Pre-stroke physical activity and adverse health outcomes after stroke in the Atherosclerosis Risk in Communities study

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Abstract

Background and Purpose: The association of physical activity (PA) prior to stroke (pre-stroke PA) with long-term prognosis after stroke is still unclear. We examined the association of pre-stroke PA with adverse health outcomes in the Atherosclerosis Risk in Communities (ARIC) study.

Methods: We included 881 participants with incident stroke occurring between 1993–1995 (visit 3) and December 31st, 2016. Follow-up continued until December 31st, 2017 to allow for at least 1-year after incident stroke. Pre-stroke PA was assessed using a modified version of the Baecke questionnaire in 1987–1989 (visit 1) and 1993–1995 (visit 3), evaluating PA domains (work, leisure and sports) and total PA. We used Cox proportional hazards models to quantify the association between tertiles of accumulated pre-stroke PA levels over the 6-year period between visits 1 and 3, and mortality, risk of cardiovascular disease and recurrent stroke after incident stroke.

Results: During a median follow-up of 3.1 years after incident stroke, 676 (77%) participants had adverse outcomes. Highest pre-stroke total PA was associated with decreased risks of all-cause

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mortality (HR 0.78, 95%CI 0.63–0.97) compared to lowest tertile. In the analysis by domain-specific PA, highest levels of work PA were associated with lower risk for all-cause (HR 0.77, 95%CI 0.62–0.96) and cardiovascular mortality (0.45, 0.29–0.70), and highest levels of leisure PA were associated with lower all-cause mortality (HR 0.72; 95%CI 0.58 to 0.89) compared to lowest tertile of PA. No significant associations for sports PA were observed.

Conclusions: Higher levels of total pre-stroke PA as well as work and leisure PA were associated with lower risk of mortality after incident stroke. Public health strategies to increase lifetime PA should be encouraged to decrease long-term mortality after stroke.

Keywords

Stroke; Physical Activity; Work; Leisure; Sports; Mortality; Cardiovascular disease

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Physical activity (PA) is important for primary and secondary prevention of cardiovascular disease (CVD), including stroke [1–3]. A meta-analysis of prospective cohort studies reported >16% reduction in the relative risk for stroke among physically active individuals (>600 MET-minutes/week) [4]. Moreover, studies demonstrated associations between PA after stroke and better clinical and functional outcomes, as well as lower mortality rates [5], reinforcing the importance of PA not only for stroke prevention, but also as a therapeutic strategy [6].

Compared to established contributions of PA to primary and secondary prevention of stroke, it is less clear whether PA prior to stroke (pre-stroke PA) is associated with long-term prognosis after incident stroke. The few studies that examined the association of pre-stroke PA on outcomes after stroke were retrospective and based on self-reported information at stroke admission, increasing the possibility of recall bias and underrepresentation of the most severely affected patients[7]. Moreover, most evaluated a single measurement of PA focused in one domain, usually leisure-time or sports PA, which can result in misclassifications of total PA levels since an increase in PA in one domain may be compensated by decreased activity in other domains[8]. Also, most studies reported only short-term outcomes, usually functional outcomes, but not mortality and CVD events, leaving uncertainty regarding long-term associations between PA and post-stroke outcomes[9, 10]. To address these caveats, we examined the association of pre-stroke PA with adverse outcomes after stroke in the Atherosclerosis Risk in Communities (ARIC) study. The prospective design of the ARIC study and availability of repeated PA measurements, together with strict clinical outcomes monitoring provides an opportunity to address this gap in the literature.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Participants

ARIC is a prospective cohort study designed to investigate the major CVD risk factors[11]. A total of 15,792 individuals aged 45–64 years were recruited in 1987–1989 (visit 1) from four different US communities: Washington County, Maryland; Jackson, Mississippi; Forsyth

County, North Carolina; and suburbs of Minneapolis, Minnesota. After visit 1, six subsequent visits have been completed (1990–92, 1993–95, 1996–98, 2011–13, 2016–17 and 2018–19). In addition, follow-up telephone calls have been conducted annually until 2012 and semiannually afterwards. All participants provided written informed consent at each examination and the Institutional Review Board at each site approved the study. Staffs were trained and certified to all data collection procedures, as previously described[11].

