Gait speed and handgrip strength as predictors of all-cause mortality and cardiovascular events in hemodialysis patient

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Abstract

Background Low physical performance in patients undergoing maintenance hemodialysis is associated with a high mortality rate. We investigated the clinical relevance of gait speed and handgrip strength, the two most commonly used methods to assess physical performance.

Methods We obtained data regarding gait speed and handgrip strength from 277 hemodialysis patients and evaluated their relationship with baseline parameters, mental health, plasma inflammatory markers, and major adverse clinical outcomes. Low physical performance was defined by the recommendations suggested by the Asian Working Group on Sarcopenia.

Results The prevalence of low gait speed and handgrip strength were 28.2% and 44.8%, respectively. Old age, low serum albumin levels, high comorbidity index, and impaired cognitive functions were associated with low physical performance. Patients with isolated low gait speed exhibited a general trend for worse quality of life than those with isolated low handgrip strength. Gait speed and handgrip strength showed very weak correlations with had different determinant factors (older age, the presence of diabetes, and lower serum albumin for low gait speed, and lower body mass index, and the presence of previous cardiovascular events for low handgrip strength). Patients with low gait speed and handgrip strength had elevated levels of plasma endocan and matrix metalloproteinase-7 and the highest risk of all-cause mortality and cardiovascular events among the groups (adjusted hazard ratio of 2.72, $p = 0.024$).

Conclusion Gait speed and handgrip strength reflected distinctive aspects of patient characteristics and that their combination improved the prediction of adverse clinical outcomes in hemodialysis patients. Gait speed seems to be a better indicator for poor patient outcomes compared with handgrip strength.

Background

The increasing prevalence of end-stage renal disease (ESRD) is a major public health problem in most developed countries, including South Korea [1, 2]. Despite remarkable advances in dialysis modality and patient care, the mortality rate of ESRD patients is still exceedingly high compared with that of the general population [3]. Well-established risk factors for major adverse events associated with ESRD include old age, preexisting cardiovascular disease, the presence of diabetes, and underdialysis [4-10]. Nonetheless, hemodialysis patients exhibit high interindividual variability, and it is frequently difficult to predict the clinical course accurately on an individual level. The identification and management of potential risk factors is of particular importance because individualized therapeutic interventions might improve the clinical outcomes of ESRD patients.

Sarcopenia is defined as quantitative and qualitative loss of skeletal muscle that is frequently linked to adverse effects in patients [11]. Uremic toxins in chronic kidney disease (CKD) patients are often associated with not only the chronic catabolic state of inflammation, oxidative stress, and nutritional imbalance but also a high prevalence of cardiovascular events, both of which eventually lead to clinically evident sarcopenia. Recent studies have highlighted that reduced physical performance is independently

associated with poor patient survival as well as low quality of life among CKD patients [12, 13], indicating the importance of physical activity in risk stratification among these patients. Currently, however, the optimal method to assess physical performance in these populations has not yet been defined.

Measurements of gait speed (GS) and handgrip strength (HS) were used as reliable tests to determine the functions of skeletal muscle [14, 15]. Both tests are simple, rapid, inexpensive, and can be performed in the geriatric population [16]. Accumulating evidence suggests that these parameters are useful for predicting outcomes in CKD [17-19] and ESRD patients [20-24]. Nonetheless, both tests have several limitations, such as a nonstandardized protocol or intraindividual variability. Moreover, performing either test may result in the misinterpretation of the performance status because dialysis patients frequently exhibit isolated problems in their upper or lower extremities but not the other parts of their body. Therefore, it can be speculated that combining these two simple tests may compensate for the shortcomings of each test individually. The aim of this study was to determine whether GS and HS have distinctive clinical relevance and whether combining these tests could offer a better indicator of patient outcomes than performing a single test.

Methods

Participant and study design

This study was performed using the data obtained from a prospective cohort study that enrolled 460 hemodialysis patients in six hospitals between June 2016 and January 2018 (CRIS no. KCT0003281). After excluding 183 patients who did not perform GS or HS tests, a total of 277 patients were finally enrolled in this study. We subsequently classified the enrolled patients into 4 groups based on their physical performance: normal GS and HS (n=119, 43.0%), normal GS and low HS (n=80, 28.9%), low GS and normal HS (n=34, 12.3%), and low GS and HS (n=44, 15.9%). Baseline demographics and clinical parameters, including the Charlson [25] and Liu [26] comorbidity indexes, were obtained at the time of study entry. All patients were monitored for major adverse events composed of all-cause mortality and cardiovascular events including acute coronary syndrome, symptomatic heart failure, cerebral infarction and hemorrhage, and peripheral arterial disease until June 2019.

Measurements of gait speed and handgrip strength

Baseline GS and HS were measured before dialysis therapy on a treatment day within one month of patient enrollment. GS was assessed by measuring the walking speed over a 4-m course at the participant's usual pace. The test was repeated three times, and the average speed was calculated. HS was measured by a Jamar hand dynamometer (Sammons Preston Inc., Bolingbrook, IL) on the dominant hand unless contraindicated. Each measurement was repeated three times, and the highest value was noted. Based on the suggestions by the Asian Working Group for Sarcopenia [27], low GS was defined as less than 0.8 m/s, and low HS was defined as less than 26 kg for men and less than 18 kg for women.

