# Association of physical activity with all-cause and cardiovascular mortality in 7666 adults with hypertrophic cardiomyopathy (HCM): more physical activity is better

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## ABSTRACT

**Objectives** Recommendations on physical activity (PA) for adults with hypertrophic cardiomyopathy (HCM) are not well established. We investigated the association of PA intensity with mortality in the general adult HCM population.

**Methods** A nationwide population-based cohort of individuals with HCM who underwent health check-ups including questionnaires on PA levels were identified from the years 2009 to 2016 in the National Health Insurance Service database. Subjects who reported no PA at baseline were excluded. To estimate each individual's PA level, the PA score (PAS) was calculated based on the self-reported questionnaires, and the study population was categorised into three groups according to tertiles of PAS. The associations of PAS with all-cause and cardiovascular mortality were analysed.

**Results** A total of 7666 participants (mean age 59.5 years, 29.9% were women) were followed up for a mean 5.3±2.0 years. All-cause and cardiovascular mortality progressively decreased from the lowest to the highest tertiles of PA intensity: 9.1% (4.7%), 8.9% (3.8%) and 6.4% (2.7%), respectively (*p-for-trend*=0.0144 and 0.0023, respectively). Of note, compared with the middle PA group, the highest PA group did not have an increased risk of all-cause and cardiovascular mortality (HR 0.78, (95% CI 0.63 to 0.95) and HR 0.75 (95% CI 0.54 to 1.03), respectively). All subgroup and sensitivity analyses consistently showed that all-cause and cardiovascular mortality did not increase with higher PA levels.

**Conclusions** Moderate-to-vigorous-intensity PA, in a middle-aged population of patients with HCM, was associated with progressive reduction of all-cause and cardiovascular mortality. The impact of vigorous-intensity PA on a younger age group requires further investigation.

## INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is the most common inheritable cardiomyopathy. It is characterised by left ventricular hypertrophy without any secondary causes and has a prevalence of approximately 1:500.[1] The clinical presentation of HCM is variable. Many individuals experience a normal life span and others experience serious complications which can include sudden cardiac death (SCD).[2 3] HCM is the leading cause of SCD in young athletes.[3 4] International consensus recommendations disqualify athletes with HCM from engaging in competitive physical activities (PAs)[5–8] because of safety concerns over triggering lethal ventricular arrhythmias.

PA recommendations for young athletes are currently extrapolated to the general HCM population.[9 10] However, documented exercise-induced ventricular arrhythmias are rare, and there is a lack of concrete association between such arrhythmias and SCD events or appropriate implantable cardioverter-defibrillator (ICD) discharges in HCM, even in individuals who participate in competitive sports.[7 11–13] Therefore, there is an ongoing controversy regarding whether it is safe for the general population with HCM to participate in more-than-light-intensity PA.

Individuals with HCM intentionally reduce their PA at work and leisure time after being diagnosed with HCM.[14] Although it is currently considered appropriate to restrict PA to some extent,[6 15] individuals with HCM are not immune from cardiovascular diseases that are strongly associated with low levels of PA and physical inactivity.[16–18] How much PA is safe and salutatory for adults with HCM? In this context, it is timely to highlight the potential association of PA restrictions on the prognosis of the general HCM adult population and explore the current ambiguity regarding the advice on optimal PA levels in these patients. We used a large-scale, nationwide database provided by the National Health Insurance Service (NHIS) in Korea to investigate the association of PA intensity with all-cause and cardiovascular mortality in the general HCM adult population.

## METHODS

### Source of the database and HCM diagnosis

This study used data from the NHIS database, which is a mandatory universal health insurance service covering up to 97% of the entire Korean population. The NHIS database is based on claims for medical service expenses and includes each patient's demographics, diagnoses, healthcare utilisation, prescription data and mandatory health

