Association between physical activity and risk of renal function decline and mortality in community-dwelling older adults: a nationwide population-based cohort study

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Abstract

Background: Physical activity (PA) is an important risk factor associated with health outcomes. However, the relationship between PA and kidney function decline in older adults remains unclear. We examined the influence of PA on kidney function decline and mortality in community-dwelling older adults.

Methods: Adults aged $\geq$ 65 years with an estimated glomerular filtration rate (eGFR) > 60 mL/min/1.73 m^2 who had available health checkup data from 2009 to 2010 were included. The cohort was followed annually through December 2015 for anthropometric, sociodemographic, and medical information including outcomes and biennially for laboratory information from the health checkup. We divided these patients into three groups according to self-reported PA (Inactive group: no leisure-time PA, Active group: vigorous activity for at least 80 min/week or a sum of moderate-intensity activity and walking for at least 300 min/week, Low-active group: level of PA between the definitions of the other two groups). Associations between the intensity of PA and death, cardiovascular death, and $\geq$ 50% eGFR decline were investigated.

Results: Among 102,353 subjects, 32,984 (32.23%), 54,267 (53.02%), and 15,102 (14.75%) were classified into the inactive, low-active, and active groups, respectively. The active group was younger, contained a higher proportion of men, and had higher frequencies of hypertension, diabetes mellitus, drinking, and smoking than the other groups. The active group had significantly lower incidence rates of mortality, cardiovascular mortality, and kidney function decline than the other groups (all $p < 0.001$). The active group also showed lower all-cause (hazard ratio [HR], 0.76; 95% confidence interval [CI], 0.70–0.82) and cardiovascular mortality (HR, 0.64; 95% CI, 0.53–0.78) and protection against $\geq$ 50% eGFR decline (HR, 0.81; 95% CI, 0.68–0.97) compared with the inactive group in the fully adjusted Cox proportional hazards regression model.

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Conclusions: High PA was an independent modifiable lifestyle factor for reducing mortality and protecting against declines in kidney function in older adults.

Keywords: Physical activity, Renal function, Mortality, Older adults

Background

Longer life expectancies and low birth rates have led to substantial increase in the proportion of older people worldwide. Given that aging is a well-established risk factor for various chronic diseases [1], it is not surprising that the prevalence of chronic kidney disease (CKD) is increasing, particularly in developed countries with a growing aged population [2]. Because CKD in older people is closely associated with increased risk of cardiovascular disease, cognitive dysfunction, and functional impairment, the increasing prevalence of CKD is a substantial economic, social, and medical concern [3].

Aging is associated with sarcopenia, progressive decline in muscle mass and strength that leads to frailty [4]. Frailty reduces physiologic reserves, increases vulnerability upon exposure to stressors, and is closely related to harmful outcomes such as falls, functional impairment, cognitive dysfunction, and cardiovascular comorbidity and death in older adults [5]. Increased physical activity (PA) has been regarded as a potential strategy for mitigating sarcopenia in older adults [6]. Sarcopenia and frailty are prevalent in both older population and CKD patients and strongly associated with higher risk of hospitalization and all-cause mortality in these patients [7]. Low PA is also related to poor clinical outcomes and reduced quality of life in patients with CKD, including worsening kidney function [8–12]. Some previous studies suggested that an increase in PA reduces the risk of decline in estimated glomerular filtration rate (eGFR) and development of albuminuria in patients with CKD or general population [13–15]. However, the impact of PA on worsening kidney function remains unclear in older people.

