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Impact of Nutritional Status and Cardiopulmonary Exercise Testing-Based Exercise Education on Long-Term Outcomes in Acute Coronary Syndrome

— Insights From the Mie ACS Registry —

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Background: Exercise training based on cardiopulmonary exercise testing (CPET) improves outcomes in patients with acute coronary syndrome (ACS), while nutritional status is also crucial. This study evaluated CPET implementation and the impacts of clinical parameters, including CPET and nutritional status, on 2-year outcomes in ACS patients.

Methods and Results: Data from 2,621 ACS patients enrolled in the Mie ACS registry were analyzed. Of these, 938 were hospitalized in CPET-equipped facilities, while 1,683 were not. Nutritional status was assessed using controlling nutritional status (CONUT) score. Cox regression analysis evaluated the associations between nutritional status, CPET-based exercise education, and 2-year prognosis. Among the 938 patients in CPET facilities, 359 underwent CPET and received exercise education. During the 2-year follow up, 60 all-cause deaths occurred. Univariate Cox regression revealed that CPET implementation was associated with lower all-cause mortality. Other predictors included hemoglobin levels, age, hospitalization length, Killip class ≥2, mechanical support, and malnutrition. In multivariate Cox regression, CPET implementation remained an independent predictor of mortality (hazard ratio 0.47; P=0.04). However, when nutritional status was included, moderate to severe malnutrition emerged as an independent predictor of all-cause mortality (hazard ratio 2.47; P=0.02), diminishing the significance of CPET (P=0.058).

Conclusions: Moderate to severe malnutrition is a powerful independent prognostic factor for mortality in the Mie ACS registry. CPET implementation may enhance survival in ACS patients.

Key Words: Acute coronary syndrome; Cardiopulmonary exercise testing; CONUT score; Prognosis

Exercise training is recommended for patients with cardiovascular diseases, including acute coronary syndrome (ACS), as well as healthy individuals as it improves physical, psychological, and social functioning.[1,2] Cardiac rehabilitation (CR) includes exercise training, exercise education, and strategies to reduce modifiable cardiovascular risk factors.[3–5] Cardiopulmonary exercise testing (CPET) plays an important role in determining exercise capacity, stratifying cardiovascular risk, and guiding the intensity of CR.[1,6]

Nutritional status is a critical prognostic factor in patients with ACS[7] and heart failure.[8] One commonly used measure to assess nutritional status is the controlling nutritional status (CONUT) score.[9] CONUT scores are simple and accessible, and are derived from serum albumin, total cholesterol, and lymphocyte count, serving as a comprehensive marker of malnutrition.[9] Previous studies have demonstrated that in patients with cardiovascular disease, such as coronary artery disease or previous myocardial infarction, a higher CONUT score is associated with poorer outcomes.[10,11]

To date, the extent to which CPET-based exercise education and prescription were provided to ACS patients around the time of hospital discharge remains unclear.

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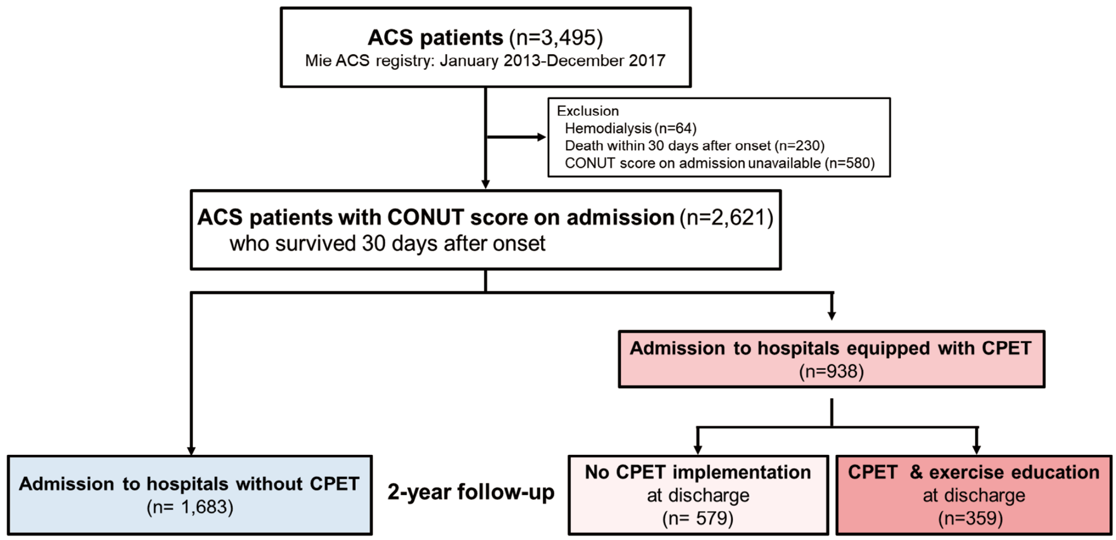

Figure 1. Flow chart of patient enrollment. ACS, acute coronary syndrome; CONUT, controlling nutritional status; CPET, cardiopulmonary exercise testing.