Questionnaires related to physical performance and mental health

Patients were asked to complete three kinds of questionnaires at the time of initial enrollment: the Korean version of the mini-mental status examination (K-MMSE) [28], the Beck Depression Inventory (BDI) [29], and the Korean version of the Kidney Disease Quality Of Life-Short Form (KDQOL-SF) [30]. We specifically obtained information regarding 11 ESRD-targeted domains on the KDQOL-SF, and these data were subsequently categorized into three components: physical, mental, and social. The physical components included domains of physical functioning, pain, general health, and energy/fatigue. The mental components included domains of cognitive function, sleep, and emotional well-being. Finally, the social components included work status, quality of social interaction, social support, and social function.

Measurement of plasma inflammatory markers

Plasma samples were collected before the initiation of dialysis and stored at -80°C until analysis. Multiple plasma inflammatory markers were simultaneously measured by multiplex enzyme-linked immunosorbent assay as previously described [31]. We reviewed the previous literature and selected the following candidate inflammatory markers: a proliferation-inducing ligand, B-cell activating factor, CXCL16, endocan, endostatin, follistatin, IL-6, IL-25, IL-18, monocyte chemoattractant protein-1, MCP-2, MCP-4, matrix metalloproteinase-7 (MMP-7), MMP-8, osteoprotegerin, PCSK9, receptor activator of nuclear factor-κB ligand, and tumor necrosis factor-α (TNF-α).

Statistical analysis

All statistical analyses were performed with SPSS for Windows, version 20.0 (SPSS, Chicago, IL). Baseline characteristics and clinical parameters are expressed as the mean ± standard deviation or as the numbers of patients and percentages. Analysis of variance with Bonferroni post hoc analysis, chi-square test, and Fisher's exact test were used to compare these variables, as appropriate. We used Pearson's correlation analyses to determine the relationship between GS and HS. Multiple logistic regression analysis was used to determine the risk factors for low GS and HS. Levels of plasma inflammatory markers are expressed as box-and-whisker plots, and their comparisons were made by Analysis of variance with Bonferroni post hoc analysis. Finally, Kaplan-Meier curves were generated to assess the probabilities of the patient outcomes according to the results of GS and HS, and the Cox proportional hazards model was used for further multivariate adjustments with possible confounders including age, sex, previous history of cardiovascular disease, and serum albumin levels. *p* values under 0.05 were considered to indicate statistical significance.

Result

Baseline clinical characteristics of patients

The baseline demographics and laboratory parameters of patients according to physical performance status are shown in **Table 1**. The prevalence rates of low GS and HS were 78 (28.2%) and 124 (44.8%), respectively. Patients with low GS and HS were older and had a lower body mass index and a shorter duration of dialysis than those in the other groups. The prevalence of previous cardiovascular events and

diabetes was also higher in these patients. The predialysis serum albumin and creatinine levels were significantly lower in patients with poor physical performance, while spKt/V was inversely correlated with GS and HS. Mid-arm muscle circumference (MAMC) was positively correlated with GS and HS, although the statistical significance was marginal. Finally, higher prescription rate of statins was observed in patients with low GS than in those with normal GS.

Association between physical performance, comorbidity index, and mental health

We performed correlation analysis to determine the relationship between GS and HS and found that the two parameters were significantly correlated with each other, but the correlation coefficient was weak (R^2 = 0.070 and $p < 0.001$; **Figure 1**). We next evaluated the relationship between physical performance, comorbidity indexes, and mental health. As shown in **Table 2**, GS and HS were significantly associated with comorbidity scores and poor physical status (Charlson comorbidity scores of 3.4±1.2 vs. 4.0±1.5 vs. 4.4±1.3 vs. 4.7±1.2 and Liu comorbidity scores of 3.9±2.1 vs. 4.6±2.8 vs. 5.1±2.4 vs. 6.1±2.7 for the normal GS and HS, normal GS and low HS, low GS and normal HS, and low GS and HS groups, respectively; $p < 0.001$ for both comparisons). In addition, patients with low GS and HS showed profoundly impaired cognitive functions as assessed by the MMSE and the KDQOL-SF (27.4±2.7, 25.8±4.2, 26.4±3.6, and 25.2±4.8; and 86.1±14.3, 80.8±18.0, 73.3±23.8, and 73.5±22.1 for the normal GS and HS, normal GS and low HS, low GS and normal HS, and low GS and HS groups; $p = 0.010$ and 0.001, respectively). The social activity index was relatively maintained in the low GS and HS group. Notably, the comorbidity scores, depression index, and the quality of life scores were mostly worse in patients with low GS and normal HS compared to those with normal GS and low HS, although statistical significance was only observed in physical functioning status.

Risk factors for low gait speed and poor handgrip strength

Logistic regression analysis was performed to identify the determining factors of poor physical performance (**Table 3**). Older age was the only common risk factor for both low GS (adjusted odds ratio [OR] of 1.51, 95% confidence interval [CI] of 1.20 – 1.91; $p < 0.001$) and HS (adjusted OR of 1.30, 95% CI of 1.07 – 1.57; $p = 0.008$). The presence of diabetes and low serum albumin levels were risk factors for low GS (adjusted OR of 2.12, 95% CI of 1.16 – 43.86 and adjusted OR of 3.37, 95% CI of 1.32 – 8.62, respectively) but not for HS. On the other hand, low HS, but not low GS, was significantly associated with low body mass index (adjusted OR of 0.92, 95% CI of 0.86 – 0.99; $p = 0.022$) and a previous history of cardiovascular events (adjusted OR of 1.73, 95% CI of 1.02 – 2.95; $p = 0.043$).

