European Journal of Preventive Cardiology (2025) **00**, 1–12
https://doi.org/10.1093/eurjpc/zwaf170

FULL RESEARCH PAPER
Prevention in practice

Aerobic exercise and cardiovascular outcomes in patients with diabetes undergoing percutaneous coronary intervention: a nationwide population-based study

Jung-Kyu Han [1,2]*†, Kyungdo Han [3]†, You-Jeong Ki [4], Jin-Eun Song [1], Doyeon Hwang[1], Jeehoon Kang [1], Han-Mo Yang [1,2], Kyung Woo Park [1,2], Hyun-Jae Kang [1,2], Bon-Kwon Koo [1,2], and Hyo-Soo Kim [1,2]

[1]Cardiovascular Center, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea; [2]Department of Internal Medicine, College of Medicine, Seoul National University, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea; [3]Department of Statistics and Actuarial Science, Soongsil University, 369 Sangdo-ro, Dongjak-gu, Seoul 06978, Republic of Koreaa; and [4]Cardiovascular Center, Uijeongbu Eulji Medical Center, 712 Dongil-ro, Uijeongbu-si 11759, Gyeonggi-do, Republic of Korea

Received 18 July 2024; revised 1 January 2025; accepted 19 March 2025; online publish-ahead-of-print 24 March 2025

Aims

We investigated the impact of aerobic exercise on clinical outcomes in patients with diabetes undergoing percutaneous coronary intervention (PCI).

Methods and results

We analyzed a nationwide prospective population database from the Korean National Health Insurance System. We included 8225 patients with diabetes who had undergone PCI and documented their aerobic exercise habits before and after the procedure (mean interval: 2.0 years). The patients were categorized into four groups: persistent non-exercisers, new exercisers, exercise discontinuers, and exercise maintainers. The primary outcome was major adverse cardiovascular events (MACE), a composite of all-cause death, myocardial infarction, revascularization, and heart failure. We assessed the risk of clinical events using inverse probability-weighted Cox proportional hazards models. During a mean follow-up of 4.9 years, exercise maintainers, discontinuers, and new exercisers were associated with a significantly lower risk of MACE compared to non-exercisers. The lowest risk was observed in exercise maintainers (maintainers: aHR, 0.78; 95% CI: 0.71–0.86; discontinuers: aHR, 0.88; 95% CI: 0.79–0.98; new exercisers: aHR, 0.89; 95% CI: 0.80–1.00). A J-curve relationship between the amount of aerobic exercise and adverse clinical outcomes was observed, with the lowest risk identified at 1000–1499 MET-min/week. Benefits diminished with exercise intensity ≥1500 MET-min/week.

Conclusion

Aerobic exercise maintenance after PCI was associated with a reduced risk of cardiovascular events in patients with diabetes, with a moderate amount of exercise providing maximal benefit. Therefore, aerobic exercise is advisable for patients with diabetes undergoing PCI, and the optimal exercise dosage warrants further research.

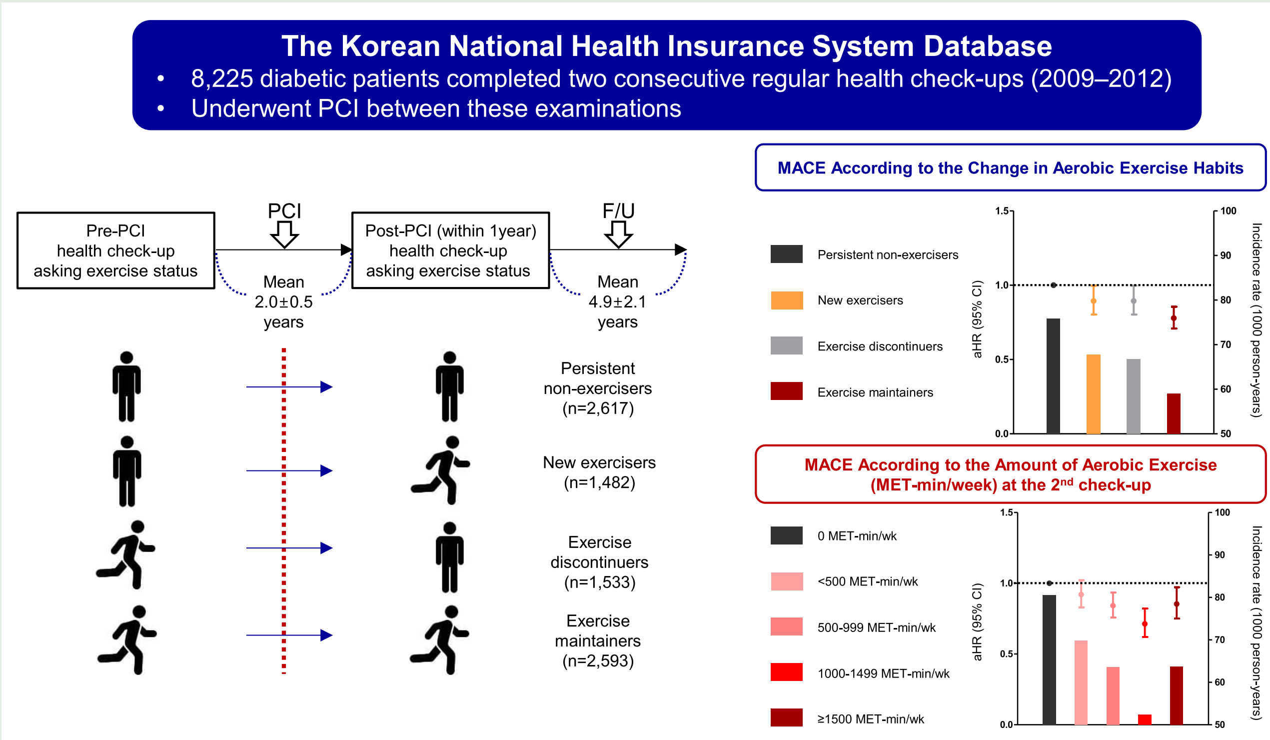
Lay summary

This large-scale prospective population study, based on the Korean National Health Insurance System, demonstrated that maintaining aerobic exercise in patients with diabetes undergoing percutaneous coronary intervention is significantly associated with a lower risk of cardiovascular events.

- A J-curve relationship was observed between the amount of aerobic exercise and clinical outcomes, with the lowest risk observed at 1000–1499 MET-min/week for both new exercisers and the entire study population.
- However, exercising beyond 1500 MET-min/week offers diminishing returns, highlighting the need for balanced exercise intensity.

* Corresponding author. Tel: 82 2 2072 4870, Fax: 82 2 766 8904, Email: hpcrates@gmail.com
† The first two authors are the co-first authors of the current study.

Graphical Abstract



Keywords Exercise • Diabetes • Percutaneous coronary intervention • Cardiovascular event

Introduction

Diabetes mellitus (DM) is a significant risk factor for cardiovascular diseases,[1] which are the leading causes of death and complications in patients with diabetes.[2] Globally, the rate of diabetes is increasing,[3] with an estimated prevalence of 20–30% among individuals with coronary artery disease receiving percutaneous coronary intervention (PCI).[4] Aerobic exercise is a cornerstone of the maintenance and improvement of cardiovascular health, both for primary prevention[5,6] and management of diabetes.[7] Regular aerobic exercise is crucial for preventing and controlling weight gain, lowering blood pressure, enhancing insulin sensitivity and glucose management, and improving lipid profiles.[8] These benefits counter critical risk factors for type 2 diabetes development, underscoring the importance of exercise in managing the disease and promoting overall cardiovascular health.[9] However, the impact of aerobic exercise on the clinical outcomes of patients with diabetes undergoing PCI is yet to be comprehensively studied. Key questions include how exercise habits and their changes before and after PCI affect outcomes in this patient group, as well as the relationship between aerobic exercise dose and clinical outcomes. Therefore, we aimed to address these issues using a large-scale population database from the Korean National Health Insurance System (NHIS), a single insurer in the Republic of Korea that covers 97% of the Korean population.

