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Original article

Association of age at menarche, reproductive lifespan and age at menopause with the risk of atrial fibrillation: The HUNT study

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ABSTRACT

Background: Age at menarche, reproductive lifespan, and age at menopause are associated with several cardiovascular diseases, but their relationship with atrial fibrillation (AF) is uncertain.
Methods: We linked information on all women who participated in the third survey of the population-based, longitudinal HUNT study in Norway with medical records from all local hospitals. A total of 14,632 women aged 60 or more were followed for validated incident AF. We retrieved age at menarche and age at menopause from the HUNT questionnaires. Reproductive lifespan was defined as the difference between age at menarche and age at menopause. We used Cox proportional hazards regression models to assess associations between AF and age at menarche, reproductive lifespan, and age at menopause.
Results: During a median follow-up of 8.17 years (136,494 person-years), 1217 (8.3 %) participants developed AF. In multivariable-adjusted analyses, we observed no associations between early or late age at menarche and AF (hazard ratios (HRs): <12 years: 0.85 [95 % confidence interval (CI), 0.65–1.12]; ≥16 years: 0.99 [95 % CI, 0.80–1.24] compared to those who attained menarche at 13–14 years). The HR for a reproductive lifespan shorter than 30 years was 0.91 [95 % CI, 0.72–1.15] compared to 34–37 years. Likewise, there was no clear association between premature or early age at menopause and AF (HRs: <40 years: 1.21 [95 % CI, 0.83–1.75]; 40–44 years: 0.97 [95 % CI, 0.77–1.22] compared to 50–54 years).
Conclusions: In this population of women aged 60 years and over, the risk of AF was not associated with age at menarche, reproductive lifespan, or age at menopause.

1. Introduction

Atrial fibrillation (AF) is the most common chronic arrhythmia in adults, affecting over thirty million people across the globe [1]. The incidence of AF is sharply increasing due to the aging of populations worldwide [1]. Moreover, AF is one of the major risk factors for heart failure, stroke, and all-cause mortality [1]. Women with AF have higher absolute risk of all-cause and cardiovascular mortality, stroke and heart failure compared with men with AF [2].

Early menarche, a shorter reproductive lifespan, and early menopause have been consistently associated with higher risk of cardiovascular disease (CVD) [3–6]. However, few studies have examined

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whether these reproductive factors are associated with higher risk of AF, with inconsistent results. Most previous studies used unvalidated AF diagnoses which might have led to substantial misclassification [7]. Although some studies have investigated the association between age at menopause and AF [8–14], far fewer have quantified the associations between age at menarche or reproductive lifespan and risk of AF [8,10,14].

To improve our limited understanding of female-specific risk factors for AF, we examined the associations between age at menarche, reproductive lifespan, and age at menopause with risk of AF using longitudinal data and validated follow up diagnoses of AF from the population-based Trøndelag Health Study (HUNT) in Norway.

2. Methods

2.1. Study population

The HUNT study is an ongoing, population-based open cohort study that has invited all residents aged 20 years or older residing in the northern part of Trøndelag county, Norway [15]. The study includes data from questionnaires, interviews, clinical measurements, and biological samples and the participants' data can be linked to other local and national health registries and hospital data by the unique identification number of Norwegian residents [15]. The HUNT study consists of 4 surveys, each of which included open enrollment and in-person examinations: HUNT1 (1984–86), HUNT2 (1995–97), HUNT3 (2006–08), and HUNT4 (2017–19) [15]. We linked the HUNT data with information on AF diagnosis from the electronic patient administrative systems of both hospitals providing acute medical care in the region (Levanger Hospital and Namsos Hospital) and with data from the Medical Birth Registry of Norway (MBRN) [7,16].

Our study population included 17,262 women who participated in HUNT3 and were ≥60 years old at HUNT3 or reached age 60 during the follow-up. We chose to start follow-up at 60 years to avoid immortal time bias [17] as it reflects an age beyond which natural menopause is extremely unlikely [18]. We excluded 2630 women for the following reasons (the numbers shown below are not mutually exclusive): 537 diagnosed with AF before HUNT3 examination, 141 missing age at menarche, 791 missing age at menopause, 24 with menopausal age over 60 years, 1002 with unknown time of bilateral oophorectomy, 1264 with premenopausal hysterectomy or unknown time of hysterectomy (Fig. 1). After exclusions, the final study population comprised 14,632 women.

