The association of physical activity fragmentation with all-cause mortality in Hispanics: a prospective cohort study

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Summary

Background Physical activity fragmentation represents the frequency of transitioning from an active to sedentary state. The prognostic information of physical activity fragmentation is unclear in Hispanics/Latinos. This study examined the association of PA fragmentation with all-cause mortality in Hispanic/Latino adults.

Methods We investigated 11,992 participants from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) (18–74 yr; 52.2% women), from four United States urban communities (Bronx, New York; Chicago, Illinois; Miami, Florida; San Diego, California), that wore an accelerometer for one week. Physical activity fragmentation was calculated using the active-to-sedentary transition probability (ASTP) as the reciprocal of the average active bout duration. Daily total log-transformed activity count (TLAC) was used as a measure of total physical activity. The residual of ASTP regressed on TLAC (TLAC-adjusted ASTP) was explored to investigate the association of ASTP independent of total physical activity. Deaths were identified from annual follow-up interviews, obituary searches, or matches to the National Death Index through December 31, 2021. Cox regression models were fitted according to physical activity fragmentation.

Findings There were 745 deaths (6.2%) over a mean follow-up of 11.2 (SD 2.2) years. The highest compared to the lowest tertile of ASTP showed a HR of 1.45 (95% CI 1.10–1.92) of all-cause mortality after accounting for confounders. The mortality risk also increased for each 0.10-unit increase of ASTP, as a continuous variable, by 22% (HR 1.22; 95% CI 1.07–1.39). The results were similar considering TLAC-adjusted ASTP.

Interpretation Among Hispanic/Latino adults, more fragmented physical activity was associated with elevated all-cause mortality, independent of total physical activity volume.

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Keywords: Physical activity; Fragmentation; Sedentary; Mortality; Hispanics; Latinos

Introduction

Higher physical activity volumes, at any intensity, and less time spent in sedentary behaviors are associated with reduced risk of all-cause mortality.[1] The use of device-measured physical activity using wearable accelerometers in epidemiological studies adds to this

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Research in context

Evidence before this study

Physical activity fragmentation, measured as active-to-sedentary transition probability (ASTP), is an emerging concept of daily physical activity pattern that provides information on how fragmented physical activity is during the day. Higher values of ASTP indicate a more fragmented pattern of physical activity. Previous studies have suggested that ASTP may serve as an early indicator of declining health and functional capacity, potentially linked to increased mortality risk. We conducted a search of articles from PubMed using the terms "Physical Activity Fragmentation" OR "Active to Sedentary Transition Probability" in the Title/Abstract, with no language restrictions, limited to studies published before May 21, 2024 (no start date restrictions). Reference lists of selected studies were also reviewed. Of the 36 identified studies, most were cross-sectional (n = 28). Of the eight longitudinal studies, only four evaluated the association between ASTP and mortality, demonstrating that higher ASTP was associated with an increased mortality risk. However, these studies were limited by the inclusion of mostly older adults and non-Hispanic whites, with a relatively short follow-up period of less than five years. Therefore, there is limited literature on studies examining physical activity fragmentation and its association with mortality in a more diverse population with long-term follow-up. Investigating the association between ASTP with mortality in a larger population with different characteristics and a longer follow-up may provide additional insights for the identification of a more sensitive marker of impending mortality.

Added value of this study

Our study extends the knowledge from previous studies by demonstrating that higher physical activity fragmentation was associated with higher mortality risk in large sample of middle-age and older Hispanic/Latino adults, independent of total physical activity levels and potential demographic, clinical, and lifestyle confounders.

Implications of all the available evidence

Physical activity fragmentation by means of ASTP may be a new phenotypic marker of free-living physical activity patterns associated with reduced physical functioning and higher all-cause mortality. Interventions to increase length of daily active bouts (e.g., continuous walking), that can be more easily performed in a less-fragmented pattern in comparison to moderate and vigorous activities, may be effective for decreasing physical activity fragmentation and contributing to reduce all-cause mortality.

knowledge, providing detailed information about physical activity that is challenging to obtain using self-reported measurements.[2] Moreover, accelerometers provide the opportunity to define physical activity patterns beyond traditional physical activity measures of total volume and intensity, which may be uniquely associated with health outcomes.[3,4]

Physical activity fragmentation is an emerging concept that indicates the frequency of transitioning from a physically active state to a sedentary state. Physical activity fragmentation is calculated as the active-to-sedentary transition probability (ASTP), which is the reciprocal of the mean bout duration of active (i.e., non-sedentary) bouts of any intensity on a per-minute basis.[5] For example, two individuals both engage in 10 min of physical activity, but one completes it in a single 10-min bout while the other splits it into five bouts (a mean bout duration of 2 min), making an ASTP of 0.10 (calculated as 1 divided by the mean bout duration of 10 min) for the first person and 0.50 (1 divided by 2 min) for the second person. Thus, higher ASTP values indicate a more fragmented physical activity pattern.

Some cross-sectional and prospective studies have investigated the association of higher physical activity fragmentation with reduced physical functioning and higher all-cause mortality[5–11]; however, these studies were limited by including only individuals older than 50 years, with restricted racial/ethnic diversity (60–85% non-Hispanic Whites), and a short mean follow-up period (<5 years). Therefore, further research investigating physical activity fragmentation and its association with mortality in a more diverse population with a longer follow-up period is needed.

