ORIGINAL RESEARCH

Arrhythmias and Adaptations of the Cardiac Conduction System in Former National Football League Players

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***Background*—**Habitual high-intensity endurance exercise is associated with increased atrial fibrillation (AF) risk and impaired cardiac conduction. It is unknown whether these observations extend to prior strength-type sports exposure. The primary aim of this study was to compare AF prevalence in former National Football League (NFL) athletes to population-based controls. The secondary aim was to characterize other conduction system parameters.

***Methods and Results*—**This cross-sectional study compared former NFL athletes (n=460, age 56±12 years, black 47%) with population-based controls of similar age and racial composition from the cardiovascular cohort Dallas Heart Study-2 (n=925, age 54±9 years, black 53%). AF was present in 28 individuals (n=23 [5%] in the NFL group; n=5 [0.5%] in the control group). After controlling for other cardiovascular risk factors in multivariable regression analysis, former NFL participation remained associated with a 5.7 (95% CI: 2.1–15.9, $P<0.001$) higher odds ratio of AF. Older age, higher body mass index, and nonblack race were also independently associated with higher odds ratio of AF, while hypertension and diabetes mellitus were not. AF was previously undiagnosed in 15/23 of the former NFL players. Previously undiagnosed NFL players were rate controlled and asymptomatic, but 80% had a CHA_2DS_2-VASc score ≥1. Former NFL players also had an 8-fold higher prevalence of paced cardiac rhythms (2.0% versus 0.25%, $P<0.01$), compared with controls. Furthermore, former athletes had lower resting heart rates (62±11 versus 66±11 beats per minute, $P<0.001$), and a higher prevalence of first-degree atrioventricular block (18% versus 9%, $P<0.001$).

***Conclusions*—**Former NFL participation was associated with an increased AF prevalence and slowed cardiac conduction when compared with a population-based control group. Former NFL athletes who screened positive for AF were generally rate controlled and asymptomatic, but 80% should have been considered for anticoagulation based on their stroke risk. **(*J Am Heart Assoc*. 2019;8:e010401. DOI: 10.1161/JAHA.118.010401.)**

Key Words: athlete's heart • atrial fibrillation • conduction disease • National Football League

The health benefits of regular moderate exercise are well established. Recently, concerns have been raised about the cardiovascular risk of long-term, strenuous endurance activity, in particular as it relates to atrial fibrillation (AF) and cardiac conduction disease. In a meta-analysis, the prevalence of AF was 5-fold higher in veteran endurance athletes compared with age-matched sedentary controls.[1] Long-term alterations in autonomic tone with increased atrial refractory period, atrial dilation caused by increased preload, heightened inflammation, and atrial fibrosis are some of the mechanisms postulated to induce AF in athletes.[2] Cardiac conduction system disease, including the need for permanent pacemaker implantation, is also more common in former endurance athletes compared with age-matched, more sedentary peers.[3]

Prior studies have focused on the effects of long-term participation in endurance sports; however, the impact of prolonged exposure to strength-type sports on the cardiac conduction system is largely unknown. Therefore, the primary aim of this study was to evaluate the prevalence of AF in former National Football League (NFL) players compared with a population-based non-elite athlete control group. The secondary aim was to characterize other cardiac conduction system parameters in both groups.

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Clinical Perspective

What Is New?

- While several studies have associated long-term participation in endurance-type sports with an increased risk of atrial fibrillation (AF), this is the first study associating participation in strength-type sports with AF.
- The majority of former NFL athletes with AF were previously undiagnosed, rate controlled, and asymptomatic, but 80% met indications for anticoagulation, highlighting the need for a high level of clinical suspicion for occult AF in this group.
- Sinus bradycardia and first-degree atrioventricular block are typically benign findings in former athletes, but more severe conduction abnormalities requiring cardiac pacing also appear more prevalent in this population.

What Are the Clinical Implications?

- These data should be placed in the context of recently published work indicating that former participation in the NFL is associated with overall reduced all-cause and cardiovascular mortality compared with the general population.

