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Cardiovascular risk factors, ECG abnormalities and quality of life in subjects with atrial fibrillation

Summary

In Central European regions epidemiologic findings for atrial fibrillation (AF) in a randomly selected population are not available. Therefore, information obtained by a standardized examination procedure including resting 12 lead ECG of 4003 participants (2014 men, 1989 women), aged 25 to 64 years, of the MONICA-Augsburg Survey 1984/85 were analysed. Reexamination of 3753 subjects took place three years later (Follow-up Study 1987/88). Persons with AF in the baseline survey (n = 13) were compared with an age-and sex-matched control group (n = 156) without AF, chosen from the same population sample, with regard to cardiovascular risk factors, associated diseases and disturbances in the subjects' general well-being. In 1984/85 thirteen cases with AF (6 males, 7 females) were observed, giving an age-standardized prevalence of AF in males of 0.22% and in females of 0.34%. The age of men with AF ranged between 50 and 63 years and of women between 61 and 64 years. No significant differences were observed in persons with AF compared to the control group in risk factor levels and alcohol consumption; however, significant differences could be seen concerning disturbances in quality of life like self-reported health status ($p < 0.001$), sleep disturbances ($p < 0.05$), antihypertensive medication ($p < 0.001$). AF cases were found to have further ECG abnormalities significantly more often (left anterior hemiblock: $p < 0.05$; ventricular premature beats: $p < 0.05$). In all subjects with AF in the initial examination 1984/85 AF was found three years later (chronic AF). Overall 13 new cases (7 men, 6 women) were identified in the 1987/88 follow-up. The prevalence of AF in a South German population is comparable with AF prevalences reported from studies in other populations (e.g.) Framingham 1950, Reykjavik 1967/70). Associated ECG abnormalities were found more frequently in subjects with AF. Cases with AF have considerable disturbances in their general well-being.

Atrial fibrillation (AF) is a cardiac rhythm disturbance commonly encountered in clinical practice. From epidemiologic studies it is well-known that AF is associated with an increased risk of mortality. Whereas since the beginning of the century numerous studies have investigated the electrophysiological, clinical, and pharmacotherapeutic aspects of AF, epidemiological studies have been reported only since the early 1960s[1–5]. Prevalence and incidence reported in the literature vary greatly in relation to the population groups studied. There are no studies on the epidemiology of AF based on a representative investigation of an unselected adult population from Central European regions.

We therefore analysed the data of 4003 men and women aged 25–64 years who participated in the first cross-sectional study (Survey 1984/85) of the Augsburg MONICA study.

Besides providing an estimate of the frequency of AF, we particularly focussed on the differences between individuals of the same age and gender with and without AF regarding coronary risk factors and attendant conditions. Furthermore, we analysed the self-assessment of subjects with AF regarding their general health status in order

to evaluate their quality of life. The follow-up conducted in 1987/88 provides an insight into the incidence of this rhythm disorder.

Materials and Methods

The Augsburg MONICA Project

The Augsburg MONICA Project is part of the international MONICA Project (Monitoring trends and determinants in cardiovascular disease) conducted under World Health Organization (WHO) guidance in 41 centers in 26 countries in order to investigate changes in cardiovascular risk factors and changes in morbidity and mortality[6,7].
During the 10-year duration of this project, all centers are uniformly conducting three cross-sectional studies to determine trends in risk factor profiles[8,9] and concurrently maintaining continuous coronary event registers to establish event rates[10]. Beyond this, the Augsburg MONICA project re-examined the participants of the Survey 1984/85 after three years according to the same study protocol[11] in order to establish individual changes in the risk factor profile. Baseline results from the study region Augsburg have been published elsewhere[12–18].

Study population and response rates

The study region comprises the city of Augsburg and the counties of Aichach-Friedberg and Augsburg. For the first cross-sectional study (Survey 1984/85), an age- and sex-stratified random sample of 5312 persons aged 25–64 years was drawn[19]. A total of 76% (n = 4022) of these individuals participated in the 1984/85 survey and 3753 persons were available for the follow-up in 1987/88.
The analyses presented here include 4003 persons (2014 men, 1989 women) in the survey and 3533 persons (1771 men, 1762 women) in the follow-up for whom complete data were available.