The relationship between plasma inflammatory markers and physical performance

We next measured various plasma inflammatory markers and compared their levels across groups. Among measued cytokines and chemokines, the levels of plasma endocan and MMP-7 were significantly higher in patients with low GS and HS than in those with normal GS and HS (**Figure 2A and B**). In contrast, levels of traditional inflammatory markers, including TNF-α, IL-6, and high sensitivity C-reactive protein (hs-CRP), were not associated with physical performance (**Figure 2C-E**).

Impact of gait speed and handgrip strength on all-cause mortality and cardiovascular events

The mean duration of follow-up since the recruitment of patients was 25.3 months, and a total of 19 deaths (6.9%) and 30 (10.8%) cardiovascular events occurred during this period. Patients with low GS and HS showed the highest cumulative incidence rate for major adverse events (11.8%, 15.0%, 17.6%, and 29.5% for the normal GS and HS, normal GS and low HS, low GS and normal HS, and low GS and HS groups, respectively, p = 0.004 for overall comparisons; **Figure 3**).

The observed hazard ratios (HRs) for major adverse events are shown in **Table 4**. Multivariate Cox regression analysis revealed that patients with low GS and HS had the highest risk for major adverse events (adjusted HR of 2.72, 95% CI of 1.14 – 6.46; p = 0.024) compared to the risks of those with normal GS and HS after multivariate adjustments of possible confounders. Patients with normal HS but low GS also exhibited an increasing trends in the major adverse events (adjusted HR of 2.38, 95% CI of 0.86 – 6.53; p = 0.084). In contrast, isolated low HS was not related to increased risk for adverse outcomes, although the adjusted HRs were slightly elevated. There was a significant interaction between GS and HS for the major adverse events (p = 0.019).

Discussion

Although sarcopenia was originally described as an age-related structural and functional decline in skeletal muscle, recent investigations have consistently acknowledged that decreased kidney function is also involved in sustained muscle wasting and the subsequent development of sarcopenia. Compared to the elderly population, in which the prevalence of sarcopenia is 11% [32], CKD patients are likely to be much more prone to its occurrence, with an estimated prevalence of 30 - 60% [20, 21, 24, 33-35]. The two main components of sarcopenia, muscle strength and mass, which are dissociated in the settings of ESRD and the functional aspects of skeletal muscle, are more important than muscle mass in terms of patient outcomes [20, 34]. In this regard, we extensively investigated the effects of skeletal muscle dysfunction on major adverse events in hemodialysis patients. Our findings suggest that GS and HS represent different aspects of patient characteristics and that their combination could identify those at the highest risk for mortality and cardiovascular events. Of note, MAMC showed a tendency to decrease in patients with low physical performance but was not related to either clinical outcome (data not shown). Together, our data support the idea that the functional assessment of skeletal muscle is more important than its quantitative assessment and measuring GS and HS is a suitable method for the evaluation of skeletal muscle function in hemodialysis patients.

We noticed that spKt/V, currently used as a standard method for the assessment of dialysis adequacy, was highest in patients with low GS and HS and lowest in patients with normal GS and HS (**Table 1**). The inverse relationship between Kt/V and physical performance was consistently shown in other studies [24, 33, 35, 36], suggesting that this relationship is likely to be a universal phenomenon. We speculate that the low muscle mass and subsequent decreased volume of distribution of urea in the body (V) in patients with low GS and HS resulted in a relative increase in the value of Kt/V without affecting the true dialysis

efficacy [37]. Therefore, sarcopenic patients may be underdialyzed if their dialysis time and dialyzer filter are selected solely based on the levels of Kt/V. Further study is warranted to define the optimal target of Kt/V in dialysis patients based on the severity of sarcopenia.

Although both GS and HS represent the physical performance of dialysis patients, we found that a substantial portion of patients exhibited low performance in one test while demonstrating normal performance in the other (114/277, 41.2%). Moreover, the correlation coefficient between GS and HS was very weak despite its statistical significance, suggesting that the contributing factors of these two conditions might be different. We consider that this finding is at least in part due to the differences in the involved muscles and neurologic systems during the execution of the HS and GS tests. In accordance with our data, Roshanravan *et al*. showed a discrepancy in upper and lower muscle strength in a nondialysis CKD cohort study [19]. Thus, these data provide a rationale that the combination of the GS and HS tests could integrate the different components of patient information, thereby allowing us to predict future outcomes better.

Despite the fact that the clinical relevance of GS and HS as predictors of mortality and cardiovascular outcomes was documented in previous studies, direct comparisons between these two tests have not been performed so far. Interestingly, patients with isolated low GS had a tendency to exhibit worse comorbidity indexes and physical functions than those with isolated low HS (**Table 2**). Furthermore, GS was significantly superior than HS for the prediction of all-cause mortality in the analysis of our cohort, implying that the muscle function of the lower extremities might be more important than that of the upper extremities in terms of patient outcomes. Several recent studies also revealed that skeletal muscle function in the lower extremities, but not in the upper extremities, was associated with overall physical performance and hospitalization rate [38, 39], emphasizing the clinical importance of lower extremity performance. Moreover, the GS test was still valuable because low GS was associated with increased HRs of death and cardiovascular mortality regardless of HS (**Figure 3 and Table 4**).

