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Association between exercise habit changes and mortality following a cardiovascular event

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ABSTRACT

Objective To investigate the associations between exercise habit changes following an incident cardiovascular event and mortality in older adults.

Methods We analysed the relationship between exercise habit change and all-cause, cardiovascular and non-cardiovascular deaths in adults aged ≥ 60 years between 2003 and 2012 who underwent two consecutive health examinations within 2 years before and after diagnosis of cardiovascular disease (CVD). They were categorised into four groups according to exercise habit changes: persistent non-exercisers, exercise dropouts, new exercisers and exercise maintainers. Differences in baseline characteristics were adjusted using inverse probability of treatment weighting.

Results Of 6076 participants, the median age was 72 (IQR 69–76) years and men accounted for 50.6%. Compared with persistent non-exercisers (incidence rate (IR) 4.8 per 100 person-years), new exercisers (IR 3.5, HR 0.73, 95% CI 0.58 to 0.91) and exercise maintainers (IR 2.9, HR 0.53, 95% CI 0.38 to 0.73) were associated with reduced risk of all-cause death. The rate of non-cardiovascular death was significantly lower in new exercisers (IR 2.3, HR 0.73, 95% CI 0.56 to 0.95) and exercise maintainers (IR 2.3, HR 0.61, 95% CI 0.42 to 0.90) than in persistent non-exercisers (IR 3.2). Also, trends towards reduced cardiovascular death in new exercisers and exercise maintainers were observed (p value for trend < 0.001).

Conclusions More virtuous exercise trajectories in older adults with CVD are associated with lower mortality rates. Our results support public health recommendations for older adults with CVD to perform physical activity.

INTRODUCTION

Previous studies have proven that incorporating an exercise habit is inversely related to the risk of mortality.¹ Current guidelines recommend regular exercise to reduce the risk of all-cause or cardiovascular death and morbidity.² However, evidence supporting the benefits of exercise in older adults with cardiovascular diseases (CVDs) is scarce because studies on exercise and mortality have been mainly performed in healthy and middle-aged persons.³ Although some studies have attempted to demonstrate the impact of exercise habits on death in patients with CVD, the results were inconsistent.^{4,5} In addition, most studies were based on a single baseline assessment of exercise with subsequent follow-up for mortality. Several

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Current guidelines recommend regular exercise to reduce the risk of mortality and morbidity.
- ⇒ Data on the prognostic effect of starting or maintaining exercise are mainly based on general healthy populations.

WHAT THIS STUDY ADDS

- ⇒ In patients with ischaemic stroke, heart failure or acute myocardial infarction, maintaining regular exercise was associated with reduced all-cause, cardiovascular and non-cardiovascular death.
- ⇒ Incorporating exercise habits was related to lowered risk of all-cause and non-cardiovascular death.
- ⇒ Although patients aged ≥ 75 years had reduced benefits with respect to preventing death compared with those aged < 75 years, the benefits were still statistically significant.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

- ⇒ Recommendations for exercise are important and should be promoted among older adults with cardiovascular disease.

studies have shown that such an assessment has time-limited predictive power and may be unable to accurately differentiate the effect of exercise per se from the influences of confounding factors such as genetic background, undetected comorbidities and changes in the variable of interest during follow-up.⁶ Engeseth *et al*⁷ described that physical fitness at inclusion was a significant predictor of early cardiovascular death but not late cardiovascular death. To overcome these limitations, some studies have suggested using change in exercise habits as a variable for evaluating long-term outcomes.^{8,9}

Considering the lack of information on the impact of exercise in older patients with CVD, this study aimed to analyse the association between change in exercise habits after a new CVD diagnosis and risk of all-cause, cardiovascular or non-cardiovascular death.

METHODS

Data were extracted from the Korean National Health Insurance Service (NHIS)-Senior database,



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which incorporates data of 558 147 participants recruited through a 10% simple random sampling method from a total of 5.5 million individuals aged ≥ 60 years in the National Health Information Database.^{10 11} Individuals enrolled in the insurance system undergo a general health screening examination every 2 years. The NHIS-Senior database includes information from self-report questionnaires, demographic data, anthropometric and blood pressure measurements, and information on income-based insurance status. Low income denotes income in the lowest 30% among the entire Korean population. The questionnaires collect information on participants' medical history, family history and lifestyle factors (smoking, alcohol intake and physical activity). Current smokers and drinkers were defined as people who currently smoke cigarettes and have consumed a drink containing alcohol in the last 12 months. All variables have no missing data. The need for informed consent was waived.

