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Association Between Relevant Co-morbidities and Dementia in Patients with Atrial Fibrillation—A National Swedish Study

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Abstract

Background.—The risk of dementia is increased in patients with atrial fibrillation (AF).

Objective. To study relevant co-morbidities and incident dementia (vascular dementia, Alzheimer's disease, other dementia and all dementia) in AF patients.

Methods.—All adults ($n = 537,513$) 45 years diagnosed with AF in hospitals in Sweden 1998–2012 were included. Cox regression was used to estimate hazard ratios (HR) with 95% CIs for association between comorbidities, and incident dementia, after adjustment for age, residence place in Sweden, and socio-economic factors.

Results.—Totally 30,332 patients (5.6%) were diagnosed with dementia during the follow-up, with 14,097 men (4.9%) and 16,235 women (6.5%). After adjustments (HRs; 95% CI), hypertension was associated with lower risk of incident dementia (all types) in men (0.79; 0.76–0.82) and women (0.77; 0.74–0.79). Higher risk of dementia was seen in patients with stroke, diabetes, depression and anxiety. Lower risks of dementia were also seen in AF patients with concomitant coronary heart disease and congestive heart failure.

Conclusions.—The findings regarding incident dementia need to be interpreted with great caution, owing to possible “survival bias” or reversed causation. However, the lower associated risks of dementia associated with hypertension could possibly be explained by protective effects of certain antihypertensive drugs.

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Conflict of Interest

The authors have no conflict of interest to disclose.

Keywords

Atrial fibrillation; Dementia; Gender; Hypertension; Depression; Stroke

Introduction

Atrial fibrillation (AF) is the most common arrhythmia worldwide, and is also increasing in the world, and have a great impact on public health (1), also including dementia [Alonso, 2016 #1128

When looking at clinically relevant comorbidities with an increased risk of dementia inpatients with AF, diseases such as stroke [Pendlebury, 2009 #24], diabetes (2,3), and depression (4,5) are important. In contrast, studies on the association between heart diseases and dementia have found some contradictory results, with one meta-analysis suggesting an increased risk of dementia in patients with coronary heart disease (CHD) (6), and another meta-analysis reporting a lower risk of Alzheimer's disease in patients with heart disease in general (7). As regards the association between hypertension and dementia, there are also conflicting findings and views on this. One review emphasized the risk of accelerated atherosclerosis in long-standing hypertension, with subsequent increased risk of cognitive decline and dementia (8). Another review also admitted this association, but also pointed to the fact that, strict blood pressure control also during sleep may have neuroprotective effects (9). Besides, also too low blood pressure in later life with cerebral hypo-perfusion in combination with atherosclerosis may increase the risk of cognitive dysfunction and dementia (8).

In an earlier Swedish study of patients with AF in primary care, prevalent dementia was found to be more common in men and women with congestive heart failure (CHF), stroke, and depression, but less common in women with hypertension (10). However, when studying incident dementia, diabetes and depression were associated with a higher risk in men, while CHF was associated with a lower risk in both men and women, and hypertension, myocardial infarction, and cerebrovascular diseases with a lower risk among women (10). We wanted to see if these results from a smaller study could be replicated in a larger study using national data on AF patients in Sweden.

The aim was to study the association between background clinically relevant co-morbidities and incident dementia (vascular dementia, Alzheimers disease, other dementia and all dementia) in men and women with AF in Sweden.

Methods

Design

The study used individual-level patient data from the National Patient Register (NPR), with data from hospitals, both in-patients and out-patients. National identification numbers were replaced with new unique serial numbers to ensure anonymity. The files were linked to a dataset including data from the Total Population Register and the Swedish Cause of Death Register, which contains individual-level data on age, sex, education, cause of death and

hospital diagnosis for all residents registered in Sweden. Ethical approvals were obtained from regional boards at Karolinska Institutet and the University of Lund.

