



The psoas muscle index as a predictor of long-term survival after cardiac surgery for hemodialysis-dependent patients

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Abstract

Sarcopenia represented by skeletal muscle depletion is closely related to frailty and predicts prognoses in the general population. However, its predictive value for hemodialysis (HD)-dependent patients undergoing cardiac surgery has not been fully investigated. We aimed to clarify the impact of sarcopenia on the outcomes of HD-dependent patients after cardiac surgery. We retrospectively reviewed 138 HD-dependent patients who underwent cardiac surgery between January 2006 and December 2017. Sarcopenia was assessed using the psoas muscle index (PMI), which was calculated using values measured on preoperative computed tomography images and the following formula: cross-sectional area of bilateral psoas muscle/height². Patients were divided into two groups according to the PMI: the sarcopenia group (≤ 443 mm²/m² for men and ≤ 326 mm²/m² for women; $n = 35$) and the non-sarcopenia group (> 443 mm²/m² for men and > 326 mm²/m² for women; $n = 103$). Preoperative characteristics and surgical outcomes were compared. Overall in-hospital mortality did not differ between the sarcopenia and non-sarcopenia groups. However, the patients with sarcopenia had significantly decreased long-term survival. Multivariate analysis revealed that low PMI was a significant independent predictor of long-term mortality (hazard ratio, 1.92; 95% confidential interval, 1.19–3.17; $p < 0.01$). Long-term survival rates in HD-dependent patients undergoing cardiac surgery are severely affected by the presence of preoperative sarcopenia defined by PMI. Preoperative risk analysis using the PMI might contribute to risk stratification of and decision-making for HD-dependent patients undergoing cardiac surgery.

Keywords Hemodialysis · Sarcopenia · Cardiac surgery · Artificial valve · Artificial kidney/dialysis

Introduction

Despite recent advances in dialysis technology and surgical treatment, the mortality and morbidity rates of hemodialysis (HD)-dependent patients undergoing cardiac surgery remain high [1]. Studies have reported that sarcopenia comprising decreased skeletal muscle mass was frequently observed in HD patients and affected their prognoses [2–4]. In such a fragile patient cohort, risk analysis from the viewpoint of sarcopenia is essential for improving surgical outcomes.

Sarcopenia has been identified as a useful prognostic tool for patients undergoing major surgeries [5–8], and the

negative impact of sarcopenia on surgical outcomes of cardiac surgery has been reported [9–13]. However, the impact of sarcopenia in HD-dependent patients has not been fully investigated. Recently, it was noted that the psoas muscle index (PMI), which represents the volume of skeletal muscle in the entire body, reflects sarcopenia and predicts surgical outcomes [10–13]. In this study, we assessed the usefulness of the PMI as a predictor of surgical outcomes in HD-dependent patients who underwent cardiac surgery.

Materials and methods

Patients and study design

The study protocol was approved by the Ethics Committee on Human Research of Jichi Medical University Hospital (A18-052). The requirement for informed consent was

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waived due to the retrospective observational nature of this study.

Among 1720 consecutive patients who underwent valve surgery and coronary artery bypass grafting at the Jichi Medical University Hospital between January 2006 and December 2017, 152 (8.8%) were chronic HD-dependent patients. Of these patients, PMI data were missing for 14 (8.6%) patients; therefore, a total of 138 patients were included in this study [99 men and 39 women; mean age, 66 ± 9 years (range 28–83)]. In 79 (57%) patients, renal failure secondary to diabetes was present. Non-diabetic nephropathy was observed in 59 (43%) patients. Preoperatively, all patients underwent maintenance HD. The mean duration of dialysis before the surgery was 103 ± 84 months (range 1–432 months).

First, 21 preoperative variables were evaluated to determine the risk factors for in-hospital and long-term mortality. Each variable was evaluated by univariate analysis, and variables with $p < 0.05$ were included in the multivariate logistic regression analysis. Subsequently, we divided the patients into two groups, those with and those without sarcopenia, based on the PMI measured using preoperative computed tomography (CT) imaging. The clinical characteristics of patients in both groups were compared, and the in-hospital mortality, postoperative complications, long-term survival, and duration of hospital stay were assessed.