Methods

Data source and study population

This study utilized the Korean NHIS database, which comprises various subsets of health-related data for individuals in the Republic of Korea. Specifically, this database provides information regarding baseline demographics, health check-ups, and diagnostic codes for diseases, medication prescription, and mortality. All Koreans enrolled in the NHIS are encouraged to undergo health check-ups at least every 2 years. Among 2 741 135 patients with DM who underwent check-ups between 1 January 2009 and 31 December 2012, 1 970 945 adult (aged ≥20 years) completed two consecutive regular check-ups. Among them, 20 006 patients underwent PCI between the two examinations. To avoid confounding by pre-existing diseases, individuals with a history of heart failure ($n = 6541$) or myocardial infarction (MI, $n = 5081$) before the second check-up were excluded from the analysis. After excluding patients with missing data ($n = 159$), the final study population comprised 8225 individuals (*Figure 1*). Time intervals between the first health check-up and the index PCI, as well as between the index PCI and the second check-up, were measured. The follow-up duration began on the date of the second check-up for each individual and extended until the occurrence of any clinical event or 31 December 2018, whichever came first. This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Seoul National University Hospital (Approval Code: E-2310-004-1472).

Measurements and definitions

Data on aerobic exercise intensity (light, moderate, or vigorous) and frequency (number of days per week) were collected using a self-reported questionnaire. This questionnaire included three questions asking about the frequency (days per week) of the following activities during the past week: (i) light exercise (e.g. slow walking, carpet sweeping)[10] for at least 30 min per day, (ii) moderate exercise (e.g. brisk-paced walking, tennis, leisurely bicycling)[10] for at least 30 min per day, and (iii) vigorous exercise (e.g. running, climbing, fast cycling, aerobics)[10] for at least 20 min per day.

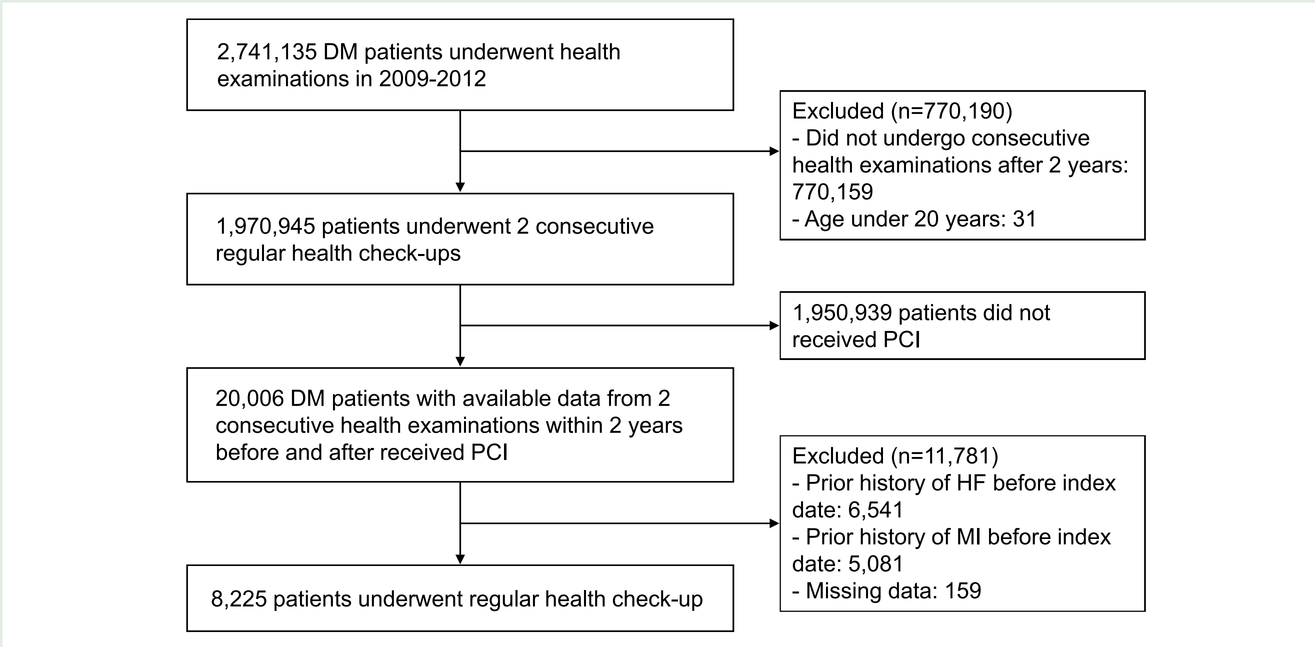


Figure 1 Selection and categorisation of the study population. (*A*) Flowchart illustrating the selection process of the study population. (*B*) Categorisation of the study population-based on the change in exercise habits. DM, diabetes mellitus; HF, heart failure; MI, myocardial infarction; PCI, percutaneous coronary intervention.

To define aerobic exercise status, 'yes' was assigned to individuals who engaged in moderate or vigorous exercise for >30 or >20 min, respectively, at least once a week. In contrast, 'no' was designated for those who did not perform any moderate or vigorous exercise, irrespective of engagement in light exercise. The study population was divided into the following four groups based on exercise status before and after PCI: (i) persistent non-exercisers (no/no), individuals who exercised neither before nor after PCI; (ii) new exercisers (no/yes), patients who did not exercise before PCI but started exercising after the procedure; (ii) exercise discontinuers (yes/no), individuals who exercised before PCI but stopped afterwards; and (iv) exercise maintainers (yes/yes), patients who exercised both before and after PCI. To distinguish the impact of low-intensity exercise from no exercise, we also conducted an analysis re-assigning 'yes' to patients with any amount of exercise and 'no' to those with no exercise.

To determine the optimal amount of aerobic exercise required to improve cardiovascular outcomes, we analyzed hazard ratios (HR) based on stratified exercise amount. Exercise amount was determined using a self-reported questionnaire that recorded the frequency of each aerobic exercise intensity type over a specific duration. To calculate the total amount of exercise, we first assigned metabolic equivalents of task (METs) to different exercise intensities as follows: 2.9 METs for light exercise, 4.0 METs for moderate exercise, and 7.0 METs for vigorous exercise.[11] The total amount of exercise was then calculated as the sum of products obtained by multiplying these MET values by the reported weekly frequency and minimum duration of light, moderate, and vigorous exercise, respectively. Subsequently, we stratified the amount of exercise into four categories as follows: (i) <500, (ii) 500–999, (iii) 1000–1499, and (iv) ≥1500 MET-min, using an explorative approach. For instance, 500 MET-min/week equates to either 125 min/week of moderate- or 71 min/week of vigorous-intensity exercise.

Covariates and outcome measurement

Demographic data, comorbidities, medications, laboratory findings, anthropometric measurements, self-reported questionnaire results, and income-based insurance contributions were collected during the health examination following the index PCI. The primary outcome of interest for this study was major adverse cardiovascular events (MACE), which comprised all-cause death, MI, revascularization, and heart failure. The individual components of MACE were considered secondary outcomes. Clinical outcomes were identified using codes from the International Classification of Diseases, 10th Revision, Clinical Modification, in both in- and out-patient records. The date of the health check-up conducted after PCI was considered the index date, and the study population was followed up until the date of the first occurrence of any clinical event or 31 December 2018, whichever occurred first.

Statistical analyses

Continuous variables are presented as mean ± SD, whereas categorical variables are reported as percentages. The incidence rate for each outcome was calculated as the number of events divided by the follow-up duration (per 1000 person-years). For cases in which combined endpoints occurred in one patient, the first event was recorded. An inverse probability-weighted (IPW) Cox proportional hazards regression model was employed to address potential selection or predisposition bias. The propensity score, derived from baseline covariates, including demographic characteristics, comorbidities, medications, laboratory findings, anthropometric measurements, lifestyle, and income-based insurance contributions, was used to balance the weights across the four patient groups. A maximum absolute standardized difference (ASD) < 0.1 was considered a satisfactory covariate balance. The risk of clinical events was assessed using Cox proportional hazards models weighted by IPW. To elucidate the effects of aerobic exercise habits, the persistent non-exerciser (no/no) group was defined as the reference group, and adjusted HRs (aHRs) with 95% confidence intervals (CIs) were computed. Multivariable Cox proportional hazards regression analyses adjusting for age, sex, comorbidities, smoking status, social income, medications, and body mass index were also performed to estimate aHR and the corresponding 95% CIs for the association between exercise amount and clinical outcomes.

