Dynapenia is an independent predictor of cardio-cerebrovascular events in patients undergoing hemodialysis

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Original Articles

Dynapenia is an independent predictor of cardio-cerebrovascular events in patients undergoing hemodialysis

Short title: Dynapenia in patients undergoing hemodialysis

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Key words: sarcopenia, dynapenia, CV events, HD, AWGS

Abstract

Background: The number of patients on maintenance hemodialysis (HD) diagnosed with sarcopenia has been increasing through as individuals age. Recent focus is on the condition termed, “dynapenia,” which reduces only muscle function, as opposed to sarcopenia, which reduces both muscle mass and function. However, the association between dynapenia and cardio-cerebrovascular (CV) events in patients undergoing HD is largely unknown.

Objectives: The purpose of this study was to evaluate whether sarcopenia and dynapenia are associated with the onset of CV events in patients undergoing HD.

Methods: We retrospectively analyzed 342 patients undergoing HD between January and December 2018. Patients who underwent HD thrice per week for > 3 months were included in the analysis. We adopted the Asian Working Group on Sarcopenia criteria for the diagnosis of sarcopenia and dynapenia.

Results: In this study, 244 patients undergoing HD were enrolled. The prevalence of sarcopenia was 38.5%. Sarcopenia was determined to be an independent contributor to CV events in patients undergoing HD. To investigate the clinical relevance of dynapenia in patients with HD, patients without sarcopenia were further divided into dynapenia and non-dynapenia groups. Among 150 patients without sarcopenia, 46 were diagnosed with

dynapenia. In the Kaplan–Meier analysis, the rate of CV events was significantly different among the three groups in a stratified manner, with the highest rate in the sarcopenia group and the lowest rate in the non-sarco-dynapenia group. Both patients with sarcopenia and dynapenia had significantly increased CV events compared to those with non-sarco-dynapenia (HR 8.00; 95% CI 2.73–34.1; $p < 0.0001$ vs. HR 4.85; 95% CI 1.28–23.0; $p < 0.02$).

Conclusions: Both sarcopenia and dynapenia resulted in significantly higher CV events than non-sarco-dynapenia in patients undergoing HD. Therefore, clinicians should evaluate muscle function in addition to muscle quantity to estimate CV events in patients undergoing HD.

Abbreviations

HD = hemodialysis

AWGS = The Asian Working Group on Sarcopenia

CV = cardiovascular and cerebrovascular

DEXA = Dual-energy X-ray absorptiometry

SMI = Skeletal mass index

MI = Myocardial infarction

Introduction

Sarcopenia is a progressive and systemic skeletal muscle disorder involving the accelerated loss of muscle mass and function [1]. The Asian Working Group on Sarcopenia (AWGS) stated a consensus on the definition of sarcopenia in the Asian population in 2019 with consideration for ethnic variation [2]. It is well known that there exists an association between sarcopenia and cardiovascular and cerebrovascular (CV) events and mortality [3-5].

In recent years, attention has been focused on the condition termed “dynapenia,” which reduces only muscle function, as opposed to sarcopenia, which reduces muscle mass and function. Although a definition for dynapenia has not yet been available, several algorithms have been reported [6-8]. Clark BC. et al. proposed the term dynapenia to define age-related loss of muscle strength and power [9]. Recent reports define dynapenia as a condition in which a person has reduced walking speed and/or handgrip strength; however, the skeletal mass index (SMI) remains unaltered [10]. Dynapenia increase the risk of physical disability, poor physical performance, and even death [11, 6, 12-14]. However, little is known about the relationship between dynapenia and the occurrence of cardiovascular events.

The increase in patients undergoing hemodialysis (HD) with an aging population

is an important issue, because CV events significantly increase in these patients [15-18]. Furthermore, complication of sarcopenia is associated with increased mortality and CV events in patients undergoing HD [19, 20]. As one cause of sarcopenia in patients undergoing HD is that significantly more sedentary behaviors occur on dialysis days compared with non-dialysis days [21-23]. Therefore, a sedentary lifestyle is associated with an increased risk of mortality in patients undergoing HD [24, 25]. To date, however, the relationship between dynapenia and future adverse CV events in patients undergoing HD treatment is unknown. Therefore, this study aimed to evaluate whether sarcopenia and dynapenia are associated with the onset of CV events in patients undergoing HD.

Materials and Methods

Study Subjects

This retrospective observational study included 342 patients undergoing HD between January 2018 and December 2018 at Inoue Hospital in Suita, Japan. Patients who underwent HD thrice per week for > 3 months were included in the analysis. Of these, the current study excluded the following subjects: patients with missing or inappropriate dual-energy X-ray absorptiometry (DEXA) measurements (n=18), handgrip strength (n=21), or walking test results (n=25) and those with missing data (n=34). The remaining 244 patients were enrolled in the study (Fig. 1). The research protocol was

approved by the ethics committees of Osaka City University Hospital (2021-049) and Inoue Hospital (255).

