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Locomotive syndrome in hemodialysis patients and its association with quality of life—a cross-sectional study

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Abstract

Background: Locomotive syndrome (LS) is defined as impairment of mobility function. This study aimed to clarify LS and its association with quality of life in hemodialysis patients.

Methods: This is a cross-sectional study. The subjects were chronic kidney disease patients undergoing maintenance hemodialysis treatment. LS was assessed using two physical tests (two-step test, stand-up test) and one self-reported test (Geriatric Locomotive Function Scale-25). LS has two stages of severity; the beginning of the decline in mobility function is known as Locomo stage 1, and the progression of the decline of mobility function is known as Locomo stage 2. We used SF-36 to assess quality of life and examined their relationships with the Locomo stages. Chi-square test, Kruskal-Wallis test, Jonckheere-Terpstra test, and Mantel-Haenszel test were used for analysis. Multiple linear regression was used to model the cross-sectional association of Locomo stages with each component and summary score of SF-36.

Results: A total of 76 hemodialysis patients were included. The number of subjects with Locomo stage 1 and stage 2 were 19 (25%) and 53 (70%), respectively, while only four (5%) subjects did not have mobility dysfunction. Each component and summary score of the SF-36 for physical function, role emotional, physical component summary, and mental component summary were significantly associated with Locomo stages.

Conclusion: A high prevalence and severity of LS in hemodialysis patients was found, and the severity was associated with quality of life.

Keywords: Locomotive syndrome, Hemodialysis, Quality of life, Body composition, Physical assessment

Background

Activities of daily living (ADL) and the quality of life (QOL) of patients with chronic kidney disease (CKD) undergoing dialysis treatment are known to be worse than those of non-dialysis patients [1–3]. One of the reasons for poor ADL/QOL in CKD patients is the impairment of physical functions, including locomotive organ dysfunction, secondary to several CKD-related factors

such as protein–energy wasting, frailty, sarcopenia, bone disorder, and amyloidosis [4–8]. Thus, the proper assessment of physical function, especially that of locomotive organs, is necessary in CKD patients.

The Japanese Orthopedic Association proposed the concept of Locomotive syndrome (LS), which is a condition of reduced mobility due to impairment of the locomotive organs including muscles, nerves, bones, and joints [9]. The impairment of locomotive organs is associated not only with ADL, but also with psychological condition [10, 11]. LS can be assessed using two physical tests (two-step test, stand-up test) and one self-report

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test (the question Geriatric Locomotive Function Scale-25 (GLFS-25)) [12]. LS comprises two stages, the beginning of the decline of mobility function, which is known as Locomo stage 1, and the progression of the decline of mobility function, which is known as Locomo stage 2 [13]. Elderly patients develop LS earlier than sarcopenia or frailty [14], and it is related to falls, cognitive decline, depression, and impairment of QOL [15–18]. CKD patients have a high risk of sarcopenia and frailty, as well as reduced QOL; however, no data are available on the frequency or severity of LS, as well as related factors in dialysis patients.

In this article, we report (1) the prevalence and severity of LS and (2) the association of LS with QOL in patients undergoing maintenance hemodialysis.

Methods

Design and setting

A cross-sectional study was conducted at two hemodialysis centers in Japan from May 2018 to November 2018. Subjects underwent regular hemodialysis therapy three times per week for more than 1 year. We excluded patients who had severe respiratory, cardiovascular disease, or inability to answer questionnaires (impairment of reading comprehension, vision impairment, or cognitive impairment). All subjects provided written informed consent prior to enrolment. The protocol of this study is compliant with the Helsinki Declaration of 1975, as revised in 2013. The study protocol was approved by the Shinkohkai Murakamikenin Hospital ethics committee (No.1701, August 2, 2017) and registered at the University Hospital Medical Information Network center (UMIN000038246).

Assessment of LS (Locomo test)

Two-step test

This test measured the stride length to assess walking ability, including muscle strength, balance, and flexibility of the lower limbs. The two-step test was performed as follows: (1) subjects stood behind the start line with their toes aligned; (2) subjects were instructed to take two steps as long as possible and then align both feet; (3) we measured the length of the two steps from the starting line to the tips of the subject's toes. The two-step test score was calculated using the following formula: length of the two steps (cm) ÷ height (cm) [12].