Surgical procedures

The surgical procedures are listed in Table 1. Isolated coronary artery bypass grafting was performed in 51 patients, valve surgery was performed in 47, and combined surgery was performed in 40. In valve surgeries, mechanical heart valves were used in 74 patients, bioprostheses were used in 8, and an annular ring for annuloplasty was used in 5. Ten

Table 1 Surgical procedures performed in the study cohort

Procedures	Total (%)
Isolated CABG	
Off-pump	18 (13%)
On-pump	33 (24%)
Valve surgery	
Single valve (+ TAP)	33 (24%)
Double valve (+ TAP)	10 (7%)
Aortic root replacement	2 (1%)
Apico-aortic bypass	2 (1%)
Combined surgery	
Valve + CABG	34 (25%)
Valve + congenital	3 (2%)
Valve + ascending aorta	3 (2%)

CABG coronary artery bypass grafting, TAP tricuspid annuloplasty

patients underwent emergency/urgent surgeries, which were defined as those performed within 24 h of consultation.

Surgical techniques

Surgery was performed through a median sternotomy, except for 4 patients who underwent an apico-aortic bypass. Patients who underwent valve and concomitant cardiac procedures received moderate hypothermic cardiac arrest with the standard cardiopulmonary bypass (apico-aortic bypass was performed under ventricular fibrillation). Cold blood cardioplegic solution was administered in an antegrade or retrograde manner.

HD was performed on the day before surgery using the standard method. We performed hemofiltration using a hemoconcentrator incorporated within a circuit to manage excess hemodilution during cardiopulmonary bypass. Washed red blood cells treated with an autotransfusion system (Haemoneics Corporation, Braintree, MA) were used to avoid hyperkalemia associated with blood transfusion during surgery. After surgery, most patients resumed their routine intermittent HD in the intensive care unit starting on the first postoperative day; however, those who were hemodynamically unstable or had advanced hyperkalemia alternatively underwent continuous veno-venous hemofiltration/hemodiafiltration.

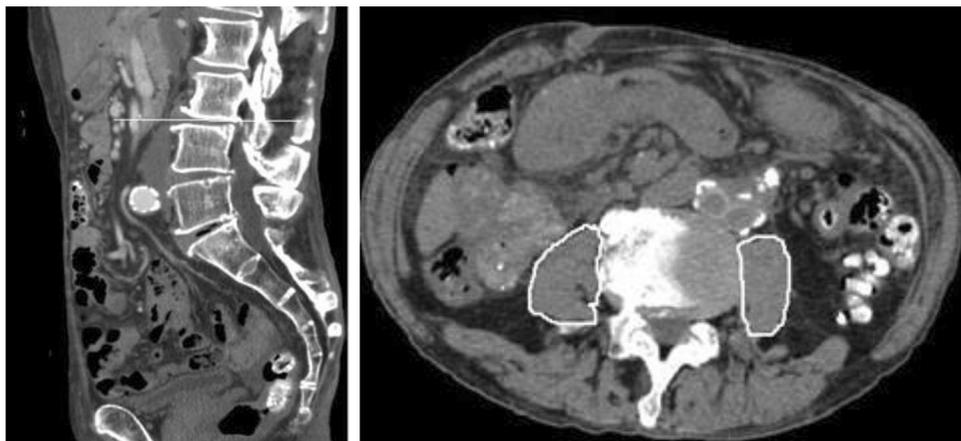
Definition of sarcopenia

We measured the psoas muscle area the preoperative CT scan and calculated the PMI. All preoperative CT scans were performed within 2 months before surgery. Using preoperative plain CT images at the lower border of the third lumbar vertebra (L3), the cross-sectional area of the bilateral psoas muscle was measured using manual tracing. The PMI (mm^2/m^2) was calculated using the following formula: $\text{PMI} = \text{cross-sectional area of the bilateral psoas muscle (lower border of L3)} / \text{height}^2$ (mm^2/m^2) (Fig. 1). In this study, sarcopenia was defined as a PMI below the 25th sex-specific percentile, based on the definitions used in the original description of the frailty phenotype and a prior analysis [14, 15].

