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Objectively measured physical activity reduces the risk of mortality among Brazilian older adults

Physical activity and risk of mortality

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PROGRAMA DE PÓS-GRADUAÇÃO EM EPIDEMIOLOGIA

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Abstract

Background/Objectives: Use of objectively measured physical activity (PA) in older adults to assess relationship between PA and risk of all-causes mortality is scarce. This study evaluated the associations of PA based on accelerometry and questionnaire with the risk of mortality among older adults from a city in Southern Brazil.

Design: A cohort study.

Setting: Urban area of Pelotas, Southern Brazil.

Measurements: Study with a representative sample of older adults (60+ years) from Pelotas, enrolled in 2014. Overall (mg), light (LPA) and moderate-to-vigorous PA (MVPA) were estimated by raw accelerometer data. International Physical Activity Questionnaire estimated leisure-time and commuting PA. Hazard ratios (excluding deaths in the first 6 months) stratified by sex were estimated by Cox regression analysis considering adjustment for confounders.

Results: From the 1,451 older adults interviewed in 2014, 145 died (10%) after a follow-up of on average 2.6 years. Men and women in the highest tertile of overall PA had on average 77% and 92% lower risk of mortality than their less active counterparts (95%CI: 0.06; 0.84 and 95%CI: 0.01; 0.65, respectively). The highest tertile of LPA was also related to lower risk of mortality in individuals of both genders (74% and 91% lower risk among men and women). MVPA statistically reduced the risk of mortality only among women (HR: 0.30 and HR: 0.07 in the 2nd and 3rd tertiles). Self-reported leisure-time PA was statistically associated with lower risk of mortality only among men. Women in the highest tertiles of commuting PA showed lower risk of mortality than those in the reference group.

Conclusion: Accelerometry-based PA was associated with lower risk of mortality among Brazilian older adults. Older individuals should practice any type of physical activity.

Keywords: Physical activity; mortality; longitudinal study; older adults.

Introduction

Physical activity (PA) is an important determinant of health worldwide. It is estimated that inactivity causes 9% of premature mortality – around 5.3 million deaths a year[1]. Although non-communicable diseases (NCD) that can be prevented by PA [1] are associated with a higher proportion of deaths in high-income countries, high mortality rates due to these diseases are also observed in middle- or low-income countries, in coexistence with important mortality from communicable diseases [2].

Brazil is an upper-middle income country in which non-communicable diseases predominate in all regions of the country, especially cardiovascular diseases, mental disorders, diabetes, and chronic obstructive pulmonary disease [3]. The number of older adults in Brazil grew 40% between 2002 and 2012, and both prevalence and mortality due to NCD are elevated in this population [4].

Several studies have described an existing relationship between PA in older adults and risk of all-causes mortality [5-15]. These studies differed concerning PA assessment, length of follow-up, ethnicity, age at baseline, stratifications variables and other aspects, making comparison difficult. Use of objectively measured PA in community-dwelling older adults to assess such association is uncommon [6, 9, 14] and no study was found using accelerometry in Latin America.

Newer literature with objectively measured PA suggests that increasing light PA (LPA) may also be important for reducing mortality in adults and older adults [10, 16-17]. Longitudinal studies from low- and middle-income countries are especially

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important for elucidating these relationships. Findings from more affluent countries may not translate well to poorer societies due to different macrodeterminants of life conditions [18]. This study aims to overcome some of the previous gaps in the scientific literature by evaluating the relationship between PA, measured by accelerometry and questionnaire, and risk of all-cause mortality in community-dwelling older adults from a Southern Brazilian city.

Methods

Study setting and sampling

The "COMO VAI?" study (*Consórcio de Mestrado Orientado para a Valorização da Atenção ao Idoso*) – "HOW ARE YOU?" (Masters Consortium for Valuation of Older Care) is a cohort study that has been conducted in Pelotas, a middle-sized city located in Southern Brazil (~340,000 inhabitants in 2016).

From January to August 2014, community-dwelling older adults were located and interviewed at their homes. A representative sample was obtained from two sampling stages. Initially, 133 census tracts were selected considering the size of census tracts after being sorted by mean income. Thirty one households were selected in each tract, considering that at least 12 older adults would be identified per tract. Inclusion criteria were age older than 60 years and not being institutionalized (i.e. long-term care institution, long hospital stay, etc.).

