

Estimation of All-Cause and Cardiovascular Mortality Risk in Relation to Leisure-Time Physical Activity: A Cohort Study

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Key Words: physical activity; all-cause mortality; cardiovascular mortality; population; cohort study.

Summary. Background and Objective. Epidemiologists agree that physical activity has a protective role in morbidity and mortality mainly through its positive impact on risk factors. So far, most studies have confirmed that CVD risk decreases with an increasing physical activity level, but it is not known what level of physical activity is already sufficient for mortality risk reduction. Thus, the aim of this study was to explore long-term associations between leisure-time physical activity and mortality risk in the Lithuanian urban population.

Material and Methods. The MONICA study (1992–1993) and the repeated health examination survey in 2001–2002 were organized as a cohort study of 2642 middle-aged inhabitants from the general Lithuanian population of Kaunas. Two random samples aged 35–64 years were examined in 1992–2002. Leisure-time physical activity was assessed by an interview method, asking about physically demanding activities at leisure time measured in hours. The study sample was pooled into 2 groups: inactive (first quartile) and active (second to fourth quartiles). Follow-up was carried out in terms of the endpoints reached from the baseline until December 31, 2010. Mortality data from the National Death Register were obtained.

Results. Multivariate adjusted Cox proportional hazards analyses revealed an HR of 1.46 (95% CI, 1.15–1.85) for all-cause mortality and 1.73 (95% CI, 1.23–2.45) for CVD mortality in the lowest quartile of leisure-time physical activity compared with the higher ones. As much as 16.2% of all-cause mortality and 22.2% of CVD mortality was attributable to the lowest quartile of leisure-time physical activity.

Conclusions. This study demonstrated a beneficial effect of leisure time physical activity on predicting all-cause and CVD mortality risk.

Introduction

Over the past 5 decades, a substantial accumulation of epidemiological and experimental data has established a causal relationship between the low levels of leisure-time physical activity (LTPA) and an increased risk of cardiovascular disease (CVD) (1). Physical inactivity is considered the fourth leading cause of death worldwide (2). It is well known that physical activity (PA) has a protective role in the morbidity and mortality from CVD mainly through its positive impact on the risk factors, such as increased body weight, high blood pressure, glucose intolerance, and abnormal blood lipid profile (3, 4). A major question regarding this amendable risk factor is to what extent PA has an effect on longevity beyond the recognized mediators of blood pressure, lipid profile, and body weight (5).

The World Health Organization recommendations for PA are based on evidence linking a physically active lifestyle to reduced mortality (6). Despite these strong evidences of PA benefits, the humans of the 21st century are immersed within an environment explicitly designed to eliminate physical labor (1). The lack of exercise and sedentary work in industrialized countries is becoming increasingly common.

There is scientific evidence that LTPA, but not the work requiring many physical efforts, has a positive impact on human's health (7). Epidemiologists agree that the protective effect of PA on CVD mortality is approximately 750–2000 kcal a week of moderate intensity exercise (walking or jogging about 12–32 kilometers per week) (8). If a person is physically inactive during leisure time, a minimum of 1 hour per week of continuous very strenuous exercise is recommended (9). So far, it is unknown whether the relationship between PA and CVD is linear. In addition, most studies have confirmed

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that CVD risk decreases with an increase in moderate-intensity PA, but it is not known how much of movement is already sufficient for a reduction in CVD mortality risk at the population level: the dose-response relationship between LTPA and mortality risk remains a subject of discussion.

In Lithuania, the mortality from CVD remains one of the highest in Europe and is the first in the death structure (10). According to the 2010 data, only 28% of Lithuanian adult men and 29% of women achieved the WHO recommended PA level during leisure time (11). Moreover, there is a lack of population-based PA studies in Lithuania, and insufficient attention is paid to the promotion of PA (12).

Thus, the aim of this study was to explore the long-term associations between LTPA and all-cause and CVD mortality risk in the Lithuanian urban population.