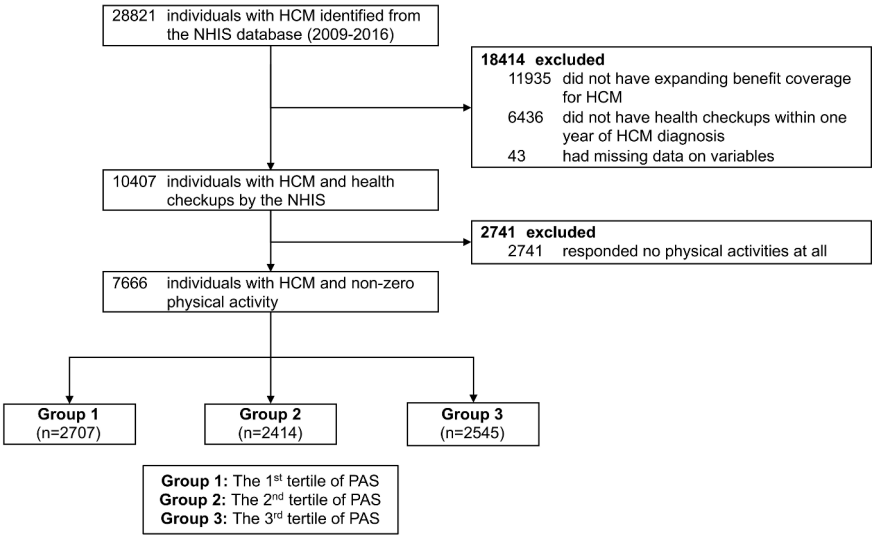


**Figure 1** Flowchart for selection of the study population. HCM, hypertrophic cardiomyopathy; NHIS, National Health Insurance Service; PAS, physical activity score.

check-up results.[19] Details of the health examinations and data are available in the online supplemental methods.

HCM was defined by (1) claims for diagnostic codes (*International Classification of Disease, Tenth Revision, Clinical Modification; ICD-10-CM*) of I42.1 or I42.2 with at least one admission or outpatient visit and (2) registration in the rare intractable diseases (RID) programme providing insurance benefits, which is tightly controlled with imaging evidence and review by medical experts and health insurance professionals. Definitions of other comorbidities are detailed in online supplemental table 1.

## Study population

Among the 28 821 individuals with the diagnostic code of I42.1 or I42.2 between 2009 and 2016, we excluded those who were not registered as HCM in the RID programme (n=11 935). We excluded individuals who did not undergo health check-ups within 1 year after the diagnosis of HCM (n=6436) or those with missing data on the study variables (n=43). We further excluded individuals who reported no PA at all in the health examination questionnaires (n=2741), due to the concern that such individuals may have severe comorbidities preventing them from performing PA. A total of 7666 HCM individuals who underwent health examinations within 1 year of HCM diagnosis were finally included (figure 1).

This study conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the institutional review board of our institution (E-1805-051-944). Informed consent from participants was waived because the data used were anonymised. This research was done without direct patient involvement.

## Assessment of PA levels

The grade of PA was estimated based on three questions regarding PA in the survey on health behaviours provided by the NHIS, and the English-translated version is presented in online supplemental table 2.

Conceptually, each question regards the frequency of light, moderate and vigorous PA. Each individual responded on how many days during the past week they performed each grade of PA. This survey form, that is, last 7-day recall, has been reported to be reliable for use in the evaluation of individual PA levels in national monitoring.[20] To estimate the overall grade and the amount of PA in a quantitative manner, we devised the following metrics: PA score (PAS) and minimum energy expenditure (MEE). The purpose of PAS was to approximate one's average workload of daily PA based on the concept of metabolic equivalent of tasks (METs). The METs are widely used in medical research to quantitatively measure PA intensities.[21] Moreover, it has been well recognised to have a close relationship with mortality among patients with cardiovascular diseases.[12 22 23] For each question, we gave appropriate METs (8, 5 and 3 METs to questions 1, 2 and 3, respectively) according to *The 2011 Updates on Compendium of Physical Activity* (Compendium).[21] The Compendium has been accepted as a reference standard to estimate the energy expenditure of any given PA in the field of survey research.[21 24] PAS was calculated as $(8a + 5b + 3c)/7$ in METs per day, where *a*, *b* and *c* were answers to the survey questions Q1, Q2 and Q3, respectively. Meanwhile, MEE was intended to represent the minimum weekly energy expenditure relevant to the given PA. The concept of energy expenditure measured in MET-min per week has been globally accepted by health professionals as a standard quantification of an individual's PA.[25] Moreover, calculating this metric based on an appropriate survey of PA has been well validated.[20] Given that the minimal times consumed for PA for the survey questions Q1, Q2 and Q3 were 20, 30 and 30 min, respectively, we calculated MEE as $(8*20a + 5*30b + 3*30c)$ in MET-min per week, where *a*, *b* and *c* were defined as answers of the survey questions Q1, Q2 and Q3, respectively. Activities such as running, aerobics, climbing, biking at a fast pace and mountain climbing correspond to eight METs; activities such as brisk walking, tennis doubles and biking at a regular pace correspond to five METs; light activities such as usual walking during commute correspond to three METs. We not only used PAS as the main measure of PA throughout the study but also performed MEE-based analyses, which are presented in more detail in the online supplemental data.

