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Changes in exercise frequency and cardiovascular outcomes in older adults

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Aims Little is known about the association of changes in moderate to vigorous physical activity (MVPA) level with cardiovascular disease (CVD), especially in older adults whose ability to engage in frequent MVPA naturally wanes as they age. We aimed to examine the association of changes in MVPA and CVD in older adults.

Methods and results In a nationwide cohort study of older adults aged 60 years or older, we identified more than 1.1 million subjects without previous history of CVD at baseline who underwent two consecutive national health screening from 2009 to 2012. We prospectively assessed the risk of CVD occurred between 2013 and 2016 according to changes in frequency of MVPA by initial MVPA status. Compared to those who were continuously physically inactive, those who increased their frequency of MVPA from physically inactive to 1–2 times per week [0.7/1000 person-years (PY) decrease in incidence rate (IR); adjusted hazard ratio (aHR) 0.95; 95% confidence interval (CI) 0.92–0.99], 3–4 times per week (1.5/1000 PY decrease in IR; aHR 0.89; 95% CI 0.84–0.94), ≥5 times per week (0.4/1000 PY decrease in IR; aHR 0.91; 95% CI 0.85–0.97) had a significantly reduced risk for total CVD (*P* for trend <0.001). Older adults who became physically inactive from engaging in more than 1–2 times of MVPA per week had a higher CVD risk compared to those who maintained their frequency of MVPA.

Conclusion Among older adults, engaging in higher frequency of MVPA or maintaining MVPA level was associated with reduced risk of CVD.

Keywords Exercise • Health behaviour • Older adults • Cardiovascular diseases

Introduction

Insufficient physical activity is one of the easily modifiable risk factors for cardiovascular events and mortality worldwide along with other lifestyle-associated risk factors such as cigarette smoking and high sodium consumption.[1,2] Preventive association of high frequency of physical activity with cardiovascular disease (CVD) has been well established through multiple cohort studies and meta-analyses.[3–6] These studies suggest that high frequency of physical activity is inversely related to risk of CVD in a dose-response manner, but whether changes in physical activity level is associated with CVD risk remains unclear, especially in older adults whose frequency of moderate-to-vigorous physical activity (MVPA) begins to decline as they age.[7] Based on the recent evidence on physical activity and cardiovascular health, the sixth joint task force of the *European Society of Cardiology (ESC)* and other societies on CVD prevention in clinical practice and the US Department of Health and Human Services released the *2016 European Guidelines on cardiovascular disease prevention in clinical practice* and *Physical Activity Guidelines for Americans, 2nd edition* (PAG) in 2018, respectively.[8,9] They provide evidence-based guidelines for older adults that they should do multicomponent physical activity for substantial health benefits. Furthermore, the PAG suggests that older adults with disabilities or chronic conditions should follow the same recommendations.

The effect of changes in frequency of physical activity on CVD among older adults remains uncertain. One study examined the

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association of changes in physical activity and CVD outcome in a Spanish cohort of older adults and found that those who increased physical activity had a 25% reduction and decreased physical activity had a non-significant increase in risk of cardiovascular mortality, but this study did not measure the intensity and frequency of changes in physical activity.[10] Moreover, among older adults with disabilities and chronic conditions, physical activity could also play a key role in CVD prevention, but little is known about the cardiovascular health benefits and disadvantages of changes in frequency of physical activity in these groups, especially in the Asian population.

Using a large, population-based data consist of older adults with records on sociodemographic factors, health survey, examination, and medical claims from the National Health Insurance Service (NHIS) in the Republic of Korea, we assessed the association of changes in MVPA frequency with subsequent CVD events and also tested whether this association differs by disabilities and presence of chronic conditions such as diabetes, hypertension, and hyperlipidaemia.

Methods

Study population

Details of the NHIS cohort design, methods, and validity of the records are available in previous studies.[11] Briefly, the NHIS is a quasi-government entity established under the Ministry of Health and Welfare that serves as a single-insurer for healthcare services with a coverage rate of ~97% in the Republic of Korea. The NHIS database is available for population-based cohort study since information on demographics, national health screening, medical treatment, and drug prescription is routinely collected and undergoes quality control before being realized for research purpose. We enrolled 1 119 925 men and women who were aged at least 60 years of age and underwent the two consecutive biennial national health screening provided by the NHIS from 2009 to 2010 and 2011 to 2012. This study excluded participants without physical activity data, experienced CVD, or were dead prior to follow-up of events (*Figure 1*). Institutional Review Board (IRB) at the Seoul National University Hospital (IRB no. E-1806-076-951) and the NHIS Big Data Steering Department (NHIS-2018-1-404) approved this study. We were exempted from obtaining written consent from the participants because the NHIS data contains strictly anonymized clinical data that follow the guidelines of the Personal Data Protection Act.

Classification of change in physical activity

At each national health screening period, the participants of the NHIS cohort provided responses to a series of self-administered questionnaire on physical activity and other lifestyle behaviours. Based on the responses in the NHIS survey data, we used the records on the number of moderate (≥30 min per day; e.g. brisk walking, dancing, gardening) or vigorous (≥20 min per day; e.g. running, fast cycling, aerobic) per week at the two consecutive biennial health screening (2009–10 and 2011–12) to determine changes in MVPA among the participants. For primary analyses, we created categories for increase of MVPA at the second examination (2011–12) from physically inactive at the first examination (2009–10) as follows: (i) continually physically inactive, (ii) physically inactive to 1–2 times of MVPA per week, (iii) physically inactive to 3–4 times of MVPA per week, and (iv) physically inactive to more than five times of MVPA per week. Similarly, we created categories for decrease in MVPA between the two health screening periods as follows: (i) continuously more than five times of MVPA per week, (ii) more than five times of MVPA per week to 3–4 times of MVPA per week, (iii) more than five times of MVPA per week to 1 to 2 times of MVPA per week, and (iv) more than five times of MVPA per week to physically inactive. Changes of physical activity among the participants who responded that they were doing 2–3 or 4–5 times of MVPA per week at the first examination were used in the secondary analyses. Validity and reliability of the physical activity questionnaire in the NHIS cohort are described in a previous study.[12] Details for the categorization of changes in MVPA is provided in Supplementary material online, *Appendix Figure S1*.