Data collection

The data for the first survey were collected from October 1984 through May 1985, those for the follow-up during the same months in 1987/88. The examinations were performed by specially trained personnel in 16 centers distributed across the study region[20]. The analyses are based on the following data collection instruments:
Data on sociodemography, medical care, self-assessed health status, medication use, physical activity, and smoking status were collected in a standardised interview. The interview was followed by three blood pressure measurements as well as body height and weight measurements. After this, blood samples were taken and ECGs were registered. The ECG was taken with a computer-aided ECG evaluation system (SICARD 803). The 12 conventional leads were registered for a duration of 20 seconds[21,22]. All computer ECG findings were cardiologically evaluated.
After routine data collection had been concluded, additional data were obtained from the family physicians of those subjects with AF who had signed a consent form.

Statistical methods

The group of subjects with AF in the first examination (Survey 1984/85) was compared to a control group without AF. In order to increase statistical power, 12 controls of the same age and sex were randomly chosen for each case of AF, so that the 13 cases with AF were compared with 156 controls. This corresponds to a case-control study within the survey 1984/85 (nested case control study).
The chi-square test (two-sided) was used to test for differences between AF cases and controls. The 1:12 matching study design was considered in the calculation of the odds ratio according to Mantel-Haenszel. The prevalence and incidence were age-standardized for the population between 25 to 64 years, i.e. the values found for each age group were weighted according to the age distribution of the poplation of Germany (as of 31 December 1980) and summarized to give the age-adjusted value.

Results

Prevalence and incidence

Table 1 shows the prevalence of AF in the first survey by age and sex indicating a marked increase with age. No AF was found among men in the two younger age groups (25–34 years and 35–44 years). As shown in Table 2, the average age of men with AF (n = 6) was 58 years (range 50–63 years). Women with AF were found only in the oldest age group (55–64 years), and their average age was 62 years (61–64 years).
The age-standardized prevalence in relation to the age distribution of 25–64 year old men and women in Germany was 0.22% in men and 0.34 % in women.
All subjects with AF in the first survey who participated in the follow-up study also showed AF at follow-up (Table 3). We were unable to re-examine four of the subjects found to be AF-positive in the first survey; two of them had died, and two did not participate in the follow-up. In the 1987/88 follow-up, 13 new cases with AF (7 men, 6 women) were discovered, corresponding to an age-standardized 3-year incidence of 0.34% in men and 0.35% in women.

Age (years)	AF positive n	%	Total
Men	6	0.22*	2014
25–34	0	–	461
35–44	0	–	485
45–54	1	0.2	539
55–64	5	0.9	529
Women	7	0.34	1989
25–34	0	–	460
35–44	0	–	522
45–54	0	–	513
55–64	7	1.4	494

* Age-weighted according to the age distribution of the population in the study area.

Table 1. *Prevalence of atrial fibrillation (AF) by age and sex (Survey 1984/85).*

	Survey 1984/85 age (4 years)			Follow-up 1987/88 age (4 years)		
	n	$\bar{x}$	Range	n	$\bar{x}$	Range
Men	6	57.8	50–63	7	57.4	47–67
Women	7	62.4	61–64	6	62.3	59–67
Total	13	60.3	50–64	13	59.7	47–67

Table 2. *Age and sex distribution of persons with atrial fibrillation in the baseline examination (Survey 1984/85) and of persons with first manifestations of atrial fibrillation in the re-examination (Follow-up 1987/88).*

1. Survey 1984/85	Follow-up 1987/88 Atrial fibrillation positive	negative	No ECG*	Total
Positive	9	0	4	13
Negative	13	3511	466	3990
Total	22	3511	470	4003

* This category comprises persons who were unavailable for ECG examination for various reasons (migration, death, "non-response", technical reasons).