Results

Baseline characteristics and study population

A total of 8225 patients with DM who had undergone PCI were included in the analysis. The mean age of the study cohort was 64.7 ± 8.6 years, and 5728 patients (69.6%) were male. At the time of the second health check-up, 2617 patients (31.8%) were classified as persistent non-exercisers, 1482 (18.0%) as new exercisers, 1533 (18.6%) as exercise discontinuers, and 2593 (31.5%) as exercise maintainers. The new exerciser and exercise maintainer groups were comparatively younger, had a higher proportion of male patients, and exhibited a lower prevalence of conditions such as hypertension, peripheral arterial disease, chronic obstructive pulmonary disease, stroke, and chronic kidney disease (*Table 1*). The maximum ASDs, indicating successful covariate balancing after IPW, were all ≤0.1. Additional multiple comparisons of covariates and analysis of the degree of balance achieved among the four groups were performed by calculating ASDs (see Supplementary material online, *Table S1*). The mean time period from the first health check-up to the index PCI was 0.9 ± 0.6 years, while the mean duration from the index PCI to the second check-up was 1.0 ± 0.6 years. The average interval between the two check-ups was 2.0 ± 0.5 years.

Changes in aerobic exercise habits and clinical outcomes

The mean follow-up durations since the second check-up for MACE, all-cause death, cardiovascular death, MI, revascularization, and heart failure were 4.9 ± 2.1, 5.8 ± 1.4, 5.8 ± 1.4, 5.7 ± 1.6, 5.2 ± 2.0, and 5.5 ± 1.6 years, respectively. The clinical outcomes of the four exercise groups after IPW adjustment are summarized in *Table 2*. New exercisers, discontinuers, and exercise maintainers exhibited progressively lower risks of MACE compared with persistent non-exercisers (maintainers: aHR, 0.78; 95% CI: 0.71–0.86, discontinuers: aHR, 0.88; 95% CI: 0.79–0.98, new exercisers: aHR 0.89; 95% CI: 0.80–1.0). Regarding other clinical outcomes, including all-cause death, cardiovascular death, MI, revascularization, and heart failure, exercise maintainers showed a significantly lower risk than that of persistent non-exercisers. Although new exercisers and discontinuers displayed numerically lower risks of adverse clinical outcomes, these differences were not statistically significant (*Table 2* and *Figure 2*). Further analysis, in which any amount of exercise was categorized as the exercise group, also showed a similar trend (see Supplementary material online, *Table S2*). When the amount of exercise was categorized using a cutoff value of 500 MET-min/week, a similar trend was observed regarding the impact of exercise habits on clinical outcomes (see Supplementary material online, *Table S3*). Individuals who engaged in exercise for ≥500 MET-min/week both before and after the index PCI showed better clinical outcomes than those of individuals who engaged in exercise for <500 MET-min/week before and after PCI.

Relationship between exercise amount and risk of clinical events

To determine the appropriate amount of exercise required after PCI, a multivariable-adjusted Cox proportional hazards analysis was conducted based on the amount of exercise recorded at the time of the second health check-up (*Table 3* and *Figure 3*). Notably, a J-curve relationship was observed between the amount of exercise and adverse clinical outcomes adjusted by multivariable analysis, with the lowest risk occurring at 1000–1499 MET-min/week. The benefits of exercise appeared to diminish at ≥1500 MET-min/week. Finally, when the analysis was conducted for new exercisers alone, a similar J-curve trend was evident between the amount of exercise and clinical outcomes (see Supplementary material online, *Table S4*).

Subgroup analysis of MACE

The relationship between aerobic exercise habits and MACE, with the lowest risk observed in exercise maintainers, remained consistent across various subgroups, including those classified according to age, sex, DM duration, insulin usage, and number of DM medications (*Figure 4*).

Discussion

To our knowledge, this is the first population-based study to investigate the impact of aerobic exercise on cardiovascular outcomes in patients with DM who underwent PCI. The key findings of this study were as follows: (ⅰ) among patients with diabetes, the maintenance of aerobic exercise after PCI was significantly associated with a lower risk of cardiovascular events; and (ⅱ) a J-curve relationship was observed between aerobic exercise amount and clinical outcomes, with the lowest risk observed at 1000–1499 MET-min/week for both new exercisers and the entire study population.

Current evidence and clinical guidelines supporting aerobic exercise in patients with diabetes

Aerobic exercise plays a pivotal role in improving cardiovascular risk factors, including insulin resistance, elevated blood glucose, poor lipid profiles, and high blood pressure.[12] Glucose uptake by skeletal muscle occurs through facilitated diffusion, which is dependent on the glucose transporter 4 (GLUT4) on the cell surface.[13] Notably, muscle contraction translocates GLUT4 to the plasma membrane in an insulin-independent manner. Therefore, exercise is the most effective stimulus for increasing skeletal muscle GLUT4 expression.[13] Furthermore, although nitric oxide-mediated endothelial function is impaired in individuals with diabetes, exercise improves endothelial-dependent vasodilation in these patients.[14] Data from a prospective cohort study and a meta-analysis of prospective studies showed that exercise significantly reduces the risk of overall mortality in patients with diabetes.[15] Specifically, randomized trials and meta-analyses have shown that engaging in aerobic exercise for ≥150 min/week decreases haemoglobin A1c levels in people with diabetes or prediabetes.[16–18] Consequently, current guidelines for individuals with diabetes recommend engaging in ≥150 min/week of moderate-to-vigorous aerobic exercise.[7,19,20] Similarly, the guidelines for patients with chronic coronary disease[21] and for primary prevention of cardiovascular disease[5,6] advise ≥150 min/week of moderate- or ≥75 min/week of vigorous-intensity aerobic exercise. However, the effect of aerobic exercise on the clinical outcomes of patients with diabetes undergoing PCI has not yet been fully explored. Our large-scale population-based study offers significant evidence in favor of promoting aerobic exercise in this patient population.

Long lasting effects of aerobic exercise

The effects of aerobic exercise on insulin sensitivity are known to be short-lived, lasting only for 24–72 h. Based on this finding, an interval

