

Sedentary behavior, physical activity and renal function in middle-aged and older adults: isotherm substitution modelling

Keisei Kosaki

Waseda University

Koichiro Tanahashi

Kyoto Pharmaceutical University

Masahiro Matsui

University of Tsukuba

Nobuhiko Akazawa

Japan Institute of Sports Sciences

Yosuke Osuka

Tokyo Metropolitan Institute of Gerontology

Kiyoji Tanaka

University of Tsukuba

David W. Dunstan

Baker Heart and Diabetes Institute

Neville Owen

Baker Heart and Diabetes Institute

Ai Shibata

University of Tsukuba

Koichiro Oka

Waseda University

Seiji Maeda (✉ maeda.seiji.gn@u.tsukuba.ac.jp)

University of Tsukuba <https://orcid.org/0000-0003-1642-4644>

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Abstract

Background: Both physical inactivity and sedentary behavior (too much sitting) can contribute to renal dysfunction. However, the potential benefits of behavior change (e.g., replacing sedentary behavior with physical activity) on renal function are not fully understood. We used isotemporal substitution to model potential impacts on renal function of replacing time from one behavior to another in middle-aged and older adults. **Methods:** For 174 Japanese adults (aged 50 – 83 years; 76 % women), the time spent in sedentary behavior, light-intensity physical activity (LPA), and moderate to vigorous-intensity physical activity (MVPA) were assessed using uniaxial accelerometers. Renal function was evaluated by the estimated glomerular filtration rate (eGFR) from serum creatinine and cystatin C levels. **Results:** In univariate analyses, eGFR was significantly, albeit weakly, correlated with time spent in sedentary behavior ($r_s = -0.229$), LPA ($r_s = 0.265$) and with MVPA ($r_s = 0.353$). In the isotemporal substitution models, replacement of 30 min/day of sedentary behavior with equivalent LPA time was not significantly associated with eGFR ($\beta = 2.25$, $p = 0.111$); however, replacement with the same amount of MVPA was beneficially associated with eGFR ($\beta = 5.51$, $p < 0.05$). **Conclusions:** These cross-sectional findings suggest that both sedentary behavior (detrimentally) and physical activity (beneficially) may be contributors to maintaining renal function and that replacing sedentary behavior with MVPA may benefit renal health in middle-aged and older adults.

Background

Chronic kidney disease (CKD), defined as persistent renal dysfunction or renal damage, is one of the major non-communicable diseases with a high prevalence worldwide [1]. For example, CKD in the Japanese adult population is estimated to affect about one in eight and has been increasing among those who are middle-aged and older [2]. As these trends of CKD prevalence are expected to continue, especially in countries with ageing populations, including Japan [3], there is the need to identify practical countermeasures for preventing the onset and progression of CKD in middle-aged and older adults.

Insufficient moderate- to vigorous-intensity physical activity (MVPA) is associated with the onset of renal dysfunction [4]. Subsequently, physical inactivity has been recognized recently as one of the important targets for intervention in renal care [5]. In addition, new evidence suggests that sedentary behavior defined as any waking behavior characterized by an energy expenditure ≤ 1.5 metabolic equivalents, such as television viewing time [6] may be another risk factor for renal dysfunction [7, 8]. Taken together, these epidemiological findings suggest the importance of behavioral approaches for renal care and the possibility that specific behavior change (e.g., replacing sedentary behavior with physical activity) may contribute to preventing renal dysfunction. However, the potential impacts of replacing sedentary behavior with physical activity on renal function are not well-understood.

Isotemporal substitution modelling is a novel statistical approach that enables the estimation of associations when replacing time from one behavior to another, whilst keeping total time fixed and other behaviors fixed [9]. Recent cross-sectional studies using this approach have demonstrated that replacing time spent in sedentary behavior with equivalent physical activity can be associated beneficially with cardio-metabolic biomarkers, health-related quality of life, and physical function [10–13].

We used isotemporal substitution modelling to examine cross-sectional associations of accelerometer-derived sedentary behavior and the different physical activity intensities (LPA and MVPA) with renal function in middle-aged and older adults.

Methods

Participants

This cross-sectional study used the data from 200 participants who were recruited for an interventional study via local newspaper advertisements between 2014 and 2015. In total, there were 180 eligible participants, after excluding those without objectively evaluated sedentary behavior and physical activity or those who had insufficient accelerometer data. After excluding participants who had missing values of required variables such as blood samples ($n = 6$), the final analyses were conducted 174 middle-aged and older Japanese adults (Fig. 1). This study was approved by the Ethics Committee in University of Tsukuba (Tai 019-19) and conformed to the principles outlined in the Declaration of Helsinki, and all participants provided written informed consent.