We hypothesized that high PA is associated with reduced mortality and slow progression of kidney function decline in community-dwelling older adults who were not diagnosed as CKD and investigated that possibility using the Senior Cohort Database of the National Health Insurance Service (NHIS-Senior cohort) in Korea.
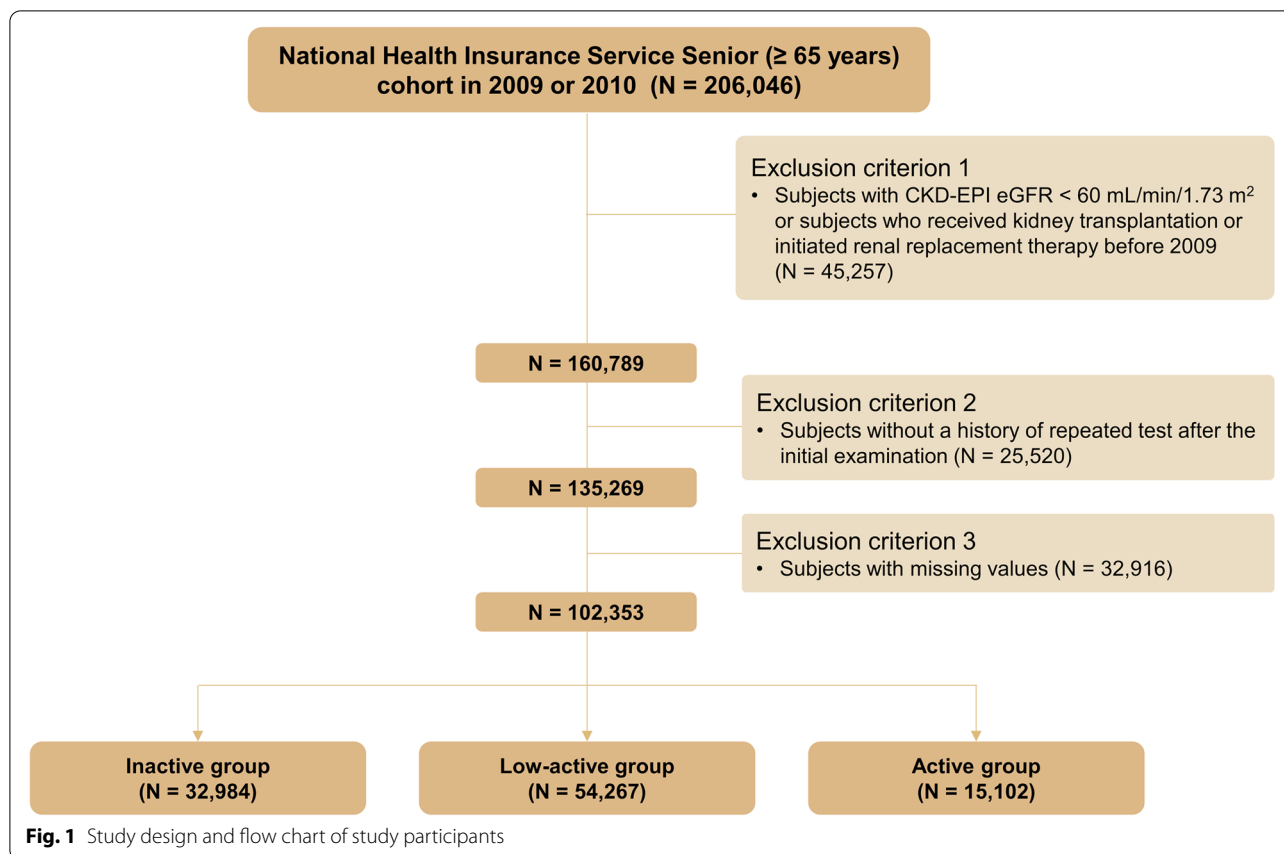
Methods

Data source and study participants

This nationwide, retrospective, observational study was performed using data from the NHIS-Senior cohort between 2009 and 2015. The NHIS-Senior cohort was established to support research about older people in Korea [16]. The research database contains de-identified data from approximately 558,147 individuals aged ≥ 60 years who were eligible for National Health Insurance and Medical Aid as of the end of December 2002. The cohort was followed annually through December 2015 for anthropometric, sociodemographic, and medical information including outcomes and biennially for laboratory information from the health checkup. Because serum creatinine level was added to the health checkup in 2009, study participants who underwent baseline health checkups between 2009 and 2010 were initially screened for enrollment.

We initially recruited 206,046 individuals aged ≥ 65 years who underwent an initial health checkup between 2009 and 2010. We excluded individuals who had baseline eGFR < 60 mL/min/1.73m^2 or previously had received a kidney transplant or dialysis ($n = 45,247$). We also excluded individuals without follow-up data of serum creatinine level after the initial visit ($n = 25,520$) and those with missing values in the PA questionnaire ($n = 32,916$). Therefore, 102,353 individuals were included in our final analysis and followed until 2015 (Fig. 1).

Classification of physical activity

The intensity and frequency of PA were assessed using a self-reported questionnaire, the Korean version of the International Physical Activity Questionnaire (IPAQ)-short form [17]. The IPAQ-short form asks about the frequency and duration of walking, moderate-intensity, and vigorous-intensity PA in the preceding 7 days. The World Health Organization (WHO) Guidelines recommend that older adults engage in at least 150 min/week of moderate-intensity aerobic activity, 75 min/week of vigorous-intensity aerobic activity, or an equivalent combination [18]. However, it is difficult for most older adults to achieve those targets because of age-related limitations, such as comorbidities, mobility problems, or increased risk of injury. Although the current guidelines do not include a recommendation for light-intensity PA, a recent study found that participating in at least 300 min/week of light-intensity PA was associated with favorable health outcomes in older adults [19]. Therefore, we categorized subjects into the inactive, low-active, and active groups according to reported intensity of PA, including light-intensity PA. The inactive group contained those who said that they did not engage in any PA. The active group was defined as those who performed vigorous activity for

Kim *et al. BMC Geriatrics* (2022) 22:973

Page 3 of 10

Fig. 1 Study design and flow chart of study participants

at least 80 min/week or the sum of moderate-intensity activity and walking for at least 300 min/week. The low-active group was defined as those whose PA fell between the definitions of the other two groups.

