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Change in Physical Activity and Cardiac Structure over 10 Years: The MESA Study

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Abstract

Introduction: Physical activity (PA) is inversely associated with risk of heart failure and cardiovascular disease (CVD), whereas increased left ventricular (LV) mass and mass to volume (M:V) ratio are unfavorable CVD risk factors. We assessed whether changes in leisure-time PA were associated with longitudinal changes in cardiac structure in a community-based population.

Methods: We included 2,779 MESA participants, free of baseline CVD, who had available data on PA and cardiac MRI at Exams 1 (2000-2002) and 5 (2010-2012). PA was measured by a Typical Week PA Survey and converted to MET*min/week of moderate+vigorous activity. We used linear mixed effect models to estimate the associations of baseline and change in PA with baseline and change in cardiac structure, adjusting for CVD risk factors and body size.

Results: At baseline, the mean age was 59 years, 53% were women, and 58% of non-white race/ethnicity. During average 10-year follow-up, and after accounting for baseline PA levels, the highest quintiles of PA increase were significantly associated with increases in LV mass [2.3g (95% CI 0.4, 4.2)], LV end diastolic volume [4.7ml (2.4, 7.0)], and stroke volume [3.3ml (1.6, 5.1), but lower M:V ratio [−2.9 (−5.0, −0.8)], compared to the lowest quintile. Increasing exercise PA was associated with increases in LV diameter and reductions in M:V ratio, whereas

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occupational PA was associated with increases in M:V ratio. Increasing PA over 10-years was also associated with greater risk of eccentric dilated LV hypertrophy at exam 5.

Conclusions: After accounting for baseline PA, greater positive changes in leisure-time PA levels were associated with a more eccentric-type of LV remodeling pattern over 10-years. The clinical implications of such findings remain to be determined.

Keywords

heart failure; prevention; lifestyle; physical activity

Introduction

Adverse cardiac remodeling is independently associated with higher rates of coronary heart disease (CHD), stroke, heart failure (HF), and cardiovascular death (1, 2). Pathological remodeling may be characterized by increases in left ventricular (LV) mass, defined as left ventricular hypertrophy (LVH) or concentric remodeling, defined by relative increased wall thickness in relation to LV diameter. LVH may by further categorized according to LV wall thickness and LV dilation, into 4 tiers, that may have different associations with clinical outcomes (3). LVH and concentric LV remodeling are associated with several traditional risk factors, and there may be modifiable pathways through which these conditions lead to increased cardiovascular events (1, 4, 5). Importantly, studies have demonstrated that reversal of adverse remodeling resulting from therapeutic interventions can reduce the risk of cardiovascular events and mortality in these high-risk populations (6-8)

Physical activity (PA) is a healthy behavior associated with myriad cardiovascular benefits, including lower risk of CHD and HF events. The mechanisms underlying such protective associations are not well understood but may involve changes in cardiac structure and preventions of adverse LV remodeling (9). While prior studies have evaluated cardiac remodeling that occurs in highly trained athletes (10), few have assessed the impact of more modest levels of PA on cardiac structure, in general community-based populations. Moreover, prior community-based studies have been limited to cross-sectional analyses with single assessment of PA and LV structure (11), and/or by the use of echocardiographic data, which is subject to higher inter- and intra-observer variability in LV measurements and is less accurate for the characterization of LV remodeling (12, 13) compared to magnetic resonance imaging (MRI) assessment, which is the gold standard for assessment of cardiac volume, mass and function (14).

For the study presented below, we hypothesized that higher levels of baseline and increases in leisure-time PA would be associated with more pronounced changes in cardiac remodeling over time, as assessed by cardiac MRI. Furthermore, we aimed to assess how various domains of PA may be associated with LV remodeling. Lastly, we use a 4-tier classification of LVH to determine the associations of PA with specific patterns of LV remodeling previously associated with clinical outcomes (3, 15).

Methods

Study Population

The Multi-Ethnic Study of Atherosclerosis (MESA) is a prospective cohort study of U.S. adults from 6 U.S. communities: Forsyth County, North Carolina; Northern Manhattan and the Bronx, New York; Baltimore City and Baltimore County, Maryland; St. Paul, Minnesota; Chicago, Illinois; and Los Angeles, California. Details of the study have been previously described (16). Briefly, MESA enrolled 6,814 men and women between the ages of 45 and 84, from diverse ethnic backgrounds and who were free of clinical cardiovascular disease (CVD) and HF at baseline. Five exams were conducted between the years of 2000 and 2012. All study participants signed written informed consents, and the institutional review boards of each study site approved the study protocols. After excluding participants with incident CVD between Exams 1 and 5 (n=459), those who were missing information on PA (n=19), LV structure and function variables (n=1,658), other covariates of interest (n=51), and 1,848 without follow up cardiac MRI, a total of 2,779 participants who underwent baseline (Exam 1, 2000-2002) and follow up cardiac MRI at Exam 5 (2010-2012) were included in our analyses (see Figure, Supplemental Digital Content 1, Flowchart of the study population with exclusions).