Physical activity level assessment

The leisure-time exercise levels at each health examination were evaluated using self-report questionnaires with a 1-week recall.¹² This short form survey was developed from the International Physical Activity Questionnaire, the reliability and validity of which have been confirmed in previous studies.^{13–15} The questionnaire incorporated three questions that assessed the frequency (days per week) of at least 30 min/day of light-intensity exercise, at least 30 min/day of moderate-intensity exercise and at least 20 min/day of vigorous-intensity exercise. Exercise status at each health examination was dichotomised as satisfying ('yes') versus not satisfying ('no') according to the current guidelines: ≥ 5 day/week of moderate-intensity exercise or ≥ 3 day/week of vigorous-intensity exercise or an equivalent combination of moderate-intensity and vigorous-intensity exercise, regardless of any amount of light-intensity exercise. Thereafter, the participants were divided into four groups according to exercise habit change: persistent non-exercisers (no to no), exercise dropouts (yes to no), new exercisers (no to yes) and exercise maintainers (yes to yes). Figure 1A illustrates the design of the study.

Covariates, follow-up and clinical outcomes

The diagnoses of selected comorbidities were confirmed using the International Classification of Diseases 10th revision codes and prescription medications before enrolment.^{10 11} To ensure diagnostic accuracy, participants were considered to have comorbidities or CVD when they had a discharge diagnosis of the conditions or were confirmed to have the conditions at least twice in an outpatient setting (online supplemental table 1).^{10 11 13–18}

The primary outcomes were all-cause, cardiovascular and non-cardiovascular deaths. The secondary outcomes were heart failure hospitalisation, ischaemic stroke, acute myocardial infarction (MI), new-onset atrial fibrillation and sudden cardiac arrest. We defined cardiovascular death if CVD was considered as the initial cause of death on death certificates.^{10 11 13–18} The participants were followed up from the date of the second health examination to the date of death or 31 December 2014, whichever came first. Information on death (date and causes) was confirmed from the National Population Registry of the Korea National Statistical Office, which conducts central registration of death based on death certificates. The NHIS and the National Statistical Office are national agencies covering the entire Korean population; thus, their databases allowed us to completely investigate the events.

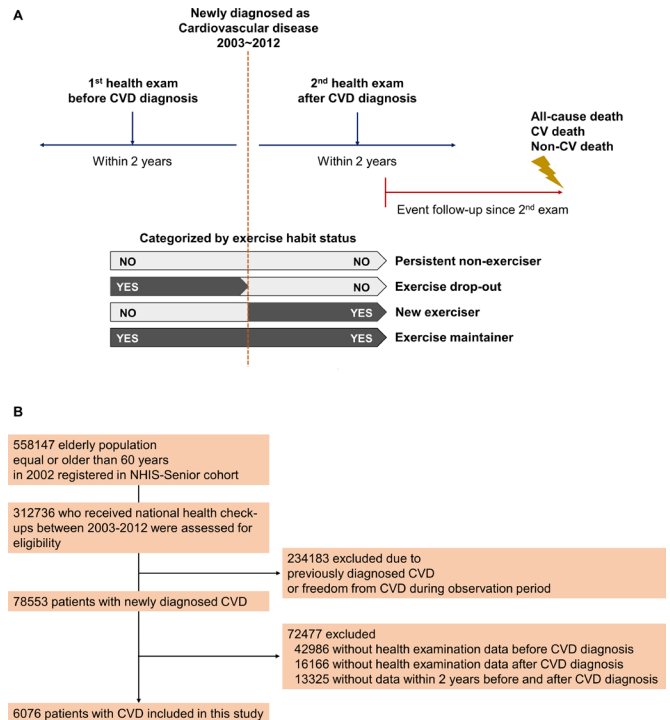


Figure 1 Selection and categorisation of the study population. (A) Categorisation of participants according to exercise habit change and the overall scheme of the study. (B) Selection of participants from the NHIS. CV, cardiovascular; CVD, cardiovascular disease; NHIS, National Health Insurance Service.

Patient and public involvement

Patients were not invited to contribute to study design, analysis, and writing or editing this manuscript.

Statistical analysis

Categorical variables are reported as frequencies (percentages), and continuous variables are expressed as median with IQR. Baseline characteristics were compared using Pearson's χ^2 test for categorical variables and Kruskal-Wallis test for continuous variables. Inverse probability of treatment weighting (IPTW) using propensity scores derived from all the baseline covariates including demographics, comorbidities, anthropometric measures, lifestyle behaviours, medications and income status was performed to correct for systematic differences among the four study groups. A standardised mean difference of <0.1 was considered to indicate acceptable differences among the study groups.¹⁹ The weighted incidence rates of all-cause, cardiovascular and non-cardiovascular deaths were estimated by dividing the number of weighted events by the sum of the follow-up duration and are presented as rates per 100 person-years. Persistent non-exercisers were defined as the reference group, and cumulative incidence curves for the outcomes were generated and compared using the log-rank test. Weighted Cox proportional hazards models with IPTW were used to compute the HR and 95% CI, considering all-cause death as a competing risk, by using the Fine and Gray method. When estimating the risk of all-cause death, the Fine and Gray method was not performed.

