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Original Article

A Novel Nomogram that Predicts Chronic Hemodialysis Patients' Survival Based on Their Sedentary Behavior

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Appropriate treatments for chronic hemodialysis patients are a public health challenge in Japan. Sedentary behavior appears to be closely associated with these patients' survival. We thus sought to develop a nomogram that predicts survival based on the duration of chronic hemodialysis patients' sedentary behavior. One hundred twenty-four patients under chronic hemodialysis (73 men, 51 women, age 71.7 ± 11.1 years) were enrolled in this cohort study. The patients wore a triaxial accelerometer that measured both their sedentary behavior, *i.e.*, total sedentary behavior (minutes) and their maximum sedentary bouts (min) on non-hemodialysis days. We obtained the Kaplan-Meier curve and used the log-rank test and a Cox proportional hazards model to evaluate the relationship between the patients' sedentary behavior and their survival. We also used a Cox proportional hazards model to develop a nomogram for the patients' 5-year survival rate. Forty-six patients died during the follow-up period. When we stratified the patients by the medians of total sedentary behavior and maximum sedentary bouts, we observed significant between-group differences. After adjustment for confounding factors in a Cox proportional hazards model, total sedentary behavior and maximum sedentary bouts were identified as critical survival factors, and we generated a nomogram using an index of sedentary behavior. Our analysis results demonstrated that sedentary behavior on non-dialysis days was closely associated with the survival of the chronic hemodialysis patients, suggesting that a decrease in sedentary behavior would prolong their survival. The nomogram developed herein based on sedentary behavior may be useful for predicting the outcomes of chronic hemodialysis patients.

Key words: nomogram, chronic hemodialysis, sedentary behavior, Cox proportional hazards model, Kaplan-Meier curve

The number of patients who were undergoing chronic hemodialysis in Japan in 2023 was 343,508, and the average age of these patients was 70.1 years <https://docs.jsdt.or.jp/overview/file/2023/pdf/2023all.pdf> (December, 2024). Effective treatment to improve the prognosis of chronic hemodialysis patients is thus urgently required in Japan. Sedentary behavior, which is defined as any waking behavior that is characterized by energy expenditure (metabolic

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equivalents) ≤ 1.5 while in a sitting or reclining posture [1], has been strongly implicated in various health outcomes [2-13], including those of chronic hemodialysis patients. Our research group has examined the relationship between sedentary behavior and health-related quality of life (HRQOL) in a cross-sectional study [14, 15], and we also observed a relationship between sedentary behavior and survival in a longitudinal study [16, 17]. In another group's investigation of parameters of prolonged sedentary bouts on non-hemodialysis days, the subjects' total sedentary behavior (measured in minutes) and their maximum sedentary bouts (min) were closely associated with HRQOL [18].

Although sedentary behavior has been shown to be closely associated with patients' survival in several contexts [8-13], the relationship between sedentary behavior and survival in Japanese individuals undergoing chronic hemodialysis has not been established, and we speculated that survival predictions based on sedentary behavior could be useful for the proper management of chronic hemodialysis patients. We thus developed a nomogram that predicts a commonly used survival parameter, *i.e.*, the 5-year survival rate, by using several parameters of sedentary behavior in chronic hemodialysis patients.

Patients and Methods

Patients. Of the 207 patients eligible for this cohort study, 124 (73 men and 51 women, aged 71.7 ± 11.1 years) met the following inclusion criteria (Fig. 1): (1) receiving outpatient treatment at Innoshima General Hospital (Onomichi, Japan) between September 2013 and September 2024, (2) parameters including sedentary behavior were measurable by a triaxial accelerometer, and (3) written informed consent was provided. Ethical approval of this study was obtained from the Ethical Committee of Innoshima General Hospital, Onomichi, Japan [H25-2-27, H26-1-23, H26-12-16, H27-12-25, H28-12-9, H29-12-4, H30-11-1, H31-2-25, R1-12-23, R2-11-9, R3-11-10, R6-4-22, and R7-1-7].

Sedentary behavior. The patients' physical activity, including sedentary behavior, was measured by a triaxial accelerometer called the Active Style Pro HJA-350IT® (Omron, Kyoto, Japan). The availability and accuracy of this device have been described [19-21]. The patients were asked to wear the triaxial accelerometer on their waist for 14 consecutive days, except when they were sleeping and bathing. A non-wearing time was defined as the period when estimated the physical activity's intensity revealed by the triaxial accelerometer showed a value of 0 for > 60 consecutive min. The total wearing time was defined as 24 h (1,440 min) minus the non-wearing time (min). We calculated each patient's total sedentary behavior (min) and maximum prolonged sedentary bouts (min) and used these data in our analyses as described [14-18].