Physical performance parameters

Physical performance was assessed at the baseline. A walking test was performed along a 4 m walkway with a 1 m start-up from the starting point at the patient's usual pace. All participants started walking in the standing position. Gait speed was calculated as 4 m divided by the time taken to walk this distance in seconds (m/s). Handgrip strength was measured using a hand-held dynamometer (Grip D; Model T.K.K. 5101, Takei Scientific Instruments Co. Ltd., Niigata, Japan). After adjusting the dynamometer for hand comfort, the handgrip strength was measured in a sitting position with the arm hanging by the side and the elbow fully extended. The highest grip strength after maximal effort was recorded twice for each hand. We used the maximum values based on the measurements obtained from both hands [26].

Body composition

Muscle mass was measured using DEXA (Horizon A, Hologic, USA). SMI was calculated by dividing the appendicular skeletal muscle mass by the body height in meters squared [2].

Definition of sarcopenia and dynapenia

We adopted the AWGS 2019 criteria for the diagnosis of sarcopenia. We used the cut-off values recommended by AWGS 2019 for muscle strength and muscle mass measurements as follows: low muscle strength was defined as handgrip strength, < 28 kg for men and < 18 kg for women and/or 6 m walk (< 1.0 m/s). Low muscle mass was measured using DEXA, defined as SMI < 7.0 kg/m^2 in men and < 5.4 kg/m^2 in women [2].

Dynapenia is a condition in which muscle mass is preserved with reduced muscle function. According to the previous reports, we defined dynapenia based on handgrip strength, < 28 kg for men and < 18 kg for women and/or 6 m walk (< 1.0 m/s) and SMI, > 7.0 kg/m^2 in men and > 5.4 kg/m^2 in women [9, 10].

Primary outcome assessments

The primary outcome was the occurrence of CV events, which included myocardial infarction (MI), angina, stroke, and hospitalization for congestive heart failure. MI and angina were confirmed using coronary angiography. Stroke was defined as the occurrence of hemorrhagic or ischemic stroke. The secondary outcome was hospitalization for non-CV events. These outcomes were obtained by reviewing the medical records, and when necessary, follow-up through a questionnaire by e-mail and telephone.

Statistical analyses

Normally distributed data are presented as median and interquartile range or mean ± SD. Comparisons between groups were performed using Student's t test, the Mann–Whitney U test, analysis of variance, or Kruskal-Wallis test for continuous variables and $\chi 2$ statistics or Fisher's exact test for categorical variables, as appropriate. For the combined endpoint analysis and survival rate, log-rank tests and Kaplan–Meier survival analyses were performed. We estimated the relative risk of CV events and non-CV events using the Cox proportional hazard regression model. In this study, all tests were two-tailed; $P < 0.05$ was considered statistically significant. These analyses were performed using the JMP software (version 13.0.0; SAS, Cary, NC, USA) for Windows.

Results

Patient characteristics

In this study, 244 patients undergoing HD aged 35 to 91 years were enrolled. Table 1 shows the baseline clinical characteristics of patients with and without sarcopenia. The prevalence of sarcopenia was determined to be 38.5%, with no significant difference in the duration of HD (in years) compared with non-sarcopenia. Male sex and age were significantly higher in patients with sarcopenia than in those without sarcopenia. On the other hand, BMI, diastolic blood pressure, heart rate, albumin, and LDL-cholesterol levels were significantly lower in patients with sarcopenia than in those without sarcopenia.

Echocardiographic parameters and coronary risk morbidity rates did not differ between the groups.

Clinical factors associated with CV events

To examine the association between various clinical factors and CV events in all participants, multivariate regression analyses were performed (Table 2). The presence of sarcopenia was determined to be an independent factor for CV events in patients undergoing HD (OR, 3.31; 95% CI, 1.12–9.76; p = 0.030). On the other hand, age and BMI, but not the presence of sarcopenia, were independent contributors to non-CV events in patients undergoing HD. Kaplan–Meier analysis revealed that the rate of CV events was higher in patients with sarcopenia than in those without sarcopenia [Fig. 2 (a)]. We observed no differences in the rate of non-CV events between the groups [Fig. 2 (b)].

Clinical relevance of dynapenia in patients undergoing HD

To investigate the clinical relevance of dynapenia in patients undergoing HD, patients without sarcopenia were further divided into dynapenia and non-dynapenia groups (Table 3). Among 150 patients without sarcopenia, 46 were diagnosed with dynapenia. In the comparison between the three groups, we observed a significant difference in sex, age, BMI, diastolic blood pressure, heart rate, albumin, calcium, phosphorous, and LDL-cholesterol levels. In the Kaplan–Meier analysis, the rate of CV events was significantly

different among the three groups in a stratified manner, with the highest rate in the sarcopenia group and the lowest rate in the non-sarco-dynapenia group (Fig. 3). Table 4 shows the hazard ratios for the CV events. Patients with sarcopenia and dynapenia had significantly increased CV events compared to the non-sarco-dynapenia group (HR 8.00; 95% CI 2.73–34.1; $p < 0.0001$ vs. HR 4.85; 95% CI 1.28–23.0; $p < 0.02$).