Assessment of Physical Activity

In MESA, leisure time PA was assessed using the MESA Typical Week Physical Activity Survey, which was adapted from the Cross-Cultural Activity Participation Study (17). Participants were asked questions regarding frequency and duration of participation in various activities within a typical week. The questionnaire included nine categories of PA: household chores, lawn/yard/garden/farm, care of children/adults, transportation, walking (not at work), dancing and sports activities, conditioning activities, leisure activities, and occupational and volunteer activities. Additional questions characterized the intensity of each activity as light, moderate, or vigorous. For our main analyses, we derived a variable considering the sum of minutes spent on all moderate and vigorous activities, including occupational activities, as done in prior MESA analyses. We conducted additional analyses considering three domains of PA: exercise (walking not at work, dancing/sports, conditioning, and leisure time activity), occupational, and household (household chores, lawn/yard/garden/farm, and care of children/adults). For the 3 domains of PA, all levels of activity (mild, moderate and vigorous were included. In our primary analyses, PA was categorized as baseline quintiles of PA, as well as quintiles of change in PA between Exams 1 and 5. In supplemental analysis, we also considered quintiles of the average PA levels between Exams 1 and 5. We additionally modeled PA at baseline as well as change in PA between Exams 1 and 5 as continuous variables scaled per 1 standard deviation (SD).

Covariates of Interest

Information about participant’s demographics such as age, sex, race/ethnicity, as well as level of education, was assessed by questionnaire at Exam 1. Other covariates included in our adjustment models were measured at both Exams 1 and 5, and we considered change over time in these factors. Smoking history and medication use were obtained via standardized questionnaires. Additionally, participants were required to bring their

medications to the study visits for inventory. Height and weight were measured by trained clinic staff, and body mass index (BMI) was calculated in kg/m^2. Resting blood pressure was calculated based on the average of the last 2 of 3 measurements. Total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were measured from plasma samples after a 12-hour fast. Estimated glomerular filtration rate (eGFR) was calculated based on serum creatinine levels using the Chronic Kidney Disease Epidemiology Collaboration Equation (18). Diabetes was defined as a fasting serum glucose ≥126 mg/dL, a self-reported history of a physician-diagnosis of diabetes or use of insulin or diabetes medications. High-sensitivity C-reactive protein (CRP) was measured from stored blood samples (from Exam 1 only) using the BNII nephelometer (Dade Behring Inc, Deerfield, IL) at the Laboratory for Clinical Biochemistry Research, University of Vermont, VT. Intra and inter-assay coefficients of variation for CRP have been previously reported (19).

Cardiac Structure and Function

In MESA, data regarding cardiac structure and function were measured from cardiac MRI. MRI studies were performed at both Exams 1 (2000-2002) and 5 (2010-2012), using 1.5 T magnets with a four-element phased-array surface as previously described (1, 20). Cardiac MR images were obtained according to a previously published protocol and included short and long axis cine images (21). Technical changes including MRI scanners and sequences over the 10-year interval were accounted for as described previously (20).

All images were analyzed by trained Technologists at Johns Hopkins University using MASS software ([version 4.2] Medis) and confirmed by an MRI-expert physician. The endocardial and epicardial borders were traced semi-automatically at end-systole and end-diastole and corrected manually. LV end diastolic and systolic volumes were calculated using the summation of areas on each separate sliced multiplied by the sum of slice thickness and image gap, as per the Simpson's rule. LV mass was derived from the sum of the difference between epicardial and endocardial areas, multiplied by slice thickness, plus image gap in the end-diastolic phase multiplied by the specific gravity of myocardium (1.05 g/mL). LV stroke volume was calculated as the difference between LV end diastolic and systolic volumes, and LVEF was calculated as LV stroke volume divided by LV end diastolic volume multiplied by 100. The inter-observed variability, assessed using technical error of measurement percentage of the mean, was: 4.4% for LV end-diastolic volume; 12.8% for end-systolic volume; and 6% for LV mass (21). For our main analyses, we considered the following MRI derived measures as outcomes of interest: LV mass; LV end-diastolic volume; LV stroke volume; LV mass to volume ratio; and LVEF, all modeled as continuous variables. While we did not index these variables to body size, all analyses were conducted with adjustments to height and weight.

We conducted additional analyses considering LVH as the outcome of interest. LVH was defined according to previously published studies as LV mass/height$^{2.7}$ ≥39 g/m$^{2.7}$ for women and ≥48 g/m$^{2.7}$ for men (15). We then further categorized LVH according to previously described measures of concentricity (LV mass/vol$^{0.67}$ ≥ 8.1 g/mL$^{0.67}$ for women and ≥9.1 g/mL$^{0.67}$ for men) and dilation (LV end diastolic volume/body surface area ≥68 mL/m^2 for women and ≥74 mL/m^2 for men) as: eccentric LVH indeterminate (LVH without

either increased concentricity or dilation); eccentric LVH dilated (LVH without increased concentricity but dilation is present); concentric LVH thick (LVH with increased concentricity but no dilation); and LVH thick and dilated (LVH with both increased concentricity and dilation) (15).