Furthermore, it is also unclear how exercise prescription and nutrition status are related to outcomes in ACS patients. Therefore, the present study aimed to assess the implementation of CPET and to evaluate the impacts of clinical parameters, including CPET implementation and nutritional status, on 2-year outcomes in ACS patients in Mie Prefecture, Japan.

Methods

Study Population

The Mie ACS registry is a prospective multicenter registry that was initiated in Mie Prefecture in 2013.[12,13] In the present study, ACS patients (age 68±12 years; 78% male) who had not previously received maintenance hemodialysis and were 30 days post-onset were enrolled from 15 hospitals participating in the Mie ACS registry between 2013 and 2017. Among patients enrolled in the Mie ACS registry, there were 3,421 ACS patients who survived 30 days after onset and were not on maintenance hemodialysis between 2013 and 2017. Of these, 2,621 patients whose data on the components of the CONUT score on admission were available were included in the present study (**Figure 1**). We compared clinical characteristics between patients who underwent CPET at hospital discharge and those who did not, as well as their CONUT score on admission. Prognostic factors, including CPET-based exercise education, and CONUT score, were evaluated.

This registry study conformed to the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Mie University Graduate School of Medicine and each participating hospital's ethics committee (Reference no. 2881). This study was also registered in a clinical trial registry (https://www.umin.ac.jp/ctr/index-j.htm; UMIN 000036020).[12,13]

CONUT Score on Admission

The CONUT score was used to evaluate nutritional risk and was calculated based on serum albumin concentration, total cholesterol level, and total lymphocyte count, as previously reported.[9] In the present study, patients were classified into 3 groups according to their CONUT score on admission: normal (0–1 point), mild malnutrition (2–4 points), and moderate to severe malnutrition (5–12 points).

CPET

CPET for patients with cardiovascular disease can help increase cardiac and lung function, increase exercise capacity, and enhance quality of life.[14,15] A maximal symptom-limited exercise testing was performed using a cycle ergometer with a ramp protocol to determine the anaerobic threshold and peak oxygen uptake. All patients who underwent maximal CPET were instructed to exercise at 60–80% of their peak heart rate achieved during maximal CPET, or at the anaerobic threshold level, at discharge or 2 weeks after onset.[16]

CR After Discharge

CR is an effective intervention to improve exercise capacity, quality of life, and the health of patients with ACS. Patients who wanted to participate in outpatient CR after discharge were offered outpatient CR that was covered by Japan's universal health insurance system.[17] At the outpatient CR, exercise training was provided under the supervision of an exercise physiologist and a cardiologist at least once a week. Patients admitted to hospitals without outpatient CR, or those who did not want to participate even if CR facilities were available, were instructed to exercise at home at least 3 times a week for 15–30 min each session. Patients who did not receive CPET were also advised to perform aerobic exercise at home.

Outcomes

Outcome data were collected through patient interviews, hospital chart reviews, and telephone interviews with the patient or their relatives. Clinical events were recorded in a web-based system by a well-trained cardiologist.[12,13] The