Baseline data collection

Baseline demographic and clinical data were analyzed for all participants. Blood samples were obtained after ≥ 8-h fasting state and serum creatinine level was measured using an isotope dilution mass spectrometry–calibrated method, and eGFR was calculated using the creatinine-based CKD Epidemiology Collaboration equation [20]. Deciles of the National Health Insurance premium were investigated as a proxy measure for precise income and re-categorized into five groups.

Outcomes

The primary outcomes were death, cardiovascular death, and a decline in eGFR within the observation period. Deaths and causes of death were ascertained from records linked with the Korean Statistical Information Service using unique personal identification numbers [21]. Cardiovascular death was defined using the following codes from the Korean Classification of Diseases

version 5 or 6: E10–E14, I10–I15. I20–I25, I60–I69, I70–I79. A decline in eGFR was defined as ≥ 50% eGFR decrease from baseline [22, 23]. The change in eGFR was assessed using the baseline eGFR and the last eGFR of health checkup during the follow-up period, and the percent change in eGFR was calculated as follows: (last eGFR − baseline eGFR)/(baseline eGFR) × 100%.

Statistical analysis

Continuous variables are expressed as mean and standard deviation, and categorical variables are presented as frequency with percentage. To test whether the variables are normally distributed, the Kolmogorov–Smirnov test was used. *P* values were obtained from Chi-square testing for categorical variables. Survival curves according to level of PA were estimated using the Kaplan–Meier method, and the significance of the survival curve was assessed by log rank testing. Hazard ratios (HRs) with 95% confidence intervals (CIs) were obtained from Cox proportional hazards regression analysis. Univariable analyses using Cox proportional hazards regression analysis were performed to determine the risk factors for death, cardiovascular death, and decline in eGFR during follow up and were followed by multivariable analyses

Kim *et al. BMC Geriatrics*   (2022) 22:973

Page 4 of 10

to determine significant factors. A *p* for trend in the Cox proportional hazards model was calculated using the Wald test. Subgroup analyses were conducted using age, sex, body mass index (BMI), smoking, drinking, income, and various comorbidities. The linearity assumption for continuous variables was verified. The proportional hazards assumption for categorical variables was verified using a log-minus-log plot. All analyses were performed using R software 3.3.3 and SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). *P* values < 0.05 were considered to indicate statistical significance.

Results

Baseline characteristics

Table 1 shows the baseline characteristics of the study population by PA level. The mean age of the total population was 72.0 ± 4.0 years, and 46,183 subjects (45.12%) were male. The subjects were categorized into the

inactive group ($n = 32,984$, 32.23%), low-active group ($n = 54,267$, 53.02%), and active group ($n = 15,102$, 14.75%). The active group was relatively young, containing many 65- to 74-year-old subjects. The subjects in the active group were more likely to be men (61.28%) compared with the inactive and low-active groups. Interestingly, the participants in the active group were more likely than the others to be ex-smokers (23.16%) and alcohol consumers (34.66%) and less likely to be non-smokers (65.69%). The proportion of current smokers was similar among the three groups. The active group also had higher prevalence of diabetes mellitus (20.29%), hypertension (54.85%), and dyslipidemia (7.4%) than the other groups. Baseline eGFR level did not differ among the groups. The proportion of very high decile of income was relatively high in the active group (42.52%).

Table 1 Baseline characteristics of the subjects according to the levels of physical activity in older adults