Methods

Study Design

This is a cross-sectional study comparing a self-selected sample of former NFL players to a population based non-elite athlete control group from the Dallas Heart Study-2 (DHS). An invitation to participate in voluntary cardiovascular screening, as part of the NFL Players Care Foundation Healthy Body and Mind Screening Program, was extended to former NFL players. All former players who had participated in at least 1 NFL game were eligible to participate in screening. Details of this screening have been described previously.[4] Briefly, screening was conducted between January 2014 and January 2015 at multiple locations across the United States (Canton, OH; Chicago, IL; Cincinnati, OH; Dallas, TX; Indianapolis, IN; Las Vegas, NV; New York City, NY; Orlando, FL; Phoenix, AZ; and Pittsburgh, PA). The screening was performed by experienced personnel from the Cleveland Clinic Foundation. The data were de-identified and stored in a secure database with MedStar Sports Medicine. Screening comprised a cardiovascular history questionnaire that was reviewed with the player by a cardiologist to ensure accuracy of data, basic biometrics (height and weight), blood pressure readings, lipid profile, HbA1c, a 12-lead ECG, and an echocardiogram. The study was approved by the MedStar Institutional Review Board. All study participants provided written informed consent. The data that support the findings of this study are available from the corresponding author upon reasonable request.

The DHS was selected as the control group, given the racial diversity of the cohort with a significant black population. The design details of the DHS have been described previously.[5] Briefly, it is a probability-based population cohort of 3072 adults from Dallas County approved by the University of Texas Southwestern Medical Center Institutional Review Board. All participants provided written informed consent. Participants were enrolled between 2000 and 2002 (DHS-1), and there was intentional oversampling of blacks. The second phase was performed between 2007 and 2009 (DHS-2) and included follow-up visits of 2485 DHS participants along with 916 spouses of the original cohort. For the present analysis, we prespecified selection of male, white and black DHS-2 participants at least 40 years of age and with a body mass index (BMI) of at least 20 kg/m^2. All individuals meeting those criteria were included in the analysis. The DHS-2 was chosen as the comparison cohort because it was better matched for age (as compared with the DHS-1) with the NFL group.

Definitions

In both the NFL and DHS groups, hypertension and hyperlipidemia were defined as self-reported history of disease or the use of antihypertensive or lipid-lowering drugs. Diabetes mellitus was defined as self-reported history of diabetes mellitus, hemoglobin A1c ≥6.5%, or use of oral hypoglycemic drugs or insulin. Coronary artery disease, stroke, and heart failure were defined as self-reported history of disease. Current smoking was defined as any cigarette smoking at time of evaluation. In the NFL group, current level of physical activity was defined by frequency of weekly exercise: low (<1 time per week), medium (1–2 times per week), or high (≥3 times per week).

Former NFL players who played in the tackle, guard, center, defensive tackle, defensive end, or linebacker were classified as linemen; those who played in the quarterback, running back, wide receiver, tight end, cornerback, safety, kicker, or punter position were classified as nonlinemen.

Twelve-lead ECGs were measured using a General Electric (GE) Marquette Medical System with a MAC 5000 hardware and software configuration. The 12-lead ECGs were interpreted according to the 2017 International Recommendations for ECG interpretation in athletes.[6] AF was classified as history of physician-diagnosed AF (previously known AF), or AF detected for the first time on the 12-lead study ECG (previously unknown AF).

Transthoracic echocardiograms using Vivid q (GE Medical, Milwaukee, WI) and Philips iE33 (Philips Healthcare, Andover, MA) ultrasound systems were performed in all former NFL

players. The following measurements were prospectively performed according to the American Society of Echocardiography guidelines: ejection fraction (EF) using disc summation algorithm calculated from left ventricular (LV) volumes from apical 2- and 4-chamber windows, left atrial volume index using a disc summation algorithm, end-diastolic interventricular septal and posterior wall thickness and LV internal dimension in diastole. LV mass index was calculated based on modeling the LV as a prolate ellipse. Mitral valve inflow waves (E and A waves) and the average of the medial and lateral mitral annular velocities (e′) were measured using standard techniques.[7]

Statistical Methods

Summary statistics for continuous variables are reported as mean (1 SD) and categorical variables are reported as frequency (percentage). Participant characteristics were compared between the retired NFL and DHS groups using a Student unpaired *t* test for continuous variables and the χ^2 test for categorical variables. ANOVA was applied for the analysis of continuous variables across more than 2 groups. Univariable and multivariable (stepwise selection) logistic regression models were used to assess the association of baseline covariates with AF. Analysis limited to the NFL group, including echocardiographic parameters, was also performed.

To further address the question of AF rates between the 2 groups, given baseline differences between NFL participants and DHS-2 participants, propensity score matching was used. For the purpose of propensity matching with the NFL cohort, DHS participants were restricted to males and black/white race. NFL participants were matched in a 2:1 ratio, as the model allowed. Propensity matching was performed using a greedy matching algorithm for individual variables included in the $CHADS_2VASC$ score, as they were available. Specifically, we matched for age (within 5 years), BMI (within 5 kg/m^2), clinical heart failure, the presence of coronary artery disease or clinical heart failure (yes/no), hypertension status (yes/no), and diabetes mellitus status (yes/no). No information on peripheral vascular disease, stroke, or transient ischemic attack was available in the NFL group; thus, these variables of the $CHADS_2VASC$ were not included in the matching algorithm. After matching, the odds ratio for the outcome of AF based on the exposure of a former NFL player was calculated.