A total of 12,887 individuals participated in visit 3. We excluded those with history of stroke before visit 3 (n=252) and those with missing information on PA (n=525). We also excluded participants neither white nor black (n=38), and those black participants from the Minnesota and Washington County centers (n=41) owing to small numbers, resulting in 12,031 participants. Among those, 881 incident stroke events were reported between visit 3 (1993–95) and December 31st, 2016: 807 ischemic stroke, 89 intracerebral hemorrhage and 22 subarachnoid hemorrhage. Stroke was defined as a sudden or rapid onset of neurologic symptoms lasting >24 hours or leading to death, in the absence of evidence for a non-stroke cause. In ARIC, hospitalizations with discharge codes of cerebrovascular disease (ICD-9 codes 430 to 438 until 1997, ICD-9 codes 430 to 436 afterwards and ICD-10 codes I60 to I67, I69, G45) are identified, hospital charts are reviewed and events validated as stroke are further adjudicated by trained study physicians as ischemic or hemorrhagic stroke. The present analysis includes events defined as definite or probable strokes[12, 13].

Pre-Stroke PA

Pre-stroke PA was assessed using an interviewer administered modified version of the Baecke questionnaire at visits 1 and 3, that is easy to administrate and demonstrated good reliability and validity properties for both male and female subjects, similar to many other physical activity instruments[14, 15]. The questionnaire consisted of 16 items to evaluate habitual PA in the previous 12 months, through a score ranging from 1 (low) to 5 (high) for each item, in 3 different PA domains (work, leisure, and sports)[15].

Work PA score was determined from the mean score of 8 questions that addressed main occupation, time spent during different work activities such as sitting, standing, walking or carrying heavy loads, fatigue after work, sweat during work activities and a comparison with other people of the same age regarding physical effort at work. Unemployed individuals were given a work score of 1.0. Leisure PA (that included only non-sports activities) was derived from the mean score of 4 questions related to watching television (scored inversely), walking, bicycling and walking/biking to work, school or shopping. Sports PA was assessed from the mean score of 4 questions: one question about frequency, duration and intensity of up to four sports activities and 3 questions on the frequency of sweating, the general frequency of playing sports, and a self-rating of the amount of PA compared with others of same age. The sum of the scores obtained in each domain (work, leisure and sports) determined the total score of PA[15, 16]. To comprehensively characterize pre-stroke PA levels over the 6-year period between the visits, accumulated scores for total and domain-specific PA were created by summing up PA scores at visit 1 and 3. Exposures were categorized by tertiles of the accumulated PA scores. In addition, to examine the pattern of changes in pre-stroke PA during this period, PA levels at visits 1 and 3 (total and domain-specific PA) were

divided into tertiles for each visit and four different cross-categories were generated[17]: stable low PA (lowest tertile at visit 1 and lowest tertile at visit 3); decreasing PA (intermediate/highest tertiles at visit 1 and lowest tertile at visit 3); increasing PA (lowest tertile at visit 1 and intermediate/highest tertile at visit 3); and stable high PA (intermediate/highest tertiles at visit 1 and intermediate/highest tertile at visit 3).

Definition of Outcomes

The outcomes of interest were post-stroke mortality (all-cause and CVD mortality including stroke, myocardial infarction [MI], coronary heart disease [CHD] and heart failure [HF] deaths), risk of CVD (incidence of MI/HF after stroke or recurrent stroke), risk of recurrent stroke and a composite outcome including all the above. CVD events and death in ARIC were ascertained through annual and semiannual telephone calls, as well as identification of potential CVD events in hospitalization reports and death certificates[11]. Events subsequent to an incident stroke adjudicated as definite or probable stroke or MI[18, 19] were categorized as recurrent CVD. Incident HF after stroke was defined as hospitalization based on ICD-9 code 428 or ICD-10 code I50 in any position on the medical record [20]. The follow-up time was measured from the time of incident stroke until occurrence of the study outcome, the time of final participant contact (including lost to follow-up, at which point follow-up was censored), or until the administrative censoring on December 31st, 2017, allowing for at least 1-year of follow-up after incident stroke.