Material and Methods

Study Sample. The data from the 2 surveys are presented in this article. The first health examination in the framework of the Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study was performed in 1992–1993 (13). The second survey was conducted in 2001–2002 in accordance with the MONICA project protocol. These surveys were carried out in Kaunas, which is the second largest city in Lithuania with a population of 348 624 inhabitants. Two random samples of 2642 Kaunas men and women aged 35–64 years, stratified by gender and age so that at least 200 men and women could be screened in every 10-year age group (35–44, 45–54, and 55–64), were randomly selected from the Lithuanian population register of Kaunas. During 1992–1993, 611 men and 628 women were screened (a total sample of 1239 persons), and during 2001–2002, 626 men and 777 women were examined (a total sample of 1403 persons). The response rates were 58.6% in the first survey during 1992–1993 and 62.4% in the second survey during 2001–2002. Both samples were selected using the same registry. The updating of the Kaunas population registry is continuous. Over the 1992–2002 period, the middle-aged Kaunas population did not change significantly. Two random samples were pooled together for the analysis to increase the sample size and the number of the endpoints. The studies were approved at the Regional Ethics Committee at the Lithuanian University of Health Sciences.

Baseline Health Examination. Lifestyle habits were evaluated using a frequency questionnaire. The standard questionnaire included questions regarding the respondent's age, education, smoking and alcohol consumption habits, etc. Education was

measured by 4 levels: primary, incomplete secondary, secondary/vocational/college, and university. Smoking habits were assessed according to a current smoking status. A subject who smoked at least one cigarette per day was classified as a current smoker. According to the frequency of alcohol consumption, the number of standard drinks per month, usually consumed per one occasion and type of alcoholic beverage, was calculated.

At the study site, specially trained nurses measured height (with an accuracy of 0.5 cm) and weight (with an accuracy of 0.1 kg). The responders were classified in 3 categories by body mass index (BMI): 18.5 to 24.9 kg/m² (normal weight), 25.0 to 29.9 kg/m² (overweight), and ≥ 30 kg/m² (obese). Ten persons with underweight (BMI, <18.5 kg/m²) were excluded from the further analysis. Blood pressure was measured by physicians two times with a mercury device at the appearance of sounds (first-phase Korotkoff) in a sitting position. The average of 2 blood pressure measurements was used for the analysis.

Biochemical analyses for glucose and lipids were done for responders (fasting for at least for 12 hours) on an empty stomach. The concentration of glucose in capillary blood was determined by a Glucotrend blood glucose monitor (14). The concentration of serum cholesterol was determined enzymatically.

Arterial hypertension (AH) was defined by systolic blood pressure of 140 mm Hg or more and/or diastolic blood pressure of 90 mm Hg or more or normal blood pressure (<140/90 mm Hg), if the person had been taking antihypertensive medications within the last 2 weeks.

Coronary heart disease (CHD) was determined according to the following criteria: 1) a documented history of myocardial infarction (MI) and/or ischemic changes on electrocardiography (ECG) coded by the Minnesota codes (MC) 1–1 or 1–2 (15); 2) angina pectoris defined by the Rose questionnaire (without MI and/or MC 1–1 or 1–2) (16); and 3) ECG findings by MC 1–3, 4–1, 4–2, 4–3, 5–1, 5–2, 5–3, 6–1, 6–2, 7–1, 8–3 (without MI and/or MC 1–1, 1–2 and without angina pectoris). Previous stroke was determined by interview information and documented history of stroke.

Assessment of Physical Activity. LTPA was assessed by the interview method using a standard questionnaire, asking about physically demanding activities at leisure time: going to work on foot, walking, running, gardening, maintenance of the house, and engagement in sports in a typical week during the summer and winter seasons. LTPA was measured by hours a week. Before the analysis, the averages of actively spent hours in summer and winter were calculated, and all the responders were divided into 4 equal groups (quartiles) according to LTPA: 1st, <8.4 hours/week; 2nd, 8.4–12.6 hours/

week; 3rd, 12.7–18.1 hours/week; and 4th, >18.1 hours/week. Based on the results of further analysis, the study population was divided into 2 groups: physically inactive (first LTPA quartile) and physically active (second to fourth LTPA quartiles).