		Inactive	Low-active	Active
Number, *n* (%)		32,984 (32.23)	54,267 (53.02)	15,102 (14.75)
Age (year)		72.4 ± 4.2	71.6 ± 3.9	71.4 ± 3.6
Age group (year, *n* (%))	65–74	24,730 (74.98)	43,182 (79.57)	12,746 (84.4)
	75–84	7,879 (23.89)	10,748 (19.81)	2,296 (15.2)
	85-	375 (1.14)	337 (0.62)	60 (0.4)
Sex (male, *n* (%))		12,616 (38.25)	24,312 (44.8)	9,255 (61.28)
BMI (kg/m^2, *n* (%))	< 18.5	1,289 (3.91)	1,726 (3.18)	331 (2.19)
	18.5–24.9	20,027 (60.72)	33,120 (61.03)	9,437 (62.49)
	≥ 25	11,668 (35.37)	1,9421 (35.79)	5,334 (35.32)
BMI (kg/m^2)		23.95 ± 3.27	24.01 ± 3.07	24.02 ± 2.86
SBP (mmHg)		131.38 ± 16.56	130.45 ± 15.76	130.37 ± 15.38
Smoking, *n* (%)	Non-smoker	25,883 (78.47)	40,105 (73.9)	9,920 (65.69)
	Ex-smoker	3,288 (9.97)	8,367 (15.42)	3,498 (23.16)
	Current smoker	3,813 (11.56)	5,795 (10.68)	1,684 (11.15)
Alcohol, *n* (%)		6,541 (19.83)	13,749 (25.34)	5,234 (34.66)
CVD, *n* (%)		1,124 (3.41)	1,797 (3.31)	507 (3.36)
Heart disease, *n* (%)		2,546 (7.72)	4,417 (8.14)	1,205 (7.98)
Diabetes mellitus, *n* (%)		5,030 (15.25)	9,300 (17.14)	3,064 (20.29)
Hypertension, *n* (%)		16,963 (51.43)	29,302 (54)	8,284 (54.85)
Dyslipidemia, *n* (%)		1,604 (4.86)	3,662 (6.75)	1,117 (7.4)
Creatinine (mg/dL)		0.82 ± 0.17	0.84 ± 0.17	0.88 ± 0.17
eGFR (mL/min /1.73 m^2)		79.08 ± 11.71	78.87 ± 11.57	78.68 ± 11.48
Fasting glucose (mg/dL)		102.74 ± 25.98	103.7 ± 26.14	105.5 ± 26.82
Total cholesterol (mg/dL)		197.19 ± 39.13	195.76 ± 38.29	192.95 ± 37.66
Income, *n* (%)	0–2	5,314 (16.11)	8,269 (15.24)	2,175 (14.4)
	3–4	4,136 (12.54)	6,248 (11.51)	1,539 (10.19)
	5–6	5,113 (15.5)	7,417 (13.67)	1,976 (13.08)
	7–8	6,696 (20.3)	10,633 (19.59)	2,990 (19.8)
	9–10	11,725 (35.55)	21,700 (39.99)	6,422 (42.52)

Abbreviations: BMI Body mass index, *CVD* Cerebrovascular disease, *DBP* Diastolic blood pressure, *eGFR* estimated glomerular filtration rate, *HDL-C* High-density lipoprotein cholesterol, *LDL-C* Low-density lipoprotein cholesterol, *SBP* Systolic blood pressure

Kim *et al. BMC Geriatrics* (2022) 22:973

Page 5 of 10

Table 2 Mortality and renal events according to the levels of physical activity in older adults

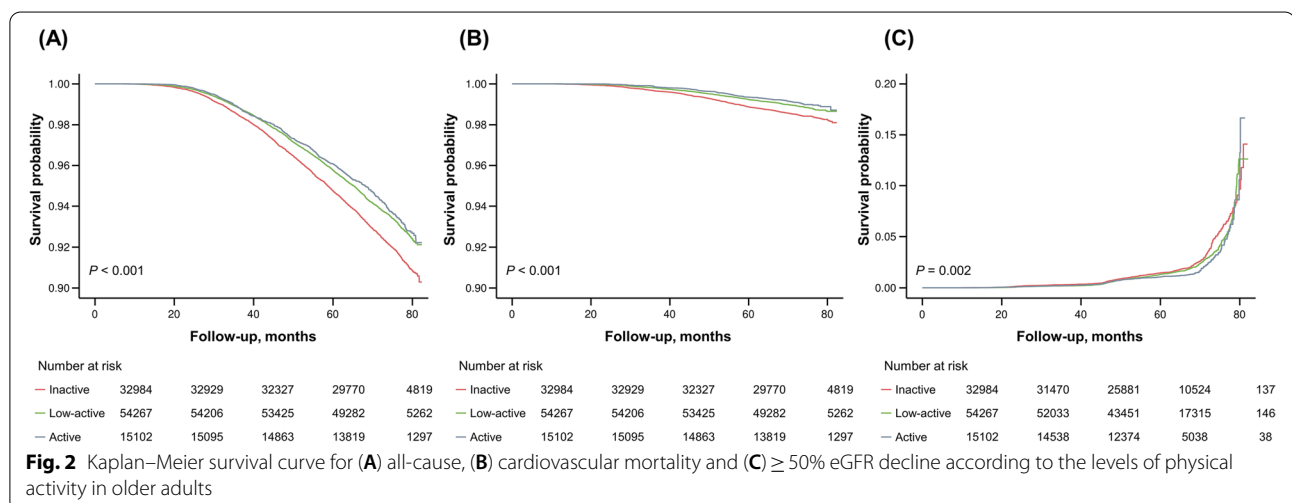|	Observed (*n*)	Events, *n* (%)	Person-years	Incidence rates /1,000 person-years	*p* value
All-cause mortality					< 0.001
Inactive	32,984	2,470 (7.49)	196,482.95	12.57	
Low-active	54,267	3,268 (6.02)	321,152.13	10.18	
Active	15,102	8,54 (5.65)	89,379.36	9.55	
Cardiovascular mortality					< 0.001
Inactive	32,984	482 (1.46)	196,482.95	2.45	
Low-active	54,267	560 (1.03)	321,152.13	1.74	
Active	15,102	132 (0.87)	89,379.36	1.48	
≥ 50% eGFR decline					< 0.001
Inactive	32,984	487 (1.48)	141,650.55	3.44	
Low-active	54,267	686 (1.26)	234,851.68	2.92	
Active	15,102	172 (1.14)	66,356.70	2.59	