Study Population

The study included all patients with diagnosed AF, identified by the presence of the ICD-10 code (10th version of the WHO's International Classification of Diseases) for atrial fibrillation (I48) in the National Patient Register (NPR). In total, 537,513 individuals (287,959 men and 5,637 women), aged 45 years or older at the time of AF diagnosis identified in the National Patient Register (NPR) from January 1, 1998, until December 31, 2012, were included in the study.

Outcome Variable

Time from first AF diagnosis to first hospital diagnosis of dementia during 1 January 1998 until 31 December 2012.

Diagnosis of dementia (with the following groups: F00 Alzheimer's disease, F01 Vascular dementia, F02 Other dementia diseases, F03 Unspecified dementia, F10.7A Alcohol-related dementia, G30 Alzheimer).

Patients with dementia diagnoses earlier than first AF diagnoses were excluded.

Co-morbidities

The following clinically relevant co-morbid conditions were identified: hypertension (I10–I15); coronary heart disease (CHD; I20–I25); congestive heart failure (CHF; I50 or I110); cerebrovascular diseases (CVD; I60–I69); obesity (E65–E68); diabetes mellitus (E10–E14); COPD (J40–J47); depression (F32–F34, F38–F39); anxiety disorders (F40–F41); and alcoholism and related disorders (F10 and K70).

Demographic and Socio-economic Variables

The following demographic and socio-economic variables was used in the analysis (defined according to the information in the year of AF diagnosis): variables of educational level, marital status, neighbourhood socioeconomic status, and region of residence in Sweden. Furthermore, sex, age-group, and immigrant status was defined.

Educational level was categorized as 9 years (partial or complete compulsory schooling), 10–12 years (partial or complete secondary schooling) and >12 years (college and/or university studies).

Marital status was classified as married, unmarried, divorced or widowed.

Neighbourhood socioeconomic status (SES) The neighbourhood deprivation index was categorized into four groups: more than one standard deviation (SD) below the mean (low deprivation level or high SES), more than one SD above the mean (high deprivation level or low SES), and within one SD of the mean (moderate SES or moderate deprivation level) used as reference group, and also unknown neighbourhood SES. The neighborhood index was based derived from the following four variables: low educational status (<10 years of

formal education), low income (<50% of the median individual income from all sources), unemployment and receipt of social welfare (11).

Region of residence: Individuals were classified as living in a large city, Southern Sweden, and Northern Sweden.

Sex: males and females.

Age-groups: Individuals were divided into the following age groups 45–54, 55–64, 65–74, 75–84 and 85 years. Individuals younger than 45 years were excluded.

Immigrant status was classified as born in Sweden and other countries.

Statistical Analyses

Analyses were Performed Stratified by Sex

For patients with incident dementia, follow-up analyses were performed by using Cox regression estimating hazard ratios (HRs) with 95% confidence intervals (CIs), using time to the first hospital diagnosis of dementia as the outcome. The regression models were adjusted for the following variables: all socio-demographic factors (educational level, marital status, neighborhood socio-economic status, age, region of Sweden and immigrant status) and all co-morbidities (hypertension, CHD, CHF, stroke, obesity, diabetes, COPD, depression, anxiety and alcoholism and alcohol-related disorders) and anticoagulant treatment. We also performed sensitivity analyses, with excluding individuals <65 years of age, and competing risk analysis with mortality as competing risk.

We also estimated the adjusted population attributable fraction (PAF), or population attributable risk (PAR) in percent for risk factors, as prevalence (%) among cases multiplied by $HR-1/HR$ (12), using adjusted HRs for the different factors. PAF is useful in order to compare the impact of different risk factors on the incidence of the outcome, in this case all dementia diagnoses.

A two-sided p -value of <0.05 was considered statistically significant for variables in the Cox regression. All analyses were performed in SAS.

Results

Characteristics of the entire study population consisting of 537,513 patients with AF stratified by sex (287,959 men and 5,637 women) and into those with a diagnosis of dementia (yes/no) are shown in Table 1 (men and women combined in Supplementary Table 1). Totally 30,332 patients (5.6%) were diagnosed with dementia during the follow-up, with 14,097 men (4.9%) and 16,235 women (6.5%). In the specified groups, in men 3,392 (24.1%) had AD, 3,942 VaD (28.0%) and 6,673 (48.0%) other types of dementia, and in women 4,021 (24.8%) had AD, 3,670 (22.6%) VaD and 8,544 (52.6%) other types of dementia. The median follow-up time was 4 years and the mean follow-up time was 4.8 years (Supplementary Table 2). Total number of person-years were 2571578 (1433236 for men and 1138342 for women).

