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Temporal trends in mortality and causes of death in patients with incident atrial fibrillation: a nationwide register study from 2010 to 2018

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ABSTRACT

Objectives Atrial fibrillation (AF) is associated with increased mortality. Previous studies have reported conflicting results in temporal trends of mortality after AF diagnosis. We aim to address this disparity by investigating the 1-year mortality and causes of death in Finnish patients diagnosed with AF between 2010 and 2017.

Design The Finnish AntiCoagulation in Atrial Fibrillation (FinACAF) study is a nationwide retrospective register-based cohort study.

Setting The FinACAF study has gathered information on all Finnish AF patients between 2004 and 2018, with information from all national healthcare registers and data from all levels of care (primary, secondary and tertiary care).

Participants We included patients with an incident AF diagnosis (International Classification of Diseases, 10th Revision code I48) between 2010 and 2017. To ensure a cohort of only incident AF, we excluded patients who used any oral anticoagulant during the year before cohort entry as well as patients with a recorded use of warfarin between 2004 and 2006. Patients under 20 years of age were excluded, and patients with permanent migration abroad before 1 January 2019 were excluded, N=157 658.

Primary outcome measures 1-year all-cause, cardiovascular (CV) and cause-specific mortality following AF diagnosis.

Results The study cohort consisted of 157 658 incident AF cases (50.1% male, mean age 72.9 years). Both all-cause and CV mortality declined from cohort entry years 2010–2017 (from 12.9% to 10.6%, mortality rate ratio (MRR) 0.77; 95% CI 0.73 to 0.82 in cohort entry year 2017 with 2010 as reference; and from 7.4% to 5.2%, MRR 0.68; 95% CI 0.63 to 0.74, respectively). Overall mortality and CV mortality were lower in women than in men throughout the study period (MRR 0.66; 95% CI 0.63 to 0.69 and MRR 0.53; 95% CI 0.50 to 0.56, respectively). Deaths attributable to ischaemic heart disease decreased during the study period (from 30.7% to 21.6%, MRR 0.51; 95% CI 0.49 to 0.62 in 2017 vs 2010), whereas dementia and Alzheimer's disease increased as a cause of death over time (6.2% to 9.9%, MRR 1.19; 95% CI 0.96 to 1.48 in 2017 vs 2010). The CHA_2DS_2-VASc score associated strongly with 1-year survival (p<0.0001).

Conclusions Our study reiterates that mortality after diagnosis of AF has decreased. The CHA_2DS_2-VASc score highlights the need to treat comorbidities as it strongly associates with patient 1-year survival after initial AF diagnosis.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is a large nationwide register-based cohort study with data from all Finnish national healthcare registers, including information from primary, secondary and tertiary care.
⇒ In Finland, every resident is given an official personal identity code, which allows reliable identification of the patient in all official registers.
⇒ The study suffers from the usual limitations of a register study, in that the data were based on administrative recording, and the entries have taken place in connection with clinical practice.

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. The prevalence of AF is rising, with current prevalence estimates as high as 5.2% in adults.[1 2] Furthermore, projections indicate a twofold increase in AF prevalence by 2050.[3] Ischaemic stroke is the major adverse event of AF and one of the most common cardiovascular (CV) causes of death in AF patients. The clinical risk factor-based CHA_2DS_2-VASc score (congestive heart failure, hypertension, age ≥75 years, diabetes, history of stroke/transient ischaemic attack (TIA), vascular disease, age 65–74 years and sex category) is used for evaluating the risk of stroke in AF patients.[4]

AF is associated with an impairment in quality of life as well as increased morbidity and mortality. Previous studies have reported conflicting results regarding temporal trends in mortality after AF diagnosis, a matter essential to assessing the effectiveness of AF care, with some reporting a decline and others no difference at all.[5–9]

This nationwide retrospective register study aims to address the conflicting results of previous studies by investigating the 1-year mortality and causes of death in patients diagnosed with AF between 2010 and 2017 using nationwide registry data from all levels of care (primary, secondary and tertiary care). Our data are, to the best of our knowledge, the only nationwide cohort with all AF patients from all levels of care.[1]

METHODS

Study population

This study is part of the Finnish AntiCoagulation in Atrial Fibrillation study (FinACAF) (ClinicalTrials Identifier: NCT04645537; ENCePP Identifier: EUPAS29845), a retrospective nationwide register-based cohort study gathering information on all Finnish AF patients between 2004 and 2018. A detailed description of the study methods has been published previously.[1] This substudy includes patients over 20 years of age with their first ICD-10 (International Classification of Diseases, 10th Revision) diagnosis code of I48 recorded between 1 January 2010 and 31 December 2017.