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

Exercise	Total	Before IPW					After IPW				
		Persistent non-exercisers	New exercisers	Exercise discontinuers	Exercise maintainers	Maximum ASD	Persistent non-exercisers	New exercisers	Exercise discontinuers	Exercise maintainers	Maximum ASD
n		2599	1468	1529	2597		2616.4	1476.4	1530.0	2612.1	
Age	64.7 ± 8.6	66.7 ± 8.2	64.1 ± 8.4	65.6 ± 8.4	62.4 ± 8.6	0.5042	64.6 ± 8.7	64.7 ± 8.4	64.7 ± 8.7	64.8 ± 8.6	0.0179
Male	5728 (69.6)	1498 (57.2)	1023 (69.0)	1041 (67.9)	2166 (83.5)	0.6013	1823.1 (69.7)	1027.3 (69.6)	1064.9 (69.6)	1808.8 (69.2)	0.0093
Comorbidities											
Hypertension	7318 (89.0)	2379 (90.9)	1310 (88.4)	1353 (88.3)	2276 (87.8)	0.1019	2338.8 (89.4)	1315.5 (89.1)	1362.7 (89.1)	2338.9 (89.5)	0.0152
Dyslipidemia	7417 (90.2)	2351 (89.8)	1345 (90.8)	1373 (89.6)	2348 (90.6)	0.0403	2350.1 (89.8)	1330.6 (90.1)	1384.1 (90.5)	2370.0 (90.7)	0.0307
PAD	2046 (24.9)	696 (26.6)	353 (23.8)	414 (27.0)	583 (22.5)	0.1051	652.3 (24.9)	367.0 (24.9)	379.9 (24.8)	647.2 (24.8)	0.0035
COPD	1214 (14.8)	443 (16.9)	199 (13.4)	245 (16.0)	327 (12.6)	0.1220	390.9 (14.9)	220.4 (14.9)	224.8 (14.7)	387.4 (14.8)	0.0070
Stroke	958 (11.7)	361 (13.8)	172 (11.6)	201 (13.1)	224 (8.6)	0.1638	86.2 (3.3)	50.4 (3.4)	53.4 (3.5)	89.8 (3.4)	0.0111
Cancer	276 (3.4)	89 (3.4)	52 (3.5)	58 (3.8)	77 (3.0)	0.0449	463.0 (17.7)	261.3 (17.7)	273.0 (17.8)	475.9 (18.2)	0.0138
CKD (GFR ≤60)	1457 (17.7)	572 (21.9)	230 (15.5)	297 (19.4)	358 (13.8)	0.2115	95.5 (3.7)	52.8 (3.6)	55.84 (3.7)	98.2 (3.8)	0.0096
Dementia	294 (3.6)	137 (5.2)	38 (2.6)	59 (3.9)	60 (2.3)	0.1542	305.0 (11.7)	168.2 (11.4)	180.7 (11.8)	313.8 (12.0)	0.0196
Smoking status											
Non-smoker	4258 (51.8)	1641 (62.7)	772 (52.1)	834 (54.4)	1011 (39.0)	0.4884	1350.7 (51.6)	767.1 (52.0)	793.5 (51.9)	1365.5 (52.3)	0.0130
Ex-smoker	2780 (33.8)	584 (22.3)	496 (33.5)	499 (32.6)	1201 (46.3)	0.5225	887.0 (33.9)	498.2 (33.75)	515.2 (33.67)	871.1 (33.4)	0.0116
Current-smoker	1187 (14.4)	392 (15.0)	214 (14.4)	200 (13.1)	381 (14.7)	0.0556	378.7 (14.5)	211.1 (14.3)	221.3 (14.5)	375.5 (14.4)	0.0048
Low income[a]	1207 (14.7)	422 (16.1)	234 (15.8)	234 (15.3)	317 (12.2)	0.1120	393.837 (15.1)	223.237 (15.1)	225.14 (14.7)	389.7 (14.9)	0.0115
Medications											
HTN medication	7832 (95.2)	2503 (95.6)	1401 (94.5)	1469 (95.8)	2459 (94.8)	0.0607	2504.3 (95.7)	1406.2 (95.2)	1456.0 (95.2)	2492.9 (95.4)	0.0268
Statin	7568 (92.0)	2400 (91.7)	1358 (91.6)	1407 (91.8)	2403 (92.7)	0.0387	2399.9 (91.7)	1358.3 (92.0)	1408.9 (92.1)	2410.1 (92.3)	0.0199
Aspirin	7968 (96.9)	2519 (96.2)	1432 (96.6)	1496 (97.6)	2521 (97.2)	0.0771	2537.2 (97.0)	1430.5 (96.9)	1481.8 (96.9)	2531.1 (96.9)	0.0069
Clopidogrel	7723 (93.9)	2469 (94.3)	1383 (93.3)	1443 (94.1)	2428 (93.6)	0.0424	2451.5 (93.7)	1386.0 (93.9)	1436.8 (93.9)	2442.4 (93.5)	0.0169
Warfarin	115 (1.4)	37 (1.4)	20 (1.4)	24 (1.6)	34 (1.3)	0.0218	39.0 (1.5)	21.2 (1.4)	21.0 (1.4)	41.8 (1.6)	0.0190
NOAC	9 (0.1)	5 (0.2)	0 (0)	3 (0.2)	1 (0.0)	0.0633	2.9 (0.1)	0 (0)	1.7 (0.1)	3.3 (0.1)	0.0510
Number of OHA											
0	1046 (12.7)	303 (11.6)	205 (13.8)	189 (12.3)	349 (13.5)	0.0676	329.1 (12.6)	185.0 (12.5)	194.8 (12.7)	321.7 (12.3)	0.0124
1	2146 (26.1)	687 (26.3)	377 (25.4)	403 (26.3)	679 (26.2)	0.0194	686.8 (26.3)	385.1 (26.1)	394.6 (25.8)	692.9 (26.5)	0.0166
2	3550 (43.2)	1125 (43.0)	615 (41.5)	672 (43.8)	1138 (43.9)	0.0483	1124.5 (43.0)	638.0 (43.2)	665.6 (43.5)	1119.1 (42.8)	0.0133
≥3	1483 (18.0)	502 (19.2)	285 (19.2)	269 (17.6)	427 (16.5)	0.0721	476.1 (18.2)	268.2 (18.2)	275.0 (18.0)	478.5 (18.3)	0.0091
Insulin	806 (9.8)	288 (11)	139 (9.4)	157 (10.2)	222 (8.6)	0.0822	259.4 (9.9)	144.3 (9.8)	150.2 (9.8)	258.6 (9.9)	0.0047
DM duration, years	6.8 ± 3.9	7.0 ± 3.8	6.7 ± 4.0	7.0 ± 3.8	6.5 ± 4.0	0.1176	6.8 ± 3.8	6.8 ± 3.9	6.8 ± 3.8	6.8 ± 4.0	0.0090

Continued

Table 1 *Continued*

Exercise	Total	Before IPW					After IPW				
		Persistent non-exercisers	New exercisers	Exercise discontinuers	Exercise maintainers	Maximum ASD	Persistent non-exercisers	New exercisers	Exercise discontinuers	Exercise maintainers	Maximum ASD
n		2599	1468	1529	2597		2616.4	1476.4	1530.0	2612.1	
Laboratory findings											
Fasting glucose, mg/dL	133 ± 43	134 ± 44	130 ± 41	133 ± 44	134 ± 43	0.0909	134 ± 43	134 ± 45	133 ± 44	133 ± 41	0.0217
Total cholesterol, mg/dL	148 ± 43	151 ± 56	148 ± 35	149 ± 35	146 ± 36	0.1078	148 ± 45	149 ± 36	149 ± 35	148 ± 37	0.0186
Triglyceride, mg/dL, median (IQR)	119 (118–121)	122 (120–125)	120 (117–123)	119 (117–122)	116 (114–118)	0.1006	120 (117–122)	119 (116–122)	120 (117–123)	120 (118–122)	0.0100
High-density lipoprotein, mg/dL	46 ± 12	46 ± 12	46 ± 11	46 ± 14	47 ± 12	0.0382	46 ± 12	46 ± 11	46 ± 14	46 ± 12	0.0159
Low-density lipoprotein, mg/dL	76 ± 43	78 ± 59	75 ± 30	76 ± 30	73 ± 36	0.0981	75 ± 45	75 ± 31	76 ± 30	76 ± 53	0.0198
Estimated GFR, mL/min/1.73 m^2	81.1 ± 52.1	78.7 ± 46.8	83.7 ± 67.0	79.1 ± 36.4	83.3 ± 55.1	0.0897	82.0 ± 56.6	81.0 ± 53.3	80.5 ± 40.2	81.5 ± 58.3	0.0308
BMI, kg/m^2	24.9 ± 2.9	24.9 ± 3.1	24.9 ± 2.8	24.8 ± 3.0	24.9 ± 2.7	0.0435	24.9 ± 3.0	24.9 ± 2.9	24.9 ± 3.1	24.9 ± 2.8	0.0203
Waist circum	86.3 ± 7.8	86.4 ± 8.2	86.3 ± 7.8	86.2 ± 8.0	86.3 ± 7.4	0.0241	86.3 ± 8.1	86.3 ± 7.8	86.4 ± 8.0	86.3 ± 7.6	0.0154
Blood pressure											
Systolic blood pressure, mmHg	128 ± 16	129 ± 17	128 ± 16	129 ± 16	127 ± 15	0.1384	128 ± 16	128 ± 16	128 ± 16	128 ± 16	0.0175
Diastolic blood pressure, mmHg	76 ± 10	76 ± 10	76 ± 10	76 ± 10	76 ± 10	0.0403	76 ± 10	76 ± 10	76 ± 10	76 ± 10	0.0211

Figures are numbers of patients (percentage) for categorical variables or mean ± SD for continuous variables, unless stated otherwise.
BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; GFR, glomerular filtration rate; HTN, hypertension; IQR, interquartile range; NOAC, non-vitamin K antagonist oral anticoagulant; OHA, oral hypoglycaemic agents; PAD, peripheral arterial disease
[a]Low income denotes income that belongs to lower 20% among the entire Korean population and supported by the Medical Aid program.