2.2. Exposures

Participants were asked about age at menarche ("How old were you when you started menstruating?") and age at menopause ("How old were you when you stopped menstruating?") in HUNT2, HUNT3, and HUNT4. We used the first available self-reported information on age at menarche and menopause. Reproductive lifespan was defined as the difference between age at menarche and age at menopause. In HUNT3, participants were also asked about whether and at what age they had bilateral oophorectomy and hysterectomy. Surgical menopause was defined by bilateral oophorectomy before natural menopause. Use of hormonal replacement therapy (HRT) was self-reported in HUNT2 and HUNT3 and categorized as never, former or current use of systemic estrogen. In HUNT3, women were asked whether they have ever used or currently used any other hormonal contraceptives than oral ones, including hormonal IUDs, vaginal rings, subdermal implants, and contraceptive injections.

2.3. Atrial fibrillation

Atrial fibrillation diagnoses were retrieved from electronic diagnosis registers at the two local hospitals in the northern part of Trøndelag county by the International Classification of Diseases (ICD) 10 code I48. One cardiologist and two specialists in internal medicine reviewed the retrieved diagnoses and validated the AF diagnoses by electrocardiogram. If participants had an acute episode of AF within the first 7 days after cardiac surgery, during the acute phase of a myocardial infarction or during episodes of major haemodynamic instability (for example, during sepsis or non-cardiac surgery), these were not regarded as an incident AF. Details of the AF validation are presented elsewhere [7].

2.4. Covariates

Data on sociodemographic, lifestyle, and health characteristics were collected via questionnaires and interviews at each HUNT survey. We used the highest obtained educational level; lower secondary (up to 9 years), upper secondary (10–12 years) and tertiary education (college or university), the self-reported smoking status (never, former and current smoker), total alcohol units per week (none, ≤7 and >7 units per a week), exercise frequency (once a week or less, 2–3 times a week, and nearly every day), self-reported history of diabetes mellitus (DM), and body mass index (BMI). Fig. 2 shows which survey of the HUNT study was used for each covariate. We used answers from earlier HUNT surveys if information regarding smoking status, alcohol consumption, DM,

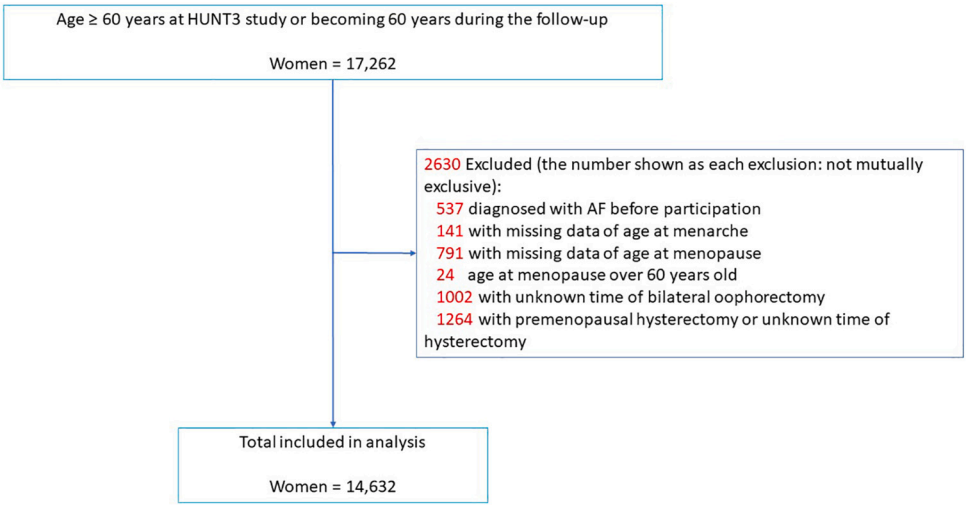

Fig. 1. Flowchart of study sample. AF, atrial fibrillation.