Besides its potential role as an early marker of impending functional decline and mortality,[5–8,10] the identification of physical activity fragmentation patterns may also serve as an important basis for physical activity recommendations. The 2020 World Health Organization (WHO) guideline on physical activity and sedentary behavior[12] recommended the accumulation of greater aerobic moderate-to-vigorous physical activity in bouts of any duration, in contrast to previous guidelines encouraging less fragmented moderate-to-vigorous physical activity with longer bouts (e.g., ≥10 min) to decrease the risk of adverse health outcomes.[13] However, the studies that supported this updated recommendation primarily focused on moderate-to-vigorous physical activity,[14] not including light activities that may substantially contribute to total physical activity levels and better represent daily-living physical activity patterns, especially among middle-aged and older adults.[15,16] Therefore, the influence of physical activity fragmentation on health outcomes considering all activities performed during the day as a more comprehensive evaluation of physical activity patterns, as in the case of ASTP, needs to be clarified.

Hispanic/Latinos are an underrepresented population in epidemiological studies, despite being the largest minority group in the U.S.[17] Many Hispanics/Latinos live in distinct social and cultural environments–such as different professional settings and experiences with health inequities–and adopt unique lifestyles, including relatively higher levels and specific patterns of physical activity, compared to other racial/ethnic groups.[18,19] These factors may result in different associations between physical activity and health outcomes for Hispanics compared to non-Hispanics.[20] Thus, a dedicated investigation focusing on this population is necessary.[21] The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) provides an unmatched opportunity to investigate the association of physical activity fragmentation with mortality risk given its prospective design, accelerometer physical activity measurements, and active outcome monitoring. Moreover, the wide age range from 18 to 74 years in HCHS/SOL allows for the examination of this relationship across different age subgroups. Therefore, the present study evaluated the association between physical activity fragmentation and mortality risk in HCHS/SOL. We hypothesized that higher physical activity fragmentation would be associated with higher all-cause mortality, regardless of total physical activity levels.

Methods

Study population

The present study included participants from the HCHS/SOL, a community-based prospective cohort study of Hispanic/Latino adults aged 18–74 years old, with baseline assessments performed between 2008 and 2011. Details of the sampling methods and study design can be found elsewhere.[22,23] Participants were recruited and enrolled from randomly selected households using a 2-stage area probability sample design in four United States urban communities (Bronx, New York; Chicago, Illinois; Miami, Florida; San Diego, California). Census block groups were randomly selected in each of the four communities and then households were randomly selected in each sampled block group. The 45–74 yr age group was oversampled to enrich clinical outcomes of interest (≈60% of the study sample). Sampling weights were generated to reflect the probabilities of selection at each stage. Informed consent was obtained from all participants. The HCHS/SOL was approved by the institutional review boards at each participant institution. The present study is a secondary analysis of de-identified data and thus does not require specific oversight by an institutional review board.

Of the 16,415 HCHS/SOL participants, 14,913 participants provided accelerometer data. Of this group, 655 participants were excluded because of missing information for ASTP, 1536 were excluded because <3 valid days of accelerometer data (defined as at least 10 h of wear per day), and 730 due to missing information for covariates, leaving a final analytic sample of 11,992 participants (Fig. 1).

Objectively-measured physical activity and fragmentation

Daily physical activity was assessed at the baseline visit by an omnidirectional accelerometer (Actical, model 198-0200-03; Respironics Co. Inc., Bend, OR) using a waist-worn belt with the device centered over the right-side iliac crest during waking hours, except when swimming, bathing, and sleeping. Participants were asked to wear it for seven consecutive days. The accelerometer captured accelerations at a sampling rate of 32 Hz that were summarized into activity counts in 1-min epochs. For consistency across the four study sites, the accelerometer data started at 5:00 AM in the morning following the clinic visit and truncated at 12:00 AM on day 6, providing a consistent 6-day wear period across all participants. Non-wear time was defined as ≥90 min of consecutive zero counts, with an allowance of up to 2-min interval with nonzero counts if no counts were detected within a 30-min window upstream or downstream from that interval.[24] Valid days were defined as the days in which wear time was ≥10 h and a minimum of three valid days was required for the inclusion in the analysis as a standard procedure to ensure the quality of physical activity measurement.[25] Minute-level activity counts were averaged across all valid days to calculate the mean counts per minute for every minute that the accelerometer was worn.

The thresholds used to classify each minute spent in sedentary and active states (i.e., all non-sedentary behavior) were <10 counts/min and ≥10 counts/min, respectively. These thresholds were considered according to analyses demonstrating consistency with sedentary behaviors in Hispanic participants of the National Health and Nutrition Examination Survey (NHANES).[26,27] Briefly, thresholds between 0 counts/min and 100 counts/min were explored in increments of 10 counts/min for consistency with age, sex, and body mass index (BMI) matched Hispanic participants of NHANES (n = 1,991). Values were mapped to approximate the population level distribution from NHANES for total activity counts, counts per minute, and sedentary and active time using quantile mapping procedures. The 10 count/min threshold provided the best match to NHANES data and is consistent with previous trunk-worn device threshold used in other studies.[28,29]

In the present study, a bout refers to a continuous period of active or sedentary behavior lasting at least 1 min. Bout lengths were defined as the number of consecutive minutes spent in either an active or sedentary state. The total bout length in each state was calculated by summing the durations of bouts (active or sedentary) throughout the day, while the number of bouts per day was determined by counting each distinct

Fig. 1: Flow chart of study participants included in the analysis.

bout of activity or sedentary behavior within the day. A measure of total physical activity volume, termed total log-transformed activity counts (TLAC), was calculated for each participant by taking the logarithm of minute-level total activity counts (i.e., including activity of any intensity), summing the values across the day, and averaging the daily sum across all valid days.[30,31] TLAC was used to account for the highly skewed distribution of the total activity counts. Physical activity fragmentation was assessed using ASTP. To calculate ASTP, each minute was labeled as active or sedentary and the number of active bouts ≥1 min was divided by total active bout length (i.e., the reciprocal of the mean bout length).[5–7]

Mortality

The outcome of interest was all-cause mortality. Deaths were identified from annual follow-up interviews with responses from family members or other proxy, obituary searches, or matches to the National Death Index.[32] The length of follow-up time was considered from the time of study entry until occurrence of death or the time of the last completed annual follow-up before January 31, 2022.