Table 3. *Cases with atrial fibrillation in the first examination (Survey 1984/85) and in the re-examination (Follow-up 1987/88).*

Special features in subjects with AF compared to the control group

Self-assessed health status, medical history, health care utilization and employment status

The responses to the standardized interview of the subjects revealed a significantly poorer health status for subjects with AF compared to the control group (Table 4). Indications for reduced quality of life were found in the poorer self-assessed health status (54% vs. 13%), reduced physical activity (69% vs. 45%) and increased sleep disturbances (85% vs. 53%).

The self-reported medical history more frequently included cardiac insufficiency (46% vs. 10%) and symptoms of angina pectoris (31% vs. 10%). Subjects with AF were less frequently employed (15% vs. 30%). Of the subjects with AF, 69% stated that they had seen a physician within the last four weeks compared to 49% in the control group.

Cardiovascular risk factors, body weight, and alcohol consumption

There were no significant differences between subjects with AF and the control group with regard to the cardiovascular risk factors hypercholesterolemia, smoking, and high blood pressure values (Table 5). With regard to the measured blood pressure, however, a much higher proportion of probands with AF were receiving antihypertensive medication compared to the control group. Adding subjects with antihypertensive treatment to those with elevated blood pressure results in a distinctly higher proportion of "actual hypertensives" (77% vs. 31%) among persons with AF. Generally, cardiac medication played a major role in subjects with AF. Twelve out of 13 took one or more cardiac medications; in addition to anti-

Feature	Atrial fibrillation (n = 13)		Control (n = 156)		
	n	%	n	%	p
Poor health status (self-reported)	7	54	20	13	< 0.001
Reduced physical activity	9	69	70	45	n.s.
Sleep disturbance	11	85	82	53	< 0.05
Cardiac insufficiency	6	46	15	10	< 0.001
Angina pectoris	4	31	15	10	< 0.05
Physician consultation within the last 4 weeks	9	69	76	49	n.s.
Hospital stay within the preceding year	5	39	24	15	< 0.05
Antihypertensive treatment	9	69	31	20	< 0.001
Still employed	2	15	47	30	n.s.

Table 4. *Self-reported health status, medical history, medical care utilization, and employment status of persons with atrial fibrillation compared with persons from the control group (Survey 1984/85).*

Feature	Atrial fibrillation (n = 13)		Control (n = 156)		$\hat{OR}_{MH}$ +	p
	n	%	n	%		
High blood pressure (BP ≥ 160/≥ 95 mmHg)	3	23	30	19	1.26	n.s.
High blood pressure or antihypertensive treatment	10	77	49	31	6.0	< 0.01
Hypercholesterolemia (≥ 260 mg/100 ml)	3	23	58	37	0.56	n.s.
Smoking (≥ 5 cigarettes per day)	2	15	28	18	0.88	n.s.
Overweight (BMI * ≥ 27.8 in men ≥ 27.3 in women)	10	77	73	47	3.52	< 0.05
Alcohol consumption ≥ 40 g pro Tag	1	8	34	22	0.27	n.s.

+) $\hat{OR}_{MH}$ = Mantel-Haenszel odds ratio adjusted for 1 : 12 matching.
* BMI = Body weight/height² (kg/m²).

Table 5. *Cardiovascular risk factors in persons with atrial fibrillation as compared with persons of the control group (Survey 1984/85).*

hypertensives these were predominantly glycosides (n = 10). The prevalence of overweight was higher among persons with AF (77% vs. 47%). There was no association between self-reported alcohol consumption and AF.

Electrocardiographic features

Additional ECG-abnormalities were found significantly more often among subjects with AF than in the control group (Table 6). These included ventricular extrasystoles (15% vs. 1%) and left anterior hemiblocks (23% vs. 3%). Signs of left ventricular hypertrophy were also more frequent among subjects with AF (31% vs. 12%), but the difference did not quite reach the 5% level of significance. The summary ECG-evaluation (disregarding the rhythm diagnoses), which separated the findings into normal/abnormal categories, also showed that the AF-positive group deviated from the norm more often than the control group (77% vs. 47%). The high prevalence of 47% abnormal ECG findings among controls can be explained by the relatively advanced age of these persons.