AF patients were identified from three national healthcare registers; Hilmo (hospitalisations and outpatient specialist visits), AvoHilmo (primary healthcare visits) and the National Reimbursement Register for reimbursed medication upheld by the Social Insurance Institute (KELA). Follow-up continued until 31 December 2018 or death, whichever came first. Patients entering the cohort during 2018 had less than 1 year of follow-up and were therefore excluded from this substudy to ensure a full year of follow-up in all patients who did not die. Patients with permanent migration abroad before 1 January 2019 were excluded from the study, which in this older cohort only comes to a total of 702 patients (0.17% of the FinACAF study population). We ran preliminary robustness checks and found that the inclusion of these patients would not change the statistical significance of the results. To ensure a cohort of only incident AF, patients with a recorded AF diagnosis between 2004 and 2009 were excluded, as well as patients with a fulfilled warfarin prescription during 2004–2006, as these patients had a brief recorded medical history and a high likelihood of a prior AF diagnosis before the study inception. Patients with recorded use of any oral anticoagulant (OAC) up to 1 year before cohort entry were also excluded. online supplemental figure S1 demonstrates the patient selection flow chart.

In addition to the aforementioned registers, the National Prescription register (KELA), National Cancer Register and the laboratory databases of the six largest central laboratories in Finland were used to obtain baseline characteristics and patient data. Individual patient data from all the used registers was linked using a unique personal identification number given to every Finnish citizen.

Baseline characteristics

The baseline clinical characteristics including comorbidities were gathered from 1 January 2004 up to the cohort entry date. Medication at baseline was defined as purchase of a medication up to 1 year before cohort entry, and baseline laboratory values were defined as the value nearest to, but no more than 12 months before the cohort entry date. CHA_2DS_2-VASc and HAS-BLED scores were calculated at cohort entry based on the information obtained from the registers (information on warfarin control quality at baseline was not available). The definitions and details of baseline characteristics are presented in online supplemental tables S1 and S2.

Outcomes

The primary outcomes were 1-year all-cause-mortality and CV mortality as well as causes of death (cause-specific mortality). Causes of death were grouped as follows: CV disease (ICD-10 I00–I42.5, I42.7–I99), ischaemic heart disease (ICD-10 I20–I25), cerebrovascular disease (ICD-10 I60–I69), other CV disease (ICD-10 I00–I15, I26–I28, I30–I42.5, I42.7–I52 and I70–I99), dementia and Alzheimer's disease (ICD-10 F01, F03, G30, R54) and cancer (ICD-10 C00–C97). The outcomes of interest were determined during 1-year follow-up after the AF diagnosis date for each cohort entry year. Causes of death and time of death were obtained from the National Causes of Death Register upheld by Statistics Finland.[10]

Patient and public involvement

This study is based on retrospective register data. Thus, no patient contacts were involved in any phase of the study and no patient consent was required according to Finnish legislation. The study conforms to the Declaration of Helsinki as revised in 2013 and to European General Data Protection Regulation (EGDPR).

Statistical analysis

Statistical analyses were performed with the IBM SPSS Statistics for Windows software (V.28.0, IBM) and R Statistical Software (V.4.2.1; R Foundation for Statistical Computing, Vienna, Austria. URL: https://www.R-project.org/). A linear-by-linear χ^2 test was used to assess associations between categorical variables, and Spearman's correlation test was used to analyse continuous variables. One-year mortality rates and causes of death (cause-specific mortality) were analysed as crude-specific and age-specific mortality. We calculated mortality rate ratios (MRRs) using the Poisson regression model. Adjusted MRRs accounted for the following variables: sex, age (age groups 20–64 years; 65–74 years and ≥75 years), calendar year of diagnosis, CHA_2DS_2-VASc score and baseline comorbidities (hypertension, heart failure, hyperlipidaemia, diabetes, ischaemic stroke or TIA, vascular disease, thyrotoxicosis, cardiomyopathy, pulmonary embolism, venous thromboembolism, prior

Table 1 Baseline characteristics of Finnish atrial fibrillation patients at time of diagnosis, n=157 658