## Study design and outcome measurement

We divided all HCM participants into three groups according to the tertiles of increasing PAS: group 1 for the tertile with the lowest level of PA; group 2, the middle tertile and group 3, the tertile with the highest level of PA. Likewise, we also categorised the study population into three groups based on MEE. Both PAS and MEE were adopted to investigate the association of PA

intensity with all-cause and cardiovascular mortality. The date of the baseline health check-up was the index date. The study population was followed from the index date to the date of mortality or until 31 December 2017, whichever came first. Mortality and the causes of death were ascertained from the governmental mortality database (Statistics Korea; KOSTAT). Cardiovascular mortality was defined when the *ICD-10-CM* code for the cause of death belonged to the categories I00–I99. We also performed exploratory analyses for SCD using the *ICD-10-CM* code of I46.

## Statistical analysis

Groups by PA were compared using one-way analysis of variance or $\chi^2$ test as appropriate. Kaplan-Meier curves for all-cause and cardiovascular mortality were compared among the groups using the log-rank test. Multivariable Cox proportional hazards regression analyses adjusting for age, sex, body mass index, systolic blood pressure, smoking status, alcohol consumption, low-income status and history of hypertension, diabetes mellitus, dyslipidaemia, atrial fibrillation and ischaemic heart disease were performed to estimate adjusted HR and the corresponding 95% CI for the association between PA levels and mortality. We performed statistical analysis with group 2 as the reference, because they had a daily average PA level of 3.4 METs that represents 'usual' PA levels of daily living. Group 1 represented very sedentary individuals with 'less-than-usual' daily PA and group 3, participants with 'more-than-usual' PA. p Values for linear trends of all-cause and cardiovascular mortality among the PA groups were calculated. Sensitivity analysis excluding participants with a history of ischaemic heart disease was performed to minimise bias caused by underlying ischaemic heart disease. All statistical analyses were performed using SAS V.9.4 (SAS Institute, Cary, North Carolina, USA), and two-sided $p<0.05$ was considered statistically significant.

# RESULTS

## Baseline characteristics

Baseline characteristics of the three groups according to PAS are presented in table 1. Based on the Physical Activity Guideline,[26] group 1 with a mean PAS of 1.4±0.6 represents HCM individuals with light PA levels and group 3 with a mean PAS of 8.4±3.1 METs/day represents those with highly active or vigorous PA levels. There were no significant differences in age across the three groups (p=0.1543), whereas group 3 had the