Discussion

The main findings of the present study on patients undergoing HD demonstrated that 1) the rate of CV events was significantly increased in the sarcopenia group, 2) the presence of sarcopenia was an independent predictor of CV events, and 3) grouping patients without sarcopenia based on the presence or absence of dynapenia could further stratify the CV event risk. To the best of our knowledge, this is the first study to investigate the clinical utility of evaluating the status of dynapenia in patients undergoing HD.

Age-related loss of muscle function is known as dynapenia [6], and it is recognized as a condition different from sarcopenia. This definition of dynapenia is important, as there is no linear relationship between skeletal muscle size and strength [27]. Our present data showed that both sarcopenia and dynapenia are independent predictors of CV events (Fig. 3). The risk of developing CV events in the dynapenia group was not

as high as that in the sarcopenia group; however, it was significantly higher than that in the non-sarco-dynapenia group (Table 4). Muscle function was reported to be a more powerful predictor of clinically relevant outcomes than muscle mass alone; however, the most important one is controversial [28, 27, 29, 4]. Recently, it was reported that slow gait speed and handgrip strength were associated with the onset of cardiovascular events in patients undergoing HD [26]. Muscle strength, power, and performance are determined based on multiple components of the skeletal muscle, including size, fiber type, quality, and innervation. Therefore, even if the patient exhibits a normal range of muscle/body composition, functional activity may be weak, given the potential impairment of other components of muscle function.[30].

The prevalence of sarcopenia is higher in CKD patients than in the general population, increasing with progression of CKD and more pronounced in patients undergoing HD [31, 32]. Many factors are involved in increasing the incidence of sarcopenia in CKD patients, including limited protein intake, energy deficiency, aging, sedentary lifestyle, inflammation, metabolic acidosis, and deficiency of natural vitamin D [33, 34]. Since many of these factors are related to CV events, we recognize a relationship between sarcopenia and HD and CV events.

In this study, the Kaplan–Meier analysis revealed that the rate of CV events was

significantly higher in the sarcopenia group than in the non-sarcopenia group. However, no difference was observed between the two groups in the case of non-CV events. These data indicate that patients undergoing HD with sarcopenia have a poor prognosis, specifically with respect to CV events. The results shown in Table 2 indicate that the presence of sarcopenia is an independent predictor of CV events; however, it was not a predictor of non-CV events. Previous studies have suggested that patients undergoing HD with sarcopenia showed significantly higher all-cause mortality rates or cardiovascular risk indices than those without sarcopenia [19, 20]. On the other hand, it was reported that sarcopenia was not a good predictor of other causes of mortality in patients undergoing HD [35]. Changes in early systemic indices, including atherosclerosis and endothelial dysfunction, are thought to be the mechanisms of increased CV events in patients with sarcopenia undergoing HD [19]. This may be because the patients were at a high risk of CV events. The trend showed that patients undergoing HD with sarcopenia had more non-CV events, which could have made a difference if the follow-up period was extended.

The current study had several limitations. First, the study was an observational retrospective study; thus, selection bias was inevitable. Second, the sample size was relatively small in this single-center study. Hence, a prospective study is warranted to

collect all necessary data to analyze the pathophysiology of sarcopenia/dynapenia and CV events. Finally, we did not evaluate medications, brain natriuretic peptide, or past history. These factors may explain the underlying mechanisms between sarcopenia/dynapenia and the occurrence of CV events.

Conclusions

Both sarcopenia and dynapenia resulted in significantly higher CV events than non-sarco-dynapenia in patients undergoing HD. Clinicians should evaluate muscle function in addition to muscle quantity to estimate CV events in patients undergoing HD in future.

Conflict of interest

The authors declare that they have no conflict of interests.

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Table 1. Patients' characteristics of the groups at the baseline

	With sarcopenia (n=94)	Without sarcopenia (n=150)	P value
Age (years)	72.4 ± 9.7	63.0 ± 11.6	<0.0001
Male gender, n (%)	77 (82)	95 (63)	0.001
Height (cm)	161.4 ± 8.1	163.1 ± 9.5	0.129
Dry weight (kg)	54.1 ± 9.2	63.3 ± 15.9	<0.0001
BMI (kg/m2)	20.7 ± 2.8	23.6 ± 4.7	<0.0001
Duration of HD (years)	11.9 (5.1)	10.8 ± 9.9	0.384
Systolic blood pressure (mmHg)	153 ± 21	153 ± 24	0.857
Diastolic blood pressure (mmHg)	75 ± 13	83 ± 13	<0.0001
Heart rate (bpm)	76 ± 13	81 ± 14	0.009
Handgrip strength (kg)	20.8 ± 5.7	27.0 ± 8.9	<0.0001
Gait speed (m/sec)	0.89 ± 0.26	1.17 ± 0.30	<0.0001
SMI (kg/m^2)	5.81 ± 0.74	6.88 ± 1.21	<0.0001
Comorbidity			
HT, n (%)	68 (72)	111 (74)	0.776
DLP, n (%)	20 (21)	34 (23)	0.487
DM, n (%)	39 (41)	62 (41)	0.981
AF, n (%)	5 (5)	9 (6)	0.825
PAD, n (%)	7 (7)	3 (2)	0.0369
Laboratory data			
Blood Urea Nitrogen (mg/dl)	55.2 ± 12.2	61.5 ± 9.9	<0.0001
Creatinine (mg/dl)	9.8 ± 2.4	11.2 ± 2.3	<0.0001
Sodium (mEq/l)	138.9 ± 2.4	139.4 ± 2.5	0.091
Potassium (mEq/l)	4.7 ± 0.6	4.8 ± 0.5	0.099
Calcium (mg/dl)	8.7 ± 0.7	8.9 ± 0.5	0.072
Magnesium (mg/dl)	2.5 ± 0.3	2.6 ± 0.4	0.327
Phosphorous (mg/dl)	5.0 ± 1.0	5.3 ± 10.7	0.015
Hemoglobin (g/dl)	11.1 ± 0.7	11.2 ± 0.6	0.291
Albumin (g/dl)	3.5 ± 0.2	3.7 ± 0.2	<0.0001
TSAT (%)	25.4 ± 8.5	25.0 ± 8.0	0.658
Ferritin (ng/ml)	101.4 (35.0)	93.0 ()	0.633
CRP (mg/dl)	0.41 (0.13)	0.33 ± 0.4	0.201

