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Early life predictors of atrial fibrillation-related mortality: Evidence from the health and retirement study

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ABSTRACT

Prior research found that Americans born in 6 southeastern states (the AF-risk zone) had elevated risk of AF-related mortality, but no mechanisms were identified. We hypothesized the association between AF-related mortality and AF-risk zone birth is explained by indicators of childhood social disadvantage or adult risk factors. In 24,323 participants in the US Health and Retirement Study, we found that birth in the AF-risk zone was significantly associated with hazard of AF-related mortality. Among whites, the relationship was specific to place of birth, rather than place of adult residence. Neither paternal education nor subjectively assessed childhood SES predicted AF-related mortality. Conventional childhood and adult cardiovascular risk factors did not explain the association between place of birth and AF-related mortality.

1. Introduction

Lifecourse cardiovascular epidemiology has demonstrated that early life risk factors such as low birthweight and childhood socio-economic adversity predict greater risk for angina and atherosclerosis as well as adult mortality from coronary heart disease and stroke (Galobardes et al., 2006; Fabsitz and Feinleib, 1980; Batty et al., 2007; Glymour et al., 2007). Atrial fibrillation (AF) is the most common cardiac arrhythmia, (Benjamin et al., 2009; Magnani et al., 2011) and is responsible for significant morbidity from heart failure, dementia, and stroke, and increased mortality. Few articles have addressed whether early life conditions contribute to the development of AF. Preliminary evidence suggests that early life factors may influence AF, but via mechanisms distinct from those established for most other cardiovascular outcomes. For example, higher birthweight predicted increased risk of AF in the Women's Health Study (Conen et al., 2010). We recently showed that birth in a band of six Southeastern states (the AF-risk zone) predicted AF-related mortality (Patton et al., 2011). Surprisingly, given the close association between AF and stroke, the geography of the AF-risk zone only partially overlapped with the U.S. Stroke Belt (Glymour et al., 2009; Glymour et al., 2007; Howard, 1999; Casper et al., 1995; Howard et al., 1997). Place of birth sets the stage for a host of subsequent childhood and adult exposures that may influence risk of AF (Fig. 1). No prior study has examined whether the association between place of birth and AF-related mortality may be explained by childhood socio-economic disadvantage or common cardiovascular risk factors.

In the current analysis, we used a national cohort to confirm and further examine our previous report that individuals born in the AF-risk zone had elevated risk of AF-related mortality, regardless of state of adult residence (Patton et al., 2011). We tested the following hypotheses: (1) birth in any of 6 high risk states – previously identified from the national mortality files to have the strongest relationship with AF-related mortality – predicts AF-related mortality in this nationally representative cohort; (2) indicators of childhood adversity, previously associated with stroke and heart disease mortality, predict AF-related mortality; and (3) associations of place of birth with AF-related mortality are attenuated when adjusted for indicators of childhood adversity and for adult behavioral and physical risk factors.

2. Methods

The national Health and Retirement Study (HRS) is an ongoing cohort study of US adults age ≥ 50 years and their spouses

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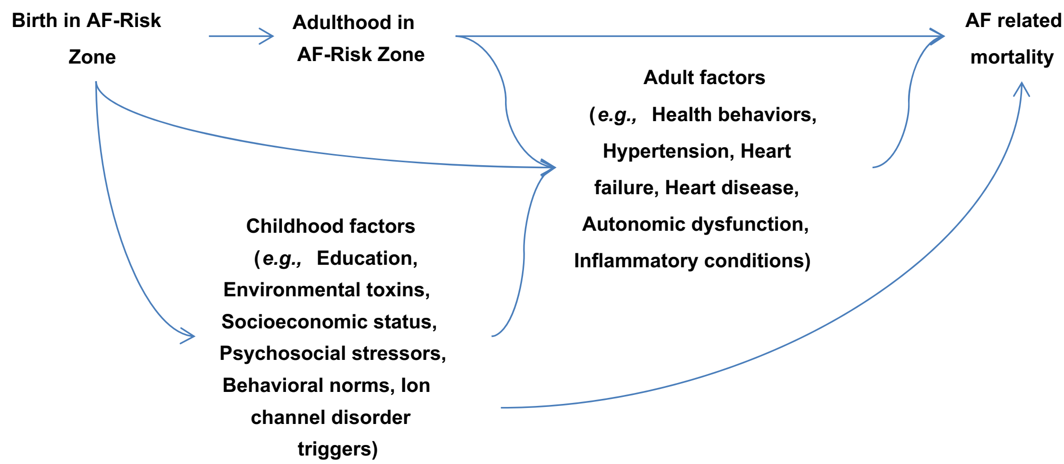

Fig. 1. Hypothesized causal structure linking place of birth and atrial fibrillation related mortality.