Data collection and follow-up

The clinical characteristics of patients were acquired retrospectively from their medical records. Mortality was defined as death that occurred during the follow-up period due to any cause. Patients were either examined at our outpatient clinic or contacted by telephone and all patients were followed-up. The time between the surgery and examination or other contact ranged from 1 to 129 months (mean 35 ± 33 months).

Fig. 1 Psoas muscle area on the preoperative computed tomography scan. The cross-sectional area of the bilateral psoas muscle at the lower border of the third lumbar vertebra was measured



Statistical analyses

Categorical variables were presented as numbers. Differences between groups were assessed using Fisher's exact test. Overall survival was defined as the time from surgery to death from any cause. Time-related survival was estimated using the Kaplan–Meier method and compared using the log-rank test. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using a multivariate Cox proportional hazards regression model. Long-term mortality predictions included in-hospital mortality. Statistical analysis was performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). $p < 0.05$ was considered statistically significant.

Results

Sarcopenia

The distribution of the PMI is shown in Fig. 2. The average PMI was $532 \pm 154 \text{ mm}^2/\text{m}^2$ for men and $413 \pm 138 \text{ mm}^2/\text{m}^2$ for women. Based on the definition of sarcopenia in this study, the cut-off value for sarcopenia was $443 \text{ mm}^2/\text{m}^2$ in male and $326 \text{ mm}^2/\text{m}^2$ in female patients. Thus, it was determined that there were 35 patients with sarcopenia and 103 without sarcopenia.

Clinical outcomes

In-hospital mortality occurred in 13 patients (9.4%). The causes of in-hospital mortality were pneumonia ($n=6$ patients), heart failure ($n=3$), myocardial infarction ($n=2$), and cerebral infarction ($n=2$).

A total of 69 patients died after hospital discharge. The causes of death included heart failure ($n=10$), arrhythmia

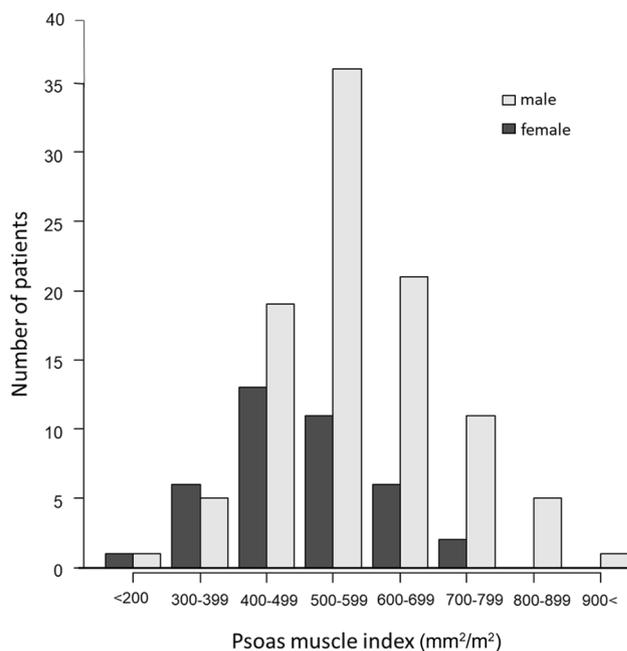


Fig. 2 Distribution of psoas muscle index. The cut-off value of the psoas muscle index was defined as the lowest sex-specific quartile. The cut-off value for sarcopenia was $443 \text{ mm}^2/\text{m}^2$ in men and $326 \text{ mm}^2/\text{m}^2$ in women

($n=8$), multiple organ failure ($n=8$), withdrawal from dialysis ($n=7$), pneumonia ($n=6$), cerebral hemorrhage/infarction ($n=5$), myocardial infarction ($n=3$), malignancy ($n=2$), rupture of abdominal aortic aneurysm ($n=1$), peritonitis ($n=1$), ileus ($n=1$), lower leg ischemia ($n=1$), blood access trouble ($n=1$), prosthetic valve endocarditis ($n=1$), and unknown causes ($n=14$). The 1-, 3-, and 5-year survival rates (including in-hospital deaths) were $71 \pm 4\%$, $57 \pm 5\%$, and $41 \pm 5\%$, respectively.