**Table 1** Baseline characteristics of the study population according to PAS

| Characteristic | Group 1 (n=2,707) | Group 2 (n=2414) | Group 3 (n=2545) | P value |
|---|---|---|---|---|
| Demographics | | | | |
| Age, mean (SD), y | 59.4 (12.6) | 59.9 (12.2) | 59.3 (11.4) | 0.1543 |
| Age, median (IQR), y | 59 (51–70) | 60 (52–70) | 60 (52–68) | 0.1543 |
| Male | 1,767/2,707 (65.3) | 1,711/2,414 (70.9) | 1,974/2,545 (77.6) | <0.0001 |
| PAS, mean (SD), METs/day | 1.4 (0.6) | 3.4 (0.7) | 8.4 (3.1) | <0.0001 |
| PAS, median (IQR), METs/day | 1.3 (0.9–2.1) | 3.1 (3.0–4.0) | 7.3 (6.1–10.0) | <0.0001 |
| BMI, mean (SD), kg/m$^2$ | 25.2 (3.3) | 25.2 (3.1) | 25.1 (2.9) | 0.8923 |
| Waist circumference, mean (SD), cm | 85.9 (8.9) | 86.0 (8.5) | 85.7 (8.4) | 0.6600 |
| SBP, mean (SD), mm Hg | 125.3 (16.1) | 126.3 (16.1) | 125.3 (15.1) | 0.0472 |
| DBP, mean (SD), mm Hg | 76.2 (10.4) | 76.8 (10.7) | 76.5 (10.5) | 0.1544 |
| Low income | 591/2,707 (21.8) | 487/2,414 (20.2) | 502 (19.7) | 0.1374 |
| Laboratory tests | | | | |
| Fasting glucose, mean (SD), mg/dL | 102.6 (23.9) | 102.9 (23.7) | 102.5 (22.6) | 0.8628 |
| Total cholesterol, mean (SD), mg/dL | 186.7 (38.7) | 183.2 (38.0) | 184.0 (37.5) | 0.0019 |
| Triglyceride, median (IQR), mg/dL | 124.6 (122.2–127.1) | 120.6 (118.2–123.1) | 118.2 (115.9–120.6) | 0.0009 |
| HDL, mean (SD), mg/dL | 51.7 (22.5) | 51.1 (20.3) | 51.7 (15.1) | 0.4653 |
| LDL, mean (SD), mg/dL | 108.3 (40.5) | 106.3 (39.3) | 106.9 (45.4) | 0.1976 |
| Smoking status | | | | |
| Non-smoker | 1,411/2,707 (52.2) | 1,151/2,414 (47.7) | 1,192/2,545 (46.9) | <0.0001 |
| Ex-smoker | 669/2,707 (24.8) | 739/2,414 (30.6) | 889/2,545 (35.0) | |
| Current smoker | 623/2,707 (23.1) | 522/2,414 (21.6) | 462/2,545 (18.2) | |
| Alcohol consumption | | | | |
| None | 1,554/2,707 (57.7) | 1,302/2,414 (54.1) | 1,301/2,545 (51.4) | 0.0002 |
| Mild | 983/2,707 (36.5) | 964/2,414 (40.1) | 1,053/2,545 (41.6) | |
| Heavy | 156/2,707 (5.8) | 140/2,414 (5.8) | 176/2,545 (7.0) | |
| Comorbidity | | | | |
| Hypertension | 1,792/2,707 (66.5) | 1,633/2,414 (67.8) | 1,711/2,545 (67.3) | 0.6211 |
| Diabetes mellitus | 472/2,707 (17.4) | 460/2,414 (19.1) | 471/2,545 (18.5) | 0.3099 |
| Dyslipidaemia | 1,259/2,707 (46.6) | 1,089/2,414 (45.2) | 1,177/2,545 (46.3) | 0.5696 |
| Metabolic syndrome | 1,654/2,707 (61.7) | 1,436/2,414 (59.9) | 1,509/2,545 (59.6) | 0.2422 |
| Atrial fibrillation | 434/2,707 (16.0) | 357/2,414 (14.8) | 390/2,545 (15.3) | 0.4644 |
| Ischaemic heart disease | 1,666/2,707 (61.5) | 1,514/2,414 (62.7) | 1,603/2,545 (63.0) | 0.5165 |
| Ischaemic heart disease requiring prior coronary revascularisation | 11/2,707 (0.4) | 9/2,414 (0.4) | 12/2,545 (0.5) | 0.8596 |
| Heart failure | 102/2,707 (3.8) | 74/2,414 (3.1) | 73/2,545 (2.9) | 0.1532 |

BMI, body mass index; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; METs, metabolic equivalents of task; PAS, physical activity score; S(D)BP, systolic (diastolic) blood pressure.