(regardless of spousal age). Details on study design and measures have been previously published (Juster and Suzman, 1995; Heeringa and Connor, 1995). Briefly, the study was initiated in 1992, with additional enrollments in 1993, 1998, and 2004, depending on birth cohort. Participants are interviewed biennially; following each wave a linkage to National Death Index US Department of Health and Human Services (2009). NDI records are searched for participants lost to follow-up and individuals previously reported as deceased but not yet successfully linked to NDI data (Health And Retirement Study, 2011). We followed HRS participants with non-missing data from their date of first interview to date of death, drop-out, or last HRS interview (in the 2008 wave).

From 31,022 respondents, we excluded 6696 (21.6%) participants who were not age eligible (younger than 50 years at baseline) and 3 (0.01%) missing date of last interview. The analytic sample comprised 24,323 respondents followed an average of 9.7 years. The parent study is approved by the University of Michigan Institutional Review Board and the current analyses were approved by the Human Subjects Committee of the Harvard School of Public Health.

2.1. Data collection and measurements

The outcome was defined as death with AF (ICD-9 code 427.3 or ICD-10 code I48) listed as a contributing cause. At enrolment (average age 63.7), respondents identified their state of current residence and state of birth. The AF-risk zone was defined to include 5 states (Maryland, North Carolina, South Carolina, Virginia, and West Virginia) and the District of Columbia (henceforth referred to collectively as the AF-risk zone). Study participants were classified as having lived in the AF-risk zone at birth or at study enrolment based on self-reported state of residence. These states were selected based on our previous analyses in a separate data set (National Center for Health Statistics mortality records), which identified these six states as the highest risk states of birth for AF-related mortality (Patton et al., 2011). In supplemental analyses, we examined all-cause mortality, death with stroke (ICD-9 codes: 430 to 438 or ICD-10 codes: I60 to I69, or G458, or G459) as a contributing cause and death with heart failure (ICD-9 428 or ICD-10 I50) as a contributing cause.

In the current paper, we conduct supplemental analyses contrasting AF-related mortality in the AF-risk zone against AF-related mortality in Stroke Belt states not in the AF-risk zone. We defined the Stroke Belt exactly as in our previous publications to include the states of: North Carolina, South Carolina, Georgia, Tennessee, Arkansas, Mississippi, or Alabama (Glymour et al., 2009; Glymour et al., 2007).

We examined years of completed schooling (0–17) and three indicators of childhood socio-economic adversity (father's education, perceived childhood socio-economic status (SES), and height) previously shown to predict other aspects of health in HRS or other studies. Father's education (<8, ≥ 8 years, unknown) predicted stroke onset in HRS (Glymour et al., 2008) and several cardiovascular outcomes in other studies (Lemelin et al., 2009; Galobardes et al., 2006). To assess perception of childhood socio-economic disadvantage, respondents were asked: "Now think about your family when you were growing up, from birth to age 16. Would you say your family during that time was pretty well off financially, about average, or poor?" Responses were scaled from 1 (pretty well off) to 5 (poor), and the small fraction of participants who volunteered "it varied" were coded as 3. Three additional questions related to childhood SES were asked including "did financial difficulties ever cause you or your family to move to a different place?", "was there a time when you or your family received help from relatives because of financial difficulties?" and "was there a time of several months or more when your father had no job?" These measures were combined into a single scale from 1 to 5, with a missing indicator for respondents who did not complete the question. These items regarding perceived childhood SES predict several domains of adult health (Luo and Waite, 2005). Height was self-reported at baseline interview. Adult height is sensitive to childhood nutrition, infections, and psychosocial conditions, (Steckel, 1995; Kuh and Wadsworth, 1989; Peck and Lundberg, 1995) and short stature has been linked to cardiovascular conditions and stroke (Hebert et al., 1993; Krahn et al., 1994; Glymour et al., 2008). Based on prior evidence linking tall stature to elevated AF risk, we first considered height in sex specific categories and then as a single linear term expressed in inches. We found no evidence that the association between height and AF-related mortality differed by sex (p-value for test of interaction between height and sex$=0.69$; detailed sex-stratified results in web Table 1), so we estimated a common coefficient.

We also examined adult risk factors including first available report of: household wealth (in 1992 dollars, divided by the square root of household size and natural log transformed); smoking status (never, past, current); self-reported body mass index (BMI); and self-reported physician's diagnoses of hypertension, diabetes, stroke and heart disease. We used the missing indicator method to retain observations missing BMI information ($n=203$, 0.8%). All models were adjusted for age at enrolment and sex. We present models stratified or adjusted for race (black vs. all other; nearly all "others" described themselves as white).