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Long-term Outcomes of Left Anterior Fascicular Block in the Absence of Overt Cardiovascular Disease

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To the Editor

Left anterior fascicular block (LAFB) is considered a benign electrocardiographic (ECG) finding,¹ but its long-term consequences have not been comprehensively studied. Conduction blocks occur due to conduction system fibrosis and are associated with myocardial fibrosis, even in the absence of other cardiovascular disease.^{2,3} Therefore, LAFB may be an immediately accessible marker of left heart fibrosis, a substrate for atrial fibrillation (AF)⁴ and congestive heart failure (CHF).⁵ We investigated the long-term outcomes of participants with LAFB in the absence of manifest cardiovascular disease in the Cardiovascular Health Study (CHS).

Methods

Established in 1989, CHS is a prospective cohort study of individuals aged 65 years or older sampled from Medicare eligibility lists nationwide.⁶ Institutional review board approval was waived for the current study. Participants provided written consent and were followed up semiannually. We excluded participants with a history of diabetes, hypertension, coronary disease, myocardial infarction (MI), AF, and CHF. We defined LAFB as a QRS axis between -45° and -90° and QRS duration of less than 0.12 seconds in the absence of left

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Study concept and design: Mandyam, Soliman, Marcus.

Acquisition of data: Mandyam, Soliman, Heckbert.

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ventricular hypertrophy, inferior MI, and ventricular preexcitation on the baseline ECG.¹ Outcome ascertainment for this study ended on June 30, 2008. We identified AF by study visit ECGs or hospital discharge diagnosis, and CHF was identified by physician diagnosis plus either pharmacological therapy or clinical findings. Deaths were identified from obituaries, the Social Security Death Index, Medicare claims, and participant proxies. Outcomes were compared using Kaplan-Meier estimates and Cox proportional hazards models. Adjusted comparative incidence rates (IRs) obtained from Poisson regressions are reported per 100 person-years. Covariates were chosen a priori or when associated with the predictor and outcome using a *P* value of less than .10 in the predictor and outcome. Participants having 1 or more covariates with missing data (*n*=183, 8%) were excluded from analyses involving missing variables. Data analysis was performed using Stata version 12 (StataCorp). Two-tailed *P* values of less than .05 were considered statistically significant.

Results

Of the eligible 1664 participants, the 39 individuals (2.3% [95% CI, 1.6%–3.1%]) with baseline LAFB were older and more likely male (TABLE). At follow-up (median 15.7, IQR 10.6–18.4 years), 380 participants had developed AF; 328, CHF; and 954 had died. Sixteen participants (41% [95% CI, 25%–57%]) with LAFB developed AF; 17 (44% [95% CI, 27%–60%]), CHF; and 33 (85% [95% CI, 73%–96%]) died. Through 10 years of annual ECGs, 0 LAFB participants developed left bundle branch block (LBBB) and 4 developed right bundle branch block, whereas 2 exhibited pacing. Participants with LAFB had an increased risk of AF, CHF, and death (FIGURE). After adjusting for age, race, sex, body mass index, systolic blood pressure, smoking, alcohol consumption, income, and study center, LAFB remained significantly associated with AF (hazard ratio [HR], 1.89 [95% CI, 1.11–3.24], *P*=.02; IR, 3.4 vs 1.8), CHF (HR, 2.43 [95% CI, 1.44–4.12], *P*=.001; IR, 3.5 vs 1.6), and death (HR, 1.57 [95% CI, 1.08–2.26], *P*=.02; IR, 6.2 vs 4.5). No meaningful differences were found when various baseline age cutoffs were applied. Also, LAFB was associated with death limited to cardiovascular causes (adjusted HR, 2.02 [95% CI, 1.08–3.77], *P*=.03; IR, 3.3 vs 1.8).

Discussion

In an older population without clinically manifest cardiovascular disease, LAFB was associated with an increased risk of AF, CHF, and death. Because no participants with LAFB went on to LBBB, and only 2 exhibited pacing throughout 10 years, it does not appear that progression of conduction disease was the reason for these observations.

