International Journal of Cardiology 178 (2015) 149–152

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Incidence of atrial fibrillation in relation to birth weight and preterm birth

Susanna C. Larsson [a,*,1], Nikola Drca [b], Mats Jensen-Urstad [b], Alicja Wolk [a]

[a] Unit of Nutritional Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden
[b] Department of Cardiology, Karolinska University Hospital, Stockholm, Sweden

ARTICLE INFO

Article history:
Received 24 June 2014
Received in revised form 27 August 2014
Accepted 21 October 2014
Available online 23 October 2014

Keywords:
Atrial fibrillation
Birth weight
Preterm birth
Prospective studies

ABSTRACT

Background: Hypertension, type 2 diabetes and other cardiovascular diseases, all risk factors for atrial fibrillation, are associated with birth weight. It remains unclear, however, whether risk of atrial fibrillation is also associated with birth weight. We investigated the associations of birth weight and preterm birth (i.e., born more than one month before term) with risk of atrial fibrillation (AF).
Methods: The study population comprised 29 551 men and 23 454 women who were free from AF at baseline. Information on birth weight, preterm birth, and risk factors for AF was obtained from a questionnaire. Incident AF cases were ascertained by linkage to the Swedish Inpatient Register.
Results: During 12 years of follow-up, AF developed in 2711 men and 1491 women. High birth weight (≥5000 g) was associated with an increased risk of AF after adjustment for age and other risk factors for AF, but the association did not persist after further adjustment for adult height. In men but not in women, low birth weight was associated with an increased risk of AF. Compared with men weighing 2500–3999 g at birth, the multivariable RR was 1.86 (95% CI, 1.15 to 3.00) for those weighing <1500 g. This association was stronger in men who were born full-term (RR 2.53; 95% CI, 1.35 to 4.73).
Conclusions: Both high birth weight and low birth weight (in men), in particular in men born full-term, were associated with an increased risk of AF. The association with high birth weight appeared to be mediated through adult height.

1. Introduction

Hypertension [1], cardiovascular disease [2,3] and type 2 diabetes [4], all risk factors for atrial fibrillation (AF), are associated with birth weight within the normal range. It remains unclear whether birth weight is also associated with risk of AF, which is the most common cardiac arrhythmia and a major risk factor for stroke, congestive heart failure, and dementia [5]. A large part of the AF morbidity is still unexplained, the so-called lone AF. Genetic factors have been proposed [6], and it remains unknown how early the predisposition for AF is developed. To our knowledge, only two previous studies have examined the association between birth weight and risk AF, with conflicting results [7,8]. In a cohort of female health professionals, a high birth weight was associated with an increased risk of AF, but the association was attenuated after adjustment for adult height [8]. In contrast, the Atherosclerosis Risk in Communities cohort found a higher risk of AF in individuals with a low birth weight [7]. No study has evaluated whether preterm birth is associated with the risk of AF. Preterm birth has been found to be associated with global myocardial structural and functional differences in adult life, including smaller ventricular size and increased mass as well as reductions in systolic and diastolic function [9,10].

Given the inconsistent results regarding the relation between birth weight and risk of AF, we investigated this association in men and women from two prospective cohort studies. Furthermore, because data on preterm birth and risk of AF are lacking, we also evaluated this association and the joint association of birth weight and preterm birth with AF risk.

2. Methods

2.1. Study population

This study was based on data from two population-based prospective cohorts of Swedish men (Cohort of Swedish Men) and Swedish women (Swedish Mammography Cohort). Detailed information about these cohorts has been published previously [11,12]. Briefly, in the autumn of 1997, 48 850 men (born between 1918 and 1952) who resided in Västmanland and Örebro counties and 39 227 women (born between 1914 and 1948) who resided in Västmanland and Uppsala counties completed a 350-item questionnaire about weight at different ages, height, lifestyle factors, medication use etc. This study was approved by the Regional Ethical Review Board at Karolinska Institutet in Stockholm,

* Corresponding author at: Unit of Nutritional Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Box 210, SE-17177 Stockholm, Sweden.
E-mail address: susanna.larsson@ki.se (S.C. Larsson).
[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

http://dx.doi.org/10.1016/j.ijcard.2014.10.138
0167-5273/

Sweden. Return of the completed questionnaire was considered to imply informed consent.