Information from the family physicians

Of the 26 individuals with AF in the first and follow-up examinations, 14 had consented that their family physician could be questioned. Twelve of 14 of the family physicians responded (8 by telephone, 4 by questionnaire). None of the patients with AF had a known medical history of rheumatic fever, nor an acquired or congenital heart defect. However, chest X-rays were available for only 7 of 12 patients, ECGs only for 3, echocardiographic and coronary angiographic results for none. The physicians reported on embolic events for 4 of the patients (3 transient ischemic attacks, 1 pulmonary embolism). One patient was treated for a hyperthyroid condition.
In 6 cases, AF was recognized and electrocardiographically documented for the first time during the MONICA examinations.

ECG-feature	Atrial fibrillation (n = 13)		Control (n = 156)		
	n	%	n	%	p
Ventricular premature beats	2	15	2	1	< 0.05
Left anterior hemiblock	3	23	5	3	< 0.05
Left ventricular hypertrophy	4	31	18	12	n.s.
ECG abnormalities (any, excluding rhythm disorders)	10	77	73	47	< 0.05

Table 6. *ECG abnormalities in persons with atrial fibrillation as compared with persons from the control group (Survey 1984/85).*

Discussion

The data on prevalence of AF vary considerably in relation to the population studied. Thus the prevalence ranges between 0.004% among male pilots (Air Force Study, USA[1]) up to 15% in men over 75 years of age (Busselton Study, West Australia[23]) and over 8.4% among women of the same age. Evidently, the prevalence of AF depends on the general health status and on the age of the groups under study.
The age standardized prevalences of 0.22% among 25–64 year old men and 0.34% for women of the same age compare very well with the results of the baseline examinations of the Framingham study in 1950[24] with 0.30% for both sexes. The Reykjavik study (baseline survey 1967/70[25]) showed AF prevalences of 0.41% for men and 0.15% for women.
Both of the above studies, like the one in the Augsburg region, were population-based investigations of samples of persons with a similar age structure (Reykjavik study 32–64 years, Framingham 30–62 years). The average age of men with AF in Augsburg was 5 years younger than that of women with AF (57.8 vs. 62.4 years). This is confirmed in the follow-up study conducted after three years. In contrast to this, the average age of cases with AF in the Reykjavik study was lower and almost identical for both sexes with 52.7 years for men (45–64 years) and 51.0 years for women (37–60 years). All studies showed a pronounced increase of AF with age[2,23,25–29].
Regarding the question of whether the AF-positive subjects in the current study had chronic or paroxysmal AF, we found that all re-examined AF-positive subjects of the first cross-sectional study 1984/85 also presented with AF during the follow-up examination in 1987/88. These subjects can therefore be considered to have the chronic form of AF which, according to Kannel et al.[5], constitutes about 60% of all AF.
As several other studies have shown, AF frequently occurs in association with other medical conditions, some of which can be considered the causal disorder. The proportion of persons with AF and without concurrent conditions (lone atrial fibrillation) is, relative to the base population of persons with AF in the 30 year follow-up of the Framingham study[30] only

16.6% for men and 6% for women. The Reykjavik study[25] reports a proportion of 32% (1967 study) and of 24% (1984 study), with the lower percentage in the study from 1984 possibly being attributable to improved diagnostics. Clinical patients show a significantly lower proportion of AF without concurrent medical conditions. Thus Kopecky et al.[31] report a proportion of only 2.7% (97/3623) in the Olmsted County Register, Minnesota, for patients aged 15 to 60 years who were examined between 1950 and 1980 in the Mayo Clinic.