Clinical parameters. We investigated the following clinical parameters as described [14-18]: sex, age

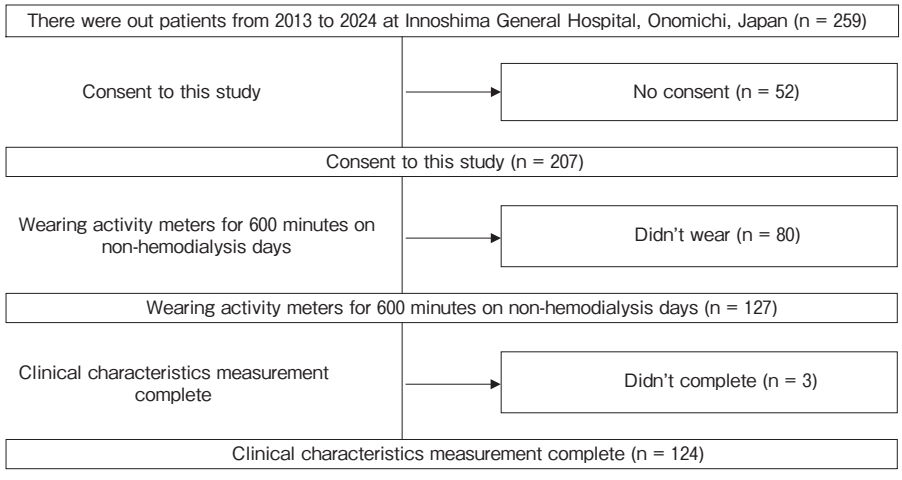

Fig. 1 Flow diagram of the enrollment of patients undergoing chronic hemodialysis as outpatient treatment at our hospital between September 2013 and September 2024.

(years), height (cm), body weight (kg), body mass index (BMI: kg/m^2), dialysis vintage (months), history of diabetes mellitus (yes/no), history of hypertension (yes/no), low back pain (yes/no), and knee pain (yes/no). The BMI was calculated as body weight (kg)/[height (m)]^2. The following results of a blood examination were also obtained: albumin (g/dl), blood glucose (mg/dl), and triglycerides (mg/dl). The blood tests were performed using conventional laboratory methods. Information about patients' deaths (date and cause of death) were collected from medical records.

Statistical analyses. The results of our analyses are expressed as the mean ± standard deviation (SD) or the number of patients (%). A Kaplan-Meier curve with the log-rank test was used to examine the significance of differences in survival rates between two groups of patients stratified by the medians of sedentary behavior parameters, *i.e.*, the total sedentary behavior (min) and the maximum sedentary bouts (min). We also used a Cox proportional hazards model to adjust for confounding factors. It has been demonstrated that in a Cox proportional hazards model, approx. 10 events are required per independent variable [22], and we therefore selected age, sex, history of diabetes mellitus, and BMI based on clinical relevance in addition to the sedentary behavior parameters (total sedentary behavior and maximum sedentary bouts) [18]. To estimate the patients' 5-year survival rate, we developed a nomogram using a Cox proportional hazards model [23]. The statistical analyses were performed using JMP Pro 17 (SAS, Cary, NC, USA) and BellCurve for Excel (Social Survey Research Information Co., Tokyo).

Results

The clinical profiles of the 124 chronic hemodialysis patients are summarized in Table 1. On the patients' non-hemodialysis days, the amount of time that the triaxial accelerometer was worn was 979.1 ± 210.5 min; the total sedentary behavior was 727.4 ± 253.9 min and the maximum sedentary bouts time was 133.3 ± 67.1 min (Table 1). During the follow-up period, 46 patients died (heart failure: n = 9, pneumonia: n = 6, sepsis: n = 5, cancer: n = 4, renal failure: n = 4, cerebral infarction: n = 3, intestinal hemorrhage: n = 3, and others: n = 12).

