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CLINICAL RESEARCH
Imaging

Cardiac structure and function and leisure-time physical activity in the elderly: The Atherosclerosis Risk in Communities Study

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Aims Adults who engage in leisure-time physical activity (LTPA) have a reduced risk of developing heart failure. We hypothesized that high levels of LTPA are associated with diminished adverse age-related changes in cardiac structure and function.

Methods and results We studied 4342 Atherosclerosis Risk in Communities Study participants free of cardiovascular disease who underwent standardized echocardiography. In a cross-sectional analysis, we related LTPA (poor, intermediate, or ideal) to cardiac structure and function. We also related cumulative average LTPA over 24 years and changes in LTPA categories to echocardiographic measures. Cross-sectional analysis demonstrated that ideal LTPA, compared with poor LTPA, was associated with better diastolic function [prevalence of normal diastolic function: 39.8% vs. 31.5%, $P < 0.001$; mean E/E′ ratio (95% CI): 9.8 (9.6, 9.9) vs. 10.4 (10.2, 10.5), $P = 0.001$] and better systolic function [left-ventricular (LV) longitudinal strain: −18.3 (−18.4, −18.2) vs. −17.9 (−18.0, −17.8), $P < 0.001$] after adjusting for age, sex, race, and centre. Higher cumulative average LTPA over 24 years or an improvement in LTPA category were also, respectively, related to a more favourable E/E′ ratio ($P < 0.0001$, $P = 0.004$) and longitudinal LV strain ($P = 0.0002$, $P = 0.002$).

Conclusion Ideal LTPA, higher average levels of LTPA over a 24-year period, and an improvement in LTPA even later in life were associated with more favourable indices of LV diastolic and systolic function in older adults. Sustaining higher levels of LTPA, and even increasing physical activity later in life, may be beneficial for older adults in attenuating expected age-related changes in cardiac structure and function.

Keywords Exercise • Leisure-time physical activity • Echocardiography • Elderly

Introduction

Participation in leisure-time physical activity (LTPA) has been associated with lower incident heart failure in several populations,[1–6] including in the elderly Atherosclerosis Risk in Communities (ARIC) Study participants.[1] The mechanisms by which physical activity reduces the risk of heart failure are likely multifactorial with many downstream effects at the molecular and cellular level ultimately resulting in changes in cardiac structure and function.[7] Much of what is known about cardiac remodelling in response to exercise comes from studies in trained athletes. The cardiac response to exercise in the elderly, however, is less well studied.

Longitudinal data from the Framingham population demonstrate that the cardiac remodelling associated with ageing is characterized by increasing LV wall thickness, decreasing LV dimensions, and increasing fractional shortening.[8] Furthermore, age has been associated with a rising prevalence and progression of diastolic dysfunction.[9] These age-related changes in cardiac structure and function, including age-related diastolic dysfunction, have been associated with the incidence of heart failure in older age.[9] Recommendations

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for exercise in those with heart failure[10] are based on previously demonstrated improvements in functional capacity, peak myocardial oxygen consumption, and quality of life. Regular physical activity may also play an important role in mitigating the changes in cardiac structure and function that occur with ageing and precede the development of heart failure. We hypothesized that high levels of LTPA are associated with diminished adverse age-related changes in cardiac structure and function. To test this hypothesis, we assessed measures of cardiac structure and function in relation to LTPA measured at the time of echocardiography and over the 24-year course of study of the elderly ARIC population.

Methods

Study design and population

The ARIC study has been described previously.[11] The intent of the ARIC Study was to identify the causes and outcomes of atherosclerosis. Initial enrolment (1987–89) included 15 792 participants aged 45–64 years from four communities: Forsyth County, NC; Jackson, MS; suburban Minneapolis, MN; and Washington County, MD. These adults participated in four serial examinations at ~3-year intervals. A fifth examination of 6538 participants was conducted between 1 June 2011 and 30 August 2013; this exam included physical activity questionnaires and echocardiograms in all participants. Physical activity was also assessed at Visits 1 (1987–89) and 3 (1993–95). Our study sample included all patients who underwent echocardiography during Visit 5 with images of acceptable quality for analysis ($n = 6118$). Those excluded were those with prevalent cardiovascular disease [coronary heart disease (CHD), stroke, heart failure, severe valvular disease] ($n = 1626$) and those with missing physical activity data at Visit 5 ($n = 138$). Twelve remaining participants who were not white or black were also excluded from the study. The final analytic sample population included 4342 participants.