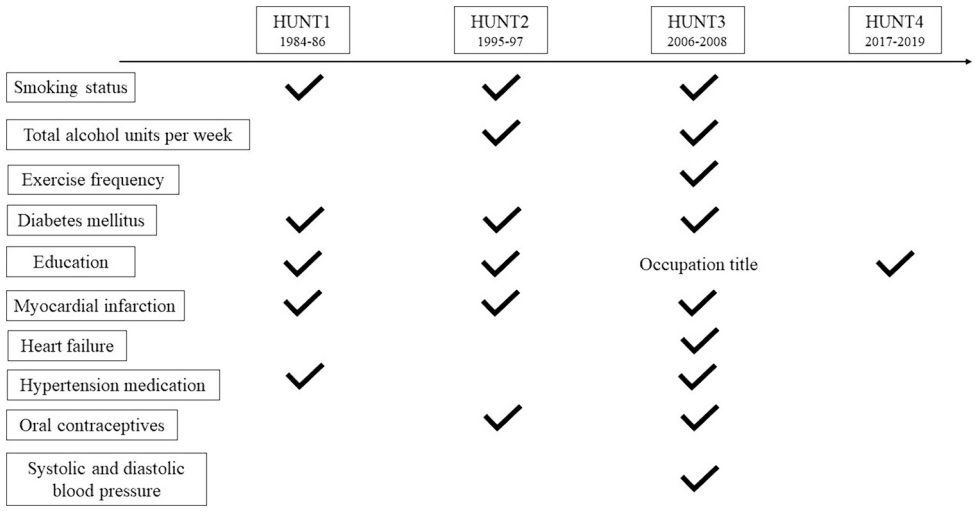

Fig. 2. Which HUNT survey was used for covariates.

and education was missing at HUNT3. Because HUNT3 did not include educational information, we derived educational status from work titles based on recommendations from Statistics Norway. We also retrieved further data to describe the baseline characteristics of the population: self-reported history of myocardial infarction, heart failure, use of hypertension medications, oral contraceptive, systolic and diastolic blood pressure.

Information on parity was retrieved from the MBRN and from self-reported information on number of children from HUNT questionnaires if births were not registered in the MBRN.

2.5. Statistical analyses

The participants' baseline characteristics are shown as means, standard deviations, medians, and interquartile ranges (IQR) for continuous variables and as numbers and percentages for categorical variables.

We used Cox proportional hazards models to estimate the hazard ratios (HRs) and corresponding 95 % confidence intervals (CI) for AF, comparing women with different categories of age at menarche, reproductive lifespan, and age at menopause. We used age as the time scale, and women entered the study on HUNT3 participation date or at age 60 years, whichever occurred later. Women were followed up until a first AF diagnosis, emigration from the county, death, or 31 January 2021, whichever came first. Supplementary Fig. S1 shows schematic summaries of the association between age at menarche, reproductive lifespan, age at menopause and AF. In analyses of reproductive lifespan and age at menopause, HRs were additionally adjusted for smoking status, alcohol consumption, DM, educational level, exercise frequency and parity. We tested the proportional hazards assumption by Schoenfeld residuals, which showed violation of proportionality in case of history of DM, and smoking status. Thus, we specified these three to be interacted with a function of time in the analyses. Furthermore, we assessed the interaction between age at menarche and age at menopause in our statistical models to test whether age at menarche and age at menopause interact with each other to modify the risk for AF. We used multiple imputation by chained equations [19] (mi command in STATA) to impute smoking status (proportion of missing: 0.27 %), alcohol consumption (proportion of missing: 2.33 %), DM (proportion of missing: 0.01 %), education level (proportion of missing: 0.25 %), and exercise frequency (proportion of missing: 2.69 %). The number of imputed datasets was 20, and we created imputed datasets by including each exposure, covariates, outcome including the censoring indicator and Nelson-Aalen estimate of the cumulative baseline hazard function, and age at covariate ascertainment.