Statistical Methods

The baseline (Exam 1) characteristics for the main study population were described as means and standard deviations, and proportions, according to the quintiles of change in PA levels observed in follow-up. We used ANOVA to compare means of continuous variables and the chi square test for categorical variables.

We first evaluated the cross-sectional associations of PA and cardiac structure and function (both assessed at Exam 1) using multivariable adjusted linear regression. Our first model was adjusted for the following baseline variables: age, sex, race/ethnicity, study center, height, weight, education, and smoking status. Model 2 included the variables from Model 1 as well as cardiovascular risk factors, which could be intermediary factors of the associations of PA with cardiac structure and function. Additional variables included in the second model were: waist-hip-ratio, systolic blood pressure, use of anti-hypertensive medications, diabetes, total cholesterol, HDL cholesterol, use of lipid lowering medications, CRP, and eGFR.

We then used multivariable-adjusted linear mixed effects models to evaluate the longitudinal associations of changes in PA from Exam 1 to Exam 5 with changes in cardiac structure and function during the same average 10-year period, after adjusting for baseline PA levels, and baseline and change in the variables listed in Models 1 and 2 described above. We performed these analyses in the overall study population, as well as stratified by pre-specified groups defined by sex and race/ethnicity. We also modeled change in PA as a continuous variable and used adjusted (Model 2) restricted cubic splines to illustrate the continuous association with changes in LV mass. In sensitivity analyses, we assessed the association of the average PA between Exams 1 and 5 and changes in cardiac structure and function over time.

Finally, we conducted additional analyses using adjusted multinomial logistic regression to evaluate the cross-sectional and longitudinal associations of PA with overall and specific patterns of LVH present at Exam 5. For these analyses, PA was modeled as a continuous variable and scaled per 1-SD.

All reported p-values were two-sided, and the level of statistical significance level was set as $p < 0.05$. Statistical analyses were performed using STATA version 14 (StataCorp LP, College Station, Texas).

Results

Baseline (Exam 1) characteristics of the main study population according to quintiles of PA change over follow-up are described in Table 1. Participants in the lowest quintile of PA change had the highest baseline levels of total moderate + vigorous activity (therefore all our longitudinal analyses account for baseline levels of PA). Those in the highest quintile of PA

change were younger and more likely men. There were significant differences in the proportion of race/ethnicities within quintiles of change in PA. Overall, persons performing higher levels of PA had healthier cardiovascular risk profiles with lower BMI, blood pressure, and LDL-cholesterol, and were less likely to have diabetes or to be current smokers, than persons in the lowest quintile of PA. Persons in the lowest and highest quintiles of PA change had the lowest use of anti-hypertensive medications and of lipid-lowering medications.

In cross sectional analyses at baseline, using the lowest quintile of PA as the reference category, we confirmed previously reported findings (11) of a graded association of higher levels of PA and higher LV mass, higher LV end diastolic volume, and higher stroke volume, after adjusting for sociodemographics, smoking, and body size (Table 2, Model 1). Results were essentially unchanged after additional adjustment for CVD risk factors (Model 2). We did not find significant cross-sectional associations between PA and LV mass to volume ratio or ejection fraction.

We then assessed the longitudinal associations of changes in PA (between Exams 1 and 5) with changes in LV structure and function (between Exams 1 and 5), after accounting for baseline PA levels, and baseline and change in covariates. After adjustment for socio-demographics, smoking, and body size (Model 1), persons in the highest quintile of PA increase had greater increases in LV mass [2.2 g (95% CI 0.3, 4.2)], LV end diastolic volume [5.0 ml (2.6, 7.3)], and LV stroke volume [3.5 ml (1.8, 5.2)], but lesser change in LV mass to volume ratio [−3.2 (−5.4, −1.1)] (Table 3), compared to the lowest quintile of PA change. Findings remained similar and statistically significant after further adjustment for CVD risk factors (Model 2). No association was present between changes in PA over time and changes in LV ejection fraction.

In supplemental analysis, we also examined the associations of the average levels of PA between Exams 1 and 5 with the parameters of cardiac structure and function measured at Exam 5 (See Table, Supplemental Digital Content 2, Cross-sectional differences in LV structure and function assessed at Exam 5 associated with average physical activity). Similar positive relationships were seen between higher average PA with higher Exam 5 LV mass, LV end diastolic volume, and LV stroke volume, but the association with mass: volume ratio was no longer statistically significant.

In restricted cubic splines adjusted for baseline PA, we noted a J-shaped association between higher changes in PA and changes in LV mass (Figure 1). Persons with the largest decreases in PA (i.e. negative PA change over 10-years) had a trend towards higher LV mass, but confidence intervals were wide and this did not meet statistical significance. On the other hand, a steep association was noted between higher increases PA levels and increased LV mass.