Baseline assessment

Female interviewers previously trained to interview and take anthropometric measurements applied a questionnaire about several aspects of health. Sex and skin color were observed by the interviewers while age was obtained by self-report. Years

of education were calculated based on the highest reported educational attainment. Economic status was categorized from A (wealthiest) to E (poorest) according to criteria of the *Associação Brasileira de Empresas de Pesquisa* – ABEP (Brazilian Association of Research Companies) [19] which considered the possession of consumer goods, the head of the household's schooling and the presence of a maid.

Older adults were also asked about smoking habits and classified as a smoker (smoked at least one cigarette in the last 30 days), never smoker, or previous smoker. Participants also self-classified their health as very good, good, regular, bad or very bad. Pre-existing morbidities were investigated based on self-reported previous medical diagnosis of the following list of diseases: high blood pressure, diabetes, heart problem, heart failure, Parkinson's disease, kidney failure, hypercholesterolemia, depression, stroke and cancer.. Physical capability was evaluated by the Katz [20] index of independence in activities of daily living (bathing, dressing, toileting, transferring, continence and feeding).

Physical activity assessment

Weekly time spent in self-reported physical activity during commuting (walking and cycling) and leisure-time (walking, moderate and vigorous activities) was estimated using the International Physical Activity Questionnaire (IPAQ) – long version [21]. Time spent in vigorous physical activity during the leisure-time domain was multiplied by two [21]. Commuting and leisure time PA were analyzed separately and an additional variable considering both domains was also included.

Objectively measured PA was measured from GENEActiv® accelerometers (Activinsights Ltd, Kimbolton, Cambs, UK, http://www.geneactiv.org) after the interview. The GENEActiv® accelerometer measures acceleration in three axes and

provides raw data expressed in gravitational equivalent units (1000mg=1g). Participants wore the accelerometer on their non-dominant wrist during seven days using a 24 hour-protocol, including water-based activities. The research team was responsible for attaching and collecting the accelerometers at the subject's home as previously described [22]. Bed-bound and disabled older adults were excluded from this assessment.

Accelerometers were initialized to collect data in 85.7 Hz time resolution. Data were processed with the GENEActiv software and analyzed using the R-package GGRI v1.1-5 (https://cran.r-project.org/web/packages/GGIR/vignettes/GGIR.html#citing-ggir). Raw data were calibrated to local gravity [23], scored for non-wear based on periods greater than 60 minutes of low acceleration variability (SD <13 mg) and abnormally high values were removed. Participants providing fewer than two days of measurement were excluded from the analyses. Activity-related acceleration was calculated using the Euclidian Norm (vector magnitude of the three axes) minus 1 g (ENMO = $\sqrt{(x^2 + y^2 + z^2)}$ - 1 g) [24]. Invalid data segments were imputed – within individual – by the average of similar time of day data points from other days of the measurement.

Overall physical activity – the total volume of movement – was expressed by the daily average of acceleration (mg). Activity intensities (light, moderate to vigorous) were estimated from 5-s aggregated time-series (epoch). Time spent in acceleration between 50 and 99 mg defined daily time in light physical activity (LPA), while activities with acceleration higher than 100 mg were considered as moderate to vigorous physical activity (MVPA) [25-27]. MVPA in 5-min bouts – defined as five consecutive minutes in which participants spent at least 4 minutes > 100 mg – was also considered.

Follow-up

Between November 2016 and April 2017 participants were interviewed again by phone. In addition to the follow-up interview, this second visit also assessed complete surnames and birth dates in order to allow monitoring of vital statistics. The baseline survey had not correctly collected this information (especially surnames), as the study was not initially planned to be longitudinal. In case of non-response or change of phone number home visits were conducted.

Relatives or neighbors reported deaths, cause of death, and dates. Those deceased were confirmed by the vital statistics sector of the Department of Epidemiologic Surveillance of the Municipal Health Secretary of Pelotas. We recorded deaths occurring up to April 30, 2017. Since causes of death were poorly described in approximately 13% of deaths in Pelotas from 2013 to 2015 (http://www2.datasus.gov.br/DATASUS/index.php?area=0205&id=6937), and defining cause-of-death is known to be problematic [28-29], only all-cause mortality was considered for this study. Losses to follow-up were assumed to be proportional during the time. Thus, we assumed losses were followed-up up to mid-way between the end of first interview phase (2014 August 31th) and the beginning of second interview (2016 November 1st) – to calculate person-time at risk. The second visit or date of death was used to obtain time of follow-up from the first interview.