We identified that endocan and MMP-7 were elevated in patients with low GS and HS. Endocan is a water-soluble proteoglycan consisting of amino acid polymers and a single dermatan sulfate chain [40]. Plasma endocan is known to exclusively originate from the vascular endothelium, and its levels reflect endothelial activation and systemic inflammation. Several previous studies have demonstrated the clinical values of plasma endocan in the prediction of cardiovascular mortality as well as the progression of kidney diseases [41-44]. It should be confirmed whether elevated levels of plasma endocan resulted from sarcopenia itself or from other confounding factors, such as vascular injuries or infection [45, 46]. MMP-7 is an endopeptidase that belongs to a member of the MMP family. In addition to its basic functions in cleaving extracellular matrix substrates, MMP-7 is also involved in the development of local and systemic inflammation [47-49]. Although MMP-2 and MMP-9 seem to play major roles in the degradation of the extracellular matrix that leads to muscle wasting, the pathophysiological relevance of MMP-7 in the development and progression of sarcopenia is still mostly unknown. Increased MMP-7 activity is observed in a hereditary form of muscular dystrophy [50], suggesting that the upregulated MMP-7 might have detrimental effects on skeletal muscle. In contrast, with a previous report [20], the

levels of hs-CRP, IL-6, and TNF-α were not elevated in sarcopenic patients in our study. We speculate that these inconsistent findings were attributed to the differences in the degree of overall inflammation; the absolute concentrations of hs-CRP and IL-6 were lower and the levels of serum albumin were higher in patients in our study than in those in the previous study [20].

The limitations of this study should be mentioned. There is a concern about selection bias because patients who were incapable of performing the GS and/or HS tests were excluded from our study. Indeed, a previous study reported that dialysis patients who could not complete a walking test showed the highest comorbidity index and worst survival rate, even when compared to those who could walk very slowly (< 0.6 m/s) [21]. We could not analyze the excluded patients since we could not distinguish between patients who simply refused to perform the tests and those who were unable to participate in the tests. Finally, we could not determine the possible mechanisms underlying the association between low physical performance and high mortality. We speculate that chronic sustained inflammation might be an essential mediator that contributes to both phenomena (**Figure 3**). This hypothesis should be explored in further studies.

Conclusion

We demonstrated that poor physical performance, assessed by GS and HS, was significantly associated with high all-cause mortality and cardiovascular diseases in hemodialysis patients. GS and HS seemed to capture different sets of skeletal muscle function, neurological impairments, and malnutrition that develop in ESRD patients. Given that the measurements of GS and HS are relatively easy to perform, the combination of these two tests would provide clinicians opportunities for better patient assessment and individualized care.

Abbreviations

ESRD, end-stage renal disease

CKD, chronic kidney disease

GS, gait speed

HS, handgrip strength

K-MMSE, Korean version of the mini-mental status examination

BDI, Beck Depression Inventory

KDQOL-SF, Kidney Disease Quality Of Life-Short Form

MMP, matrix metalloproteinase

TNF, tumor necrosis factor

MAMC, Mid-arm muscle circumference

OR, odds ratio

CI, confidence interval

hs-CRP, high sensitivity C-reactive protein

HR, hazard ratio

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki, and the Institutional Review Board of each participating center approved the study protocol (KHNMC IRB No. 2016-04-039, Kyung Hee University at Gangdong). Written informed consent was obtained from all patients.

Consent for publication

Not applicable.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

We declare no conflict of interest.

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Author's contributions

YHL and JSK drafted the article, performed the analysis and interpretation of the data. SWJ, HSH, JYM, KHJ, SHL, DHY, GJK, DYL, and HJL were responsible for the analysis and interpretation of the work. YGK was responsible for the study concept and design, analysis and interpretation of the data. All authors have read and approved the manuscript

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Tables

Table 1. Baseline characteristics and clinical parameters of enrolled patients according to gait speed and handgrip strength.