In analyses stratified by sex, we found the associations of changes in PA and changes in cardiac structure and function were stronger among men, with statistically significant interactions for all cardiac structure/function parameters assessed (Table 4). Among men only, the highest quintile of increases in PA between Exams 1 and 5 was associated with

increases in LV end diastolic volume and LV stroke volume, and decreases in LV mass to volume ratio, whereas in women the highest quintile of PA increase was only associated with increases in LV stroke volume. There were also some statistically significant differences in associations when stratified by race/ethnicity (see Table, Supplemental Digital Content 3, Longitudinal changes in LV structure and function associated with changes in physical activity over a 10-year period, stratified by race/ethnicity); however, in the absence of any *a priori* hypothesis regarding racial differences in cardiac remodeling, these results should be considered exploratory only.

We conducted additional supplemental analyses considering specific domains of PA. In cross-sectional analyses we found similar positive associations of exercise PA with LV mass, LV end diastolic volume and stroke volume, whereas the highest quintile of occupational activity was associated with higher LV mass to volume ratio (see Table, Supplemental Digital Content 4, Cross-sectional associations of baseline specific domains of physical activity and LV structure and function). In longitudinal analyses, we found that higher increases in exercise PA were associated with higher increases LV end diastolic volume and lesser change in LV mass to volume ratio, but no statistically significant associations with LV mass (see Table, Supplemental Digital Content 5, Longitudinal associations of changes in specific domains of physical activity and changes in LV structure and function over an average 10-year period). Conversely, higher increases in occupational activity were associated with modestly lower change in LV mass, LV end diastolic volume, and stroke volume, and mild increases in LV mass to volume ratio. No associations between highest quintile of household activity and LV structure were noted in longitudinal analyses.

There were 89 (3.4%) participants who met criteria for LVH at Exam 5. We did not find an association between baseline or change in PA with LVH (prevalence ratios 1.11, 95% CI 0.91, 1.35 and 1.22, 95% CI 0.97, 1.54, respectively). When considering specific patterns of LVH, we found that high increases in PA over 10-years were associated with a greater risk of having eccentric dilated LVH at Exam 5 (relative risk ratio 1.40, 95% CI 1.08, 1.82), but not the other forms of LVH (see Table, Supplemental Digital Content 6, Patterns of LV remodeling at Exam 5 associated with changes in physical activity over a 10-year period, among participants without LVH at baseline).

Discussion

In this ethnically-diverse community-based sample from MESA, we found that higher average PA levels and higher PA increase over an average 10-year period were associated with increases in LV mass and LV end-diastolic volume resulting in a lesser change in LV mass to volume ratio and increases in stroke volume. Additionally, increasing PA over 10-years was associated with a greater prevalence of eccentric, dilated LVH at the follow-up visit. These findings were independent of traditional cardiovascular risk factors such as age, hypertension, and the presence of diabetes. They were also stronger among men compared to women. We additionally found that while increases in exercise PA were associated with increase in LV volume without significant changes in LV mass (leading to lower LV mass to volume ratio), occupational PA showed opposite associations with increases in LV mass to volume ratio. Our findings suggest significant and complex associations of baseline and

changes in leisure time PA with changes in cardiac structure, which may be a pathway through which PA leads to reduced cardiovascular events.

Several studies have demonstrated an association between higher levels of PA and lower risk of cardiovascular events (22), including HF (23). The mechanisms underlying the associations of PA and reduced risk of HF are complex and incompletely understood. Several have speculated that changes in cardiac structure and preservation of normal diastolic and systolic functions may play important roles. Few studies have tried to address whether higher levels of leisure-time PA are associated with changes in cardiac structure and function, and these prior studies have yielded conflicting results. Cross-sectional data from the Framingham Heart Study showed an association of higher values of PA with lower vascular stiffness and higher LV mass among middle-aged adults (24). These findings contrast with a recent study from the Atherosclerosis Risk in Communities (ARIC) Study where higher levels of PA were associated with lower LV mass index and lower prevalence of LVH among elderly participants (9). Such studies have been limited by single assessments of cardiac structure and function as well as limitations of echocardiographic data, in particular with regard to the assessment of LV mass.

To our knowledge this is the first study to demonstrate the longitudinal associations of changes in leisure-time PA and with changes in LV structure parameters as measured by cardiac MRI, which is considered the gold standard method for assessment of LV structure. Our data add to a cross-sectional prior report from MESA linking PA with cardiac structural parameters (11) by now assessing continued cardiac remodeling over 10-years associated with PA. We additionally demonstrate that various domains of PA may be associated with different patterns of LV remodeling. While exercise activity may be associated with LV dilation without changes in LV mass leading to reduced mass to volume ratio, occupational activity was associated with increased LV mass to volume ratios. Such differences in patterns of LV remodeling could have important clinical implications and affect PA prescription in the clinical practice. Indeed, prior data from MESA has associated higher LV mass to volume ratio, defined as concentric remodeling, with increased risk of coronary heart disease and stroke (1).