Leisure-time physical activity

Participants completed an interviewer-administered modified Baecke Physical Activity questionnaire at Visits 1, 3, and 5,[12] and this analysis focused on the sports questions. A composite measure was calculated using up to four sports or exercises that participants reported in the past year along with categorical choices of usual frequency and duration for each sport/exercise. The activities were assigned a metabolic equivalent (MET) value[13] to classify intensity as moderate or vigorous activity; duration and frequency were multiplied to obtain minutes per week of moderate or vigorous activity. Physical activity was further defined according to the analysis. The reliability and validity of the modified Baecke Physical Activity questionnaire have been previously evaluated, and the questionnaire performs similarly to other physical activity instruments.[14] Good correlation between sport activity and 48 h physical activity records in men and women ($r = 0.73$, $r = 0.63$, respectively) and peak oxygen consumption by VO_2 peak ($r = 0.67$, $r = 0.45$, respectively) has been previously demonstrated within the ARIC cohort.[15]

Cross-sectional analysis leisure-time physical activity categories

Minutes per week of moderate or vigorous activity were converted to intensity categories of LTPA (poor, intermediate, and ideal) in relation to the American Heart Association (AHA) recommended levels due to the skewness of the variable as previously described in other ARIC studies.[1] Ideal LTPA was defined as ≥150 min/week of moderate activity, ≥75 min/week of vigorous activity, or ≥150 min/week of moderate + vigorous activity. Intermediate LTPA was defined as 1–149 min/week of moderate activity, 1–74 min/week of vigorous activity, or 1–149 min/week of moderate + vigorous activity. Poor LTPA was defined as 0 min/week of moderate + vigorous activity.

Cumulative average leisure-time physical activity over 24 years

Cumulative LTPA over the 24-year course of the study was measured as a continuous index. Metabolic equivalent values using the updated compendium of physical activities[16] were multiplied by usual duration and frequency to obtain estimated total MET-minutes per week of sport activity.

Change in leisure-time physical activity category over 18 years

We also categorized the change in AHA-assigned LTPA categories between Visit 3 (1993–95) and Visit 5 (2011–13) as persistently poor activity, decreased activity, increased activity, or persistently active. Those who maintained either intermediate or ideal LTPA over both visits were categorized as persistently active, and those who maintained poor LTPA over both visits were categorized as persistently poor activity. Those who increased or decreased their activity level from one AHA category to another were categorized accordingly.

Echocardiography protocol

Details of the echocardiographic imaging and analysis protocol have been thoroughly described.[17] All echocardiograms were acquired during Visit 5 with a dedicated machine (Phillips iE33 Ultrasound systems with Vision 2011) according to a detailed acquisition protocol that included comprehensive two-dimensional, Doppler, tissue Doppler, and speckle-tracking echocardiography.[17] Dedicated and blinded analysts at the Brigham and Women's Hospital Cardiac Imaging Core Laboratory performed quantitative measures on all echocardiograms according to American Society of Echocardiography (ASE) recommendations.[18] Cardiac structure measurements included left-ventricular (LV) end-diastolic volume index (LVEDVi), right-ventricular end-diastolic area index (RVEDAi), left-atrial volume index (LAVi), LV mass index (LVMi), and relative wall thickness (RWT). Left-ventricular dimensions and mass were indexed to body surface area as per ASE guidelines. Left-ventricular hypertrophy (LVH) was defined as LV mass index >115 g/m^2 in men or >95 g/m^2 in women. Left-ventricular geometry was categorized as normal, concentric remodelling (RWT >0.42, normal LVMi), concentric hypertrophy (RWT >0.42, elevated LVMi), or eccentric hypertrophy (RWT <0.42, elevated LVMi). Cardiac function measurements included LV ejection fraction (LVEF), longitudinal LV strain, RV fractional area change (RV FAC), and tricuspid annulus peak systolic velocity (TAPSV). Diastolic indices included peak early transmitral (E-wave) velocity, peak late transmitral (A-wave) velocity, E-wave deceleration time, and lateral mitral annular early relaxation velocity (E′); diastolic function was classified by Olmsted criteria.[19]

Covariates

Standardized interviewer-administered questionnaires ascertained age, sex, race, and smoking status at Visit 5. Education level [basic (≤ grade 11), intermediate (≥ grade 12 or vocational school), advanced (college or graduate school)] was assessed at Visit 1. Height, weight, body mass index (BMI), blood pressure, and resting heart rate were measured at Visits 1, 3, and 5. The presence of hypertension, diabetes, CHD, heart failure, and stroke at all visits was determined using established definitions by the ARIC study.[20] Spirometry was performed at Visit 5 and moderate–severe chronic obstructive pulmonary disease (COPD)

was defined as per American Thoracic Society guidelines.[21] Fasting plasma total cholesterol, low-density lipoprotein, and high-density lipoprotein levels were measured in a central laboratory, and results from Visit 5 were analysed for this study.[22] N-terminal pro B-type natriuretic peptide (NT-proBNP) levels were also measured at Visit 5 using electrochemiluminescent immunoassay (Roche Diagnostics) with a lower detection limit $\leq$5 pg/mL.[23]

Statistical analyses

Descriptive statistics for the sample by LTPA category at Visit 5 are presented as means $\pm$ standard deviation, proportions, or medians [interquartile range (IQR)] for skewed variables. We related AHA-assigned LTPA category at Visit 5 to echocardiographic measures at Visit 5 in a cross-sectional analysis. In addition and complementary to the cross-sectional analysis, we also conducted analysis of the cumulative average LTPA over 24 years and change in LTPA category from Visit 3 to Visit 5 in relation to cardiac structure and function.