	Normal GS and HS (n=119)	Normal GS and low HS (n=80)	Low GS and normal HS (n=34)	Low GS and HS (n=44)	*p* value
(year)	58.6±14.3	61.5±11.1	63.7±10.3	68.6±12.0	<0.001[c,e]
(male, %)	75 (63.0)	61 (76.2)	19 (55.9)	28 (63.6)	0.118
I (kg/m^2)	23.2±4.2	22.5±3.3	24.5±4.5	22.1±3.2	0.024[e]
e on dialysis (year)	4.4±5.3	5.7±6.8	3.0±5.6	2.7±3.1	0.017[e]
vious cardiovascular nts (n, %)	26 (21.8)	28 (35.0)	11 (32.4)	19 (43.2)	0.039[a,c]
betes mellitus (n, %)	55 (46.2)	44 (55.0)	23 (67.6)	31 (70.5)	0.017[b,c]
HD SBP (mmHg)	141±20	142±25	143±19	140±21	0.949
ess type (n, %)					
riovenous fistula	101 (84.9)	61 (76.2)	24 (70.6)	36 (81.8)	0.343
riovenous graft	15 (12.6)	16 (20.0)	10 (29..4)	6 (13.6)	
neter	3 (2.5)	3 (3.8)	0 (0)	2 (4.5)	
gle-pool Kt/V	1.54±0.29	1.59±0.26	1.57±0.29	1.68±0.27	0.039[c]
noglobin (g/dL)	10.6±1.3	10.4±1.3	10.6±1.2	10.2±1.3	0.417
umin (g/dL)	3.9±0.3	3.9±0.3	3.8±0.4	3.7±0.3	0.002[c,e]
HD BUN (mg/dL)	62.8±17.8	58.4±13.9	55.9±17.7	54.5±23.1	0.027[c]
HD creatinine (mg/dL)	9.7±3.1	9.4±2.2	8.1±2.8	7.5±2.6	<0.001[b,c,e]
(mg/dL)	8.5±0.8	8.7±0.8	8.3±0.7	8.7±0.9	0.037[d]
ng/dL)	5.0±1.4	4.7±1.2	4.7±1.4	4.4±1.6	0.153
ct PTH (pg/mL)	241±190	254±211	220±151	168±153	0.084
al CO2 (mEq/L)	22.5±3.0	23.3±3.1	22.6±2.9	23.3±2.9	0.246
microglobulin (mg/L)	25.2±8.6	24.4±7.4	21.4±7.3	25.1±9.3	0.142
al cholesterol (mg/dL)	143±29	132±28	145±32	141±31	0.019[e]
cholesterol (mg/dL)	78±24	73±25	75±26	85±28	0.095
cholesterol (mg/dL)	45±15	45±12	45±16	45±13	1.000
speed* (m/s)	1.14±0.24	1.09±0.18	0.66±0.13	0.62±0.13	<0.001[b,c,d,e]
dgrip strength* (kg)					
e	31.9±9.2	19.4±4.2	26.3±13.6	18.9±4.9	<0.001[a,b,c,d,f]
nale	21.4±9.6	14.2±2.1	18.4±6.1	13.7±2.2	<0.001[a,c]
MC† (cm)	23.3±3.4	22.5±4.4	22.3±2.5	21.6±3.5	0.074
-hypertensive lication (n, %)					
in-angiotensin system ker	67 (56.3)	42 (52.5)	23 (67.6)	25 (56.8)	0.524
cium channel blocker	74 (62.2)	44 (55.0)	21 (61.8)	30 (68.2)	0523
ocker	46 (38.7)	30 (37.5)	19 (55.9)	20 (45.5)	0.250
G-CoA reductase bitor	51 (42.9)	31 (38.8)	21 (61.8)	27 (61.4)	0.022[c,d,e]

Abbreviations: GS, gait speed; HS, handgrip strength; BMI, body mass index; HD, hemodialysis; CV, cardiovascular; SBP, systolic blood pressure; BUN, blood urea nitrogen;

PTH, parathyroid hormone; LDL, low-density lipoprotein; HDL, high-density lipoprotein; MAMC, mid-arm muscle circumference.

*Low GS was defined as a gait speed of less than 0.8 m/s, and low HS was defined as < 26 kg for men and < 18kg for women.

†MAMC was calculated by the following: MAMC = Midarm Circumference - (3.14163 X Triceps Skinfold Thickness / 10).

[a]$p<0.05$, Normal GS and HS vs. Normal GS and low HS; [b]$p<0.05$, Normal GS and HS vs. Low GS and normal HS; [c]$p<0.05$, Normal GS and HS vs. Low GS and HS; [d]$p<0.05$, Normal GS and low HS vs. Low GS and normal HS; [e]$p<0.05$, Normal GS and low HS vs. Low GS and HS.

Data are expressed as mean ± standard deviation or the number of patients (percentage).

Table 2. Association between physical performance, comorbidity index, and quality of life.

	Normal GS and HS	Normal GS and low HS	Low GS and normal HS	Low GS and HS	*p* value
n comorbidity	3.4±1.2	4.0±1.5	4.4±1.3	4.7±1.2	<0.001[a,b,c,e]
CI comorbidity	3.9±2.1	4.6±2.8	5.1±2.4	6.1±2.7	<0.001[c,e]
E†	27.4±2.7	25.8±4.2	26.4±3.6	25.2±4.8	0.010[c]
	15.1±9.8	14.5±8.6	17.1±11.3	19.6±10.8	0.061
†					
l components					
l functioning	78.5±17.5	69.0±25.0	54.4±33.0	43.2±26.0	<0.001[b,c,d,e]
	74.5±21.4	73.4±23.3	68.2±27.7	60.5±24.8	0.026[c]
health	38.9±20.1	42.2±22.9	35.7±19.7	26.6±16.1	0.006[c,e]
fatigue	46.8±18.7	45.8±18.7	45.9±17.7	35.5±19.0	0.031[c]
components					
ve function	86.1±14.3	80.8±18.0	73.3±23.8	73.5±22.1	0.001[b,c]
	59.9±18.2	62.0±16.9	57.4±17.2	55.7±17.0	0.359
ıal well-being	58.4±19.5	63.4±18.2	59.6±16.9	52.0±20.2	0.053
omponents					
atus	32.3±38.0	24.2±34.5	27.8±34.9	16.1±27.0	0.136
of social ion	70.8±17.9	70.9±19.6	64.9±24.8	67.3±18.5	0.447
upport	69.4±26.1	72.1±25.0	71.6±24.4	69.4±26.7	0.911
ınction	73.3±25.5	71.6±26.4	65.7±32.3	57.7±24.5	0.030[c]

Abbreviations: GS, gait speed; HS, handgrip strength; K-MMSE, Korean-version of mini-mental state exam; BDI, Beck's depression inventory; KD-QOL, kidney disease quality of life.