2.2. Baseline data collection

The 1997 questionnaire requested information on weight at different ages (including weight at birth), height at age 20, waist circumference at baseline, education, smoking status and history, physical activity, history of hypertension, family history of myocardial infarction before 60 years of age, alcohol consumption, and diet. Participants were further asked whether they had been born more than 1 month before term (hereafter referred to as preterm birth). Information on birth weight was obtained using five predefined categories: <1500 g, 1500–2499 g, 2500–3999 g, 4000–4999 g, and ≥5000 g. Participants could also answer "do not know" on the question about birth weight. BMI was computed as the weight (in kg) divided by the square of height (in meters). We calculated pack-years of smoking history by multiplying the number of packs of cigarettes smoked per day by the number of years of smoking. Information on diabetes was obtained from the Swedish National Diabetes Register and complemented with self-reported data about diabetes on the questionnaire. Data on coronary heart disease and heart failure was obtained from the Swedish Inpatient Register.

2.3. Follow-up and case ascertainment

Participants were followed-up from January 1, 1998 through December 31, 2009 by record linkage (using the unique Swedish Personal Identification number) with Swedish health care registers. Information on dates of AF diagnosis and dates of death for deceased participants was obtained from the Swedish Inpatient Register and the Swedish Cause of Death Register, respectively. Diagnoses in the Swedish Inpatient Register are coded according to the Swedish International Classification of Disease (ICD) system. Atrial fibrillation was defined as either atrial fibrillation or atrial flutter (ICD-10 code I48) due to their close interrelationship and the difficulties to make a distinction between these two diseases.

2.4. Participants for analyses

We excluded men and women with an incorrect or a missing personal identification number ($n = 297$ men and $n = 243$ women) as well as those with a previous diagnosis of AF ($n = 1496$ men and $n = 634$ women) or cancer ($n = 2592$ men and $n = 1811$ women), or who had died before the start of follow-up ($n = 55$ men and $n = 26$ women). We further excluded those with missing information on birth weight ($n = 1438$ men and $n = 8931$ women) or who had answered "do not know" on birth weight ($n = 12\,056$ men and $n = 2544$ women) as well as those with missing information on preterm birth ($n = 406$ men and $n = 382$ women) or extreme values for BMI (<15 or >50 kg/m^2; $n = 959$ men and $n = 1202$ women). After these exclusions, 29 551 men, 45–79 years of age, and 23 454 women, 49–83 years of age, remained for the analyses.

2.5. Statistical analysis

Each participant contributed follow-up time from January 1, 1998 until the date of diagnosis of AF, date of death, or end of follow-up (December 31, 2009), whichever occurred first. We used Cox proportional hazards regression models stratified by age (in months) to estimate relative risks (RR) and 95% confidence intervals (CI) of AF for each of the five categories of birth weight, using the middle category (2500–3999 g) as the reference, and for preterm birth. We also examined the joint association of birth weight (3 categories: <1500 g, 1500–2499 g, and ≥2500 g) and preterm birth with risk of AF. Four multivariable models were created. In the first multivariable model, birth weight was controlled for preterm birth (yes or no) and vice versa. The second multivariable model was further adjusted for education (less than high school, high school, or university), a combined variable for smoking status and pack-years of smoking (never, past <20 pack-years, past ≥20 pack-years, current <20 pack-years, or current ≥20 pack-years), history of coronary heart disease or heart failure (yes or no), and family history of myocardial infarction before 60 years of age (yes or no). In the third multivariable model, we additionally adjusted for potential intermediates, including history of hypertension (yes or no), history of diabetes (yes or no), and BMI (continuous). The fourth multivariable model was further adjusted for height (continuous). Adjustment for walking/bicycling, exercise, and alcohol consumption did not alter the results materially and therefore, these variables were not included in the final models.