Follow-up for cardiovascular outcomes

We collected information on medical claims records of the NHIS to identify CVD events during the follow-up period between 1 January 2013 and 31 December 2016. In the NHIS health insurance system, we used the *International Classification of Diseases, Tenth Revision (ICD-10)* and hospitalization records to identify the causes for total CVD events [composite CVD events, includes coronary heart disease (CHD) and stroke] (ICD-10: I20–I25 and I60–I69), CHD (ICD-10: I20–I25), and stroke (ICD-10: I60–I69). To exclude the CVD cases that did not turn out to be true events in the NHIS database, we only included the records with at least 48 h (2 days) of hospital admission. Definitions for CVD outcomes using the NHIS medical claims records have been previously reported.[13]

Key variables for adjustment and subgroup analyses

Relevant information in the NHIS cohort database were collected to determine key variables used for adjustment and subgroup analyses. Socioeconomic factors [age, sex, insurance premium (proxy for income status), insurance type (self-employed insured, employed insured, medical aid beneficiary), place of residence (proxy for urbanization level), and presence of disability] and medical conditions {medication use [aspirin, antihypertensive medication, antidiabetic medication, statin, and non-steroidal anti-inflammatory drugs (NSAIDs)] and comorbidity (Charlson comorbidity index; calculated using cumulative records of medical claims until follow-up)} were obtained from the NHIS insurance eligibility and medical claims database,[14] respectively. Other lifestyle behaviours (cigarette smoking and alcohol consumption), bioclinical laboratory results and measurement (body mass index, blood pressure, total cholesterol, and fasting serum glucose), and family history of CVD were determined from the NHIS national health screening database. Diabetes (fasting serum glucose ≥126 mg/dL or use of antidiabetic medication), hypertension (systolic blood pressure ≥140 or diastolic blood pressure ≥90 mmHg or use of antihypertensive mediation such as beta-blockers and angiotensin-converting enzyme inhibitors), and hypercholesterolaemia (total cholesterol ≥240 mmHg or use of statin) were defined using biochemical tests and use of medication as described in previous studies.[15]

Statistical analyses

The follow-up period in this study started on 1 January 2013 and ended on 31 December 2016. During the follow-up, each participant included in the analytic cohort was censored at the first event of CVD or death from CVD or other causes, whichever happened first. If no events occurred during the follow-up period, the participants were observed and followed up until 31 December 2016. Characteristics of participants at baseline recruitment were calculated using *n* (%) for categorical variables and means [standard deviations (SDs)] for continuous variables. We computed incidence rate (IR) based on incidence per 1000 person-years (PY) from the number of total cardiovascular events and PY in each group according to changes of MVPA and also assessed changes in IR. We calculated hazard ratio (HR) and 95% confidence intervals (CIs) for CVD outcomes according to changes in MVPA between the two biennial national health screening periods (2009–10 and 2011–12) using Cox proportional hazards

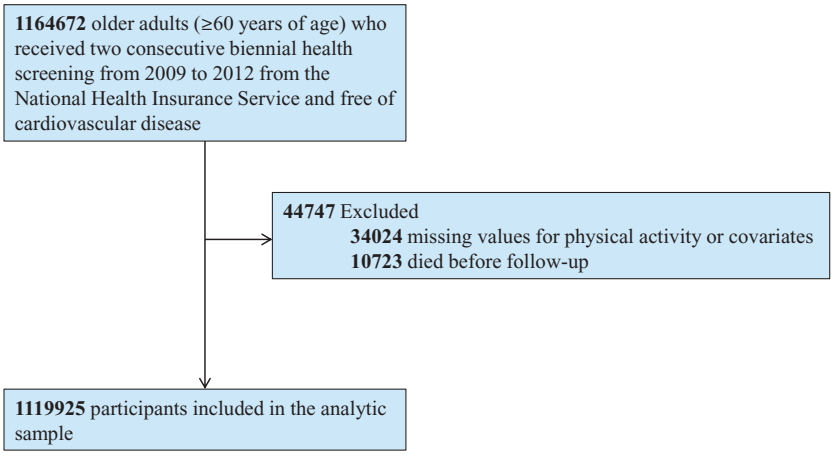


Figure 1 Flow diagram of the study population selection from the national health insurance service database.

model. We first developed a minimally adjusted model using age as the only adjustment variable. Adjusted HRs and 95% CIs for CVD outcomes were calculated from adjusting the following variables in the Cox regression model: age, sex, place of residence, insurance premium, insurance type, body mass index, systolic blood pressure, total cholesterol, fasting serum glucose, cigarette smoking, alcohol consumption, medication use (aspirin, antihypertensive medication, antidiabetic medication, statin, NSAIDs), Charlson comorbidity index, and family history of CVD. To assess the fitness of the Cox proportional hazards models, we graphically tested the proportionality assumption with log–log plot and also with Schoenfeld residual.