*Charlson comorbidity score and 2010 KI comorbidity score are adapted from reference 25 and 26.

†The detailed information regarding the list of questionnaire can be checked in reference 28, 29, and 30.

[a]$p<0.05$, Normal GS and HS vs. Normal GS and low HS; [b]$p<0.05$, Normal GS and HS vs. Low GS and normal HS; [c]$p<0.05$, Normal GS and HS vs. Low GS and HS; [d]$p<0.05$, Normal GS and low HS vs. Low GS and normal HS; [e]$p<0.05$, Normal GS and low HS vs. Low GS and HS.

Table 3. Logistic regression on the determinant factors of low gait speed and low handgrip strength.

	Low gait speed				Low handgrip strength			
	Univariate		Multivariate		Univariate		Multivariate	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age (per 10 years increment)	1.61 (1.28-2.01)	<0.001	1.51 (1.20-1.91)	0.001	1.32 (1.10-1.59)	0.004	1.02 (1.00-1.4)	0.026
Male (vs. female)	1.42 (0.83-2.45)	0.202			0.63 (0.38-1.04)	0.072		
BMI (per 1 kg/m^2 increment)	1.01 (0.95-1.08)	0.702			0.92 (0.86-0.98)	0.014	0.92 (0.86-0.99)	0.022
Time on dialysis (per 1 year increment)	0.91 (0.86-0.98)	0.008	0.94 (0.88-1.01)	0.081	1.02 (0.97-1.06)	0.451		
Diabetes (vs. absent)	2.27 (1.30-3.96)	0.004	2.12 (1.16-43.86)	0.014	1.47 (0.91-2.38)	0.114		
Previous cardiovascular event (vs. absent)	1.68 (0.97-2.92)	0.066			1.91 (1.14-3.21)	0.014	1.73 (1.02-2.95)	0.043
Albumin (per 1 g/dL decrement)	4.90 (2.03-11.83)	<0.001	3.37 (1.32-8.62)	0.011	1.69 (0.79-3.62)	0.177		

Abbreviations; OR, odds ratio; CI, confidence interval; BMI, body mass index; HD, hemodialysis; SBP, systolic blood pressure.

Table 4. Incidence and hazard ratios of cumulative composite event rate based on the physical performance.

	No. of events (%)	*p* for interaction	Adjusted HR* (95% CI)	*p* value
Cumulative composite event rate†				
Normal GS and HS	14 (11.8)	0.019	Reference	-
Normal GS and low HS	12 (15.0)		1.08 (0.49-2.39)	0.843
Low GS and normal HS	6 (17.6)		2.38 (0.86-6.53)	0.084
Low GS and HS	13 (29.5)		2.72 (1.14-6.46)	0.024

* Adjusted by age, sex, previous history of cardiovascular disease, and serum albumin levels.

† Cumulative incidence of all-cause mortality and cardiovascular events

Abbreviations: HR, hazard ratios; CI, confidence interval; GS, gait speed; HS, handgrip strength.