Important limitations of this study include the small number of patients with LAFB and that this was an older cohort. Though CHS thoroughly identifies cardiovascular disease, it remains possible that LAFB is simply a marker of undetected underlying hypertension or coronary disease. Given previous histopathological studies,^{2,3} these findings suggest that LAFB may be a clinically relevant marker of an individual's propensity to left heart fibrosis. Further research is needed to determine if LAFB is an important predictor of consequent adverse outcomes.

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References

1. Elizari MV, Acunzo RS, Ferreiro M. Hemiblocks revisited. *Circulation*. 2007; 115(9):1154–1163. [PubMed: 17339573]
2. Davies M, Harris A. Pathological basis of primary heart block. *Br Heart J*. 1969; 31(2):219–226. [PubMed: 5775292]
3. Demoulin JC, Simar LJ, Kulbertus HE. Quantitative study of left bundle branch fibrosis in left anterior hemiblock: A stereologic approach. *Am J Cardiol*. 1975; 36(6):751–756. [PubMed: 1199930]
4. Marcus GM, Yang Y, Varosy PD, et al. Regional left atrial voltage in patients with atrial fibrillation. *Heart Rhythm*. 2007; 4(2):138–144. [PubMed: 17275746]
5. Querejeta R, López B, González A, et al. Increased collagen type I synthesis in patients with heart failure of hypertensive origin: relation to myocardial fibrosis. *Circulation*. 2004; 110(10):1263–1268. [PubMed: 15313958]
6. Fried LP, Borhani NO, Enright P, et al. The cardiovascular health study: Design and rationale. *Ann Epidemiol*. 1991; 1(3):263–276. [PubMed: 1669507]

Figure.

Unadjusted Kaplan Meier estimates of proportions of individuals with left anterior fascicular block free of atrial fibrillation, congestive heart failure, or death.

Differences in proportions are compared using log-rank tests. Individuals with left anterior fascicular block more often developed atrial fibrillation ($p<0.001$), congestive heart failure ($p<0.001$), and death ($p<0.001$), when compared to those without conduction disease.

TableBaseline Characteristics of Participants Without Overt Cardiovascular Disease^a

	No. (%) of Patients ^b	
	No Conduction Disease (n = 1625) ^c	Left Anterior Fascicular Block (n = 39)
Age, mean (SD), y	71.4 (5.0)	74.9 (6.8) ^d
Male sex	618 (38)	25 (64) ^d
Body mass index, mean (SD) ^e	25.1 (4.2)	25.5 (4.2)
Systolic blood pressure, median (IQR), mm Hg	122 (113–130)	120 (114–128)
Race/ethnicity ^f		
White	1471 (91)	33 (85)
Black	147 (9)	6 (15)
American Indian/Alaskan Native	3 (<1)	0
Asian/Pacific Islander	1 (<1)	0
Other	3 (<1)	0
Annual income, \$		
<25 000, No./total (%)	820/1512 (54)	23/37 (62)
25 000–49 999	427 (28)	10 (27)
50 000	265 (17)	4 (11)
Current smoker, No./total (%)	235/1624 (14)	6/39 (15)
No. of alcoholic beverages consumed/wk		
0, No./total (%)	698/1617 (43)	17/39 (44)
<1	331 (20)	5 (13)
1–6	329 (20)	9 (23)
7–13	133 (8)	5 (13)
>14	126 (8)	3 (8)

Abbreviation: IQR, interquartile range.

^aThe normally distributed continuous variables were compared using *t* tests. Nonnormally distributed variables were compared using the Wilcoxon rank sum test. Categorical variables were compared using the χ^2 and Fisher exact tests.

^bUnless otherwise indicated.

^cReferent group.

^dComparison with referent group yielded a *P* value of less than .05.

^eCalculated as weight in kilograms divided by height in meters squared.

^fParticipants self-identified their race from the 5 investigator-specified categories listed. Race was assessed in the Cardiovascular Health Study to explore potential associations with cardiovascular disease. Race was included in this study as a potential confounder.