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Published in:
European Heart Journal - Quality of Care and Clinical Outcomes

DOI (link to publication from Publisher):
10.1093/ehjqcco/qcac071

Publication date:
2023

Document Version
Accepted author manuscript, peer reviewed version

Social determinants of health and recurrence of atrial fibrillation after catheter ablation. A Danish nationwide cohort study.

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Word count:
Abstract: 249
Main text: 2732
Tables: 4
Figures: 1

Abstract

Aim: To examine the associations between three social determinants of health (SDOH) and recurrence of AF after ablation.

Methods: We selected patients who underwent a first ablation after an incident hospital diagnosis of AF between 2005 and 2018 from the entire Danish population. Educational attainment, family income, and whether the patient was living alone were assessed at the time of ablation. We used cause-specific proportional hazard models to estimate hazard ratios (HR) with 95% CI adjusted for age and sex. In secondary analyses, we adjusted for comorbidities, antiarrhythmic medication, and prior electrical cardioversion.

Results: We selected 9,728 patients (mean age 61 years, 70% men), and 5,881 patients had AF recurrence over an average of 1.37 years after ablation (recurrence rate 325.7 (95%CI 317.6-334.2) per 1000 person-years). Lower education (HR 1.09 [1.02-1.17] and 1.07 [1.01-1.14] for lower and medium vs. higher), lower income (HR 1.14 [1.06-1.22] and 1.09 [1.03-1.17] for lower and medium vs. higher), and living alone (HR 1.07 [1.00-1.13]) were associated with increased rates of recurrence of AF. We found no evidence of interaction between sex or prior HF with SDOH. The association between family income and AF recurrence was stronger among patients <65 years compared to those aged ≥65 years. The associations between SDOH and AF recurrence did not persist in the multivariable model.

Conclusions: AF was more likely to recur among patients with lower educational attainment, lower family income, or those living alone. Multidisciplinary efforts are needed to reduce socioeconomic inequity in the effect of ablation.

Key words: Atrial fibrillation, ablation, income, education, living alone

Introduction

Atrial fibrillation (AF) is the most frequently encountered arrhythmia, and both the incidence and prevalence are increasing globally.[1,2] AF patients may lose up to two years of expected lifetime compared to AF-free individuals over 10 years after diagnosis.[3] Restoration and maintenance of sinus rhythm are important components of the AF management strategy, hence the use of catheter ablation has increased considerably over the past decade. Catheter ablation is associated with improved quality of life, reduced risk of AF recurrence, and lower healthcare utilization.[4,5]

About 30% to 45% of patients experience AF recurrence one year after catheter ablation.[6,7] Risk factors for AF recurrence include age, comorbidities, left atrial enlargement, and type of AF (persistent and long standing persistent); however, robust prediction models are still needed.[8] Socioeconomic determinants of health (SDOH), including educational attainment, family income, and cohabitation status, are associated with use of catheter ablation for AF.[9-12] SDOH also correlate with cardiovascular risk factors associated with AF recurrence, such as hypertension, obesity, and lifestyle.[13-15] No study has examined the association between SDOH and recurrence of AF after catheter ablation, and current international guidelines for catheter ablation do not address the impact of SDOH.[16] Use of SDOH as markers for risk of AF recurrence after ablation may be relevant to guide shared decision-making, optimize preventive efforts, and address healthcare service needs.

Our objective was to examine the association between SDOH and recurrence of AF after catheter ablation in the Danish healthcare system.

Methods

Data sources

The data from this study originated from the four following nationwide registries:

The Danish National Patient Registry contained nationwide prospectively registered information on inpatients, and also outpatients from after 1995.[17] Individual-level information was available on admission and discharge, surgical procedures performed, primary diagnosis and secondary diagnoses at discharge. Coding of diagnoses followed the Danish version of the International Classification of Diseases 8th Revision (ICD-8) before 1994 and the 10th revision (ICD-10) from 1994 and onwards.

The Danish National Prescription Registry provided individual-level data on all dispensed prescriptions since 1994.[18] Coding of medications followed the Anatomical Therapeutic Chemical Classification System.