**Table 2** Multivariate Cox proportional hazard regression analysis on the incidence rates and risks of all-cause and cardiovascular mortality by the PAS-based physical activity grades

| | All-cause mortality | | | | Cardiovascular mortality | | | |
|---|---|---|---|---|---|---|---|---|
| | Event | Follow-up duration, PY | Incidence rate, /1000 PY | Adjusted HR (95% CI)* | Event | Follow-up duration, PY | Incidence rate, /1000 PY | Adjusted HR (95% CI)† |
| Group 1 (n=2,707) | 245/2,707 (9.1%) | 14396 | 17.0 | 1.01 (0.84 to 1.21) | 128/2,707 (4.7%) | 14396 | 8.9 | 1.19 (0.91 to 1.57) |
| Group 2 (n=2414) | 215/2,414 (8.9%) | 12652 | 17.0 | 1 (reference) | 92/2,414 (3.8%) | 12653 | 7.3 | 1 (reference) |
| Group 3 (n=2545) | 164/2,545 (6.4%) | 13685 | 12.0 | 0.78 (0.63 to 0.95) | 69/2,545 (2.7%) | 13685 | 5.0 | 0.75 (0.54 to 1.03) |

*p-for-trend=0.0144.
†p-for-trend=0.0023.
PAS, physical activity score; PY, person-year.

highest male proportion (77.6%; p<0.0001). Body mass index and waist circumference were similar among the three groups. Although systolic blood pressure was slightly higher in group 2, the absolute difference was negligible. Fasting blood glucose levels showed no significant differences among the three groups. Lipid profiles were also similar across the three groups except for total cholesterol and triglyceride levels, which were both the highest in group 1. There were no significant differences in comorbidities across the three groups. Similar results were obtained in the MEE-based analyses (online supplemental table 3).

## All-cause and cardiovascular mortality

Over a mean follow-up duration of 5.3±2.0 years, a total of 624 all-cause mortality events (8.1%; 15.3 per 1000 person-years) were identified. All-cause mortality event and its incidence rate progressively decreased from group 1 to group 3: 9.1%, 8.9% and 6.4% for all-cause mortality events and 17.0, 17.0 and 12.0 per 1000 person-years for incidence rates in groups 1, 2 and 3, respectively. In terms of cardiovascular mortality, a total of 289 events (3.8%; 7.1 per 1000 person-years) were identified, accounting for 46.3% of all-cause mortality. The cardiovascular mortality event and rate also decreased progressively from group 1 to group 3: 4.7%, 3.8% and 2.7% for cardiovascular mortality events and 8.9, 7.3 and 5.0 per 1000 person-years in groups 1, 2 and 3, respectively (table 2). The ratios of cardiovascular mortality to all-cause mortality showed a decreasing trend from group 1 to group 3: 128/245 (0.52:1), 92/215 (0.43:1) and 69/164 (0.42:1) for groups 1, 2 and 3, respectively.

Figure 2 presents the Kaplan-Meier survival curves for all-cause and cardiovascular mortality in the three PA groups, showing that cumulative incidences of all-cause and cardiovascular mortality were the lowest in group 3 (ie, the highest PA group). The survival curves of group 3 began to separate from the other two groups approximately 1 year after the index date and remained diverged throughout the follow-up period (log-rank p=0.0006 for both all-cause and cardiovascular mortality analyses). After adjusting for covariates, multivariate Cox proportional hazards regression analysis showed progressively decreased risks of all-cause mortality from group 1 to group 3 (p-for-trend=0.0144, table 2). With group 2 as a reference, group 1 had a comparable risk of all-cause mortality, whereas group 3 demonstrated a 22% lower risk of all-cause mortality (HR 1.01, 95% CI 0.84 to 1.21 for group 1; HR 0.78, 95% CI 0.63 to 0.95 for group 3). Multivariate Cox proportional hazards regression analysis also showed a significantly decreased risk of cardiovascular mortality from group 1 to group 3 (p-for-trend=0.0023), though neither group 1 nor group 3 showed significant differences in the risk of cardiovascular mortality from the reference group 2 (HR 1.19, 95% CI 0.91 to 1.57 for group 1; HR 0.75, 95% CI 0.54 to 1.03 for group 3), possibly due to the low cardiovascular events of each group. We did not observe any evidence showing increased risks of all-cause and cardiovascular mortality in group 3. Analysis using MEE instead of PAS showed no evidence of significantly higher risk of mortality in group 3 as well (online supplemental table 4, online supplemental figure 1). Also, on exploratory analysis, there was no evidence of increased risk of SCD with vigorous PA (online supplemental tables 5 and 6).