Covariates

Baseline sociodemographic, clinical and lifestyle covariates were considered. Sociodemographic covariates were self-reported and included age, sex, Hispanic/Latino background, education level (less than high school diploma, at most high school diploma, or some college or higher), health insurance coverage (yes/no), and annual household income.

BMI was defined as weight in kilograms divided by the square of height in meters, and obesity was defined as BMI ≥30 kg/m^2. Blood pressure was determined in a

sitting position by the mean of three measurements following 5 min of rest using an automated sphygmomanometer (Omron model HEM-907 XL; Omron Healthcare, Inc, Bannockburn, IL). Hypertension was defined according to systolic or diastolic blood pressure ≥140/90 mmHg or using antihypertensive medications. Blood glucose was measured using a hexokinase enzymatic method (Roche Diagnostics, Indianapolis, IN) in EDTA plasma and hemoglobin A1c was measured using a Tosoh G7 automated high-performance liquid chromatography analyzer in EDTA whole blood (Tosoh Bioscience, Inc, South San Francisco, CA). Diabetes was defined as fasting blood glucose ≥126 mg/dL, glucose tolerance test with a 2-h plasma glucose test ≥200 mg/dL, hemoglobin A1c ≥6.5%, or using anti-diabetic medications. Serum total cholesterol was measured using a cholesterol oxidase enzymatic method (Roche Diagnostics, Indianapolis, IN). Triglycerides were measured using a glycerol blanking enzymatic method (Roche Diagnostics). High density lipoprotein (HDL) cholesterol was measured using a direct magnesium/dextran sulfate method (Roche Diagnostics), and low density lipoprotein (LDL) cholesterol was calculated using the Friedewald equation.[33] Dyslipidemia was considered when triglycerides ≥200 mg/dL, HDL-cholesterol <40 mg/dL, LDL-cholesterol ≥160 mg/dL, or the use of lipid-lowering medications.

Prior history of coronary heart disease was determined by electrocardiography findings and self-report of heart attack, angina, or revascularization procedure. Cerebrovascular disease included self-reported stroke, transient ischemic attack, or any related procedure (e.g., carotid balloon angioplasty or endarterectomy). Chronic kidney disease was defined as estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2. Peripheral artery disease was determined based on self-report, intermittent claudication in one or both legs, or an ankle-brachial index <0.9. Chronic obstructive pulmonary disease (emphysema and chronic bronchitis) and cancer were self-reported on whether they were ever informed that they had any of these conditions.

Depression symptoms in the past week were evaluated using the 10-item center for epidemiological studies depression scale (CES-D-10).[34] Each item comprised four response categories ranged from "rarely or none of the time" (score of 0) to "all of the time" (score of 3). A summary score with a range of zero to 30 was calculated, with higher scores indicating greater depression symptoms. Diet quality was determined using the alternative healthy eating index-2010 score (AHEI-2010) that comprised 11 dietary components with evidence of association with chronic diseases obtained from two 24-h recalls.[35] Each component was assigned a minimum score of 0 and a maximum score of 10, with intermediate values being scored proportionally. AHEI-2010 scores vary from 0 to 110 as the sum of the 11 dietary components, with a higher number indicating a better diet quality. Smoking status was self-reported and categorized as current vs. former/never smoker. Smokers were defined as having smoked at least 100 cigarettes in their lifetime, and those who reported currently smoking every day or in some days were classified as current smokers.[36]

Statistical analysis

Stratification, clustering, and sampling weights were used to account for the complex survey design. Complex survey methodology accommodated the 2-stage sampling probability and non-responses in the selected sample at the household and individual levels. The weights were trimmed and calibrated to the 2010 U.S. Census data based on age, sex, and Hispanic/Latino background within the Census block groups of the four HCHS/SOL field centers, making the sample representative of the original sampled population. More details about the study design and sampling structure can be found elsewhere.[23,37] We further adjusted for missing accelerometer data using inverse probability weights, which predicted accelerometer adherence based on associated variables, with the final weight being the product of the sampling weights and the inverse probability weights.[25,38]

Distributions were visually inspected using histograms. Baseline characteristics of the study population were presented as mean (95% confidence intervals [CI]) for continuous variables or absolute frequencies (percentages) for categorical variables. p-values for trend across tertiles of baseline ASTP were calculated by modeling ASTP tertiles as a continuous variable.

ASTP was considered as categories (stratified by tertiles) as well as a continuous variable in the survival analyses. We estimated cumulative survival across tertiles of ASTP using the Kaplan–Meier method and compared them using the Wald test. We explored Cox regression models to account for potential confounders, as follows: Model 1 minimally adjusted for sociodemographic confounders age, sex, study site, and accelerometer wear time; Model 2 additionally adjusted for other sociodemographic confounders Hispanic/Latino background, education level, and health insurance coverage; and Model 3 further adjusted for clinical and lifestyle factors such as obesity, hypertension, diabetes, dyslipidemia, prior history of coronary heart disease or cerebrovascular disease, pulmonary disease, chronic kidney disease, peripheral artery disease, cancer, depression symptoms, diet quality, and current smoking. The proportional hazard assumption for Cox regression models was verified by Schoenfeld residuals. A restricted cubic spline model with three knots located at percentiles 10, 50 and 90 and reference point set at the median of the first tertile was constructed to characterize the continuous association of ASTP with mortality. This model was adjusted for covariates in Model 3, noted above. Nonlinearity was assessed by comparing

the coefficients of the two middle splines in the restricted cubic spline model using the Wald test, with a p-value of <0.05 considered indicative of a statistically significant nonlinear relationship.