Furthermore, by using a 4-tier classification of LVH, we were able to demonstrate an association between higher PA over 10-years and a later life prevalence of eccentric dilated LVH. Prior studies have demonstrated an association between dilated eccentric LVH and elevated markers of myocardial injury and stress, as well as adverse clinical outcomes (3, 15). However, there are important differences between the populations between various studies, with the current study having a healthier population that was free of CVD and HF at baseline. It is also possible that LVH resulting from higher PA may have different prognostic implications compared to LVH resulting from hypertension or aging. As such, the clinical implications of our findings remain to be determined. Given the protective associations of PA with CVD, it is conceivable that such modest eccentric changes in LV structure in the context of higher PA may be associated with favorable clinical outcomes.

In the current study, changes in LV structure were more prominent among men than women, and some differences were noted by race/ethnicity as well; of which these findings should be

considered exploratory only. It is important to mention that we may not have had sufficient power to detect significant differences in the outcomes in these subgroup analyses. Furthermore, we cannot exclude that some of these findings may have been related to chance due to multiple testing. Nonetheless, these results are in line with prior reports of differences in cardiac remodeling associated with exercise according to sex and race/ethnicity (11, 25-27). Further studies are needed to better understand these findings.

Limitations of the current study include its observational nature yielding the possibility of unmeasured and residual confounding, and as such, causality of these associations cannot be determined. Additionally, PA was self-reported with the use of a semi-quantitative questionnaire, which could be associated with reporting bias and measurement error. This analysis included only participants who underwent MRI at both Exam 1 and 5, and there may be bias due to attrition during study. Nevertheless, our study has many important strengths including the use of data from a diverse well-characterized community-based sample, with repeated measures of PA over 10-years, and ability to update confounding covariates over-time. Additionally, LV structure parameters were measured by the gold standard cardiac MRI.

In summary, the present study shows higher levels of moderate + vigorous PA and higher increases in PA over time are associated with modest increases in LV mass, LV volume, and LV mass to volume ratio, as well as with a greater risk of eccentric dilated LVH in later life. Various domains of PA may have different associations with LV remodeling. The clinical implications of such findings remain to be determined.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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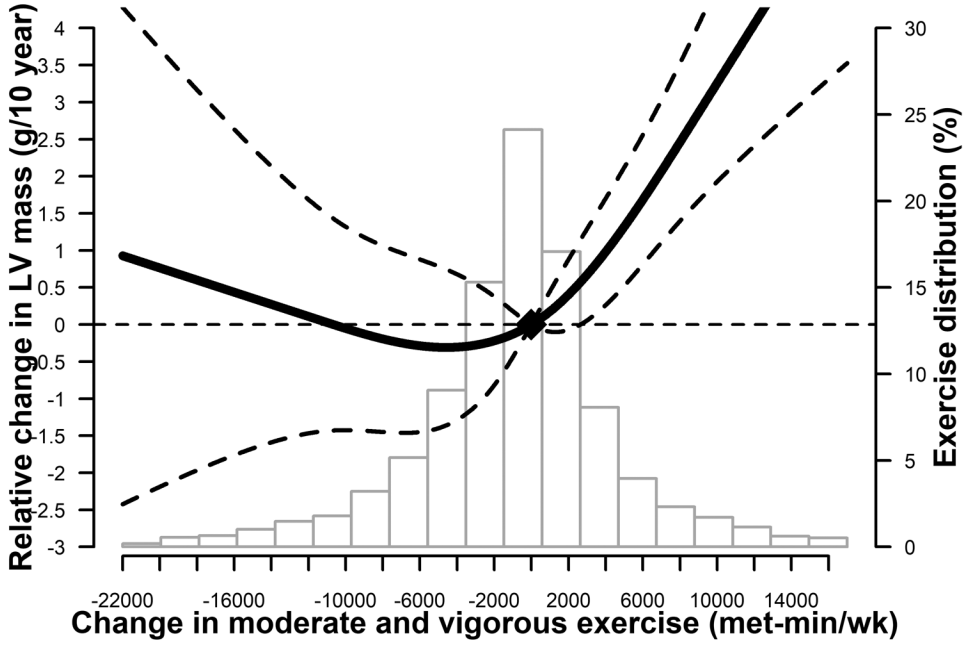

Figure 1.

Adjusted change in LV mass (g) associated with change in levels of moderate and vigorous exercise from Exam 1 to 5: the MESA study (2000-2012).

* The curves represent the adjusted longitudinal changes in LV mass (g, solid line) and their 95% confidence intervals (dashed lines) based on restricted cubic splines for exercise levels change (moderate and vigorous combined) from visit 5 to visit 1 (mean of 10 years) with knots at 5th, 35th, 65th and 95th percentiles and constrained to be 0 at baseline. Results were obtained from linear mixed models with random variations in baseline LV mass levels, and adjusted for baseline exercise levels (restricted cubic splines), sex, race/ethnicity, study center, education, CRP, and baseline levels and changes over time in age, cigarette smoking, height, weight, waist-to-hip ratio, systolic blood pressure, use of hypertension medication, total cholesterol, HDL cholesterol, use of lipid lowering medication, diabetes status, and eGFR.

Table 1.