Stand-up test

This test assessed leg strength by having the subject stand up on one or both legs from a specified height [12]. After preparing two seats of different heights (40 and 20 cm); first, the subjects stood up from a height of 40 cm with one leg (right or left). If subjects were unable

to stand up, the subjects were then asked to stand up from a height of 20 cm using both legs.

GLFS-25

The GLFS-25 is a self-reported comprehensive measure that consists of 25 questions that refer to experiences in the preceding month. The scale addresses four dimensions using 25 questions (four questions regarding pain, 16 questions regarding ADL, three questions regarding social functions, and two questions regarding mental health status). These 25 questions were graded using a 5-point scale from no impairment (0 points) to severe impairment (4 points), and then arithmetically added to produce a total score (minimum 0, maximum 100) [19].

Operational definition for severity of LS

The subjects were categorized as Locomo stage 1 if any of the following three conditions were met: stand-up test, inability to perform one-leg standing from a 40-cm-high seat; two-step test, < 1.3; and GLFS-25 score, ≥ 7. The subjects were categorized as Locomo stage 2 if any of the following three conditions were met: stand-up test, inability to stand using both legs from a 20-cm-high seat; two-step test, < 1.1; GLFS-25 score, ≥ 16 [13].

Physical assessment

Body mass index was calculated based on body weight after hemodialysis. Body composition was measured using bioelectrical impedance analysis (In Body S10, In Body Co., Ltd., Seoul, Korea). The measurement was conducted in the supine position after hemodialysis to obtain data regarding skeletal muscle mass, body fat, extracellular water/total body water ratio (ECW/TBW), and phase angle (measured at 50 kHz). The skeletal muscle index (SMI) was calculated using the following formula: skeletal muscle mass (kg) ÷ height² (m²). We defined muscle mass as SMI < 7.0 kg/m² for men and < 5.7 kg/m² for women; obesity was defined as > 25% body fat for men and > 35% body fat for women [20, 21].

Biochemical measurement

Non-fasting blood samples were drawn before hemodialysis sessions. We analyzed serum albumin, C-reactive protein, blood urea nitrogen, serum creatinine, calcium, phosphorus, and hemoglobin. If there was hypoalbuminemia (< 4.0 g/dL), the calcium was corrected using the following formula: Corrected calcium concentration = Measured calcium concentration (mg/dL) + (4 – Serum albumin (g/dL)) [22].

Nutritional assessment

The Mini Nutritional Assessment®–short form (MNA®-SF) is an assessment tool consisting of six items. The items are as follows: declining food intake over 3 months

(score: no decrease = 2, moderate decrease = 1, severe decrease = 0), weight loss during the past 3 months (score: no weight loss = 3, weight loss between 1 and 3 kg = 2, does not know = 1, weight loss greater than 3 kg = 0), mobility (score: goes out = 2, able to get out of bed/chair but does not go out = 1, bed- or chair-bound = 0), psychological stress or acute disease in the past 3 months (score: no = 2, yes = 0), neuropsychological problems (score: no psychological problems = 2, mild dementia = 1, severe dementia or depression = 0), and body mass index (BMI) (score: BMI 23 or greater = 3, BMI 21 to less than 23 = 2, BMI less than 19 = 0). A total score of 12–14 reflects normal nutritional status, 8–11 reflects at risk of malnutrition, and 0–7 represents malnourishment [23].

The geriatric nutritional index (GNRI) was calculated from the serum albumin and body weight using the following equation: $GNRI = [14.89 \times \text{Albumin (g/dL)}] + [41.7 \times \text{Body weight after hemodialysis (kg)/Ideal body weight (kg)}]$. If the patient's body weight exceeded their ideal body weight, body weight was set to 1 [24].

We used the SF-36 v2[®], Japanese version to assess QOL. Subject responses to the SF-36 were used to determine scores for eight subscales (physical functioning (PF), role physical (RP), bodily pain (BP), social functioning (SF), general health perceptions (GH), vitality (VT), role emotional (RE), and mental health (MH)), and three component scores (physical component score (PCS), mental component score (MCS), and role-social component score (RCS)). All domain scores were transformed such that 50 represents the mean of the general Japanese population, and the standard deviation was 10 using software (iHope International Inc. Kyoto, Japan).