Statistics Denmark provided information on family income, highest level of education, and whether the patient was living alone. Statistics Denmark holds registers on the variables of SDOH. The register of the population's education collects information regarding completed education for each individual in the population The register is based on an assessment of the series of educations that each individual has completed at a given time.[19] The registry includes automatically all individuals attending an education in Denmark. The registry of income includes anyone who has submitted a tax return to the Tax Administration. Accordingly, the registry includes anyone who is economically active.[20] Information on whether patients were living alone originates from a registry that includes all individuals residing in Denmark with information on family and household relations.

The Danish Civil Registration System provided individual-level information on sex, date of birth, vital statistics, and migration.[21] Assignment of a unique 10-digit Civil Registration number to

all Danish citizens enabled unambiguous linkages of data across registries. Supplemental Table 1 shows definition of diseases and medication.

Design and study population

We conducted a nationwide registry-based cohort study of all patients undergoing a first catheter ablation for AF. The study population included all Danish patients aged 35 years or older who underwent a first-time ablation for AF (procedure code: BFFB04) between 2005 and 2018. Baseline was the day of the registered ablation procedure. Follow-up of patients for recurrence was up to and including 2018. We excluded residents in Greenland, patients without a registered diagnosis of AF prior to ablation, patients not living in Denmark for at least five years before the ablation procedure, and patients with missing information on at least one of the three SDOH parameters.

Social determinants of health

Statistics Denmark provided individual-level information on three measures of SDOH, including family income, education, and whether a patient was living alone prior to the day of the catheter ablation. If data on one or more SDOH parameters were unavailable for the year of ablation, we attempted to identify the information for up to three years back. The three SDOHs reflected different aspects of social status, including acquisition of knowledge, non-material resources, material resources, and social support from both marital and non-marital relationships.

Total family income was the sum of business income, public transfers, private pensions, interest income, other property income, and other non-classifiable income that could be attributed directly to the individual in the family. The amounts were before taxes for all persons belonging to the same family. We categorized income into tertile groups (lower, medium, and higher) by calendar year of the ablation procedure to account for potential inflation.

Highest educational attainment was categorized into lower, medium, and higher groups. as per the International Standard Classification of Education (ISCED). The lower group included early childhood, primary education, and lower secondary education (ISCED 0-2). The medium group included general upper secondary education and vocational upper secondary education (ISCED 3). The higher group included short-cycle tertiary, medium-length tertiary, bachelor's-level educations or equivalent, second-cycle, Masters-level or equivalent, and PhD level (ISCED 5-8). ISCED 4 does not exist in Denmark.

Patients living alone were compared to patients not living alone, i.e., couples with registered partnership and cohabiting couple.

Recurrence of AF

The definition of AF recurrence followed a previous study that originated from the Danish nationwide registries.[7] Recurrent AF was defined as a composite of hospital admission (one or more days) with AF as the primary diagnosis, cardioversion for AF, a second ablation for AF, or a redeemed prescription of an antiarrhythmic drug (amiodarone, dronedarone, or class 1C anti-arrhythmic medication) (Supplemental Table 2). We applied a blanking period of 90 days after the baseline ablation to account for early recurrence.[7,16]

In a sensitivity analysis, we examined an alternative definition of recurrence as composite of an electrical cardioversion or a recurrent ablation for AF.

Covariates

Covariates included age, sex, prior electrical cardioversion, years since diagnosis of AF, and use of antiarrhythmic drugs, and history of heart failure, myocardial infarction, valvular heart disease, stroke, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, chronic kidney

disease, and cancer (Supplemental Table 1). History of comorbidity was assessed on the day of ablation or before, with no time window. Antiarrhythmic drug use was defined as at least one prescription within six months before the ablation procedure (Supplemental Table 1).

Statistical analyses

Patients were followed from the day of the first ablation until the date of first AF recurrence, death, emigration, or end of follow-up, whichever came first. Our interest was the etiological association between SDOH and recurrence of AF and not to predict recurrence before dying. Therefore, we fitted cause-specific proportional hazard models, which is equivalent to fitting a Cox model after censoring the competing events (death and emigration). We estimated cause-specific hazard ratios (HR) with 95% confidence intervals (95%CI). We assessed the proportional hazards assumption by using graphs of the Schoenfeld residuals and we found no violation of the assumption.