LDL-cholesterol (mg/dl)	78.8 ± 29.1	91.5 ± 30.0	0.003
HDL-cholesterol (mg/dl)	46.2 ± 12.5	47.4 ± 14.0	0.515
TTE findings			
LVDd (mm)	45.8 ± 6.5	46.6 ± 6.3	0.374
LVDs (mm)	29.0 ± 6.2	28.7 ± 6.1	0.700
IVS (mm)	11.7 ± 1.8	11.7 ± 1.8	0.964
PW (mm)	11.5 ± 1.2	11.8 ± 1.6	0.139
LAD (mm)	40.6 ± 5.5	41.3 ± 6.7	0.406
%FS (%)	37.0 ± 8.1	38.7 ± 7.1	0.083
EF (%)	60.8 ± 10.7	63.1 ± 9.1	0.077
E/A	0.83 ± 0.4	0.90 ± 0.4	0.218
DCT (mm)	212 ± 62	217 ± 65	0.576
E/e'	13.7 ± 6.4	12.8 ± 6.0	0.297
TRPG (mmHg)	25.2 ± 9.1	24.7 ± 9.0	0.742

Values expressed as the median and interquartile range (IQR), or mean ± SD. Values in parentheses are percentages.

BMI; body mass index, HD; hemodialysis, SMI; skeletal mass index , HT; hypertension , DLP; dyslipidemia, DM; diabetes mellitus, AF; atrial fibrillation, PAD; peripheral arterial disease, TSAT; transferrin saturation, CRP; C-reactive protein, LDL; low density lipoprotein, HDL; high density lipoprotein, TTE; transthoracic echocardiography, LVDd; left ventricular end-diastolic diameter, LVDs; left ventricular end-systolic diameter, IVS; interventricular septum, PW; posterior left ventricular wall, LAD; left atrial dimension, FS; fractional shortening, EF; ejection fraction, DCT; deceleration time, TRPG; transtricuspid pressure gradient,

Table 2. Multivariate analyses of events

Variable	Hazard ratio* (95%CI)	P value
CV events		
Sarcopenia	3.31 (1.12 - 9.76)	0.030
Male gender	1.46 (0.48 - 4.47)	0.504
Age	1.03 (0.98 - 1.08)	0.251
Duration of HD	0.98 (0.93 - 1.04)	0.471
BMI	1.01 (0.90 - 1.15)	0.817
Diastolic blood pressure	1.02 (0.98 - 1.06)	0.270
albumin	0.86 (0.12 - 6.40)	0.885
EF	0.96 (0.93 - 1.00)	0.065
non-CV events		
Sarcopenia	1.27 (0.65 - 2.45)	0.483
Male gender	0.82 (0.44 - 1.54)	0.533
Age	1.05 (1.01 - 1.08)	0.005
Duration of HD	1.01 (0.98 - 1.04)	0.494
BMI	1.10 (1.02 - 1.19)	0.011
Diastolic blood pressure	1.01 (0.99 - 1.03)	0.417
albumin	0.45 (0.08 - 2.59)	0.370
EF	1.41 (0.34 - 5.91)	0.636

* The effect estimate represents the change in score per 1 unit change in the parameter after adjusting for all other terms in the model.

CV; cardiovascular and cerebrovascular.

The other abbreviations are same as in Table 1.