Analysis: A *p* value obtained from the Chi-square test

Association between physical activity and risks of deaths and renal function decline

During a mean follow-up period of 69.8 ± 9.0 months (range, 6.9–82.4 months), 6,594 (6.44%) subjects died, and 1,345 (1.31%) subjects experienced a greater than 50% decrease in renal function (Table 2). Overall, the incidence rates of all-cause death and cardiovascular death per 1000 person-years were 12.57 and 2.45, respectively, in the inactive group; 10.18 and 1.74 in the low-active group; and 9.55 and 1.48 in the active group. The incidence rate of decline in eGFR was 3.44 in the inactive group, 2.92 in the low-active group, and 2.59 in the active group. The active group had significantly lower incidence rates of mortality, cardiovascular mortality, and renal function decline than the other groups (all *p* < 0.001). The inactive group had poorer survival than the low-active and active groups (both *p* < 0.001 by log rank, Fig. 2A and

B). The cumulative incidence of renal function decline was higher in the inactive group than in the low-active and active groups (*p* = 0.002, by log rank, Fig. 2C).

Next, we analyzed the relative risk of mortality and renal function decline during follow up according to PA level to determine the relationships between clinical outcomes and intensity of PA in older people (Table 3). The inactive group was used as the reference category for calculating HRs. In the crude model, the HRs for all-cause and cardiovascular mortality were 0.82 (95% CI, 0.78–0.86) and 0.72 (95% CI, 0.63–0.81), respectively, for the low-active group and 0.77 (95% CI, 0.71–0.83) and 0.61 (95% CI, 0.50–0.74) for the active group. Consistent with mortality rates, the HRs for renal function decline in the crude model of the low-active (HR, 0.87; 95% CI, 0.77–0.97) and active groups (HR, 0.75; 95% CI, 0.63–0.89) were significantly lower than in the inactive group.

Fig. 2 Kaplan–Meier survival curve for (**A**) all-cause, (**B**) cardiovascular mortality and (**C**) ≥ 50% eGFR decline according to the levels of physical activity in older adults

Kim *et al. BMC Geriatrics* (2022) 22:973

Page 6 of 10

Table 3 Associations between the levels of physical activity and clinical outcomes in the elderly

	Crude			Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI		HR	95% CI	
		Lower	Upper		Lower	Upper		Lower	Upper		Lower	Upper
All-cause mortality												
Inactive (Ref.)	1			1			1			1		
Low-active	0.82	0.78	0.86	0.83	0.79	0.87	0.84	0.80	0.89	0.84	0.80	0.89
Active	0.77	0.71	0.83	0.73	0.68	0.79	0.76	0.70	0.82	0.76	0.70	0.82
p for trend	< 0.001			< 0.001			< 0.001			< 0.001		
Cardiovascular mortality												
Inactive (Ref.)	1			1			1			1		
Low-active	0.72	0.63	0.81	0.75	0.66	0.85	0.75	0.66	0.85	0.75	0.67	0.85
Active	0.61	0.50	0.74	0.63	0.52	0.77	0.64	0.53	0.78	0.64	0.53	0.78
p for trend	< 0.001			< 0.001			< 0.001			< 0.001		
≥ 50% eGFR decline												
Inactive (Ref.)	1			1			1			1		
Low-active	0.87	0.77	0.97	0.90	0.80	1.03	0.88	0.78	0.99	0.91	0.81	1.03
Active	0.75	0.63	0.89	0.82	0.68	0.97	0.78	0.65	0.93	0.81	0.68	0.97
p for trend	0.001			0.014			0.004			0.021		

Analysis: A *p* for trend obtained from the Wald test, and hazard ratios with 95% confidence intervals were obtained from Cox proportional hazards regression analysis

Model 1: age, sex, body mass index, Model 2: Model 1 + smoking, alcohol, income, cerebrovascular disease, heart disease, diabetes mellitus, hypertension, dyslipidemia, Model 3: Model 2 + systolic blood pressure, fasting glucose, total cholesterol, baseline estimated glomerular filtration rate

In models 1 and 2 of the multivariable analysis, the active group had significantly lower risk for all-cause mortality, cardiovascular mortality, and renal function decline than did the inactive group. In model 3, the fully adjusted Cox model that controlled for age, sex, comorbidities, income, SBP, and baseline biochemical characteristics, the active group had a 25% risk reduction for all-cause mortality (HR, 0.76; 95% CI 0.70–0.82) and an about 35% risk reduction for cardiovascular mortality (HR, 0.64; 95% CI 0.53–0.78). Similar results were observed in the association between the low-active group and all-cause mortality (HR 0.84, 95% CI 0.80–0.89) and cardiovascular mortality (HR 0.75, 95% CI 0.67–0.85). The active group remained associated with a significantly lower risk of renal function decline in the fully adjusted Cox regression model (HR 0.81, 95% CI 0.68–0.97), but the low-active group did not. The *p* for trends across the three groups were all significant indicating that the higher PA, the lower all-cause mortality, cardiovascular mortality, and renal function decline.