We applied two models. Model 1 was the main analysis and we adjusted for age and sex. Model 2 was a secondary analysis and included age, sex, any prior electrical cardioversion, years since AF diagnosis, use of antiarrhythmic drugs before the ablation, and history of comorbidities (Table 1). We performed stratified analyses by age (<65 vs. ≥65 years), sex, and history of HF; we tested for statistical interaction between each variable and SDOH by including interaction terms in Model 1. Data suggest that an ablation strategy among AF patients with HF is associated with a better prognosis than medical therapy.[22]

We examined mediation according to the Judd & Kenny's Difference of Coefficients Approach.[23] We added each covariate listed in Table 1 to Model 1 one by one. We then estimated the indirect effect by subtracting the partial regression coefficient for SDOH obtained from the resulting model from the regression coefficient for SDOH obtained from Model 1. The indirect effect is interpreted as the change in AF recurrence rate associated with SDOH that is mediated by

the corresponding covariate. We calculated the associated 95%CI by using percentile bootstrap resampling with 500 repetitions. When the 95%CI did not include zero, indicating evidence that the indirect effect is different from zero, we further calculated the proportion of the association between SDOH and AF recurrence that is mediated by the covariate.

Analyses were performed in Stata (StataCorp. 2019: Release 17.0, College Station, TX: StataCorp LLC).

Ethics

The Danish Health Data Authority, Statistics Denmark, and the Danish Data Protection Agency approved this study. Registry-based studies do not require approval from an ethics committee according to Danish law.

Results

Study participants

We identified 9,728 patients undergoing ablation between 2005 and 2018 (Figure 1). On the day of the ablation procedure, the mean age was 61.3 years (SD 9.6), 70% of the patients were male, and the median time from the first AF diagnosis to the first ablation was 2.6 (Q1-Q3: 0.9-6.2) years (Table 1). The proportion of patients with history of comorbidities increased with decreasing levels of education attainment and family income, and was higher among patients living alone (Supplemental Tables 5-7). The mean age on day of ablation was lower in those with higher level of family income (Supplemental Table 6). The proportion of male patients increased by level of family income and was highest for patients with lowest for education level (Supplemental Table 7). Patients with lower socioeconomic status had the highest prevalence of comorbidities (Supplemental Tables 8-19).

Association between SDOH and AF recurrence following ablation

The median follow-up time was 1.37 years (Q1-Q3: 0.43-6.27), and the longest follow-up was 13.9 years. During follow-up, 5,881 patients had recurrence of AF, for a recurrence rate of 325.7 (95%CI 317.6-334.2) per 1000 person-years.

The recurrence rate was 343.7 (95%CI 325.6-362.9) per 1000 person-years among patients with lower education, 334.0 (95% CI 321.6-347.0) for patients in the medium group, and 304.6 (95% CI 291.2-318.5) in the higher group. The corresponding recurrence rate for income were 365.7 (95%CI 350.1-382.0) for lower income, 331.0 (95%CI 316.7-345.9) for medium income, and 287.4 (95%CI 274.7-300.7) for higher income. The recurrence rate was 360.2 (95%CI 341.9-379.4) for patients living alone and 316.2 (95%CI 307.0-325.6) for patients not living alone.

In the age- and sex-adjusted cause-specific Cox regression models, lower educational attainment, lower income, and living alone were associated with higher rates of recurrence of AF (Table 2). However, there was no evidence of associations after adjustment for potential confounders and mediators (Model 2, Table 2).

Subgroup analyses

In sex-specific analyses, we found no evidence of interaction by sex (Table 3). When stratifying by age group, we found that lower family income was associated with higher hazards rates of recurrence among the younger patients (Table 3). Finally, we found no statistical interaction by history of HF (Table 4).