Table 2 Hazard ratios and 95% CIs of MACE, all-cause death, cardiovascular death, revascularization, and MI according to aerobic exercise status

	n	Events (*n*)	Follow-up Duration (person-years)	Incidence rate (per 1000 person-years)	IPW-adjusted HR (95% CI)
MACE[a]					
Persistent non-exercisers	2616.4	962.3	12 703.2	75.8	1 (ref.)
New exercisers	1476.4	492.2	7274.8	67.7	0.89 (0.80–1.00)
Exercise discontinuers	1530.0	506.5	7609.5	66.7	0.89 (0.79–0.98)
Exercise maintainers	2612.1	775.1	13 146.1	59.0	0.78 (0.71–0.86)
All-cause death					
Persistent non-exercisers	2616.4	271.0	15 083.7	18.0	1 (ref.)
New exercisers	1476.4	128.2	8497.2	15.1	0.84 (0.68–1.04)
Exercise discontinuers	1530.0	143.0	8849.3	16.2	0.90 (0.73–1.10)
Exercise maintainers	2612.1	183.8	15 118.5	12.2	0.68 (0.56–0.82)
Cardiovascular death					
Persistent non-exercisers	2616.4	69.1	15 083.7	4.6	1 (ref.)
New exercisers	1476.4	33.7	8497.2	4.0	0.87 (0.58–1.31)
Exercise discontinuers	1530.0	37.0	8849.3	4.2	0.91 (0.61–1.36)
Exercise maintainers	2612.1	46.3	15 118.5	3.1	0.67 (0.46–0.97)
Myocardial infarction					
Persistent non-exercisers	2616.4	168.8	14 643.1	11.5	1 (ref.)
New exercisers	1476.4	82.0	8302.4	9.9	0.86 (0.66–1.12)
Exercise discontinuers	1530.0	87.9	8675.8	10.1	0.88 (0.68–1.14)
Exercise maintainers	2612.1	120.4	14 819.5	8.1	0.71 (0.56–0.89)
Revascularization					
Persistent non-exercisers	2616.4	471.5	13 429.2	35.1	1 (ref.)
New exercisers	1476.4	259.9	7593.1	34.2	0.98 (0.84–1.13)
Exercise discontinuers	1530.0	256.6	7949.8	32.3	0.92 (0.79–1.07)
Exercise maintainers	2612.1	388.2	13 678.6	28.4	0.81 (0.71–0.93)
Heart failure					
Persistent non-exercisers	2616.4	413.6	14 296.0	28.9	1 (ref.)
New exercisers	1476.4	221.6	8111.7	27.3	0.95 (0.81–1.12)
Exercise discontinuers	1530.0	226.0	8429.6	26.8	0.93 (0.79–1.09)
Exercise maintainers	2612.1	334.6	14 547.6	23.0	0.79 (0.69–0.92)

CI, confidence interval; HR, hazard ratio; IPW, inverse probability-weighted; MACE, Major adverse cardiovascular events.
[a]Defined as a composite of all-cause death, MI, revascularization, and heart failure.

of no more than 72 h between successive aerobic exercise sessions was recommended.[22] However, a recent study revealed that the total volume of exercise, rather than an even distribution of exercise throughout the week, is more relevant for reducing the risk of future disease.[23] Furthermore, improvements in hepatic lipid content and insulin sensitivity persisted even after 4 weeks following the completion of a 12-week high-intensity interval training program.[24] This may be attributed to a sustained increase in antioxidant proteins and small extracellular vesicles.[24]

Interestingly, our study found that exercise discontinuers (those who stopped exercising after PCI) still had a lower risk of MACE than persistent non-exercisers. Aerobic exercise may have long-lasting effects that persist for some time, even after the discontinuation of exercise. Data from the 10-year follow-up of the Studies Targeting Risk Reduction Interventions through Defined Exercise (STRIDE) trial, in which overweight or obese men and women with mild-to-moderate dyslipidemia were randomized into the control or exercise group for 8 months, revealed that the benefits of exercise to waist circumference and fasting insulin levels persisted 10 years later. This suggests the long-lasting effects of 8 months of exercise training.[25] The exact mechanism behind these long-lasting effects is unclear, but they may result from an improved baseline health status that persists over time. Additionally, individuals who have engaged in exercise may become more health-conscious, maintaining healthier lifestyles even after discontinuing regular exercise.

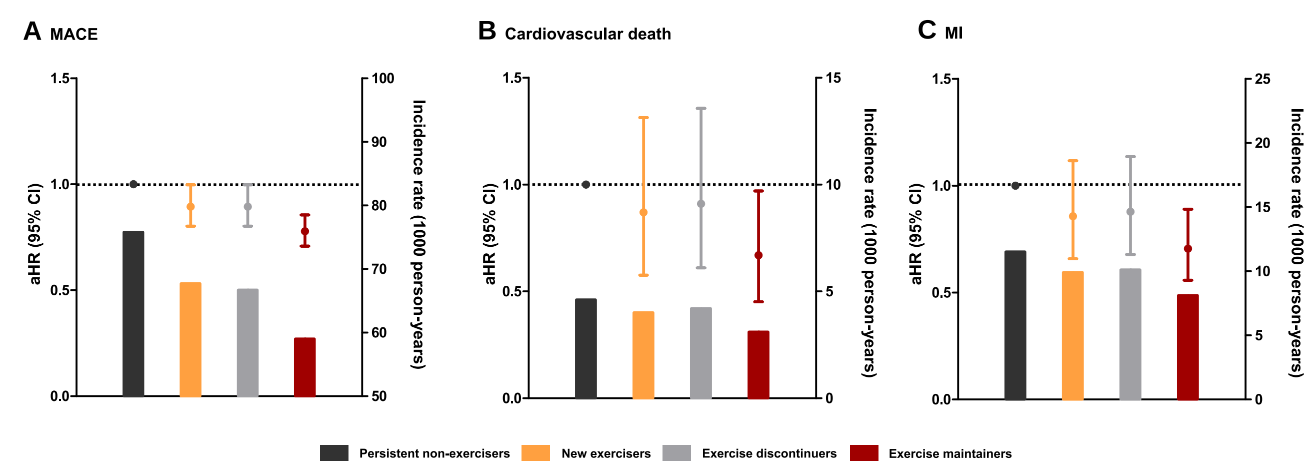


Figure 2 HRs and 95% CIs for adverse clinical outcomes according to the change in aerobic exercise habits. Bars represent weighted incidence rates, dots indicate adjusted HRs, and whiskers represent 95% CIs. aHR, adjusted hazard ratio; MACE, major adverse cardiovascular events; MI, myocardial infarction.

Table 3 Hazard ratios and 95% CIs for MACE, all-cause death, cardiovascular death, revascularization, and MI according to aerobic exercise amount (MET-min/week) after PCI

MET-min/week	*n*	Events	Follow-up Duration (person-years)	Incidence rate (per 1000 person-years)	Unadjusted HR (95% CI)	Multivariable-adjusted HR (95% CI)
MACE[a]						
0 MET-min/week	1977	765	9507.4	80.5	1 (ref.)	1 (ref.)
<500 MET-min/week	2006	686	9825.3	69.8	0.87 (0.78–0.96)	0.92 (0.83–1.02)
500–999 MET-min/week	2126	674	10 598.0	63.6	0.79 (0.71–0.88)	0.84 (0.76–0.93)
1000–1499 MET-min/week	1010	273	5209.6	52.4	0.65 (0.56–0.75)	0.71 (0.62–0.82)
≥1500 MET-min/week	1106	351	5506.2	63.7	0.79 (0.70–0.90)	0.85 (0.75–0.97)
All-cause death						
0 MET-min/week	1977	250	11 285.0	22.2	1 (ref.)	1 (ref.)
<500 MET-min/week	2006	173	11 570.2	15.0	0.68 (0.56–0.82)	0.78 (0.64–0.95)
500–999 MET-min/week	2126	164	12 282.4	13.4	0.60 (0.50–0.73)	0.70 (0.57–0.85)
1000–1499 MET-min/week	1010	66	5961.6	11.1	0.49 (0.38–0.65)	0.64 (0.49–0.85)
≥1500 MET-min/week	1106	83	6440.5	12.9	0.58 (0.45–0.74)	0.66 (0.51–0.85)
Cardiovascular death						
0 MET-min/week	1977	55	11 285.0	4.9	1 (ref.)	1 (ref.)
<500 MET-min/week	2006	51	11 570.2	4.4	0.90 (0.62–1.32)	1.05 (0.71–1.5)
500–999 MET-min/week	2126	39	12 282.4	3.2	0.65 (0.43–0.98)	0.78 (0.51–1.18)
1000–1499 MET-min/week	1010	16	5961.6	2.7	0.54 (0.31–0.95)	0.72 (0.40–1.27)
≥1500 MET-min/week	1106	23	6440.5	3.6	0.73 (0.45–1.18)	0.90 (0.54–1.48)
Myocardial infarction						
0 MET-min/week	1977	146	10 969.2	13.3	1 (ref.)	1 (ref.)
<500 MET-min/week	2006	112	11 287.2	9.9	0.75 (0.58–0.95)	0.79 (0.62–1.02)
500–999 MET-min/week	2126	107	12 022.7	8.9	0.67 (0.52–0.86)	0.75 (0.58–0.96)
1000–1499 MET-min/week	1010	37	5871.6	6.3	0.47 (0.33–0.67)	0.53 (0.37–0.77)
≥1500 MET-min/week	1106	56	6291.9	8.9	0.67 (0.49–0.91)	0.76 (0.55–1.04)
Revascularization						
0 MET-min/week	1977	351	10 034.2	35.0	1 (ref.)	1 (ref.)
<500 MET-min/week	2006	356	10 320.3	34.5	0.99 (0.85–1.14)	0.99 (0.85–1.15)