	Male	Female	All
Sex, n (%)	78 921 (50.1)	78 737 (49.9)	
Mean age (SD)	69.2 (13.3)	76.6 (11.7)	72.9 (13.1)
Age, years, n (%)			
<65	26 596 (33.7)	11 789 (15.0)	38 385 (24.3)
65–74	23 966 (30.4)	19 388 (24.6)	43 354 (27.5)
≥75	28 359 (35.9)	47 560 (60.4)	75 919 (48.2)
Comorbidities, n (%)			
Hypertension	54 805 (69.4)	64 175 (81.5)	118 980 (75.5)
Heart failure	12 278 (15.6)	15 161 (19.3)	27 439 (17.4)
Hyperlipidaemia	38 181 (48.4)	40 366 (51.3)	78 547 (49.8)
Diabetes	18 538 (23.5)	16 857 (21.4)	35 395 (22.5)
Ischaemic stroke	8651 (11.0)	9576 (12.2)	18 227 (11.6)
Transient ischaemic attack (TIA)	2839 (3.6)	3993 (5.1)	6832 (4.3)
Vascular disease	23 303 (29.5)	21 270 (27.0)	44 573 (28.3)
Coronary artery disease	19 191 (24.3)	16 827 (21.4)	36 018 (22.8)
Myocardial infarction	7778 (9.9)	6137 (7.8)	13 915 (8.8)
Thyrotoxicosis	326 (0.4)	1236 (1.6)	1562 (1.0)
Cardiomyopathy	1957 (2.5)	846 (1.1)	2 803 (1.8)
Dilated cardiomyopathy	1443 (1.8)	496 (0.6)	1 939 (1.2)
Hypertrophic cardiomyopathy	322 (0.4)	269 (0.3)	591 (0.4)
Pulmonary embolism	984 (1.2)	1232 (1.6)	2216 (1.4)
Venous thromboembolism	3321 (4.2)	5905 (7.5)	9226 (5.9)
Prior bleeding	10 210 (12.9)	7535 (9.6)	17 745 (11.3)
Alcohol use disorder	5478 (6.9)	1403 (1.8)	6881 (4.4)
COPD	5444 (6.9)	2682 (3.4)	8126 (5.2)
Sleep apnoea	4639 (5.9)	1715 (2.2)	6354 (4.0)
Cancer	15 437 (19.6)	17 753 (22.5)	33 190 (21.1)
Dementia	2977 (3.8)	5381 (6.8)	8358 (5.3)
Psychiatric disease	11 394 (14.4)	11 229 (14.3)	22 623 (14.3)
Laboratory values, mean (SD)			
Hb, g/L*	140.5 (19.5)	130.3 (16.5)	135.4 (18.8)
Trom, 10‡/L†	223.5 (79.8)	248.5 (82.6)	236.0 (82.2)
GFR, mL/min/1.73 m^2§	76.4 (22.1)	69.1 (21.0)	72.7 (21.8)
HbA1c, mmol/mol¶	44.2 (11.9)	43.5 (10.8)	43.8 (11.4)
Chol-LDL, mmol/l**	2.6 (0.9)	2.8 (0.9)	2.7 (0.9)
CHA_2DS_2-VASc, mean (SD)††	2.68 (1.77)	4.27 (1.64)	3.47 (1.88)
HAS-BLED, mean (SD)‡‡	2.02 (1.15)	2.25 (0.96)	2.13 (1.06)
Medication, n (%)			
Beta-blocker	34 884 (44.2)	42 344 (53.8)	77 228 (49.0)
Platelet aggregation inhibitor‡	7549 (9.6)	7711 (9.8)	15 260 (9.7)
Statin	28 710 (36.4)	28 306 (36.0)	57 016 (36.2)
Lipid-lowering medication, other	1309 (1.7)	944 (1.2)	2253 (1.4)
Diuretic, all	22 645 (28.7)	33 112 (42.1)	55 757 (35.4)
Diuretic, loop	10 065 (12.8)	15 229 (19.3)	25 294 (16.0)
Diuretic, thiazide	2261 (2.9)	3553 (4.5)	5814 (3.7)

Continued

Table 1 Continued

	Male	Female	All
Diuretic, potassium sparing	1656 (2.1)	1995 (2.5)	3651 (2.3)
Dihydropyridine, CCB	20 936 (26.5)	24 114 (30.6)	45 050 (28.6)
Diltiazem	458 (0.6)	772 (1.0)	1230 (0.8)
Verapamil	334 (0.4)	603 (0.8)	937 (0.6)
Angiotensin receptor blocker	17 876 (22.7)	22 394 (28.4)	40 270 (25.5)
ACE-inhibitor	19 433 (24.6)	17 854 (22.7)	37 287 (23.7)
Insulin	5290 (6.7)	4038 (5.1)	9328 (5.9)
Non-insulin hypoglycaemic drug	13 358 (16.9)	11 525 (14.6)	24 883 (15.8)
Metformin	11 708 (14.8)	9722 (12.3)	21 430 (13.6)
Antidepressant drug	7139 (9.0)	11 506 (14.6)	18 645 (11.8)
Antipsychotic drug	3248 (4.1)	4521 (5.7)	769 (4.9)