Sensitivity analysis

When we did not consider hospital admission for AF as part of the definition of recurrence, 5,519 patients had recurrence of AF, for a recurrence rate of 275.4 (95%CI 268.3-282.8) per 1000 person-

years. The recurrence rate was 287.6 (95% CI 272.0-304.2) per 1000 person-years among patients with lower education, 285.0 (95% CI 274.1-296.4) for patients in the medium group, and 256.0 (95% CI 244.4-268.1) in the higher group. The recurrence rate for income were 300.8 (95% CI 287.5-314.6) for lower income, 283.3 (95%CI 270.7-296.4) for medium income, and 246.1 (95%CI 234.9-257.9) for higher income. The recurrence rate was 297.6 (95% CI 282.0-314.1) for patients living alone and 269.1 (95%CI 261.1-277.4) for patients not living alone.

In the age- and sex-adjusted cause-specific Cox regression models, lower educational attainment and lower income were associated with higher rates of recurrence of AF (Supplemental Table 20). Our analysis of living alone suggested a higher rate of recurrence associated with patients living alone, but we found no statistical evidence of an association (HR 1.05, 95%CI 0.99-1.12, p=0.12). Similar to our main analysis, there was no evidence of associations after adjustment for potential confounders and mediators (Supplemental Table 20).

Mediation analyses

For the association between educational attainment and AF recurrence, there was evidence that prior electrical cardioversion, use of antiarrhythmic drugs, heart failure, myocardial infarction, diabetes, hypertension, and chronic obstructive pulmonary disease were potential mediators (Supplemental Table 21). For the association between income level and AF recurrence, we found evidence that prior electrical cardioversion, heart failure, myocardial infarction, diabetes, hypertension, chronic obstructive pulmonary disease, and cancer were potential mediators (Supplemental Table 22). For the association between living alone and AF recurrence, we found statistical evidence that heart failure, myocardial infarction, diabetes, hypertension, chronic obstructive pulmonary disease, and cancer were mediators (Supplemental Table 23). Hypertension, heart failure, and chronic obstructive pulmonary disease consistently gave the largest proportions mediated for the three associations, ranging between 10.5% and 44.4%.

Discussion

In this nationwide cohort study of patients undergoing first-time catheter ablation for AF, we found that lower level of education, lower family income, and living alone were associated with higher hazard rates of recurrence of AF. We found no statistical evidence of interaction by sex. In the age-stratified analyses adjusted for sex, we found statistical evidence of interaction by income level that suggested higher hazard rates among younger patients. When stratifying by history of HF, we found no statistical evidence of interaction. The results of our sensitivity analysis were in agreement with the results of our primary outcome.

In the multivariable-adjusted model, there was no longer evidence of association between SDOH and recurrence of AF after ablation. The underlying causal relationship is unknown and likely complex and multifactorial. The fact that the associations did not persist suggests that common factors associated with AF progression account for the socioeconomic disparity in recurrence after catheter ablation. Comorbidities and AF duration may reflect underlying structural and electrical remodeling processes, which directly affect the likelihood of long-term sinus rhythm maintenance. In simple single mediator analyses, we found that prior hypertension, heart failure, and chronic obstructive pulmonary disease were potential mediators across all associations between SDOH and AF recurrence. However, limited knowledge is available to distinguish confounders from mediators.

In our sample, patients in lower socioeconomic positions had a higher prevalence of comorbidities. The disparities observed in our study may suggest suboptimal efforts to improve the risk profiles among patients in the lowest socioeconomic positions. However, to our knowledge, no study has so far described the preventive or treatment-related efforts implemented in connection with ablation by levels of SDOH. Future studies should examine the association between SDOH

and electrophysiological and imaging characteristics, to further elucidate the underlying pathophysiological mechanisms.