Results

Study Population

A total of 484 former NFL players underwent screening. Of these, 460 former players (age 56±12 years, black 47%) had complete data and were included in the study. Of the 2485 participants in the DHS group, 925 participants (age 53.9±8.6 years, black 53%) met the inclusion criteria. Baseline characteristics of study participants are shown in Table 1. While the NFL group was older and had higher BMIs than the DHS group, the differences were small (55.9±12 versus 53.9±8.5 years, P=0.002 and 32.3±5 versus 30.5±6.3 kg/m^2, P<0.0001). Other risk factors associated with AF and cardiac conduction disease were higher in the DHS group, including the following: any history of smoking (56% versus 22%, P<0.001), hypertension (57% versus 50%, P=0.002), hyperlipidemia (45% versus 35%, P<0.001), diabetes mellitus (19% versus 13%, P=0.002), coronary artery disease (7.0% versus 3.7%, P=0.01), and heart failure (2.5% versus 1.2%, P=0.04).

Atrial Fibrillation

AF was present in 28 individuals (NFL group: n=23, 5%; DHS group: n=5, 0.5%). In the NFL group, AF was a previously known diagnosis in 8 (35%) and previously unknown in 15/23 (65%). All former NFL with previously unknown AF were asymptomatic from an AF perspective. All individuals in the DHS group had previously known AF.

In univariable regression analysis, former NFL player status was associated with 9.7 (95% CI: 3.7–25.6, P<0.001) times higher odds of AF. Stepwise multivariable regression analysis controlling for age, hypertension, diabetes mellitus, BMI, and race showed that former NFL players had 5.7 times higher odds of AF (adjusted odds ratio 5.7, 95% CI: 2.1–15.9, P<0.001) (Table 2).

Differences between former NFL players with and without AF are presented in Table 3. Compared with former NFL players without AF, former players with AF were older, larger, more inactive, and more likely to be white. They also had higher heart rate (HR), lower ejection fractions, larger left atria, and higher E/e′ on echocardiography (all P<0.05). However, the prevalence of hypertension, hyperlipidemia, diabetes mellitus, or history of coronary artery disease, player position (lineman versus non-lineman), or the number of years played in the NFL did not differ (Table 3).

In stepwise multivariable regression analysis including only former NFL players, a larger left atrial volume index (adjusted odds ratio 3.1, 95% CI: 2.1–4.6) and higher BMI (adjusted odds ratio 1.1, 95% CI: 1.0–1.3) were independently associated with higher odds of AF. Conversely, black race was independently associated with lower odds of AF (adjusted odds ratio 0.1, 95% CI: 0.02–0.4). Other parameters including age, hypertension, and diabetes mellitus were not significantly associated with AF (Table 4).

With regard to propensity score matching, the matched cohort included a total of 1013 participants; 377 former NFL

Table 1. Baseline Characteristics

	NFL Group (N=460)	DHS Group (N=925)	*P* Value
Age, y	55.9±12	53.9±8.5	0.002
Race			
Black, %	46.5	53.3	0.002
White, %	51.5	46.7	0.01
Other, %	2.0	0	<0.001
BMI, kg/m^2	32.3±5.0	30.5±6.3	<0.001
Smoking			
Current, %	9.8	26.4	<0.001
Former, %	12.0	29.1	<0.001
Hypertension, %	49.8	57.0	0.002
Hyperlipidemia, %	34.6	44.7	<0.001
Diabetes mellitus, %	13.0	18.5	0.002
Coronary artery disease, %	3.7	7.0	0.01
Stroke/TIA, %	2.6	3.3	0.34
Heart failure, %	1.2	2.5	0.04
Heart rate, bpm	62±11	66±11	<0.001
PR-interval, ms	179±31	167±26	<0.001
First-degree atrioventricular block, %	18.0	9.0	<0.001
QRS-interval, ms	96±17	93±13	<0.001
QTc interval, ms	417±28	414±22	0.001
Left anterior hemiblock, %	6.3	7.7	0.06
Right posterior hemiblock, %	0	0.1	0.63
Left bundle branch block, %	0.7	0.8	0.26
Right bundle branch block, %	2.2	1.6	0.13
Incomplete right bundle branch block, %	10.0	7.1	0.02
Left ventricular hypertrophy, %	7.4	8.2	0.07
Right ventricular hypertrophy, %	0.2	0.3	0.44
Left atrial enlargement, %	7.8	8.7	0.07
Right atrial enlargement, %	0	1.8	0.002
Pathologic Q-waves, %	0.7	4.8	<0.001
T-wave inversions, %	3.7	12.2	<0.001
ST-segment depression, %	0.4	3.9	<0.001
Premature atrial contractions, %	1.3	1.4	0.2
Premature ventricular contractions, %	3.9	1.8	0.01
Atrial fibrillation, %	5.0	0.5	<0.001
Paced rhythm, %	2.0	0.25	0.002
Echocardiographic parameters			
Ejection fraction, %	59±4.8	…	…
Left ventricular mass, g	213±54	…	…
Left ventricular mass index, g/m^2	89±20	…	…
LVEDV, mL	135±32	…	…