*Hb, percentage of cohort with lab value 63.8.
†Trom, percentage of cohort with lab value 63.7.
‡Excluding heparin.
§GFR, percentage of cohort with lab value 62.0.
¶HbA1c, percentage of cohort with lab value 24.1.
**Chol-LDL, percentage of cohort with lab value 30.5.
††CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes, history of stroke/TIA, vascular disease, age 65–74 years, sex category).
‡‡HAS-BLED (hypertension, abnormal renal or liver function, prior stroke, bleeding history, age >65 years, alcohol abuse, concomitant antiplatelet/nonsteroidal anti-inflammatory drugs (no labile INR available, max score 8).
CCB, calcium channel blocker; chol-LDL, low-density lipoprotein cholesterol; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; Hb, haemoglobin; HbA1c, glycated haemoglobin; Trom, thrombocytes.

bleedings, alcohol use disorder, chronic obstructive pulmonary disease, sleep apnoea, cancer, dementia and psychiatric disease). Survival analyses were performed by Kaplan-Meier analysis using a log-rank test. A p<0.05 was considered as a statistically significant finding.

RESULTS

Study cohort and patient characteristics

We identified 157 658 cases (50.1% male) of incident AF that fulfilled the criteria of this study. The mean age of the AF population was 72.9±13.1 years at the time of cohort entry. Women were on average 7.4 years older than men at the time of AF diagnosis (76.6±11.7 years vs 69.2±13.3 years, p<0.001, respectively). online supplemental figure S2 demonstrates the age distribution of men and women at cohort entry. The number of new AF patients per year increased from 16 259 to 22 127 from 2010 to 2017, and the mean age at cohort entry increased from 71.8±13.9 years to 73.7±12.5 years.

At time of cohort entry, three-quarters of the AF patients presented with hypertension, and the other most common comorbidities were hyperlipidaemia (49.8%), coronary artery disease (22.8%), diabetes mellitus (22.5%), heart failure (17.4%), prior stroke or TIA (15.9%) and psychiatric disease (14.3%) (table 1). The average CHA_2DS_2-VASc score was 3.47 (SD 1.88), and the average HAS-BLED score 2.13 (SD 1.06). CHA_2DS_2-VASc scores were ≥2 in 83.6% of patients.

All-cause 1-year mortality

Crude all-cause mortality of the cohort was 11.2% and it was higher in women than in men (12.0% vs 10.4%). The age-specific mortality was lower in women when compared with men in all age categories: 2.7% vs 3.7% (<65 years), 4.9% vs 7.9% (65–74 years), 17.3% vs 18.8% (≥75 years), p<0.001. In the adjusted Poisson regression, overall mortality was lower in women when compared with men throughout the study period (MRR 0.66; 95% CI 0.63 to 0.69). Table 2 and online supplemental figures S3 and S4 depict the 1-year survival by age and sex.

All-cause mortality decreased from 12.9% to 10.6% during the study period, with an adjusted MRR of 0.77 (95% CI 0.73 to 0.82) in cohort entry year 2017 with 2010 as reference. Figure 1A depicts the temporal trend in all-cause mortality by calendar year of AF diagnosis. The age-specific mortality in patients aged 65 years or more decreased when comparing cohort entry years 2010–2017 (65–74 years, 7.9%–6.2%; ≥75 years, 21.5%–16.3%, p<0.001). Whereas in patients aged 20–64 years, mortality remained stable (3.2%–3.4% p=ns).

CV 1-year mortality

Crude 1-year CV mortality was 50% lower in women when compared with men until the age of 75 years: 0.6% vs 1.3% (<65 years) and 1.6% vs 3.1% (65–74 years), p<0.001. Among the elderly (aged ≥75 years), CV mortality was higher in women than in men (10.7% vs 9.7%, p<0.001). In the adjusted Poisson regression, CV mortality was

Table 2 Crude all-cause and cardiovascular (CV) mortality rates in 1-year follow-up by age, sex and CHA_2DS_2-VASc score