We performed several secondary analyses. First, we excluded participants with surgical menopause or a self-reported history of cancer due to the well-known association of cancer with AF [20] and because cancer treatment might induce early menopause. Second, we performed secondary analyses stratified by HRT to investigate the effect of HRT on the association of menopausal age and reproductive lifespan with AF. Third, we estimated the association of age at menarche and AF including all women participating in HUNT3 regardless of age [17]. Fourth, we additionally adjusted for parity and BMI at HUNT3 in models assessing AF from age at menopause and reproductive lifespan. Fifth, we examined the association of natural and surgical menopause with AF. Lastly, we examined the association between reproductive lifespan, age at menopause and AF among never users of hormonal IUD in order to assess the potential impact of misclassification of age at menopause.

All analyses were performed using Stata IC, version 17.0 (StataCorp, College Station, Texas).

2.6. Ethics approval

All participants in the HUNT study provided written informed consent. The present study was approved by the Regional Committee for Ethics (REC) in Medical Research on January 27th 2022 (REC Central, reference number: 418576).

3. Results

During a median follow-up of 8.17 years (136,494 person-years), 1217 (8.3 %) participants developed AF. Table 1 shows baseline characteristics of the 14,632 study participants. Median age at HUNT3 participation was 61.5 [IQR: 54.8–70.1] years. The median age of menarche was 13 [IQR: 12–14] years, median reproductive lifespan was 37 [IQR: 34–39] years, and median age of menopause was 50 [IQR: 48–53] years. Women with AF had higher systolic and diastolic blood pressure and were more likely to report use of hypertensive medication than women without AF.

3.1. Menarche and AF

No clear association was found between age at menarche and risk of AF (Table 2). Compared to women with menarche between age 13 and 14 years, the HRs for those who experienced menarche before age 12 and after age 16 years were 0.85 [95 % CI, 0.65–1.12] and 0.99 [95 % CI, 0.80–1.24], respectively.

Table 1
Baseline characteristics of the study participants.

	All women (N = 14,632)*	Women without atrial fibrillation (N = 13,415)	Women with atrial fibrillation (N = 1217)
Age at HUNT3, years	61.5 [54.8–70.1]	60.7 [54.2–68.6]	72.9 [65.9–79.3]
Education			
Lower secondary education	5224 (35.7 %)	4511 (33.6 %)	713 (58.6 %)
Upper secondary education	6061 (41.4 %)	5715 (42.6 %)	346 (28.4 %)
Tertiary education	3311 (22.6 %)	3160 (23.6 %)	151 (12.4 %)
Self-reported diabetes mellitus	771 (5.3 %)	670 (5.0 %)	101 (8.3 %)
Self-reported myocardial infarction	347 (2.4 %)	269 (2.0 %)	78 (6.4 %)
Self-reported heart failure	131 (0.9 %)	95 (0.7 %)	36 (3.0 %)
Hypertensive medication	4583 (31.3 %)	3917 (29.2 %)	666 (54.7 %)
Systolic blood pressure, mmHg	132.5 (119.5–146.5)	131.5 (119.0–145.5)	140.5 (127.0–155.5)
Diastolic blood pressure, mmHg	72.0 (65.0–79.0)	72.0 (65.0–79.0)	71.5 (64.5–80.0)
Smoking status			
Never smoker	5936 (40.6 %)	5344 (39.8 %)	592 (48.6 %)
Former smoker	5022 (34.3 %)	4639 (34.6 %)	383 (31.5 %)
Current smoker at HUNT3	3635 (24.8 %)	3394 (25.3 %)	241 (19.8 %)
Alcohol consumption			
None	4968 (34.0 %)	4382 (32.7 %)	586 (48.2 %)
≤7 units a week	9042 (61.8 %)	8460 (63.1 %)	582 (47.8 %)
Over 7 units a week	281 (1.9 %)	271 (2.0 %)	10 (0.8 %)
Exercise frequency			
Once a week or less	5222 (35.7 %)	4743 (35.4 %)	479 (39.4 %)
2–3 times a week	5999 (41.0 %)	5580 (41.6 %)	419 (34.4 %)
Nearly every day	3017 (20.6 %)	2763 (20.6 %)	254 (20.9 %)
Parity			
Nulliparous	865 (5.9 %)	773 (5.8 %)	92 (7.6 %)
One birth	1166 (8.0 %)	1078 (8.0 %)	88 (7.2 %)
Two births	5174 (35.4 %)	4849 (36.1 %)	325 (26.7 %)
3+ births	7427 (50.8 %)	6715 (50.1 %)	712 (58.5 %)
Oral contraceptive use, ever	5712 (39.0 %)	5546 (41.3 %)	166 (13.6 %)
Hormone replacement therapy			
Never	10,162 (69.5 %)	9313 (69.4 %)	849 (69.8 %)
Former	3275 (22.4 %)	3011 (22.4 %)	264 (21.7 %)
Current	1195 (8.2 %)	1091 (8.1 %)	104 (8.5 %)
Age at menarche, years	13 [12–14]	13.0 [12–14]	14 [13–15]
Reproductive lifespan, years	37 [34–39]	37 [34–39]	36 [34–39]
Age at menopause, years	50 [48–53]	50 [48–53]	50 [48–53]
Surgical menopause	349 (2.4 %)	317 (2.4 %)	32 (2.6 %)