The risks of a first hospital diagnosis for dementia for men, also categorized according to type of dementia, are shown in Table 2. For men hypertension and COPD were significantly associated with lower dementia risk regarding all dementia types, and depression with a higher corresponding risk. A lower risk of dementia was found for CHD for dementia in general, and the subgroup of other types; for congestive heart failure for dementia in general, as well as for the subgroups of AD and other types of dementia; for obesity for dementia in general, and in the subgroups of AD and VaD; and for cerebrovascular diseases for the subgroup of AD. A higher risk of dementia was found for cerebrovascular disease for dementia in general, as well as for the subgroups of VaD and other types; for diabetes for the subgroup of VaD; for anxiety for dementia in general and for the subgroup of other types; and for alcohol-related diseases for dementia in general, and for the subgroups of VaD and other types.

The risks of a first hospital diagnosis for dementia for women are shown in Table 3. For women hypertension, obesity and COPD were significantly associated with a lower risk of incident dementia among all types, while depression was associated with a higher risk. A lower risk of dementia was found for CHD for dementia in general, and in the subgroup of other types; for congestive heart failure for dementia in general, and the subgroups of AD and other types; for cerebrovascular diseases for the subgroup of AD. A higher risk of dementia was found for cerebrovascular diseases for dementia in general and the subgroup of VaD; for diabetes for all dementia and the subgroup of VaD; for anxiety for dementia in general and the subgroup of VaD; and for alcohol-related diseases for dementia in general and the subgroups of VaD and other types.

Competing risk analyses for mortality showed similar results as the main analyses (Supplementary Tables 3 and 4). For men, the HRs for CHD and CHF were significantly lower for all dementia subgroups. For cerebrovascular diseases, the HR for AD was non-significant and, for alcoholism, the HR was significantly higher for AD. For women, the HRs for CHD were significantly lower for all dementia subgroups and, for cerebrovascular diseases, the HR was significantly lower for other dementia. For diabetes and anxiety, the HR was non-significant for VaD and, for alcoholism, the HR was significantly higher for AD.

We also performed sensitivity analyses, with excluding men and women <65 years of age (Supplementary Tables 5–7), with very similar results as in the main analyses. For men, CHD showed statistically significant result for AD, HR 0.89 (95% CI 0.83–0.96), and CHF for VaD, HR 0.91 (95% CI 0.85–0.98), while obesity neither showed statistical significance for AD, HR 0.55 (95% CI 0.31–1.00), nor for VaD HR 0.71 (95% CI 0.45–1.14). For women, CHD showed statistically significant result for AD, HR 0.92 (95% CI 0.86–0.99), and anxiety for other dementia, HR 1.15 (95% CI 1.02–1.29), while obesity did not show statistical significance for other dementia, HR 0.75 (95% CI 0.54–1.05).

We also calculated population attributable fractions (PAF; Supplementary Table 8). For cerebrovascular diseases, PAF was 10.4% (95% CI 9.4 to 11.4) in men and 2.5% (95% CI 1.6 to 3.7) in women. For hypertension, negative PAFs were found, i.e. –9.6% (95% CI –11.4 to –7.9) in men and –11.7% (–13.7 to –10.4) in women, as well as for congestive

heart failure, -9.5% (-11.4 to -7.7) in men and -11.4 (95% CI -12.7 to -9.5) in women. For other disorders PAFs were low (for alcohol-related disorders, 2.0% for men and 0.6% for women).

Discussion

The main finding of this study in patients with AF was that hypertension, congestive heart failure, obesity and COPD were associated with a lower risk of incident dementia and that cerebrovascular diseases and depression were associated with a higher risk of dementia.