Characteristics of the study population at Exam 1 (2000-2002) by quintiles of PA (MET*min/week) change over follow up

	1st quintile (−50550, −4350) (n=552)	2nd quintile (−4338, −1438) (n=556)	3rd quintile (−1433, 275) (n=546)	4th quintile (278, 2545) (n=570)	5th quintile (2550, 74250) (n=555)
Age, years	59.1 (9.5)	60.3 (9.9)	60.4 (9.5)	59.8 (8.6)	57.0 (8.5)
Men	275 (49.8)	239 (43.0)	219 (40.1)	268 (47.0)	293 (52.8)
Race/Ethnicity					
White	181 (32.8)	251 (45.1)	241 (44.1)	273 (47.9)	219 (39.5)
Chinese-American	42 (7.6)	66 (11.9)	91 (16.7)	92 (16.1)	69 (12.4)
Black	164 (29.7)	146 (26.3)	108 (19.8)	107 (18.8)	158 (28.5)
Hispanic	165 (29.9)	93 (16.7)	106 (19.4)	98 (17.2)	109 (19.6)
Education					
<High school	88 (15.9)	58 (10.4)	73 (13.4)	65 (11.4)	60 (10.8)
High school, technical school, or associate degree	309 (56.0)	243 (43.7)	219 (40.1)	216 (37.9)	262 (47.2)
College, graduate or Professional school	155 (28.1)	255 (45.9)	254 (46.5)	289 (50.7)	233 (42.0)
Smoking					
Never	293 (53.1)	282 (50.7)	300 (54.9)	306 (53.7)	292 (52.6)
Former	186 (33.7)	208 (37.4)	192 (35.2)	201 (35.3)	199 (35.9)
Current	73 (13.2)	66 (11.9)	54 (9.9)	63 (11.1)	64 (11.5)
Height, cm	167.1 (9.4)	167.1 (9.9)	166.0 (9.9)	166.8 (9.8)	168.2 (9.9)
Weight, lb	174.9 (35.1)	171.3 (35.2)	168.5 (36.2)	167.2 (34.9)	172.6 (35.4)
Waist to hip ratio	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)
BMI, kg/m^2	28.3 (4.9)	27.7 (4.9)	27.7 (5.2)	27.1 (4.6)	27.6 (4.8)
Systolic BP, mm Hg	123.1 (18.0)	123.4 (19.7)	123.4 (21.3)	122.6 (21.4)	120.8 (19.0)
Diastolic BP, mm Hg	72.2 (9.5)	71.6 (10.2)	71.1 (10.4)	71.5 (10.6)	72.0 (10.1)
Total cholesterol, mg/dl	198.5 (35.6)	193.1 (37.1)	194.5 (33.3)	193.2 (36.3)	191.8 (32.9)
HDL cholesterol, mg/dl	50.6 (14.8)	51.6 (14.2)	52.2 (14.6)	52.7 (16.9)	50.4 (13.9)
LDL cholesterol, mg/dl	121.7 (30.3)	116.2 (31.9)	116.4 (30.0)	115.1 (32.7)	116.6 (30.4)
Triglycerides, mg/dl	128.8 (73.9)	126.1 (75.8)	130.6 (74.5)	129.6 (79.2)	125.0 (67.9)

	1st quintile (−50550, −4350) (n=552)	2nd quintile (−4338, −1438) (n=556)	3rd quintile (−1433, 275) (n=546)	4th quintile (278, 2545) (n=570)	5th quintile (2550, 74250) (n=555)
eGFR, mL/min/1.73 m2	81.6 (15.3)	78.6 (15.4)	77.6 (14.6)	77.7 (14.5)	81.4 (14.3)
CRP, mg/l **	1.7 (0.8 - 4.0)	1.9 (0.8 - 4.4)	1.8 (0.8 - 4.3)	1.7 (0.7 - 3.9)	1.6 (0.7 - 3.4)
Antihypertensive medication	148 (26.8)	195 (35.1)	186 (34.1)	171 (30.0)	155 (27.9)
Lipid lowering medication	54 (9.8)	99 (17.8)	82 (15.0)	94 (16.5)	81 (14.6)
Diabetes	55 (10.0)	53 (9.5)	43 (7.9)	46 (8.1)	39 (7.0)
Total intentional exercise, MET*min/week **	11010 (8186 - 16526)	4867.5 (3638 - 6585)	2719 (1665 - 4680)	2261 (1275 - 4230)	3510 (1913 - 6210)
LV mass, g	124.2 (29.7)	118.7 (28.0)	115.3 (26.5)	117.3 (26.7)	122.6 (29.6)
LV end diastolic volume, ml	132.9 (30.8)	128.1 (28.0)	126.8 (28.7)	128.2 (26.9)	134.3 (29.5)
LV stroke volume, ml	82.1 (19.7)	80.6 (18.7)	80.0 (19.3)	80.2 (17.7)	83.9 (19.2)
LV mass to volume ratio, g/ml, (x100, expressed as %)	94.9 (18.0)	93.9 (17.8)	92.1 (15.7)	92.4 (15.8)	92.2 (16.0)
LV ejection fraction, %	61.9 (6.2)	63.0 (5.7)	63.1 (5.5)	62.6 (5.8)	62.6 (5.5)

*Data are presented as means and standard deviations, or numbers and proportion (%).