Data are presented as n (%) for categorical variables, and mean (standard deviation), or median [interquartile range] for continuous variables.
* The following data were missing: education status (n = 36), diabetes mellitus (n = 2), myocardial infarction (n = 2), heart failure (n = 10), hypertension medication (n = 3), systolic blood pressure (n = 110), diastolic blood pressure (n = 110), smoking status (n = 39), alcohol consumption (n = 341), exercise frequency (n = 394), oral contraceptive (n = 2317), and hormone replacement therapy (n = 1606).

Table 2
Age adjusted hazard ratios and 95 % confidence intervals of incident atrial fibrillation according to age at menarche.

Menarche	Event cases	Person-years of follow-up	Crude incidence per 1000 person-year	HR	95 % CI
<12 years	58	10,648	5.5	0.85	0.65–1.12
12 years	198	23,707	8.4	1.06	0.90–1.24
13 and 14 years	656	72,078	9.1		Reference
15 years	215	22,108	9.7	0.92	0.79–1.07
≥16 years	90	7953	11.3	0.99	0.80–1.24

CI = confidence interval. HR = hazard ratio.

3.2. Reproductive lifespan and AF

Likewise, there was no clear association found between reproductive lifespan and risk of AF (Table 3). Compared to women with reproductive lifespan between 34 and 37 years, the HR for those who have reproductive lifespan shorter than 30 years was 0.91 [95 % CI, 0.72–1.15].

3.3. Menopause and AF

There was no clear association between age at menopause and risk of AF (Table 4). Compared to women with menopause between age 50 and 54 years, the HRs for those who experienced menopause before age 40 and from age 40 to 44 were 1.21 [95 % CI, 0.83–1.75] and 0.97 [95 % CI, 0.77–1.22], respectively.

3.4. Secondary analyses

We found no clear interaction between age at menarche and age at menopause (Supplementary Table S1).

The complete case analyses showed similar results to the main analyses with multiple imputation (Supplementary Table S2). Restricting our analyses to women with natural menopause and no self-reported history of cancer did not substantially change the results (Supplementary Table S3). Likewise, estimates were similar when stratifying by HRT use to assess the impact of hormone therapy on the associations between age at menopause, reproductive lifespan and AF (Supplementary Table S4). Estimates remained similar when we included person-time below age 60 to assess the association between age at menarche and AF (Supplementary Table S5). Furthermore, the estimates remained similar after additionally adjusting for parity and BMI at HUNT3 in the analyses of age at menopause and reproductive lifespan (Supplementary

Table 3
Hazard ratio and 95 % confidence intervals of incident atrial fibrillation according to reproductive lifespan.

Reproductive lifespan	Event cases	Person-years of follow-up	Crude incidence per 1000 person-year	Age adjusted analysis		Multivariable-adjusted analysis*	
				HR	95 % CI	HR	95 % CI
<30 years	83	8829	9.4	0.93	0.74–1.17	0.91	0.72–1.15
30–33 years	177	18,641	9.5	0.94	0.79–1.12	0.93	0.78–1.11
34–37 years	478	49,194	9.7	Reference		Reference	
38–41 years	351	45,034	7.8	0.91	0.80–1.05	0.93	0.81–1.07
≥42 years	128	14,796	8.7	1.10	0.91–1.34	1.13	0.93–1.38

CI = confidence interval. HR = hazard ratio.
* Adjusted for smoking, alcohol, diabetes mellitus, education, and exercise frequency.