Risk factors for in-hospital death

The preoperative risk factors for in-hospital death are presented in Table 2. The univariate analysis revealed that age ≥ 70 years, concomitant procedures, body mass index ≤ 18 kg/m², total cholesterol ≤ 120 mg/dL, serum albumin ≤ 3.0 g/dL, and total lymphocyte count ≤ 700 (μ L) were risk factors for in-hospital death, but sarcopenia (low PMI) was not ($p = 0.09$).

Risk factors for long-term mortality

The preoperative risk factors for long-term mortality are presented in Table 2. The univariate analysis (including in-hospital mortality) identified the following five risk factors as statistically significant predictors of long-term mortality: age ≥ 70 years, ejection fraction $\leq 30\%$, urgent/emergency surgery, albumin ≤ 3.0 g/dL, and low PMI. The multivariate analysis using Cox proportional

hazards modeling confirmed that low PMI was a statistically significant predictor of long-term mortality (HR, 1.94; 95% CI, 1.19–3.17; $p < 0.01$), as well as ejection fraction $\leq 30\%$, emergency surgery, age ≥ 70 years, and serum albumin ≤ 3.0 g/dL (Table 3).

Table 3 Multivariate analysis of long-term mortality

Variables	Hazard ratio	95% CI	<i>p</i> value
Left ventricular ejection fraction $\leq 30\%$	2.78	1.32–1.75	0.006
Emergency surgery	2.69	1.20–5.88	0.016
Low PMI ^a	1.94	1.19–3.17	0.008
Age ≥ 70 years	1.88	1.18–3.02	0.008
Serum albumin ≤ 3.0 g/dL	1.61	1.00–2.63	0.048

CI confidence interval, PMI psoas muscle index

^a ≤ 443 mm²/m² in men and ≤ 326 mm²/m² in women

Table 2 Preoperative patient characteristics: results of the univariate analysis

Variables	In-hospital mortality			Long-term mortality		
	Died (<i>n</i> = 13)	Survived (<i>n</i> = 125)	<i>p</i> value ^a	Died (<i>n</i> = 82) ^b	Survived (<i>n</i> = 56)	<i>p</i> value
Age ≥ 70	10 (77%)	42 (34%)	0.005	35 (43%)	17 (30%)	0.041
Female	4 (31%)	35 (28%)	1.000	22 (27%)	17 (30%)	0.707
Duration of HD ≥ 100 months	4 (31%)	56 (45%)	0.391	33 (40%)	27 (48%)	0.803
Diabetes nephropathy	7 (54%)	72 (58%)	1.000	46 (56%)	33 (59%)	0.657
Smoking	5 (39%)	65 (52%)	0.395	41 (50%)	29 (52%)	0.895
LVEF $\leq 30\%$	4 (31%)	13 (11%)	0.058	10 (12%)	7 (13%)	0.005
NYHA function classes 3 and 4	9 (69%)	57 (46%)	0.146	37 (45%)	29 (52%)	0.765
Urgent/emergency surgery	3 (23%)	7 (6%)	0.054	8 (10%)	2 (4%)	0.040
Infective endocarditis	1 (8%)	2 (2%)	0.259	3 (4%)	0 (0%)	0.071
Concomitant procedure	8 (62%)	32 (26%)	0.011	25 (30%)	15 (27%)	0.212
Associated disease						
Hypertension	10 (77%)	86 (69%)	0.754	56 (68%)	40 (71%)	0.057
Cerebrovascular disease	3 (23%)	27 (22%)	1.000	18 (22%)	12 (21%)	0.607
Peripheral artery disease	3 (23%)	37 (30%)	0.754	27 (33%)	13 (23%)	0.407
Chronic lung disease	1 (8%)	7 (6%)	0.557	6 (7%)	2 (4%)	0.670
Liver dysfunction ^c	2 (15%)	12 (10%)	0.622	9 (11%)	4 (7%)	0.523
Nutritional status						
Emaciation (BMI ≤ 18 kg/m ²)	6 (46%)	15 (12%)	0.005	17 (21%)	4 (7%)	0.060
Anemia (hemoglobin ≤ 9.0 g/dL)	3 (23%)	18 (14%)	0.418	14 (17%)	7 (13%)	0.485
Total cholesterol ≤ 120 mg/dL	9 (69%)	29 (23%)	0.001	22 (27%)	16 (29%)	0.084
Serum albumin ≤ 3.0 g/dL	8 (62%)	24 (19%)	0.002	27 (33%)	5 (9%)	0.014
Lymphocytic count ≤ 700 (μ L)	8 (62%)	39 (31%)	0.035	29 (35%)	18 (32%)	0.056
Low PMI ^d	6 (46%)	29 (23%)	0.093	26 (32%)	9 (16%)	0.013