Statistical analysis

The statistical significance of differences among each Locomo stage group was calculated using the chi-square test or Kruskal-Wallis test. Trend test was examined by the Jonckheere-Terpstra trend test or Mantel-Haenszel test for trend. Values of $p < .05$ were considered significant. Multiple linear regression was used to model the cross-sectional association of Locomo stages with each component and summary score of SF-36, and the model was adjusted for age, sex, and dialysis vintage. All statistical analyses were performed using SPSS version 25 software (IBM Corp., Armonk, NY, USA).

Results

Seventy-six hemodialysis patients participated in this study, including 52 men and 24 women with a median age of 68 years old (interquartile range (IQR): 59–77 years), body mass index of 20.5 kg/m² (IQR: 19.1–24.3 kg/m²), and 7-year duration of dialysis (IQR: 2–14 years). The primary cause of CKD included diabetes

(38%), chronic glomerulonephritis (49%), renal sclerosis (8%), and others (5%). The presence of disease or complications related to physical dysfunction and QOL were included: cerebrovascular disease (8%), cardiovascular disease (12%), orthopedic disease (18%), cancer (13%), and dementia (1%). The patients underwent hemodialysis treatment three times a week. Each session was 4 h long, and Kt/V was 1.53 (IQR: 1.36–1.67). No adverse event occurred during the study protocol.

The number of Non-locomo, Locomo stage 1, and Locomo stage 2 subjects were 4 (5%), 19 (25%), and 53 (70%), respectively. Patient characteristics in each Locomo test group are shown in Table 1. There were significant differences in age, stand-up test result, two-step test result, and GLFS-25 between the groups. Figure 1 shows the results of the GLFS-25. More than half of subjects had pain in their body, reduced ability to go up and down the stairs, difficulty or inability to walk, inability to do housework, reduced sport and social activity, and anxiety over falling. Table 2 shows the body compositions, laboratory values, and nutritional parameters of the groups. SMI, phase angle, and serum creatinine and calcium levels were significantly different between the three groups. In the trend test, as worsening Locomo stage, significant trend of increase found low SMI, body fat, obesity, ECW/ TBW, and significant trend of decline found phase angle, and serum creatinine.

SF-36 components, such as PF, RE, PCS, and MCS were different among Locomo stages. In trend test, PF, RP, RE, and PCS were found in significant trend of decline as worsening Locomo stage. MCS was found in significant trend of increase as worsening Locomo stage (Table 3).

Discussion

In this study, we found that dialysis patients have LS frequently, and the LS is often of a severe level. Moreover, the severity of LS was associated with QOL. Our findings indicate the importance of assessing LS in dialysis patients, and that further studies to improve locomotive organ dysfunction will be needed for better QOL/ADL as well as survival in dialysis patients.

LS is a major cause of requiring care in the general population [11], and it is important to evaluate it in addition to sarcopenia and frailty in dialysis patients who have poor ADL and mortality. Hemodialysis patients seem to have a higher prevalence and worse Locomo stage (Table 1) than those reported previously in the general population which is estimated at 69.8% and 25.1% in Locomo stages 1 and 2, respectively [25]. The impairment of locomotive organs is induced by several CKD-related factors including dialysis therapy, protein-energy wasting, accumulation of uremic toxins,

Table 1 Demographic results of Locomo test and characteristics according to the Locomo stage