Covariates

Covariates were collected at ARIC visits, annual and semi-annual telephone calls, and abstracted medical records from the incident stroke admission and included age at incident stroke, sex, race/ARIC field center, elapsed time from visit 3 to incident stroke, atrial fibrillation at incident stroke, medical history (e.g. time-varying history of hypertension, diabetes, CHD, HF, peripheral artery disease, and chronic kidney disease), medication use (e.g., antihypertensive and antidiabetic medication), body mass index (BMI), and smoking status. For time-varying variables, a data point closest to incident stroke was used for each participant[11, 21]. A combined race/ARIC field center variable was generated because of the disparate distribution of race groups across the ARIC centers. Smoking status was reported within a year prior to incident stroke or from the last ARIC visit for those with missing information for this timeframe (n=162).

Statistical Analysis

Characteristics of participants were presented as mean (standard deviation) for continuous variables or frequencies (percentages) for categorical variables. P-values for trend were based on a nonparametric test across tertiles of accumulated pre-stroke total PA score (nptrend in Stata). Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between tertiles (highest and intermediate vs lowest) of 6-year accumulated pre-stroke total- and domain-specific PA scores with each outcome, adjusting for age at incident stroke, sex and race/ARIC field center (model 1). Additional models were fitted adjusting for time to incident stroke, hypertension, diabetes, CHD, HF, peripheral artery disease, chronic kidney disease, atrial fibrillation at stroke, smoking status (current vs non-current), and the average of BMI at

ARIC visit 1 and 3 (model 2). Tests for linear trends were performed by modeling accumulated total and domain-specific scores of pre-stroke PA as a continuous variable for the Cox regression models. Further analyses evaluating the associations between the 6-year cross-categories of pre-stroke total and domain-specific PA scores with adverse health outcomes were also performed.

Sensitivity analyses were conducted to examine the association between pre-stroke PA and adverse outcomes including only participants with ischemic stroke and considering adverse outcomes at 1-year, 3-year, and 5-year after stroke, and among those who developed incident stroke within 5 years after ARIC visit 3. Data analyses were performed using Stata 14.2 (College Station, Texas) and statistical significance was set at 2-tailed p-value of <0.05 for all analyses.

RESULTS

Participants in the highest tertile of accumulated pre-stroke total PA were more likely to be men, white, have longer elapsed time between ARIC visit 3 and incident stroke, lower BMI and lower prevalence of hypertension, diabetes, and peripheral artery disease compared to those in the lowest tertile (Table 1). Considering the pattern of changes on pre-stroke PA, most participants presented high total PA scores at both study visits (n=439; 49.8%). Detailed information on the pre-stroke PA cross-categories is described in the Supplemental Table I.

During a median (25%–75%) follow-up of 3.1 (0.8–7.2) years after incident stroke, 676 cases of composite outcomes, 588 deaths (161 attributed to CVD), 153 cases of recurrent stroke and 374 cases of CVD were reported. The number of CVD events during follow-up were 258 HF, 153 recurrent stroke, and 91 MI. The associations between tertiles of accumulated pre-stroke total PA and adverse health outcomes are presented in Table 2. Compared to those in the lowest tertile, participants in the highest pre-stroke PA tertile experienced lower risk of all-cause mortality. No statistically significant associations were observed for the composite outcome, CVD mortality, CVD, and recurrent stroke.

Results on associations between tertiles of pre-stroke domain-specific PA and adverse health outcomes are shown in Table 3. Higher tertile of accumulated pre-stroke work PA was associated with a lower risk of all-cause mortality and CVD mortality. Statistically significant lower risk was also found for the composite outcome and CVD mortality in the intermediate tertile compared with the lowest tertile. For pre-stroke leisure PA domain, high and intermediate PA levels were associated with lower risk of all-cause mortality, and intermediate PA levels was associated with lower recurrent stroke, with no significant association for other outcomes. Accumulated pre-stroke sports PA did not demonstrate significant associations with any outcome. The cumulative incidence of adverse health outcomes after stroke by tertiles of accumulated pre-stroke total PA scores are illustrated in Figure 1. The results were similar when including only participants with ischemic stroke (Supplemental Tables II and III).