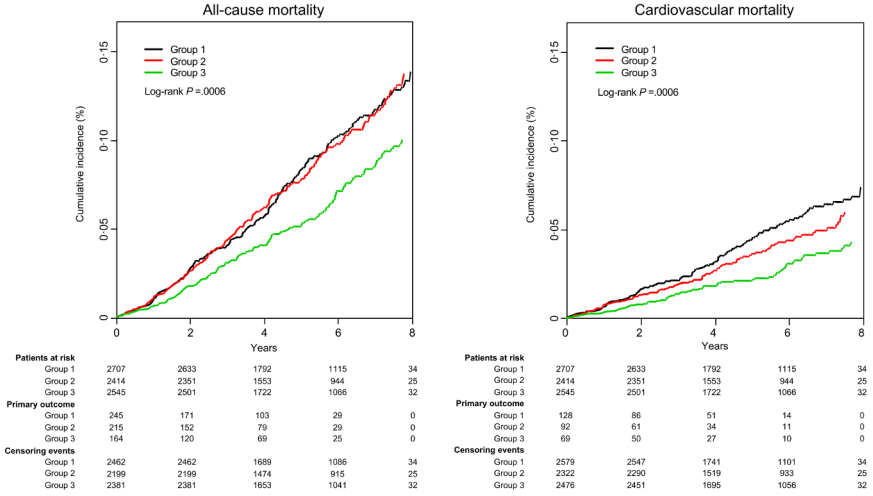


**Figure 2** Kaplan-Meier survival curves for all-cause and cardiovascular mortality by the PAS-based physical activity grade. PAS, physical activity score.