Cross-sectional analysis

Echocardiographic variables were compared for trend by LTPA category using multivariable linear or logistic regression, as appropriate. All multivariable regression models were adjusted for age, sex, race, and field centre. Continuous echocardiographic variables are presented as adjusted means $\pm$ standard error and categorical variables are presented with adjusted prevalence.

Significant correlates were tested for interaction by sex, race, education, and prevalent hypertension. Additional covariates (resting heart rate, BMI, diabetes, hypertension) were considered as mediators in the relationship between LTPA and cardiac structure and function and were therefore not included in the multivariable models. Because of low participation rates during ARIC Visit 5, we also repeated these analyses using inverse probability weights[24] to account for the propensity of participants to attend Visit 5 with results also provided in the Supplementary material online.

Cumulative average leisure-time physical activity analysis

Total cumulative average LTPA in MET-minutes per week was calculated accounting for the time intervals between Visits 1, 3, and 5 for each participant. We estimated the average amount of activity during the interval between subsequent visits by averaging the activity obtained at the beginning and end of each interval. Missing physical activity data were relatively few ($n = 268$). Any missing values were imputed using the average of available values from neighbouring visits. Linear and curvilinear associations between cumulative average LTPA and measures of cardiac structure and function were analysed using adjusted restricted cubic spline models and linear regression models adjusted for age, sex, race, and centre.

Change in leisure-time physical activity category analysis

Echocardiographic variables between groups (poor activity, decreased activity, increased activity, or persistently active) were compared relative to the persistently poor activity group by multivariable linear or logistic regression, as appropriate. Sensitivity analysis stratifying the persistently active group into those with persistently intermediate and persistently ideal LTPA was performed with results provided in Supplementary material online.

Best fit linear and curvilinear models were determined using the Akaike information criterion. A two-sided *P*-value of <0.05 was considered statistically significant. All statistical analyses were performed using Stata Software (version 13, Stata Corp., College Station, TX, USA).

Results

Cross-sectional analysis

Population characteristics

After excluding those with prevalent cardiovascular and valvular disease, 4342 participants were evaluated at Visit 5. Overall, 62.5% of participants were women, 79% were Caucasian, and the mean age was 75.6 $\pm$ 5 years (*Table 1*). The majority of the population met criteria for ideal LTPA (50.7%, $n = 2203$) while 19.3% ($n = 839$) were categorized as having intermediate LTPA, and 29.9% ($n = 1300$) were categorized as having poor LTPA. Participants in Forsyth County, NC and Minneapolis, MN were more likely to have ideal LTPA while participants in Jackson, MS and Washington County, MD were more likely to have poor LTPA (*Table 1*). Participants who were more active had on average higher education, lower BMI, lower prevalence of hypertension, less anti-hypertensive medication use, lower heart rates, and a lower prevalence of diabetes. There was no significant difference in the presence of moderate–severe COPD among LTPA categories despite a higher prevalence of current smokers in the poor LTPA category. Nearly half of the sample population represented former smokers with 243 participants (5.7%) with unknown smoking status. Those who met criteria for ideal LTPA had lower median NT-proBNP levels.

Cardiac structure and function

At Visit 5, ideal LTPA was associated with a significantly lower LV mass index [75.9 (75.2, 76.6) vs. 78.5 g/m^2 (77.5, 79.4), $P < 0.001$] and lower prevalence of LVH (7.5 vs. 12.1%, $P < 0.001$) compared with those with poor LTPA after adjusting for age, sex, race, and centre (*Table 2*). Conventional measures of systolic function, such as resting LVEF and RV fractional area change, were clinically similar between LTPA groups; however, LV longitudinal strain was more favourable in those with ideal LTPA [-18.3 (-18.4, -18.2) vs. -17.9 (-18.0, -17.8), $P < 0.001$]. Measures of diastolic function [E/A ratio: 0.86 (0.85, 0.87) vs. 0.83 (0.82, 0.85), $P = 0.005$; E/E′ ratio: 9.8 $\pm$ 0.1 vs. 10.4 $\pm$ 0.1, $P < 0.001$] were more favourable in those with ideal LTPA compared with those with poor LTPA. Ideal LTPA was also associated with a higher prevalence of normal diastolic function (39.8 vs. 31.5%, $P < 0.001$) and a lower prevalence of moderate diastolic dysfunction (31.4 vs. 36.3%, $P = 0.01$) than those with poor LTPA at Visit 5. None of the participants demonstrated diastolic indices consistent with severe diastolic dysfunction.