Table 1. Patient Characteristics

	No CPET hospital (n=1,683)	CPET hospital		P value
		No CPET implementation (n=579)	CPET implementation (n=359)	
Age (years)	69 [60–77]	71 [63–80]*	66 [56–73]*,†	<0.01
Male (%)	78	74	87*,†	<0.01
Height (cm)	163 [157–169]	164 [155–169]	165 [160–170]*,†	<0.01
Body weight (kg)	61.6 [53.0–70.0]	61.0 [53.0–69.0]	64.0 [58.0–73.0]*,†	<0.01
Body mass index (kg/m²)	23.1 [21.1–25.6]	23.0 [21.1–25.3]*	23.8 [21.9–25.7]*,†	<0.01
Length of hospitalization (days)	12 [9–17]	15 [10–21]*	16 [12–19]*,†	<0.01
<7	226 (13)	83 (14)	5 (1)*,†	
7–21	1,215 (72)	372 (64)*	304 (85)*,†	
>21	242 (14)	124 (21)*	50 (14)†	
Outpatient CR (%)	0	7*	61*,†	<0.01
Peak CPK (mg/dL)	1,682 [700–3,420]	1,456 [516–2,873]*	2,004 [981–3,733]*,†	<0.01
Hemoglobin (g/dL)	14.3 [12.8–15.4]	13.9 [12.4–15.4]*	14.7 [13.5–15.9]*,†	<0.01
eGFR (mL/min/1.73 m²)	68 [53–82]	65 [51–78]*	70 [57–84]†	<0.01
Killip class ≥2 (%)	17	21*	11†	<0.01
Nutritional risk status (%)				
Normal risk	62	58	69*,†	<0.01
Mild risk	31	35	30	
Moderate/severe risk	7	6	1*,†	
STEMI (%)	70	59*	82*,†	<0.01
Culprit LAD (%)	44	44	49	0.20
CPA prehospital (%)	2	5*	5*	<0.01
IABP/ECMO/ventilator (%)	12	11	8	0.10
Comorbidities (%)				
Hypertension	65	65	62	0.55
Diabetes	30	34	30	0.20
Dyslipidemia	52	45*	49	0.02
Medications (%)				
ACE inhibitor/ARB	85	77*	85†	0.01
β-blockers	62	51*	56*,†	<0.01
Loop diuretics	17	16	10*,†	<0.01

Unless indicated otherwise, data are presented as n (%), or median [IQR]. Patients were divided into those admitted to hospitals with CPET equipment (CPET hospital) and those admitted to hospitals without CPET equipment (No CPET hospital). Patients admitted to hospitals with CPET were divided further into those who underwent CPET at discharge (CPET implementation) and those who did not (No CPET implementation). *P<0.05 vs. patients admitted to hospital without CPET capabilities. †P<0.05 vs. patients who were admitted to CPET hospitals but without CPET implementation. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; CPA, cardiopulmonary arrest; CPET, cardiopulmonary exercise testing; CPK, creatinine kinase; CR, cardiac rehabilitation; ECMO, extracorporeal membrane oxygenation; eGFR, estimated glomerular filtration rate; IABP, intra-aortic balloon pump.

primary endpoint was all-cause mortality during the 2 years following discharge. Secondary endpoints included hospitalization due to heart failure and major adverse cardiac and cerebrovascular events (MACE), which were defined as cardiovascular death, non-fatal myocardial infarction, unstable angina requiring hospitalization, heart failure requiring hospitalization, and stroke requiring hospitalization.

Statistical Analysis

Continuous variables with a normal distribution were expressed as mean±standard deviation, while those without a normal distribution were expressed as median and interquartile range. Categorical variables were expressed as number and percentage. The chi-squared test or Mann Whitney U-test was used to compare categorical variables. The student's t-test or the Wilcoxon rank sum test was used for continuous variables, as appropriate. Event analyses were displayed using Kaplan-Meier survival curves and compared using the log-rank test. A Cox regression model was used to investigate the independent predictors of all-cause mortality. The association between all-cause mortality and clinical variables (age, male gender, length of hospitalization, peak creatinine kinase [CPK], hemoglobin, estimated glomerular filtration rate [eGFR], Killip class ≥2, malnutrition, mechanical support such as intra-aortic balloon pump, extracorporeal membrane oxygenation, and ventilator, outpatient CR, CPET implementation, ST-elevation myocardial infarction, comorbidities such as hypertension, diabetes, and dyslipidemia, and medications including angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, β-blockers, and loop diuretics) were investigated using univariate Cox regression analysis. Variables with a P value <0.10 were included in the multivariate Cox regression analysis in Model 1. Nutritional status was included in the Cox regression analysis in Model 2. Statistical significance was defined as P<0.05. Statistical analysis was performed using SPSS (version 25.0; IBM Corp., Armonk, NY, USA) and R software packages

Table 2. Factors Associated With CPET Implementation in Hospitals With CPET Equipment