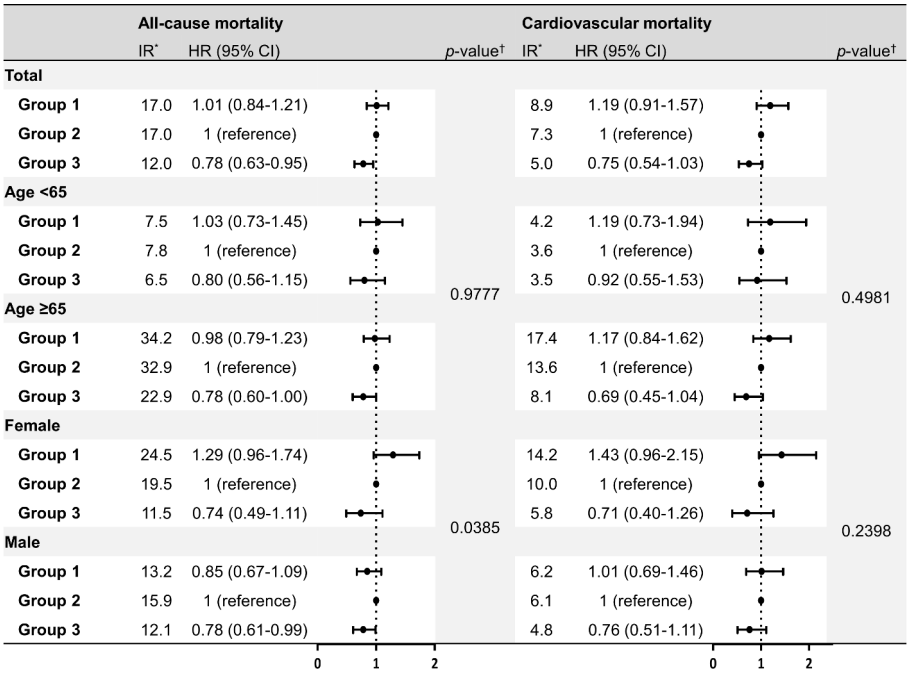


**Figure 3** Subgroup analyses by age strata and sex. *Incidence rate per 1000 person-years. †p-for-interaction.

## Subgroup and sensitivity analyses

In subgroup analyses by age strata and sex (figure 3 and online supplemental table 7), group 3 with the highest PA level showed a tendency of lower all-cause and cardiovascular mortality, without achieving statistical significance. The interaction term for age strata was insignificant. The interaction term for sex was significant for all-cause mortality (p-for-interaction=0.0385), with women showing greater benefit of increasing PA levels, but was insignificant for cardiovascular mortality. We did not note any increase in the risk of all-cause and cardiovascular mortality in HCM participants with vigorous PA in subgroup analyses.

To minimise bias that might be caused by the underlying ischaemic heart disease, we performed a sensitivity analysis after excluding individuals with a prior history of ischaemic heart disease (table 3, online supplemental table 8, online supplemental figures 2 and 3). After adjusting for covariates used in the main analysis with the exception of ischaemic heart disease, neither group 1 nor group 3 showed any statistical differences in the risk of all-cause and cardiovascular mortality from group 2. Again, all-cause and cardiovascular mortality was not significantly increased in HCM participants without ischaemic heart disease and with vigorous PA levels.

## DISCUSSION

We evaluated the effects of PA intensity on all-cause and cardiovascular mortality in a nationwide HCM adult cohort that approached 8,000 individuals. After stratifying PA levels with PAS and MEE, we found that leisure-time PA of more than light-intensity PA was not associated with any significant increase in all-cause and cardiovascular mortality in the general adult HCM population; rather, PA of moderate-to-vigorous-intensity was associated with a significant decrease in these outcomes. This trend held true in all prespecified subgroup analyses by age strata or sex as well as in the sensitivity analysis of participants without a prior history of ischaemic heart disease.

## Association between PA levels and mortality in HCM

Although a few studies were performed to prove the benefit of PA on the patients with HCM,[14 27] all previous studies included a small number of HCM individuals. Therefore, they could only preliminarily suggest potentially beneficial effects of PA on the prognosis. Importantly, one randomised controlled trial on the effect of moderate-intensity exercise training in the patients with HCM has recently been published.[27] It revealed a small but statistically significant increase in the maximal oxygen uptake (+1.35 mL/kg/min or <0.5 METs) following a 16-week

**Table 3** Sensitivity analysis in the groups according to PAS after excluding participants with a prior history of ischaemic heart disease

| | All-cause mortality | | | | Cardiovascular mortality | | | |
|---|---|---|---|---|---|---|---|---|
| | Event | Follow-up duration, PY | Incidence rate, /1000 PY | Adjusted HR (95% CI)* | Event | Follow-up duration, PY | Incidence rate, /1000 PY | Adjusted HR (95% CI)† |
| Group 1 (n=1,041) | 88/1,041 (8.5%) | 5451 | 16.1 | 1.12 (0.81 to 1.54) | 56/1,041 (5.4%) | 5451 | 10.3 | 1.80 (1.12 to 2.88) |
| Group 2 (n=900) | 70/900 (7.8%) | 4685 | 14.9 | 1 (reference) | 27/900 (3.0%) | 4685 | 5.8 | 1 (reference) |
| Group 3 (n=942) | 54/942 (5.7%) | 4958 | 10.9 | 0.81 (0.56 to 1.17) | 18/942 (1.9%) | 4958 | 3.6 | 0.67 (0.36 to 1.26) |

*p-for-trend=0.0728.
†p-for-trend=0.0002.
PAS, physical activity score; PY, person-year.

intervention, without an increased risk of SCD. The authors suggested future research addressing the safety and benefits of more vigorous exercise.[27]

According to the Advisory Committee Report's guideline,[26] PA intensity of ≥500 MET·mins/week is recommended for health benefit. As shown in online supplemental tables 3 and 4, we noted that all-cause and cardiovascular mortality in MEE group 3 achieving a mean MEE of 1511.2±524.3 MET·mins/week was not increased, with a decreasing trend of cardiovascular mortality from MEE group 1 to MEE group 3 (p-for-trend=0.0065), suggesting that the previous recommendation regarding PA can be extended to the general HCM adult population.[26]

### Mechanisms for the benefits of PA in HCM

Higher PA levels were associated with lower all-cause and cardiovascular mortality, supporting the concept that engaging in moderate-to-vigorous-intensity PA may contribute to good prognosis with no additional risk of triggering lethal arrhythmia or SCD in the general adult HCM population.