The most frequent causes of AF are atherosclerotic, hypertensive and rheumatic heart disease as well as hyperthyroid conditions. Obstructive pulmonary disease, cardiomyopathies and valvular heart disease are less frequent[32]. Based on the results of the Framingham study, Savage et al.[24] additionally regard stroke (in men), cardiac insufficiency, left ventricular hypertrophy and diabetes (in women) as precursors of AF.

In our investigations, the more frequent occurrence of signs of left ventricular hypertropy in the ECGs of subjects with AF compared to the control group indicates an association between AF and left ventricular hypertrophy. The increased occurrence of additional ECG abnormalities in subjects with AF is possibly a general indication of attendant cardiac conditions, but could also in part be induced by medications. Lake et al.[23] have referred to the increase of left bundle branch blocks among patients with AF; our study also showed a remarkably high prevalence of left anterior hemiblocks among persons with AF.

The discussion about coronary heart disease as a cause of AF is controversial. In the Busselton population study in West Australia, Lake et al.[23] showed a positive correlation of AF with angina pectoris and previous myocardial infarction. Symptoms of angina pectoris were also found more frequently in persons with AF in our investigation. It should be noted, however, that angina pectoris is not specific for coronary heart disease and might also be encountered in other myocardial and valvular conditions. The results of Cameron et al.[33] for CHD patients examined with invasive diagnostic methods showed no positive correlation of AF and narrowing of the large coronary arteries.

The coronary risk factors hypercholesterolemia and smoking were not found more frequently among AF-probands compared to the control group. This confirms the results presented by Önundarson in the Reykjavik study, which even showed a lower prevalence of coronary risk factors. The higher prevalence of overweight found among persons with AF (Odds Ratio = 3.5) in the study region Augsburg was not confirmed in the Reykjavik study.

In order to interpret the distribution of the risk factors, it should be noted that the group-specific current risk factor profiles are no indication for a past equivalent risk exposure, particularly if knowledge of the condition and the health status of the patient influenced the risk factors. This becomes clear for the risk factor hypertension. The blood pressure values of subjects with AF hardly differ from those of the control group; the majority of subjects with AF, however, were on antihypertensive treatment.

Based on the results of the Framingham study, Kannel et al.[5] consider hypertension-related cardiovascular disease (high blood pressure with signs of LVH in the ECG, cardiac enlargement, cardiac insufficiency) the most important precursors of AF in men: these explain about 15% of all cases with chronic AF. High blood pressure without signs of hypertrophy or insufficiency did not have predisposing significance for AF.

Koskinen et al.[34] state that alcohol consumption might have a triggering function for AF. We determined less alcohol consumption in our subjects with AF. Lake et al..[23] also found less alcohol consumption among persons with manifest AF compared to a control group.

Our data cannot address the question of a rheumatic causation of AF, because the MONICA study was primarily designed for other purposes. Interview and questionnaire information gathered from practitioners did not show an association with rheumatic disorders; however, it should be noted that conclusive diagnostic tests had often not been performed. Kannel et al.[5] frequently found prior rheumatic heart disease among men and women who developed AF.

The occurrence of thromboembolic events in association with AF is of great prognostic significance. In our study, practitioners reported embolic events in 4 of 12 cases with AF. Brand et al.[30] determined a greatly increased proportion of strokes in subjects with idiopathic AF compared with a control group (28.2% vs. 6.8%). This is not supported by Kopetzky et al.[31]. Kannel et al.[5] also determined a greater proportion of strokes in males with chronic AF (10.2% vs. 2.4%). Wolf et al.[35] report a five times increased risk of stroke in patients with AF. Peterson and Godfredsen[32] state that the complication rate through thromboembolic events is 25%.

Anderson et al.[36] suggest a temporal correlation between the occurrence of specific symptoms and the beginning of AF in patients with paroxysmal AF. In our study, we also addressed the question of how, and to what extent, the general well-being of persons with chronic AF is affected compared with an age- and sex-matched control group. The frequent cardiac symptoms, the hemodynamic deficits, particularly under stress, and the underlying cardiac condition and

its complications, led to the assumption of a reduction of quality of life in a considerable proportion of probands with AF. This was confirmed by the standardized interview and was expressed by a generally reduced physical condition, sleep disturbances and frequent physician visits and hospital stays, as well as a higher proportion of unemployment.
Addressing the impact of AF on the health care system, two facts should be considered: since the incidence of AF increases markedly with age, and the population is aging, AF my cause additional challenges to the health care system.