For primary analysis, we assessed increase and decrease of MVPA among the participants by restricting the analytic sample to those who were categorized as physically inactive and ≥5 times of MVPA per week at the first health screening period (2009–10). In this analysis, we used participants who were classified as continually physically inactive and continuously ≥5 times of MVPA per week as references to determine increasing and decreasing trend of MVPA among the participants, respectively. For subgroup analyses, we stratified the participants by age (60–69, 70–79, and ≥80 years), sex (male and female), presence of disability (with and without), cigarette smoking (never, past smoker, and current smoker), weight status (obese and non-obese), diabetes, hypertension, hypercholesterolaemia (yes and no), and comorbidity (Charlson comorbidity index <2 and ≥2). In secondary analyses, we assessed the association of change in MVPA among the participants who were defined as continuously 1–2 times and 3–4 times of MVPA per week with CVD events within each subpopulation using same Cox regression models used in the primary analysis. All data collection, mining and statistical analyses in this study were performed with SAS 9.4 (SAS Institute, Cary, NC, USA). Statistical significance was two-sided and was defined as *P* values <0.05 for all analyses.

Results

Baseline characteristics

Among the 1 119 925 participants, the mean (SD) age was 66.9 (5.6) and 528 744 (47.2%) were men. About two-thirds of the individuals at the first (2009–10) and second (2011–12) health screening periods responded that they were physically inactive (72.9% in the first and 71.6% in the second period, respectively). Higher proportion of women was physically inactive (78.0% and 76.9%) compared to men (67.2% and 65.7%) in both periods of the national health screening. Other characteristics of the participants who underwent the two consecutive biennial health screening between 2009 and 2012 are listed in *Table 1*.

Change of exercise frequency

Of the 973 616 participants who were physically inactive at the first health screening period (2009–10), most of the participants were continuously physically inactive (78.2%) and only 21.8% increased MVPA to 1–2, 3–4, and ≥5 times per week (11.7%, 6.1%, and 4.0%, respectively) when followed up in the second health screening period (2011–12). About half (54.4%) of the participants became physically inactive in the second examination period (2011–12) from doing ≥5 times of MVPA per week in the first examination period (2009–10). Only about one-fifth of the participants maintained the same frequency of MVPA in both examination periods.

Association of increase in exercise frequency with total cardiovascular disease

During 5.5 million PY of follow-up, there were 114 856 total CVD events, 25 407 CHDs, and 33 273 stroke events occurred. After multivariable adjustment (socioeconomic factors, lifestyle behaviours, medical characteristics, and family history), the participants who increased their frequency of MVPA from physically inactive to 1–2 times per week (0.7/1000 PY decrease in IR; HR 0.95; 95% CI 0.92–0.99), 3–4 times per week (1.5/1000 PY decrease in IR; HR 0.89; 95% CI 0.84–0.94), ≥5 times per week (0.4/1000 PY decrease in IR; HR 0.91; 95% CI 0.85–0.97) had a significantly reduced risk for total CVD events compared to those who were continuously physically inactive (*Table 2*). For CHD and stroke events, the association of increase in frequency of MVPA with these outcomes showed similar results (*Figures 2* and *3*)

Table 1 Characteristics of participants of older adults (60 years of age and older) in the national health insurance service cohort who received two consecutive biennial national health screening in 2009–10 and 2011–12

Characteristics	All	Men in the NHIS cohort	Women in the NHIS cohort
Number of participants	1 119 925	528 744	591 181
Physical activity at health screening Period I (2009–10)			
Physically inactive	816 644 (72.9)	355 541 (67.2)	461 103 (78.0)
1–2 times MVPA per week	156 972 (14.0)	92 423 (17.5)	64 549 (10.9)
3–4 times MVPA per week	82 513 (7.4)	44 685 (8.5)	37 828 (6.4)
≥5 times MVPA per week	63 796 (5.7)	36 095 (6.8)	27 701 (4.7)
Physical activity at health screening Period II (2011–12)			
Physically inactive	802 145 (71.6)	347 550 (65.7)	454 595 (76.9)
1–2 times MVPA per week	156 707 (14.0)	92 012 (17.4)	64 695 (11.0)
3–4 times MVPA per week	90 678 (8.1)	48 699 (9.2)	41 979 (7.1)
≥5 times MVPA per week	70 395 (6.3)	40 483 (7.7)	29 912 (5.0)
Age, mean (SD)	66.9 (5.6)	67.0 (5.5)	66.8 (5.6)
Income status			
1Q	264 889 (23.7)	132 028 (24.9)	132 861 (22.5)
2Q	175 758 (15.7)	91 726 (17.4)	84 032 (14.2)
3Q	263 525 (23.5)	123 758 (23.4)	139 767 (23.6)
4Q	415 753 (37.1)	181 232 (34.3)	234 521 (39.7)
Location of residence			
Capital city	405 919 (68.8)	191 747 (36.3)	214 172 (36.2)
Metropolitan	676 174 (18.6)	320 318 (60.6)	355 856 (60.2)
Rural (city/town)	37 832 (12.6)	16 679 (3.1)	21 153 (3.6)
Disability[a]	107 733 (9.6)	57 280 (10.8)	50 453 (8.5)
Cigarette smoking status			
Never	770 372 (68.8)	194 999 (36.9)	575 373 (97.3)
Past smoker	208 203 (18.6)	202 648 (38.3)	5555 (0.9)
Current smoker	141 350 (12.6)	131 097 (24.8)	10 253 (1.8)
Alcohol consumption			
None	771 855 (68.9)	235 819 (44.6)	536 036 (90.7)
1–2 times/week	207 945 (18.6)	163 443 (30.9)	44 502 (7.5)
3–4 times/week	81 697 (7.3)	74 819 (14.2)	6878 (1.2)
≥5 times/week	58 428 (5.2)	54 663 (10.3)	3765 (0.6)
BMI (kg/m^2), mean (SD)			
Baseline	23.9 (2.9)	23.7 (2.8)	24.2 (3.1)
Change	-0.07 (1.2)	-0.06 (1.2)	-0.07 (1.3)
Total cholesterol (mg/dL), mean (SD)			
Baseline	198.7 (37.6)	191.7 (35.7)	205.2 (38.0)
Change	-3.5 (39.4)	-3.0 (36.9)	-3.9 (41.5)
Fasting serum glucose (mg/dL), mean (SD)			
Baseline	102.9 (24.1)	104.1 (26.0)	100.1 (22.0)
Change	0.1 (22.8)	0.06 (25.0)	0.2 (20.6)
SBP (mmHg), mean (SD)			
Baseline	126.8 (14.9)	127.5 (14.7)	126.2 (15.1)
Change	-0.2 (16.1)	-0.4 (16.0)	0.01 (16.2)
DBP (mmHg), mean (SD)			
Baseline	77.0 (9.6)	77.8 (9.6)	76.2 (9.6)
Change	-0.5 (10.9)	-0.6 (10.9)	-0.3 (10.8)
Diabetes[b]	201 903 (18.0)	106 811 (20.2)	95 092 (16.1)
Hypertension[c]	635 835 (56.8)	303 192 (57.3)	332 643 (56.3)
Hypercholesterolaemia[d]	436 623 (38.9)	152 548 (28.9)	284 075 (48.1)
Use of medication			
Statin	375 205 (33.5)	129 652 (24.5)	245 553 (41.5)