Besides, CHD was associated with a lower risk of the group of other causes of dementia, and alcohol-related diseases and anxiety were associated with a higher risk of some subgroups of dementia.

Compared with an earlier study of AF patients in Swedish primary care, we found both similarities and differences (10), which is not surprising considering the differences data sources. There might be differences between AF patients identified in the different cohorts, with primary care patients probably older but with less severe complications or co-morbidities.

Hypertension was negatively associated with prevalent and incident dementia among women in that study, but with incident dementia in both men and women in the present. Regarding the lower risk in patients with diagnosed hypertension, this could possibly be due to a positive effect by antihypertensive drugs, in line with conclusions in a review from The Swedish Council on Health Technology Assessment in Health Care (SBU), i.e. that a good control of blood pressure in middle age reduces the risk of dementia, and also that antihypertensive drug treatment reduces the risk of developing stroke-related dementia (13). In earlier articles from a cohort of patients with AF in primary care, use of 3–4 antihypertensive drugs was associated with a lower dementia risk, and more specifically the combination of a RAAS-blocker and a thiazide was significantly associated with lower dementia risk (10).

Myocardial infarction was negatively associated with incident dementia in women in the primary care study (10), but in the present study with incident dementia in both men and women, however not with AD and VaD. In the primary care study CHF was positively associated with prevalent dementia but negatively with incident dementia among men and women, but in the present study negatively with incident dementia in both men and women. Furthermore, the lower risk of dementia associated with heart diseases (CHD and congestive heart disease) in our study, could also be an effect of effective treatment with antihypertensive drugs and statins. Another explanation to the effect in AF patients with other concomitant heart diseases, especially congestive heart failure, could be the higher mortality (14), i.e. patients die before developing dementia. As mentioned earlier, contradictory results are found in two earlier meta-analysis, with one finding heart disease to be associated with a lower risk of AD (7), and another study reporting CHD to be associated with an increased risk of dementia (6). However, we also performed a sensitivity analysis using competing risks for mortality where we found similar results as in the main analysis.

However, the HRs were lower for both men and women and for CHD and CHF for all dementia subgroups.

As regards cerebrovascular diseases these are strongly associated with dementia (15), and regarded as the most important risk factor for dementia among AF patients. In the primary care study was found that stroke was associated with a higher risk of prevalent dementia among men in all ages and women <75 years of age, but however associated with lower risk of incident dementia among women (10). In the present study we also found cerebrovascular diseases and to be associated with an increased risk of especially VaD, but a lower risk of AD. The lower risk for AD for cerebrovascular diseases in men and women could be due to difficulties in classification, or that VaD develops before AD possibly do. Besides, the higher mortality in AF patients with cerebrovascular diseases (16), is another probable explanation, introducing a risk of survival bias. The discrepancy may be due to that that patients with cerebrovascular diseases cared for in primary care are not always diagnosed for dementia even if symptoms may be at hand. Whatever the reason, this must be taken in consideration when studying risk of dementia in registers.

Regarding diabetes, this has been to be associated to dementia (2,3). In the primary care study an increased risk of incident dementia was found (10), while in the present study we found a moderately increased risk for VaD for both men and women. Thus, the results seem to be what could be expected, even if a survival bias could be present. People with diabetes do have an increased mortality compared to people without diabetes, but the mortality gap seems to have narrowed during the last decades (17).

For the psychiatric diagnoses of depression and anxiety, women more often develop this mental disorder, but possibly men with depression could be affected to a larger degree. In the primary care study depression was associated with prevalent dementia among both men and women and with incident dementia only among men (10). In the present study, however, depression was associated with incident dementia among both men and women. We have earlier found depression to be associated with increased mortality among men with AF, but not among women (18). As dementia develop over many years, the direction between especially depression and dementia may go in both directions (5), i.e. a slowly develop dementia may cause depression, as well as depression could be a risk factor in itself for dementia (19). As regards anxiety, no association was found in the primary care study, while in the present study an overall moderately increased risk was found among both men and women. As for depression, a developing dementia could be expected to cause anxiety. The association between alcohol-related disorders and dementia is also worth to comment. Many articles have been published on the possible relation between alcohol intake and development of dementia. A systematic review of earlier systematic reviews concluded, that the review “indicates that light to moderate alcohol consumption protects from Alzheimer’s disease and dementia” (20), even if alcohol abuse seems to be associated with an increased risk of dementia (21). Regarding the risk of alcohol-related dementia, an Australian study found this to be the most common type among individuals younger than 65 years of age (22). In general, alcohol-related dementia accounted for 1.4% of all dementia cases in Australia (23). However, alcohol abuse is also associated with an increased mortality, with