	Person-years*	All-cause deaths, n (%)	CV Deaths, n (%)	Mortality rate (per 1000 p-years, 95% CI)	CV mortality rate (per 1000 p-years, 95% CI)
Male	73.462	8235 (10.4)	3852 (4.9)	112.1 (109.7 to 114.6)	52.4 (50.8 to 54.1)
<65 years	25.970	996 (3.7)	345 (1.3)	38.4 (36.0 to 40.8)	13.3 (11.9 to 14.8)
65–74 years	22.703	1 904 (7.9)	743 (3.1)	83.9 (80.1 to 87.7)	32.7 (30.4 to 35.2)
≥75 years	25.790	5335 (18.8)	2 764 (9.7)	206.9 (201.4 to 212.5)	107.2 (103.2 to 111.2)
Female	72.280	9485 (12.0)	5465 (6.9)	131.2 (128.6 to 133.9)	75.6 (73.6 to 77.6)
<65 years	11.578	316 (2.7)	74 (0.6)	27.3 (24.4 to 30.5)	6.4 (5.0 to 8.0)
65–74 years	18.763	951 (4.9)	314 (1.6)	50.7 (47.5 to 54.0)	16.7 (14.9 to 18.7)
≥75 years	41.939	8218 (17.3)	5077 (10.7)	196.0 (191.7 to 200.2)	121.1 (117.7 to 124.4)
CHA_2DS_2-VASc†					
0	8.938	194 (2.1)	36 (0.4)	21.7 (18.8 to 25.0)	4.0 (2.8 to 5.6)
1	16.322	640 (3.8)	136 (0.8)	39.2 (36.2 to 42.4)	8.3 (7.0 to 9.9)
2	23.072	1339 (5.6)	333 (1.4)	58.0 (55.0 to 61.2)	14.4 (12.9 to 16.1)
3	27.821	2400 (8.2)	799 (2.7)	86.3 (82.9 to 89.8)	28.7 (26.8 to 30.8)
4	30.090	3784 (11.6)	1799 (5.5)	125.8 (121.8 to 129.8)	59.8 (57.1 to 62.6)
5	20.298	3861 (16.9)	2297 (10.0)	190.2 (184.3 to 196.3)	113.2 (108.6 to 117.9)
6	12.000	3013 (21.4)	2059 (14.6)	251.1 (242.2 to 260.2)	171.6 (164.3 to 179.2)
7	5.246	1647 (25.8)	1207 (18.9)	314.0 (299.0 to 329.5)	230.1 (217.3 to 243.4)
8	1.635	661 (31.3)	508 (24.0)	404.3 (374.0 to 436.3)	310.7 (284.3 to 338.9)
9	0.320	181 (40.7)	143 (32.1)	565.7 (486.3 to 654.4)	446.9 (376.7 to 526.5)

*1000 years.
†CHA_2DS_2-VASc: (congestive heart failure, hypertension, age ≥75 years, diabetes, history of stroke/transient ischaemic attack, vascular disease, age 65–74 years, sex category).

lower in women when compared with men throughout the study period (MRR 0.53; 95% CI 0.50 to 0.56).

One-year CV mortality decreased from 7.4% to 5.2% over the study period (MRR 0.68; 95% CI 0.63 to 0.74 in cohort entry year 2017 with 2010 as reference). Figure 1B depicts the temporal trend in CV mortality by calendar year of AF diagnosis. Comparing cohort entry years 2010–2017, there was a statistically significant decrease in age-specific 1-year CV mortality within patients aged 65 years or more from 3.4% to 2.2% in patients aged 65–74 years (p<0.001) and 13.5% to 8.7% in patients aged≥75 years (p<0.001). In patients aged 20–64 years, CV mortality remained stable (1.1%–0.9%, p=ns). Table 2 depicts crude all-cause- and CV mortality rates in a 1-year follow-up by age, sex and CHA_2DS_2-VASc scores.