Table 3. Patients' characteristics of the three groups at the baseline

	All subjects (n=244)	With sarcopenia (n=94)	without sarcopenia (n=150)		P value
			With dynapenia (n=46)	Without sarco-dynapenia (n=104)	
Age (years)	66.6 ± 11.8	72.4 ± 9.7	69.9 ± 9.5	60.0 ± 11.2	<0.0001
Male gender, n (%)	171 (70)	77 (82)	20 (43)	74 (71)	<0.0001
Height (cm)	162.5 ± 9.0	161.4 ± 8.1	158.5 ± 9.6	165.2 ± 8.7	<0.0001
Dry weight (kg)	59.7 ± 14.4	54.1 ± 9.2	63.7 ± 16.4	63.1 ± 15.8	<0.0001
BMI (kg/m2)	22.5 ± 4.3	20.7 ± 2.8	25.0 ± 4.6	22.9 ± 4.6	<0.0001
Duration of HD (years)	11.3 (3.9)	11.9 (5.1)	12.2 (3.2)	10.2 (3.6)	0.235
Systolic blood pressure (mmHg)	153 ± 23	153 ± 21	153 ± 25	154 ± 23	0.991
Diastolic blood pressure (mmHg)	80 ± 14	75 ± 13	79 ± 12	85 ± 13	<0.0001
Heart rate (bpm)	79 ± 14	76 ± 13	81 ± 16	81 ± 12	0.039
Handgrip strength (kg)	25 ± 8	20.8 ± 5.7	20.6 ± 9.6	29.8 ± 7.0	<0.0001
Gait speed (m/sec)	1.06 ± 0.32	0.89 ± 0.26	0.84 ± 0.22	1.31 ± 0.21	<0.0001
SMI (kg/m^2)	6.47 ± 1.17	5.81 ± 0.74	6.95 ± 1.09	6.85 ± 1.26	<0.0001
Comorbidity					
HT, n (%)	179 (73)	68 (72)	34 (74)	77 (74)	0.960
DLP, n (%)	59 (24)	20 (21)	13 (28)	26 (25)	0.642
DM, n (%)	101 (41)	39 (41)	23 (50)	40 (38)	0.361
AF, n (%)	14 (6)	5 (5)	5 (11)	4 (4)	0.272
PAD, n (%)	10 (4)	7 (7)	1 (2)	2 (2)	0.113
Laboratory data					
Blood Urea Nitrogen (mg/dl)	59.1 ± 11.3	55.2 ± 12.2	59.9 ± 9.2	62.2 ± 10.3	0.0003
Creatinine (mg/dl)	10.6 ± 2.4	9.8 ± 2.4	9.8 ± 1.9	11.8 ± 2.2	<0.0001
Sodium (mEq/l)	139.2 ± 2.5	138.9 ± 2.4	139.3 ± 2.4	139.5 ± 2.5	0.116
Potassium (mEq/l)	4.8 ± 0.5	4.7 ± 0.6	4.7 ± 0.5	4.8 ± 0.5	0.090
Calcium (mg/dl)	8.8 ± 0.6	8.7 ± 0.7	8.7 ± 0.5	8.9 ± 0.6	0.022
Magnesium (mg/dl)	2.6 ± 0.3	2.5 ± 0.3	2.5 ± 0.3	2.6 ± 0.3	0.095
Phosphorous (mg/dl)	5.2 ± 0.8	5.0 ± 1.0	5.1 ± 0.7	5.3 ± 0.7	0.024
Hemoglobin (g/dl)	11.1 ± 0.6	11.1 ± 0.7	11.1 ± 0.5	11.2 ± 0.6	0.208
Albumin (g/dl)	3.6 ± 0.2	3.5 ± 0.2	3.6 ± 0.2	3.7 ± 0.2	<0.0001

TSAT (%)	25.1 ± 8.2	25.4 ± 8.5	23.8 ± 7.5	25.4 ± 8.1	0.524
Ferritin (ng/ml)	96.3 (32.4)	101.4 (35.0)	119.4 (44.9)	81.4 (29.3)	0.115
CRP (mg/dl)	0.36 (0.11)	0.41 (0.13)	0.37 (0.12)	0.32 (0.1)	0.093
LDL-cholesterol (mg/dl)	86.8 ± 30.2	78.8 ± 29.1	91.1 ± 29.5	91.6 ± 30.4	0.009
HDL-cholesterol (mg/dl)	46.9 ± 13.5	46.2 ± 12.5	42.9 ± 11.9	49.3 ± 14.5	0.025
TTE findings					
LVDd (mm)	46.3 ± 6.4	45.8 ± 6.5	46.0 ± 7.3	46.9 ± 5.8	0.347
LVDs (mm)	28.8 ± 6.1	29.0 ± 6.2	28.8 ± 7.3	28.6 ± 5.4	0.932
IVS (mm)	11.7 ± 1.8	11.7 ± 1.8	11.4 ± 1.9	11.8 ± 1.8	0.527
PW (mm)	11.7 ± 1.5	11.5 ± 1.2	11.7 ± 1.7	11.8 ± 1.6	0.544
LAD (mm)	41.0 ± 6.2	40.6 ± 5.5	42.0 ± 5.8	40.9 ± 7.0	0.406
%FS (%)	38.1 ± 7.5	37.0 ± 8.1	37.8 ± 7.5	39.2 ± 6.9	0.218
EF (%)	62.2 ± 9.8	60.8 ± 10.7	61.9 ± 9.8	63.6 ± 8.8	0.233
E/A	0.88 ± 0.4	0.83 ± 0.4	0.96 ± 0.5	0.88 ± 0.3	0.179
DCT (mm)	215 ± 64	212 ± 62	220 ± 76	216 ± 59	0.810
E/e'	13.1 ± 6.2	13.7 ± 6.4	13.6 ± 5.5	12.4 ± 6.2	0.206
TRPG (mmHg)	24.9 ± 8.6	25.2 ± 9.1	27.6 ± 6.0	23.5 ± 9.0	0.081

Values expressed as the median and interquartile range (IQR), or mean ± SD. Values in parentheses are percentages.