Table 4
Hazard ratio and 95 % confidence intervals of incident atrial fibrillation according to age of menopause.

Menopause	Event cases	Person-years of follow-up	Crude incidence per 1000 person-year	Age adjusted analysis		Multivariable-adjusted analysis*	
				HR	95 % CI	HR	95 % CI
<40 years	29	2680	10.8	1.25	0.86–1.82	1.21	0.83–1.75
40–44 years	84	9312	9.0	1.00	0.80–1.26	0.97	0.77–1.22
45–49 years	345	36,618	9.4	1.05	0.92–1.20	1.03	0.90–1.17
50–54 years	614	70,699	8.7	Reference		Reference	
≥55 years	145	17,185	8.4	1.07	0.89–1.28	1.08	0.90–1.30

CI = confidence interval. HR = hazard ratio.
* Adjusted for smoking, alcohol, diabetes mellitus, education, and exercise frequency.

Table S6). We found no associations of either natural or surgical menopause and AF (Supplementary Table S7). We observed similar associations between reproductive lifespan, age at menopause and AF when restricting our main analyses to women who never used hormonal IUDs (Supplementary Tables S8 and S9).

4. Discussion

In this population-based cohort study, we observed no clear association between age at menarche, reproductive lifespan, age at menopause and risk of AF.

4.1. Age at menarche

Early age at menarche is associated with higher risk of other CVDs, [6] and several potential pathophysiological mechanisms make such an association between age at menarche and AF plausible. Early menarche is associated with higher BMI and adiposity, hypertension, metabolic syndrome, impaired glucose tolerance and type 2 DM [21] which are well known risk factors for AF [8]. On the other hand, later menarche is associated with larger adult stature, another well-known risk factor for AF [1,22].

Currently, there are only two cohort studies that have investigated the association between age at menarche and AF [8,10]. Our results contradict a previous UK Biobank study [10] where both early and late age at menarche were associated with 10 % and 8 % increased risk for AF, respectively. There are several differences between the UK Biobank and our study. First, we used validated AF diagnoses, leading to less misclassification bias. Previous studies have shown that the accuracy of AF diagnoses in the ICD systems varies widely across populations [23,24]. Furthermore, our study excluded short AF episodes related to operations or myocardial infarction, which could have possibly inflated the association between age at menarche and AF in the UK Biobank. Interestingly, our results concur with a Mendelian randomization study from the UK Biobank [8] which found that genetically predicted age at menarche was largely unassociated with AF risk.

4.2. Age at menopause and reproductive lifespan

In this study, there was no evidence of an association between menopausal age, reproductive lifespan and AF. There have been studies showing that early menopause and short reproductive lifespan are associated with higher risk of other CVD [6,25]. Menopause causes lower estrogen levels, leading to altered vascular function, enhanced inflammation, reduced nitric oxide-dependent vasodilation and lipid profile change [26]. These pathophysiological mechanisms contributing to CVD and cardiovascular aging could presumably also increase the risk of AF. Moreover, early menopause is associated with hypertension, which is a major modifiable risk factor of AF [1,27].

A meta-analysis of 5 cohort studies concluded that early menopause was associated with 8 % higher risk for AF [9,11–14,28]. To our knowledge, two additional studies not included in the meta-analysis also examined the association between menopausal age and AF [8,10]. In five studies of all the seven studies, the point estimates of hazard ratios for early menopausal age and AF risk ranged from 0.82 to 1.30 [9–12,14]. Data on the relationship between reproductive lifespan and AF is limited but indicated that women with shorter reproductive lifespan (below 30 years) were at higher risk of AF [10,14]. Each study uses different categories of menopause and reproductive lifespan which make the direct comparison difficult. Geographical location, race-ethnicity and socioeconomic status influence menopausal age and the association between menopausal age and CVD risk [29]. These socio-demographic differences may also affect the association between menopausal age and AF risk. Other than the Framingham Heart Study [11], ours is the only study using validated AF diagnosis from health registers. The Women's Heart Study validated only self-reported AF diagnoses [13]. Among the previous studies, the Framingham Heart Study [11] had the most similar approach to ours. We both used validated AF diagnoses and included women over 60 years old at participation. Like ours, the study by Magnani et al. did not show a clear association between menopausal age and AF.