great risk of survival bias (21). Even if we found a doubled risk of dementia associated with alcohol-related disorders, the PAFs were low.

Regarding COPD we found this to be overall associated with a lower risk of dementia. Earlier studies have found an association between COPD and cognitive dysfunction, even if there are some contradictive results (24), and patients in nursing homes with COPD often have cognitive dysfunction (25). However, COPD is associated with an increased risk of CHF in general (26), and also with AF specifically (27). Thus, the lower risk is most likely to be influenced by survival bias.

There are several limitations of this study. This is an observation study that only can show associations and no causal findings. The findings may have been subject to bias, especially to survival bias (28), even if the sensitivity analyses with competing risk showed similar results as the main analysis. Unfortunately, we were unable to find a validation of AF diagnoses in Sweden. However, Norway has a health care system that is similar to Sweden and the specificity of an AF diagnosis in Norway was 99.7% (29).

We used incident dementia in the present study, and the results differ when assessing results on incident and prevalent dementia. As time is of importance when studying incident dementia, setting the dementia diagnosis later in the course could affect the results. We don't know the validity of the dementia diagnoses, and there might be miss-classification into the different dementia subgroups. However, the Swedish in-patient register (hospital diagnoses) has been shown to have a high validity (30).

Diagnosis of obesity is most likely underreported, and this diagnosis is seldom set in patient records. Besides, patients with hypertension and diabetes are most often receiving their care in primary health care, why the rates could be under-reported in our study. However, as diagnoses are from in-and out-patients in hospitals, hypertension and diabetes could be expected to be reported in dementia patients, why the risk rather could be expected to be high in our results. Further more we did not have access to life-style factors. However, to some extent socio-economic factors both on an individual and neighborhood level do reflect lifestyle factors and their impact on morbidity and mortality (31), including also dementia (32,33). All these mentioned factors could have affected the results. A major strength of this study was that we were able to link clinical data from individual EPRs to data from national demographic and socioeconomic registers with less than 1% of information missing. In conclusion, in this national study of AF patients, we found hypertension to be associated with a lower dementia risk, probably due to a good antihypertensive treatment, and it is warranted that further studies analyze the association between different antihypertensive compounds and dementia. The association between heart diseases and decreased risk of dementia could be influenced by survival bias, especially in patients with CHF. A higher risk of dementia in patients with especially cerebrovascular diseases is to be expected, but the risk we found could be underestimated owing to survival bias and that diagnoses probably are not set in all cases. The risk of dementia in patients with diabetes and also depression are in earlier studies. However, some of the results must be interpreted with some caution, especially owing to survival bias, but also to problems in classifying the dementia type, or even setting a diagnosis in stroke patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights

- Dementia in patients with atrial fibrillation was associated with stroke, diabetes, depression and anxiety
- A lower risk of dementia was found in patients with atrial fibrillation and hypertension
- Presence of heart diseases was associated with a lower risk of dementia in patients with atrial fibrillation, possibly due to a higher mortality risk

Table 1. Baseline characteristics for patients aged 45 years with diagnoses of AF ($N=537513$), and with or without dementia in Sweden