	All patients (n = 76)	Non-locom (n = 4)	Locomo stage 1 (n = 19)	Locomo stage 2 (n = 53)	P value
Male, n (%)	52 (68)	4 (100)	14 (74)	34 (64)	.28
Age (years)	67.5 (59.3–76.8)	59.5 (50.8–62.3)	62.0 (56.0–72.0)	72.0 (64.5–79.5)	.005
Stand-up test, n (%)					
Difficulty standing from					
40-cm-high seat (either leg)	37 (49)	0 (0)	12 (63)	27 (51)	< .001
20-cm-high seat (both legs)	23 (30)	0 (0)	0 (0)	23 (43)	
Two-step test					
< 1.3, n (%)	22 (29)	0 (0)	16 (84)	6 (11)	< .001
< 1.1, n (%)	44 (58)	0 (0)	0 (0)	44 (83)	
GLFS-25 score					
≥ 7, n (%)	25 (33)	0 (0)	10 (53)	15 (28)	< .001
≥ 16, n (%)	33 (43)	0 (0)	0 (0)	33 (62)	
Active VD use, n (%)	60 (79)	4 (100)	15 (79)	41 (77)	.56
L-carnitine use, n (%)	17 (22)	2 (50)	5 (26)	10 (19)	.31
Dialysis vintage (years)	7 (2–14)	16 (2–29)	7 (4–18)	6 (2–14)	.80
Primary cause of ESRD, n (%)					
Diabetes mellitus	29 (38)	1 (25)	7 (37)	21 (40)	.39
Chronic glomerulonephritis	37 (49)	2 (50)	12 (63)	23 (43)	
Renal sclerosis	6 (8)	1 (25)	0 (0)	5 (9)	
Other	4 (5)	0 (0)	0 (0)	4 (8)	
Kt/V	1.53 (1.36–1.67)	1.41 (1.33–1.52)	1.45 (1.32–1.67)	1.55 (1.45–1.68)	.10

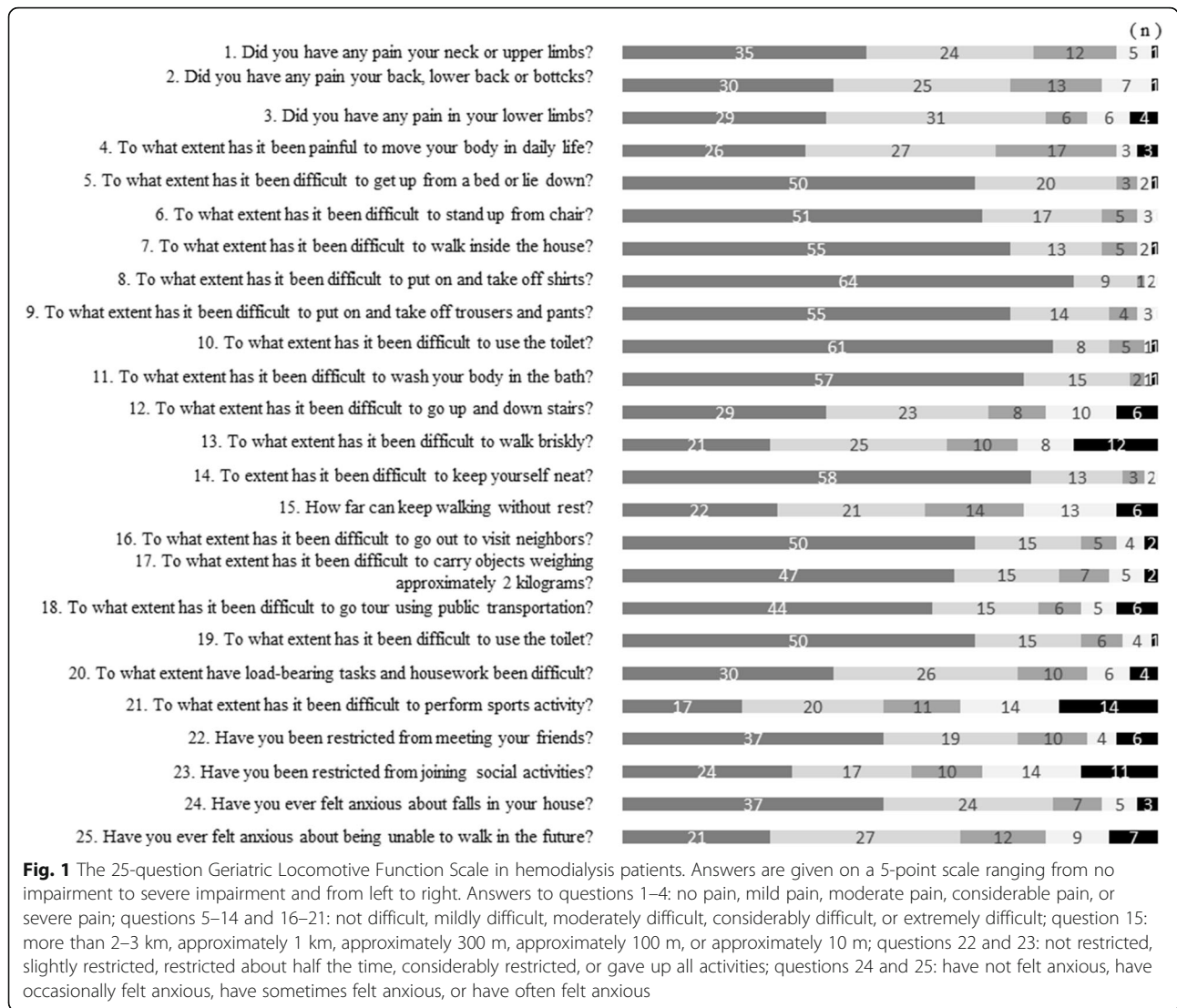
ESRD, end-stage renal disease; GLFS, geriatric locomotive functional scale; VD, vitamin D