Table 1 Clinical characteristics of the chronic hemodialysis patients

	Mean ± SD	Minimum	Maximum
All patients = 124			
Men/Women	73/51	–	–
Age (years)	71.7 ± 11.1	41.0	92.0
>65 years (%)	77.4	–	–
Height (cm)	155.9 ± 8.6	133.6	175.6
Body weight (dry weight) (kg)	54.1 ± 10.9	19.6	91.0
Body mass index (kg/m^2)	22.3 ± 3.4	16.5	31.5
Dialysis vintage (months)	63.5 ± 76.9	2.0	338.0
History of diabetes mellitus (%)	40.3	–	–
Hypertension (%)	90.3	–	–
Low back pain (%)	28.2	–	–
Knee pain (%)	13.7	–	–
Blood sample			
Albumin (g/ml)	3.7 ± 0.5	2.4	5.2
Blood glucose (mg/dl)	131.8 ± 41.9	81.0	302.0
Triglycerides (mg/dl)	110.8 ± 63.3	29.0	431.0
HDL cholesterol (mg/dl)	54.6 ± 16.1	19.1	108.7
Physical activity (non-hemodialysis days)			
Wearing time (min/day)	979.1 ± 210.5	682.8	1,436.8
Total sedentary behavior (min)	727.4 ± 253.9	304.5	1,312.5
Maximum sedentary bouts (min)	133.3 ± 67.1	33.5	312.0

SD, standard deviation.

We then compared the survival of two groups of patients stratified by the median of the total sedentary behavior (658.8 min) and the median of the maximum sedentary bouts (112.3 min), by conducting a Kaplan-Meier curve with the log-rank test (Figs. 2, 3). The results revealed significant between-group differences in survival; the survival of the patients with shorter total sedentary behavior group ($p=0.011$) and that of the patients with shorter maximum sedentary bouts group ($p=0.012$) was significantly longer. The total sedentary behavior ($p=0.014$) and the maximum sedentary bout ($p=0.017$) were both identified as significant factors affecting survival after adjustments for confounding factors (age, sex, history of diabetes mellitus, and BMI) in the Cox proportional hazards model (Table 2).

Based on these results, we developed a nomogram to estimate 5-year survival rates by performing another a Cox proportional hazards model (Figs. 4, 5). For example, a male chronic hemodialysis patient aged 41 years with a BMI of 16.5 kg/m^2, no history of diabetes mellitus, and total sedentary behavior at 304.5 min had a 90.9% probability of achieving 5-year survival (Fig. 4); another male patient also aged 41 years with a 16.5 kg/m^2 BMI, no history of diabetes mellitus, and a

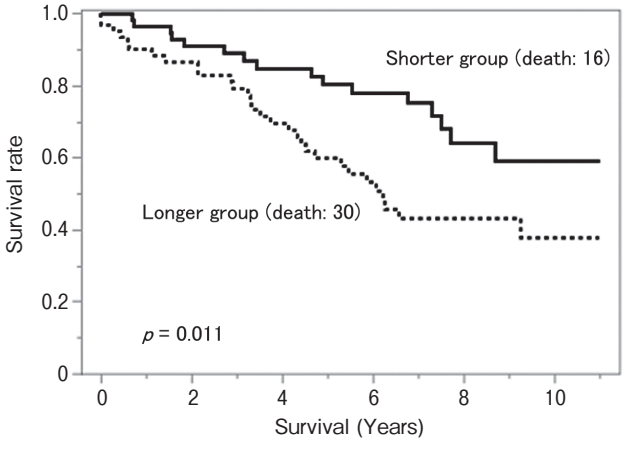

Fig. 2 Kaplan-Meier and log-rank analysis of the survival rate of the 124 chronic hemodialysis patients stratified based on the median value of their total sedentary behavior (min) on their non-hemodialysis days. Shorter group: the patient's total sedentary behavior was less than the median. Longer group: the patient's total sedentary behavior was longer than the median.