The abbreviations are same as in Table 1.

Table 4. Hazard ratios for CV events

Variable	Hazard ratio* (95%CI)	P value
non sarco-dynapenia	1.00 (Reference)	
dynapenia	4.85 (1.28 - 23.0)	0.020
sarcopenia	8.00 (2.73 - 34.1)	<0.0001

* The effect estimate represents the change in score per 1 unit change in the parameter.

The abbreviations are same as in Table 2.

Figure Titles and Legends

Fig. 1 The flowchart of the study. HD, hemodialysis; DEXA, dual-energy X-ray absorptiometry.

This retrospective observational study included 342 patients undergoing HD between January 2018 and December 2018 and 244 patients were enrolled in the study.

Fig. 2 Kaplan–Meier analysis of (a) CV events and (b) non-CV events in patients undergoing HD with or without sarcopenia.

Kaplan–Meier analysis revealed that the rate of CV events was higher in patients with sarcopenia than in those without sarcopenia, in the other hands, the rate of non-CV events was no significant difference of two groups.

Fig. 3 Kaplan–Meier analysis of CV events in patients undergoing HD with sarcopenia, dynapenia, or without these conditions.

In the Kaplan–Meier analysis, the rate of CV events was significantly different among the three groups in a stratified manner, with the highest rate in the sarcopenia group and the lowest rate in the non-sarco-dynapenia group

Fig.1

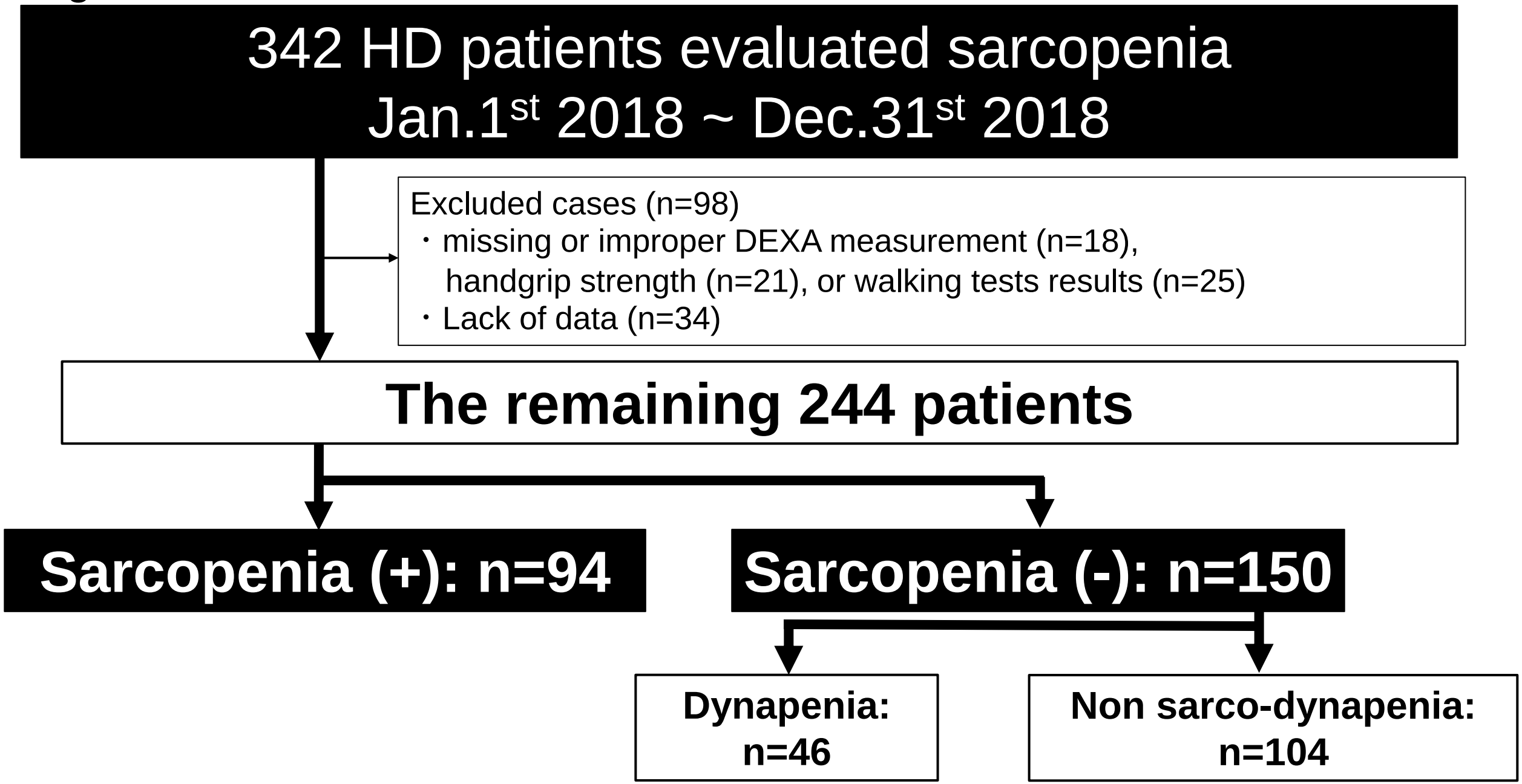
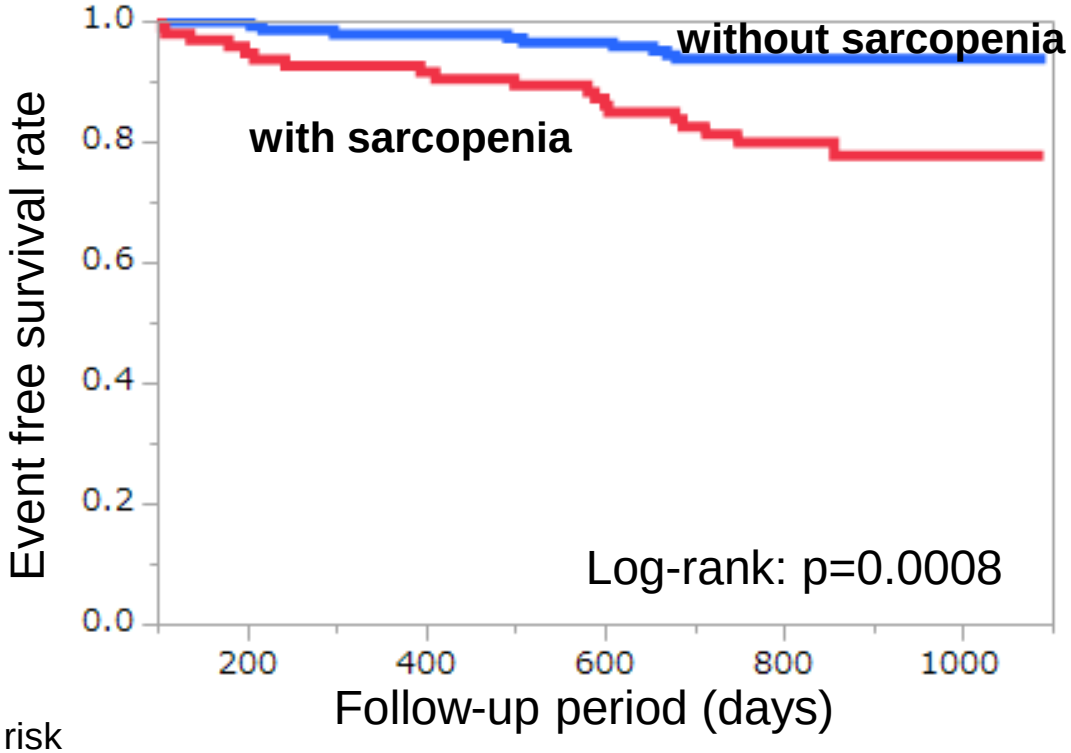