Sedentary behavior and physical activity

The time spent in sedentary behavior, light-intensity physical activity (LPA), and MVPA were assessed using a uniaxial accelerometer (Lifecorder, Suzuken Co., Ltd., Nagoya, Japan) that samples vertical acceleration signals in the range from 0.06 to 1.94 G at 32 Hz. The accuracy and detailed algorithm of this accelerometer has been described elsewhere [14]. The epoch length was 1 minute, the time used by the accelerometer for measuring activity. Participants were instructed to wear constantly the accelerometer on the level of participant's waist

during waking and sleeping hour for 7 consecutive days, except while bathing and swimming. A day with at least 10 hours of wear time was considered valid. This accelerometer records the scores of physical activity intensity consisted of a scale from 0 – 9 (level 0: rest; level 0.5: micro activity; level 1 – 9: movement) according to the acceleration signal patterns [15]. In the present study, these scores were reclassified into four activity levels based on the previous investigation [16] as follows: sedentary or sleep (≤ 1.5 Mets: level 0 – 0.5), light (1.6 – 2.9 Mets: level 1 – 3), moderate (3.0 – 6.0 Mets: level 4 – 6), and vigorous (> 6.0 Mets: level 7 – 9), and were reported as the time spent in each activity level. The time spent in sedentary behavior was calculated as the time of sedentary or sleep (< 1.5 Mets: level 0 – 0.5) minus the sleep time assessed by the validated questionnaire (The Japanese version of the Pittsburgh Sleep Quality Index). Also, the moderate and vigorous physical activity time were combined to form the time spent in MVPA.

Renal function

Estimated glomerular filtration rate (eGFR) was calculated by the Japanese eGFR equations based on standardized serum creatinine or cystatin C as follows: $eGFR_{cr}$ (mL/min/1.73 m²) = $194 \times \text{serum creatinine}^{-1.094} \times \text{Age}^{-0.287} \times 0.739$ (if female), $eGFR_{cys}$ (mL/min/1.73 m²) = $\{104 \times \text{serum cystatin C}^{-1.019} \times 0.996^{\text{Age}} \times 0.929$ (if female) $\} - 8$ [17, 18]. To improve estimated accuracy, the average values of $eGFR_{cr}$ and $eGFR_{cys}$ were used as the index of renal function.

Covariates

Brachial systolic and diastolic blood pressure and heart rate were simultaneously measured using semi-automatic vascular testing device with electrocardiogram and oscillometric extremities cuffs (form PWV/ABI, Colin Medical technology, Japan). Fasting blood samples were collected in the morning following a more than 12-hour overnight fasting to measure serum or plasma concentrations of high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglyceride, glucose, creatinine, and cystatin C.

Statistical analysis

All statistical analyses were performed using SPSS Statistics 25.0 (IBM Corp., Tokyo, Japan). Data were presented as the means \pm SD (for normal distribution), median with interquartile range (for skewed distribution), or frequency counts (for categorical data), as appropriate. Univariate linear associations of sedentary behavior, LPA, and MVPA with eGFR were examined using Spearman's rank correlation coefficients (r_s). Joint associations of sedentary behavior, LPA, and MVPA (four groups stratified according to each median value: higher sedentary behavior/higher physical activity, higher sedentary behavior/lower physical activity, lower sedentary behavior/higher physical activity, lower sedentary behavior/lower physical activity) with eGFR were examined using two-way analysis of co-variance (ANCOVA) to adjust for total waking time and covariates including age, sex, body mass index, systolic blood pressure, heart rate, HDL cholesterol, LDL cholesterol, triglycerides, fasting blood glucose, antihypertensive medicine, lipid-lowering medicine, hypoglycemic medicine, and current smoking. Independent associations of the exposure variables (sedentary behavior, LPA, and MVPA) with the outcome variable (eGFR) were assessed using three multiple linear regression models including a single factor model, partition model, and isothermal substitution model. For enhanced interpretability of the results, the exposure variables (sedentary behavior, LPA, and MVPA) were scaled to 30 min/day units, respectively [13]. Briefly, the single factor models evaluated separately the associations between each exposure variable and eGFR, with adjustment for total waking time and covariates (Model 1 – 3). The partition model evaluated simultaneously the associations between all exposure variables and eGFR, with adjustment for covariates, but without adjusting for total waking time (Model 4). The isothermal substitution models estimated the substitution associations between replacing one exposure variable with an equal amount of time in another exposure variable (e.g., replacement of 30 min/day of sedentary behavior with 30 min/day of MVPA) and GFR_{average} (Model 5 – 7). This estimation can be accomplished by omitting replacing target exposure variable from the model and entering total waking time and covariates. A more detailed description of these regression models is presented elsewhere [9].