Figures

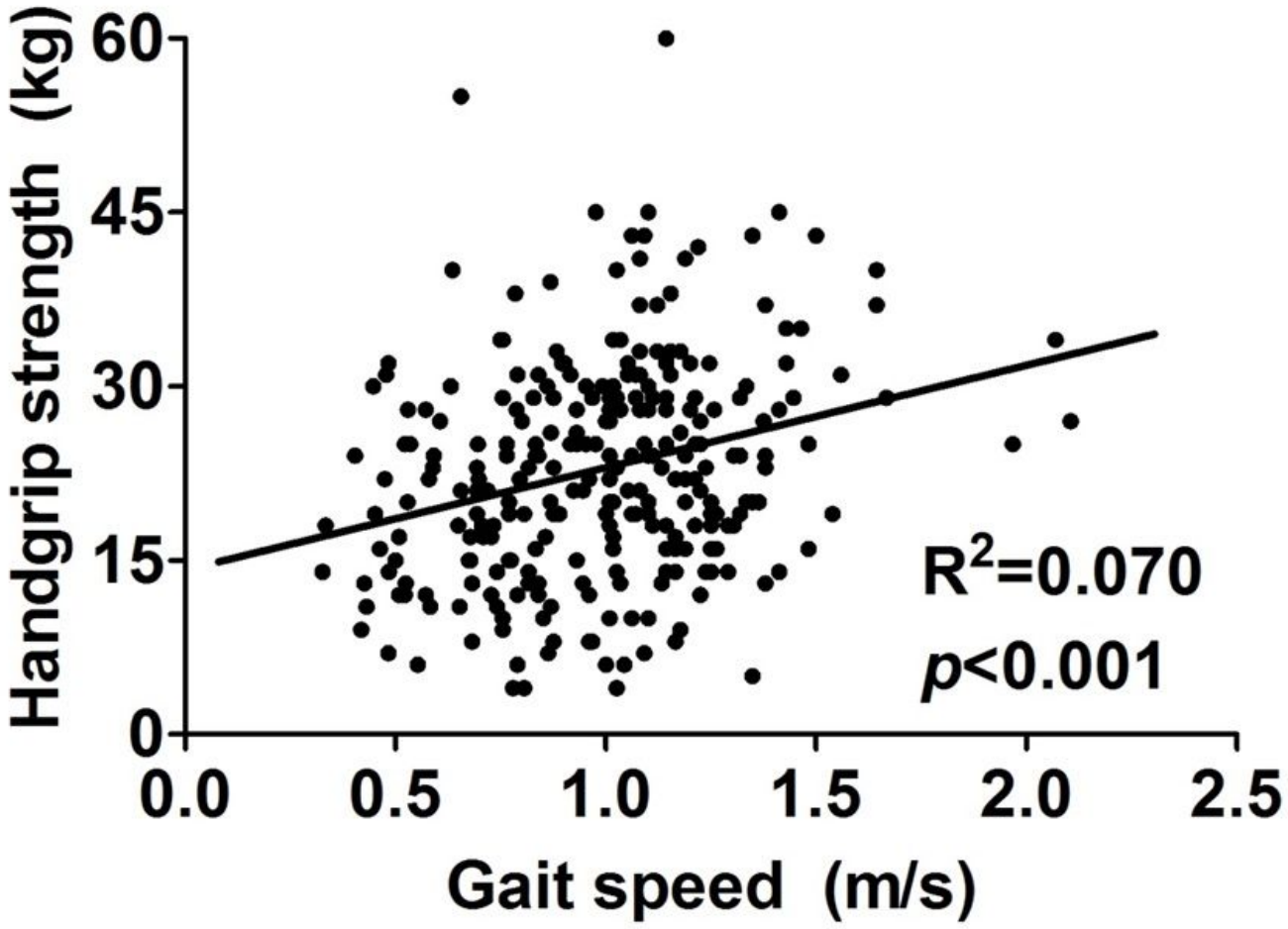

Figure 1

Correlation between gait speed and handgrip strength. hown is the scatter plot displaying the relationship between gait speed and handgrip strength. Although these two parameters were significantly correlated with each other, the correlation coefficient was very weak (R2 = 0.070, p < 0.001).