342 HD patients evaluated sarcopenia
Jan.1st 2018 ~ Dec.31st 2018
Excluded cases (n=98)
・missing or improper DEXA measurement (n=18),
handgrip strength (n=21), or walking tests results (n=25)
・Lack of data (n=34)
The remaining 244 patients
Sarcopenia (+): n=94
Sarcopenia (-): n=150
Dynapenia: n=46
Non sarco-dynapenia: n=104

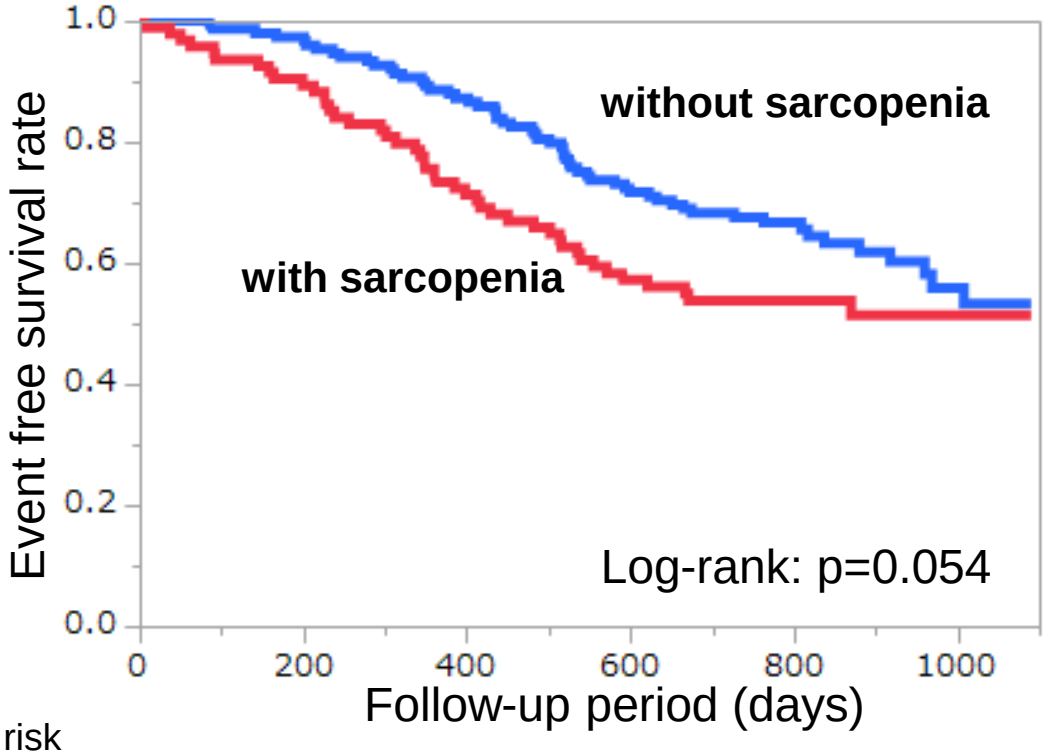
Fig.2

(a) CV events



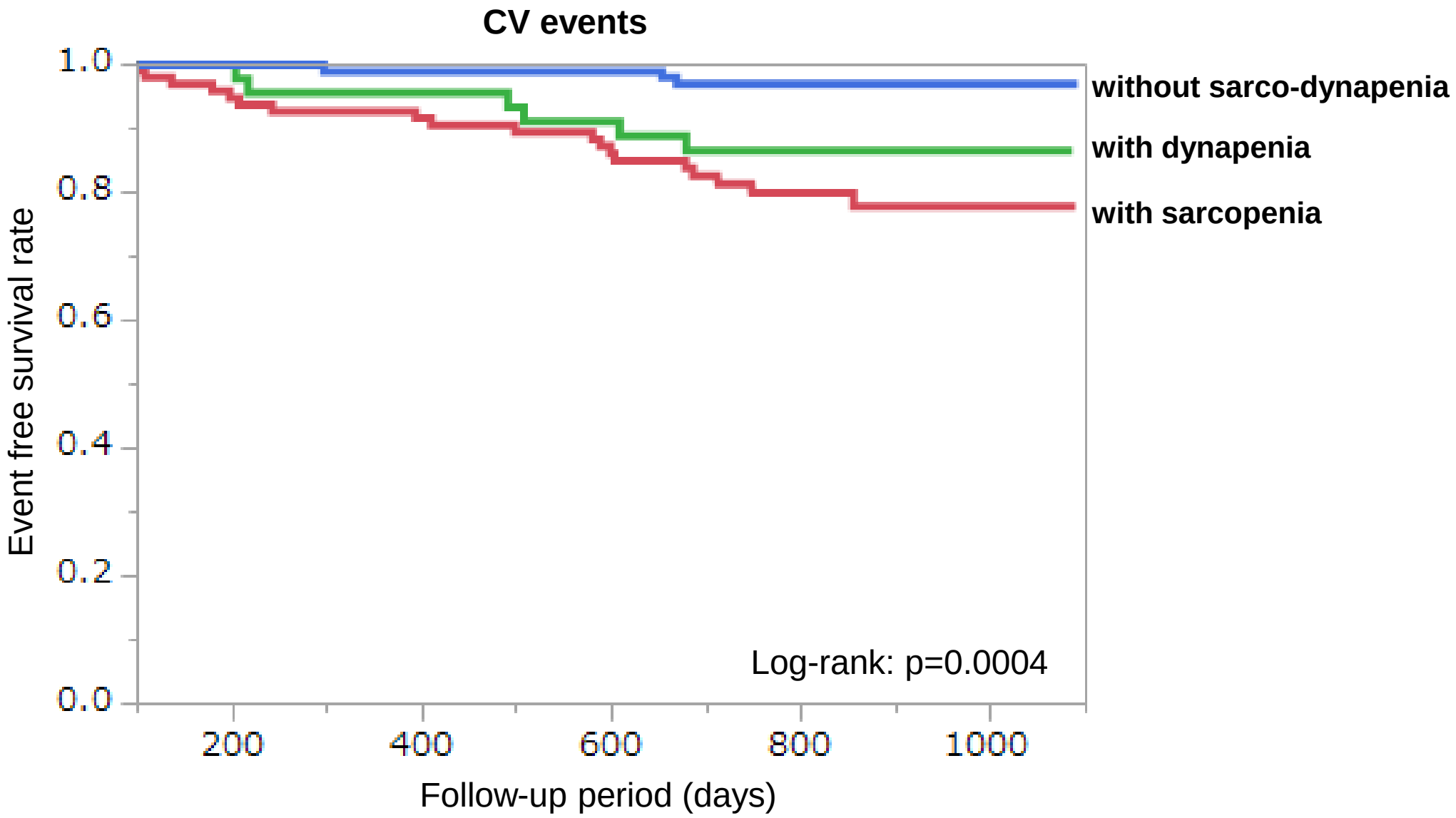
Number at risk					
With sarcopenia	94	86	77	48	13
Without sarcopenia	150	147	144	94	41

(b) non-CV events



Number at risk					
With sarcopenia	94	68	52	32	10
Without sarcopenia	150	130	107	66	25

Fig.3



Number at risk					
With sarcopenia	94	86	77	48	13
Without sarcopenia	46	44	41	27	13
Without sarco-dynapenia	104	103	103	66	28