Statistical analyses

Analyses were performed using Stata version 13.0 (Stata Corp., College Station, USA). Significance level was set at 5%. Description of the characteristics of the sample was reported based on life status. Distribution of the variables according to tertiles of overall PA was also described. Since the proportion of deaths, life expectancy and type

of physical activity (Supplementary Table 1) was different between males and females, the analyses for risk of mortality were stratified by sex, assuming a p-value <0.10 for interaction. The statistical adjustment was based on a hierarchical model and included variables that presented a p-value≤0.2 in the crude analysis with mortality or physical activity, with exception of smoking (since better information for this exposure, e.g. pack-years, is not available), using four different levels of adjustment: adjustment for age (model 1); adjustment for model 1 + skin color, schooling, economic level and smoking (model 2); adjustment for model 2 + self-perceived health and number of morbidities (model 3); and adjustment for model 3 + functional capability. This strategy allowed observing the relationship between exposures and outcome considering only sociodemographic and behavior confounders and also including preexisting conditions to reduce the influence of possible reverse casualty.

Hazard ratios and 95% confidence intervals were obtained using Cox regression (proportional hazards regression) according to the models described above. Physical activity variables (overall physical activity, LPA, MVPA, self-report leisure-time and commuting PA) were analyzed in tertiles to examine at the dose-response association. A graph of cumulative hazard function according to time was set to assess whether the findings could be influenced by time between the events. Deaths in the first 6 months were excluded from analysis, and a sensitivity analyses was conducted to exclude deaths in the first year of follow-up.

Ethical aspects

Both phases of the "COMO VAI?" study were submitted for consideration and approved by the Research Ethics Committee of the School of Medicine of Federal University of Pelotas. Informed consent was obtained from all participants prior to the

interviews at baseline and follow-up. Relatives or neighbors who reported deaths also signed the informed consent - in the phone-based interviews, the agreement in response to the questions was the consent.

Results

In 2014, 1,451 older adults were interviewed (78.7% from the 1,844 located after sampling procedures – most non-interviewed individuals were women and were aged between 60 and 69 years). Objectively measured physical activity was obtained for 971 participants (66.9% of those interviewed). Individuals in the economic groups A/B had a higher probability of providing valid accelerometry data [22]. Up to April 2017 (3,614 person-year at risk), 145 deaths were identified (10%), 92 (6.3%) participants were lost to follow-up, and 61 (4.2%) were refusals to the second follow-up assessment. Thus, time of follow-up was on average 2.6 years (median: 2.7 years; IQR: 2.5-2.8 years). Follow-up status differed according to marital status, economic level, nutritional status, and smoking. Older adults who were married or living with a partner, richer, were overweight and never smoked had a higher probability of follow-up (data not shown). A total of 23 participants died in the first six months of follow-up and were excluded in the main analysis.

Table 1 describes the total sample according to life status. Percentage of deaths was higher among men (12.9% vs. 8.3% among women – p=0.005), individuals aged > 80 years at baseline (p<0.001), with lower educational level (p=0.033), presenting bad or very bad self-perceived health (p<0.001), with at least four self-reported morbidities (p<0.001) and dependent for two or more functional activities (p<0.001). Participants who died were not statistically different than survivors according to skin

color, economic status and smoking. All physical activity measurements were lower among older adults who died (p<0.001).

Figure 1 shows that mortality rate was higher among men and women in the lowest tertile of overall PA compared with individuals classified in the second and third tertiles. Older males and females classified in the second and third tertiles of accelerometer-based PA had similar survival probability although dose-response associations were observed.

Table 2 shows the distribution of independent variables according to tertiles of overall PA (acceleration). Percentages of men and women were not statistically different among the tertiles (p=0.692). The highest tertile of overall PA showed a higher proportion of participants aged 60 to 69 years (p<0.001). The proportion of more educated participants and those classified in A/B economic groups was higher in the third tertile of PA (p=0.010; p=0.025). A higher percentage of older adults who perceived their health as very good or good were classified in the highest tertile of overall physical activity (p<0.001) as well as those with none or a lesser number of morbidities and those who reported being functionally independent (p<0.001; p<0.001). All other physical activity measurements were statistically higher in the third tertile of PA (p<0.001).