Results

Characteristics of the participants are shown in Table 1. The mean age was 64 ± 7 years and most of the participants were women (76%). On average, the majority of total waking time (1056 ± 61 min/day) was spent in sedentary behavior (970 ± 64 min/day), with 67 ± 25 min of LPA and 19 ± 14 min of MVPA per day. The mean values of eGFR were 85 ± 14 mL/min/1.73 m², and a small number of participants ($n = 6$) were less than 60 mL/min/1.73 m². Several participants were taking medications, including an antihypertensive agent (20%), lipid-lowering agent (10%), and/or hypoglycemic agent (1%).

Table 1
 Characteristics of selected participants (n = 174)

Variables	Total		
Age, years	64	±	7
Women, n (%)	132 (76)		
Height, cm	158	±	7
Weight, kg	57.1	±	9.1
Body mass index, kg/m ²	22.9	±	2.9
Sleep time, min/day	365 [360–420]		
Total waking time, min/day	1075 [1020–1080]		
Sedentary behavior, min/day	970	±	64
Light-intensity physical activity, min/day	64 [50–84]		
Moderate- to vigorous-intensity physical activity, min/day	16 [9–25]		
Systolic blood pressure, mmHg	122 [113–132]		
Diastolic blood pressure, mmHg	75	±	9
Heart rate, bpm	61 [56–66]		
High-density lipoprotein cholesterol, mg/dL	64	±	14
Low-density lipoprotein cholesterol, mg/dL	132	±	29
Triglyceride, mg/dL	82 [59–110]		
Fasting blood glucose, mg/dL	91 [86–96]		
eGFR, mL/min/1.73 m ²	85	±	14
Antihypertensive medicine, n (%)	20 (11)		
Lipid-lowering medicine, n (%)	10 (6)		
Hypoglycemic medicine, n (%)	1 (1)		
Current smoking, n (%)	3 (2)		
Data are presented as the means ± SD, median [interquartile range], or frequency counts (%), as appropriate. eGFR, average value of estimated glomerular filtration rate calculated from serum creatinine or cystatin C.			

The results of univariate linear analyses are presented in Fig. 2. The time spent in sedentary behavior was significantly and negatively, albeit weakly, correlated with eGFR ($r_s = -0.229$, $p < 0.05$). The time spent in LPA and MVPA were significantly and positively correlated with eGFR ($r_s = 0.265$, $p < 0.001$, $r_s = 0.353$, $p < 0.001$, respectively).

Figure 3 shows the joint associations of sedentary behavior, LPA and MVPA (four groups stratified according to each median value) with eGFR. Although there was no statistically significant interaction between sedentary behavior and LPA ($p = 0.184$) or MVPA ($p = 0.834$) in their association with eGFR, the mean values of eGFR were lowest in those with higher sedentary behavior and lower LPA (81.1 [95% CI: 76.9, 85.3] mL/min/1.73 m²) or MVPA (79.3 [95% CI: 74.9, 83.7] mL/min/1.73 m²), respectively.

The results from three multiple linear regression models with adjusting for covariates are summarized in Table 2. The single factor models (Model 1–3) showed that sedentary behavior was significantly and negatively associated with eGFR ($\beta = -3.31$, $p < 0.001$), conversely, both LPA and MVPA were significantly and positively associated with eGFR ($\beta = 3.61$, $p < 0.05$, $\beta = 7.07$, $p < 0.05$, respectively). The partition model (Model 4) showed that only MVPA was significantly associated with eGFR ($\beta = 4.71$, $p < 0.05$). The isotemporal substitution models (Model 5–7) showed that replacement of 30 min/day of sedentary behavior with equivalent LPA time was not significantly associated with eGFR ($\beta = 2.25$, $p = 0.111$), however, replacement with the same amount of MVPA was modestly but significantly associated with the eGFR ($\beta = 5.51$, $p < 0.05$). Replacement of 30 min/day of LPA with equivalent MVPA time was not significantly associated with eGFR ($\beta = 3.25$, $p = 0.312$).