Continued

Table 1 *Continued*

Characteristics	All	Men in the NHIS cohort	Women in the NHIS cohort
Aspirin	264 735 (23.6)	122 424 (23.2)	142 311 (24.1)
NSAIDs	869 872 (77.7)	367 313 (69.4)	502 559 (85.0)
Antidiabetic medication	171 064 (15.3)	87 524 (16.6)	83 540 (14.1)
Antihypertensive medication	565 357 (50.5)	265 055 (50.1)	300 302 (50.8)
Family history			
Heart disease	26 454 (3.8)	10 274 (3.2)	16 180 (4.5)
Stroke	76 457 (11.0)	34 043 (10.5)	42 414 (11.5)
Charlson comorbidity index			
0	108 900 (9.7)	62 320 (11.8)	46 580 (7.9)
1	125 819 (11.2)	66 433 (12.6)	59 386 (10.1)
≥2	885 206 (79.1)	399 991 (75.6)	485 215 (82.1)

All values above are presented as *n* (%) unless otherwise specified. SI conversion factors: multiply by 0.0259 and 0.0555 to convert total cholesterol and glucose to mmol/L, respectively. Baseline was defined as the national health screening Period II (2011–12). Change of BMI, total cholesterol, fasting serum glucose, and blood pressure was defined as the difference of values at the national health screening Period II (2011–12) from the national health screening Period I (2009–10).
BMI, body mass index (calculated by weight in kg divided by height in m^2); DBP, diastolic blood pressure; MVPA, moderate to vigorous physical activity; NHIS, National Health Insurance Service; NSAID, non-steroidal anti-inflammatory drugs; Q, quartile; SBP, systolic blood pressure.
[a]Based on the enrolment records for the NHIS.
[b]Defined as fasting serum glucose of more than 126 mg/dL or use of antidiabetic medication.
[c]Defined as SBP ≥140 or DBP ≥90 mmHg or use of antihypertensive medication according to the Korean Society of Hypertension.
[d]Defined as total cholesterol ≥240 mg/dL or with statin treatment.

Association of decrease in exercise frequency with total cardiovascular disease

Compared to the individuals who were continuously doing ≥5 times of MVPA per week, those who decreased their frequency of MVPA from ≥5 times of MVPA per week to 3–4 times per week (1.1/1000 PY decrease in IR; HR 1.11; 95% CI 0.91–1.35), 1–2 times per week (1.2/1000 PY increase in IR; HR 1.19; 95% CI 0.98–1.44), and physically inactive (1.3/1000 PY increase in IR; HR 1.27; 95% CI 1.11–1.46) had an increase in risk for composite outcome of CVD events. The trends in both increasing and decreasing frequency of MVPA with CVD risk showed dose-response relationship ($P_{trend} < 0.001$).

Association of changes in exercise frequency with total cardiovascular disease

Compared to the participants who were continuously doing 1–2 times of MVPA per week, those who became physically inactive had an elevated risk of total CVD, but among these participants, increasing MVPA to 3–4 times and ≥5 times per week from 1 to 2 times of MVPA per week did not significantly lower the risk for CVD. Similarly, decrease of MVPA from 3 to 4 times per week to physically inactive was associated with an increase in CVD risk, but increase of MVPA to ≥5 times per week from 3 to 4 times per week was not associated with a decreased risk of CVD (*Table 2*).

Subgroup analysis

For the composite CVD outcome, the subgroup analyses were conducted by stratifying the participants by age, sex, disability, cigarette smoking, weight status, chronic conditions (presence of diabetes, hypertension, and hypercholesterolaemia), and comorbidity (Charlson comorbidity index). Among the participants with disability and chronic conditions, those who increased MVPA up to 3–4 times per week from being physically inactive had a significantly decreased risk of total CVD compared to those who were consistently physically inactive (Supplementary material online, *Appendix Table S1*). The trend and strength of association between decrease in frequency of MVPA and composite outcome of CVD were similar in most of the subgroups. (Supplementary material online, *Appendix Table S2*).