Continued

Table 3 *Continued*

MET-min/week	*n*	Events	Follow-up Duration (person-years)	Incidence rate (per 1000 person-years)	Unadjusted HR (95% CI)	Multivariable-adjusted HR (95% CI)
500–999 MET-min/week	2126	354	11 066.6	32.0	0.92 (0.79–1.06)	0.94 (0.81–1.09)
1000–1499 MET-min/week	1010	147	5370.7	27.4	0.79 (0.65–0.96)	0.79 (0.65–0.96)
≥1500 MET-min/week	1106	187	5753.8	32.5	0.93 (0.78–1.11)	0.95 (0.79–1.14)
Heart failure						
0 MET-min/week	1977	344	10 669.2	32.2	1 (ref.)	1 (ref.)
<500 MET-min/week	2006	306	10 990.7	27.8	0.87 (0.74–1.01)	0.97 (0.83–1.14)
500–999 MET-min/week	2126	284	11 774.6	24.1	0.75 (0.64–0.87)	0.85 (0.72–1.00)
1000–1499 MET-min/week	1010	101	5771.1	17.5	0.53 (0.43–0.66)	0.65 (0.52–0.81)
≥1500 MET-min/week	1106	152	6164.5	24.7	0.76 (0.63–0.92)	0.89 (0.73–1.08)

CI, confidence interval; HR, hazard ratio; MACE, Major adverse cardiovascular events; MET, metabolic equivalents of task.
[a]Defined as a composite of all-cause death, MI, revascularization, and heart failure.

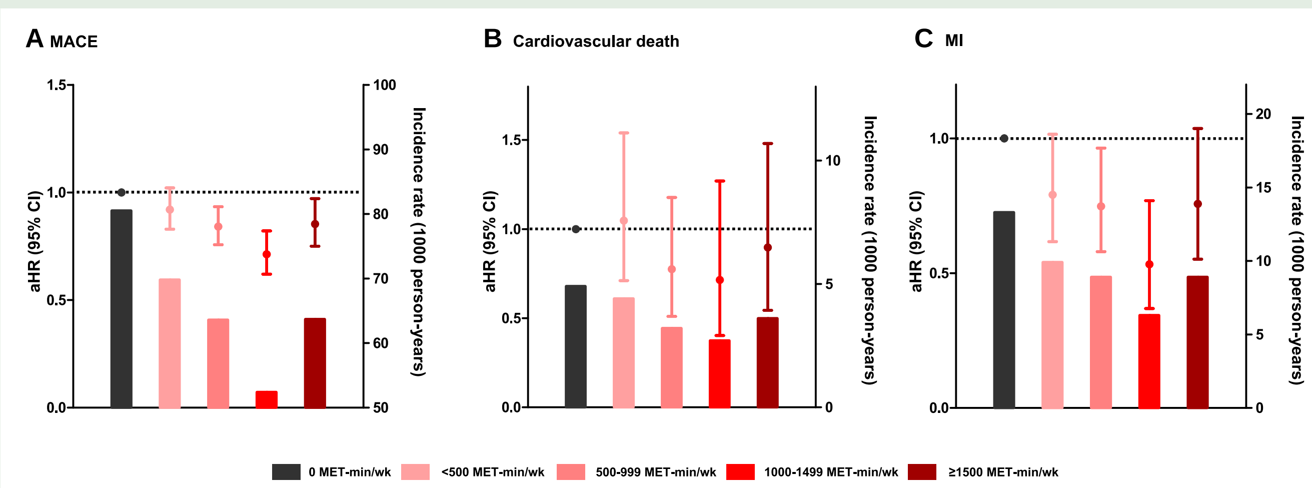


Figure 3 HRs and 95% CIs for adverse clinical outcomes according to aerobic exercise amount (MET-min/week). Bars represent weighted incidence rates, dots indicate adjusted HRs, and whiskers represent 95% CIs. aHR, adjusted hazard ratio; MACE, major adverse cardiovascular events; MET, metabolic equivalents of task; MI, myocardial infarction.

J-curve relationship between aerobic exercise amount and cardiovascular outcomes

The impact of high amounts of aerobic exercise on clinical outcomes is complex and not yet fully understood. Long-term excessive endurance exercise may lead to pathological structural remodelling of the heart and arteries, including myocardial fibrosis,[26] diastolic dysfunction,[27] and coronary artery calcification,[27] as well as an elevated risk of atrial fibrillation.[28] A prospective observational study on jogging found that light and moderate joggers had lower mortality rates than non-joggers, whereas the mortality rate of strenuous joggers was not statistically different from that of sedentary individuals.[29] A cohort study of patients with stable coronary heart disease identified a curvilinear relationship between exercise amount and mortality.[30] While increasing exercise was associated with a lower risk of mortality, particularly among those who were initially sedentary, the incremental benefits diminished at higher levels of habitual physical activity.[30] Individuals who were already engaging in regular moderate or vigorous exercise experienced less pronounced mortality benefits from further increasing their activity levels.[30] Additionally, a recent study identified a non-linear relationship between exercise intensity and cardiovascular outcomes in patients with diabetes, with an increased risk of adverse outcomes among individuals with a high polygenic risk score for type 2 diabetes.[31]

To the best of our knowledge, this is the first study to explore the relationship between aerobic exercise dose and clinical outcomes in patients with diabetes undergoing PCI. We observed that the greatest benefits of aerobic exercise were seen in patients who engaged in 1000–1499 MET-min/week of activity, with diminished benefits at ≥1500 MET-min/week. Given that heavy physical exertion may trigger MI and sudden cardiac death,[32] and considering the elevated risk for complex coronary artery disease and high ischaemic burden in patients with diabetes, we speculate that excessive aerobic exercise may raise