Characteristic	Men ($n = 287959$)					Women ($n = 249554$)				
	No dementia $n = 273862$		Dementia $n = 14097$		p	No dementia $n = 233319$		Dementia $n = 16235$		p
	Numbers	%	Numbers	%		Numbers	%	Numbers	%	
Mortality	143665	52.5	11878	84.3	<0.001	141268	60.5	13770	84.8	<0.001
Age groups (years)					<0.001					<0.001
45–54	18517	6.8	75	0.5		6120	2.6	32	0.2	
55–64	47740	17.4	717	5.1		20465	8.8	351	2.2	
65–74	79686	29.1	3594	25.5		50093	21.5	2504	15.4	
75–79	45362	16.6	3496	24.8		40338	17.3	3583	22.1	
80–84	41121	15.0	3438	24.4		47076	20.2	4575	28.2	
85	41436	15.1	2777	19.7		69227	29.7	5190	32.0	
Educational level					<0.001					<0.001
Compulsory schooling	122078	44.6	6988	49.6		123163	52.8	9443	58.2	
Secondary schooling	94042	34.3	4463	31.7		66360	28.4	4257	26.2	
College and/or university studies	57742	21.1	2646	18.8		43796	18.8	2535	15.6	
Marital status					<0.001					<0.001
Married	178153	65.1	9293	65.9		99758	42.8	5532	34.1	
Unmarried	28176	10.3	915	6.5		13982	6.0	859	5.3	
Divorced	35542	13.0	1633	11.6		28166	12.1	1877	11.6	
Widowed	31991	11.7	2256	16.0		91413	39.2	7967	49.1	
Region of residence					0.1506					<0.001
Large cities	144895	52.9	7653	54.3		126796	54.3	9409	58.0	
Southern Sweden	87158	31.8	4226	30.0		72401	31.0	4424	27.2	
Northern Sweden	41809	15.3	2218	15.7		34122	14.6	2402	14.8	
Immigrant status					<0.001					0.0541
Born in Sweden	248186	90.6	12947	91.8		207779	89.1	14537	89.5	
Foreign Born	25676	9.4	1150	8.2		25540	10.9	1698	10.5	
Neighborhood deprivation					<0.001					<0.001
Low	34800	12.7	1722	12.2		24354	10.4	1713	10.6	

Characteristic	Men (<i>n</i> = 287959)					Women (<i>n</i> = 249554)				
	No dementia <i>n</i> = 273862		Dementia <i>n</i> = 14097		<i>p</i>	No dementia <i>n</i> = 233319		Dementia <i>n</i> = 16235		<i>p</i>
	Numbers	%	Numbers	%		Numbers	%	Numbers	%	
Middle	134552	49.1	6544	46.4		111104	47.6	7160	44.1	
High	35257	12.9	1775	12.6		33684	14.4	2031	12.5	
Unknown	69253	25.3	4056	28.8		64177	27.5	5331	32.8	
Hospital Diagnoses										
Hypertension	114409	41.8	5082	36.1	<0.001	103368	44.3	6344	39.1	<0.001
Coronary heart disease	98003	35.8	5278	37.4	<0.001	69936	30.0	5014	30.9	0.0145
Congestive heart failure	105199	38.4	5692	40.4	<0.001	92230	39.5	6544	40.3	0.0499
Cerebrovascular diseases	64431	23.5	5239	37.2	<0.001	65967	28.3	5557	34.2	<0.001
Obesity	5360	2.0	77	0.5	<0.001	4122	1.8	81	0.5	<0.001
Diabetes mellitus	46977	17.2	2414	17.1	0.9282	33943	14.5	2185	13.5	<0.001
COPD	31122	11.4	1383	9.8	<0.001	27910	12.0	1476	9.1	<0.001
Depression	8979	3.3	988	7.0	<0.001	9835	4.2	1251	7.7	<0.001
Anxiety	6011	2.2	408	2.9	<0.001	7426	3.2	695	4.3	<0.001
Alcoholism and related disorders	11317	4.1	630	4.5	0.0506	2335	1.0	200	1.2	0.0045

Cox regression models (with hazard ratios (HRs) and 95% confidence interval (CI)) for incident hospital diagnosis of dementia among men aged 45 years with diagnoses of AF in Sweden; patients with an earlier known hospital episode of dementia before AF diagnosis excluded

Table 2.