Follow-up. Person-years were calculated from the beginning of follow-up until the date of death or end of the study period (December 31, 2010), whichever occurred first. The mean follow-up time was 12.6 years. Data from the National Death Register were used to analyze mortality among the persons observed. All death cases were registered every month from the beginning of the baseline health examinations and categorized into specific causes of death, which were obtained from death certificates. Deaths from CVD were verified by the myocardial infarction registry data (13). Two groups of death cases were analyzed in this study: all-cause deaths, 001-E999 codes of the International Classification of Diseases (ICD), 9th revision (until January 1, 1997), and A00–Z99 codes of the ICD, 10th revision (after January 1, 1997); and deaths from CVD, 390–458 codes of the 9th ICD and I00–I99 codes of the 10th ICD. CVD deaths included CHD, stroke, and other vascular causes (17, 18).

Statistical Analysis. Firstly, the chi-square (χ^2) test was used to compare the prevalence of categorical variables among the groups of subjects with the different quartiles of LTPA at the baseline. To compare the estimates of continuous variables in the LTPA quartiles with normal distribution, an analysis of variance (ANOVA) test was used, and for SAU with nonnormal distribution, the Kruskal-Wallis test was employed.

Secondly, all-cause and CVD mortality rates in the LTPA quartiles were calculated. The population attributable risk fraction (PARF) was interpreted as the proportional reduction in the average population mortality rate that would occur if low LTPA was eliminated from the population. The PARF was estimated using the following equation (19, 20):

$$\text{PARF} = ((r_{\text{pop}} - r_0) / r_{\text{pop}}) \times 100(\%),$$

where r_{pop} indicates the mortality rate of the overall population, and r_0 indicates the mortality rate of the unexposed population.

The cut-off point for the exposed population was set at the first LTPA quartile, which divided the study population in 2 groups: exposed (first LTPA quartile) and unexposed (second to fourth LTPA quartiles).

Finally, survival analyses were accomplished for all-cause mortality as well as separately for CVD. Kaplan-Meier curves were generated. The probability of surviving to any point was estimated from the cumulative probability of surviving each of the preceding time intervals. The estimates of hazard

functions in the different LTPA quartiles were tested using a log-rank procedure. For the estimation of hazard ratios (HR), we fitted Cox regression models including relevant independent variables (age, sex, education, risk factors, and CVD) and adjusting for the study year. As HRs in the second, third, and fourth LTPA quartiles did not differ significantly, these 3 quartiles were pooled together as a risk factor-unexposed (physically active) category for further analyses. The association between LTPA and death was increasingly adjusted for additional variables using 3 models: 1) unadjusted; 2) adjusted for age, sex, education, and study year; 3) adjusted for age, sex, education, study year, smoking, alcohol consumption, hypertension, fasting glucose, total cholesterol, CHD, and previous stroke. Age, glucose concentration, total cholesterol level, and alcohol consumption, recalculated to standard drinks, were entered as continuous variables, whereas LTPA (active vs. inactive), gender, study year, education (3 levels), body mass index (normal weight, overweight, obesity), smoking (no, yes), hypertension (no, yes) and CVD (no, yes) were entered as categorical variables. A P value of <0.05 was considered as statistically significant.

All mortality analyses were initially conducted separately for those free of CVD and those with CVD. Those who had a diagnosed CVD at the baseline were at higher mortality risk as compared with the initially healthy, but the relative risk between LTPA groups was the same in healthy and subjects with CVD at the baseline. Therefore, the adjustment for a chronic disease did not change significantly the LTPA estimates when the whole group was analyzed, and the data are presented for the whole group throughout the article.

General descriptive analyses and survival estimations were performed with the Stata, version 10.1; Kaplan-Meier curves were generated with the SPSS, version 19.0.

Results

The frequency distribution and the mean values of the key variables used for the adjustment in the survival analyses for each quartile of LTPA are shown in Table 1. Younger age was associated with higher LTPA. The educational level of the participants was positively associated with LTPA ($P < 0.0001$). The percentages of current smokers ($P < 0.0001$) and persons with hypertension ($P < 0.0001$), CVD ($P = 0.001$), and obesity ($P > 0.05$) were negatively related to LTPA. The mean values of fasting blood glucose and consumed alcohol amount decreased with each increasing LTPA quartile ($P < 0.05$).