We estimated the primary and secondary outcomes using unweighted and various multivariable Cox models to verify the robustness of the results. Model 1 included age and sex. Model 2 was adjusted for body mass index, waist circumference, drinking, smoking, low income, Charlson comorbidity index,

hypertension, diabetes mellitus and dyslipidaemia, in addition to variables in model 1. Model 3 incorporated peripheral artery disease, chronic obstructive pulmonary disease, malignancy, chronic kidney disease, sleep apnoea, CHA₂DS₂-VASc score, use of aspirin, use of P2Y12 inhibitors, use of statins and use of oral anticoagulation, in addition to variables in model 2. In addition, we analysed the outcomes in prespecified subgroups, divided according to age (<75 or ≥75 years), sex, severity of comorbidities (Charlson comorbidity index <4 or ≥4) and each component of newly diagnosed CVD. We calculated the p value for interaction to examine the consistency of the patterns in the main results.²⁰ All tests were two-tailed, with p<0.05 considered to indicate statistical significance. All analyses were performed using R programming (V4.1.0; The R Foundation for Statistical Computing, Vienna, Austria).^{11 15 16 18}

RESULTS

Study population

From the Korean NHIS-Senior database, we identified 312 736 patients who underwent a health screening examination between 2003 and 2012. We defined CVD as a composite of acute MI, ischaemic stroke or hospitalisation for heart failure (online supplemental table 1). We excluded participants diagnosed with CVD before enrolment and those free from CVD between 2003 and 2012. Among the remaining participants, 6076 participants who had data from two consecutive health examinations within 2 years before and after the CVD diagnosis were finally included in this study (figure 1B).

Baseline characteristics

Table 1 shows the baseline characteristics of the 6076 study participants. The median age was 72 (IQR 69–76) years and men accounted for 50.6%. There were 2871 persistent non-exercisers (47.3%), 754 exercise dropouts (12.4%), 1363 new exercisers (22.4%) and 1088 exercise maintainers (17.9%). New exercisers and exercise maintainers were predominantly men. All variables were well balanced after IPTW (table 1, online supplemental figure 1).

Risks of all-cause, cardiovascular and non-cardiovascular deaths according to exercise habit change

Before estimating the risk of primary and secondary outcomes, the Cox proportionality assumption was tested based on the Schoenfeld residuals. No relevant violations were found. During the median follow-up of 3.8 years (IQR 2.2–5.7 years), the weighted all-cause mortality rate was 4.8, 4.6, 3.5 and 2.9 per 100 person-years in the persistent non-exerciser, exercise dropout, new exerciser and exercise maintainer groups, respectively. New exercisers (HR 0.73, 95% CI 0.58 to 0.91) and exercise maintainers (HR 0.53, 95% CI 0.38 to 0.73) had a lower risk of all-cause death than persistent non-exercisers.

Exercise maintainers also had a lower risk of cardiovascular death (HR 0.34, 95% CI 0.17 to 0.64). New exercisers exhibited a numerically improved survival with respect to cardiovascular death, although it was not statistically significant (HR 0.76, 95% CI 0.49 to 1.17, p=0.21). The risk of non-cardiovascular death was lower in both new exercisers (HR 0.73, 95% CI 0.56 to 0.95) and exercise maintainers (HR 0.61, 95% CI 0.42 to 0.90) than in persistent non-exercisers. Exercise dropouts showed similar risks of the three mortality outcomes compared with the reference group (table 2, figure 2). The cumulative incidence curves of all-cause, cardiovascular and non-cardiovascular deaths are shown in online supplemental figure 2, with the

concordant results of the log-rank test. Trends towards a reduced risk of primary outcomes in patients with favourable exercise changes were observed (p value for trend <0.001 in all-cause death, p<0.001 in cardiovascular death, p=0.006 in non-cardiovascular death).

Risks of other outcomes according to exercise habit change

The incidence rates and risks of other outcomes, including heart failure hospitalisation, ischaemic stroke, acute MI, new-onset atrial fibrillation and sudden cardiac death, are presented in online supplemental table 2 and online supplemental figure 3. No significant associations between exercise changes and these outcomes were observed. The risk of acute MI could not be estimated due to the small number of events.

Subgroup and sensitivity analyses

Sensitivity analyses were conducted to examine whether unweighted (online supplemental table 3) and various weighted (online supplemental table 4) Cox proportional hazards models showed consistent results. As shown in online supplemental table 3, new exercisers tended to experience a reduced risk of cardiovascular death (HR 0.63, 95% CI 0.42 to 0.93). Except for this, other results were consistent with the main results. As seen in online supplemental table 4, all estimates of model 1 and model 2 were comparable with the main results (model 3).