Zusammenfassung

Risikofaktoren, EKG-Anomalien und Lebensqualität bei Vorhofflimmern

Da Studien zur Epidemiologie des Vorhofflimmerns (VF) in der Durchschnittsbevölkerung aus dem deutschsprachigen Raum nicht vorliegen, wurden Daten aus dem standardisierten Untersuchungsprogramm (mit Routine-EKG) von 4003 Teilnehmern (2014 Männer, 1989 Frauen) im Alter zwischen 25 und 64 Jahren der 1. Querschnittsstudie 1984/85 des MONICA-Projekts Augsburg analysiert. Es wurde untersucht, inwieweit sich Probanden mit VF (n = 13) von Probanden gleichen Alters und Geschlechts ohne VF (n = 156) hinsichtlich kardiovaskulärer Risikofaktoren, EKG-Anomalien und einer allgemeinen Beeinträchtigung ihres Befindens unterscheiden. Die altersstandardisierte Prävalenz des VF betrug bei Männern 0,22%, bei Frauen 0,34%. Bezüglich kardiovaskulärer Risikofaktoren und Alkoholkonsum zeigten sich bei Probanden mit VF gegenüber Probanden ohne VF keine statistisch signifikanten Unterschiede; hingegen wurden bei Probanden mit VF signifikant häufiger Merkmale eingeschränkter Lebensqualität und zusätzliche EKG-Anomalien gefunden. Da alle Probanden, die in der Querschnittsstudie 1984/85 VF aufwiesen und an der Nachuntersuchung 1987/88 teilnahmen, auch hier VF aufwiesen, handelt es sich hier offensichtlich um die chronische Form. Darüber hinaus wurden nach drei Jahren 13 Neuerkrankungen festgestellt.
Die Häufigkeit von VF in einer süddeutschen Bevölkerung ähnelt der in anderen Regionen (Framingham 1950, Island 1967–1970).

Résumé

Facteurs de risque cardiovasculaire, perturbations électro-cardio-graphiques et qualité de vie des sujets présentant une fibrillation auriculaire

Des études concernant l'épidémiologie de la fibrillation auriculaire (FA) ne sont pas disponibles dans les populations de langue germanique. C'est pourquoi les données de la 1ére étude MONICA Augsburg 1984/85 ont été analysées. Il s'agit d'une étude standardisée (aves pratique d'ECG régulière) auprès de 4003 sujets (2014 hommes, 1989 femmes), agés de 25 à 64 ans. Les personnes présentant lors de la 1ére étude une FA (n = 13) ont été comparées à un groupe témoin sans FA (n = 156), apparié sur l'âge, le sexe et sélectionné dans le même échantillon en fonction des facteurs de risque cardiovasculaire, de maladies associées ou autres troubles de la santé. La prévalence de la FA standardisée sur l'âge était chez les hommes de 0,22 % et chez les femmes de 0,34 %. Le niveau des facteurs de risque cardiovasculaire et celui de la consommation d'alcool ne sont pas significativement différents entre le groupe présentant une FA et le groupe témoin. En revanche des différences significatives ont été observées en ce qui concerne la qualité de la vie. Les cas présentant une FA avaient de façon significative plus de perturbations à l'ECG. Une FA persistait 3 ans plus tard chez tous les patients ayant présenté une FA lors du 1er examen en 84/85 (FA chronique). 13 nouveaux cas ont été dépistés lors du suivi 87/88.
La prévalence de la FA dans la population d'Allemagne du Sud est comparable avec celle rapportée par des études effectuées sur d'autres populations (Framingham 1950, Reykjavik 1967/70).

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