Overall, during the follow-up period, there were 330 deaths, including 150 CVD deaths (Table 2). The percentage of all-cause deaths decreased from

Table 1. Sample Characteristics According to Leisure-Time Physical Activity at the Baseline

| Characteristic | Quartile of Leisure-Time Physical Activity, Hours per Week | | | | χ^2 (P) |
|---|--|------------|------------|------------|----------------|
| | <8.4 | 8.4–12.7 | 12.8–18.1 | >18.1 | |
| Gender | | | | | |
| Male | 311 (47.0) | 343 (51.1) | 301 (46.4) | 282 (42.7) | 9.5 (0.024) |
| Female | 351 (53.0) | 328 (48.9) | 348 (53.6) | 378 (57.3) | |
| Age group, years | | | | | |
| 35–44 | 186 (28.1) | 221 (32.9) | 215 (33.1) | 218 (33.0) | 11.7 (0.07) |
| 45–54 | 217 (32.8) | 226 (33.7) | 222 (34.2) | 236 (35.8) | |
| 55–64 | 259 (39.1) | 224 (33.4) | 212 (32.7) | 206 (31.2) | |
| Education | | | | | |
| Primary/incomplete secondary | 133 (20.1) | 113 (16.9) | 91 (14.0) | 87 (13.2) | 27.1 (<0.0001) |
| Secondary/vocationally/college | 357 (53.9) | 351 (52.4) | 369 (56.9) | 332 (50.4) | |
| University | 172 (26.0) | 206 (30.7) | 189 (29.1) | 240 (36.4) | |
| Body mass index, kg/m ² | | | | | |
| 18.5–24.9 | 194 (29.5) | 201 (30.1) | 187 (29.0) | 206 (31.4) | 10.5 (0.104) |
| 25.0–29.9 | 237 (36.0) | 264 (39.6) | 278 (43.2) | 260 (39.7) | |
| ≥30.0 | 227 (34.5) | 202 (30.3) | 179 (27.8) | 189 (28.9) | |
| Smoking | | | | | |
| No | 490 (74.0) | 514 (76.6) | 536 (82.6) | 540 (81.8) | 20.1 (<0.0001) |
| Yes | 172 (26.0) | 157 (23.4) | 113 (17.4) | 120 (18.2) | |
| Arterial hypertension | | | | | |
| No | 313 (47.4) | 331 (49.4) | 329 (50.7) | 394 (59.7) | 23.6 (<0.0001) |
| Yes | 348 (52.6) | 339 (50.6) | 320 (49.3) | 266 (40.3) | |
| Coronary heart disease | | | | | |
| No | 529 (79.9) | 569 (84.8) | 564 (86.9) | 575 (87.1) | 17.1 (0.001) |
| Yes | 133 (20.1) | 102 (15.2) | 86 (13.1) | 85 (12.9) | |
| Previous stroke | | | | | |
| No | 646 (97.6) | 667 (99.4) | 644 (99.2) | 657 (99.5) | 15.8 (0.001) |
| Yes | 16 (2.4) | 4 (0.6) | 5 (0.8) | 3 (0.5) | |
| Total cholesterol, mean (SD), mmol/L | 6.1 (1.3) | 6.2 (1.4) | 6.2 (1.3) | 6.2 (1.4) | 0.5* (0.69) |
| Fasting blood glucose, mean (SD), mmol/L | 5.6 (1.8) | 5.6 (1.4) | 5.4 (1.1) | 5.3 (1.4) | 7.9* (<0.0001) |
| Alcohol consumption, median, drinks/month | 4.9 | 6.3 | 4.7 | 4.4 | 9.9† (0.02) |

Values are number (percentage) unless otherwise stated.

*F test (ANOVA), †Kruskal-Wallis test.