Data are presented as median (interquartile range)

mineral and bone disorders, and dialysis-related amyloidosis. Those factors can lead to impairment of ADLs after the initiation of dialysis treatment [26]. Protein–energy wasting reduces muscle mass and muscle strength in hemodialysis patients [27]. The serum level of indoxyl sulfate, a uremic toxin, is associated with skeletal muscle mass in peritoneal dialysis patients [28]. Parathyroid hormone (PTH), which is positively correlated with CKD stage, may be associated with the reduction of muscle mass because in mice that underwent subtotal nephrectomy, fat-specific knockout of PTH receptor inhibited muscle mass reduction and improved muscle strength [29]. In addition, a multicenter cross-sectional study showed that knee joint pain was associated with impaired ADL in hemodialysis patients with dialysis-related amyloidosis [8]. Thus, the severity of LS in hemodialysis patients may be explained by the high prevalence of pain in bone, joints, and skeletal muscle [30]. Although exercise is effective in improving physical function and QOL in dialysis patients, advanced locomotive organ dysfunction and joint pain are major causes of limiting exercise and physical activity [31–33]. Locomo test including GLFS-25 can examine locomotive organ function and joint pain, but sarcopenia or frailty assessment cannot examine those. Thus, to evaluate and manage LS as well

as frailty and sarcopenia in hemodialysis patients will be important because impaired locomotive organs will be associated with worse ADL/QOL, especially those who need frequent visit to their hospitals for dialysis treatment. We showed the severity of LS in maintenance hemodialysis patients with average age and dialysis duration compared with those reported by Japanese Society of Dialysis Therapy [34]. In this study, 95% of them had LS, and we must pay attention to adopt it for elderly dialysis patients who will have severe locomotive organ dysfunction compared with younger patients. However, even in those high-risk population, it may be important to check the Locomo stage regularly to find the effect of the intervention, such as exercise, nutrition, and dialysis therapy on the locomotive organs management in the future. Locomo test is consisted with subjective and objective information focused on the condition of locomotive organs, and further studies will be needed for a direct comparison between LS and sarcopenia/frailty in hemodialysis patients.

LS is associated with the impairment of QOL in hemodialysis patients (Table 3). It is known that hemodialysis patients have a worse physical component with respect to QOL [35].



LS causes deteriorating ADL in the general population [36], and impairment of ADL is associated with a lower physical component summary of QOL in hemodialysis patients [37]. Taken together, LS may be the major cause of the impairment of QOL via deteriorating ADL. GLFS-25 is a tool to understand ADL with questionnaire and subjective, and we may need to examine the association of GLFS-25 with objective and instrumental ADL in hemodialysis patients. MCS was found in significant trend of increase as worsening Locomo stage (Table 3). Previous study did not find significant difference between Locomo stages 1 and 2 in MCS in the general population [18], and further study will be needed to examine the association in hemodialysis patients with a large sample size.