Discussion

In this large, population-based cohort study from the NHIS database in the Republic of Korea, we found real world evidence that the older adults with insufficient physical activity who increased frequency of MVPA to more than 3–4 times per week had a significantly lower risk of CVD events as compared to those who were continuously physically inactive, and this association was consistent among those with disabilities and chronic conditions. In contrast, decrease in frequency of MVPA was associated with a significantly elevated risk of CVD events as compared to consistently engaging in more than five times of MVPA per week in older adults.

Comparison with other studies

Our findings on the association of increased frequency of MVPA with decreased CVD risk was similar with previous studies, which showed that the individuals with high frequency of physical activity had a significantly lower CVD risk compared to those with low frequency of physical activity, although physical activity in these studies was measured at a single time-point.[4–6,16] A recent meta-analysis of observational studies showed the inverse association of physical activity with CHD and stroke in men and women, but the participants included in

Table 2 Association of changes in frequency of moderate to vigorous physical activity between the two biennial health screening periods (2009–10 and 2011–12) with subsequent risk of total cardiovascular disease events in older adults aged 60 years and older in the national health insurance service cohort

Category	Number of participants	Incidence per 1000 PY[a]	Age-adjusted hazard ratio (95% CI)	Multivariable-adjusted hazard ratio (95% CI)[b]
Physically inactive at the NHIS health screening Period I (2009–10)				
Continuously physically inactive	761 248	10.8	Reference	Reference
Physically inactive to 1–2 times of MVPA/week	114 079	10.1	0.99 (0.96–1.02)	0.95 (0.92–0.99)[c]
Physically inactive to 3–4 times of MVPA/week	58 943	9.3	0.90 (0.86–0.94)[e]	0.89 (0.84–0.94)[e]
Physically inactive to ≥5 times of MVPA/week	39 346	10.4	0.95 (0.90–0.99)[c]	0.91 (0.85–0.97)[d]
P value for trend			<0.001	<0.001
1–2 times of MVPA/week at the NHIS health screening Period I (2009–10)				
Decrease of MVPA from 1–2 times of MVPA/week to physically inactive	151 660	9.8	1.04 (0.99–1.10)	1.10 (1.02–1.18)[c]
Continuously 1–2 times of MVPA/week	54 014	8.8	Reference	Reference
Increase of MVPA from 1–2 times of MVPA/week to 3–4 times of MVPA/week	25 065	9.0	0.99 (0.91–1.07)	0.96 (0.86–1.07)
Increase of MVPA from 1–2 times of MVPA/week to ≥5 times of MVPA/week	8746	8.2	0.88 (0.77–0.99)[c]	0.90 (0.76–1.06)
P value for trend			<0.001	<0.001
3–4 times of MVPA/week at the NHIS health screening Period I (2009–10)				
Decrease of MVPA from 3–4 times of MVPA/week to physically inactive	86 295	10.3	1.09 (1.01–1.16)[c]	1.16 (1.06–1.27)[d]
Decrease of MVPA from 3–4 times of MVPA/week to 1–2 times of MVPA/week	21 913	10.2	0.95 (0.87–1.05)	1.00 (0.88–1.13)
Continuously 3–4 times of MVPA/week	30 002	10.1	Reference	Reference
Increase of MVPA from 3–4 times of MVPA/week to ≥5 times of MVPA/week	8099	9.9	1.05 (0.92–1.20)	1.06 (0.90–1.27)
P value for trend			0.019	<0.001
≥5 times of MVPA/week at the NHIS health screening Period I (2009–10)				
Continuously ≥5 times of MVPA/week	14 204	9.6	Reference	Reference
Decrease of MVPA from ≥5 times of MVPA/week to 3–4 times of MVPA/week	7717	8.5	0.91 (0.79–1.06)	1.11 (0.91–1.35)
Decrease of MVPA from ≥5 times of MVPA/week to 1–2 times of MVPA/week	7182	10.8	1.15 (0.99–1.32)	1.19 (0.98–1.44)
Decrease of MVPA from ≥5 times of MVPA/week to physically inactive	34 693	10.9	1.08 (0.98–1.19)	1.27 (1.11–1.46)[d]
P value for trend			<0.001	<0.001

Each time of MVPA indicates more than 20–30 min based on the self-reported survey of the NHIS national health screening records. CVD event is defined as more than 2 days of hospitalization for total cardiovascular disease (ICD-10 codes: I20–I25 and I60–I69) according to the medical claims records of the NHIS.
CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; ICD-10, international classification of diseases, 10th revision; MVPA, moderate to vigorous physical activity; NHIS, national health insurance service; NSAIDs, non-steroid anti-inflammatory drugs; PY, person-years.
[a]Computed from the number of CVD events occurred and PYs in each group during the follow-up period (2013–16).
[b]Calculated from Cox proportional hazards model adjusted for age, sex, place of residence, insurance premium (proxy for income status), insurance type, body mass index, systolic blood pressure, total cholesterol, fasting serum glucose, cigarette smoking, alcohol consumption, aspirin, antihypertensive medication, antidiabetic medication, statin, NSAIDs, Charlson comorbidity index, and family history of cardiovascular disease.
[c]$P < 0.05$.
[d]$P < 0.01$.
[e]$P < 0.001$.