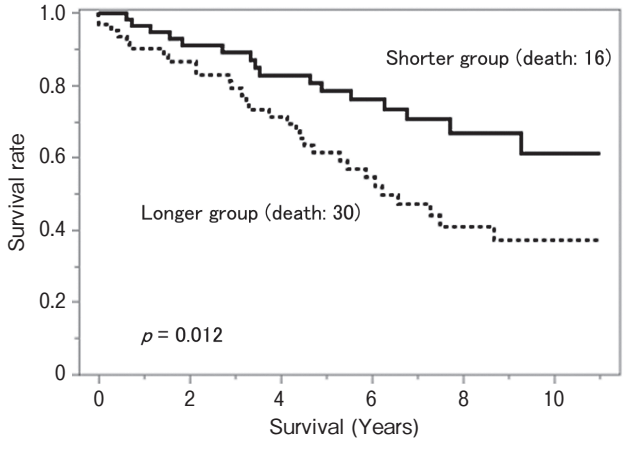

Fig. 3 Kaplan-Meier and log-rank analysis of the survival rate of the patients stratified based on the median value of the maximum sedentary bout on their non-hemodialysis days. Shorter group: the patient's maximum sedentary bout was less than the median, Longer group: the patient's maximum sedentary bout was longer than the median.

Table 2 Multivariate analysis of the survival rate of the chronic hemodialysis patients (Cox proportional hazards model)

	Hazard ratio	95%CI		*P*-value
Total sedentary behavior (h)	1.09	1.02	1.17	**0.014**
Age (years)	1.05	1.01	1.08	**0.005**
Sex (male/female)	2.08	1.10	3.94	**0.021**
History of diabetes mellitus	1.21	0.67	2.21	0.527
BMI (kg/m^2)	0.89	0.80	0.98	**0.018**
Maximum sedentary bouts (h)	1.37	1.06	1.75	**0.017**
Age (years)	1.05	1.02	1.09	**0.001**
Sex (male/female)	2.32	1.22	4.43	**0.008**
History of diabetes mellitus	1.20	0.65	2.21	0.555
BMI (kg/m^2)	0.90	0.81	0.99	**0.029**

BMI, body mass index.

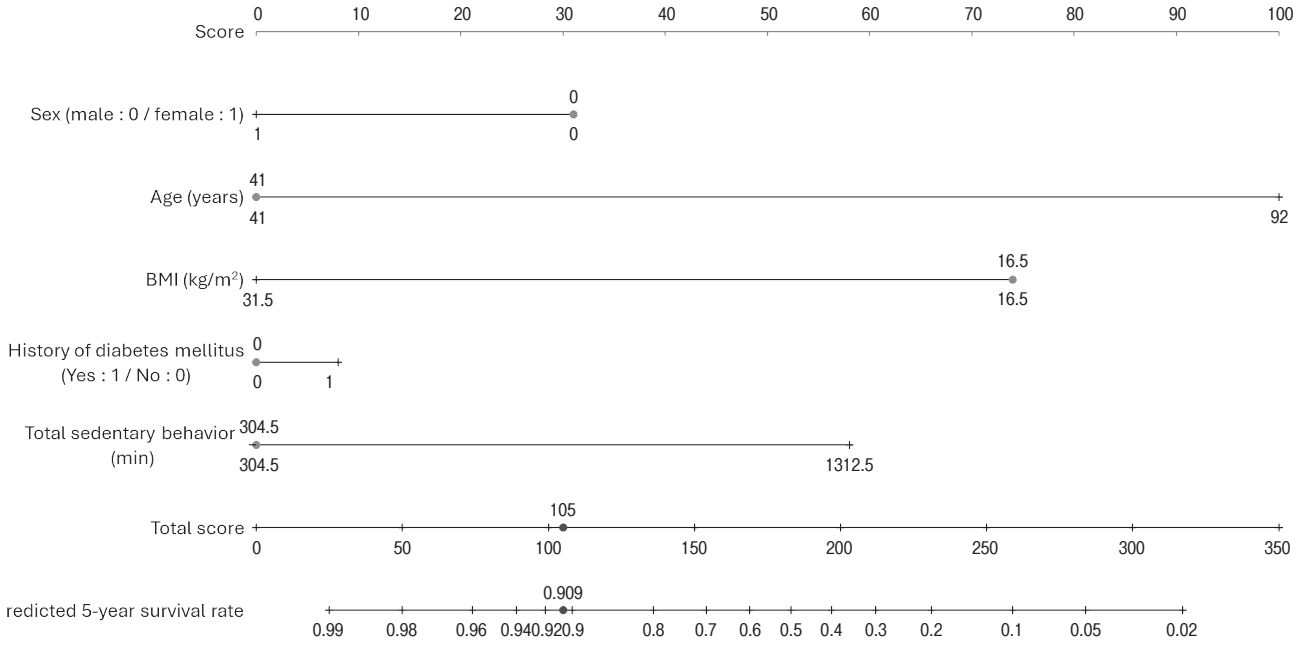

Fig. 4 The nomogram developed for the 5-year survival rate of chronic hemodialysis patients based on their total sedentary behavior (min) on non-hemodialysis days.

