)	676	4	0.6 (0.2–1.5)
60–64	1411	24	1.7 (1.2–2.5)	620	16	2.6 (1.6–3.4)	791	8	1.0 (0.5–2.0)
65–69	1291	51	4.0 (3.0–5.2)	597	31	5.2 (3.7–7.3)	694	20	2.9 (1.9–4.4)
70–74	1130	68	6.0 (4.8–7.6)	464	32	6.9 (5.0–9.6)	666	36	5.4 (4.1–7.0)
75–79	855	77	9.0 (7.3–11.1)	330	43	13.0 (9.8–17.1)	525	34	6.5 (4.7–8.9)
80–84	533	72	13.5 (10.9–16.7)	164	25	15.2 (10.5–21.5)	369	47	12.7 (9.7–16.5)
≥85	427	76	17.8 (14.5–21.7)	95	17	17.9 (11.5–26.8)	332	58	17.5 (13.8–21.9)
All	6808	376	5.5 (5.0–6.1)	2590	165	6.0 (5.0–7.0)	4053	206	5.1 (4.5–5.8)

^aDenotes % (95% CI).

Table 3 Incidence rates of AF with 95% CI by gender and age. The Rotterdam Study 1990–99 ($n = 6432$)

Age groups (years)	All		Men		Women	
	Cases/py	Rate (95% CI) ^a	Cases/py	Rate (95% CI) ^a	Cases/py	Rate (95% CI) ^a
55–59	3/2741	1.1 (0.3–2.9)	3/1140	2.6 (0.7–7.0)	–	–
60–64	27/8361	3.3 (2.2–4.7)	17/3496	4.9 (2.9–7.6)	10/4821	2.1 (1.1–3.7)
65–69	54/9817	5.5 (4.2–7.1)	28/4269	6.6 (4.5–9.3)	26/5548	4.7 (3.1–6.8)
70–74	100/8662	11.5 (9.5–14)	45/3627	12.4 (9.2–16.4)	55/5035	10.1 (8.3–14.1)
75–79	101/6899	14.7 (12.0–17.7)	51/2566	19.9 (15.7–25.9)	50/4332	11.5 (8.7–15.1)
80–84	92/4445	20.7 (16.8–25.3)	36/1414	25.5 (18.1–34.8)	56/3031	18.2 (14.1–23.8)
≥85	60/3294	18.2 (14.0–23.3)	18/709	25.4 (15.6–39.2)	42/2585	16.2 (11.9–21.7)
All	437/44175	9.9 (9.0–10.9)	198/17223	11.5 (10.0–13.2)	239/26952	8.9 (7.8–10.2)

py, person-years.

^aDenotes per 1000 person-years.

Table 4 Cumulative risk of AF in percentages at different ages in men and women. The Rotterdam Study 1990–99 (*n* = 6432)

Age (years)	Period risk (%) in 5-years intervals							Lifetime risk (95% CI)
	5 years	10 years	15 years	20 years	25 years	30 years	35 years	
Men								
55	0.8	2.8	5.4	9.6	15.2	20.1		23.8 (15.6–26.9)
60	2.1	4.7	8.9	14.6	19.6			23.3 (15.1–26.4)
65	2.8	7.3	13.4	18.7				22.7 (14.3–25.8)
70	5.0	11.6	17.5					21.9 (13.3–25.2)
75	7.9	14.9						20.2 (11.1–23.8)
80	9.2							16.1 (6.4–20.3)
>85								11.8 (1.3–17.2)
Women								
55	0	1.0	2.9	7.2	11.1	16.3		22.2 (14.7–24.8)
60	0.9	2.9	7.2	11.2	16.4			22.3 (14.8–24.9)
65	2.0	6.4	10.6	19.1				22.1 (14.6–24.8)
70	4.6	9.0	14.7					21.1 (13.4–23.8)
75	4.8	11.2						18.3 (10.2–21.2)
80	7.4							15.3 (7.4–18.9)
>85								11.8 (1.9–14.1)

men than in women. The lifetime risk of AF was high with only small differences between the sexes.