Sensitivity analysis demonstrated no significant effect modification by sex, race, education, or prevalent hypertension. In sensitivity analyses intended to generalize results to all eligible Visit 5 ARIC participants, our major findings remained unchanged (Supplementary material online, *Tables S1* and *S2*).

Cumulative average leisure-time physical activity analysis

The median cumulative average LTPA was 602.5 MET-min/week [IQR: 239.5, 1089.8]. The majority of participants remained active over all three visits with median total LTPA as follows: Visit 1—470.1 MET-min/week [IQR: 0.0, 1075.7]; Visit 3—546.7 MET-min/week [IQR: 0.0, 1096.7], and Visit 5—633.4 MET-min/week [IQR: 0.0, 1306.8].

Evaluation of cumulative average LTPA over 24 years revealed more favourable LV longitudinal strain ($P = 0.002$) with higher

Table 1 Sample characteristics at Visit 5 (2011–2013) by physical activity level, ARIC

	Poor activity $n = 1300$	Intermediate activity $n = 839$	Ideal activity $n = 2203$	*P*-value (trend)
Age (years)	76.1 ± 5.1	75.8 ± 5.1	75.2 ± 4.9	<0.001
Men, *n* (%)	399 (30.7)	267 (31.8)	963 (43.7)	<0.001
Race, *n* (%)				<0.001
White	944 (72.6)	612 (72.9)	1875 (85.1)	
African American	356 (27.4)	227 (27.1)	328 (14.9)	
Field Centre (*n*, %)				
Forsyth County, NC	184 (14.2)	172 (20.5)	599 (27.2)	<0.001
Jackson, MS	341 (26.3)	200 (23.8)	287 (13.0)	<0.001
Minneapolis, MN	267 (20.5)	247 (29.4)	856 (38.9)	<0.001
Washington County, MD	508 (39.1)	220 (26.2)	461 (20.9)	<0.001
Education level, *n* (%)				
Basic	247 (19.0)	103 (12.3)	137 (6.2)	
Intermediate	619 (47.7)	388 (46.3)	841 (38.2)	
Advanced	432 (33.3)	347 (41.4)	1221 (55.5)	
BMI (kg/m^2)	30.0 ± 6.3	28.8 ± 5.3	27.5 ± 4.9	<0.001
Heart rate (b.p.m.)	64 ± 11	63 ± 10	61 ± 10	<0.001
SBP (mmHg)	131 ± 19	131 ± 17	129 ± 17	<0.001
Hypertension, *n* (%)	1127 (86.7)	695 (82.8)	1634 (74.2)	<0.001
Anti-hypertensive use, *n* (%)	1009 (77.8)	604 (72.1)	1371 (62.3)	<0.001
Diabetes, *n* (%)	524 (40.3)	313 (37.3)	599 (27.2)	<0.001
Moderate-severe COPD, *n* (%)	315 (30.7)	214 (32.4)	587 (33.0)	0.22
Smoking status, *n* (%)				
Current smoker	97 (7.6)	42 (5.0)	112 (5.1)	<0.001
Former smoker	555 (46.1)	382 (49.0)	1060 (51.3)	0.004
Never smoker	551 (43.1%)	356 (43.1%)	893 (40.9%)	0.17
Total cholesterol (mg/dL)	182 [157, 210]	183 [159, 211]	186 [161, 213]	0.01
HDL (mg/dL)	52 ± 14	53 ± 14	55 ± 14	<0.001
LDL (mg/dL)	107 ± 35	108 ± 32	110 ± 33	0.02
NT-proBNP (pg/mL)	129 [63, 243]	120 [67, 224]	101 [56, 195]	<0.001
Sports Index Score	1.9 ± 0.5	2.5 ± 0.5	3.1 ± 0.7	<0.001

Numbers represent mean ± standard deviation or median [interquartile range] for continuous variables and *n* (%) for categorical variables. Education levels described as: Basic (≤grade 11), Intermediate (≥grade 12 or vocational school), Advanced (college or graduate school).
BMI, body mass index; COPD, chronic obstructive pulmonary disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NT-proBNP, N-terminal pro-brain natriuretic peptide; SBP, systolic blood pressure.

amounts of activity despite no significant difference in LVEF across the range of leisure activity (*Figure 1*). Higher average LTPA was also associated with favourable diastolic function (E/E′ ratio: $P < 0.0001$). Left-ventricular mass index, however, showed an inverse association with average LTPA only at low levels (*Figure 1*). Curvilinear models also demonstrated larger cardiac chamber dimensions (LVEDVi: $P < 0.0001$; RVEDAi: $P < 0.0001$; LAVi $P = 0.02$) with higher average LTPA (Supplementary material online, *Figure S1*).