	Univariate regression		Multivariate regression	
	P value	OR (95% CI)	P value	OR (95% CI)
Age	<0.01	0.96 (0.95–0.97)	<0.01	0.97 (0.95–0.98)
Sex, male	<0.01	2.38 (1.67–3.41)	<0.01	1.93 (1.29–2.89)
Length of hospitalization (days)				
<7		1.00		1.00
7–21	<0.001	13.57 (5.43–33.88)	<0.01	7.17 (2.09–24.60)
>21	<0.001	6.69 (2.56–17.49)	0.04	4.76 (1.30–17.47)
Log peak CPK	<0.01	2.14 (1.59–2.88)	<0.01	1.67 (1.17–2.39)
Hemoglobin (g/dL)	<0.01	1.24 (1.16–1.33)	0.27	–
eGFR (mL/min/1.73 m²)	<0.01	1.01 (1.01–1.02)	0.13	–
Killip class ≥2	<0.01	0.48 (0.32–0.70)	<0.01	0.51 (0.32–0.80)
Normal nutritional status		1.00		1.00
Mild malnutrition	0.02	0.71 (0.54–0.95)	0.87	1.03 (0.74–1.44)
Moderate/severe malnutrition	<0.01	0.18 (0.07–0.48)	0.02	0.29 (0.10–0.79)
IABP/ECMO/ventilator support	0.10	0.68 (0.44–1.07)		
STEMI	<0.01	3.08 (2.24–4.22)	0.02	1.64 (1.10–2.45)
Hypertension	0.33	0.87 (0.66–1.15)		
Diabetes	0.24	0.84 (0.63–1.12)		
Dyslipidemia	0.28	1.16 (0.89–1.50)		

CI, confidence interval; OR, odds ratio; STEMI, ST-elevation myocardial infarction. Other abbreviations as in Table 1.

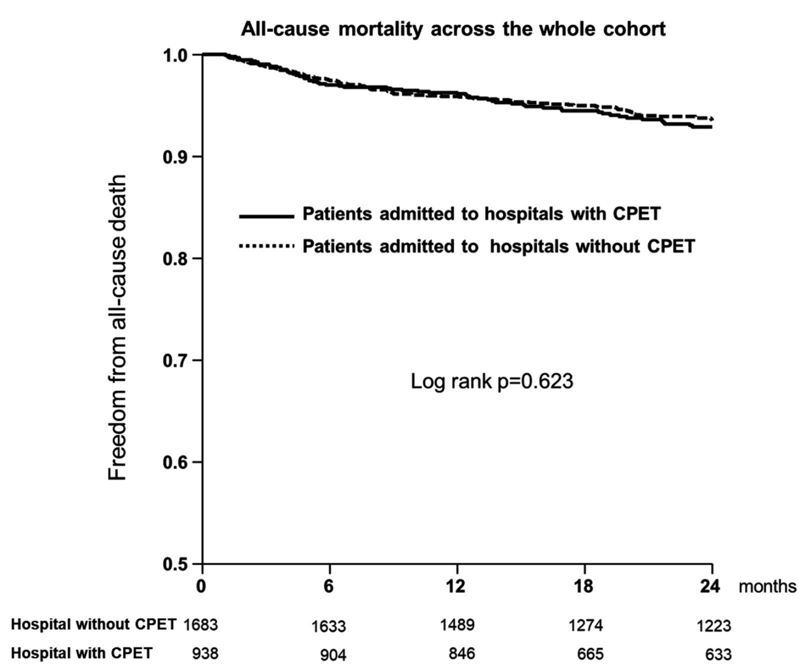

Figure 2. Kaplan-Meier curves for all-cause mortality during the 2-year follow up of patients admitted to hospitals with cardiopulmonary exercise testing (CPET) equipment compared with those admitted to hospitals without CPET equipment.

(V.4.0.0 for Windows; R Development Core Team).

Results

Patient Characteristics

In the present study, 2,621 patients (mean age 68±12 years; 78% male) were enrolled, as shown in **Figure 1** and **Table 1**. Six (40%) out of 15 hospitals participating in the Mie ACS registry had CPET equipment and an outpatient CR system, and 938 patients were admitted to these hospitals. Of those 938 patients, 359 (37%) underwent CPET. The average peak oxygen uptake (peak VO_2) in patients with CPET was 19.1±5.0 mL/kg/min. Most patients who underwent CPET (85%) were hospitalized for 7–21 days, while 14% were hospitalized for >21 days. Patients who underwent CPET were younger, more likely to be male, had higher body weight, and were more likely to have ST-elevation myocardial infarction, higher peak CPK, higher hemoglo-

