

Evaluation of the Effects of Outpatient Cardiac Rehabilitation in the Maintenance Phase With and Without Renal Dysfunction

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Abstract

Background: In recent years, the number of patients with cardiovascular disease (CVD) complicated by chronic kidney disease (CKD) has increased due to population aging and the rising prevalence of diabetes. However, it remains unclear whether the effectiveness of outpatient cardiac rehabilitation (CR) during the maintenance phase differs based on the presence of CKD.

Methods: This single-center retrospective study included 63 patients who initiated outpatient cardiac CR at our hospital between June 2020 and February 2025 and continued for one year. Demographic and clinical data were obtained from medical records. Assessments—including handgrip strength, knee extension strength, body composition analysis, questionnaires, and cardiopulmonary exercise testing—were conducted at CR initiation (baseline) and after one year.

Results: Participants were divided into two groups: a normal renal function group ($n = 28$) and a reduced renal function group ($n = 35$). At baseline, the groups differed significantly only in age and renal function. Anaerobic threshold (AT) and peak oxygen uptake (peak VO_2) were significantly lower in the reduced renal function group at baseline, and this trend remained after one year. In an analysis of covariance using changes in AT and peak VO_2 as dependent variables, the reduced renal function group showed a significantly lower improvement, even after adjusting for baseline renal function, age, sex, and weekly CR frequency.

Conclusions: These findings suggest that patients with CVD complicated by CKD may experience less improvement in exercise tolerance after one year of maintenance-phase outpatient CR compared to those without CKD.

Introduction

In recent years, the number of cardiac patients with comorbid chronic kidney disease (CKD) has increased due to the aging population and rising prevalence of diabetes [1]. Multiple studies have identified CKD as an independent risk factor for poor prognosis. Hallan et al. [2] reported that a low estimated glomerular filtration rate (eGFR) and elevated albuminuria levels are independent predictors of increased mortality and progression to end-stage renal disease in patients with CKD. Anavekar et al. [1] investigated 14,527 patients with acute myocardial infarction (AMI) and CKD, classifying them into four groups based on baseline eGFR: ≥ 75 mL/min/1.73 m² (normal renal function), 60–74 (mildly decreased), 45–59 (moderately decreased), and < 45 (severely decreased). The three-year mortality rates were 14.1%, 20.5%, 28.9%, and 45.5%, respectively, indicating that all-cause mortality increases with declining renal function. Notably, the three-year mortality rate in the mildly decreased group exceeded 20%, suggesting that even mild renal impairment is a significant risk factor in patients with AMI.

Sato et al. [3] evaluated 505 patients hospitalized for heart failure, dividing them into a CKD group (eGFR < 60) and a non-CKD group (eGFR ≥ 60), and examined cardiac events over a two-year follow-up. A total of 115 cardiac events were recorded, with the incidence significantly higher in the CKD group compared to the non-CKD group (34% vs. 14%, $p < 0.001$). Peak oxygen uptake (Peak VO_2) was identified as an independent predictor of cardiac events in both groups.

These findings highlight that CKD is significantly associated with poor long-term prognosis and an increased incidence of cardiac

events in patients with AMI and heart failure, with Peak VO_2 independently influencing these outcomes.

The benefits of outpatient cardiac rehabilitation (CR) for patients with stable heart disease—particularly for preventing recurrence and improving long-term outcomes—are well established [4]. Moreover, exercise therapy has been shown not to exacerbate renal dysfunction in patients with CKD [5], and CR in patients with AMI and CKD may help slow the progression of renal decline [6]. Takaya et al. [7] assessed Peak VO_2 before and after a 3-month outpatient CR program in post-AMI patients stratified by CKD status and found significant improvements in both groups. However, it remains unclear whether the effectiveness of outpatient CR differs by renal function.

Therefore, in this study, we classified patients with stable cardiac disease who continued outpatient CR for one year into two groups based on renal function and examined whether renal status influenced changes in exercise capacity.

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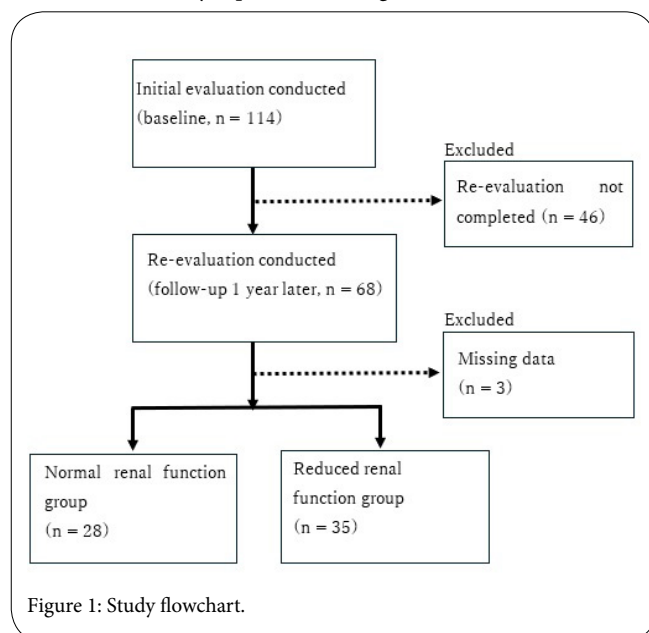
Materials and Methods

Study design

This single-center retrospective study utilized data obtained from medical records.