Change in leisure-time physical activity category analysis

Of the 4342 participants analysed, 4149 had available LTPA data at both Visits 3 and 5. The majority of participants maintained intermediate or ideal activity LTPA (36.0%, $n = 1494$) or increased their LTPA category (27.3%, $n = 1134$). The remaining population decreased their LTPA category (21.5%, $n = 894$) or maintained persistently poor activity over 18 years (15.1%, $n = 627$).

Participants who remained active over 18 years demonstrated a lower LV mass index and a lower prevalence of LVH compared with those with persistently poor activity after controlling for age, gender, race, and centre (*Table 3*). Systolic function measured by LV longitudinal strain was more favourable in the persistently active [−18.3 (−18.4, −18.1) vs. −17.9 (−18.1, −17.7), $P = 0.001$] and increased activity groups [−18.3 (−18.4, −18.2) vs. −17.9 (−18.1, −17.7), $P = 0.002$] compared with the persistently poor activity groups. Furthermore, diastolic function measured by the E/E′ ratio

Table 2 Cardiac structure and function by physical activity level at Visit 5 (2011–2013), ARIC

	Poor activity $n = 1300$	Intermediate activity $n = 839$	Ideal activity $n = 2203$	*P*-value*
LV EDVi (mL/m^2)	42.5 (41.9, 43.0)	42.4 (41.8, 43.0)	43.4 (43.0, 43.8)	0.002
RV EDAi (cm^2/m^2)	10.4 (10.2, 10.5)	10.3 (10.2, 10.5)	10.6 (10.5, 10.7)	0.009
LAVi (mL/m^2)	25.1 (24.7, 25.6)	24.5 (23.9, 25.0)	25.2 (24.8, 25.5)	0.67
LVMi (g/m^2)	78.5 (77.5, 79.4)	76.7 (75.5, 77.9)	75.9 (75.2, 76.6)	<0.001
RWT (cm)	0.43 (0.42, 0.43)	0.43 (0.43, 0.43)	0.42 (0.42, 0.43)	0.02
LV hypertrophy (%)	12.1 (10.4, 13.9)	8.7 (6.8, 10.6)	7.5 (6.3, 8.6)	<0.001
LV geometry (%)				
Normal	49.8 (47.0, 52.6)	51.4 (48.0, 54.7)	53.7 (51.5, 55.8)	0.03
Concentric remodelling	40.4 (37.7, 43.1)	40.2 (36.9, 43.5)	38.0 (35.9, 40.1)	0.16
Concentric hypertrophy	6.3 (4.9, 7.7)	5.0 (3.5, 6.5)	4.3 (3.5, 5.1)	0.02
Eccentric hypertrophy	3.7 (2.6, 4.8)	3.4 (2.1, 4.7)	4.0 (3.2, 4.8)	0.60
LV EF (%)	65.6 (65.3, 66.0)	65.8 (65.5, 66.2)	66.1 (65.9, 66.3)	0.03
Longitudinal LV strain (%)	−17.9 (−18.0, −17.8)	−18.1 (−18.2, −17.9)	−18.3 (−18.4, −18.2)	<0.001
RV FAC	0.52 (0.52, 0.53)	0.52 (0.52, 0.53)	0.53 (0.53, 0.53)	0.007
TAPSV (cm/s)	12.0 (11.8, 12.1)	12.0 (11.8, 12.2)	12.0 (11.9, 12.1)	0.43
E/A ratio	0.83 (0.82, 0.85)	0.84 (0.82, 0.85)	0.86 (0.85, 0.87)	0.005
Lateral E/E′ ratio	10.4 (10.2, 10.5)	10.0 (9.7, 10.2)	9.8 (9.6, 9.9)	<0.001
LV diastolic function, *n* (%)				
Normal	31.5 (28.6, 34.5)	34.9 (31.4, 38.5)	39.8 (37.6, 42.1)	<0.001
Mild	31.9 (29.1, 34.7)	32.2 (28.9, 35.6)	28.7 (26.6, 30.8)	0.06
Moderate	36.3 (33.3, 39.3)	32.7 (29.3, 36.1)	31.4 (29.3, 33.5)	0.01

Values represent adjusted means (95% confidence interval) for continuous variables and adjusted prevalence (95% confidence interval) for categorical variables.
EDAi, end-diastolic area index; EDVi, end-diastolic volume index; EF, ejection fraction; FAC, fractional area change; LAVi, left-atrial volume index; LV, left ventricle; LVMi, left-ventricular mass index; RV, right ventricle; RWT, relative wall thickness; TAPSV, tricuspid annular peak systolic velocity.
**P*-value for trend based on multivariable regression adjusted for age, gender, race, and centre.

was more favourable in those who were persistently active [9.8 (9.7, 10.0) vs. 10.4 (10.1, 10.6), $P \leq 0.001$] and those who increased their activity [9.9 (9.7, 10.1) vs. 10.4 (10.1, 10.6), $P = 0.004$] compared with those with persistently poor activity. Participants who were persistently active (37.9 vs. 32.2%, $P = 0.03$) and those who became more active (37.8 vs. 32.2%, $P = 0.04$) had a greater prevalence of normal diastolic function compared with those with persistently poor activity.