Table 2
Single factor, partition, and isotemporal substitution models for renal function evaluated by eGFR

Models	Sedentary behavior			LPA		MVPA			R-Square	
	β	(95% CI)	β	(95% CI)	β	(95% CI)
Single factor model ^{a,b}	1	-	(- 5.17, - 1.45)**						0.262**	
	2			3.61	(1.05, 6.18)*			0.242**	
	3						7.07	(2.81, 11.33)*	0.255**
Partition model ^a	4	-	(- 1.76, 0.16)	1.45	(- 1.32, 4.23)	4.71	(0.01, 9.40)*	0.267**
	5	Dropped		2.25	(- 0.53, 5.03)	5.51	(0.85, 10.17)*	0.267**
Isotemporal substitution model ^{a,b}	6	-	(- 5.03, 0.53)	Dropped			3.25	(- 3.08, 9.59)	0.267**
	7	-	(- 10.17, 0.85)*	-	(- 9.59, 3.08)	Dropped			0.267**

^aAll models adjusted for age, sex, body mass index, systolic blood pressure, heart rate, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, fasting blood glucose, antihypertensive medicine, lipid-lowering medicine, hypoglycemic medicine, and current smoking. ^bsingle factor and isotemporal substitution models were also adjusted for total waking time. Regression coefficients (β) correspond to a 30 min/day of each behavior. ** $p < 0.001$, * $p < 0.05$. LPA, light-intensity physical activity; MVPA, moderate-to vigorous-intensity physical activity.

Discussion

In this cross-sectional study of middle-aged and older adults, we examined the associations of accelerometer-derived sedentary behavior and physical activity with renal function and potential renal impacts of replacing sedentary behavior with the different intensities of physical activity. Time spent in sedentary behavior, LPA, and MVPA were significantly associated with eGFR. Furthermore, isotemporal substitution modelling showed that replacement of 30 min/day of sedentary behavior with equivalent MVPA time was significantly associated with the better eGFR. These findings suggest that both sedentary behavior (detrimentally) and physical activity (beneficially) may be contributing factors to maintaining renal function, and replacing sedentary behavior with physical activity (MVPA) may benefit renal health in middle-aged and older adults.

Several previous studies have reported the associations of sedentary behavior and physical activity with renal function [7, 8, 19–25]. However, only a few studies have used accelerometer-derived measures of sedentary behavior and physical activity [19, 20, 23], most studies have relied on self-reported measures derived from questionnaires which may be limited in quantifying the degree of behavior. In addition, there is no study examining the potential impacts of replacing sedentary behavior with physical activity on renal function using the isotemporal substitution modelling. To our knowledge, this is the first study to examine the associations of accelerometer-derived sedentary behavior and physical activity with renal function using the isotemporal substitution modelling in Japanese adults who have been reported to have the highest sitting times (medians ≥ 360 min/day) [26].

This study has also shown the mean values of eGFR were lowest in those with higher sedentary behavior and lower physical activity (LPA and MVPA). However, there was no statistically significant interaction between sedentary behavior and physical activity with respect to the association with the eGFR. This is because the influences of physical activity, especially MVPA on eGFR might be apparently stronger than those of sedentary behavior. Univariate analyses also showed that the associations between MVPA and eGFR ($r_s = 0.353$) were stronger than those of sedentary behavior ($r_s = 0.229$). Therefore, the combination of higher sedentary behavior and lower physical activity are likely to be strongest with respect to having a lower renal function; however, the MVPA emerged as potentially having a more significant influence on renal function than did sedentary behavior.

Beneficial effects of regularly performed physical activity (i.e., exercise training) on several medical conditions have been demonstrated in the general population and in patients with CKD. The Kidney Disease: Improving Global Outcomes (KDIGO) guideline mainly intends to maintain and improve cardiovascular health and tolerance and recommends that patients with CKD should undertake moderate physical activity for at least 30 min five times per week in line with recommendations for the general population [27]. Furthermore, recent meta-analyses have also shown the possibility that exercise training slightly improves eGFR in patients with CKD [28, 29]. However, the beneficial effects of exercise training on renal function are not likely to be conclusive and remain controversial due to a limited small number of studies in both meta-analyses. We estimated the potential impacts of specific behavior change on renal function using isothermal substitution modelling and revealed that replacement of 30 min/day of sedentary behavior with equivalent physical activity (MVPA) was significantly associated with the better eGFR (+ 5.51 [95% CI: 0.85, 10.17] mL/min/1.73 m²). This finding supports and expands on the results of several previous interventional studies and the KDIGO recommendation of physical activity.