To investigate the association of ASTP with mortality independent of total physical activity levels, due to the high correlation between ASTP and TLAC (Pearson coefficient correlation; r = –0.76; Supplementary Figure S1), we modeled the residual of ASTP from linear regression of ASTP on TLAC, corresponding to the variation of ASTP unexplained by total physical activity. We called this variable as TLAC-adjusted ASTP. The same Models 1–3 were fitted to estimate the association between TLAC-adjusted ASTP and with mortality. We also explored total physical activity volume (i.e., TLAC) as an exposure.

For sensitivity analyses, we fitted the same models considering only those participants with ≥5 valid accelerometer days. We also fitted the models censoring deaths within the first 2 years of follow-up to account for the potential confounding due to poor health status leading to reduced physical activity.[39] In addition, we conducted subgroup analyses stratified by sex and age categories (<60 and ≥60 years) to verify the consistency of the results across different subgroups. The interaction was tested by modeling the interaction terms of ASTP and sex or age categories. The data analysis was performed using complex survey procedures in Stata version 17.0 software (College Station, Texas) and considered a 2-tailed p-value of <0.05 statistically significant. This manuscript adheres to the guidelines of the STrengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist (Supplementary Material).

Role of funding sources

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript.

Results

The clinical, demographic, and lifestyle characteristics of participants are shown in Table 1 (total and stratified by tertiles of ASTP). Overall, individuals with higher ASTP tended to have a worse clinical and lifestyle profile, with a higher BMI, a higher prevalence of comorbidities, more depressive symptoms, worse diet quality, lower physical activity, and higher sedentary time. Moreover, they were more likely to be Dominicans, Cubans, and Puerto Ricans (less likely Mexicans), and have higher educational levels and higher insurance coverage. Those in the intermediate and highest tertiles were more likely to be women in comparison to those in the lowest tertile of ASTP.

There were 745 deaths (154 in the lowest, 212 in the intermediate, and 379 in the highest tertile of ASTP) during a mean follow-up of 11.2 (SD 2.2) years (mortality rate 4.8 per 1,000 person-years). 10-year cumulative mortality was 7.0% in the highest tertile, 3.7% in the intermediate tertile, and 2.7% in the lowest tertile of ASTP (Wald test p < 0.001) (Fig. 2).

The association between ASTP and mortality remained significant after accounting for potential confounders (Table 2). Greater ASTP (more fragmented physical activity) was consistently associated with elevated mortality risk, with HR 1.45 (95% CI 1.10–1.92) in the highest vs. the lowest tertile in Model 3. A similar result was observed when modeling ASTP continuously, with a greater mortality risk for each 0.1-unit increment of ASTP (HR 1.22, 95% CI 1.07–1.39). In restricted cubic spline analyses, the association of ASTP with mortality was mostly linear (Wald test p = 0.93; Fig. 3).

The results were largely similar across all models when we explored the independent association of ASTP beyond total physical activity volume, by fitting TLAC-adjusted ASTP (Table 3). In Model 3, the highest tertile demonstrated a HR of 1.46 (95% CI 1.06–2.00) for mortality in comparison to the lowest tertile of ASTP. Similar results for TLAC-adjusted ASTP modeled as a continuous variable were observed, with a greater mortality risk for each 0.1-unit increment (HR 1.28; 95% CI 1.01–1.61). We confirmed that higher TLAC (as a measurement of total physical activity volume) was also significantly associated with lower mortality risk in our study population (HR 0.76; 95% CI 0.55–1.00) (Table 3).

Similar results were observed in the sensitivity analyses exploring the association between ASTP and mortality considering the 9,210 participants with ≥5 valid accelerometer days (Supplementary Table S1) and also censoring 62 deaths within the first 2 years of follow-up (Supplementary Table S2). Greater ASTP was significantly associated with higher mortality risk among sex (men and women) and age (<60 yrs and ≥60 yrs) subgroups (Supplementary Figure S2).

Discussion

The use of accelerometers provides information beyond the traditional measures of physical activity volume and intensity, allowing a more comprehensive investigation about patterns of daily-living physical activity and its association with health outcomes.[2] The present study demonstrated that higher daily-living physical activity fragmentation (more transitions from a physical activity of any intensity to a sedentary state) was robustly associated with higher mortality risk in a large sample of Hispanic/Latino adults in the US, independent of total physical activity levels and potential confounders. This finding was consistent even after censoring for early deaths within the first two years of follow-up and across subgroups of sex and age (<60 yrs and ≥60 yrs), supporting that physical activity fragmentation may emerge as a comprehensive new physical activity measure associated with poor prognosis, not only among older