Table 2. Sample Characteristics and Mortality During the Follow-Up Period According to Leisure-Time Physical Activity Quartile

| Characteristic | Leisure Time Physical Activity Quartiles, Hours per Week | | | | Total |
|--|--|------------|------------|------------|--------------|
| | <8.4 | 8.4–12.7 | 12.8–18.1 | >18.1 | |
| Total cohort at the baseline n (%) | 662 (25.1) | 671 (25.4) | 649 (24.6) | 660 (25.0) | 2642 (100.0) |
| All-cause deaths, total n (%) | 117 (35.5) | 91 (27.6) | 66 (20.0) | 56 (17.0) | 330 (100.0) |
| All-cause deaths, men n (%) | 76 (32.3) | 70 (29.8) | 50 (21.3) | 39 (16.6) | 235 (100.0) |
| All-cause deaths, women n (%) | 41 (43.2) | 21 (22.1) | 16 (16.8) | 17 (17.9) | 95 (100.0) |
| CVD deaths n, total (%) | 60 (40.0) | 38 (25.3) | 26 (17.3) | 26 (17.3) | 150 (100.0) |
| CVD deaths n, men (%) | 43 (39.1) | 29 (26.4) | 21 (19.1) | 17 (15.5) | 110 (100.0) |
| CVD deaths n, women (%) | 17 (42.5) | 9 (22.5) | 5 (12.5) | 9 (22.5) | 40 (100.0) |
| Person years | 7773.6 | 8599.5 | 8509.1 | 8454.1 | 33 336.3 |
| All-cause death rate per 1000 person-years | 15.1 | 10.6 | 7.8 | 6.6 | 9.9 |
| CVD death rate per 1000 person-years | 7.7 | 4.4 | 3.1 | 3.1 | 4.5 |

CVD, cardiovascular disease; PARF, population attributable risk fraction.

PARF (all-cause mortality) = $((9.9 - 8.3) / 9.9) \times 100 = 16.2\%$; PARF (CVD mortality) = $((4.5 - 3.5) / 4.5) \times 100 = 22.2\%$.

35.5% in the lowest LTPA quartile to 17.0% in the highest (from 40.0% to 17.3% for CVD deaths, respectively). The all-cause and CVD mortality rates per 1000 person-years decreased from 15.1 to 6.6 and from 7.7 to 3.1 in the lowest vs. highest LTPA quartile, respectively).

Table 3 shows the comparisons of the pairwise probability of death and the probability of death from CVD in different PA quartiles. Figs. 1 and 2 represent the pooled probability of death and the

probability of death from CVD comparisons in 4 PA quartiles. In the Kaplan-Meier analysis, physical inactivity (<8.4 hours/week) was associated with a significantly greater probability of death from any cause and CVD as compared with all higher LTPA quartiles (log-rank test, $P < 0.01$). In addition, in all-cause death structure, people in the second LTPA quartile (8.4–12.6 hours/week) also had a higher probability of death as compared with the highest LTPA quartile ($P = 0.006$).

Table 3. Probability of Death Comparison in Different Leisure-Time Physical Activity Quartiles

| | Leisure Time Physical Activity Quartiles, Hours per Week | | | | | | | |
|---------------------|--|---------|----------|-------|-----------|---------|----------|---------|
| | <8.4 | | 8.4–12.7 | | 12.8–18.1 | | >18.1 | |
| | Log Rank | P | Log Rank | P | Log Rank | P | Log Rank | P |
| All-Cause Mortality | | | | | | | | |
| <8.4 | – | – | 8.0 | 0.005 | 21.4 | <0.0001 | 29.5 | <0.0001 |
| 8.4–12.7 | 8.0 | 0.005 | – | – | 3.7 | 0.053 | 7.5 | 0.006 |
| 12.8–18.1 | 21.4 | <0.0001 | 3.7 | 0.053 | – | – | 0.70 | 0.40 |
| >18.1 | 29.5 | <0.0001 | 7.5 | 0.006 | 0.70 | 0.40 | – | – |
| CVD mortality | | | | | | | | |
| <8.4 | – | – | 8.7 | 0.003 | 19.5 | <0.0001 | 18.8 | <0.0001 |
| 8.4–12.7 | 8.7 | 0.003 | – | – | 2.1 | 0.15 | 2.0 | 0.16 |
| 12.8–18.1 | 19.5 | <0.0001 | 2.1 | 0.15 | – | – | 0.003 | 0.95 |
| >18.1 | 18.8 | <0.0001 | 2.0 | 0.16 | 0.003 | 0.95 | – | – |

CVD, cardiovascular disease.