**Data presented as median and inter-quartile range.

¶BMI = body mass index; BP = blood pressure; HDL = high-density lipoprotein; LDL = low-density lipoprotein; eGFR = estimated glomerular filtration rate; CRP = C-reactive protein; MET = metabolic equivalent of task; LV = left ventricle.

Table 2:

Cross-sectional differences in LV structure and function associated with baseline (Exam 1) physical activity: the MESA study (2000-2002)

Physical Activity, MET*min/week	LV mass, g	LV end diastolic volume, ml	LV stroke volume, ml	LV mass-to-volume ratio, g%/ml	LV ejection fraction, %
Model 1					
Quintile 1 (n=552)	Reference (0)	Reference (0)	Reference (0)	Reference (0)	Reference (0)
Quintile 2 (n=556)	0.21 (−1.93, 2.35)	−0.20 (−2.64, 2.25)	0.16 (−1.43, 1.75)	0.28 (−1.53, 2.10)	0.23 (−0.38, 0.84)
Quintile 3 (n=546)	1.78 (−0.38, 3.95)	1.80 (−0.68, 4.28)	1.22 (−0.39, 2.83)	0.28 (−1.57, 2.13)	0.08 (−0.54, 0.69)
Quintile 4 (n=570)	**3.03 (0.86, 5.19)**	**4.26 (1.79, 6.74)**	**2.80 (1.18, 4.41)**	−0.84 (−2.68, 1.01)	0.08 (−0.54, 0.70)
Quintile 5 (n=555)	**4.11 (1.86, 6.37)**	**4.02 (1.44, 6.61)**	**2.48 (0.79, 4.18)**	0.13 (−1.82, 2.08)	0.04 (−0.61, 0.70)
Model 2					
Quintile 1 (n=552)	Reference (0)	Reference (0)	Reference (0)	Reference (0)	Reference (0)
Quintile 2 (n=556)	0.15 (−1.87, 2.17)	−0.36 (−2.75, 2.03)	0.03 (−1.52, 1.58)	0.36 (−1.39, 2.10)	0.21 (−0.39, 0.81)
Quintile 3 (n=546)	1.85 (−0.19, 3.90)	1.74 (−0.68, 4.17)	1.16 (−0.41, 2.73)	0.38 (−1.40, 2.15)	0.07 (−0.54, 0.68)
Quintile 4 (n=570)	**3.31 (1.26, 5.36)**	**3.98 (1.55, 6.40)**	**2.72 (1.14, 4.30)**	−0.36 (−2.14, 1.43)	0.16 (−0.45, 0.78)
Quintile 5 (n=555)	**4.18 (2.03, 6.32)**	**3.70 (1.16, 6.25)**	**2.41 (0.75, 4.08)**	0.44 (−1.45, 2.33)	0.13 (−0.53, 0.78)

*Baseline (Exam 1) PA quintile range in MET*min/week: Quintile 1: 0 – 1695; Quintile 2: 1700 – 3195; Quintile 3: 3202 – 5220; Quintile 4: 5228 – 8760; Quintile 5: 8775 – 103320.

**Values are beta coefficients obtained from multivariable adjusted linear regression models. Results in bold font are statistically significant at $p<0.05$.

¶Model 1: Adjusted for baseline age, sex, race/ethnicity, study center, education, cigarette smoking, height, and weight.

‡Model 2: Adjusted for Model 1 + baseline waist-to-hip ratio, systolic blood pressure, use of hypertension medication, total cholesterol, HDL cholesterol, use of lipid lowering medication, diabetes, CRP, and eGFR.

Table 3:

Longitudinal changes in LV structure and function associated with changes in physical activity over an average 10-year period (from Exam 1 to Exam 5): the MESA study (2000-2012)

	LV mass, g	LV end diastolic volume, ml	LV stroke volume, ml	LV mass-to-volume ratio, g%/ml	LV ejection fraction, %
Model 1					
Quintile 1 (n=552)	Reference (0)	Reference (0)	Reference (0)	Reference (0)	Reference (0)
Quintile 2 (n=556)	−0.03 (−1.99, 1.93)	**2.41 (0.10, 4.72)**	1.69 (−0.02, 3.41)	−2.06 (−4.17, 0.05)	0.48 (−0.25, 1.21)
Quintile 3 (n=546)	−0.28 (−2.27, 1.71)	**2.59 (0.25, 4.93)**	**2.16 (0.41, 3.90)**	**−2.66 (−4.81, −0.51)**	0.57 (−0.18, 1.31)
Quintile 4 (n=570)	0.41 (−1.57, 2.39)	**3.55 (1.22, 5.89)**	**2.89 (1.14, 4.63)**	**−2.75 (−4.90, −0.60)**	0.66 (−0.08, 1.41)
Quintile 5 (n=555)	**2.22 (0.25, 4.19)**	**4.96 (2.64, 7.28)**	**3.49 (1.76, 5.21)**	**−3.23 (−5.35, −1.11)**	0.41 (−0.32, 1.14)
Model 2					
Quintile 1 (n=552)	Reference (0)	Reference (0)	Reference (0)	Reference (0)	Reference (0)
Quintile 2 (n=556)	0.46 (−1.44, 2.36)	**2.69 (0.40, 4.98)**	**1.84 (0.14, 3.55)**	−1.96 (−4.04, 0.12)	0.43 (−0.30, 1.15)
Quintile 3 (n=546)	−0.23 (−2.16, 1.69)	**2.53 (0.21, 4.85)**	**2.10 (0.37, 3.83)**	**−2.64 (−4.76, −0.52)**	0.51 (−0.23, 1.25)
Quintile 4 (n=570)	0.80 (−1.11, 2.72)	**3.46 (1.14, 5.77)**	**2.76 (1.03, 4.49)**	**−2.39 (−4.51, −0.27)**	0.58 (−0.16, 1.32)
Quintile 5 (n=555)	**2.25 (0.35, 4.16)**	**4.67 (2.36, 6.97)**	**3.34 (1.63, 5.05)**	**−2.91 (−5.00, −0.81)**	0.41 (−0.33, 1.14)