We performed subgroup analysis according to age. The incidence rate of cardiovascular death showed significant interactions with an increased risk thereof in exercise dropouts (HR 1.99, 95% CI 1.04 to 3.82) and increased benefits in exercise maintainers (HR 0.15, 95% CI 0.05 to 0.45) among those aged <75 years (p value for interaction=0.017; online supplemental table 5). Subgroup analysis according to sex, severity of comorbidities and type of CVD showed no significant interactions (online supplemental tables 6–8).

Compared with enrolled patients, patients who did not receive the second health examination were older with more comorbidities (online supplemental table 9). However, compared with non-exercisers at the first examination, exercisers also tended to have significantly lower all-cause, cardiovascular and non-cardiovascular death rates (online supplemental table 10).

DISCUSSION

The principal findings of this nationwide population-based cohort study that categorised patients according to changes in exercise habits after a first incident CVD event are summarised in figure 3. First, exercise maintenance was associated with a reduced risk of all-cause, non-cardiovascular or cardiovascular death. Second, a trend of progressively lower mortality rates was observed with an increase of exercise from persistent non-exercisers to exercise maintainers. Finally, among patients aged <75 years, those who were physically inactive tended to have a higher risk of cardiovascular death and those with a regular exercise habit tended to obtain greater benefits from exercise than their counterparts among patients aged ≥75 years.

Single assessment of exercise habit versus assessment of exercise habit change

Most studies on exercise relied on long-term follow-up of a single baseline assessment of physical activity. However, temporal changes in exercise habits could affect the risk of mortality during a long follow-up period.²¹ Moreover, previous studies have already described not only that a single assessment of exercise habits has limited predictive power in estimating the

Table 1 Baseline characteristics of the total study population according to exercise habit change