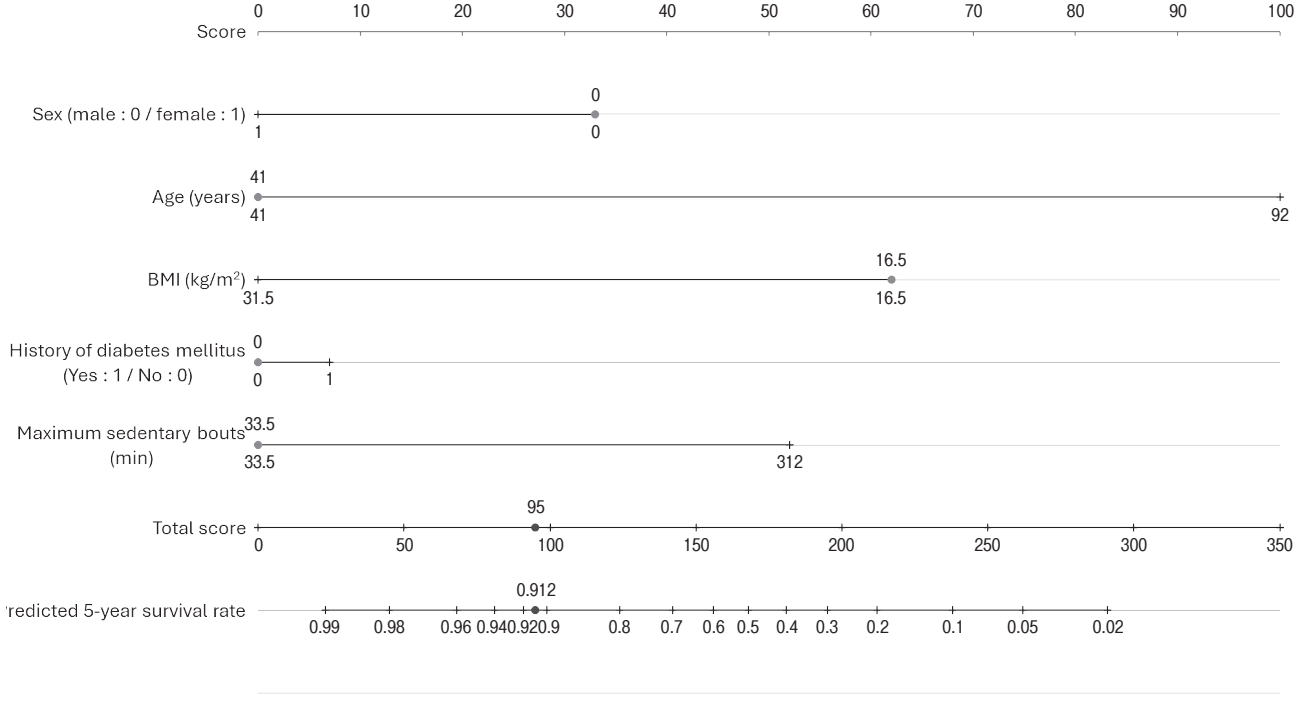

Fig. 5 The nomogram developed for the 5-year survival rate of the chronic hemodialysis patients based on their maximum sedentary bouts (min) on non-hemodialysis days.

33.5-min maximum sedentary bout had a 5-year survival probability value of 91.2% (Fig. 5).

Discussion

We examined the clinical significance of two parameters of sedentary behavior, *i.e.*, the total sedentary behavior and the maximum sedentary bouts, in a population of Japanese patients under chronic hemodialysis conditions. After adjustments for confounding factors, the patients' total sedentary behavior and maximum sedentary bouts on non-hemodialysis days were significantly associated with the patients' survival. We also developed a nomogram based on these sedentary behavior parameters to estimate the patients' 5-year survival rate.