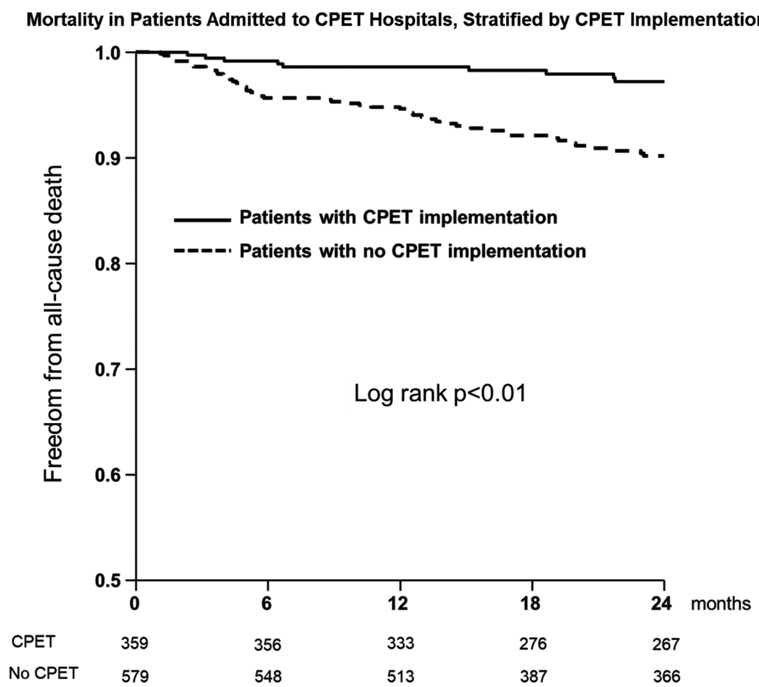

Figure 3. Kaplan-Meier curves for patients admitted to hospitals with cardiopulmonary exercise testing (CPET) equipment, comparing those who underwent maximal CPET and received CPET-based exercise education at discharge with those who did not undergo CPET.

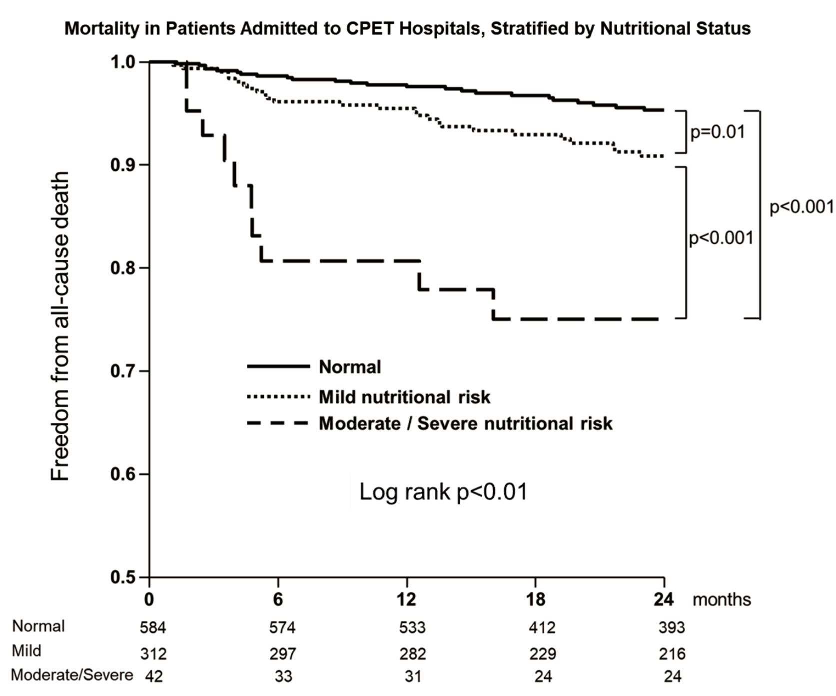

Figure 4. Kaplan-Meier curves for patients admitted to hospitals with cardiopulmonary exercise testing (CPET) equipment, comparing those with normal nutrition status, mild malnutrition, and moderate to severe malnutrition according to the controlling nutritional status (CONUT) score.

bin levels, higher eGFR, Killip class 1, normal nutrition status, and hospital stays of 7–21 days. Of the 938 patients, 261 (28%) participated in outpatient CR after discharge. The percentage of patients who participated in outpatient CR was significantly higher (61%) among those who underwent CPET at discharge compared with those who did not (7%; P<0.01).