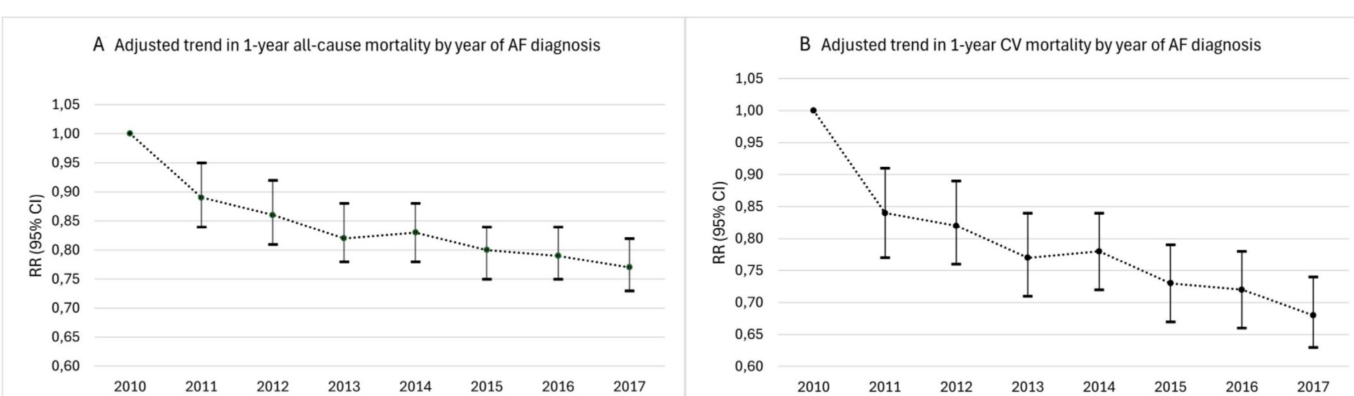
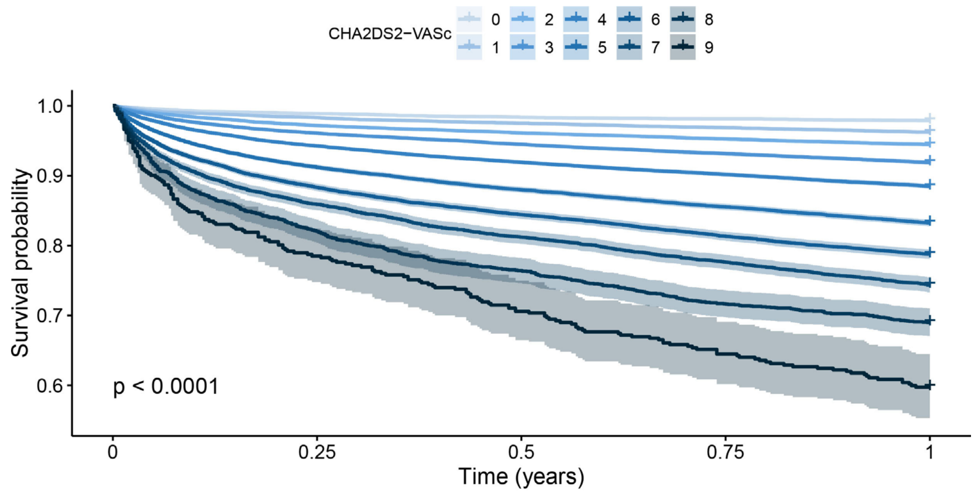


Figure 1 Temporal trends in all-cause- and cardiovascular (CV) mortality during the year following AF diagnosis with mortality rate ratios (RR) from Poisson regression models adjusting for age, sex, CHA_2DS_2-VASc-score and baseline comorbidities, with cohort entry year 2010 as reference. (A) All-cause mortality by cohort entry year with 95% CI; (B) CV mortality by cohort entry year with 95% CI. AF, atrial fibrillation.



Number at risk

CHA2DS2−VASc	0	0.25	0.5	0.75	1
0	9073	8972	8923	8902	8881
1	16721	16439	16305	16199	16090
2	23945	23267	23012	22808	22618
3	29355	28204	27735	27345	26970
4	32559	30686	29928	29360	28804
5	22877	20863	20128	19569	19040
6	14063	12420	11873	11440	11077
7	6377	5478	5178	4951	4742
8	2104	1726	1608	1508	1452
9	442	347	312	285	264

Time (years)

Figure 2 1 year survival by CHA_2DS_2-VASc score.

CHA_2DS_2-VASc and 1-year mortality

CHA_2DS_2-VASc score at cohort entry was associated significantly with mortality during 1-year follow-up after AF diagnosis (p<0.0001). One-year survival was >95% in patients with CHA_2DS_2-VASc scores 0–1 and ≤80.0% in patients with scores from 6 to 9. Figure 2 depicts 1-year survival distribution by CHA_2DS_2-VASc score.

Causes of death after incident AF

Greater differences in crude 1-year mortality from cohort entry years 2010 to 2017 were found within causes of death in cancer (increase from 18.5% to 24.4%), ischaemic heart disease (decrease from 30.7% to 21.6%) and dementia/Alzheimer's disease (increase from 6.2% to 9.9%) (figure 3). However, after adjusted Poisson