Our study identifies socioeconomic inequity as a determinant of AF recurrence following ablation. This issue requires attention and has not yet been addressed in clinical guidelines. Cardiovascular and comorbidity risk management is a central component of the ABC approach for AF,[24] and the current European consensus statement on ablation also recommend addressing modifiable risk factors to improve the outcome of ablation.[16] Relevant modifiable risk factors include obesity, obstructive sleep apnea, hypertension, and diabetes, as well as lifestyle factors such as smoking and alcohol consumption.[25] Our results may imply that a strategy that aggressively targets risk factor modification in those with worse socioeconomic circumstances could reduce inequality in AF recurrence. It is well-known that specialized nurse-led AF clinics are of great benefit in improving patient compliance and clinical outcomes.[26] Expansion of such clinics for patients undergoing ablation, especially for those with lower socioeconomic circumstances, may be of benefit.

Health literacy is the ability of an individual to obtain, process, and grasp fundamental health information and services to inform and participate in health decisions.[27] Health literacy is associated with socioeconomic position and education,[28] and a recent scientific statement from the American Heart Association underlines that health literacy is a barrier to prevention of cardiovascular diseases.[29] Reduced health literacy may explain unhealthy lifestyle habits and non-adherence to treatment, thereby increasing the risk of AF recurrence. Thus far, health literacy has not been integrated into the European guidelines, and how to best address health literacy remains uncertain.

Limitations

We had no information on type of AF or had access to data from monitoring devices to determine the exact duration of AF. We were unable to follow the patients systematically after the ablation

procedure. Patients with recurrent AF may be unregistered if they do not report to the healthcare system about recurrent symptoms or stay away from planned clinical follow-up. Accordingly, patients with asymptomatic or minimally symptomatic recurrence would not have been identified by our definition. Furthermore, we had no data on procedural characteristics, such as completeness of pulmonary vein isolation, number of AF foci, or AF inducibility, all of which are associated with recurrence.[30] Our Model 2 included many essential covariates, including mediators and confounders. Unfortunately, we had no information on other important factors, such as symptoms, diet, body mass index, physical activity, smoking, alcohol, or health literacy.

Finally, the results originated from the Danish healthcare system, which is based on the idea that all individuals should have free and equal access to healthcare and education. The tax-financed Danish National Health Service guarantees no-cost, partial reimbursement of consumer costs of medical treatment, and equal access to general practitioners and hospitals. All of which ensure a high level of equity in healthcare. However, even in universal healthcare systems, socioeconomic disparities in access to and in quality of care may still remain.[31] For instance, a previous Danish study has shown that individuals with higher income and education have lower incidence of AF.[32] Generalizability to other healthcare systems may be limited, and the observed associations in our study may potentially be even more dominant in countries without similar social security.

Conclusion

Among men and women undergoing a first-time ablation procedure for AF, lower educational attainment, lower family income, and living alone were associated with increased hazard rates of AF recurrence. This study identifies socioeconomic inequity in AF ablation outcomes a new issue that requires further research. The associations originated from a universal healthcare system, and

potentially may be more dominant in countries without similar social security. Multidisciplinary efforts are needed to reduce socioeconomic inequity in the effect of AF ablation.

Conflict of Interest

NV: None declared.

PC: None declared.

MDK: speaker fee for BMS/Bayer

JCN: Grants from Novo Nordisk Foundation outside this work.

DG: Grant from Biosense Webster outside this submitted work.

WYD: None.

LT: Ludovic Trinquart received funding from the American Heart Association (18SFRN34150007).

SPJ: Consultant work for BMS and Pfizer. Institutional research grants from BMS and Pfizer.

LF: Supported by a grant from the Health Research Foundation of Central Denmark Region. Consultant and speaker for BMS/Pfizer and AstraZeneca.

GYHL: Consultant and speaker for BMS/Pfizer, Boehringer Ingelheim and Daiichi-Sankyo. No fees are received personally.

Data Availability Statement

Permission to access the data used on this study can be obtained following approval from the Danish Health Authority.