	Total (n = 11,992)	Tertiles of ASTP			p-value for trend[a]
		Lowest (n = 3,998)	Intermediate (n = 3,997)	Highest (n = 3,997)	
Age (Years), mean (95% CI)	41.1 (40.6–41.7)	40.6 (39.9–41.3)	41.7 (40.9–42.5)	41.1 (40.2–42.0)	0.41
Women, % (95% CI)	52.2 (50.8–53.6)	45.5 (43.0–47.9)	57.4 (40.5–44.8)	53.6 (44.0–48.9)	<0.001
Hispanic/Latino background, % (95% CI)					
Dominican	9.8 (8.3–11.4)	6.0 (4.6–7.7)	9.5 (7.9–11.4)	13.3 (10.8–16.1)	<0.001
Central American	7.5 (6.4–8.7)	8.5 (6.9–10.4)	6.7 (5.5–8.1)	7.3 (6.2–8.6)	0.18
Cuban	21.0 (17.6–24.7)	19.0 (15.5–23.2)	21.1 (17.8–24.7)	22.5 (18.9–26.7)	0.02
Mexican	77.8 (34.4–41.1)	47.6 (43.3–52.0)	38.3 (34.9–41.9)	28.4 (25.1–32.0)	<0.001
Puerto Rican	15.3 (13.8–16.9)	11.5 (9.6–13.7)	15.7 (13.8–17.8)	18.2 (16.1–20.6)	<0.001
South American	5.0 (4.3–5.7)	4.3 (3.5–5.2)	5.4 (4.4–6.6)	5.2 (4.3–6.3)	0.11
Mixed/other	3.8 (3.2–4.6)	3.1 (2.3–4.2)	3.3 (2.4–4.5)	5.0 (3.7–6.8)	0.04
Education level, % (95% CI)					
Less than high school	31.9 (30.3–33.6)	34.6 (32.2–37.0)	31.7 (29.6–34.1)	29.7 (27.1–32.3)	0.003
High school graduation	28.2 (26.9–29.6)	29.7 (27.6–31.9)	27.4 (25.3–29.6)	27.6 (25.1–30.3)	0.22
Some college or higher	39.9 (38.1–41.7)	35.7 (33.0–38.5)	40.8 (38.4–43.3)	42.8 (39.9–45.7)	<0.001
Health insurance coverage, % (95% CI)	50.1 (48.1–52.2)	40.8 (37.9–43.8)	51.3 (48.4–54.1)	57.3 (54.4–60.1)	<0.001
Body mass index (kg/m^2), mean (95% CI)	29.4 (29.2–29.6)	28.8 (28.5–29.0)	29.4 (29.1–29.7)	29.8 (29.4–30.2)	<0.001
Depression symptoms, mean (95% CI)	6.9 (7.7–7.0)	6.3 (6.0–6.6)	7.1 (7.0–7.4)	7.1 (6.8–7.4)	<0.001
Obesity, % (95% CI)	39.4 (37.9–40.9)	36.8 (34.6–39.2)	39.6 (37.3–42.1)	41.4 (39.0–43.8)	0.005
Hypertension, % (95% CI)	24.2 (22.9–25.2)	19.3 (17.6–21.2)	25.5 (23.6–27.5)	27.3 (25.1–29.5)	<0.001
Diabetes, % (95% CI)	14.4 (13.5–15.4)	11.5 (10.2–13.0)	14.6 (13.1–16.2)	16.8 (15.3–18.4)	<0.001
Dyslipidemia, % (95% CI)	42.9 (41.4–44.3)	40.3 (38.0–42.7)	44.4 (42.2–46.7)	43.7 (41.0–46.4)	0.06
Coronary heart/cerebrovascular disease, % (95% CI)	7.1 (6.4–7.8)	5.0 (4.1–6.1)	6.6 (5.7–7.7)	9.3 (8.0–10.7)	<0.001
Chronic obstructive pulmonary disease, % (95% CI)	6.0 (5.4–6.6)	3.8 (3.1–4.7)	6.3 (5.3–7.5)	7.7 (6.7–8.8)	<0.001
Chronic kidney disease, % (95% CI)	4.5 (4.0–5.1)	3.0 (2.8–3.8)	4.3 (3.5–5.2)	6.1 (5.1–7.1)	<0.001
Peripheral artery disease, % (95% CI)	1.3 (0.9–1.8)	1.5 (0.7–3.0)	0.9 (0.6–1.3)	1.5 (1.0–2.3)	0.87
Cancer, % (95% CI)	3.6 (3.1–4.1)	2.8 (2.0–3.9)	3.6 (2.9–4.5)	4.2 (3.5–5.0)	0.04
Total cholesterol (mg/dL), mean (95% CI)	194.9 (193.7–196.1)	195.6 (193.7–197.5)	195.3 (193.0–197.5)	193.9 (192.1–195.8)	0.19
Triglycerides (mg/dL), mean (95% CI)	133.4 (130.4–136.4)	129.1 (124.9–133.4)	134.8 (128.6–141.0)	136.0 (131.0–140.9)	0.05
HDL-cholesterol (mg/dL), mean (95% CI)	48.6 (48.2–49.0)	48.9 (48.3–49.5)	48.8 (48.2–49.4)	48.1 (47.5–48.7)	0.05
LDL-cholesterol (mg/dL), mean (95% CI)	120.2 (119.2–121.2)	121.2 (119.6–122.8)	120.4 (118.5–122.2)	119.2 (117.6–120.9)	0.08
Current smoking, % (95% CI)	20.4 (19.1–21.8)	20.3 (18.1–22.7)	19.1 (17.2–21.2)	21.7 (19.6–24.1)	0.37
AHEI 2010, mean (95% CI)	47.5 (47.2–47.9)	48.5 (48.0–49.0)	47.5 (47.0–47.9)	46.8 (46.3–47.2)	<0.001
Number of valid accelerometer days, mean (95% CI)	5.1 (5.0–5.1)	5.0 (5.0–5.1)	5.1 (5.0–5.2)	5.1 (5.1–5.2)	0.01
Accelerometer wear time per day (minutes), mean (95% CI)	949.8 (941.5–958.2)	934.5 (923.4–945.6)	942.6 (932.0–953.2)	969.8 (958.8–980.8)	<0.001
TLAC (counts), mean (95% CI)	2239.1 (2212.2 to 2266.1)	2951.5 (2910.5 to 2992.6)	2190.7 (2165.5 to 2216.0)	1654.7 (1631.9 to 1677.6)	<0.001
ASTP, mean (95% CI)	0.23 (0.22–0.23)	0.15 (0.14–0.15)	0.22 (0.21–0.22)	0.30 (0.30–0.31)	<0.001
Active bout length per day (minutes), mean (95% CI)	6.8 (5.0–8.6)	13.0 (7.3–18.7)	4.6 (4.5–4.6)	3.4 (3.3–3.4)	0.001
Sedentary bout length per day (minutes), mean (95% CI)	5.0 (5.0–5.1)	4.3 (4.2–4.3)	4.9 (4.8–4.9)	5.8 (5.7–5.9)	<0.001
Number of daily active bouts per day, mean (95% CI)	98.7 (97.8–99.7)	83.8 (82.8–84.8)	101.6 (100.6–102.7)	109.4 (107.7–111.0)	<0.001
Number of daily sedentary bouts per day, mean (95% CI)	97.2 (96.3–98.2)	82.3 (81.3–83.3)	100.2 (99.1–101.2)	107.7 (106.0–109.4)	<0.001
Total time active per day (minutes), mean (95% CI)	468.6 (463.9–473.4)	586.0 (579.0–592.9)	464.6 (459.6–469.5)	368.9 (363.6–374.1)	<0.001
Total time sedentary per day (minutes), mean (95% CI)	486.7 (479.9–493.6)	353.1 (345.6–360.6)	483.5 (476.4–490.7)	607.4 (599.1–615.7)	<0.001