	Before IPTW						After IPTW									
	Persistent non-exerciser (n=2871)		Exercise dropouts (n=754)		New exerciser (n=1363)		Exercise maintainer (n=1088)		Persistent non-exerciser (n=5664)		Exercise dropouts (n=5042)		New exerciser (n=5019)		Exercise maintainer (n=4663)	
	n	SMD	n	SMD	n	SMD	n	SMD	n	SMD	n	SMD	n	SMD	n	SMD
Age	73 (69, 77)	0.056	73 (69, 77)	0.056	72 (69, 76)	0.056	72 (70, 75)	0.056	73 (69, 76)	0.056	72 (69, 76)	0.056	72 (69, 76)	0.056	72 (69, 76)	0.051
Male sex	1271 (44.3)	0.212	384 (50.9)	0.212	719 (52.8)	0.212	702 (64.5)	0.212	2804 (49.5)	0.212	2622 (52.0)	0.212	2640 (52.6)	0.212	2630 (56.4)	0.071
BMI (kg/m ²)	23.5 (21.4, 25.8)	0.056	23.5 (21.5, 25.6)	0.056	23.7 (21.6, 25.7)	0.056	23.8 (22.0, 25.8)	0.056	23.6 (21.5, 25.8)	0.056	23.6 (21.6, 25.5)	0.056	23.7 (21.7, 25.7)	0.056	23.8 (21.8, 25.7)	0.029
Waist circumference (cm)	84.0 (78.0, 90.0)	0.072	83.0 (77.0, 90.0)	0.072	83.0 (78.0, 89.3)	0.072	85.0 (79.0, 90.0)	0.072	84.0 (78.0, 90.0)	0.072	83.0 (78.0, 90.0)	0.072	83.0 (78.0, 89.0)	0.072	83.0 (78.0, 89.0)	0.024
Systolic BP (mm Hg)	130 (120, 140)	0.015	130 (120, 140)	0.015	130 (120, 140)	0.015	130 (120, 140)	0.015	130 (120, 140)	0.015	130 (120, 140)	0.015	130 (120, 140)	0.015	130 (120, 140)	0.021
Diastolic BP (mm Hg)	80 (70, 85)	0.066	80 (70, 84)	0.066	80 (70, 85)	0.066	80 (70, 84)	0.066	80 (70, 85)	0.066	80 (70, 84)	0.066	80 (70, 83)	0.066	80 (70, 83)	0.021
Economic status*		0.135		0.135		0.135		0.135		0.135		0.135		0.135		0.066
Low	688 (24.0)		150 (19.9)		292 (21.4)		192 (17.6)		1229 (21.7)		1049 (20.8)		1104 (22.0)		951 (20.4)	
Middle	654 (22.8)		179 (23.7)		264 (19.4)		201 (18.5)		1263 (22.3)		1190 (23.6)		974 (19.4)		957 (20.5)	
High	1529 (53.3)		425 (56.4)		807 (59.2)		695 (63.9)		3172 (56.0)		2803 (55.6)		2941 (58.6)		2755 (59.1)	
Current drinker	380 (13.2)		90 (11.9)		227 (16.7)		199 (18.3)		815 (14.4)		689 (13.7)		824 (16.4)		743 (15.9)	
Current smoker	236 (8.2)		46 (6.1)		137 (10.1)		78 (7.2)		488 (8.6)		333 (6.6)		434 (8.6)		358 (7.7)	
Charlson comorbidity index	5 (3.7)		6 (4.8)		6 (4.8)		6 (4.8)		5 (4.7)		5 (4.7)		5 (4.7)		5 (3.7)	
Fasting glucose (mg/dL)	98 (88, 111)		99 (89, 115)		99 (89, 113)		100 (90, 114)		99 (88, 112)		99 (89, 112)		98 (89, 111)		99 (89, 112.61)	
Total cholesterol (mg/dL)	185 (160, 215)		178 (150, 211)		182 (152, 211)		173 (147, 202)		183 (156, 212)		181 (153.4, 211)		184 (155, 211)		180 (154, 209)	
eGFR (mL/min/1.73 m ²)	66.7 (53.0, 82.7)		66.7 (54.8, 82.7)		69.1 (56.2, 84.2)		69.6 (55.6, 84.2)		68.1 (54.9, 83.8)		67.7 (55.5, 83.0)		67.7 (55.3, 83.8)		67.7 (56.0, 83.8)	
Newly diagnosed CVD		0.094		0.094		0.094		0.094		0.094		0.094		0.094		0.044
HF hospitalisation	811 (28.2)		212 (28.1)		329 (24.1)		248 (22.8)		1507 (26.6)		1346 (26.7)		1245 (24.8)		1139 (24.4)	
Ischaemic stroke	1991 (69.3)		518 (68.7)		984 (72.2)		809 (74.4)		4021 (71.0)		3545 (70.3)		3619 (72.1)		3376 (72.4)	
Acute MI	69 (2.4)		24 (3.2)		50 (3.7)		31 (2.8)		136 (2.4)		151 (3.0)		155 (3.1)		148 (3.2)	
Hypertension	1957 (68.2)		564 (74.8)		981 (72.0)		800 (73.5)		3982 (70.3)		3610 (71.6)		3483 (69.4)		3217 (69.0)	
Diabetes mellitus	660 (23.0)		231 (30.6)		380 (27.9)		348 (32.0)		1111 (20.5)		1321 (26.2)		1315 (26.2)		1268 (27.2)	
Dyslipidaemia	1775 (61.8)		545 (72.3)		973 (71.4)		828 (76.1)		3755 (66.3)		3489 (69.2)		3438 (68.5)		3213 (68.9)	
Peripheral artery disease	267 (9.3)		99 (13.1)		180 (13.2)		165 (15.2)		606 (10.7)		585 (11.6)		567 (11.3)		611 (13.1)	
COPD	1019 (35.5)		267 (35.4)		528 (38.7)		379 (34.8)		2022 (35.7)		1755 (34.8)		1787 (35.6)		1567 (33.6)	
Malignancy	536 (18.7)		153 (20.3)		304 (22.3)		292 (26.8)		1161 (20.5)		1018 (20.2)		1079 (21.5)		1054 (22.6)	
CKD	98 (3.4)		41 (5.4)		57 (4.2)		50 (4.6)		215 (3.8)		212 (4.2)		186 (3.7)		191 (4.1)	
Sleep apnoea	2 (0.1)		1 (0.1)		1 (0.1)		3 (0.3)		6 (0.1)		5 (0.1)		5 (0.1)		14 (0.3)	
Medication																
Aspirin	661 (23.0)		221 (29.3)		403 (29.6)		347 (31.9)		1478 (26.1)		1361 (27.0)		1365 (27.2)		1301 (27.9)	
P2Y12 inhibitor	180 (6.3)		62 (8.2)		111 (8.1)		97 (8.9)		436 (7.7)		373 (7.4)		366 (7.3)		345 (7.4)	
Statin	278 (9.7)		117 (15.5)		194 (14.2)		214 (19.7)		685 (12.1)		676 (13.4)		652 (13.0)		657 (14.1)	
OAC	58 (2.0)		21 (2.8)		31 (2.3)		32 (2.9)		125 (2.2)		131 (2.6)		125 (2.5)		117 (2.5)	
Warfarin	58 (2.0)		21 (2.8)		31 (2.3)		32 (2.9)		125 (2.2)		131 (2.6)		125 (2.5)		117 (2.5)	

Values are presented as median (Q1, Q3 quartiles; 25th and 75th percentiles) or n (%).
 *Low-income and high-income denote income in the lowest and highest 30% among the entire Korean population; individuals with low income are supported by the medical aid programme.
 BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; HF, heart failure; IPTW, inverse probability of treatment weighting; MI, myocardial infarction; OAC, oral anticoagulant; SMD, standardised mean difference.