A relationship between sedentary behavior and mortality has been observed by several research groups [8-13]. van der Ploeg *et al.* demonstrated that among 222,497 Australians, the mortality rate in the subjects with a long sitting duration (≥ 11 h/day) was 40% higher than that of the subjects with a short sitting duration (< 4 h/day) [8]. Warren *et al.* also showed that among 7,744 males in the U.S., those who drove a car for > 10 h/week had a 48% higher risk of mortality due to cardiovascular disease compared to those who drove < 4 h/week [9]. Among 11,168 subjects in the UK, women who stood or walked during their jobs had a 32% lower risk of all-cause mortality and a 40% lower risk of cancer death than those who worked sedentary jobs [10]. Analyses by Koyama *et al.* revealed that among 64,456 Japanese individuals, the all-cause mortality rate of the subjects with a long sitting duration (≥ 9 h/day) was 33% higher than that of the subjects with a shorter sitting duration (< 5 h/day) [11].

Ukawa *et al.* used a questionnaire to survey 76,688 Japanese individuals (33,414 men and 43,274 women) about their TV viewing time, and their analysis results demonstrated that the men who watched TV > 4 h/day had a 63% higher rate of mortality due to chronic obstructive pulmonary disease than those who watched TV < 2 h/day [12]. Another survey of 85,899 Japanese individuals about their TV viewing time by Ikehara *et al.* identified a 19% higher risk of death from cardiovascular disease in the subjects who watched TV ≥ 6 h/day compared to those who watched TV < 2 h/day [13].

In the above-cited studies, the subjects' sedentary behavior was described in a self-report questionnaire, and although a relationship was observed between sedentary behavior and all-cause mortality, our present study appears to be the first to investigate the relationship between sedentary behavior based on objective data recorded by a triaxial accelerometer and all-cause mortality in chronic hemodialysis patients in Japan.

The nomogram that we developed in this study was achieved with the use of a Cox proportional hazards model. A nomogram is a statistical method for predicting the outcomes of individual patients [24-26]. For example, Shi *et al.* developed nomogram to predict the survival of chronic hemodialysis patients in China, with the degree of calcification of the abdominal aorta being the main factor [27]. Jiang *et al.* also developed nomogram to predict survival in chronic hemodialysis patients in China, but they used the patients' serum levels of nucleotide-binding oligomerization domain-like receptor family pyrin domain-containing 3, a marker of inflammation, as a major factor [28]. Nomogram developed by Honglan *et al.* to predict survival in chronic hemodialysis patients in China used the number of valvular insufficiencies as the main factor [29]. We newly developed a nomogram that predicts the 5-year survival rate of chronic hemodialysis patients by using a Cox proportional hazards model, which uses commonly measured variables such as age, sex, history of diabetes, and BMI in addition to sedentary behavior parameters (total sedentary behavior and maximum sedentary bout). This nomogram is easy to use in daily clinical practice and will be very useful for motivating chronic hemodialysis patients to improve their lifestyle and reduce their sedentary behavior.

There are some study limitations to address. The patient population was drawn from a single hospital in Onomichi, Japan, and the results obtained may not be representative of chronic hemodialysis patients throughout Japan. Second, among 207 patients, only 124 met the study's inclusion criteria, and the enrolled patients may thus have been more health conscious than the non-enrolled patients. Third, the prolonged sedentary bouts of the study's elderly patients on their non-dialysis days may have reflected a better or worse general condition rather than the patients' lifestyles. Fourth, the mechanisms by which sedentary behavior parameters affect survival in chronic hemodialysis patients remain unclear. Hamilton *et al.* speculated that a longer duration of sedentary behavior reduces lower-limb muscle movements, which decreases the body's

blood flow and metabolism, resulting in arteriosclerosis and lifestyle-related diseases [7]. Lower-limb muscles account for approx. 60% of all muscles in the body [30]. Fifth, since we did not perform a statistical validation of the nomogram, as it is not possible to evaluate the external validity of the nomogram. Further studies are thus required to determine the external validity of the nomogram.

Despite these study limitations, our analyses revealed that decreases in the total sedentary behavior and the maximum sedentary bout on non-hemodialysis days were beneficial for the survival of chronic hemodialysis patients. Multicenter cohort studies are urgently required to confirm this relationship.

The total amount of sedentary behavior and the maximum sedentary bout on non-hemodialysis days were identified as important factors affecting the survival of patients under chronic hemodialysis, and we developed a nomogram for these patients' 5-year survival rate. The nomogram will be beneficial for estimating the 5-year survival rate of other chronic hemodialysis patients and will be a useful indicator in clinical practice for reducing patients' sedentary behavior.

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