Subgroup	No. of patients	Events	IPW-adjusted HR (95% CI)	P for interaction
Age				
<65 years				
Persistent non-exercisers	1297.0	413.4	1 (reference)	
New exercisers	697.3	194.1	0.855 (0.720 - 1.014)	
Exercise discontinuers	736.7	223.4	0.947 (0.804 - 1.115)	
Exercise maintainers	1240.6	320.5	0.789 (0.682 - 0.913)	
65-74 years				
Persistent non-exercisers	1019.1	403.1	1 (reference)	
New exercisers	628.7	229.7	0.935 (0.795 - 1.100)	0.80
Exercise discontinuers	631.8	219.7	0.848 (0.719 - 0.999)	
Exercise maintainers	1084.8	339.4	0.752 (0.651 - 0.870)	
≥75 years				
Persistent non-exercisers	300.3	145.8	1 (reference)	
New exercisers	150.5	68.4	0.892 (0.668 - 1.190)	
Exercise discontinuers	161.5	63.5	0.817 (0.608 - 1.099)	
Exercise maintainers	286.8	115.3	0.811 (0.634 - 1.037)	
Sex				
Male				
Persistent non-exercisers	1823.1	678.6	1 (reference)	
New exercisers	1027.3	349.0	0.895 (0.786 - 1.019)	
Exercise discontinuers	1064.9	347.4	0.858 (0.754 - 0.976)	
Exercise maintainers	1808.8	557.8	0.799 (0.714 - 0.894)	
Female				0.43
Persistent non-exercisers	793.3	283.7	1 (reference)	
New exercisers	449.1	143.2	0.895 (0.732 - 1.095)	
Exercise discontinuers	465.1	159.2	0.943 (0.776 - 1.145)	
Exercise maintainers	803.3	217.3	0.717 (0.600 - 0.856)	
DM duration				
<5 years				
Persistent non-exercisers	877.9	286.4	1 (reference)	
New exercisers	509.8	139.6	0.826 (0.675 - 1.012)	
Exercise discontinuers	503.9	138.2	0.803 (0.655 - 0.985)	
Exercise maintainers	902.7	233.4	0.758 (0.637 - 0.901)	
≥5 years				0.65
Persistent non-exercisers	1738.5	675.9	1 (reference)	
New exercisers	966.6	352.7	0.925 (0.813 - 1.052)	
Exercise discontinuers	1026.1	368.4	0.917 (0.807 - 1.041)	
Exercise maintainers	1709.4	541.7	0.781 (0.697 - 0.875)	
Insulin use				
No				
Persistent non-exercisers	2357.0	838.3	1 (reference)	
New exercisers	1332.1	428.9	0.889 (0.791 - 0.998)	
Exercise discontinuers	1379.8	437.1	0.865 (0.771 - 0.971)	
Exercise maintainers	2353.5	660.7	0.753 (0.680 - 0.834)	
Yes				0.50
Persistent non-exercisers	259.4	124.0	1 (reference)	
New exercisers	144.3	63.3	0.937 (0.691 - 1.269)	
Exercise discontinuers	150.2	69.5	1.006 (0.749 - 1.351)	
Exercise maintainers	258.6	114.4	0.923 (0.715 - 1.192)	
Number of DM medication				
<2				
Persistent non-exercisers	1015.8	390.6	1 (reference)	
New exercisers	570.1	194.7	0.847 (0.713 - 1.007)	
Exercise discontinuers	589.4	198.1	0.838 (0.706 - 0.995)	
Exercise maintainers	1014.6	314.7	0.774 (0.667 - 0.899)	
≥2				0.75
Persistent non-exercisers	1600.6	571.7	1 (reference)	
New exercisers	906.3	297.5	0.929 (0.807 - 1.069)	
Exercise discontinuers	940.6	308.5	0.914 (0.795 - 1.050)	
Exercise maintainers	1597.5	460.4	0.774 (0.685 - 0.876)	

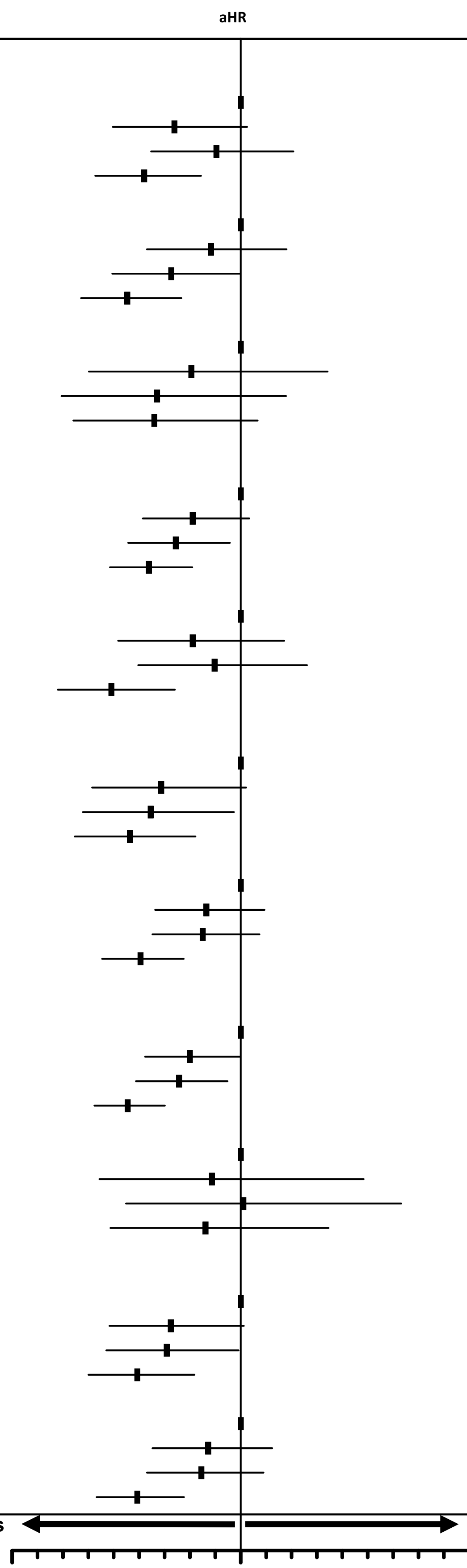


Figure 4 Subgroup analysis of MACEs. DM, diabetes mellitus; HR, hazard ratio; IPW, inverse probability weighting.

the risk-benefit ratio. The potentially increased risk of exercise-induced hypoglycaemia in patients with diabetes who take glucose-lowering therapies, such as insulin and sulfonylureas, should also be considered.[9] The current guidelines recommend ≥150 min/week of moderate-to-vigorous aerobic exercise,[7,19,20] which is equivalent to 600–1050 MET-min/week. Our study indicates that an exercise amount approximately 1.5–2.5-fold greater than this threshold may reduce the benefits of aerobic exercise in patients with diabetes undergoing PCI. Hence, while aerobic exercise should be encouraged in this patient group, recommending a suitable dosage may be important to ensure ideal outcomes. This finding, as well as the optimal range of aerobic exercise quantity in patients with diabetes undergoing PCI, requires verification through future research.

Study limitations

Our study has several limitations that should be considered when interpreting the results. First, exercise, especially resistance training, effectively lowers blood sugar levels and insulin resistance.[33] However, due to limited questionnaire data, only aerobic exercise was included in this study, potentially overlooking the impact of resistance training on patient outcomes. Second, despite our efforts to perform multivariable analysis and IPW adjustments, unmeasured confounders might have influenced our results, given the nature of non-randomized data. Third, we could not determine why patients in the exercise discontinuers group stopped aerobic exercise after PCI. While some may have discontinued due to PCI-related complications, the proportion of exercise discontinuers (1529 of 8225, or 19%) suggests that such cases represent only a subset. Moreover, their better clinical outcomes compared with persistent non-exercisers indicate that most were unlikely to have experienced severe complications, which would likely have negatively impacted outcomes. Fourth, the self-reported questionnaire used to assess aerobic exercise intensity covered only the past week, which may not fully capture patients' usual exercise levels. However, this method is based on the seven-day Physical Activity Recall (PAR),[34] a widely used tool in epidemiological studies. The seven-day PAR has demonstrated good correlation with seven-day diaries[35] and directly measured energy expenditure,[36] and its validity has been supported by comparisons with heart rate monitoring records.[37] Fifth, the Korean NHIS database used in this study does not include variables specific to cardiac rehabilitation, limiting our ability to analyze its potential impact on outcomes. However, in South Korea, the systematic implementation of cardiac rehabilitation programs is not widespread due to limited insurance coverage. As a result, the proportion of patients who received cardiac rehabilitation after PCI is likely to be small. Additionally, our study followed patients for a mean duration of 4.9 years after their second health check-up. This extended follow-up period likely exceeds the typical duration of most cardiac rehabilitation programs, suggesting that the observed results may reflect long-term lifestyle changes rather than relatively short-term effects of rehabilitation. Finally, this study utilized an existing large-scale database that was not specifically collected for the analysis presented in this manuscript. As a result, the study design is exploratory in nature and was not statistically powered to detect the observed associations, raising the possibility that some significant results may have occurred by chance. Further prospective studies are warranted to validate these findings in a more controlled setting.

Conclusion

Based on a large nationwide population database, our study showed that maintaining aerobic exercise after PCI in patients with diabetes was associated with a lower risk of adverse cardiovascular events. In addition, we observed a J-curve relationship between the amount of aerobic exercise and clinical outcomes. Aerobic exercise should be encouraged to achieve better outcomes in patients with diabetes who undergo PCI, although the optimal exercise dosage warrants further investigation.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

Author contribution

J.-K.H. contributed to the conception, and design of the work. K.H. contributed to the acquisition, and analysis of data for the work. J.-K.H. and Y.-J.K. contributed to the interpretation of data for the work. J.-K.H. drafted the manuscript. All authors critically reviewed the manuscript. All gave final approval and agreed to be accountable for all aspects of the work, ensuring both its integrity and accuracy.