Table 2 HR with 95% CI for all-cause, cardiovascular and non-cardiovascular deaths according to exercise habit change

		Individuals (n)	Events (n)	IR* (per 100 PY)	Subdistribution HR (95% CI)	P value	P value for trend
All-cause death†	Persistent non-exercisers	2871	671	4.8	1 (reference)		<0.001
	Exercise dropouts	754	131	4.6	0.92 (0.70 to 1.22)	0.562	
	New exercisers	1363	174	3.5	0.73 (0.58 to 0.91)	0.006	
	Exercise maintainers	1088	88	2.9	0.53 (0.38 to 0.73)	<0.001	
CV death	Persistent non-exercisers	2871	231	1.5	1 (reference)		<0.001
	Exercise dropouts	754	48	1.6	1.30 (0.85 to 1.99)	0.233	
	New exercisers	1363	53	1.2	0.76 (0.49 to 1.17)	0.205	
	Exercise maintainers	1088	18	0.6	0.34 (0.17 to 0.64)	0.001	
Non-CV death	Persistent non-exercisers	2871	440	3.2	1 (reference)		0.006
	Exercise dropouts	754	83	3.0	0.73 (0.52 to 1.04)	0.079	
	New exercisers	1363	121	2.3	0.73 (0.56 to 0.95)	0.021	
	Exercise maintainers	1088	70	2.3	0.61 (0.42 to 0.90)	0.012	

P values were evaluated by the likelihood ratio test.

*Weighted incidence rates were computed after inverse probability of treatment weighting.

†The Fine and Gray method was not used when calculating the risk of all-cause death.

CV, cardiovascular; IR, incidence rate; PY, person-years.

long-term cardiovascular risk but also that the change in exercise habits between the time of inclusion and the second assessment remains an independent predictor of death.²² In addition, the impact of selection bias on the association between exercise habits and death in large prospective cohort studies, which were mainly based on contemporary exercise guidelines, should be considered. For these reasons, we classified the participants into four groups according to exercise habit change. This may have allowed discriminating the benefits of exercise by itself from the influence of other confounding risk factors that have been improved by the accumulated gains from exercise.²³ Thus, the present study confirms the benefits of exercise in preventing death, especially when considering the results among exercise maintainers.

Exercise habit change after CVD diagnosis and death

Physical inactivity is a well-known risk factor for all-cause and cardiovascular deaths in adults.²⁴ Contemporary physical activity guidelines recommend substituting physical inactivity with regular exercise and establishing a target exercise level to improve life expectancy. However, most previous studies cited in these guidelines were based on results in healthy adults or

patients with hypertension, diabetes mellitus or HIV infection.²⁵ Guidelines for CVD management have also supported the benefits of exercise training, although uncertainty remains about its effects on mortality because the evidence was mainly based on small-sized randomised trials or non-randomised subgroup analyses of prospective cohort studies. A recent cohort study found that a higher level of exercise not only tended to reduce the risk of all-cause death among patients with CVD but also resulted in greater survival benefit than in individuals without CVD.²⁶ Our results were consistent with these findings and were robust even after adjusting for covariates in the Cox regression models and after analysing the outcomes in subgroups divided according to age, sex, degree of comorbidities and type of CVD.

Exercise habit change and death in older adults

The WHO guideline describes the impact of regular moderate-intensity exercise on all-cause and cardiovascular deaths in

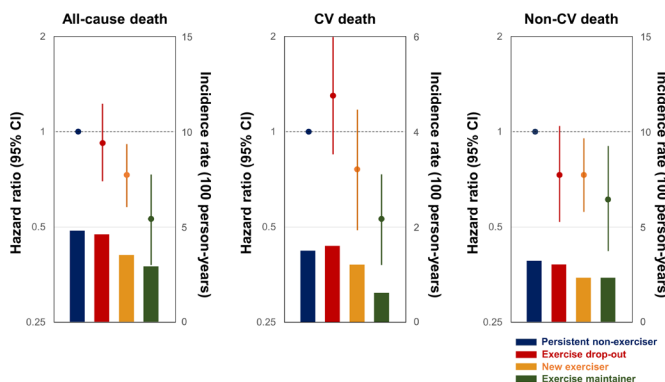


Figure 2 Dual-axis graph for all-cause, cardiovascular and non-cardiovascular deaths according to exercise habit change. Bars denote weighted incidence rates. Dots and whiskers indicate HR and 95% CI computed using weighted Cox proportional hazards models with inverse probability of treatment weighting. CV, cardiovascular.