	Alzheimer's disease (<i>n</i> = 3,392)			Vascular dementia (<i>n</i> = 3,942)			Other dementia (<i>n</i> = 6,673)			All dementia (<i>n</i> = 14,097)		
	HR	95% CI		HR	95% CI		HR	95% CI		HR	95% CI	
Hospital Diagnoses												
Hypertension (ref. No)	0.77	0.72	0.83	0.90	0.84	0.96	0.73	0.70	0.77	0.79	0.76	0.82
Coronary heart disease (ref. No)	0.93	0.86	1.00	1.01	0.95	1.08	0.82	0.78	0.86	0.90	0.86	0.93
Congestive heart failure (ref. No)	0.72	0.67	0.77	0.94	0.88	1.00	0.78	0.75	0.82	0.81	0.78	0.84
Cerebrovascular diseases (ref. No)	0.91	0.85	0.99	2.57	2.41	2.74	1.15	1.10	1.22	1.39	1.34	1.44
Obesity (ref. No)	0.56	0.34	0.92	0.63	0.42	0.95	0.74	0.53	1.04	0.66	0.53	0.83
Diabetes mellitus (ref. No)	0.97	0.88	1.07	1.34	1.24	1.45	1.02	0.96	1.10	1.10	1.05	1.15
COPD (ref. No)	0.81	0.72	0.91	0.84	0.75	0.93	0.82	0.76	0.89	0.82	0.78	0.87
Depression (ref. No)	2.03	1.75	2.36	2.69	2.39	3.03	2.00	1.80	2.22	2.21	2.06	2.36
Anxiety (ref. No)	1.07	0.85	1.35	1.05	0.86	1.28	1.36	1.18	1.58	1.20	1.08	1.33
Alcoholism and related disorders (ref. No)	0.92	0.73	1.16	1.42	1.20	1.67	2.63	2.35	2.94	1.80	1.65	1.96

Ref. No. Denotes that the actual condition not being present is the reference group.

Cox regression models (with hazard ratios (HRs) and 95% confidence interval (CI)) for incident hospital diagnosis of dementia among women aged 45 years with diagnoses of AF in Sweden; patients with an earlier known hospital episode of dementia before AF diagnosis excluded

Table 3.

	Alzheimer's disease (<i>n</i> = 4,021)			Vascular dementia (<i>n</i> = 3,670)			Other dementia (<i>n</i> = 8,544)			All dementia (<i>n</i> = 16,235)		
	HR	95% CI		HR	95% CI		HR	95% CI		HR	95% CI	
Hospital Diagnoses												
Hypertension (ref. No)	0.80	0.75	0.85	0.86	0.80	0.92	0.71	0.68	0.75	0.77	0.74	0.79
Coronary heart disease (ref. No)	0.94	0.88	1.01	1.01	0.94	1.08	0.84	0.80	0.88	0.90	0.87	0.93
Congestive heart failure (ref. No)	0.73	0.69	0.79	0.87	0.82	0.94	0.77	0.74	0.81	0.78	0.76	0.81
Cerebrovascular diseases (ref. No)	0.74	0.69	0.79	1.92	1.80	2.05	0.99	0.94	1.04	1.08	1.05	1.12
Obesity (ref. No)	0.43	0.27	0.68	0.45	0.28	0.73	0.73	0.54	0.98	0.57	0.45	0.71
Diabetes mellitus (ref. No)	0.87	0.79	0.96	1.20	1.10	1.31	0.99	0.92	1.05	1.00	0.96	1.05
COPD (ref. No)	0.78	0.70	0.87	0.87	0.78	0.97	0.82	0.76	0.89	0.82	0.78	0.87
Depression (ref. No)	1.72	1.51	1.95	2.24	2.00	2.52	1.72	1.58	1.88	1.84	1.73	1.96
Anxiety (ref. No)	1.06	0.89	1.25	1.30	1.12	1.51	1.12	0.99	1.26	1.15	1.06	1.25
Alcoholism and related disorders (ref. No)	1.27	0.92	1.75	2.02	1.54	2.65	2.39	1.95	2.92	1.97	1.70	2.27

Ref. No. Denotes that the actual condition not being present is the reference group.