Continued

Table 1. Continued

	NFL Group (N=460)	DHS Group (N=925)	*P* Value
IVSeD, mm	11.5±1.9	…	…
PWTeD, mm	10.8±1.6	…	…
LVDeD, mm	50±6	…	…
Left atrial diameter, mm	39±6	…	…
Left atrial volume index, mL/m^2	27±8	…	…
E/A	1.15±0.70	…	…
E/e′	8.7±3.0	…	…

BMI indicates body mass index; bpm, beats per minute; DHS, Dallas Heart study; E/A, ratio between peak early and late diastolic flow velocity; E/e′, ratio of early peak mitral flow velocity to the average of the medial and lateral mitral annular velocities; IVSeD, interventricular septum end-diastolic diameter; LVDeD, left ventricular dimension in end-diastole; LVEDV, left ventricular end-diastolic volume; NFL, National Football League; PWTeD, posterior wall thickness in end-diastole.

participants matched to 651 DHS participants. Fifteen total AF events occurred (11 in former NFL participants and 4 in DHS participants.) After matching, former NFL players demonstrated a 4.86 greater odds (95% CI 1.54–15.4) of having AF when compared with the matched DHS participants.

The characteristics of NFL players with AF are shown in Table 5. The average resting HR in NFL players with AF at the time of screening was 77±19 beats per minute. NFL players without previously unknown AF had a higher HR compared with players with previously unknown AF (84±19 versus 66±15 beats per minute, *P*=0.03), but almost all had a HR of <100 beats per minute and all were asymptomatic.

The CHA_2DS_2-VASc score in NFL players with AF ranged from 0 to 6 with an average score of 2.1±1.7. In players with previously undiagnosed AF, 3 (20%) had a score of 0, 4 (27%) had a score of 1, and 8 (53%) had a score ≥2.

Table 2. Uni- and Multivariable Regression of AF Predictors

	Odds Ratio	95% CI	*P* Value
Univariable analysis			
Former NFL player	9.7	3.7–25.6	<0.001
Age, y	2.8	1.9–4.1	<0.001
BMI, kg/m^2	1.6	1.2–2.1	0.002
Black race	0.3	0.1–0.6	0.003
Hypertension	1.0	0.5–2.2	0.92
Diabetes mellitus	0.9	0.3–2.5	0.79
Multivariable analysis			
Former NFL player	5.7	2.1–15.9	<0.001
Age, y	2.1	1.4–3.1	<0.001
BMI, kg/m^2	1.9	1.2–2.8	0.002
Black race	0.3	0.1–0.8	0.02

Hypertension and diabetes mellitus did not reach statistical significance in the stepwise selection model. AF indicates atrial fibrillation; BMI, body mass index; NFL, National Football League.

Cardiac Conduction and Ectopy

Compared with the DHS group, former NFL athletes had an 8-fold higher prevalence of paced rhythms (2.0% versus 0.25%, *P*<0.01). Former NFL players also had lower resting HR, longer PR intervals, a higher prevalence of first-degree atrioventricular block, and longer QRS intervals (Table 1). The prevalence of ventricular (3.9% versus 1.8%, *P*=0.01) but not atrial (1.3% versus 1.4%, *P*=0.2) premature contractions was also higher in the NFL group.

Discussion

The main finding in this study was a higher prevalence of AF in former NFL athletes compared with population-based controls, despite a similar age and racial composition and a lower prevalence of cardiovascular risk factors in the NFL group. The majority of former NFL athletes with AF were previously undiagnosed, rate controlled, and asymptomatic, but met indications for anticoagulation, highlighting the need for a high level of clinical suspicion for occult AF in this group. Furthermore, former NFL athletes had a higher prevalence of paced cardiac rhythms, as well as lower resting HRs, a higher prevalence of first-degree atrioventricular blocks, and longer QRS intervals compared with controls, all in line with slower cardiac impulse formation and propagation.