ASTP tertiles range: lowest from 0.0001 to 0.19, intermediate from 0.19 to 0.25, and highest from 0.25 to 0.72. HCHS/SOL: Hispanic Community Health Study/Study of Latinos; CI: confidence interval; HDL: HDL: high-density lipoprotein; LDL: low-density lipoprotein; AHEI: Alternative Healthy Eating Index; ASTP: active-to-sedentary transition probability; TLAC: total log activity counts. [a]P-value for trend based upon linear regression model (for continuous variables) or logistic regression model (for categorical variables) using ASTP tertiles as a continuous variable.

Table 1: **Baseline characteristics overall and by tertiles of ASTP, HCHS/SOL (2008–2011).**

adults but also within middle-aged populations. Moreover, our results confirmed that higher accelerometer-measured total physical activity volume was significantly associated with lower mortality risk, as demonstrated in previous studies conducted in non-Hispanic/Latino populations.[40,41]

Although physical activity fragmentation has recently emerged as a potential predictor of elevated mortality risk in older adults and non-Hispanic Whites,[6–8] our study adds to previous research by demonstrating that higher fragmentation levels were linked to an increased mortality risk among middle-age and older Hispanics/

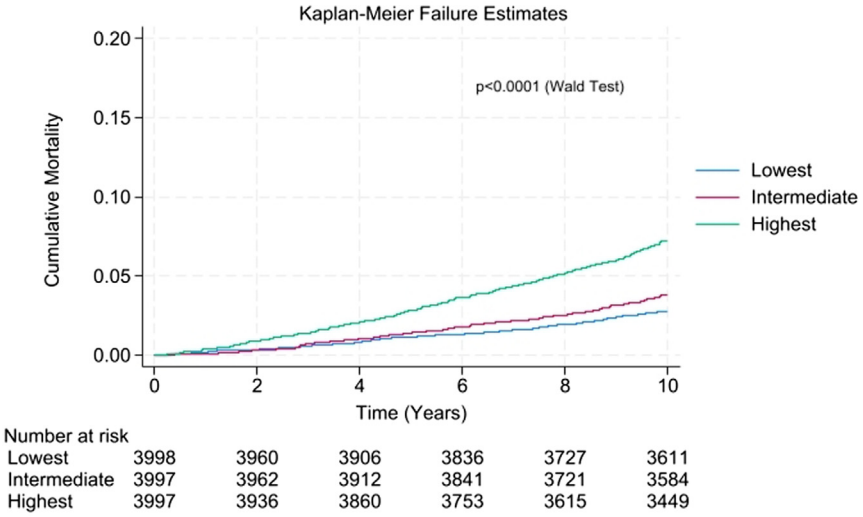

Fig. 2: Cumulative mortality by tertiles of ASTP, HCHS/SOL. ASTP: active-to-sedentary transition probability; HCHS/SOL: Hispanic Community Health Study/Study of Latinos; 745 deaths: 348 women and 397 men; 386 < 60 yr and 359 ≥ 60 yr.

Latinos, a population that typically engages in higher amounts of physical activity due to increased transportation and work-related activities compared to other races/ethnicities in US.[18,42,43] In contrast, previous studies that used a more simplistic measure of physical activity fragmentation by differentiating the time spent in short (<10 min) vs. long (≥10 min) bouts of moderate-to-vigorous physical activity found no mortality differences.[14,44,45] In this context, ASTP may provide a more detailed evaluation of activity fragmentation patterns considering all daily active bouts (regardless of physical activity intensity) on a minute-by-minute basis,[7] which is more representative of engagement in daily living activities.

The mechanisms underlying the association of physical activity fragmentation with adverse health outcomes are yet to be determined, but there are a few plausible mechanisms. For example, reduced energy availability to carry out daily living activities is one potential physiological process linked to more fragmented physical activity.[46,47] In this context, the more fragmented physical activity patterns may manifest as an early compensatory strategy, allowing individuals to maintain their usual daily activities by performing them in shorter periods, avoiding longer bouts of continuous activities that are usually more physically demanding.[10,47] In addition, factors other than physiological mechanisms, including psychological (e.g., low self-efficacy and motivation) and environmental aspects (e.g., lack of accessibility to recreational spaces, parks, and trails to perform sustained physical activity) may also contribute to a more fragmented physical activity pattern and also poor prognosis. Nonetheless, further studies are needed to understand mechanisms linking greater physical activity fragmentation to higher risk of adverse outcomes.