The associations between cross-categories of pre-stroke total and adverse health outcomes are depicted in Supplemental Table IV. Compared to those in the stable low total PA category, participants in the stable high total PA category experienced lower rates of CVD mortality, whereas no statistically significant associations were observed for the composite outcome, all-cause mortality, CVD, and recurrent stroke. No statistically significant associations with outcomes were observed for the other total PA cross-categories. Considering domain-specific PA categories, participants that maintained high work PA scores demonstrated a lower risk of composite outcome, all-cause mortality, CVD mortality, and CVD. Stable high and increased leisure PA were consistently associated with lower risk of all-cause mortality. Cross-categories of sports PA score demonstrated a significant association between decreased PA and all-cause mortality (Supplemental Table V). Similar results were observed when including only participants with ischemic stroke (Supplemental Tables VI and VII).

Sensitivity analyses exploring the association between accumulated pre-stroke PA and adverse outcomes at 1-year, 3-year, and 5-year after incident stroke, and among those who developed incident stroke within 5 years after ARIC visit 3 showed more consistent associations for longer follow-up periods, especially for work PA domain (Supplemental Tables VIII and IX).

DISCUSSION

The present study demonstrates association between higher levels of accumulated 6-year pre-stroke PA levels with all-cause mortality reduction, with a significant dose-response relationship across tertiles of total PA. These results are consistent with those observed by Bell et al.[22] who found 39% greater mortality in older women that did not perform PA before the stroke, compared to those who performed >150 minutes/week of exercise. More recently, Wen et al.[23] demonstrated that 30 minutes of daily PA, 3 days/week over 6 months was associated with lower in-hospital mortality and better clinical outcomes in a prospective cohort of Taiwanese stroke patients. Conversely, a study conducted by Decourcelle et al.[24] did not support the positive influence of previous PA on mortality at 3-months in an observational multicenter study including patients treated with thrombolytic therapy by intravenous recombinant tissue-plasminogen activator at the acute ischemic stroke.

Although PA has been associated with improvement in traditional risk factors for CVD[25–27], which could lead to a reduction in the risk of recurrent stroke and CVD in stroke patients, our findings do not suggest the same beneficial influence of pre-stroke PA. Similarly, Krarup et al.[28] followed 265 ischemic stroke patients during 2 years and found no significant association between pre-stroke PA level and recurrent stroke or CVD. A possible decrease in total PA levels after stroke[29, 30] may have partially blunted the beneficial influence of pre-stroke PA levels on risk of CVD and recurrent stroke.

We also evaluated the pattern of changes in pre-stroke PA levels and its association with clinical outcomes after incident stroke. Maintaining high PA levels over 6 years before stroke decreased mortality risk, with no consistent risk reduction for any other patterns of PA changes. Likewise, a prospective Danish population-based study including 4,658 men, aimed

at assessing the influence of PA patterns reported 5 years apart on mortality rates, demonstrated a 63% risk reduction only for those who performed high PA (jogging) at both examinations[31]. These results suggest that persistent high PA promote greater health benefits than non-persistent PA practice, despite some others showing that any increase in PA levels during lifetime contributes to mortality reduction[32–34].

Considering that health-related PA benefits may result from increased levels in any PA domain, this study is strengthened by a comprehensive evaluation of PA levels including work, leisure and sports PA[8]. The PA domains that were consistently associated with reduced mortality after incident stroke were work and leisure, with no significant contribution of sports. Despite the well-recognized impact of leisure PA on health outcomes, the influence of work PA is still controversial with studies demonstrating positive, negative, or null influence[35–37]. Our findings are supported by a meta-analysis including data from more than 83,000 participants that reported a significantly inverse association between work and leisure PA and all-cause mortality (17% and 26% risk reduction, respectively), but with discrepant results for sports PA[38]. A possible explanation for the unexpected lack of associations of sports PA on death and CVD risk in our study is the inclusion of stroke individuals, that usually had lower levels of pre-stroke sports activities[39]. Nevertheless, a cohort study evaluating death and recurrent stroke after incident stroke demonstrated a reduced incidence of all-cause death (30% lower risk) but no influence on CVD (including recurrent stroke) among ski-competition participants (individuals with high pre-stroke sports PA levels) in comparison to matched individuals from the general population[40].