AF in Athletes

Multiple population-based studies have demonstrated that individuals who engage in regular light-to-moderate physical activity have a lower incidence of AF compared with sedentary controls.[8] However, there is an increasingly recognized association between long-term, habitual participation in endurance sports and an increased risk of AF.[1,3,9,10] The mechanisms linking endurance exercise and AF are incompletely understood and are likely multifactorial. In addition to

Table 3. Baseline Characteristics in Former NFL Players With and Without AF

	AF (N=23)	No AF (N=437)	*P* Value
Age, y	67±11	55±12	<0.001
Race			
Black, %	13	48	<0.001
White, %	87	50	<0.001
Other	0	2	0.54
Heart rate, bpm	77±19	61±10	<0.001
Position			
Lineman	48	30	0.15
Nonlineman	52	70	0.18
Years played in the NFL	7.3±3.4	7.4±3.7	0.88
BMI, kg/m^2	34.3±6.8	32.2±4.9	0.05
Current level of activity			
Low, %	26	12	0.04
Medium, %	13	27	0.13
High, %	57	53	0.75
Unknown, %	4	8	0.45
Hypertension, %	52	47	0.90
Hyperlipidemia, %	52	35	0.09
Diabetes mellitus, %	9	13	0.56
Coronary artery disease, %	30	23	0.40
Ejection fraction, %	57±7	60±5	0.004
Left ventricular mass index, g/m^2	96±21	88±20	0.06
LVEDV, mL	130±39	136±32	0.43
LVESV, mL	59±24	54±17	0.23
IVSeD, mm	12.3±1.5	11.5±1.9	0.06
Left atrial diameter, mm	46±6	38±6	<0.001
Left atrial volume index, mL/m^2	40±12	27±7	<0.001
E/e′	11.6±5.3	8.6±2.8	<0.001

Current physical activity was categorized into 3 groups: low <1 time per week, medium 1 to 2 times per week, and high ≥3 times per week. AF indicates atrial fibrillation; BMI, body mass index; bpm, beats per minute; E/e′, ratio of early peak mitral flow velocity to the average of the medial and lateral mitral annular velocities; IVSeD, interventricular septum end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; NFL, National Football League.

Table 4. Uni- and Multivariable Regression of AF Predictors in the NFL Group

	Odds Ratio	95% CI	*P* Value
Univariable analysis			
Age, y	2.8	1.7–4.6	<0.001
BMI, kg/m^2	1.4	1.0–2.0	0.05
Black race	0.2	0.1–0.5	0.004
Lineman	1.5	0.6–4.0	0.39
Years played in NFL	1.0	0.6–1.5	0.88
Coronary artery disease	1.1	0.7	0.43
Hypertension	1.2	0.5–2.9	0.65
Diabetes mellitus	0.7	0.2–2.9	0.58
LVMI, g/m^2	1.4	1.0–2.0	0.07
LAVI, mL/m^2	2.8	2.0–4.0	<0.001
LVEF, %	0.7	0.5–0.9	0.01
E/e′	1.8	1.3–2.5	<0.001
Multivariable analysis			
LAVI, mL/m^2	3.1	2.1–4.6	<0.001
BMI, kg/m^2	1.1	1.0–1.3	0.01
Black race	0.1	0.02–0.4	0.01

All listed univariable parameters were entered in the step-wise multivariate selection model. Only LAVI, BMI, and black race remained independently associated with higher odds of AF. AF indicates atrial fibrillation; BMI, Body Mass Index; E/e′, ratio of early peak mitral flow velocity to the average of the medial and lateral mitral annular velocities; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; NFL, National Football League.

left atrial enlargement because of prolonged increases in preload during exercise, it has been proposed that intense exercise over a prolonged time period can induce inflammation, resulting in atrial scarring and an increased risk of AF.[2] This hypothesis is supported by animal data showing an increased expression of fibrosis markers and a higher susceptibility to arrhythmias in rats after 16 weeks of intense exercise.[11] Furthermore, in humans, higher levels of cardiac fibrosis markers[12] as well as magnetic resonance imaging evidence of increased late gadolinium enhancement suggesting left atrial fibrosis have been reported in athletes.[13] Changes in autonomic tone and increased atrial ectopy in athletes have also been proposed as potential AF triggers.[3,14]