When stratified into 3 groups by malnutrition risk using the CONUT score on admission (**Supplementary Table**), patients with higher malnutritional risk were older, leaner, and had lower hemoglobin levels and eGFR. The incidence of Killip class ≥2, prehospital cardiopulmonary arrest, and the use of mechanical support were more frequently observed in patients with moderate to severe mal-

Table 3. Multivariate Cox Regression Analysis for All-Cause Mortality in Hospitals With CPET Equipment

	Multivariate regression	
	P value	Hazard ratio (95% CI)
Model 1		
Age	<0.01	1.05 (1.02–1.08)
Length of hospitalization (days)		
<7	0.09	1.00
7–21	0.24	–
>21	0.05	–
Hemoglobin (g/dL)	0.02	0.85 (0.74–0.98)
eGFR (mL/min/1.73 m²)	0.43	–
Killip class ≥2	<0.01	2.96 (1.74–5.04)
IABP/ECMO/ventilator use	0.06	–
Outpatient cardiac rehabilitation	0.91	–
CPET implementation	0.04	0.47 (0.23–0.98)
Dyslipidemia	0.19	–
Loop diuretics	0.27	–
Model 2		
Age	<0.01	1.06 (1.03–1.09)
Length of hospitalization (days)		
<7	0.07	1.00
7–21	0.16	–
>21	0.03	–
Hemoglobin (g/dL)	0.03	0.86 (0.75–0.99)
eGFR (mL/min/1.73 m²)	0.45	–
Killip class ≥2	<0.01	2.86 (1.67–4.92)
IABP/ECMO/ventilator use	0.06	–
Outpatient cardiac rehabilitation	0.24	–
CPET implementation	0.058	–
Dyslipidemia	0.10	–
Loop diuretics	0.24	–
Nutritional status		
Normal nutritional status		1.00
Mild malnutrition	0.96	0.98 (0.55–1.77)
Moderate/severe malnutrition	0.02	2.47 (1.13–5.40)

Multivariate Cox regression models for all-cause mortality in patients admitted to CPET hospitals. Age, male gender, length of hospitalization, peak CPK, hemoglobin, eGFR, nutritional status, mechanical support such as IABP, ECMO, and ventilator, outpatient CR, CPET implementation, STEMI, hypertension, diabetes, and dyslipidemia, and ACE inhibitors/ARB, β-blockers, and loop diuretics were variables included in Model 1. Nutritional status was included in Model 2. Abbreviations as in Tables 1,2.

nutrition risk. Patients with moderate to severe risk were less likely to undergo CPET at discharge and participate in outpatient CR (**Supplementary Table**).

Factors Associated With Implementation of CPET

Factors associated with CPET implementation were evaluated using univariate and multivariate binomial logistic analysis in 938 patients admitted to a hospital with CPET equipment. As shown in **Table 2**, male sex, length of hospitalization ≥7 days, peak CPK, and ST-elevation myocardial infarction were independently associated with CPET implementation. In contrast, older age, Killip class ≥2, and moderate to severe malnutrition were independently associated with non-performing CPET.

Two-Year Outcomes in ACS Patients

In the entire cohort of 2,621 patients, there were 161 all-cause deaths during the 2-year follow-up period: 60 (6.4%) occurred among 938 patients admitted to hospitals with CPET equipment, and 101 (6.0%) among 1,683 patients admitted to hospitals without CPET equipment. No difference was observed in all-cause mortality between the 2 groups as shown in **Figure 2** (Log rank P=0.62). Among the 938 patients admitted to hospitals with CPET equipment, Kaplan-Meier curves showed that those who underwent CPET and received CPET-based exercise education experienced significantly fewer all-cause deaths compared with those who did not undergo CPET (2.5% vs. 9%; Log rank P<0.001; **Figure 3**).

The number of patients hospitalized due to exacerbated heart failure over the 2-year period was 10 (2.8%) with CPET and 20 (3.5%) without CPET. The number of patients who experienced MACE was 19 (5.3%) with CPET and 44 (7.6%) without CPET, respectively. There were no statistically significant differences between patients with CPET and those without CPET in heart failure hospitalizations (2.8% vs. 3.3%; Log rank P=0.59) or MACE (5.3% vs. 7.6%; Log rank P=0.12) between the 2 groups. Malnutrition status was also significantly associated with all-cause mortality in 938 patients, with patients at moderate to severe malnutrition having markedly higher mortality rates compared with those with normal or mild malnutrition (both P<0.01; **Figure 4**). The rate of heart failure hospitalization (P≥0.18) or MACE (P≥0.08) were not statistically different among the 3 nutritional status groups.