Although there was no statistically significant interaction by sex in the association of overall PA and LPA with risk of mortality (p=0.664 and p=0.638), there was evidence of interaction by sex in the association between MVPA and risk of mortality (p=0.084). After adjustment for possible confounders included in model 4, men classified in the highest tertile of overall physical activity had on average 77% lower risk of all-causes mortality in the study period (HR= 0.23; 95%CI: 0.06; 0.84) in comparison with men in the lowest tertile. Hazard ratios did not substantially change

after inclusion of additional variables in the statistical models. Men in the highest tertile of accelerometry-based LPA showed on average 74% lower risk of mortality (HR= 0.26; 95%CI: 0.07; 0.95) compared with individuals in the first tertile. Objectively measured MVPA and self-reported measurements of PA were not significantly associated with mortality among men, although hazard ratio in those men classified in the lowest tertile of MVPA was low (HR= 0.22; 95%CI: 0.05; 1.05). (Table 3)

Table 4 shows the association between physical activity and risk of all-cause mortality among women. Older women who were classified in the highest tertile of overall physical activity had on average an 92% lower risk of mortality than those classified in the lowest tertile (95%CI: 0.01; 0.65) after adjustment for all possible confounders. Older women in highest tertile of LPA had a 91% lower risk of mortality in comparison with individuals in the lowest tertile (95%CI: 0.01; 0.67). Hazard ratios in the lowest and intermediate tertiles of both overall PA and LPA were statistically similar. Older women in the intermediate and highest tertiles of MVPA had on average 70% (95%CI: 0.13; 0.88) and 92% lower risk of mortality than participants in the lowest tertile (95%CI: 0.01; 0.59). There was no association between self-reported leisure-time PA and risk of mortality, whereas women in the intermediate and highest tertiles of commuting PA showed 67% and 74% lower risk of mortality, respectively, than individuals in the lowest tertile (95% CI: 0.14; 0.77 and 95%CI: 0.09; 0.69). Similar findings were observed for the sum of both leisure-time and commuting PA (HR=0.24 – 95%CI: 0.08; 0.72).

Sensitivity analysis (Supplementary figure 1) for association of overall PA with mortality including only deaths after 1 year of follow-up presented similar results than shown in the main analysis.

Discussion

To our knowledge, this study is the first investigation of objectively measured PA from triaxial accelerometers and risk of mortality among older adults from a low- or middle-income country. Our main findings suggest that low levels of PA are associated with higher risks of death independent of previous health, functional conditions and other factors related to higher mortality among older adults. Use of PA from accelerometry and questionnaire allowed for estimating the differences in results from different sources of information. Despite sex differences – higher mortality in men in the lowest tertile than in women – overall PA was important for avoiding early mortality in older adults of both genders.

Previous studies found inverse associations between physical activity and risk of mortality [5, 7-8, 11-13, 15, 17, 30], as observed in the current study, but an absence of association has also been reported [31]. Association between physical activity obtained by triaxial accelerometers and mortality was recently described using data from The Women's Health Study [17]. Despite differences in the measurement of overall PA (counts *vs.* m*g*), and consequently in the cut-off points used to classify intensity, light PA was not related to the risk of mortality in this study [17], unlike in our current study and in other one performed with women enrolled in the Objective Physical Activity and Cardiovascular Health Study [30]. Other studies that have compared objectively measured PA and risk of mortality are scarce and not specific to older adults [32].

A previous systematic review and meta-analysis of studies in older adults found a decrease in mortality associated with moderate-to-vigorous PA, but this review included only studies with self-reported PA [8]. Differences in the strength of association observed in the studies may reflect differences among the studies in age at baseline, length of follow-up, and especially in the measurement of physical activity. Some

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studies evaluated physical activity in all domains [11-12, 33-34], other only included leisure-time PA [7], housework [35], or walking [15, 36]. Some studies considered sex as a confounder in the statistical analysis [5, 11, 13, 34, 36] whereas others stratified the analysis by sex as a potential effect modifier [12, 35]. Studies that stratified the analysis according to sex found different results for men and women, with PA reducing mortality only in men [12, 35]. In our study, mortality by tertiles of MVPA was different between the sexes (p-value for interaction <0.10), although HR in the highest tertile of MVPA in males was nearly to the reference.

In addition to biological differences, men and women also consistently have different patterns of physical activity. Men from our study spent on average more time in objectively measured MVPA (15.0 min/day vs. 8.1 min/day) and in self-reported leisure-time PA (119 min/week vs. 64 min/week). Similar sex differences were found for time spent in commuting PA, with women having less time than men. Commuting PA is probably an important contributor to total time spent in PA by older women. However, we do not have information from the work and household domains of PA. As 27% of the men in our sample were still working at baseline interview compared to only 14% of women this might impact the gender differences (data not shown).