We found that ECW/TBW, phase angle, and obesity were related to the severity of LS in hemodialysis patients. ECW and phase angle negatively correlate with

muscle strength in hemodialysis patients [38–40], and ECW/TBW, phase angle, and obesity may suggest the existence of LS. In addition, LS is associated with increased body fat [41]. Hemodialysis patients have increased levels of intramuscular fat, which might be the cause of the reduced muscle strength [42]. Therefore, LS is related more strongly with obesity than malnutrition.

Our study has several limitations. First, our results demonstrated severe LS in hemodialysis patients, and the non-LS group was smaller than the LS group, which may be insufficient for comparison. Second, this study used a simple stand-up test because we considered the fatigue of the subjects instead of the original stand-up test. Third, QOL is associated with the life environment, for example, income, family, and intelligence; however, we did not survey those factors. Fourth, we did not examine cognitive function, while only 1% of participants was diagnosed with dementia. Finally, our study

Table 2 Body compositions, laboratory values, and nutritional parameters according to the groups of Locomo stage

	All patients (n = 76)		Non-locomo (n = 4)		Locomo stage 1 (n = 19)		Locomo stage 2 (n = 53)		Group difference P value	Trend test P value
Body composition										
BMI (kg/m ²)	20.5	(19.1–24.3)	20.8	(19.3–22.1)	19.7	(18.7–22.7)	20.5	(19.4–24.7)	.44	.26
SMI (kg/m ²)	6.3	(5.4–7.1)	7.1	(6.6–7.4)	6.7	(6.0–7.5)	6.0	(5.3–6.9)	.039	.12
Low SMI, n (%)	45	(59)	1	(25)	9	(47)	35	(66)	.13	.046
Body fat (%)	24.5	(20.6–35.1)	18.2	(15.9–23.7)	21.7	(15.6–24.5)	26.8	(22.1–37.1)	.004	.001
Obesity, n (%)	32	(42)	0	(0)	4	(21)	28	(53)	.012	.003
ECW/TBW	0.396	(0.387–0.402)	0.383	(0.374–0.388)	0.388	(0.384–0.396)	0.399	(0.393–0.405)	< .001	< .001
Phase angle (°)	4.6	(4.0–5.3)	5.9	(5.2–6.5)	5.1	(4.6–5.6)	4.2	(3.9–4.9)	< .001	< .001
Laboratory values										
Albumin (g/dL)	3.6	(3.3–3.9)	3.8	(3.5–4.1)	3.7	(3.3–3.9)	3.6	(3.3–3.9)	.35	.19
C-reactive protein (mg/dL)	0.06	(0.03–0.31)	0.71	(0.04–3.07)	0.07	(0.01–0.28)	0.06	(0.03–0.33)	.51	.99
BUN (mg/dL)	60.1	(52.4–69.1)	71.8	(60.5–88.0)	59.3	(51.0–63.0)	60.1	(53.3–68.9)	.14	.95
Creatinine (mg/dL)	10.27	(8.57–12.17)	12.62	(10.34–14.76)	12.03	(10.68–13.09)	9.67	(8.33–11.19)	< .001	< .001
Potassium (mEq/L)	4.9	(4.5–5.5)	5.4	(5.1–6.1)	4.9	(4.5–5.5)	4.8	(4.5–5.5)	.20	.22
Phosphorus (mg/dL)	5.4	(4.6–6.3)	5.5	(4.7–8.8)	5.5	(4.7–6.4)	5.4	(4.5–6.3)	.78	.65
Hemoglobin (g/dL)	10.9	(10.3–11.4)	10.9	(9.9–12.0)	10.9	(10.2–12.5)	10.9	(10.4–11.4)	.87	.64
Nutritional parameter										
GNRI (score)	92.2	(87.7–96.8)	95.1	(89.8–101.9)	93.1	(85.7–96.6)	92.0	(87.8–96.8)	.69	.58
MNA-SF, n (%)										
At risk	30	(39)	0	(0)	6	(32)	24	(45)	.12	.48
Malnutrition	5	(7)	0	(0)	3	(16)	2	(4)		

BMI, body mass index; BUN, blood urea nitrogen; ECW, extracellular water; TBW, total body water; GNRI, Geriatric Nutritional Risk Index; MNA-SF, Mini nutritional assessment-short form; SMI, skeletal muscle mass index
 Date are presented as median (interquartile range).
 Bold values are P < .05.