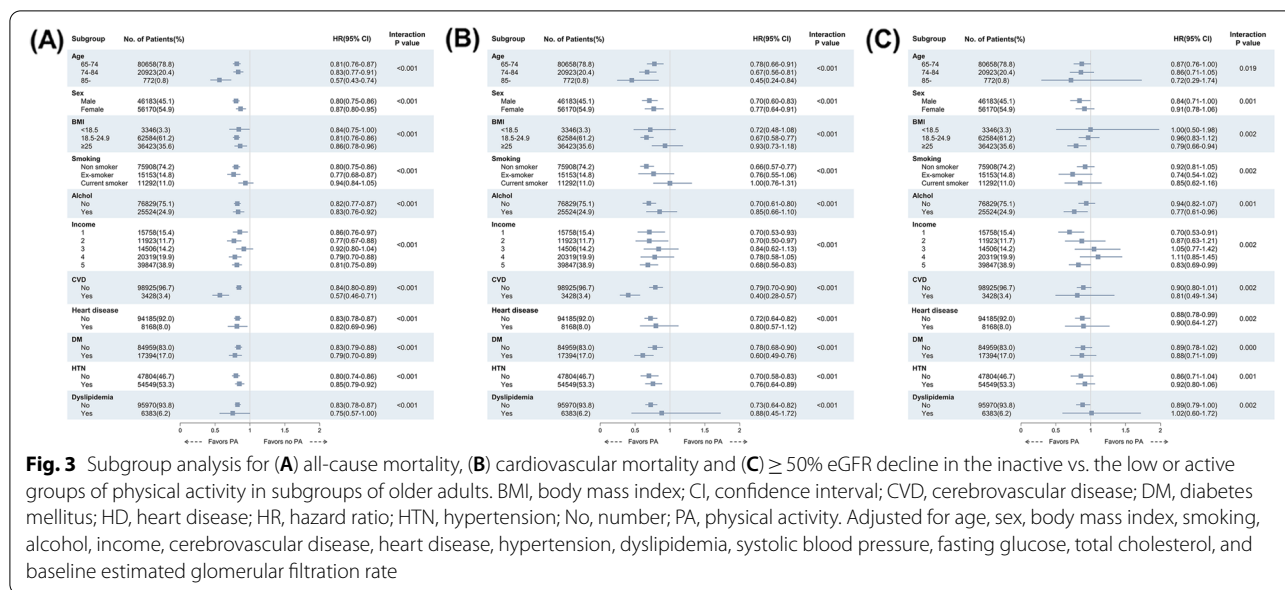### Subgroup analyses of the risks of deaths and renal function decline

To elucidate the effects of subgroups on the associations between PA and clinical outcomes, we performed subgroup analyses stratified by age, sex, BMI, smoking, alcohol, income, and comorbidities. Subgroup analyses were performed after adjustments for age, sex, BMI, smoking,

alcohol, income, cerebrovascular disease, heart disease, diabetes mellitus hypertension, dyslipidemia, SBP, fasting glucose, total cholesterol, and baseline eGFR. The effect of PA on all-cause mortality substantially prominent in subjects 85 years and older (HR 0.57, 95% CI 0.43–0.74) and subjects with cerebrovascular disease (HR 0.57, 95% CI 0.46–0.71). PA was found to be beneficial regardless of sex, alcohol consumption, and the presence of cerebrovascular disease, heart disease, diabetes mellitus, or hypertension. In the case of current smokers (HR 0.94, 95% CI 0.84–1.05) and underweight (BMI < 18.5 kg/m^2, HR 0.84, 95% CI 0.75–1.00), there was no beneficial effect of PA on all-cause mortality (Fig. 3A).

The positive effect of PA on cardiovascular death was found regardless of age, sex, and the presence of cerebrovascular disease, diabetes mellitus, or hypertension. However, in subgroup analyses according to BMI and smoking status, the effect of PA was limited only in the subjects with BMI 18.5–24.9 kg/m^2 (HR 0.67, 95% CI 0.58–0.77) or non-smokers (HR 0.66, 95% CI 0.57–0.77). In those with heart disease, PA reduced all-cause mortality but had no significant influence on cardiovascular mortality (HR 0.80, 95% CI 0.57–1.12). Consistently, PA had no significant influence on cardiovascular mortality in the subgroup with dyslipidemia (HR 0.88, 95% CI 0.45–1.72, Fig. 3B).