There are a few important clinical and public health implications from our study. Our findings support a growing body of evidence that physical activity fragmentation by means of ASTP may be a new phenotypic marker of the deterioration of free-living physical activity patterns associated with reduced physical functioning and higher all-cause mortality,[5–8] not only among

All-cause mortality, HR (95% CI)	ASTP			
	Continuous (per 0.10 unit) (n = 11,992)	Tertiles		
		Lowest (n = 3,998)	Intermediate (n = 3,997)	Highest (n = 3,997)
Model 1	1.42 (1.24–1.62) p-value < 0.0001	Reference	1.20 (0.90–1.61) p-value = 0.21	1.78 (1.38–2.30) p-value < 0.0001
Model 2	1.41 (1.23–1.61) p-value < 0.0001		1.20 (0.90–1.62) p-value = 0.22	1.79 (1.37–2.32) p-value < 0.0001
Model 3	1.22 (1.07–1.39) p-value = 0.004		1.09 (0.81–1.47) p-value = 0.57	1.45 (1.10–1.92) p-value = 0.009

ASTP: active-to-sedentary transition probability; HCHS/SOL: Hispanic Community Health Study/Study of Latinos; HR: hazard ratio; CI: confidence interval. Model 1: adjusted for study site, age, sex, and accelerometer wear time; Model 2: adjusted for model 1 + Hispanic/Latino background, education level, and health insurance coverage; Model 3: adjusted for model 2 + obesity, hypertension, diabetes, dyslipidemia, cardiovascular/cerebrovascular diseases, chronic obstructive pulmonary disease, chronic kidney disease, peripheral artery disease, cancer, depression symptoms, diet quality, and current smoking.

Table 2: **Hazard ratios (95% CI) for the association between ASTP and all-cause mortality, HCHS/SOL.**

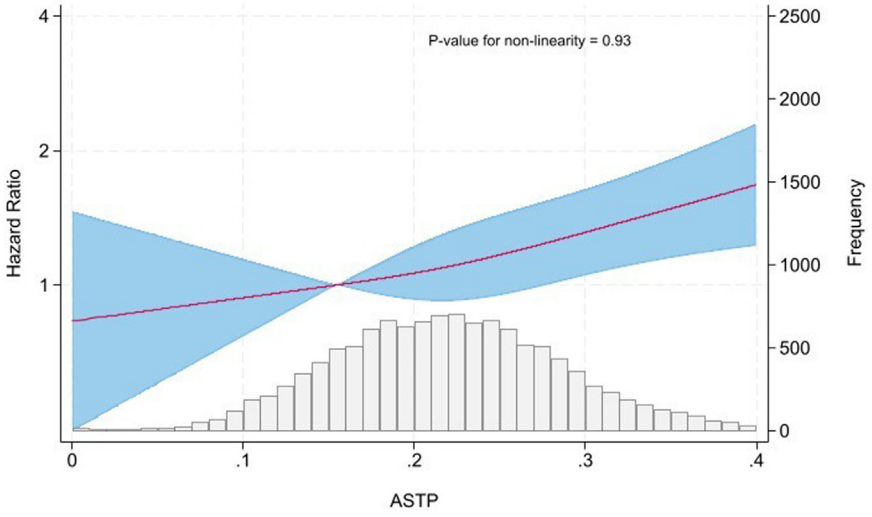

Fig. 3: Continuous associations of ASTP and all-cause mortality in a restricted cubic spline model (3 knots), HCHS/SOL. ASTP: active-to-sedentary transition probability; HCHS/SOL: Hispanic Community Health Study/Study of Latinos; *Only ASTP < 0.40 was considered in the graph due to the small number of participants above this point (n = 170); Knots located at ASTP percentiles 10th (0.135), 50th (0.219), and 90th (0.311); Reference point set at the median of the first tertile (ASTP = 0.155). Model adjusted for study site, age, sex, accelerometer wear time, Hispanic/Latino background, education level, health insurance coverage, obesity, hypertension, diabetes, dyslipidemia, cardiovascular/cerebrovascular diseases, chronic obstructive pulmonary disease, chronic kidney disease, peripheral artery disease, cancer, depression symptoms, diet quality, and current smoking.

older adults but also in a middle-aged population with a diverse Hispanic/Latino background. Consequently, interventions to increase length of daily active bouts (e.g., continuous walking), that can be more easily performed in a less-fragmented pattern in comparison to moderate and vigorous activities, may be effective for decreasing physical activity fragmentation and contributing to favorable prognoses.[12,48] Although the latest 2020 WHO guideline on physical activity and sedentary behavior[12] no longer emphasize the importance of bout duration, with more fragmented physical activity also promoting health benefits, this recommendation refers to moderate-to-vigorous activities. Our study suggests that fragmentation patterns of physical activity does matter when considering both light and moderate-to-vigorous intensity activities, as in the case of ASTP, implying