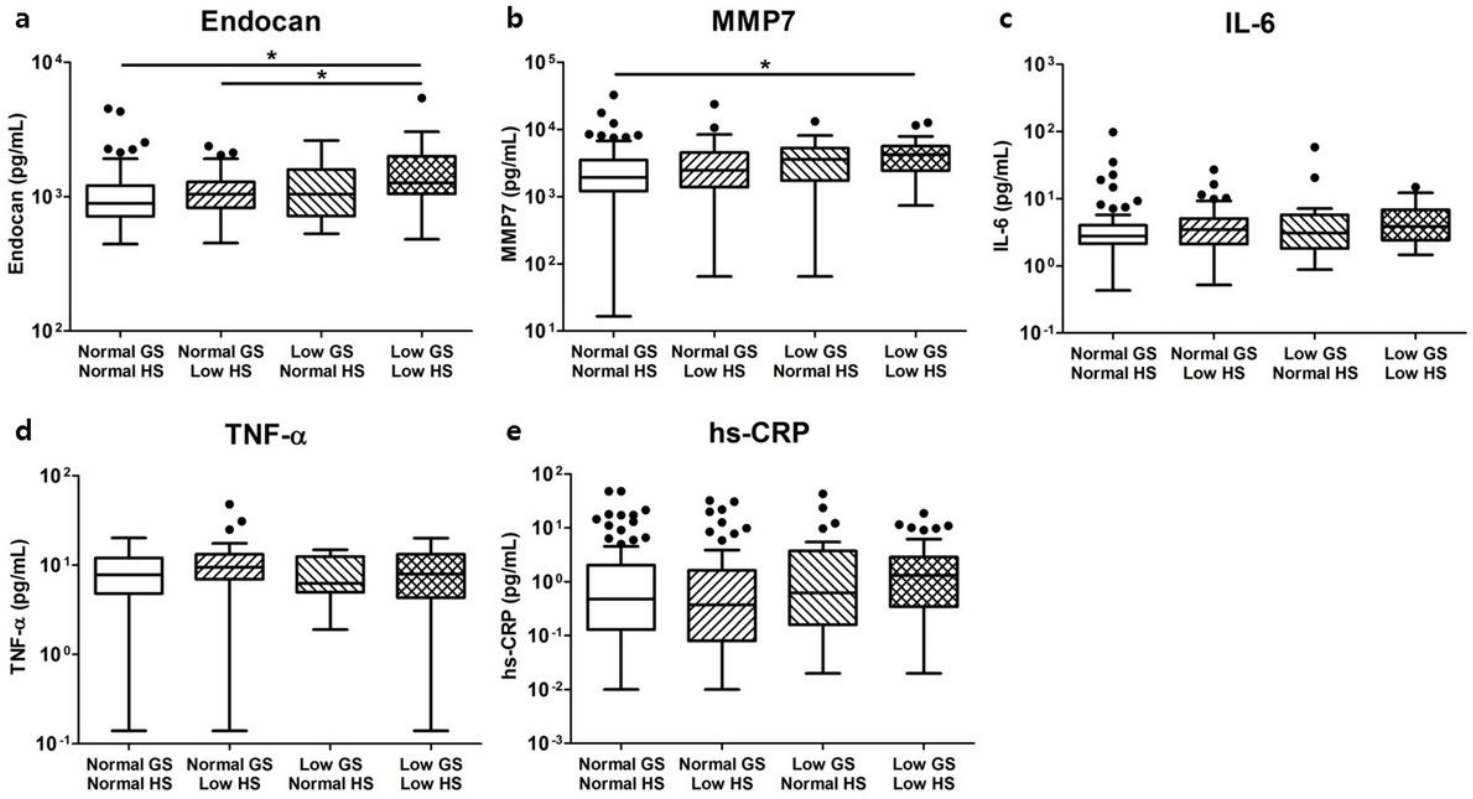

Figure 2

Levels of various plasma inflammatory markers in hemodialysis patients according to physical performance. Among the plasma inflammatory markers measured by multiplex ELISA, the levels of (A) endocan and (B) MMP-7 were significantly higher in patients with low GS and HS than in those with normal GS and HS. The levels of (C) TNF-α, (D) IL-6, and (E) hs-CRP were not different among the groups.

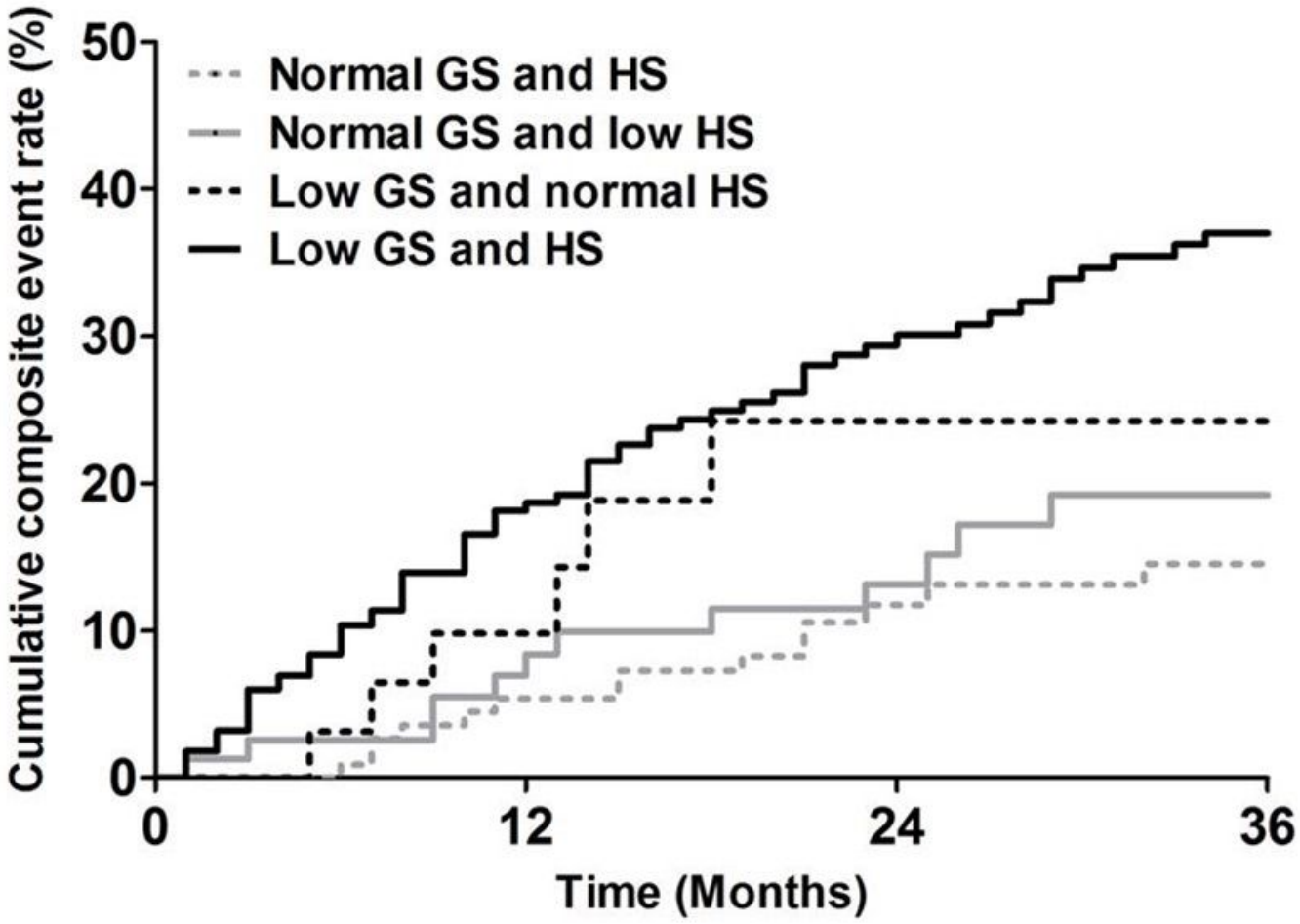

Figure 3

Cumulative event rate of all-cause mortality and cardiovascular events in hemodialysis patients according gait speed and handgrip strength. Patients with low GS and HS showed the highest cumulative composite event rate (p = 0.004 for overall trends).