HD hemodialysis, LVEF left ventricular ejection fraction, NYHA New York Heart Association, BMI body mass index, PMI psoas muscle index

^a*p* values for each variable with regard to hospital mortality

^bIncluding in-hospital mortality

^cDefined by serum aspartate transaminase and alanine transaminase > 35 IU/L

^d ≤ 443 mm²/m² for men and ≤ 326 mm²/m² for women

Sarcopenia vs. non-sarcopenia

The preoperative and operative characteristics of each group are shown in Table 4. Liver dysfunction was frequently associated with sarcopenia. Body mass index was significantly lower among patients in the sarcopenia group. However, there was no difference in-hospital mortality (sarcopenia vs. non-sarcopenia: 17.1% [6/35] vs. 6.8% [7/103], respectively; $p=0.09$) or postoperative hospitalization between the groups (29 ± 22 vs. 37 ± 51 days; $p=0.5$). Regarding the causes of hospital deaths, there was no significant difference between the groups (Appendix 1).

The long-term results in the sarcopenia and non-sarcopenia groups are shown in Fig. 3. Kaplan–Meier survival curves revealed that the 1-, 3-, and 5-year survival rates were $60 \pm 8\%$, $44 \pm 9\%$, and $28 \pm 9\%$ for patients in the sarcopenia group and $75 \pm 4\%$, $61 \pm 5\%$, and $46 \pm 6\%$ for those in the non-sarcopenia group, respectively. The log-rank test

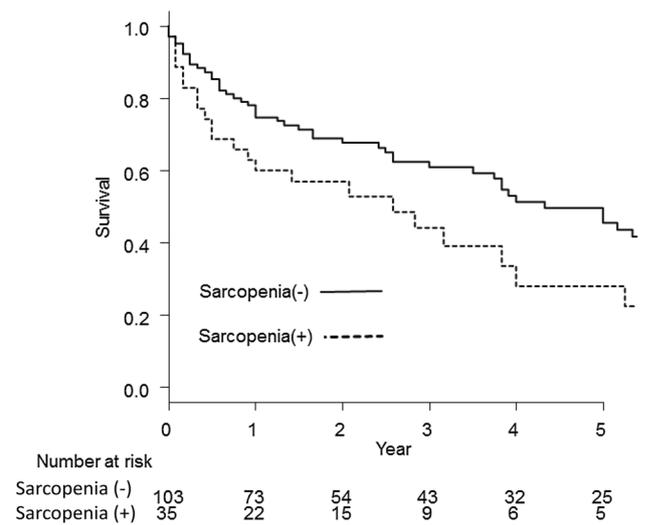


Fig. 3 Kaplan–Meier curves of long-term survival in the sarcopenia and non-sarcopenia groups

Table 4 Perioperative characteristics of patients in the sarcopenia and non-sarcopenia groups