The strengths of this study are the use of accelerometers to objectively assess each behavior, and the clinically interpretable results obtained from the isothermal substitution modelling. However, there are several limitations. First, the nature of cross-sectional investigation limits our ability to judge the precise causal links between sedentary behavior, physical activity, and renal function. We cannot deny the possibility that renal function may be contributing factors to maintaining sedentary behavior and physical activity. Second, the potential renal impacts examined using the isothermal substitution models were estimations, and the actual impacts of specific behavior change on renal function remains unknown. Third, we evaluated only an eGFR as renal function in this study; however, other comprehensive evaluations by several urinary biomarkers such as urinary albumin will be needed. Fourth, a generalization of our findings may be difficult due to the relatively small sample size, a single-center study, and the selective populations (i.e., middle-aged and older Japanese adults). Finally, the reasons for the better renal function when replacing sedentary behavior with physical activity remains equivocal. Considering the findings of previous basic research [30], several mediating factors including anti-oxidant defense and anti-inflammatory environment may be involved in the mechanism underlying the renal benefits of specific behavior change. Further interventional studies, such as randomized controlled trials, examining the effects of moderate- to vigorous-intensity exercise on renal health are needed to address these limitations and provide a more definitive interpretation of the present findings.

Conclusion

Sedentary behavior (detrimentally) and physical activity (LPA and MVPA) (beneficially) were significantly associated with renal function evaluated by eGFR. Findings from isothermal substitution modelling suggest that replacement of 30 min/day of sedentary behavior with equivalent MVPA time may contribute to the better renal function in middle-aged and older adults. These findings provide important preliminary evidence on the potential renal benefits of decreasing sedentary time and increasing physical activity time and include important public health implications.

Abbreviations

LPA: light-intensity physical activity; MVPA: moderate to vigorous-intensity physical activity; eGFR: estimated glomerular filtration rate; CKD: chronic kidney disease; HDL: high-density lipoprotein; LDL: low-density lipoprotein; KDIGO: Kidney Disease: Improving Global Outcomes

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee in University of Tsukuba (Tai 019-19) and conformed to the principles outlined in the Declaration of Helsinki, and all participants provided written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to the ongoing nature of this study but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

K.K., A.S., K.O., and S.M.: research conception; K.K., K.Tanahashi., M.M., N.A., and Y.O: data acquisition/analysis; K.K., K.Tanaka., D.D., N.O., A.S., K.O., and S.M.: data interpretation; K.K.: statistical analysis; D.D., N.O., K.O., and S.M: supervision or mentorship.

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Figures

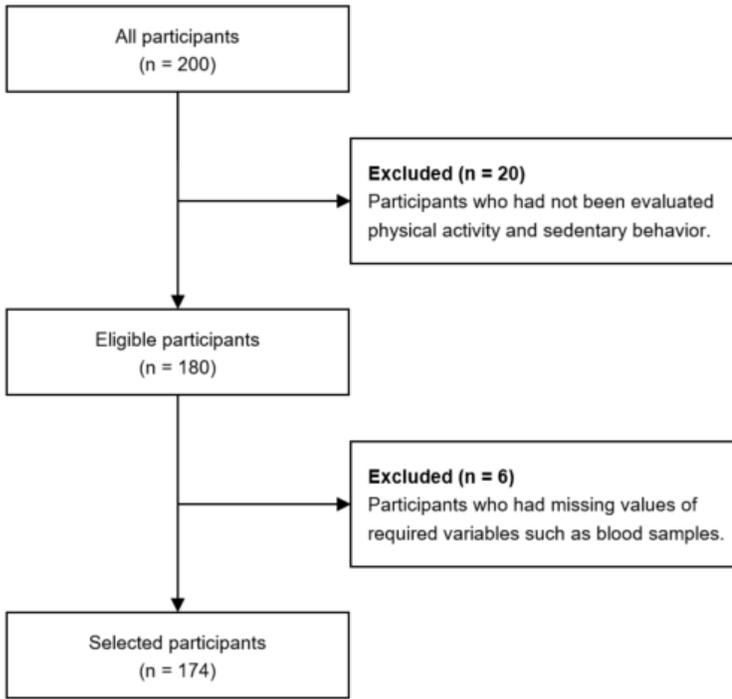


Figure 1

Flow diagram.