To our knowledge, this is the first study describing an increased prevalence of AF in former, primarily strength trained, elite athletes. Our findings are consistent with the 5-fold increased risk of AF previously reported in former endurance athletes.[1] Whether AF in former NFL players is being driven by similar mechanisms as those postulated to drive AF in endurance athletes is unclear. In the present study, except for slightly higher age and BMI, risk factors known to be associated with an increased risk of AF, including smoking, hypertension, hyperlipidemia, and diabetes mellitus, were lower in the NFL players compared with controls. Despite this, former NFL players had 5.7 times higher odds of AF after multivariable adjustment and, similarly, a 4.9 times higher odds ratio after propensity score matching. Of note, the prevalence of AF in the control group was similar to the reported national prevalence of 0.2% in males <55 years of age.[15] Interestingly, black race appeared protective against

Table 5. Former NFL Players With AF

Case	Age (y)	Race	Position	Years in NFL	Smoking	Other Conditions	Activity Level	BMI	HR	CHA_2DS_2-VASc	LVEF	LAVI	LVMI
Previously unknown AF													
1	42	White	NL	5	Current	None	High	34.2	72	0	55	34	83
2	43	White	L	8	Never	HLD	Medium	39.0	101	1	35	41	100
3	60	White	L	13	Never	HTN, HLD	Low	44.9	84	1	55	30	104
4	60	White	NL	4	Never	None	Low	32.6	105	0	60	36	70
5	60	White	L	7	Never	HTN	Low	47.8	62	1	60	30	89
6	61	Black	NL	11	Never	HLD	High	28.0	126	0	60	22	90
7	66	White	NL	6	Never	DM, HLD	High	40.7	60	2	65	26	97
8	68	White	L	11	Never	None	Medium	33.5	87	1	60	28	107
9	68	Black	L	14	Never	HTN	High	43.4	96	2	60	36	157
10	71	White	NL	6	Former	CAD, HTN	High	31.1	84	3	50	62	98
11	71	White	L	12	Never	CAD, HLD	High	28.8	60	2	65	63	101
12	72	White	NL	3	Never	Stroke, CAD, HTN, HLD	High	28.1	82	5	55	52	106
13	74	White	NL	7	Former	Stroke, CAD, HTN, HLD	Medium	25.9	62	4	65	56	84
14	77	White	L	5	Never	Stroke, CAD, HTN	Low	33.7	87	6	65	35	84
15	84	White	L	5	Former	DM, HLD	High	39.8	66	3	60	43	66
Previously known atrial fibrillation													
16	61	White	L	3	Never	HTN	Low	46.3	80	1	60	38	75
17	65	White	L	2	Never	CAD, HTN	High	32.3	85	2	55	41	139
18	67	White	NL	11	Never	None	High	26.1	81	1	50	33	108
19	69	Black	NL	7	Current	HLD	High	27.4	64	1	45	42	91
20	74	White	NL	5	Former	Stroke	High	31.1	66	3	55	21	100
21	75	White	NL	4	Former	CAD, HTN, HLD	High	32.7	46	4	60	46	103
22	76	White	L	9	Former	HTN, HLD	Low	26.6	47	3	55	51	95
23	78	White	NL	9	Former	HTN	Unknown	35.8	57	4	60	58	81

Current physical activity was categorized into 3 groups: low <1 time per week, medium: 1 to 2 times per week, and high: ≥3 times per week. AF indicates atrial fibrillation; BMI, body mass index; CAD, coronary artery disease; DM, diabetes mellitus; HLD, hyperlipidemia; HR, heart rate; HTN, hypertension; L, lineman; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; NFL, National Football League; NL, nonlineman.

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AF, which is in keeping with population studies showing a lower prevalence of AF in blacks, despite a higher AF risk factor burden. Higher BMI is associated with obstructive sleep apnea, a condition that is more prevalent in NFL players than the general population and a strong risk factor for the development of AF.[16] Unfortunately, we did not have data regarding obstructive sleep apnea in the studied populations.

In a separate analysis of the NFL group, we found a strong association between enlarged left atrial size and AF. This is in line with prior studies linking exercise, left atrial enlargement, and AF risk.[14] It is also consistent with a recent meta-analysis of left atrial dimensions in athletes, which indicated that the left atria were significantly larger in both strength athletes and combined trained athletes compared with sedentary controls.[17] However, the average left atrial volume index in the former NFL group was within established limits for the general population. Therefore, the observed left atrial enlargement may be because of AF itself, rather than prior sporting participation.

It has been suggested that the number of lifetime hours of strenuous physical activity may play a role in the risk of future AF.[18] Indeed, there appears to be a threshold of 1500 lifetime hours of exercise, beyond which AF risk increases.[19] The lack of an association between years of NFL participation and AF may be explained by this "threshold effect," because all NFL players likely had accumulated at least 1500 lifetime hours of sports through their high school, collegiate, and professional careers. In this study, the current level of activity was overall similarly distributed between former NFL athletes with and without AF.