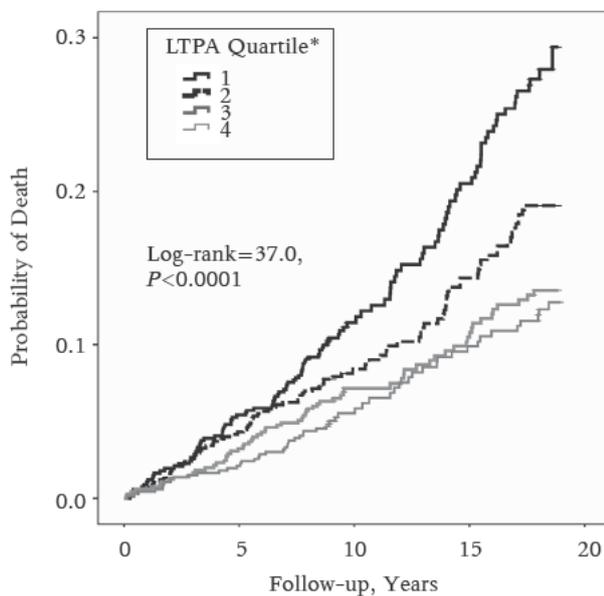


Fig. 1. Probability of death from any cause according to leisure time physical activity quartile

LTPA, leisure-time physical activity.

*Higher LTPA quartile indicates higher physical activity.

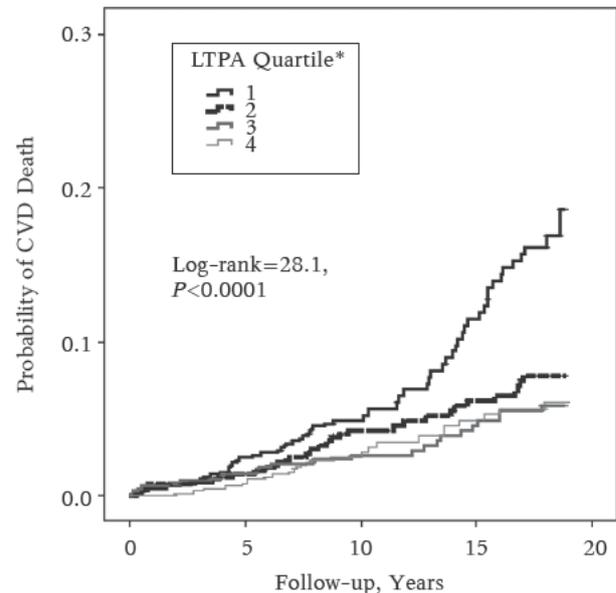


Fig. 2. Probability of cardiovascular death according to leisure time physical activity

LTPA, leisure-time physical activity; CVD, cardiovascular disease.

*Higher LTPA quartile indicates higher physical activity.

As the adjusted all-cause and CVD mortality risks were approximately the same in the second to fourth LTPA quartiles, Table 4 shows the comparisons of pooled risk estimation in these 3 quartiles (active) versus the lowest one (inactive). Cox proportional hazards analyses revealed an unadjusted HR of 1.86 (95% CI, 1.49–2.34) for all-cause mortality and 2.28 (95% CI, 1.65–3.17) for CVD mortality in the lowest LTPA quartile compared with higher LTPA quartiles: participation in physical efforts demanding activities 8.4 hours a week and more (Table 4). Sociodemographic (model 2) and multivariate adjusted (model 3) hazard ratios confirmed an independent protective LTPA effect on all-cause and CVD mortality: physically inactive

people were at a 46% higher all-cause mortality risk and a 73% higher CVD mortality risk as compared with active ones.

Again, our results showed that 16.2% of all-cause mortality and 22.2% of CVD mortality were attributable to the lowest LTPA quartile.