All-cause mortality, HR (95% CI)	TLAC-adjusted ASTP[a]			
	Continuous (n = 11,992)	Tertiles		
		Lowest (n = 3,998)	Intermediate (n = 3,997)	Highest (n = 3,997)
Model 1	1.57 (1.24–2.00) p-value < 0.0001	Reference	1.21 (0.90–1.62) p-value = 0.21	1.69 (1.24–2.31) p-value = 0.001
Model 2	1.56 (1.22–2.00) p-value < 0.0001		1.21 (0.90–1.63) p-value = 0.20	1.68 (1.22–2.30) p-value = 0.001
Model 3	1.28 (1.01–1.61) p-value = 0.04		1.22 (0.91–1.64) p-value = 0.18	1.46 (1.06–2.00) p-value = 0.02
All-cause mortality, HR (95% CI)	**TLAC**			
	Continuous (per 10% of mean) (n = 11,992)	Tertiles		
		Lowest (n = 3,998)	Intermediate (n = 3,997)	Highest (n = 3,997)
Model 1	0.91 (0.87–0.95) p-value < 0.0001	Reference	0.74 (0.58–0.95) p-value = 0.02	0.60 (0.45–0.80) p-value < 0.0001
Model 2	0.91 (0.88–0.95) p-value < 0.0001		0.75 (0.59–0.97) p-value = 0.03	0.60 (0.45–0.80) p-value = 0.001
Model 3	0.95 (0.91–0.98) p-value = 0.006		0.90 (0.70–1.17) p-value = 0.46	0.76 (0.55–1.03) p-value = 0.08

ASTP: active-to-sedentary transition probability; TLAC: total log activity counts; HCHS/SOL: Hispanic Community Health Study/Study of Latinos; HR: hazard ratio; CI: confidence interval. 10% of TLAC mean = 223.9 counts. Model 1: adjusted for study site, age, sex, and accelerometer wear time; Model 2: adjusted for model 1 + Hispanic/Latino background, education level, and health insurance coverage; Model 3: adjusted for model 2 + obesity, hypertension, diabetes, dyslipidemia, cardiovascular/cerebrovascular diseases, chronic obstructive pulmonary disease, chronic kidney disease, peripheral artery disease, cancer, depression symptoms, diet quality, and current smoking. [a]TLAC-adjusted ASTP: linear regression residuals from ASTP and TLAC (counts).

Table 3: **Hazard ratios (95% CI) for the association between all-cause mortality, TLAC-adjusted ASTP, and TLAC, HCHS/SOL.**

that continuous physical activity should last as long as possible, as evidenced by the linear relationship between ASTP and mortality. Nonetheless, future research incorporating ASTP as a measure of physical activity fragmentation is needed to expand our understanding on how intervention strategies can be effectively implemented to improve daily living physical activity patterns.

The present study has some limitations. First, the lack of information for cause of death precluded us from performing a more detailed analyses exploring cause-specific mortality. However, the evaluation of all-cause mortality provides a comprehensive measure of the relationship between physical activity fragmentation on overall health, thereby offering valuable insights into the overall health implications of physical activity fragmentation, which can be relevant for developing future public health interventions for this underrepresented population.[49] In addition, despite being considered a gold-standard method for evaluating free-living physical activity, hip-worn accelerometers may not accurately capture activities that do not involve significant body movements, such as sitting activities (biking) and upper body movements (weightlifting), or water-based activities (e.g., swimming).[50] Moreover, although we only included participants who wore accelerometers according to the study protocol, which were previously described as having an overall healthier risk factor profile than non-adherents, the use of inverse probability weights accounted for these potential differences in accelerometer wear and adherence.[25] While we acknowledge that different moderate-to-vigorous activities may exhibit distinct fragmentation patterns independent of total volume of physical activity, the HCHS/SOL population spent a relatively low time in moderate-to-vigorous leisure time physical activity (on average 22 min per day),[18] and its overall impact is likely limited. Also, some information was based on self-report and may be subject to information bias. Residual confounding is still possible due to the observational study design. Although the lack of time-varying information on physical activity fragmentation over the follow-up period can be considered a limitation, assessing a single measure simplifies the evaluation of the relationship between physical activity fragmentation and mortality, facilitating the interpretation and application of the findings in clinical settings. This approach is also commonly observed in previous epidemiological studies where physical activity is assessed as an exposure variable.[44] In contrast, strengths of the present study included the prospective design with a large sample size followed over a long period, the use of well-validated measurement procedures in HCHS/SOL, and the inclusion of ASTP as a measurement of physical activity fragmentation, which considers all active bouts in a minute-by-minute basis and includes light activities that better represents daily living physical activity patterns.[15,16]

To conclude, more fragmented physical activity was robustly associated with elevated all-cause mortality, independently of total physical activity volume in Hispanic/Latino adults. Our findings support ASTP as an emerging informative measure with prognostic information independent of total physical activity. Intervention strategies increasing time spent in more continuous activity bouts may be useful to decrease mortality risk and deserve future investigation.

Contributors

MFFM, KM, and YM contributed to conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, and writing. DSA, RK, MD, JAS contributed to conceptualization, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, and writing. SHB, FGII, YMR, JAC, SKA, MD, OGB, KRE contributed to investigation, methodology, project administration, supervision, validation, visualization, and writing. All authors contributed to writing and editing and approved the final version. KM had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing statement

The HCHS/SOL data are publicly available from the National Heart, Lung, and Blood Institute or can be requested to its coordinating center at the University of North Carolina.

Declaration of interests

MFFM, YM, FG II, OGB, and SHB declared no conflicts of interest in relation to this submitted work. DSA, MD, RK, JAC, YMR, and KRE declared that they received funding from National Institutes of Health. SKA declared that she received funding from National Cancer Institute. JAS declared that she received consulting fees from Edwards Lifesciences, an honorarium from the Villages Inc, supporting attending meetings/travel from McMaster University, and has a role as advisory board of BellSant Inc. KM declared that he received grant from National Institutes of Health and Resolve to Save Lives, consulting fees from Kowa Company and RhythmX AI, and payment from Fukuda Denshi.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2025.100996.

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