these studies were not limited to older adults.[17] In a prospective analysis of 4207 US men and women of a mean age of 73 years who participated in the Cardiovascular Health Study (CHS), a significant risk reduction of total CVD, CHD, and stroke was observed among older adults with high walking score, leisure-time activity, and exercise intensity.[18] Although the CHS survey was updated to reduce misclassification of physical activity, baseline data were used to categorize types and intensity of physical activity. Our findings show that increasing frequency of MVPA from being physically inactive is associated with a lower risk of CVD compared to remaining physically inactive. Being able to classify the association of increased physical activity and CVD risk among physically inactive older adults may add

	CHD incidence per 1000 PY	HR (95% CI)	P value for trend
Physically Inactive at the NHIS Health Screening Period I (2009-2010)			
Continuously Physically Inactive	4.6	[Reference]	0.064
Physically Inactive to 1-2 times of MVPA/week	4.5	0.96 (0.90-1.02)	
Physically Inactive to 3-4 times of MVPA/week	4.3	0.94 (0.86-1.02)	
Physically Inactive to ≥5 times of MVPA/week	4.6	0.96 (0.87-1.06)	
1-2 times of MVPA/week at the NHIS Health Screening Period I (2009-2010)			
Decrease of MVPA from1-2 times of MVPA/week to Physically Inactive	4.4	1.01(0.91-1.11)	0.009
Continuously 1-2 times of MVPA/week	4.5	[Reference]	
Increase of MVPA from 1-2 times of MVPA/week to 3-4 times of MVPA/week	4.2	0.86 (0.74-1.00)	
Increase of MVPA from 1-2 times of MVPA/week to ≥5 times of MVPA/week	3.7	0.78 (0.61-0.99)	
3-4 times of MVPA/week at the NHIS Health Screening Period I (2009-2010)			
Decrease of MVPA from 3-4times of MVPA/week to physically inactive	4.6	1.10 (0.97-1.26)	0.054
Decrease of MVPA from 3-4 times of MVPA/week to 1-2 times of MVPA/week	4.0	0.93 (0.78-1.11)	
Continuously 3-4 times of MVPA/week	4.6	[Reference]	
Increase of MVPA from 3-4 times of MVPA/week to ≥5 times of MVPA/week	4.2	0.97 (0.75-1.25)	
≥5 times of MVPA/week at the NHIS Health Screening Period I (2009-2010)			
Continuously ≥5 times of MVPA/week	4.8	[Reference]	<.001
Decrease of MVPA from ≥5 times of MVPA/week to 3-4 times of MVPA/week	4.1	1.08 (0.82-1.44)	
Decrease of MVPA from ≥5 times of MVPA/week to 1-2 times of MVPA/week	5.0	1.28 (0.97-1.68)	
Decrease of MVPA from ≥5 times of MVPA/week to physically inactive	4.9	1.29 (1.06-1.57)	

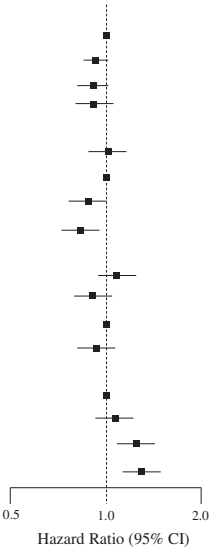


Figure 2 Adjusted hazard ratios for coronary heart disease according to changes in frequency of moderate to vigorous physical activity in older adults aged 60 years and older. Hazard ratios and 95% confidence intervals presented above are adjusted for age, sex, place of residence, insurance premium (proxy for income status), insurance type, body mass index, systolic blood pressure, total cholesterol, fasting serum glucose, cigarette smoking, alcohol consumption, aspirin, antihypertensive medication, antidiabetic medication, statin, non-steroidal anti-inflammatory drugs, Charlson comorbidity index, and family history of cardiovascular disease. CHD, coronary heart disease; CI, confidence interval; HR, hazard ratio; NSAIDs, non-steroidal anti-inflammatory drugs; PY, person-years.

further evidence to the numerous studies that have shown the preventive effects of high physical activity on CVD.

Currently, there is scant literature which explicitly examined the association between change in physical activity and CVD risk in older adults. The investigators of Universidad Autónoma de Madrid (UAM) cohort examined the change in physical activity in a representative Spanish cohort of more than 60 years of age and reported that those who had increased and maintained physical activity had a 25% and 58% risk reduction in CVD mortality as compared to those who were continuously inactive, respectively.[10] In this study, the risk of CVD mortality in older adults who decreased physical activity (HR 0.96; 95% CI 0.68–1.34) was similar to those who were continuously inactive, which was used as the reference group. In addition to these results, the UAM cohort study of older adults in Spain also suggested that the number of chronic conditions was a modifier of the association between change in physical activity and CVD mortality. Indeed, because the ability to perform high frequency of physical activity among older adults may be an indicator for general health conditions, those with low frequency of physical activity at baseline are likely to have comorbidities that potentially restrict physical activity. However, in our subgroup analyses, the older adults with chronic conditions (diabetes, hypertension, and hypercholesterolaemia) who later increased their frequency of MVPA from being physically inactive to 3–4 times per week had a significant reduction in CVD risk. Moreover, increased CVD risk in older adults who decreased their frequency of MVPA found in our study also support the evidence on the inverse relationship between physical activity and CVD. While one of the potential reasons for decreased physical activity is newly diagnosed or worsening of pre-existing diseases in older adults, our findings indicate that those without chronic conditions and low comorbidity who decreased physically activity also had elevated CVD risk, although statistical significance was attenuated. This may be accounted for limited statistical power due to the low proportion of older adults who were consistently free of chronic conditions and comorbidities at two examinations.