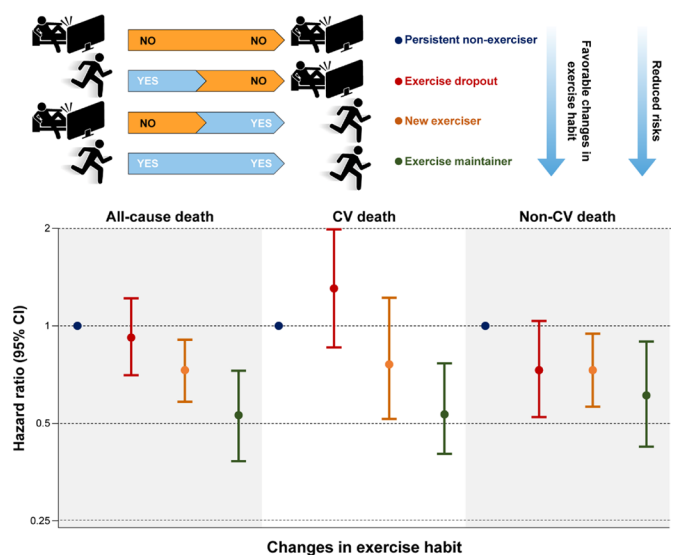


Figure 3 Graphical abstract summarising the principal findings of this study. The risks of all-cause, cardiovascular and non-cardiovascular death are reduced with more virtuous exercise trajectories in older adults with newly diagnosed cardiovascular (CV) disease.

older adults. However, it merely extrapolates the conclusion of studies that showed the benefits in middle-aged adults because no upper age limit criterion was set. Few studies to date have investigated a specific old-age group, and some studies failed to prove that exercise improves prognosis.^{27 28} Our current study showed that starting or maintaining regular exercise was associated with a lower risk of all-cause, cardiovascular or non-cardiovascular death. Although the results among new exercisers were not statistically significant for cardiovascular death, they were consistent with the tendency observed in the main analysis regardless of various sensitivity and subgroup analyses. A recently published study examined physical activity trajectories in the elderly with incident CVD and overall mortality.⁹ Some results across more virtuous trajectories of physical activity when considering cardiovascular outcomes and overall mortality go in the same direction as those found in the present paper. In our study, although patients aged ≥ 75 years had reduced benefits with respect to preventing death compared with those aged < 75 years, the benefits were still statistically significant. Barbiellini *et al*⁹ showed comparable results that interaction with age goes in support of a stronger effect of physical activity early in late-life rather than late in late-life. Therefore, our results suggest that the adoption and maintenance of regular exercise should not be ignored in older patients, even considering the reduced benefits obtained from exercise.

Study limitations

Our study had several limitations. First, as the CVD diagnosis was confirmed using claims data, errors due to incorrect coding may be present. To minimise this problem, previously verified definitions used in cohort studies based on the Korean NHIS database were applied. Second, recall bias is a major limitation because information about exercise habits relied on self-report questionnaires asking about lifestyle behaviours during the previous week. Third, physical activity level before and after the CVD diagnosis was evaluated using a questionnaire with a 1-week recall, assessing the physical activity over a period of 7 days rather than the entire period before and after the cardiovascular event. Therefore, the level of exercise could not be precisely defined. Additionally, while the validity of the International Physical Activity Questionnaire Short Form has been proven, its reliability has been shown to be low. Fourth, various types of physical activities, including light-intensity exercise, household tasks, occupational activities and transportation-related physical activities, were not included or analysed.²⁹ Fifth, multivariable Cox models were used to adjust results with potential confounders. However, the severity of CVD was not included. In fact, the severity of CVD could have both a prognostic value in terms of mortality risk and an impact on the physical activity level. Sixth, as only the Korean population could be enrolled in the study, ethnic differences might limit the external generalisability of the results. Seventh, the inclusion of patients who had two consecutive health examinations could introduce a selection bias. Information on individuals who did not undergo health examinations was not available; however, we found that the primary outcomes in patients who did not undergo a second health examination were consistent with the main results. Lastly, this was a nationwide cohort study and the causality between exercise habits and mortality cannot be proven.

CONCLUSION

Initiation or maintenance of at least 5 days of moderate-intensity activity or 3 days of vigorous-intensity activity a week

is associated with reduced risk of all-cause, cardiovascular and non-cardiovascular deaths in older adults with newly diagnosed CVD. Exercise is important and should be recommended to older adults with CVD.

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REFERENCES

- Moore SC, Patel AV, Matthews CE, *et al*. Leisure time physical activity of moderate to vigorous intensity and mortality: a large pooled cohort analysis. *PLoS Med* 2012;9:e1001335.
- World Health Organization. *Who guidelines Approved by the guidelines review Committee. who guidelines on physical activity and sedentary behaviour*. Geneva: World Health Organization, 2020.
- Koster A, Harris TB, Moore SC, *et al*. Joint associations of adiposity and physical activity with mortality: the National Institutes of Health-AARP diet and health study. *Am J Epidemiol* 2009;169:1344–51.
- Faulkner J, Stoner L, Lanford J, *et al*. Long-term effect of participation in an early exercise and education program on clinical outcomes and cost implications, in patients with TIA and minor, Non-Disabling stroke. *Transl Stroke Res* 2017;8:220–7.