Discussion

This study demonstrates a relationship between higher amounts of LTPA and favourable indices of LV diastolic and systolic function in a large elderly cohort. Moreover, we found that staying active or becoming physically active is more strongly associated with favourable measures of cardiac structure and function than not participating in LTPA.

Previous large population studies have demonstrated that normal ageing leads to decreased cardiac chamber dimensions, increased LV wall thickness, and increased fractional shortening.[8] Invasive haemodynamic measurements suggest that an increase in LV stiffness occurs between ages 50 and 64 after which LV dimensions decline and remodelling occurs.[25] Exercise, however, may be one means to counteract these changes. In small cohorts, several groups have demonstrated that LV compliance resembles a more youthful pattern in those who maintain high-level exercise, yet whether echocardiographic-based measures of diastolic function change in non-athletes who take up exercise remains inconclusive.[26,27]

In this large elderly cohort, those with higher LTPA demonstrated better diastolic indices than their inactive counterparts. This apparent benefit was observed in those who had remained active since middle age, whether by AHA recommended levels or by cumulative average activity, and among those who had increased their activity. These cross-sectional findings mirror prior results in which age-associated changes in ventricular relaxation were reduced by endurance activity.[28] However, our findings are in contrast to recent observations from the Framingham population in which there was no association with physical activity and E/E′ ratios,[29] which may reflect differences in the populations studied; age-related changes in diastolic function are less likely to have developed in this younger cohort. Although the differences in diastolic indices between activity levels are modest in this ARIC sample, the trend towards more favourable diastolic function supports the hypothesis of attenuation of age-related changes with exercise. These results may provide insight into the lower incidence of heart failure seen with exercise in the ARIC sample,[1] a finding that may be consistent with the modestly lower NT-proBNP values seen in those with ideal LTPA in this and other studies.[30] Additional studies are needed to evaluate the