Characteristic	Sarcopenia (+) (n=35)	Sarcopenia (-) (n=103)	p value
Preoperative			
Age (years)	67 ± 10	66 ± 9	0.746
NYHA classes 3 and 4	15 (43%)	51 (50%)	0.559
HD duration (month)	96 ± 83	106 ± 84	0.528
Left ventricular ejection fraction (%)	50 ± 15	52 ± 16	0.488
Diabetes nephropathy	20(57%)	59 (57%)	1.000
Hypertension	26 (74%)	70 (68%)	0.531
Liver dysfunction ^a	7 (20%)	7 (7%)	0.046
Chronic lung disease	3 (9%)	5 (5%)	0.418
Cerebrovascular accident	10 (29%)	20 (19%)	0.342
Current smoker	18 (51%)	52 (51%)	1.000
Peripheral vascular disease	12 (34%)	28 (27%)	0.518
Total cholesterol (mL/dL)	155 ± 41	147 ± 38	0.325
Hemoglobin (g/dL)	10.7 ± 1.5	10.5 ± 1.5	0.395
BMI (kg/m ²)	19.5 ± 2.9	22.6 ± 3.8	<0.001
Serum albumin (g/dL)	3.26 ± 0.55	3.43 ± 0.51	0.105
Total lymphocytic count (1000/μL)	924 ± 397	1025 ± 448	0.239
Operative			
Infective endocarditis	1 (3%)	2 (2%)	1.000
Urgent surgery	1 (3%)	9 (9%)	0.452
Repeat surgery	1 (3%)	3 (3%)	1.000
Concomitant procedure	14 (40%)	26 (25%)	0.130
Operation time (min)	388 ± 102	378 ± 109	0.646
Intraoperative fluid balance (mL)	2945 ± 1613	3003 ± 2195	0.888
Intraoperative blood transfusion (mL)	2629 ± 1342	2626 ± 1659	0.991
Postoperative			
In-hospital mortality	6 (17%)	7 (7%)	0.09
Postoperative hospitalization	29 ± 22	37 ± 51	0.50

NYHA New York Heart Association, HD hemodialysis, BMI body mass index

^aDefined by serum aspartate transaminase and alanine transaminase > 35 IU/L

revealed that patients in the sarcopenia group had significantly lower survival rates than those in the non-sarcopenia group ($p = 0.01$). Regarding the causes of remote deaths, there was no significant difference between the groups (Appendix 2).

Discussion

The term of sarcopenia was proposed by Rosenberg in the late 1980s to describe age-related decreases in muscle mass [16]. The condition is characterized by age-associated generalized loss of skeletal muscle mass and muscle strength, resulting in an insidious functional decline. Recently, sarcopenia has been used to describe loss of muscle mass and function as a result of aging, development of chronic disease, physical inactivity, and inappropriate nutrition (secondary sarcopenia) [17]. Therefore, sarcopenia is an important component of physical frailty. The previous studies reported that sarcopenia was associated with morbidity and mortality after major surgeries [5–15]. The principal finding of this study was that preoperative sarcopenia predicted the long-term mortality of HD-dependent patients undergoing cardiac surgery.

The prevalence of sarcopenia in HD-dependent patients is reportedly higher than that in the general population [2–4]. Sarcopenia is present in about 5–10% of individuals older than 65 years in the general population [18] and 33.1% of HD-dependent patients, which is over three times higher than the prevalence in the general population [4]. As for the PMI in the Japanese general population, Hamaguchi et al. reported mean PMIs of $885 \pm 161 \text{ mm}^2/\text{m}^2$ in men and $577 \pm 121 \text{ mm}^2/\text{m}^2$ in women [19], which were higher than those in our HD-dependent patients ($532 \pm 154 \text{ mm}^2/\text{m}^2$ in men and $413 \pm 138 \text{ mm}^2/\text{m}^2$ in women). Thus, HD-dependent patients are frail and vulnerable. Furthermore, HD leads to increased levels of uremic toxins, malnutrition, and the chronic inflammation, which results in muscle wasting and serious frailty [20].

HD-dependent patients with cardiac diseases are quite fragile, and concurrent sarcopenia leads to a multisystem reduction in reserve capacity. Consequently, it increases the risk of disability and death from external stress caused by various surgeries [21]. The previous reports have indicated that long-term survival after cardiac surgery is severely affected by the presence of sarcopenia. Okamura et al. reported a 5-year survival rate of $72.0 \pm 5.1\%$ in patients with sarcopenia and $91.1 \pm 1.8\%$ in those without. Compared to their results, the 5-year survival rates of our HD-dependent patients were significantly worse ($28 \pm 9\%$ in sarcopenic patients and $46 \pm 6\%$ in non-sarcopenic patients). These results suggest that the surgical insult was amplified in this vulnerable patient cohort and that concurrent sarcopenia

worsens surgical outcomes. Okamura et al. also pointed to the increased risk posed by sarcopenia in chronic renal failure patients after cardiac surgery [13].