The association between PA and more than 50% decline in eGFR became unclear when the subjects were divided

Fig. 3 Subgroup analysis for (**A**) all-cause mortality, (**B**) cardiovascular mortality and (**C**) ≥ 50% eGFR decline in the inactive vs. the low or active groups of physical activity in subgroups of older adults. BMI, body mass index; CI, confidence interval; CVD, cerebrovascular disease; DM, diabetes mellitus; HD, heart disease; HR, hazard ratio; HTN, hypertension; No, number; PA, physical activity. Adjusted for age, sex, body mass index, smoking, alcohol, income, cerebrovascular disease, heart disease, hypertension, dyslipidemia, systolic blood pressure, fasting glucose, total cholesterol, and baseline estimated glomerular filtration rate

by age. A significant effect of PA was found only in the group with BMI ≥ 25 kg/m^2 (HR 0.79, 95% CI 0.66–0.94). In addition, the HR of kidney function decline in the PA group was significantly lower in alcohol consumers (HR 0.77, 95% CI 0.61–0.96) and the very low- and very high-income subgroups (very low: HR 0.70, 95% CI 0.53–0.91, very high: HR 0.83, 95% CI 0.69–0.99). However, the effects of sex, smoking or variable comorbidities on kidney function decline were not clear (Fig. 3C).

Discussion

This nationwide observational study demonstrates that any level of PA significantly lowers the risk of all-cause and cardiovascular mortality among community-dwelling subjects aged ≥ 65 years in Korea, compared with those who are physically inactive. We also confirmed that high PA was independently associated with prevention of renal function decline in older adults. In our study population, higher PA was dose-dependently associated with lower all-cause and cardiovascular mortality and renal function decline during follow up.

The positive relationships between high PA and long-term health outcomes have been demonstrated in older population [24–28]. Nationwide studies demonstrated that older adults with high PA were associated with 0.48–0.73 lower of all-cause death compared with those with no PA [24, 25]. A Taiwan nationwide study also reported that exercise 3–5 times a week had a significantly decreased risk of mortality in older adults [26]. Regardless of the number of underlying diseases, high PA was associated with a mortality reduction of 30–47% in older adults [28]. Recently, a meta-analysis showed that the most sedentary participants had a 2.44 higher risk of all-cause mortality than the least sedentary participants, and the least active participants were associated with 3.09 higher risk of all-cause mortality compared with the most active participants for total PA in older adults [29]. We also found that high PA is associated with a 25% lower risk of all-cause mortality and a 36% lower risk of cardiovascular mortality in a community-dwelling older population.

Despite the convincing evidence of significant associations between PA and all-cause mortality, the causality within the relationship is not fully understood. Several pathophysiological mechanisms have been suggested to explain how PA delays mortality. PA protects against age-related mitochondrial fragmentation in skeletal muscle [30], reduces insulin resistance [31], modulates oxidative stress and inflammatory cytokines [32], and improves defective autophagy [33]. Clinically, PA has been identified as a potential preventive strategy to slow the development of frailty and sarcopenia in both older adults and CKD patients. Recent meta-analyses showed that PA prevents frailty or sarcopenia in adults aged ≥ 65 years [6], and regular PA improves the physical and functional capacity of CKD patients [34]. Therefore, an increase in physical capacity through appropriate PA might delay mortality by improving cardiorespiratory and metabolic fitness, regulating cardiovascular risk factors, reducing multimorbidity, and preventing frailty and disability.

The beneficial effects of PA on decline in renal function have been widely evaluated, but conflicting results have been reported about the relationship between PA and renal function. In a longitudinal cohort study, higher

Kim *et al. BMC Geriatrics*   (2022) 22:973

Page 8 of 10

PA level was associated with slower rate of eGFR loss in patients with established CKD [35]. However, other researchers reported finding no association between PA level and progression to kidney failure in patients with advanced CKD [12]. They suggested that PA might not be a modifiable risk factor in preventing CKD progression in patients whose GFR was already low [12]. Among the older adults, higher level of PA was associated with a 28% lower adjusted risk of rapid decline in kidney function (decline ≥ 3.0 mL/min/1.73m^2 per year in GFR) [36]. However, another study found that high sedentary time, not low level of PA, played an important role in incident CKD and rapidly declining kidney function in people aged 70–79 years [37]. Our results here support the beneficial effects of PA in preventing a decline in kidney function among older adults and confirm the importance of maintaining PA to renal health outcomes in the older population.