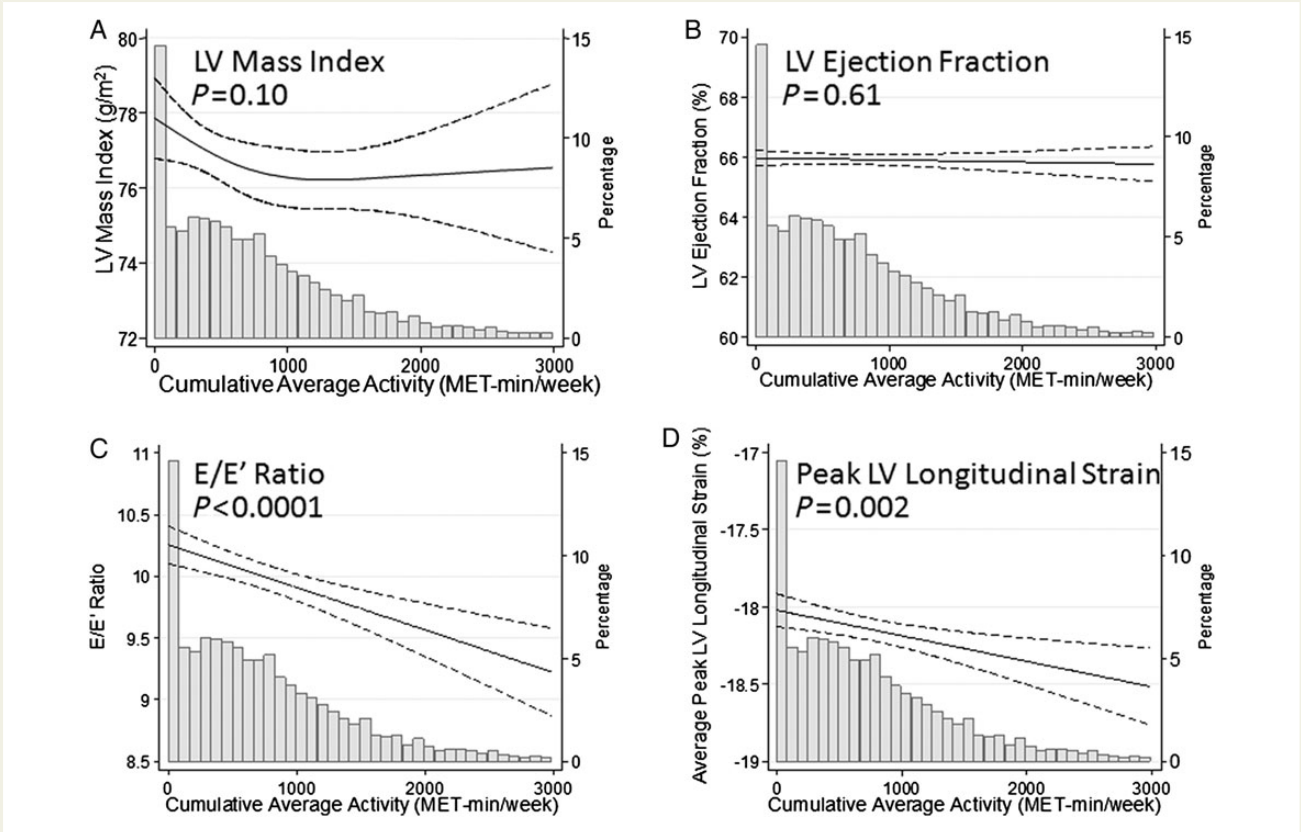

Figure 1 Multivariable analysis of parameters of cardiac structure and function by cumulative average physical activity over 24 years (1989–2013). (*A*–*D*) Fitted restricted cubic spline models and linear models of various parameters (*A*: LV mass index, *B*: LVEF, *C*: E/E′ ratio, *D*: Peak LV longitudinal strain) as a function of cumulative average physical activity (MET-min/week) over 24 years. Models are adjusted for age, sex, race, and centre with 95% confidence intervals displayed.

progression of diastolic function with age and exercise and the relationship with associated sequelae.

Our findings also demonstrate a higher LV mass index and a higher prevalence of LVH in those with poor LTPA and in those with persistently poor activity compared with those who were active or increased their activity. While regular vigorous athlete-level activity is typically associated with increased LV mass as seen in the athlete's heart, ageing and hypertension are also associated with increased LV mass and hypertrophy.[8,31,32] Despite a higher prevalence of hypertension in those that were poorly active, no significant interaction was observed between physical activity and prevalent hypertension to suggest synergism between these two risk factors. The higher LV mass index and prevalence of LVH in those who were poorly active may, however, be explained by a different mechanism. Several focused studies have reported a paradoxical effect of exercise on LV mass in those with hypertension; in these studies, those with regular physical activity had a lower risk of developing LVH compared with sedentary participants with hypertension.[33–35] In this elderly hypertensive population, regular activity may have played a role in preventing the expected increase in LV mass seen in hypertensive and athletic cohorts.

Increased global strain has been suggested to be a more sensitive marker of subclinical changes in systolic function and predictive of adverse cardiovascular outcomes than are traditional measures of systolic function, such as LVEF.[36–38] While there was no clinically significant association between LVEF and LTPA, LV longitudinal strain was significantly more favourable in those who stayed active or increased their LTPA category. Although modest in magnitude, the trend towards favourable LV longitudinal strain suggests that regular exercise could potentially help preserve systolic function in this older population.

Despite the large size of our cohort, our findings did not demonstrate any clinically significant differences in LV dimensions, LA dimensions, RV dimensions, or RV systolic function by LTPA category. While cardiac chambers may dilate as a physiological adaptation to intensive exercise in elite athletes,[31,39] we did not observe clinically significant associations in an elderly population of non-athletes when evaluated at Visit 5 or in those who increased their activity. However, those who maintained higher average physical activity over 24 years demonstrated modestly larger LV, RV, and LA dimensions, likely reflecting changes expected in a more athletic population or perhaps reflecting deceleration of the expected decline in cardiac dimensions with age.

Several limitations of this analysis should be noted. Due to the observational nature of this study, we can only describe association and cannot infer causality, and despite adjusting for covariates, we

Table 3 Cardiac structure and function by change in physical activity over 18 years (1995–2013), ARIC