Discussion

To our knowledge, this is the first report to investigate the association between LTPA and mortality risk in the middle-aged population of Lithuanian adults living in an urban area. In our study, there were a 12.6-year follow-up, a considerable number of middle-aged participants, a vast collection of potential confounders for adjustments, a satisfactory

Table 4. Mortality Risk by Leisure Time Physical Activity

| LTPA | Model 1 (unadjusted) | | Model 2 (sociodemographic adjusted) | | Model 3 (multivariate adjusted) | |
|---------------------------------|-------------------------|---------|--|---------|------------------------------------|-------|
| | HR (95% CI) | P | HR (95% CI) | P | HR (95% CI) | P |
| All-Cause Mortality Risk | | | | | | |
| Active (2nd–4th LTPA quartiles) | 1.00 | <0.0001 | 1.00 | <0.0001 | 1.00 | 0.002 |
| Inactive (1st LTPA quartile) | 1.86 (1.49–2.34) | | 1.60 (1.28–2.01) | | 1.46 (1.15–1.85) | |
| CVD mortality | | | | | | |
| Active (2nd–4th LTPA quartiles) | 1.00 | <0.0001 | 1.00 | <0.0001 | 1.00 | 0.002 |
| Inactive (1st LTPA quartile) | 2.28 (1.65–3.17) | | 1.89 (1.36–2.62) | | 1.73 (1.23–2.45) | |

LTPA, leisure-time physical activity; CVD, cardiovascular disease; HR, hazard ratio; CI, confidence interval.

Model 1, unadjusted; model 2, adjusted for age, sex, education, and study year; model 3, adjusted for age, sex, education, study year, smoking, alcohol consumption, body mass index, hypertension, total cholesterol, fasting glucose, coronary heart disease, and stroke.

number of endpoints, and 2 groups of mortality risk assessment (all-cause and CVD). Multivariate-adjusted all-cause mortality risk in the first LTPA quartile was found to be by 46% higher (95% CI, 1.15–1.85) than in the second to fourth quartiles. The survival analysis of CVD mortality with adjustments for different covariates showed even a more increased mortality risk for responders in the lowest LTPA quartile (HR, 1.73; 95% CI, 1.23–2.45) compared with the study participants in the second to fourth LTPA quartiles. The probability of death was higher in 2 groups of the lowest LTPA quartiles as compared with the highest one (>18.1 hours/week). Besides, the probability of death from CVD was higher in the lowest LTPA quartile: <8.4 hours per week of any activities as compared with the second to fourth LTPA quartiles, whereas each additional LTPA increase was no more significant.

The results of our study are consistent with those of other studies: the largest benefit was found from moving from no activity at all to the low levels of activity. In the Norwegian Women and Cancer Study, the lowest PA levels were associated with a significantly increased risk of all-cause mortality (level 1 RR=2.35; 95% CI, 1.94–2.84; level 2 RR=1.71; 95% CI, 1.45–2.00; level 3 RR=1.30; 95% CI, 1.14–1.49; level 4 RR=1.07; 95% CI, 0.95–1.22), compared with PA level 5 (21). In addition, CVD mortality risk increased in PA levels 1–3, and the size effect was even higher: level 1 RR=3.50; 95% CI, 2.41–5.10; level 2 RR=1.50; 95% CI, 0.99–2.25; and level 3 RR=1.12; 95% CI, 0.79–1.60. What is more, the magnitude of these associations was consistent across strata of age, smoking, and body mass index. A population-based study in the US older population investigated the combined effect of physical inactivity and depression on CVD mortality risk (22). Depressive symptoms and physical inactivity each independently increased the risk of CVD mortality and were strongly associated with each other. The individuals with both depressive symptoms and physical inactivity had a greater CVD mortality rate

than those with either individually (log-rank test, $P<0.001$). Physical inactivity reduced the log HR of depressive symptoms for CVD mortality by 26% after adjustment. This was similar for persons with (25%) and without (23%) established CHD. Moreover, interesting results were reported in a Danish study, where additionally to classical activities, the effect of bicycling to work was analyzed, which is quite rare in most countries (23). Compared with the sedentary, age- and sex-adjusted mortality rates in LTPA groups 2 to 4 were 0.68 (95% CI, 0.64–0.71), 0.61 (95% CI, 0.57–0.66), and 0.53 (95% CI, 0.41–0.68), respectively. Bicycling to work decreased all-cause mortality risk by approximately 40% after multivariate adjustment.