In this study, a low PMI could predict long-term but not in-hospital mortality after cardiac surgery in HD-dependent patients. Similar results have been reported in non-HD-dependent patients undergoing cardiac surgery. Paknikar et al., Hawkins et al., and Okamura et al. reported that while short-term outcomes were not significantly affected by sarcopenia, long-term results were significantly worse [8, 10, 13]. It is unclear why a low PMI can predict late but not early mortality after cardiac surgery. Sarcopenia defined by the PMI is a core component of physical frailty, which summarizes baseline vulnerability to stressors and homeostatic reserve in the chronic phase. It is not influenced by acute-phase parameters such as edema and acute inflammation. Since the PMI does not reflect the patient's condition in "real time," it might not be appropriate for the estimation of acute deterioration or short-term predictions. These factors might partially explain why the PMI has poor ability to predict short-term results.

We previously reported the prognostic nutritional index as a predictor for early and long-term surgical outcomes in HD-dependent patients [22]. This index is calculated based on acute-phase parameters (serum albumin concentration and lymphocyte counts) and reflects the patients' real-time immune-nutritional status, which is by malnutrition and acute inflammation. Therefore, the prognostic nutritional index is a powerful predictor of short-term results and can help evaluate therapeutic effects.

Our study had several limitations. It was a non-randomized, retrospective study with a small sample size. In addition, it had a relatively short follow-up period. The data were collected over the course of a decade. This means that it is likely that the outcomes may have been influenced by the differences in surgical techniques and perioperative management approaches, including HD methods. The definition of sarcopenia remains unestablished, and no definitive method or specific numerical thresholds to define the condition exist. In this study, the cut-off value for PMI was defined as the lowest sex-specific quartile, in accordance with the previous studies [14, 15]. The PMI potentially differs among age groups; therefore, distinct certain cut-off values for each age group might be necessary to develop a practical definition of sarcopenia.

Conclusion

Preoperative sarcopenia assessed by the PMI predicted long-term mortality of HD-dependent patients undergoing cardiac surgery. Left ventricular dysfunction, emergency surgery, old age, and hypoalbuminemia were also identified

as significant predictors. Preoperative evaluation of the PMI might be useful for risk stratification of and clinical decision-making for HD-dependent patients undergoing cardiac surgery.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Appendix 1: Causes of in-hospital deaths in the sarcopenia and non-sarcopenia groups

Cause of death	Sarcopenia (+) (n=6)	Sarcopenia (-) (n=7)	p value
Heart failure	1 (17%)	2 (29%)	0.562
Pneumonia	3 (50%)	3 (43%)	0.616
Cerebral hemorrhage/infarction	1 (17%)	1 (14%)	0.730
Myocardial infarction	1 (17%)	1 (14%)	0.730

Appendix 2: Causes of remote deaths in the sarcopenia and non-sarcopenia groups

Cause of death	Sarcopenia (+) (n=20)	Sarcopenia (-) (n=49)	p value
Heart failure	4 (20%)	6 (12%)	0.315
Withdrawal from dialysis	2 (10%)	5 (10%)	0.674
Pneumonia	1 (5%)	5 (10%)	0.434
Cerebral hemorrhage/infarction	3 (15%)	2 (4%)	0.141
Arrhythmia	2 (10%)	6 (12%)	0.577
Multiple organ failure	3 (15%)	5 (10%)	0.422
Myocardial infarction	2 (10%)	1 (2%)	0.199
Rupture of abdominal aneurysm	0 (0%)	1 (2%)	0.710
Malignancy	1 (5%)	1 (2%)	0.498
Peritonitis	0 (0%)	1 (2%)	0.710
Ileus	0 (0%)	1 (2%)	0.710
Lower leg ischemia	0 (0%)	1 (2%)	0.710
Blood access trouble	0 (0%)	1 (2%)	0.710
Prosthetic valve endocarditis	0 (0%)	1 (2%)	0.710
Unknown (including sudden death)	2 (10%)	12 (24%)	0.151

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