One noteworthy finding of this study is that the current recommendations for PA intensity are effective for protecting against renal function decline in older adults. Several global and national institutions now recommend that older adults participate in PA to gain health benefits, but most older adults do not meet those guidelines. One study reported that 27.3–44.3% of adults aged ≥ 65 years in the United States achieved the recommended level of PA [38]. In this study, we classified PA level based on WHO recommendations, and only 14.75% of our study population met those PA level. Although only the active group was independently associated with delay in renal function decline, even the low-active group was significantly associated with reduced all-cause and cardiovascular mortality, compared with the inactive group. This finding suggested that any level of PA is helpful to improve general health outcomes, and that the importance of encouraging increased PA, even in the slightest, should be emphasized in older adults. Further study may be needed to investigate the minimal target level of PA associated with survival and renal function decline.

Another interesting finding of this study is that PA was an independent risk factor for mortality and renal function decline after controlling for various lifestyle factors. The relationships between PA and other health-related behaviors are complex. Generally, low PA is known to be related to other unhealthy behaviors, such as overeating, heavy smoking, and excessive alcohol consumption [39]. In the present study, we observed that our active group was more likely than those in the other groups to be ex-smokers and alcohol consumers, and they already had a higher prevalence of diabetes mellitus, hypertension, and dyslipidemia. Nevertheless, high PA was significantly associated with reduced all-cause and cardiovascular mortality and delayed renal function decline

after adjustment for unhealthy behaviors and multiple comorbidities. There was a tendency for significant interactions to exist between PA and all-cause death even in older adults with alcohol consumers or those with various comorbidities in the subgroup analyses. These findings suggest that appropriate PA is an important modifiable factor to improve survivals and prevent renal function decline even in older adults with various comorbidities or alcohol consumers.

Our study has several limitations. First, although the IPAQ-short form is easily performed and widely used to assess PA, the self-reported method risks errors caused by recall bias and misinterpretation of questions. Second, because the IPAQ-short form assesses PA based mainly on leisure time PA, the actual PA level could be underestimated in participants with physically demanding occupations. Third, we used creatinine-based eGFR to assess renal function, but that equation is insufficient in older adults. Serum creatinine is produced by muscle, and loss of muscle mass associated with aging reduces creatinine generation. Recent guidelines recommend using the cystatin C-based eGFR measurement for older people [40]. Therefore, further research using the cystatin C-based eGFR might be required to redeem this weakness. Lastly, this study has some limitations due to the nature of the observational, retrospective design. As observational studies cannot establish cause-effect relationships, potential residual biases from measured or unmeasured confounders may have influenced the results. Additionally, the most enrolled participants were followed for approximately 70 months in this study, but some participants were followed for relatively short follow-up periods. Therefore, the possibility of loss due to follow-up bias due to the difference in follow-up duration may be existed. Further well-designed prospective cohort studies or randomized controlled trials may be needed to elucidate a direct association between PA and renal function decline in older adults. Despite those limitations, a major strength of our study is the reliability of the data, which we obtained from a large, nationwide, population-based database containing PA data. To our knowledge, this is the first nationwide study to identify potential association between PA level and renal function decline in community-dwelling older adults. Moreover, we adjusted for potential confounding factors and conducted extensive subgroup analyses.

Conclusions

High PA is an independent modifiable lifestyle factor for reducing mortality and protecting kidney function decline in older adults. Our findings underscore the need for interventional research to elucidate the effects

Kim *et al. BMC Geriatrics*   (2022) 22:973

Page 9 of 10

of maintaining or increasing PA on age-related decline in kidney function of older people.

Abbreviations
PA: Physical activity; eGFR: Estimated glomerular filtration rate; CKD: Chronic kidney disease; NHIS: National Health Insurance Service; IPAQ: International Physical Activity Questionnaire; WHO: World Health Organization; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HRs: Hazard ratios.

Authors' contributions
H.K and Y.A.H designed the study. S.C., S.H.K. and S.J.S. supervised the study. M.J.K. and C.L. performed the statistical analysis. E.J.B., Y.Y.H., J.C., K.D.Y., W.Y.P., I.O.S., and B.C.Y. were responsible for data acquisition. G.K., J.W.Y., W.M.H. and S.H.S. were responsible for data interpretation. H.K and Y.A.H. drafted the manuscript. All authors approved the final version of the manuscript.

Availability of data and materials
Publicly available datasets of Korea were used in this study. These can be found in the NHIS-Senior cohort at https://nhiss.nhis.or.kr, reference number [16].

Declarations

Ethics approval and consent to participate
This study was approved by the Institutional Review Board of College of Medicine, The Catholic University of Korea (DC20ZISI0013). Data usage was approved by the National Health Information Data Request Review Committee of the NHIS (NHIS-2021–2-031). The informed consent requirement was waived by the Ethics committee and Institutional Review Board of College of Medicine, The Catholic University of Korea due to retrospective nature of the study. The study was conducted in accordance with the principles of the Declaration of Helsinki. All study procedures were performed in accordance with the relevant guidelines and regulations.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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