Table 3 Each components and summary score of SF-36 according to the groups of Locomo stage

	All patients (n = 76)		Non-locomo (n = 4)		Locomo stage 1 (n = 19)		Locomo stage 2 (n = 53)		Group difference P value	Trend test P value
PF	30.6	(25.1–35.8)	35.5	(33.0–41.4)	33.8	(28.8–38.8)	28.7	(24.1–32.4)	.006	.001
RP	37.5	(35.4–40.1)	38.8	(35.8–43.2)	39.4	(37.2–41.7)	36.8	(35.1–39.1)	.068	.023
BP	44.1	(42.9–45.8)	44.2	(42.5–46.8)	45.0	(43.7–46.4)	43.8	(42.6–45.4)	.174	.086
GH	35.0	(33.1–36.2)	34.1	(31.0–37.0)	35.7	(33.2–36.3)	34.9	(33.3–36.0)	.582	.361
VT	44.8	(43.9–45.4)	43.8	(43.3–44.8)	44.7	(43.6–45.1)	45.0	(44.2–45.4)	.145	.062
SF	43.2	(40.4–47.2)	39.4	(34.2–44.3)	43.0	(41.1–44.7)	43.5	(40.2–48.8)	.431	.379
RE	40.8	(38.7–43.7)	42.8	(40.3–47.0)	43.3	(40.6–45.7)	40.2	(38.5–42.6)	.029	.008
MH	47.3	(46.6–48.0)	46.9	(46.3–47.9)	47.2	(46.2–48.0)	47.3	(46.6–48.0)	.823	.595
PCS	31.5	(28.1–36.3)	36.5	(34.6–41.2)	35.1	(30.4–39.1)	30.9	(26.8–34.1)	.007	.002
MCS	49.8	(47.4–51.9)	46.7	(45.2–48.2)	48.7	(45.3–51.0)	50.5	(48.4–52.4)	.011	.003
RCS	46.1	(43.4–48.1)	44.9	(41.6–49.1)	46.7	(45.0–48.9)	45.7	(43.3–47.8)	.442	.295

BP, bodily pain; GH, general health; MCS, mental component summary; MH, mental health; PCS, physical component summary; RCS, role-social component score; RE, role emotional; PF, physical functioning; RP, role physical; SF, social functioning; VT, vitality
 Date are presented as median (interquartile range). The model was adjusted for age, sex and dialysis vintage.
 Bold values are P < .05.

had a small sample; further research is needed to confirm the findings in a large cohort study. Even with those limitations, this study showed the severe limitation of locomotive organs in hemodialysis patients using the detailed assessment of LS, QOL, and body composition. The routine practice to manage LS by medical staff may help to maintain QOL and ADL in hemodialysis patients.

Conclusions

A highly prevalent and severe LS were found in hemodialysis patients. The severity of LS was associated with impaired physical QOL. These findings suggest that LS may be an important concept for QOL in hemodialysis patients.

Abbreviations

ADL: Activities of daily living; BMI: Body mass index; BP: Bodily pain; CKD: Chronic kidney disease; ECW: Extracellular water; GH: General health perceptions; GLFS-25: Geriatric locomotive function scale-25; GNRI: Geriatric Nutritional Risk Index; IQR: Interquartile range; LS: Locomotive syndrome; MCS: Mental component score; MH: Mental health; MNA-SF: Mini nutritional assessment-short form; PCS: Physical component score; PF: Physical functioning; PTH: Parathyroid hormone; QOL: Quality of life; RCS: Role-social component score; RE: Role emotional; RP: Role physical; SF: Social functioning; SMI: Skeletal muscle index; TBW: Total body water; VT: Vitality

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None

Authors' contributions

Conception, study design, and interpretation of the data were performed by KK, SY, and YI. Measurement and analysis were performed by KK, SY, YK, KG, IE, and KG. The manuscript was drafted by KK, SY, and IN. Approval of the final version of the manuscript by KK, SY, YK, KG, IE, YI, and IN.

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Availability of data and materials

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

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the guidelines of the Declaration of Helsinki and approved by the institutional Review Board at Shinkohkai Murakami-Kinen Hospital (approval number: 1701).

Consent for publication

Not applicable.

Competing interests

None.

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