Findings of our study also suggest that reduced CVD risk from increase in MVPA may be attributable to improved cardiorespiratory fitness (CRF). Cardiovascular health benefits of increased CRF is supported by observational data from Kuopio Ischaemic Heart Disease Risk Factor (KIHD) Study in Finland, which showed increase in objectively measured CRF is associated with reduction in deaths from CVD and other causes.[19] Whereas KIHD study lacked data on changes in MVPA, data on CRF was not available in the NHIS cohort of older adults. Because the direct association between changes in MVPA and CRF is unknown in our study, further study is necessary to investigate whether increase in MVPA also improves CRF and subsequently reduces CVD risk among older adults.

Implications

There are multiple mechanisms that support our findings on change in frequency of MVPA and CVD risk in older adults. High frequency of physical activity has both short- and long-term effect on cardiovascular health from improving lipid profile and lowering inflammation, adiposity, and blood pressure.[20,21] Physical activity, especially when performed on regular basis, positively influences the body's ability

	Stroke incidence per 1000 PY	HR (95% CI)	P value for trend
Physically Inactive at the NHIS Health Screening Period I (2009-2010)			
Continuously Physically Inactive	6.4	[Reference]	<.001
Physically Inactive to 1-2 times of MVPA/week	5.8	0.96 (0.91-1.01)	
Physically Inactive to 3-4 times of MVPA/week	5.2	0.84 (0.78-0.91)	
Physically Inactive to ≥5 times of MVPA/week	6.0	0.86 (0.78-0.94)	
1-2 times of MVPA/week at the NHIS Health Screening Period I (2009-2010)			
Decrease of MVPA from1-2 times of MVPA/week to Physically Inactive	5.7	1.18 (1.08-1.31)	0.004
Continuously 1-2 times of MVPA/week	4.5	[Reference]	
Increase of MVPA from 1-2 times of MVPA/week to 3-4 times of MVPA/week	5.0	1.08 (0.94-1.25)	
Increase of MVPA from 1-2 times of MVPA/week to ≥5 times of MVPA/week	4.9	1.00 (0.80-1.25)	
3-4 times of MVPA/week at the NHIS Health Screening Period I (2009-2010)			
Decrease of MVPA from 3-4times of MVPA/week to physically inactive	5.9	1.20 (1.06-1.37)	0.015
Decrease of MVPA from 3-4 times of MVPA/week to 1-2 times of MVPA/week	4.6	1.09 (0.93-1.29)	
Continuously 3-4 times of MVPA/week	4.7	[Reference]	
Increase of MVPA from 3-4 times of MVPA/week to ≥5 times of MVPA/week	5.5	1.16 (0.92-1.45)	
≥5 times of MVPA/week at the NHIS Health Screening Period I (2009-2010)			
Continuously ≥5 times of MVPA/week	5.1	[Reference]	0.028
Decrease of MVPA from ≥5 times of MVPA/week to 3-4 times of MVPA/week	4.7	1.17 (0.90-1.51)	
Decrease of MVPA from ≥5 times of MVPA/week to 1-2 times of MVPA/week	6.1	1.12 (0.86-1.46)	
Decrease of MVPA from ≥5 times of MVPA/week to physically inactive	6.2	1.24 (1.03-1.48)	

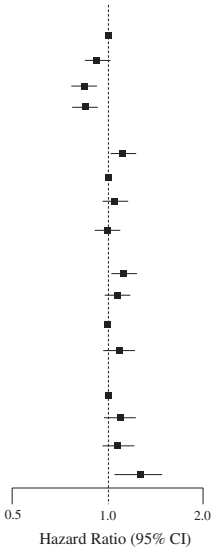


Figure 3 Adjusted hazard ratios for stroke according to changes in frequency of moderate to vigorous physical activity in older adults aged 60 years and older. Hazard ratios and 95% confidence intervals presented above are adjusted for age, sex, place of residence, insurance premium (proxy for income status), insurance type, body mass index, systolic blood pressure, total cholesterol, fasting serum glucose, cigarette smoking, alcohol consumption, aspirin, antihypertensive medication, antidiabetic medication, statin, non-steroidal anti-inflammatory drugs, Charlson comorbidity index, and family history of cardiovascular disease. CI, confidence interval; HR, hazard ratio; NSAIDs, non-steroidal anti-inflammatory drugs; PY, person-years.