The use of anabolic steroids is another risk factor that has been described in isolated case reports as a cause of AF in athletes.[20,21] However, these reports involved young active athletes developing AF at the peak of exercise, while the majority of sports-related AF occurs in middle-aged individuals, decades after cessation of professional competition.

Cardiac Conduction in Athletes

The other major finding in this study was an 8 times higher prevalence of paced cardiac rhythms in the former NFL players compared with the control group. Furthermore, former NFL players had several parameters of slower cardiac impulse formation and propagation, including lower resting HR, a higher prevalence of first-degree atrioventricular block, and longer QRS duration and QTc intervals.

While electrophysiological changes in active athletes are commonly attributed to exercise-induced alterations in autonomic tone, namely, sympathetic withdrawal and a heightened parasympathetic tone, it appears that prolonged intense exercise can permanently alter the cardiac conduction system and resting sinus bradycardia may persist decades after the athletic career has ended.[3] In fact, reduced intrinsic sinus node automaticity is an increasingly recognized mechanism of athletic bradycardia.[22,23]

We recognize that the absolute number of individuals with paced rhythms is small, and that the indications for pacemaker implantation were not defined. Still, we consider our findings hypothesis generating with regard to a potential link between strength exercise exposure and impaired cardiac conduction.

Clinical Implications

Of the former NFL players diagnosed with AF at the time of screening, 80% had a CHA_2DS_2-VASc score ≥ 1, indicating a potential benefit from anticoagulation to reduce stroke risk. Moreover, 8/15 (53%) of former athletes with AF had a score ≥ 2 and therefore a solid indication for Oral anticoagulation. Physicians caring for former athletes should also be aware that while sinus bradycardia and first-degree AV block are typically benign findings in former athletes, more severe conduction abnormalities requiring cardiac pacing also appear more prevalent in this population. However, these data should be placed in the context of recently published work indicating that former participation in the NFL is associated with overall reduced all-cause and cardiovascular mortality compared with the general population.[24]

Limitations

We acknowledge several limitations to our study. First, subjects were invited to participate, and recruitment bias cannot be excluded. By way of context, a recent mortality study of all NFL players with 1 credited season between 1986 and 2012 included 9778 players.[24] However, given the overall lower prevalence of cardiovascular risk factors and cardiac disease in the NFL group, we do not believe that the higher prevalence of AF can be explained by differential recruitment bias alone. Second, the number of AF events in both cohorts is small, limiting our ability to perform multivariable analyses. Third, our data are based on reported history of disease, as well as arrhythmias discovered on a single 12-lead ECG screening. We did not use long-term cardiac monitoring to detect clinically silent arrhythmias, and the true prevalence of electrophysiological abnormalities, including AF, is likely higher than reported. However, this limitation applies equally to both groups. Finally, sleep apnea is prevalent in former NFL players and a known AF risk factor in the general population. We lacked data on sleep apnea, along with other risk factors for AF including thyroid disease and alcohol consumption, and therefore could not assess these potential relationships.

Conclusions

Former participation in the NFL was associated with an increased prevalence of AF and slowed cardiac conduction compared with a population-based control group. Former athletes who screened positive were generally in rate-controlled AF and asymptomatic, but 80% should have been considered for anticoagulation based on their stroke risk.