- 5 Taylor RS, Walker S, Smart NA, *et al.* Impact of exercise-based cardiac rehabilitation in patients with heart failure (ExTraMATCH II) on mortality and hospitalisation: an individual patient data meta-analysis of randomised trials. *Eur J Heart Fail* 2018;20:1735–43.
- 6 Kujala UM. Is physical activity a cause of longevity? it is not as straightforward as some would believe. A critical analysis. *Br J Sports Med* 2018;52:914–8.
- 7 Engeseth K, Prestgaard EE, Mariampillai JE, *et al.* Physical fitness is a modifiable predictor of early cardiovascular death: a 35-year follow-up study of 2014 healthy middle-aged men. *Eur J Prev Cardiol* 2018;25:1655–63.
- 8 Erikssen G, Liestøl K, Bjørnholt J, *et al.* Changes in physical fitness and changes in mortality. *Lancet* 1998;352:759–62.
- 9 Barbiellini Amidei C, Trevisan C, Dotto M, *et al.* Association of physical activity trajectories with major cardiovascular diseases in elderly people. *Heart* 2022;108:360–6.
- 10 Kim D, Yang P-S, Yu HT, *et al.* Risk of dementia in stroke-free patients diagnosed with atrial fibrillation: data from a population-based cohort. *Eur Heart J* 2019;40:2313–23.
- 11 Yang P-S, Jang E, Yu HT, *et al.* Changes in cardiovascular risk factors and cardiovascular events in the elderly population. *J Am Heart Assoc* 2021;10:e019482.
- 12 Chun MY. Validity and reliability of Korean version of international physical activity questionnaire short form in the elderly. *Korean J Fam Med* 2012;33:144–51.
- 13 Kim D, Yang P-S, Kim T-H, *et al.* Ideal blood pressure in patients with atrial fibrillation. *J Am Coll Cardiol* 2018;72:1233–45.
- 14 Kim T-H, Yang P-S, Yu HT, *et al.* Effect of hypertension duration and blood pressure level on ischaemic stroke risk in atrial fibrillation: nationwide data covering the entire Korean population. *Eur Heart J* 2019;40:809–19.
- 15 Kim D, Yang P-S, You SC, *et al.* Treatment timing and the effects of rhythm control strategy in patients with atrial fibrillation: nationwide cohort study. *BMJ* 2021;373:n991.
- 16 Kim D, Yang P-S, Jang E, *et al.* 10-year nationwide trends of the incidence, prevalence, and adverse outcomes of non-valvular atrial fibrillation nationwide health insurance data covering the entire Korean population. *Am Heart J* 2018;202:20–6.
- 17 Kim D, Yang P-S, Jang E, *et al.* Increasing trends in hospital care burden of atrial fibrillation in Korea, 2006 through 2015. *Heart* 2018;104:2010–7.
- 18 Kim D, Yang P-S, Sung J-H, *et al.* Less dementia after catheter ablation for atrial fibrillation: a nationwide cohort study. *Eur Heart J* 2020;41:4483–93.
- 19 Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med* 2009;28:3083–107.
- 20 Proietti M, Marzona I, Vannini T, *et al.* Long-term relationship between atrial fibrillation, multimorbidity and oral anticoagulant drug use. *Mayo Clin Proc* 2019;94:2427–36.
- 21 Byberg L, Melhus H, Gedeberg R, *et al.* Total mortality after changes in leisure time physical activity in 50 year old men: 35 year follow-up of population based cohort. *Br J Sports Med* 2009;43:b688.
- 22 Leskinen T, Stenholm S, Heinonen OJ, *et al.* Change in physical activity and accumulation of cardiometabolic risk factors. *Prev Med* 2018;112:31–7.
- 23 Ahn H-J, Lee S-R, Choi E-K, *et al.* Association between exercise habits and stroke, heart failure, and mortality in Korean patients with incident atrial fibrillation: a nationwide population-based cohort study. *PLoS Med* 2021;18:e1003659.
- 24 Ekelund U, Tarp J, Steene-Johannessen J, *et al.* Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis. *BMJ* 2019;366:l4570.
- 25 Piercy KL, Troiano RP, Ballard RM, *et al.* The physical activity guidelines for Americans. *JAMA* 2018;320:2020–8.
- 26 Jeong S-W, Kim S-H, Kang S-H, *et al.* Mortality reduction with physical activity in patients with and without cardiovascular disease. *Eur Heart J* 2019;40:3547–55.
- 27 Munro JF, Nicholl JP, Brazier JE, *et al.* Cost effectiveness of a community based exercise programme in over 65 year olds: cluster randomised trial. *J Epidemiol Community Health* 2004;58:1004–10.
- 28 Newman AB, Dodson JA, Church TS, *et al.* Cardiovascular events in a physical activity intervention compared with a successful aging intervention: the life study randomized trial. *JAMA Cardiol* 2016;1:568–74.
- 29 Holtermann A, Schnohr P, Nordestgaard BG, *et al.* The physical activity paradox in cardiovascular disease and all-cause mortality: the contemporary Copenhagen General Population Study with 104 046 adults. *Eur Heart J* 2021;42:1499–511.