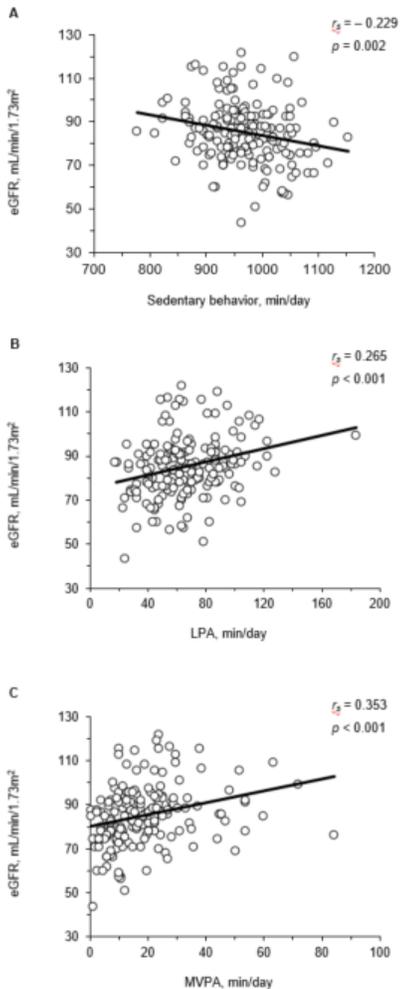


Figure 2

Univariate associations between sedentary behavior (A), light-intensity physical activity (LPA) (B), moderate-to vigorous-intensity physical activity (MVPA) (C) and estimated glomerular filtration rate (eGFR).

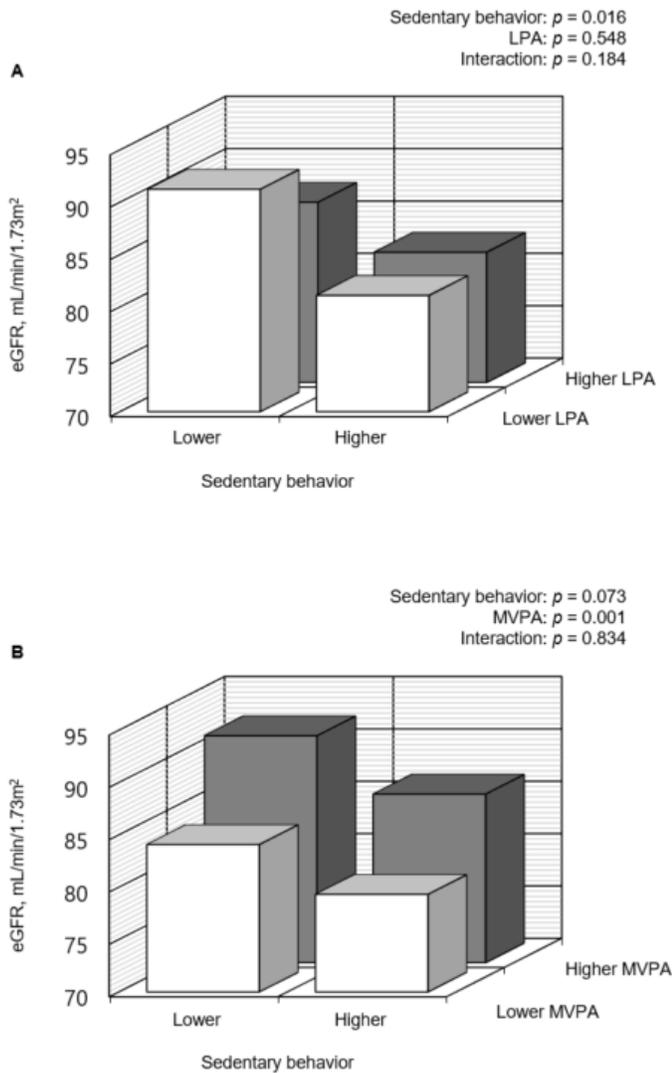


Figure 3

Associations of joint categories (four groups stratified according to each median value) of sedentary behavior, light-intensity physical activity (LPA) (A) and moderate-to vigorous-intensity physical activity (MVPA) (B) with estimated glomerular filtration rate (eGFR). p-values were evaluated using two-way ANCOVA after adjusted for age, sex, body mass index, systolic blood pressure, heart rate, HDL cholesterol, LDL cholesterol, triglyceride, fasting blood glucose, antihypertensive medicine, lipid-lowering medicine, hypoglycemic medicine, current smoking, and total waking time.