Prognostic Predictors Using Cox Regression Analyses

Among the clinical variables listed in the Methods section, age, length of hospitalization, use of mechanical support, and loop diuretics were positively associated with all-cause mortality, while hemoglobin levels, eGFR, Killip class ≥2, outpatient CR, implementation of CPET, and dyslipidemia were negatively associated with all-cause mortality using univariate Cox regression analysis. In the multivariate Cox regression analysis (Model 1) without nutritional status, CPET implementation (hazard ratio 0.47; 95% CI 0.23–0.98; P=0.04) and hemoglobin level (hazard ratio 0.85; 95% CI 0.74–0.98; P=0.02) were independent negative predictors for all-cause mortality. Older age and Killip class ≥2 were independent positive predictors for all-cause mortality (P≤0.01). When nutritional status was added to the model (**Table 3**, Model 2), hemoglobin level remained an independent predictor for better prognosis. However, the effect of CPET implementation on mortality was not statistically significant (P=0.058). Moderate to severe malnutrition (P=0.02; hazard ratio 2.47; 95% CI 1.13–5.40) as well as older age and Killip class ≥2 were the independent predictors for overall death.

Discussion

Using data from the Mie ACS registry, we demonstrated that 359 (14%) of the 2,621 ACS patients enrolled in the present study underwent CPET at discharge or 2 weeks after onset, and 10% (261/2,621) of patients participated in outpatient CR between 2013 and 2017. We also demonstrated that ACS patients who underwent CPET were younger and more likely to have ST-elevation myocardial infarction. Hemoglobin levels and CPET implementation were initially independent predictors of lower all-cause mortality in the multivariate analysis (Model 1). When nutritional status was considered in the model (Model 2), moderate to severe malnutrition, along with older age and Killip class ≥2, emerged as stronger predictors of all-cause mortality during the 2-year follow-up period. Our study was novel in that it simultaneously examined the effects of CPET-based exercise education and malnutrition on patient outcomes. By addressing both factors together, we provided a more comprehensive understanding of how these 2 important aspects interacted to influence prognosis of ACS in a real-world setting.

Impact of CPET Implementation and CEPT-Based Exercise Education on Prognosis

Lawler et al. conducted a meta-analysis of 34 randomized controlled trials of patients who had recently survived a myocardial infarction and reported that exercise-based CR reduced reinfarction, cardiovascular mortality, and all-cause mortality.[4] Schutter et al. reported that in cardiovascular patients including ACS, who underwent CPET before and after outpatient CR (median duration of 123 days), greater improvement in exercise capacity was associated with lower risk for all-cause mortality.[18] In the present study, patients who underwent CPET at discharge, or 2 weeks after onset received CPET-based exercise education from their exercise physiologists and doctors, were likely to have continued exercising at home although the duration or intensity of exercise was not monitored. We suggest that the present study provides further evidence that CPET-based exercise education may be associated with a reduction in all-cause mortality, consistent with the notion that structured CR programs could reduce all-cause and cardiac deaths in ACS patients. The hazard ratio of 0.47 indicates a substantial potential benefit, although this effect did not reach statistical significance when nutritional status was included in the multivariate Cox regression analysis.

Malnutrition as a Key Predictor for All-Cause Mortality

There are several methods to evaluate nutritional status, including CONUT score,[9] geriatric nutritional risk index (GNRI),[19] and the prognostic nutritional index.[20] We chose to use CONUT scores for assessing nutritional status because they are simple and do not require body weight and ideal body weight, as is needed for assessment of the GNRI. Previous studies using the CONUT score reported worse short- and long-term outcomes in patients with congestive heart failure[21] and acute myocardial infarction[22] with higher CONUT score (≥5 points). Takahashi et al. recently reported in a small study that higher CONUT scores were observed in 17% of patients and were associated with composite events including all-cause mortality, ACS, and target lesion revascularization.[11] A recent meta-analysis involving 37,303 ACS patients from 30 studies worldwide, including the study by Takahashi et al., also demonstrated that malnutrition was significantly associated with all-cause mortality following ACS.[23] In the present study, we excluded patients who were on maintenance hemodialysis or those who died within 30 days after onset of ACS. As a result, the percentage of patients with normal nutritional status was larger, and the percentage of patients with moderate to severe malnutrition (6%; n=125) was significantly smaller than that reported by Takahashi et al. (6% vs. 28%). Therefore, our study differs in that we exclusively enrolled ACS patients who survived the first 30 days after onset and excluded those on hemodialysis who are less likely to perform CPET in daily clinical practice. This distinction allows us to provide more relevant insights into the prognostic impact of malnutrition in a more defined population. Despite excluding patients with very high risks, we observed that those with moderate to severe malnutrition remained at high risk for all-cause mortality during the 2-year follow up. Thus, the findings from our study align with previous studies, which demonstrated a significant association between malnutrition, as evaluated using the CONUT score, and adverse clinical outcomes in ACS patients. Specifically, the highlighted risk of composite events and higher mortality observed in malnourished patients underscore the important role of nutritional status in determining prognosis. The importance of nutritional management has been a focus in patients with cardiovascular disease.[24] A small, single-center study reported that early nutritional guidance intervention by a dietitian improved nutritional status and reduced all-cause mortality in ACS patients.[25] Our results, combined with the findings from these studies, support the integration of nutritional evaluation into routine clinical practice to identify high-risk patients who may benefit from targeted interventions combined with exercise education.