The lack of information regarding stroke severity should be acknowledged as an important limitation of the present study, even though studies have demonstrated a positive influence of pre-stroke PA on stroke severity and physical functioning after incident stroke[41, 42]. Therefore, individuals with high pre-stroke PA levels were probably less impacted on their ability to participate in PA after stroke than those with low pre-stroke PA levels, then not being forced to decrease their PA levels due to the physical limitations caused by stroke. In addition, since PA levels in ARIC were not further assessed until visit 5 (2011–2013), we were not able to include PA levels after stroke in the adjusted models. Nonetheless, studies have demonstrated that PA levels after stroke were associated with PA levels before the stroke, supporting a decreased chance of differential misclassification due to marked changes in PA behavior after incident stroke[30, 43, 44]. The evaluation of PA levels using a questionnaire rather than direct measurements may have introduced some recall bias and measurement error[45]. However, PA questionnaires are the most common instrument used to evaluate PA levels in large cohort studies, with the Baecke PA questionnaire showing high reliability and validity in both men and women[46]. Finally, although our results were consistent after multiple adjustments for major potential confounders, residual confounding is still possible due to the observational design of the study.

CONCLUSION

Our findings demonstrate that higher levels of pre-stroke PA are associated with lower mortality risk after incident stroke. Sustained high levels of PA before stroke were associated with greater decreases in mortality as well. Work and leisure PA were consistently

associated with decreased risk of CVD and death after stroke, with no evidence of association for sports PA. Therefore, increasing PA levels during lifetime should be encouraged to decrease long-term all-cause and CVD mortality after stroke.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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NON-STANDARD ABBREVIATIONS AND ACRONYMS

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PA	Physical activity
CVD	Cardiovascular disease
ARIC	Atherosclerosis Risk in Communities
MI	Myocardial infarction
CHD	Coronary heart disease
HF	Heart failure
eGFR	Estimated glomerular filtration rate
BMI	Body mass index

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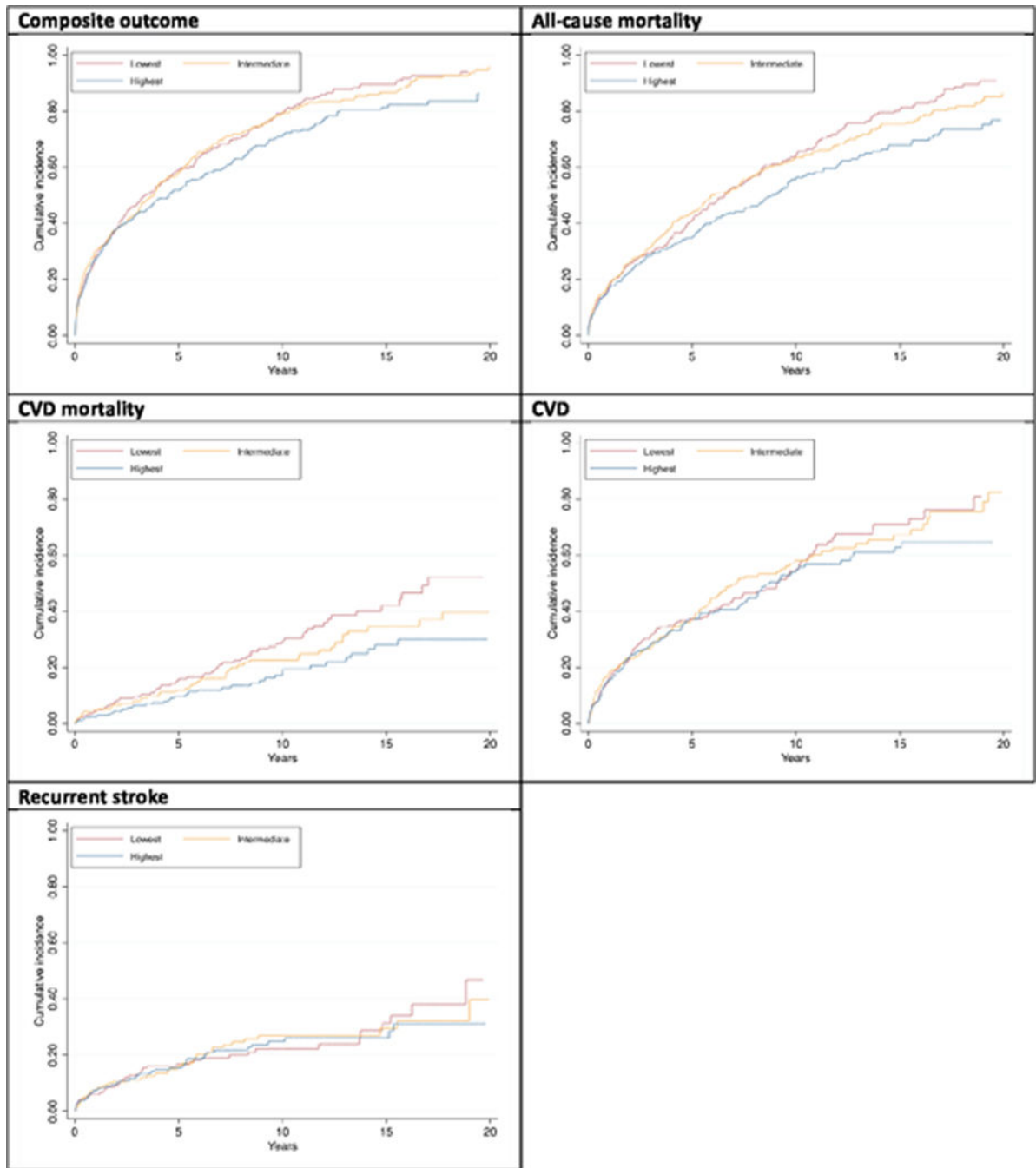
Figure 1.