4.3. Strengths and limitations

This study has several strengths. The HUNT is a large population-based study with a stable population and high participation rates. Furthermore, the Norwegian health care system provides easy accessibility for all segments of the population and participation in registers is mandatory, leading to a virtually complete follow-up and minimizing the misclassification of the clinical end point. To avoid immortal time

bias, we chose a landmark approach and included women ≥60 years old. The Immortal bias arises when periods of follow-up time are misclassified or excluded because the outcome cannot occur by design [17]. Previous studies, other than Magnani et al. [11] and Honingberg et al. [9] have neglected the immortal time bias, and could have overestimated the risk for AF.

The current study also has some limitations. First, we observed wider confidence intervals in comparison to some previous research, indicating that our findings have lower precision than those reported in larger studies. Second, as in any study, age at menarche and menopause were self-reported, which is prone to non-differential misclassification and therefore to underestimation of associations [30]. Third, the current study lacks appropriate confounders of the association between age at menarche and AF, such as childhood BMI. However, the previous UK Biobank study [10] mainly adjusted for CVD risk factors at the baseline and the point estimates changed little. Fourth, we lacked data on timing and dose of contraceptives and HRT. Fifth, we cannot rule out residual confounding from genetic factors or other unmeasured characteristics. Lastly, the participants were ethnic Norwegian women, which may reduce confounding by racial and ethnic characteristics associated with AF, but which reduces generalizability.

5. Conclusion

We observed no evidence of an association between age at menarche, reproductive lifespan, age at menopause and AF. Future studies should investigate the association between age at menarche, reproductive lifespan, age at menopause and AF in different populations using validated AF diagnoses.

Contributors

Hikaru Morooka conceived and designed the study, wrote the first draft of the manuscript, contributed to the interpretation of the results and critically revised the manuscript.

Eirin B. Haug contributed to the study concept and designed the study, supervised the statistical analyses, contributed to the interpretation of the results and critically revised the manuscript.

Vegard Malmo, Jan Pål Loennechen, Kenneth J. Mukamal and Janet Rich-Edwards contributed to the interpretation of the results and critically revised the manuscript.

Abhijit Sen, Imre Janszky and Julie Horn conceived and designed the study, contributed to the interpretation of the data and critically revised the manuscript.

All authors read and approved the final version, and no other person made a substantial contribution to the paper.

The authors declare that AI was not used in the preparation of the manuscript.

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Ethical approval

All participants in the HUNT study provided written informed consent. The present study was approved by the Regional Committee for Ethics (REC) in Medical Research on January 27th 2022 (REC Central, reference number: 418576).

Provenance and peer review

This article was not commissioned and was externally peer reviewed.

Data sharing and collaboration

There are no linked research data sets for this paper. Due to restrictions imposed by the HUNT Research Centre (in accordance with the Norwegian Data Inspectorate), data cannot be made publicly available. Data are currently stored in the HUNT databank, and there are restrictions in place for the handling of HUNT data files. Data used from the HUNT Study in research projects will be made available on request to the HUNT Data Access Committee (kontakt@hunt.ntnu.no). The HUNT data access information (available here: http://www.ntnu.edu/hunt/data) describes in detail the policy regarding data availability.

Contributors

Hikaru Morooka: Writing – review & editing, Writing – original draft, Visualization, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Eirin B. Haug:** Writing – review & editing, Validation, Supervision, Software, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Vegard Malmo:** Writing – review & editing, Supervision, Resources, Methodology, Data curation. **Jan Pål Loennechen:** Writing – review & editing, Supervision, Resources, Methodology, Data curation. **Kenneth Mukamal:** Writing – review & editing, Supervision, Methodology. **Janet Rich-Edwards:** Writing – review & editing, Supervision, Methodology. **Abhijit Sen:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Imre Janszky:** Writing – review & editing, Supervision, Resources, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **Julie Horn:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no competing interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.maturitas.2024.107979.

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