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References

1. Abdulla J, Nielsen JR. Is the risk of atrial fibrillation higher in athletes than in the general population? A systematic review and meta-analysis. *Europace*. 2009;11:1156–1159.
2. Swanson DR. Atrial fibrillation in athletes: implicit literature-based connections suggest that overtraining and subsequent inflammation may be a contributory mechanism. *Med Hypotheses*. 2006;66:1085–1092.
3. Baldesberger S, Bauersfeld U, Candinas R, Seifert B, Zuber M, Ritter M, Jenni R, Oechslin E, Luthi P, Scharf C, Marti B, Attenhofer Jost CH. Sinus node disease and arrhythmias in the long-term follow-up of former professional cyclists. *Eur Heart J*. 2008;29:71–78.
4. Gentry JL III, Carruthers D, Joshi PH, Maroules CD, Ayers CR, de Lemos JA, Aagaard P, Hachamovitch R, Desai MY, Roselli EE, Dunn RE, Alexander K, Lincoln AE, Tucker AM, Phelan DM. Ascending aortic dimensions in former National Football League athletes. *Circ Cardiovasc Imaging*. 2017;10:e006852.
5. Victor RG, Haley RW, Willett DL, Peshock RM, Vaeth PC, Leonard D, Basit M, Cooper RS, Iannacchione VG, Visscher WA, Staab JM, Hobbs HH. The Dallas Heart Study: a population-based probability sample for the multidisciplinary study of ethnic differences in cardiovascular health. *Am J Cardiol*. 2004;93:1473–1480.
6. Sharma S, Drezner JA, Baggish A, Papadakis M, Wilson MG, Prutkin JM, La Gerche A, Ackerman MJ, Borjesson M, Salerno JC, Asif IM, Owens DS, Chung EH, Emery MS, Froelicher VF, Heidbuchel H, Adamuz C, Asplund CA, Cohen G, Harmon KG, Marek JC, Molossi S, Niebauer J, Pelto HF, Perez MV, Riding NR, Saarel T, Schmied CM, Shipon DM, Stein R, Vetter VL, Pelliccia A, Corrado D. International recommendations for electrocardiographic interpretation in athletes. *J Am Coll Cardiol*. 2017;69:1057–1075.
7. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015;28:1–39.e14.
8. Morseth B, Lochen ML, Ariansen I, Myrstad M, Thelle DS. The ambiguity of physical activity, exercise and atrial fibrillation. *Eur J Prev Cardiol*. 2018;25:624–636.
9. Karjalainen J, Kujala UM, Kaprio J, Sarna S, Viitasalo M. Lone atrial fibrillation in vigorously exercising middle aged men: case-control study. *BMJ*. 1998;316:1784–1785.
10. Andersen K, Farahmand B, Ahlbom A, Held C, Ljunghall S, Michaelsson K, Sundstrom J. Risk of arrhythmias in 52 755 long-distance cross-country skiers: a cohort study. *Eur Heart J*. 2013;34:3624–3631.
11. Benito B, Gay-Jordi G, Serrano-Mollar A, Guasch E, Shi Y, Tardif JC, Brugada J, Nattel S, Mont L. Cardiac arrhythmogenic remodeling in a rat model of long-term intensive exercise training. *Circulation*. 2011;123:13–22.
12. Lindsay MM, Dunn FG. Biochemical evidence of myocardial fibrosis in veteran endurance athletes. *Br J Sports Med*. 2007;41:447–452.
13. Wilson M, O'Hanlon R, Prasad S, Deighan A, Macmillan P, Oxborough D, Godfrey R, Smith G, Maceira A, Sharma S, George K, Whyte G. Diverse patterns of myocardial fibrosis in lifelong, veteran endurance athletes. *J Appl Physiol*. 2011;110:1622–1626.
14. Wilhelm M, Roten L, Tanner H, Wilhelm I, Schmid JP, Saner H. Atrial remodeling, autonomic tone, and lifetime training hours in nonelite athletes. *Am J Cardiol*. 2011;108:580–585.
15. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, Singer DE. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA*. 2001;285:2370–2375.
16. Kim JH, Zafonte R, Pascuale-Leon A, Nadler LM, Weisskopf M, Speizer FE, Taylor HA, Baggish AL. American-style football and cardiovascular health. *J Am Heart Assoc*. 2018;7:e008620. DOI: 10.1161/JAHA.118.008620.
17. Iskandar A, Mujtaba MT, Thompson PD. Left atrium size in elite athletes. *JACC Cardiovasc Imaging*. 2015;8:753–762.
18. Mont L, Sambola A, Brugada J, Vacca M, Marrugat J, Elosua R, Pare C, Azqueta M, Sanz G. Long-lasting sport practice and lone atrial fibrillation. *Eur Heart J*. 2002;23:477–482.
19. Elosua R, Arquer A, Mont L, Sambola A, Molina L, Garcia-Moran E, Brugada J, Marrugat J. Sport practice and the risk of lone atrial fibrillation: a case-control study. *Int J Cardiol*. 2006;108:332–337.
20. Lau DH, Stiles MK, John B, Shashidhar , Young GD, Sanders P. Atrial fibrillation and anabolic steroid abuse. *Int J Cardiol*. 2007;117:e86–e87.
21. Sullivan ML, Martinez CM, Gallagher EJ. Atrial fibrillation and anabolic steroids. *J Emerg Med*. 1999;17:851–857.
22. Lewis SF, Nylander E, Gad P, Areskog NH. Non-autonomic component in bradycardia of endurance trained men at rest and during exercise. *Acta Physiol Scand*. 1980;109:297–305.
23. Bahrainy S, Levy WC, Busey JM, Caldwell JH, Stratton JR. Exercise training bradycardia is largely explained by reduced intrinsic heart rate. *Int J Cardiol*. 2016;222:213–216.
24. Lincoln AE, Vogel RA, Allen TW, Dunn RE, Alexander K, Kaufman ND, Tucker AM. Risk and causes of death among former National Football League players (1986–2012). *Med Sci Sports Exerc*. 2018;50:486–493.