Cumulative incidence of adverse health outcomes after stroke by tertiles of accumulated pre-stroke total PA score.

Accumulated 6-year pre-stroke physical activity as reported in ARIC visit 1 (1987–1989) and visit 3 (1993–1995).

CVD mortality was defined as mortality from stroke, myocardial infarction and heart failure.

CVD included recurrent stroke and the incidence of myocardial infarction and heart failure after stroke.

Composite outcome included all-cause mortality, CVD mortality, and CVD.

Table 1.

Characteristics of stroke patients according to tertiles of accumulated pre-stroke total PA score [*].

	Total (n=881)	Tertiles of accumulated pre-stroke total PA score			p-value for trend
		Lowest (n=289)	Intermediate (n=291)	Highest (n=301)	
Age at stroke [years, mean (SD)]	73.4 (7.9)	72.9 (8.1)	73.9 (8.2)	73.3 (7.5)	0.49
Time from visit 3 to incident stroke [years, mean (SD)]	11.4 (6.5)	10.8 (6.5)	11.1 (6.4)	12.3 (6.4)	<0.01
Female	52.3%	67.1%	50.5%	39.9%	<0.01
Black	32.0%	41.5%	34.0%	20.9%	<0.01
Comorbidities at stroke					
Hypertension	86.5%	90.0%	86.9%	82.7%	0.01
Diabetes	44.4%	47.4%	47.8%	38.2%	0.02
Coronary heart disease	17.8%	18.3%	18.9%	16.3%	0.51
Heart failure	22.1%	24.6%	21.3%	20.6%	0.25
Peripheral artery disease	8.1%	10.7%	7.6%	6.0%	0.04
Chronic kidney disease	23.2%	22.5%	22.0%	24.9%	0.48
Atrial fibrillation [**]	20.4%	19.4%	18.9%	22.9%	0.28
Current smoking	14.9%	17.0%	14.4%	13.3%	0.21
Average of measures at visit 1 and 3					
Body mass index (kg/m^2)	28.9 (5.4)	30.0 (6.3)	28.5 (5.0)	28.2 (4.6)	<0.01
Total score	6.7 (1.3)	5.3 (0.6)	6.6 (0.3)	8.1 (0.7)	<0.01
Work score	2.0 (0.9)	1.4 (0.5)	2.0 (0.8)	2.6 (0.8)	<0.01
Sport score	2.4 (0.7)	1.9 (0.4)	2.4 (0.5)	2.9 (0.7)	<0.01
Leisure score	2.3 (0.5)	2.0 (0.4)	2.3 (0.5)	2.6 (0.4)	<0.01

[*] Accumulated 6-year pre-stroke physical activity as reported in ARIC visit 1 (1987–1989) and visit 3 (1993–1995). For accumulated total PA score: lowest tertile (<12.25); intermediate tertile (12.25–14.49); highest tertile (14.50).