	(Reference Group)			
	Persistently poor activity $n = 627$	**Decreased activity** $n = 894$	**Increased activity** $n = 1134$	**Persistently active** $n = 1494$
LV EDVi (mL/m^2)	42.4 (41.7, 43.1)	42.5 (41.9, 43.1)	42.9 (42.3, 43.4)	43.4 (43.0, 43.9)*
RV EDAi (cm^2/m^2)	10.3 (10.1, 10.5)	10.4 (10.3, 10.6)	10.4 (10.3, 10.5)	10.7 (10.5, 10.8)*
LAVi (mL/m^2)	24.8 (24.2, 25.5)	25.0 (24.4, 25.5)	25.0 (24.5, 25.5)	25.2 (24.8, 25.6)
LVMi (g/m^2)	78.7 (77.4, 80.1)	78.1 (77.0, 79.2)	76.0 (75.0, 77.0)*	75.8 (74.9, 76.7)*
LV hypertrophy (%)	11.6 (9.1, 14.0)	12.1 (10.0, 14.2)	6.3 (4.9, 7.7)**	8.1 (6.7, 9.5)*
LV EF (%)	65.7 (65.3, 66.2)	65.7 (65.4, 66.1)	66.2 (65.9, 66.5)	65.9 (65.6, 66.2)
Longitudinal LV strain (%)	−17.9 (−18.1, −17.7)	−18.0 (−18.1, −17.8)	−18.3 (−18.4, −18.2)*	−18.3 (−18.4, −18.1)*
RV FAC	0.53 (0.52, 0.53)	0.52 (0.52, 0.53)	0.53 (0.53, 0.54)	0.53 (0.52, 0.53)
TAPSV (cm/s)	11.9 (11.7, 12.1)	12.0 (11.8, 12.2)	12.0 (11.8, 12.1)	12.1 (11.9, 12.2)
E/A ratio	0.84 (0.82, 0.86)	0.83 (0.82, 0.85)	0.85 (0.83, 0.86)	0.86 (0.84, 0.87)
Lateral E/E′ ratio	10.4 (10.1, 10.6)	10.1 (9.9, 10.3)	9.9 (9.7, 10.1)*	9.8 (9.7, 10.0)**
LV diastolic function, *n* (%)				
Normal	32.2 (28.1, 36.4)	34.4 (30.8, 38.0)	37.8 (34.8, 40.9)*	37.9 (35.2, 40.6)*
Mild	32.3 (28.4, 36.3)	31.1 (27.8, 34.4)	29.8 (26.9, 32.8)	29.7 (27.2, 32.3)
Moderate	35.2 (31.0, 39.5)	34.2 (30.7, 37.7)	32.4 (29.5, 35.3)	32.4 (29.9, 34.9)

Values represent adjusted means (95% confidence interval) for continuous variables and adjusted prevalence (95% confidence interval) for categorical variables. Pairwise comparison relative to Persistently Poor Activity group with multivariable regression adjusted for age, gender, race, and centre.
EDAi, end-diastolic area index; EDVi, end-diastolic volume index; EF, ejection fraction; FAC, fractional area change; LAVi, left-atrial volume index; LV, left ventricle; LVMi, left-ventricular mass index; RV, right ventricle; TAPSV, tricuspid annular peak systolic velocity.
*$P < 0.05$.
**$P \leq 0.001$.

cannot rule out the possibility of residual confounding or reverse causality. Measures of cardiac structure and function were only obtained at Visit 5, which also limits conclusions about causality. The questionnaire used to measure physical activity, as a self-reported variable, is subject to recall error and possible over-reporting of activity, which is likely to bias observed associations towards the null. The evaluation of Visit 5 participants in a longitudinal study over 24 years likely introduces a survival bias, and the remaining cohort may represent a more highly active, healthier elderly population than is typical for this age range although sensitivity analysis for attrition showed that findings remained unchanged. We also acknowledge that those in the persistently active group over Visits 3 and 5 may be better evaluated if stratified by persistently ideal or persistently intermediate activity subgroups; however, sensitivity analysis did not demonstrate significant differences between these subgroups.

The strengths of this study include its large size and evaluation of an elderly cohort. This population represents an active elderly population with increasing total physical activity over each visit with approximately half of the sample meeting criteria for ideal LTPA at Visit 5. This increase in physical activity may reflect a secular trend towards more leisure activity, having more time during retirement, or increased reporting of leisure activity at later visits. This population sample of a particularly active older cohort allowed for a more granular assessment of the association of physical activity with various echocardiographic measures. Moreover, we analysed cumulative average LTPA and change in LTPA category over Visits 3 and 5 to further evaluate and strengthen the associations seen by cross-sectional analysis at Visit 5.

In summary, we found that ideal LTPA, higher average levels of LTPA over 24 years, and an improvement in LTPA, even later in life, are associated with better LV diastolic and systolic function. These findings suggest that maintenance of a healthy lifestyle that includes LTPA may help attenuate age-related changes in cardiac structure and function.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

Authors' contributions

S.M.H., B.C.: Performed statistical analysis; A.R.F., S.D.S.: Handled funding and supervision; S.H., K.R.E., S.C., A.M.S.: Acquired the data; S.M.H., A.G., B.C., S.D.S.: Conceived and designed the research; S.M.H., B.C., S.D.S.: Drafted the manuscript; S.M.H., A.G., B.C., K.R.E., S.C., A.M.S., A.R.F., S.D.S.: Made critical revision of the manuscript for key intellectual content.

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