Figure 1. Flowchart

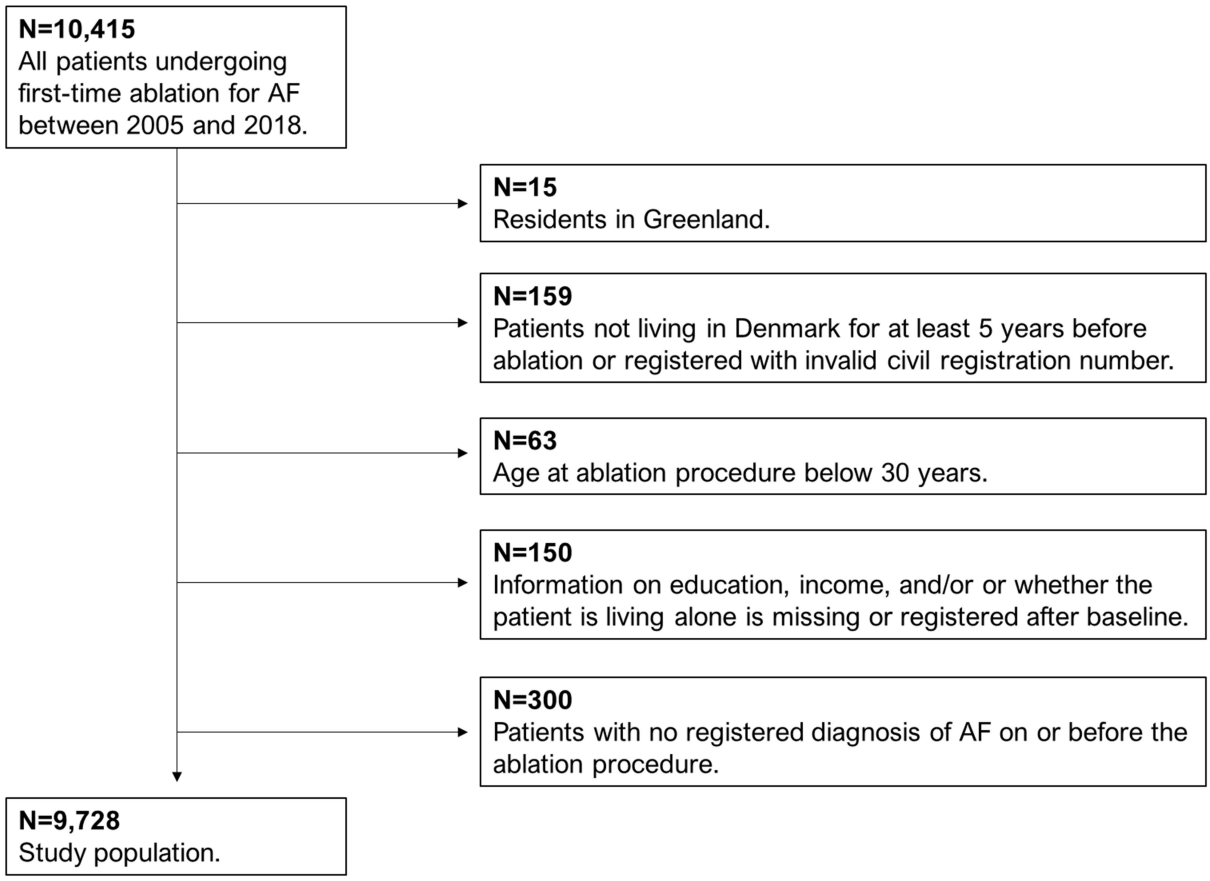

Table 1. Baseline characteristics.

Characteristics	N=9,728
Mean age, years (SD)	61.3 (9.6)
Male sex	6837 (70.3%)
Prior electrical cardioversion	5165 (53.1%)
Years since AF diagnosis, median (Q1-Q3)	2.6 (0.9-6.2)
Use of antiarrhythmic drugs*	3901 (40.1%)
History of comorbidity	
Heart failure	1793 (18.4%)
Myocardial infarction	692 (7.1%)
Valvular heart disease	839 (6.6%)
Stroke	550 (5.7%)
Diabetes mellitus	1264 (13.0%)
Hypertension	5711 (58.7%)
Chronic obstructive pulmonary disease	427 (4.4%)
Chronic kidney disease	138 (1.4%)
Cancer	1764 (18.1%)
Level of education	
Lower	2066 (21.2%)
Medium	4395 (45.2%)
Higher	3267 (33.5%)
Income group**	
Lower	3235 (33.3%)
Medium	3242 (33.3%)
Higher	3251 (33.4%)
Living alone	2328 (23.9%)

All characteristics are N (%), otherwise specified.