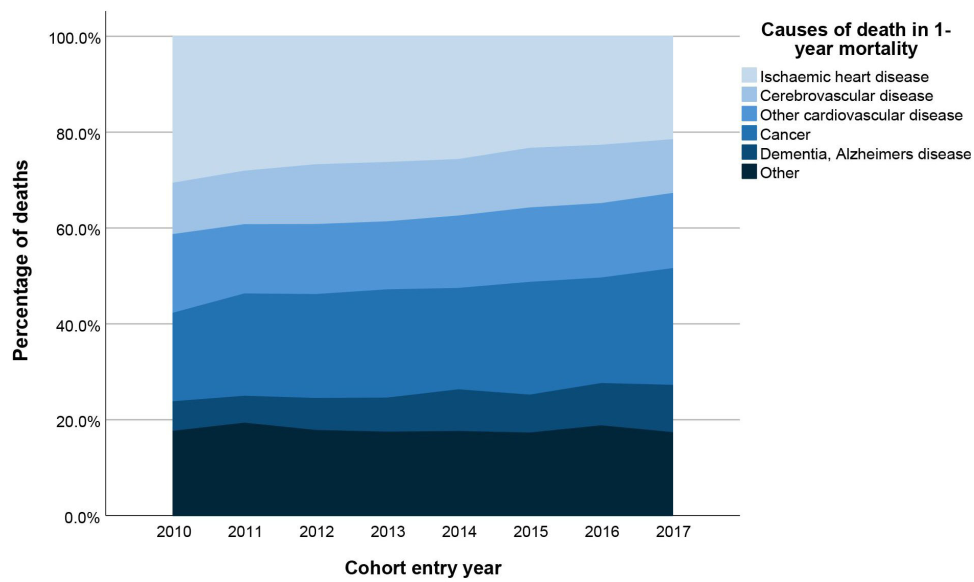


Figure 3 Causes of death in 1 year mortality from cohort entry years 2010 to 2017.

Table 3 Mortality rate ratios with 95% CIs of cause-specific mortality in 1-year follow-up by year of atrial fibrillation diagnosis

	2010	2011	2012	2013	2014	2015	2016	2017
Ischaemic heart disease	Reference	0.83 (0.74–0.92)	0.75 (0.67–0.84)	0.72 (0.63–0.79)	0.70 (0.62–0.78)	0.61 (0.54–0.68)	0.59 (0.53–0.66)	0.51 (0.49–0.62)
Cerebrovascular disease	Reference	0.79 (0.62–1.02)	0.94 (0.74–1.19)	0.96 (0.76–1.22)	1.20 (0.96–1.5)	1.00 (0.80–1.26)	1.18 (0.94–1.47)	1.19 (0.96–1.48)
Other CV disease	Reference	0.80 (0.69–0.93)	0.81 (0.70–0.95)	0.76 (0.65–0.88)	0.82 (0.70–0.95)	0.82 (0.71–0.96)	0.82 (0.71–0.95)	0.84 (0.72–0.97)
Cancer	Reference	1.01 (0.89–1.16)	1.02 (0.90–1.17)	0.98 (0.86–1.12)	0.92 (0.8–1.05)	0.97 (0.85–1.11)	0.90 (0.79–1.03)	0.96 (0.84–1.09)
Dementia, Alzheimer's disease	Reference	0.79 (0.62–1.02)	0.94 (0.74–1.19)	0.96 (0.76–1.22)	1.20 (0.96–1.50)	1.00 (0.80–1.26)	1.18 (0.94–1.47)	1.19 (0.96–1.48)

CV, cardiovascular.

analysis for cause-specific mortality, a temporal trend over the study period was only discovered in ischaemic heart disease and dementia/Alzheimer's disease (MRR 0.51; 95% CI 0.49 to 0.62 and MRR 1.19; 95% CI 0.96 to 1.48, respectively, in 2017 to the reference of 2010). Table 3 depicts the MRRs in cause-specific mortality within 1-year follow-up by year of AF diagnosis.

Ischaemic heart disease was the most common cause of death in crude mortality (25.6% of deaths) within 1 year of AF diagnosis, with no difference between the sexes. Cancer was the second most common cause of death with 21.9% of cases and was found more commonly in men than in women (27.2% vs 17.4%, p<0.001). Deaths due to cerebrovascular disease (11.8%) and dementia and Alzheimer's disease (7.6%) were less common in men than in women (9.6% vs 13.7%, p<0.001 and 5.4% vs 9.6%, p<0.001, respectively). Online supplemental figure S5 depicts causes of death by age and sex.

DISCUSSION

Our study revealed a lower 1-year mortality rate among women of all age groups after incident AF diagnosis when compared with men. Additionally, 1-year CV mortality was 50% lower in women compared with men until the age of 75 years. Over the study period, the overall 1-year mortality as well as the 1-year CV mortality declined. Deaths attributable to ischaemic heart disease decreased, whereas deaths due to dementia and Alzheimer's disease increased during the study period.

In our study, overall mortality was lower in women than in men in all age categories. Similarly, CV mortality was lower in women than men when excluding the oldest cohort (aged ≥75 years). This observation is in line with the Global Burden of Disease study finding that the number of disability-adjusted life-years due to CV diseases is higher in women compared with men after the age of 80 years.[11] In the working-age cohort (20–64 years), the most common cause of death was CV disease in men and cancer in women, as men generally develop CV disease at a younger age.