In the US large population-based cohort study, the largest benefits from both aerobic and strengthening exercises were found (24). According to the results of this study, the greatest increase in survival probabilities occurred among the responders who engaged in at least some LTPA as compared with those who engaged in none. Additional survival benefits were associated with the higher levels of aerobic LTPA. The authors concluded that strengthening activities did not reduce mortality risks, whereas aerobic activities added some survival benefits. The US prospective study involved 121 700 female registered nurses, aged 30 to 55 years (25). After the 24-year follow-up, the multivariable adjusted all-cause mortality risk was 0.63 (0.57–0.69) in the highest PA level (≥ 5.5 hours/week) compared with the lowest or almost non-PA level. Besides, a reduction in CVD mortality risk was even stronger (0.57; 0.45–0.73), when the highest PA level was compared with the lowest. The authors concluded that each additional increment in the PA level had a protective effect.

In our study, 16.2% of all-cause mortality and 22.2% of CVD mortality were attributable to the lowest LTPA quartile. According to the different sources, the PARF of no/low activity risk group was reported to be 7%–17% for all-cause and 11%–28% for CVD mortality (2, 21, 25).

The beneficial LTPA effects on health and longevity prediction have already been proven by the other studies, and protective biological mechanisms have widely been analyzed (8, 26–29). Despite this fact, the dose–response relationships between LTPA and mortality risk remain questionable: how much of PA is sufficient? A systematic review of 44 epidemiological studies confirmed that the energy expenditure of about 1000 kcal per week was associated with a significant 20%–30% reduction in all-cause mortality risk (27). Due to limited data, it remained unclear whether the activity of vigorous intensity confers an additional benefit beyond its contribution to the volume of PA when compared with the activity of moderate intensity. In this study, no data were available on the duration and frequency of PA in relation to all-cause mortality rates after controlling for volume of PA.

The comparison of the results among different studies is complicated because of different epidemiological study designs, unequal observation periods, adjustment for various confounders, and different LTPA measurements. At this moment, more than 100 valid instruments for the assessment of PA exist (30). The collection of individual PA information in populations usually is only subjective and may be affected by the underevaluation of a sedentary lifestyle and the overvaluation of moderate- and high-intensity activities. A lifetime assessment of PA may lead to recall biasing. Definitely, further longitudinal studies including the instrumental measurements of physical fitness are needed.

Conclusions

The main results of this study showed that the prevalence of the baseline risk factors was evidently higher in the participants with lower LTPA as compared with the participants with higher LTPA. This study demonstrated that lower LTPA increased all-cause and CVD mortality risk. The inverse associations between PA and mortality remained significant

even with multivariate adjustments. These data suggest that preventive health and wellness programs in the middle-aged Lithuanian population, particularly those within the lowest LTPA, should focus on encouraging enrolment and continued participation in physical exercise programs. Future research might examine the beneficial effects in the LTPA of different intensity.

Strengths of Our Study. It is the first long-term cohort study in Lithuania that aimed to explore the long-term associations between LTPA and all-cause and CVD mortality risk in the Lithuanian urban population. The mean duration of follow-up was 12.6 years. In our study, the impact of LTPA on all-cause mortality and mortality from CVD was studied using the Cox proportional hazards regression analysis in 3 separate models.

Limitations. Our research has a few limitations. First, in our study, LTPA was only self-reported, and none specialized questionnaire on PA was used. The intensity of LTPA was not taken into account; therefore, energy expenditures could not be calculated. Second, mortality HRs could not be adjusted for dietary habits because of discordance of diet information gathered in the 1992–1993 and 2001–2002 studies. Third, information about LTPA and other risk factors was collected only during the baseline health examination, and the change in risk factor profile was not taken into account. Finally, we cannot assert that the study population of Kaunas is perfectly representative of the general Lithuanian urban population.

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Statement of Conflict of Interest

The authors state no conflict of interest.

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