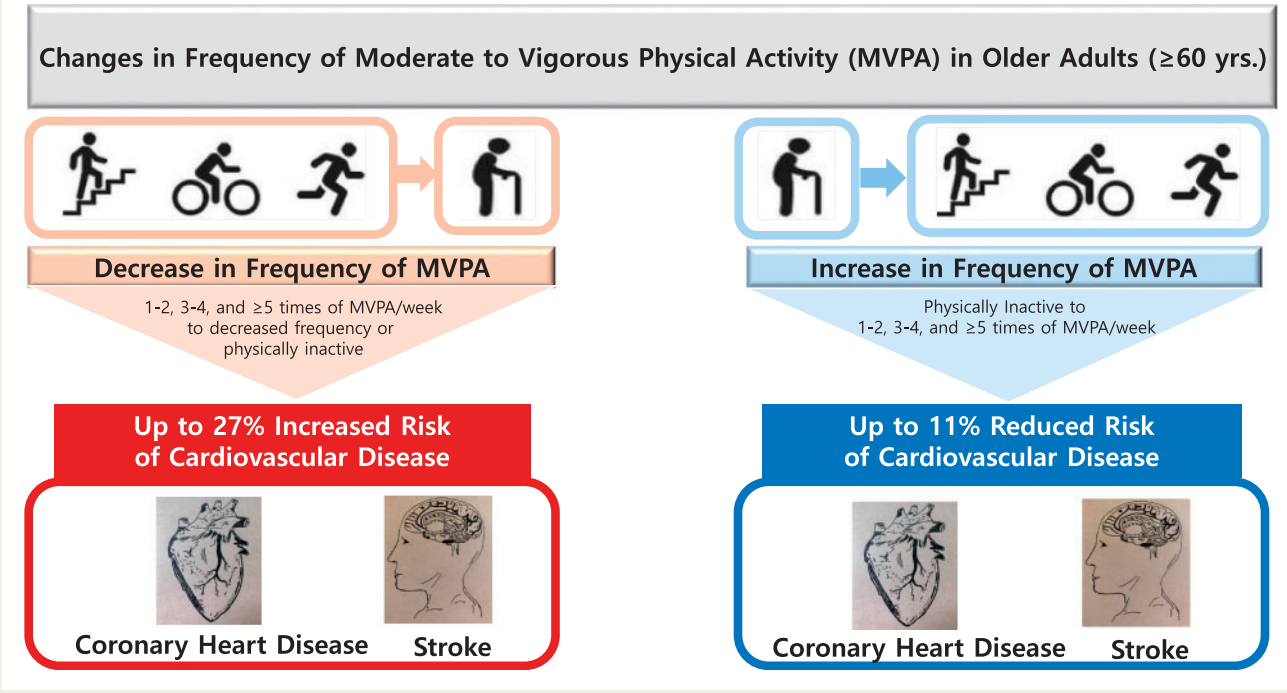
to regulate glucose level using insulin in the blood circulatory system.[22–24] Some of the cardiometabolic risk factors (waist circumference, systolic blood pressure, fasting triglycerides, high-density lipoprotein cholesterol, and insulin) are reported to improve with high MVPA independent of sedentary time.[25] Also, physical activity induces sympathoadreneric activation, which could reduce inflammation by suppressing monocytic cytokine production (e.g. IL-1beta, IL-6, TNF-alpha)[26] as well as release of nitric oxide in cardiopulmonary system.[27] In a national cohort of Sweden with 15 years of follow-up, replacing sedentary time with physical activity was associated with a significant reduction in CVD mortality.[28] In contrast, when physical activity is decreased, these cardiovascular health benefits of high physical activity are likely to be reduced.

Our results have both clinical and public health implications that support the need to encourage higher frequency of MVPA among physically inactive older adults and maintaining frequency of MVPA among those who are already physically active for substantial risk reduction in CVD risk. Although our data could not show that the older adults in the NHIS cohort followed the key guidelines of the ESC joint guideline and PAG combining aerobic exercise with balance training and muscle-strengthening activity, our findings partially add evidence that clinicians are advised to encourage their patients to increase or maintain frequency of MVPA regardless of disabilities or chronic conditions.

Strengths and limitations of study

Strengths of the current study include the ability to examine the association of change in frequency of MVPA with CVD risk in older adults using a large, population-based data, with repeated measurement for assessing change in physical activity. Ascertainment of CVD outcomes was based on the medical claims records collected on the national level, and is considered of high accuracy as compared to self-reported history of CVD or estimation with CVD risk assessment tools. Also, the analytic data were linked to other sources of database for potential confounders that were used for adjustment in the analyses. Therefore, we were also able to carry out a wide range of subgroup analyses such as participants with disabilities and chronic conditions to establish real-world evidence that support encouraging physical activities for those who are capable of doing MVPA.

There are several limitations in this study. First, information on intensity and frequency of physical activity was collected from a self-reported survey, which is subject to reporting bias and possible misclassification when assessing changes in MVPA. In addition, physical activity questionnaire in the NHIS data lacked information on exact duration and other types of non-leisure time physical activity such as domestic chores. Also, the survey data used in the NHIS had insufficient information on balance training, muscle-strengthening activities, and performance time of physical activity that could not be precisely converted into metabolic equivalent of task (MET) over time period (e.g. MET/minute MET/hour per week). Therefore, whether the participants in this study precisely followed the ESC joint guideline or PAG for prevention of CVD remains unclear. Second, additional source of information for evaluating CVD outcome such as dietary factors and left ventricular ejection fraction were not available in the NHIS database.



Take home figure Association of changes in exercise frequency and subsequent alterations in cardiovascular disease risk in adults aged 60 years and older.

Third, we could not assess the reason behind changing physical activity among the participants because this study was based on real-world data. Therefore, further studies with different intervention strategies for increase in physical activity for prevention of CVD are warranted. Fourth, the generalizability of our findings is limited to older Korean adults who were enrolled in the NHIS database, and thus more evidence from multi-ethnic cohort studies is needed.

Conclusions

Among older adults, regardless of disabilities and chronic conditions, increase in frequency of MVPA per week was associated with a significant risk reduction of CVD among those who were physically inactive. Our findings also suggest that decrease in frequency of MVPA from being continuously physically active attenuates the cardiovascular health benefits of physical activity (*Take home figure*). Given the dose-response nature of these associations, engaging in higher or consistent physical activity may help older adults prevent future risk for CVD events.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

Data sharing statement

No additional data available. The database used for this study was provided by the National Health Insurance Service (NHIS) in the Republic of Korea (NHIS-2018-1-404). Only authorized researchers were granted access to the database at the Big Data Research Center of the Big Data Steering Department at the NHIS.

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Conflict of interest: none declared.

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