Funding

This study was funded by Chong Kun Dang Inc. (Seoul National University Hospital funding number: 0620190200). The funding agency had no role in study design, analysis, interpretation of data, the writing of the manuscript or in the decision to submit the article for publication.

Conflict of interest: None declared.

Data availability

Data are available upon approval and oversight by the Korean National Health Insurance Service.

References

1. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. *Lancet* 2017;**389**:2239–2251.
2. Cheng YJ, Imperatore G, Geiss LS, Saydah SH, Albright AL, Ali MK, *et al.* Trends and disparities in cardiovascular mortality among U.S. adults with and without self-reported diabetes, 1988-2015. *Diabetes Care* 2018;**41**:2306–2315.
3. Ingelfinger JR, Jarcho JA. Increase in the incidence of diabetes and its implications. *N Engl J Med* 2017;**376**:1473–1474.
4. Chichareon P, Modolo R, Kogame N, Takahashi K, Chang CC, Tomaniak M, *et al.* Association of diabetes with outcomes in patients undergoing contemporary percutaneous coronary intervention: pre-specified subgroup analysis from the randomized GLOBAL LEADERS study. *Atherosclerosis* 2020;**295**:45–53.
5. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, *et al.* 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *J Am Coll Cardiol* 2019;**74**:e177–e232.
6. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, *et al.* 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J* 2021;**42**: 3227–3337.
7. American Diabetes Association Professional Practice Committee. 5. Facilitating behavior change and well-being to improve health outcomes: standards of medical care in diabetes-2022. *Diabetes Care* 2022;**45**:S60–S82.
8. Piercy KL, Troiano RP. Physical activity guidelines for Americans from the US department of health and human services. *Circ Cardiovasc Qual Outcomes* 2018;**11**:e005263.
9. Aune D, Norat T, Leitzmann M, Tonstad S, Vatten LJ. Physical activity and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis. *Eur J Epidemiol* 2015; **30**:529–542.

10. Herrmann SD, Willis EA, Ainsworth BE, Barreira TV, Hastert M, Kracht CL, *et al.* 2024 adult compendium of physical activities: a third update of the energy costs of human activities. *J Sport Health Sci* 2024;**13**:6–12.
11. Ahn HJ, Lee SR, Choi EK, Han KD, Jung JH, Lim JH, *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.
12. Vanhees L, Geladas N, Hansen D, Kouidi E, Niebauer J, Reiner Z, *et al.* Importance of characteristics and modalities of physical activity and exercise in the management of cardiovascular health in individuals with cardiovascular risk factors: recommendations from the EACPR. Part II. *Eur J Prev Cardiol* 2012;**19**:1005–1033.
13. Richter EA, Hargreaves M. Exercise, GLUT4, and skeletal muscle glucose uptake. *Physiol Rev* 2013;**93**:993–1017.
14. Maiorana A, O'Driscoll G, Cheetham C, Dembo L, Stanton K, Goodman C, *et al.* The effect of combined aerobic and resistance exercise training on vascular function in type 2 diabetes. *J Am Coll Cardiol* 2001;**38**:860–866.
15. Sluik D, Buijsse B, Muckelbauer R, Kaaks R, Teucher B, Johnsen NF, *et al.* Physical activity and mortality in individuals with diabetes mellitus: a prospective study and meta-analysis. *Arch Intern Med* 2012;**172**:1285–1295.
16. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, *et al.* Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;**346**:393–403.
17. Umpierre D, Ribeiro PA, Kramer CK, Leitão CB, Zucatti AT, Azevedo MJ, *et al.* Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. *JAMA* 2011;**305**:1790–1799.
18. Church TS, Blair SN, Cocreham S, Johannsen N, Johnson W, Kramer K, *et al.* Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial. *JAMA* 2010;**304**:2253–2262.
19. Kanaley JA, Colberg SR, Corcoran MH, Malin SK, Rodriguez NR, Crespo CJ, *et al.* Exercise/physical activity in individuals with type 2 diabetes: a consensus statement from the American College of Sports Medicine. *Med Sci Sports Exerc* 2022;**54**:353–368.
20. Grant PJ, Cosentino F. The 2019 ESC guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: new features and the 'ten commandments' of the 2019 guidelines are discussed by professor Peter J. Grant and professor Francesco Cosentino, the task force chairmen. *Eur Heart J* 2019;**40**:3215–3217.
21. Writing Committee Members; Virani SS, Newby LK, Arnold SV, Bittner V, Brewer LC, *et al.* 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology joint committee on clinical practice guidelines. *J Am Coll Cardiol* 2023;**82**:833–955.
22. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C. Physical activity/exercise and type 2 diabetes. *Diabetes Care* 2004;**27**:2518–2539.
23. Kany S, Al-Alusi MA, Rämö JT, Pirruccello JP, Churchill TW, Lubitz SA, *et al.* Associations of "weekend warrior" physical activity with incident disease and cardiometabolic health. *Circulation* 2024;**150**:1236–1247.
24. Mastrototaro L, Apostolopoulou M, Hartwig S, Strassburger K, Lipaeva P, Trinks N, *et al.* The role of exosomes for sustained specific cardiorespiratory and metabolic improvements in males with type 2 diabetes after detraining. *EBioMedicine* 2024;**110**:105471.
25. Johnson JL, Slentz CA, Ross LM, Huffman KM, Kraus WE. Ten-year legacy effects of three eight-month exercise training programs on cardiometabolic health parameters. *Front Physiol* 2019;**10**:452.
26. Ector J, Ganame J, van der Merwe N, Adriaenssens B, Pison L, Willems R, *et al.* Reduced right ventricular ejection fraction in endurance athletes presenting with ventricular arrhythmias: a quantitative angiographic assessment. *Eur Heart J* 2007;**28**:345–353.
27. O'Keefe JH, Patil HR, Lavie CJ, Magalski A, Vogel RA, McCullough PA. Potential adverse cardiovascular effects from excessive endurance exercise. *Mayo Clin Proc* 2012;**87**:587–595.
28. Pallikadavath S, Richards C, Bountziouka V, Sandilands AJ, Graham-Brown MPM, Robinson T, *et al.* The AFLETES study: atrial fibrillation in veteran athletes and the risk of stroke. *Clin J Sport Med* 2023;**33**:209–216.
29. Schnohr P, O'Keefe JH, Marott JL, Lange P, Jensen GB. Dose of jogging and long-term mortality: the Copenhagen city heart study. *J Am Coll Cardiol* 2015;**65**:411–419.
30. Stewart RAH, Held C, Hadziosmanovic N, Armstrong PW, Cannon CP, Granger CB, *et al.* Physical activity and mortality in patients with stable coronary heart disease. *J Am Coll Cardiol* 2017;**70**:1689–1700.
31. Lee CL, Yamada T, Liu WJ, Hara K, Yanagimoto S, Hiraike Y. Interaction between type 2 diabetes polygenic risk and physical activity on cardiovascular outcomes. *Eur J Prev Cardiol* 2024;**31**:1277–1285.
32. Eijsvogels TMH, Maessen MFH. Exercise for coronary heart disease patients: little is good, more is better, vigorous is best. *J Am Coll Cardiol* 2017;**70**:1701–1703.
33. Cuff DJ, Meneilly GS, Martin A, Ignaszewski A, Tildesley HD, Frohlich JJ. Effective exercise modality to reduce insulin resistance in women with type 2 diabetes. *Diabetes Care* 2003;**26**:2977–2982.
34. Blair SN, Haskell WL, Ho P, Paffenbarger RS Jr, Vranizan KM, Farquhar JW, *et al.* Assessment of habitual physical activity by a seven-day recall in a community survey and controlled experiments. *Am J Epidemiol* 1985;**122**:794–804.
35. Dishman RK, Steinhardt M. Reliability and concurrent validity for a 7-d re-call of physical activity in college students. *Med Sci Sports Exerc* 1988;**20**:14–25.
36. Taylor CB, Coffey T, Berra K, Iaffaldano R, Casey K, Haskell WL. Seven-day activity and self-report compared to a direct measure of physical activity. *Am J Epidemiol* 1984;**120**:818–824.
37. Sallis JF, Buono MJ, Roby JJ, Micale FG, Nelson JA. Seven-day recall and other physical activity self-reports in children and adolescents. *Med Sci Sports Exerc* 1993;**25**:99–108.