In the Rotterdam Study, we had, besides ECG data, the opportunity to survey general practitioner files over a considerable period before the start of the study and this may have helped us to obtain more reliable (but high) prevalence figures. The Cardiovascular Health Study reported prevalence figures that were lower in most age groups in comparison with our study.⁸ A study in the Mayo Clinic reported relatively high prevalence figures in the elderly.¹⁰ Also, Lake *et al.*⁹ in Australia reported prevalence figures that were similar to the present study.

Several problems in the assessment of AF may cause the differences between studies. AF is characterized by its well-documented temporal pattern and many patients with AF have no hospital contact.¹⁶ Furthermore, many patients are unaware of the presence of AF or periods of AF.³³ These problems indicate that assessment of AF indeed should be based on actual measurements by ECG, on information from general practitioners, and on hospital records.

Our incidence rates are similar to those reported from the Framingham Study. In the age category of 85 years and above, however, a higher incidence was reported in the Framingham Study, especially in women (*Table 5*). The Framingham study started much earlier than the present study, and measurements in populations may have made participants and physicians more aware of health and disease resulting in interventions. This may have caused participants with diseases that facilitate AF to have a better survival in the Framingham Study. The incidence figures of the Cardiovascular Health Study were almost twice as high as in our study, but this cohort is older than the Rotterdam study population. This alone cannot explain the difference, as in all age strata the incidence figures were still higher in the Cardiovascular Health Study. Furthermore, differences in racial demography and/or co-morbidity between the cohorts may have led to differences in the incidence figures. Other ascertainment methods in the Cardiovascular Health Study (e.g. self report of AF by participants) may also have played a role.

Table 5 Incidence rates of AF in three population-based studies

Age group	Framingham Study	Rotterdam Study	Cardiovascular Health Study
Men			
55–64	3.1	2.2	
65–74	~9.0	9.9	
65–69			12.3
70–74			22.8
75–84	~18	21.9	
75–79			34.8
≥80			58.7
≥85	38	25.4	
Women			
55–64	1.9	1.6	
65–74	~5.0	7.7	
65–69			10.9
70–74			9.1
75–84	~15	15.4	
65–69			23.1
≥80			25.1
≥85	31.4	16.2	

Rates are per 1000 person-years.

In the present study, prevalence figures were higher at two points during follow-up than at baseline. In the Framingham study, the prevalence over several biennial surveys rose, independent of changes in age and gender.^{34,35} In general, the prevalence of a disease can rise over time because of more attention from clinicians and general practitioners for the disease of interest in the course of time, leading to a smaller proportion that remains undetected, due to better survival of participants with AF and due to a better survival of those clinical conditions that are risk factors of AF. Our data, however, indicate that aging of the cohort was mainly responsible for the rise in prevalence in the Rotterdam study in the time window 1990–2000.

We calculated lifetime risks of AF of 24.8% for men aged 55 years and 22.9% for women aged 55 years, which correspond very well with recent data on the lifetime risk of developing AF in the Framingham study.³⁶ The difference between the sexes was small, and while risk in men was always higher over small time periods than in women, the similar lifetime risks probably reflect the better life expectancy of women. Lifetime risks of AF remained high and unchanged over a wide range of ages (55–75 years), indicating that there is equilibrium between rising death rate and rising incidence of AF. After the age of 75 years, lifetime risks declined in spite of the increasing incidence rate, through increasing death rates and decreasing life expectancy. However, our data from the Rotterdam study is almost totally Caucasian, and extrapolation to other populations should be done with caution.

In conclusion, prevalence and incidence figures are presented from a large prospective, population-based Dutch study. These data are the first European data that enable a comparison between populations in Western Europe and in North America. The prevalence and incidence of AF are high, increase with age, are higher in men than in women, and result in a very substantial lifetime risk.

Conflicts of interest: There are no conflicts of interest.

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