We tested the proportional hazards assumption using Schoenfeld residuals, and found that the assumption was satisfied. The analyses were conducted by using SAS (version 9.3; SAS Institute, Cary, NC). All statistical tests were 2-sided and p values <0.05 were considered statistically significant.

3. Results

Baseline characteristics of the study population by categories of birth weight are presented in Table 1. Compared with those weighing 2500–3999 g at birth, those weighing less than 1500 g were much more likely to have been born one month preterm. They were also more likely to have histories of coronary heart disease or heart failure, hypertension, and diabetes as well as a family history of myocardial infarction. Birth weight was positively associated with adult height and weight and had a U-shaped relationship with BMI.

During 12 years of follow-up, AF developed in 2711 men and 1491 women. Relative risks for the association between birth weight and risk of AF are shown in Table 2. A high birth weight (≥5000 g) was associated with an increased risk of AF in both men and women after adjustment for age and other risk factors. However, the association was substantially attenuated and did not persist after further adjustment for adult height. In models that adjusted for preterm birth, low birth weight was associated with an increased risk of AF in men but not in women. Compared with men weighing 2500–3999 g at birth, the multivariable RRs (model 4) were 1.22 (95% CI, 1.02 to 1.45) for those weighing 1500–2499 g and 1.86 (95% CI, 1.15 to 3.00) for those weighing <1500 g at birth. When we excluded men who were born preterm, the corresponding RR was 2.53 (95% CI, 1.35 to 4.73) for those who were born full-term and weighing <1500 g at birth.

Preterm birth was associated with a reduced risk of AF in men but was not associated with risk in women (Table 3). To further evaluate the association between preterm birth and AF in men, we grouped participants according to both preterm birth and weight at birth. Compared

Table 1
Age-standardized baseline characteristics by categories of birth weight among 29 551 men in the Cohort of Swedish Men and 23 454 women in the Swedish Mammography Cohort.

Characteristic[a]	Men: birth weight category, g					Women: birth weight category, g				
	<1500 ($n = 147$)	1500–2499 ($n = 1544$)	2500–3999 ($n = 21\,522$)	4000–4999 ($n = 5534$)	≥5000 ($n = 804$)	<1500 ($n = 114$)	1500–2499 ($n = 2040$)	2500–3999 ($n = 18\,573$)	4000–4999 ($n = 2486$)	≥5000 ($n = 241$)
Age, y	60.5	59.6	58.0	57.5	59.6	61.6	61.1	59.3	58.5	60.9
Adult height, cm	173	175	177	180	181	162	163	165	167	168
Adult weight, kg	79.5	79.3	80.7	85.0	87.2	66.1	66.8	67.6	70.9	73.9
Body mass index, kg/m^2	26.3	25.7	25.7	26.3	26.6	25.1	25.1	24.9	25.4	26.1
Born preterm, %[b]	68	25	1.1	0.2	0.6	76	23	0.7	0.2	0
Postsecondary education, %	15	16	19	20	18	20	21	24	25	21
Current smoker, %	33	28	25	26	27	27	25	24	25	32
History of CHD or heart failure, %	9.4	8.3	7.7	7.1	7.8	2.8	4.4	3.3	2.5	3.2
History of hypertension, %	26	26	22	21	21	23	22	19	15	19
History of diabetes, %	12	10	8	8	7	9	7	4	3	5
Family history of MI before age 60 yrs, %	27	17	15	15	15	24	20	17	17	15

CHD, coronary heart disease; MI, myocardial infarction.
[a] Values are means if not otherwise indicated.
[b] Born >1 month before term.