Numerous studies have confirmed the association between AF and higher mortality rates compared with those without AF.[12] The Framingham Heart Study reported that age-adjusted 5-year mortality in AF had steadily decreased by 25% between 1958–1967 and 1998–2007.[5] Other studies have reported conflicting results, both temporal improvement as well as no trends in overall mortality after AF diagnosis.[6–9] Our study reiterates a decline in both overall and CV 1-year mortality after AF diagnosis. This improvement can be explained by advances in the treatment of hypertension, coronary heart disease, heart failure and diabetes and even more importantly by the clinical implementation of the CHA_2DS_2-VASc score emphasising the role of advancing age and female sex among the elderly as risk factors for thromboembolism, leading to increased use of OAC.[4 13–16] Furthermore, the introduction of direct OACs has most likely further improved stroke prevention in patients with AF, but during our study period warfarin was the most commonly used anticoagulant.[17]

Most AF patients were multimorbid, suffering especially from CV diseases. Unfortunately, AF does not only coexist but also interacts with other conditions. AF and many of its concomitant conditions share mutual risk factors and have a multidirectional impact on each other, with one predisposing to or exacerbating the other.[18 19] CHA_2DS_2-VASc scores were high in our study, similar to scores reported by others.[20 21] The CHA_2DS_2-VASc score is commonly used to evaluate AF patients' risk for stroke and the need for anticoagulation (CHA_2DS_2-VASc ≥1). Furthermore, thromboembolic risk factors also exist outside of the CHA_2DS_2-VASc score, for example, obesity, impaired renal function, dyslipidaemia and obstructive sleep apnoea (OSA).[4 22] For instance, in patients with CHA_2DS_2-VASc score of 0, the presence of OSA increases the risk of stroke by up to 62%.[23] Previous studies report a high prevalence of OSA in patients with AF (varying from 21% to 87%), indicating under-reporting and diagnosing of OSA in our cohort (4.2% prevalence).[24] It is noteworthy that the CHA_2DS_2-VASc score is strongly associated with the overall 1-year survival after initial AF diagnosis, as reported also by others.[25 26] Therefore, treatment of AF patients must include consideration and optimal treatment of all comorbidities and CV risk factors in addition to OAC therapy and AF symptom management, that is, ABC pathway.[4 27]

Study strengths

The FinACAF study population is, to the best of our knowledge, the only nationwide cohort with all AF patients from all levels of care.[1] Previous studies on comorbidities and outcomes of AF patients may have been more prone to selection and information biases with data sources from limited levels of care.[13 27 28] Finland has a comprehensive and validated system of healthcare registers based on individual personal identity numbers that allowed us to gather reliable information from primary, secondary and tertiary care.[29] As a result, the risk of bias from, for instance, having data only on patients hospitalised with AF, the common issue of register-based studies, is minimised. The inclusion of primary care registers and drug prescription/reimbursement data increased the number of AF patients in the FinACAF cohort by 15 783 (9%) during 2012–2018 compared with the hospital discharge register alone.[1] Comprehensive data are needed in targeting preventive measures and healthcare resources effectively in the future.

Study limitations

Our study limitations include a lack of data regarding certain risk factors (such as smoking and obesity) and clinical parameters (ie, ejection fraction). The study suffers from the usual limitations of a register study, in that the data were based on administrative recording, and the entries have taken place in connection with clinical practice. The official guidelines for recording causes of death have not changed during our study period, but increased knowledge in diagnostics, and previous changes in the definitions of causes of death (WHO guidelines) may have reflected on the frequencies of recorded causes of death.[30] We limited the inclusion criteria to patients who were diagnosed with AF from 2010 to 2017. Including patients who were diagnosed in 2018 may have brought additional information from a later year, but since we only had follow-up data up to 31 December 2018 the inclusion of these patients could have caused temporal bias due to their follow-up time being less than a year. A small number of patients (0.17% of the FinACAF study population) who migrated abroad before 1 January 2019 were excluded from the study. Since these patients could migrate, they are also by definition survivors. To ensure that the exclusion of these patients did not cause bias in the results of the study we ran preliminary robustness checks and found that the inclusion of these patients would not change the statistical significance of the results.

Conclusion

In conclusion, our study documented a decrease in 1-year mortality after incident AF diagnosis in Finland as well as a reduction in 1-year CV mortality from 2010 to 2017. Although CV diseases remained the most common cause of death in patients with AF, the percentage of ischaemic heart disease as a cause of death decreased. Importantly, at the time of initial AF diagnosis, the CHA_2DS_2-VASc score was strongly associated with patient survival in addition to the risk of stroke, underlining the importance of comorbidity and CV risk factor treatments as emphasised in recent clinical practice guidelines.[4]

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