A plausible explanation regarding this observation is that moderate-to-vigorous-intensity PA can improve cardiorespiratory fitness, which translates into a long-term mortality benefit. Regular exercise can reduce various cardiovascular risk factors by enhancing cardiorespiratory fitness.[28] However, the evidence on the benefits of exercise in the HCM population is currently lacking. Moreover, HCM individuals are generally discouraged from participating in vigorous or competitive sports. However, the well-established link among physical inactivity, metabolic syndrome and all-cause and cardiovascular mortality may be of increasingly greater importance in contemporary HCM individuals who have extended longevity with improved modern management. However, the casual relationship between regular exercise and cardiovascular prognosis cannot be confirmed in this study. Further prospective studies are needed to address this issue.

### Strengths and limitations

The current study had at least three strengths. First, a large number of HCM adults with information on PA levels were included. Given that mortality in patients with HCM is not high in the contemporary era,[18] a large sample size is required to reliably investigate the effect of any intervention on prognosis. Second, our database was complete—it included all deaths and healthcare usage of the subjects. Third, while the diagnostic accuracy of HCM can be an issue in the claims database, the diagnosis of HCM in the current study population was verified by registration in the national RID programme, which is tightly controlled by experts review.

We note at least four limitations of the present study. First, the study population may be subjected to selection bias, as it included only the patients who underwent the routine health check-ups within 1 year of HCM diagnosis. Even though all Korean residents are entitled to the government-funded health examinations, approximately 75% of HCM individuals exercised this right, and the rest of them did not for various unknown reasons (i.e., non-compliant; too sick; too busy), potentially leading to selection bias. Second, the mean age of patients with HCM was around 59 years old, and the study results may not be generalisable to younger HCM individuals. Third, we did not provide an optimal upper limit of PA intensity, above which PA does not confer further mortality benefits or may be harmful, which may exist considering previous investigations reporting harmful cardiovascular effects, including lethal arrhythmia, induced by excessive sport activity.[29 30] Our fourth limitation relates to estimating the grade of PA based on the self-report survey. The survey depends heavily on memory of the last 7 days. Our analysis assumed that the PA level estimated from the questionnaire at baseline was maintained during the follow-up, which was not verified. Also, as the questionnaire does not explicitly ask the individual's time spent on PA in the last week, only approximation was possible. However, this 'last 7-day recall' survey has been well validated and proved to be reliable for research purposes.[20 21] We note that the beneficial effects of moderate-to-vigorous-intensity PA were demonstrated by two separate metrics, that is, PAS and MEE.

## CONCLUSIONS

In this nationwide population-based cohort study involving a 5.3-year follow-up of a large general adult HCM population, moderate-intensity or vigorous-intensity PA provided progressive benefits—lower all-cause mortality and lower cardiovascular mortality. We recommend individuals with adult HCM can participate in more-than-light-intensity leisure-time PA. Our data cannot be extrapolated to a younger HCM population. We opine that large-scale, randomised clinical trials are warranted to confirm the beneficial effects of moderate-to-vigorous-intensity PA in the general HCM population. However, careful considerations should be made to minimise ethical issues in study design.

### What are the findings?

- In a nationwide cohort study of 7666 middle-aged adults with hypertrophic cardiomyopathy, regular physical activity of moderate-to-vigorous intensity was associated with lower all-cause and cardiovascular mortality than lower levels of physical activity.

### How might it impact on clinical practice in the future?

- It may be safe for older adults with hypertrophic cardiomyopathy to participate in leisure-time physical activity of moderate-to-vigorous intensity. This counters previous safety concerns that moderate-to-vigorous physical activity was associated with poor prognosis by triggering lethal ventricular arrhythmias.

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