*Dispensing at least 1 prescription within 6 months before ablation

**Overlapping tertiles because income level was grouped by calendar year to account for inflation (Please see Supplemental Table 4).

Table 2. Cause-specific hazard ratios with 95% confidence intervals for associations between SDOH and recurrence of AF after ablation.

	Model 1	P value	Model 2	P value
Education				
Lower	1.09 (1.02-1.17)		1.02 (0.95-1.10)	
Medium	1.07 (1.01-1.14)	0.02	1.03 (0.97-1.10)	0.55
Higher	1.00 (ref)		1.00 (ref)	
Income				
Lower	1.14 (1.06-1.22)		1.06 (0.99-1.13)	
Medium	1.09 (1.03-1.17)	<0.001	1.05 (0.98-1.12)	0.20
Higher	1.00 (ref)		1.00 (ref)	
Living alone				
Yes	1.07 (1.00-1.13)	0.04	1.04 (0.98-1.11)	0.17
No	1.00 (ref)		1.00 (ref)	

Model 1: Adjusted for age and sex
Model 2: Adjusted for Model 1 and prior electrical cardioversion, years since AF diagnosis, use of antiarrhythmic drugs, history of heart failure, history of myocardial infarction, history of valvular heart disease, history of stroke, history of diabetes mellitus, history of hypertension, history of chronic obstructive pulmonary disease, history of chronic kidney disease, and history of cancer.

Table 3. Cause-specific hazard ratios (HR) with 95% confidence intervals for associations between SDOH and recurrence of AF after ablation by sex and age.

	Sex			Age group		
	Men N=6837	**Women N=2891**	**Interaction P value**	**Age <65 years N=5921**	**Age ≥65 years N=3807**	**Interaction P value**
Education						
Lower	1.12 (1.03-1.23)	1.04 (0.92-1.17)		1.14 (1.04-1.25)	1.03 (0.92-1.15)	
Medium	1.11 (1.03-1.19)	0.99 (0.89-1.10)	0.24	1.11 (1.03-1.19)	1.01 (0.92-1.12)	0.25
Higher	1.00 (ref)	1.00 (ref)		1.00 (ref)	1.00 (ref)	
Income						
Lower	1.16 (1.07-1.25)	1.08 (0.95-1.22)		1.25 (1.15-1.36)	1.02 (0.91-1.15)	
Medium	1.12 (1.04-1.21)	1.01 (0.89-1.15)	0.34	1.10 (1.02-1.18)	1.06 (0.93-1.20)	0.006
Higher	1.00 (ref)	1.00 (ref)		1.00 (ref)	1.00 (ref)	
Living alone						
Yes	1.11 (1.03-1.20)	1.00 (0.90-1.10)	0.09	1.09 (1.01-1.18)	1.03 (0.93-1.13)	0.23
No	1.00 (ref)	1.00 (ref)		1.00 (ref)	1.00 (ref)	

Analyses stratified by sex were adjusted for age.

Analyses stratified by age group were adjusted for sex.

Table 4. Cause-specific hazard ratios with 95% confidence intervals for associations between SDOH and recurrence of AF after ablation by history of HF.

	No history of HF N=7935	History of HF N=1793	Interaction P value
Education			
Lower	1.09 (1.01-1.18)	1.00 (0.85-1.17)	
Medium	1.06 (1.00-1.13)	1.04 (0.90-1.19)	0.54
Higher	1.00 (ref)	1.00 (ref)	
Income			
Lower	1.11 (1.03-1.20)	1.12 (0.96-1.31)	
Medium	1.07 (0.99-1.15)	1.13 (0.97-1.32)	0.46
Higher	1.00 (ref)	1.00 (ref)	
Living alone			
Yes	1.06 (0.99-1.13)	1.01 (0.89-1.15)	0.61
No	1.00 (ref)	1.00 (ref)	

Adjusted for age and sex.

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