[**] 10% under use of anti-coagulants (11% in the lowest, 9% in the intermediate and 10% in the highest tertile)

Table 2.

Hazard ratios (95% CI) of adverse outcomes after incident stroke by tertiles of accumulated pre-stroke total PA score.

| | Tertiles of accumulated pre-stroke total PA score | | | |
	Lowest (n=289)	Intermediate (n=291)	Highest (n=301)	*p-value for trend*
Composite outcome				
Model 1	Ref.	1.00 (0.83, 1.21)	0.82 (0.67, 1.00)	0.05
Model 2	Ref.	1.03 (0.85, 1.24)	0.90 (0.73, 1.10)	0.31
All-cause mortality				
Model 1	Ref.	0.93 (0.76, 1.13)	**0.73 (0.59, 0.91)**	<0.01
Model 2	Ref.	0.93 (0.76, 1.14)	**0.78 (0.63, 0.97)**	0.03
CVD mortality				
Model 1	Ref.	0.76 (0.53, 1.10)	**0.53 (0.35, 0.81)**	<0.01
Model 2	Ref.	0.82 (0.56, 1.19)	0.66 (0.43, 1.02)	0.06
CVD				
Model 1	Ref.	1.04 (0.81, 1.34)	0.93 (0.72, 1.21)	0.60
Model 2	Ref.	1.06 (0.82, 1.37)	1.05 (0.80, 1.39)	0.70
Recurrent stroke				
Model 1	Ref.	1.05 (0.71, 1.56)	1.07 (0.71, 1.62)	0.73
Model 2	Ref.	1.02 (0.68, 1.52)	1.10 (0.72, 1.67)	0.66

Accumulated 6-year pre-stroke PA as reported in ARIC visit 1 (1987–1989) and visit 3 (1993–1995).

CVD mortality was defined as mortality from stroke, MI and HF.

CVD included recurrent stroke and the incidence of MI and HF after stroke.

Composite outcome included all-cause mortality, CVD mortality, and CVD.

Model 1: Age at stroke, sex and race-ARIC field centers.

Model 2: Model 1 + time from visit 3 to incident stroke, history of hypertension, diabetes, CHD, HF, peripheral artery disease, chronic kidney disease, atrial fibrillation, smoking status (current vs. non-current), and average of BMI at visit 1 and 3.

For accumulated total PA: lowest tertile (<12.25); intermediate tertile (12.25–14.49); highest tertile (14.50)

Estimates in **bold** are statistically significant

Table 3.

Hazard ratios (95% CI) of adverse outcomes after incident stroke by tertiles of accumulated pre-stroke specific-domain PA scores.

	Tertiles of accumulated pre-stroke work PA score			
	Lowest (n=291)	Intermediate (n=283)	Highest (n=307)	p-value for trend
Composite outcome				
Model 1	Ref.	**0.77 (0.64, 0.93)**	**0.78 (0.65, 0.95)**	0.01
Model 2	Ref.	**0.80 (0.66, 0.97)**	0.82 (0.67, 1.01)	0.06
All-cause mortality				
Model 1	Ref.	**0.81 (0.66, 0.99)**	**0.74 (0.60, 0.92)**	<0.01
Model 2	Ref.	0.86 (0.70, 1.05)	**0.77 (0.62, 0.96)**	0.02
CVD mortality				
Model 1	Ref.	**0.60 (0.41, 0.87)**	**0.39 (0.25, 0.59)**	<0.01
Model 2	Ref.	**0.67 (0.46, 0.98)**	**0.45 (0.29, 0.70)**	<0.01
CVD				
Model 1	Ref.	0.79 (0.61, 1.02)	**0.75 (0.58, 0.98)**	0.04
Model 2	Ref.	0.82 (0.64, 1.07)	0.82 (0.62, 1.09)	0.17
Recurrent stroke				
Model 1	Ref.	0.81 (0.53, 1.24)	1.14 (0.77, 1.69)	0.45
Model 2	Ref.	0.83 (0.54, 1.27)	1.18 (0.78, 1.78)	0.39