The 2008 Physical Activity Guidelines for Americans recommended that older adults practice at least 150 min/week of MPA or 75 min/week of VPA[37]. The new 2018 US guidelines for older adults have not changed the total time for MPA or VPA but have eliminated the requirement that activity be accumulated in bouts of at least 10 minutes [38]. Newer data also show that higher time spent in LPA is associated with a better health profile [10, 39] and lower risk of all-cause mortality [30, 40], as observed in our study. In addition, independent of bout length, PA has been associated with lower adiposity and lower risk of metabolic syndrome in older adults [41]. Results based on

overall PA as in our study are less susceptible to bias due to misclassification of intensity based on different cut-points or, the complexity introduced by relative and absolute intensity differences, especially at older ages [42].

PA may be either cause or consequence of poor health status. We found a cross-sectional crude relationship between PA and number of morbidities and functional capability. Multi-morbidity is a reality in our population, increasing the importance of PA as an important factor for secondary prevention [43]. In addition to prevention of several diseases [1], PA improves general health profile among patients with chronic kidney disease [44-45]; improves strength, balance and bone mass postmenopausal [46]; reduces the risk of cardiovascular outcomes [47]; and decreases the risk of unfavorable outcomes in older adults with diabetes [48] or after stroke [49].

Evaluation of the benefits of PA among older adults should be made with caution due to high risk of reverse causality as previously noted[12]. For this reason, our analyses considered preexisting morbidities and disability. Furthermore, a higher proportion of deaths occurred after the first year of the physical activity measurements, and hazard ratios were minimally affected in the sensitivity analysis and by the adjustments. Inclusion of preexisting morbidities and functional capability as possible confounders as well as the sensitivity analysis may have reduced the influence of reverse casualty in the results, although such bias may not be discarded in the current study.

Strengths of this study include excellent follow-up of a representative population sample, the high response rate, and use of both objectively measured (accelerometry) and subjectively reported PA (questionnaire). A majority of previous studies used only questionnaires to estimate PA, potentially leading to missing the relationship between PA and mortality since LPA and short bouts of MVPA are

difficult to accurately measure by self-report. As in our study, previous publications report stronger associations between objectively measured free-living activity and risk of mortality in comparison to those observed based on questionnaires [50]. On the other hand, questionnaires provide information on the type of activities and in which domain activity occurs, both of which can inform future PA interventions.

A third of the older participants did not provide accelerometry data. This reduction in the size of the analytic sample for objectively measured PA is a limitation. However, even with larger 95% confidence intervals, important findings were seen, although is not possible to discard that important associations with the risk of mortality (i.e. for MVPA in men) were not observed due to limited statistical power. Although our study had a high retention rate, as it was not initially designed to be a cohort study, errors in the names, addresses and phone numbers of the participants contributed to losses and difficulty searching vital statistics. Short follow-up may have also limited our conclusions, since we observed small number of deaths in the first years of follow-up, reducing our statistical power. However, associations with survival are dependent of follow-up length, so that it is not possible to discard that such associations between physical activity and mortality are observed only in short periods of time in older adults. Finally, the absence of adequate measurements of other behavioral confounders such as diet and alcohol intake is also a limitation.

In conclusion, despite the many factors that affect the health-disease-disability-death process among the older population, overall and light PA were observed to be significant predictors of survival in older individuals from Southern Brazil. Higher overall and light PA reduced the risk of mortality in both older men and women, whereas MVPA statistically reduced the risk of mortality only among women. PA may contribute to reducing sex differences in mortality rates among older adults. Greater

health benefits are directly related to the intensity of PA, however higher intensity activity may be a challenge at older ages. Thus, our findings that any type of PA is associated with a reduction in mortality in older people is especially important for public health programs targeting physical activity of this population.

Competing Interests

All authors declare no conflict of interest.

Authors' contribution

RMB and MP conceived the study. RMB and PACS conducted the second data collection. RMB run the statistical analyses. RMB, AZL, ADB, ET, FFD, MCG PACS, AW, ICMS, SB, UE and MP wrote the manuscript. SB and UE supervised the collection and analyses of data from physical activity. All authors revised the final version and approved the manuscript.

Sponsor's role

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Figure 1. Cumulative survival probability according to tertiles of overall objectively measured physical activity at baseline in older men and women from Pelotas, Brazil.

Supplementary Table 1. Description of physical activity information of community-dwelling older adults from Pelotas, Brazil, 2014.

Supplementary figure 1. Sensitivity analysis (including only deaths after 12 months of follow-up) of cumulative survival probability according to tertiles of overall objectively measured physical activity at baseline in older men and women from Pelotas, Brazil.