Interaction Between CPET Implementation and Nutritional Status

When nutritional status was included in the multivariate Cox regression analysis (**Table 3**, Model 2), moderate to severe malnutrition emerged an independent predictor of all-cause mortality (P=0.02), and the effect of CPET implementation on mortality became statistically not significant (P=0.058). The reduced impact of CPET implementation on mortality in the presence of nutritional status may suggest that the benefits of CPET-based exercise education have been partly modulated by a patient's nutritional status. This interaction warrants further investigation to determine whether optimizing nutrition could enhance the efficacy of CPET-based exercise education in patients with ACS.

Outpatient CR System and CPET Equipment in Hospitals Participating in the Mie ACS Registry

We recently reported that there were large regional disparities in CR implementation across Japan, with 7- and 20-fold regional disparities in the number of CR units for inpatients and outpatients, partly due to variation in the number of hospitals providing outpatient CR and the availability of registered CR instructors.[26] In the present study, 6 out of 15 hospitals with CPET equipment had their own outpatient CR systems during the study periods, and outpatient CR was performed in 26% of patients admitted to these hospitals. As hospitals without CPET equipment did not have outpatient CR systems, no patients were able to undergo onsite outpatient CR. As previously reported by Goto et al.,[27] the number of hospitals implementing phase II outpatient CR during the study period was not large; however, the number of hospitals with outpatient CR systems in Mie Prefecture has increased since then. CR systems have advanced significantly in recent years. Therefore, follow-up studies are needed to evaluate the impacts of these improvements, particularly regarding the growing number of CPET-capable hospitals and the implementation of CPET-based education.

Study Limitations

There are several limitations. First, the attending physician's decision to order CPET may have been influenced by the patient's overall condition, which could be associated with prognosis during the 2-year follow-up period. For example, the presence of frailty and active cancer may significantly influence the physicians' decisions regarding CPET implementation. In addition, the decision to implement CPET may also be influenced by planned participation in outpatient CR, as CPET helps to determine the appropriate intensity of exercise training for patients. Second, the number of patients whose CONUT scores on admission was unavailable was relatively large. This was due to the fact that the present study was retrospective, and that differential white blood cell counts were not assessed in most cases. Third, we excluded patients on maintenance hemodialysis from this study. Hemodialysis patients are sometimes unable to perform maximal CPET and to participate in onsite outpatient CR due to fatigue related to hemodialysis, physical limitations, the risk of complications and time constraints. Last, this study evaluated 2-year prognosis and the status of CPET, outpatient CR in hospitals that participated in the Mie ACS Registry between 2013 and 2017. The duration and depth of this CPET-based exercise education may have varied among hospitals. In addition, we acknowledge that this education could have been shorter for patients without outpatient CR than those with the service. The number of hospitals with CPET equipment and an outpatient CR system is currently larger compared with the number available in 2013–2017.

Conclusions

In patients registered in the Mie ACS Registry, 14% of patients underwent CPET at discharge, and 10% of patients participated in outpatient CR between 2013 and 2017. ACS patients who underwent CPET were younger and had more ST-elevation myocardial infarction. While CPET implementation was initially one of the predictors of lower all-cause mortality, moderate to severe malnutrition emerged as a stronger predictor of all-cause death during the 2-year follow up.

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Disclosures

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IRB Information

This study was approved by the Institutional Review Board of Mie University Graduate School of Medicine (Reference no. 2881).

Data Availability

The deidentified participant data will not be shared.

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Supplementary Files

Please find supplementary file(s);
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