	Tertiles of accumulated pre-stroke leisure PA score			
	Lowest (n=280)	Intermediate (n=269)	Highest (n=332)	p-value for trend
Composite outcome				
Model 1	Ref.	0.83 (0.68, 1.01)	0.87 (0.71, 1.06)	0.20
Model 2	Ref.	0.83 (0.58, 1.01)	0.83 (0.68, 1.01)	0.07
All-cause mortality				
Model 1	Ref.	**0.79 (0.64, 0.98)**	**0.79 (0.64, 0.98)**	0.03
Model 2	Ref.	**0.78 (0.63, 0.97)**	**0.72 (0.58, 0.89)**	<0.01
CVD mortality				
Model 1	Ref.	1.00 (0.68, 1.47)	0.87 (0.57, 1.33)	0.52

	Lowest (n=291)	Intermediate (n=283)	Highest (n=307)	p-value for trend
Tertiles of accumulated pre-stroke work PA score				
Model 2	Ref.	1.04 (0.70, 1.54)	0.81 (0.53, 1.26)	0.34
CVD				
Model 1	Ref.	0.97 (0.74, 1.27)	1.19 (0.91, 1.56)	0.19
Model 2	Ref.	0.96 (0.73, 1.27)	1.12 (0.85, 1.48)	0.38
Recurrent stroke				
Model 1	Ref.	0.68 (0.44, 1.04)	1.13 (0.75, 1.70)	0.53
Model 2	Ref.	**0.64 (0.41, 0.99)**	1.04 (0.69, 1.58)	0.75

	Lowest (n=240)	Intermediate (n=307)	Highest (n=334)	p-value for trend
Tertiles of accumulated pre-stroke sports PA score				
Composite outcome				
Model 1	Ref.	0.98 (0.81, 1.19)	0.92 (0.75, 1.13)	0.41
Model 2	Ref.	1.06 (0.87, 1.30)	1.03 (0.84, 1.27)	0.79
All-cause mortality				
Model 1	Ref.	0.94 (0.76, 1.16)	0.85 (0.69, 1.06)	0.14
Model 2	Ref.	0.98 (0.79, 1.21)	0.94 (0.75, 1.17)	0.55
CVD mortality				
Model 1	Ref.	0.90 (0.61, 1.33)	0.82 (0.54, 1.23)	0.34
Model 2	Ref.	1.01 (0.67, 1.51)	1.03 (0.67, 1.59)	0.88
CVD				
Model 1	Ref.	0.98 (0.76, 1.28)	1.10 (0.84, 1.44)	0.48
Model 2	Ref.	1.09 (0.83, 1.43)	1.25 (0.94, 1.64)	0.12
Recurrent stroke				
Model 1	Ref.	0.93 (0.62, 1.40)	1.14 (0.75, 1.74)	0.50
Model 2	Ref.	0.94 (0.62, 1.43)	1.18 (0.77, 1.80)	0.41

Accumulated 6-year pre-stroke PA as reported in ARIC visit 1 (1987–1989) and visit 3 (1993–1995).

CVD mortality was defined as mortality from stroke, MI and HF.

CVD included recurrent stroke and the incidence of MI and HF after stroke.

Composite outcome included all-cause mortality, CVD mortality, and CVD.

Model 1: Age at stroke, sex, and race-ARIC field centers.

Model 2: Model 1 + time from visit 3 to incident stroke, history of hypertension, diabetes, CHD, HF, peripheral artery disease, chronic kidney disease, atrial fibrillation, smoking status (current vs. non-current), and average of BMI at visit 1 and 3.

For accumulated work PA: lowest tertile (<3.00); intermediate tertile (3.00–4.74); highest tertile (4.75)

For accumulated leisure PA: lowest tertile (<4.25); intermediate tertile (4.25–4.99); highest tertile (5.00)

For accumulated sports PA: lowest tertile (<4.00); intermediate tertile (4.00–5.24); highest tertile (5.25)

Estimates in **bold** are statistically significant (p<0.05)