*Rage of quintile of change in PA from Exam 1 to Exam 5, in MET*min/week: Quintile 1: −50550 – −4350; Quintile 2: −4337.5 – −1437.5; Quintile 3: −1432.5 – 275; Quintile 4: 277.5 – 2545; Quintile 5: 2550 – 74250.

**Values are beta coefficients obtained from linear mixed models with random variation variations in baseline LV structural variables across participants. Results in bold font are statistically significant at $p<0.05$.

¶Model 1: Adjusted for baseline PA, sex, race/ethnicity, study center, education, and baseline & changes over time in age, cigarette smoking, height, and weight.

ǂModel 2: Adjusted for Model 1 + for baseline CRP, and baseline levels & changes over time in waist-to-hip ratio, systolic blood pressure, use of hypertension medication, total cholesterol, HDL cholesterol, use of lipid lowering medication, diabetes, and eGFR.

Table 4:

Longitudinal changes in LV structure and function associated with changes in physical activity over a 10-year period (from Exam 1 to Exam 5), stratified by sex

	LV mass, g	LV end diastolic volume, ml	LV stroke volume, ml	LV mass-to-volume ratio, g%/ml	LV ejection fraction, %
Men					
Quintile 1 (n=393)	Reference (0)	Reference (0)	Reference (0)	Reference (0)	Reference (0)
Quintile 2 (n=409)	0.51 (−2.61, 3.64)	**5.38 (1.38, 9.38)**	**2.95 (0.09, 5.82)**	**−3.70 (−7.12, −0.28)**	0.08 (−1.03, 1.18)
Quintile 3 (n=398)	1.47 (−1.74, 4.68)	3.88 (−0.23, 7.99)	2.32 (−0.63, 5.27)	−1.81 (−5.35, 1.74)	0.11 (−1.04, 1.25)
Quintile 4 (n=431)	1.46 (−1.61, 4.53)	**3.95 (0.01, 7.89)**	2.28 (−0.56, 5.12)	−1.04 (−4.45, 2.37)	0.07 (−1.03, 1.18)
Quintile 5 (n=506)	2.90 (−0.08, 5.87)	**6.61 (2.80, 10.42)**	**4.10 (1.37, 6.84)**	**−3.46 (−6.72, −0.19)**	−0.07 (−1.12, 0.99)
Women					
Quintile 1 (n=537)	Reference (0)	Reference (0)	Reference (0)	Reference (0)	Reference (0)
Quintile 2 (n=518)	1.21 (−0.93, 3.34)	0.37 (−2.12, 2.86)	0.70 (−1.28, 2.69)	−0.07 (−2.54, 2.40)	0.59 (−0.37, 1.55)
Quintile 3 (n=522)	−0.21 (−2.35, 1.93)	1.05 (−1.45, 3.54)	1.40 (−0.60, 3.40)	−2.24 (−4.73, 0.25)	0.68 (−0.29, 1.65)
Quintile 4 (n=495)	0.73 (−1.47, 2.92)	**2.66 (0.10, 5.22)**	**2.82 (0.77, 4.87)**	**−2.99 (−5.54, −0.43)**	0.90 (−0.09, 1.90)
Quintile 5 (n=418)	1.46 (−0.79, 3.71)	2.12 (−0.51, 4.75)	**2.27 (0.18, 4.37)**	−2.03 (−4.63, 0.58)	0.92 (−0.09, 1.93)
P-interaction	**<0.001**	**0.01**	0.53	**<0.001**	**<0.001**

*Values are beta coefficients obtained from linear mixed effects models with random variation variations in baseline LV structural variables across participants. Results in bold font are statistically significant at p<0.05.

**Adjusted for baseline PA, race/ethnicity, study center, education, and baseline & changes over time in age, cigarette smoking, height, weight, baseline CRP, waist-to-hip ratio, systolic blood pressure, use of hypertension medication, total cholesterol, HDL cholesterol, use of lipid lowering medication, diabetes, and eGFR.