Participants

Among 114 patients who began outpatient CR at our hospital between June 2020 and February 2025, 68 completed the program for 1 year. After excluding those with missing data, 63 patients were included in the final analysis. Participants were stratified based on their eGFR at CR initiation: those with eGFR ≥ 60 mL/min/1.73 m² formed the normal renal function group, and those with eGFR < 60 mL/min/1.73 m² formed the reduced renal function group. A flowchart of the study is presented in Figure 1.



Methods

Age, sex, and body weight at the start of outpatient CR were extracted from medical records. Laboratory and echocardiographic findings were sourced from either pre-CR testing at our hospital or referral documents. Weekly CR frequency was recorded as dummy variables: 1 for once weekly, 2 for twice weekly, and 0.5 for once every 2 weeks.

Grip strength (N-FORCE, CORVETTE Inc., Wakayama, Japan) and knee extension strength (μ Tas F-1, ANIMA Co., Tokyo, Japan) were measured twice bilaterally, and the maximum value was used. For knee extension, isometric maximal voluntary contraction was recorded using a force sensor attached to a plate secured to the distal lower leg via a measurement belt while the leg was elevated [8]. Muscle mass was assessed using a body composition analyzer (MC-780MA-N, TANITA Co., Tokyo, Japan) in a standing position. Skeletal muscle index (SMI) was calculated by dividing appendicular muscle mass by height squared (m²). The Hospital Anxiety and Depression Scale-A (HADS-A) and Hospital Anxiety and Depression Scale-D (HADS-D) questionnaires were administered after physical assessments.

Cardiopulmonary exercise testing (CPET) was conducted to a symptom-limited maximum using an isokinetic ergometer (Strength Ergo8, Fukuda Denshi Co., Ltd., Tokyo, Japan), under supervision of a physician and a physical therapist. Prior to testing, the flow sensor and gas analyzer were calibrated, and a mask was secured over the nose and mouth to prevent air leakage. A breath-by-breath gas analyzer (AE310S, MINATO Medical Science Co., Ltd., Osaka, Japan) was used to continuously measure ventilation (VE), oxygen uptake (VO₂), and carbon dioxide output (VCO₂). Cardiac activity was monitored (ML-9000, Fukuda Denshi Co., Ltd., Tokyo, Japan) for arrhythmias and heart rate during exercise, and blood pressure was recorded every minute using an automatic monitor (TangoM2, SunTech Medical Inc., Miami, USA). Following 3 minutes of rest, participants performed a 3-minute warm-up at 10 W, followed by a ramp protocol (Ramp 10 or 15) increasing by 10 or 15 W/min at 40–60 rpm. A cool-down followed exercise. Anaerobic threshold (AT) and Peak VO₂ were calculated from test data. AT was determined using the V-slope or time-trend method, and Peak VO₂ was defined as the highest recorded VO₂ value [9].

Outpatient Cardiac Rehabilitation Program at Our Hospital

All patients participated in a standardized 1-hour CR session comprising warm-up, resistance training, aerobic exercise, and cool-down. Resistance training included six exercises (push-up, pull-down, chest press, leg press, leg extension, leg curl) using pneumatic machines (HUR, Inter Reha Co., Ltd., Tokyo, Japan). Aerobic prescriptions followed Japanese Circulation Society guidelines [4] based on workload 1 minute prior to AT or targeting a Borg scale rating of approximately 13. Aerobic exercises were performed continuously for 10–20 minutes.

Ethical Considerations

This study adhered to the Declaration of Helsinki and was approved by the Ethics Committee of Seijoh University (Approval No.: 2024C0019). Participants were informed via an opt-out process that their personal data would remain de-identified. They were advised that declining participation would not result in any disadvantage and could contact the research team if they did not consent.

Statistical Analysis

Basic demographic and clinical characteristics were presented as means $\pm$ standard deviation for normally distributed variables and as medians for non-normally distributed variables. Between-group comparisons at baseline and after one year were performed using unpaired t-tests for normally distributed continuous variables after confirming variance homogeneity. The Mann-Whitney U test was used for non-normally distributed variables, and chi-square (χ^2) tests were applied to categorical variables.

To assess changes in AT and Peak VO₂ pre- and post-intervention, analysis of covariance (ANCOVA) was conducted using change scores as dependent variables and baseline eGFR, age, sex, and weekly CR frequency as covariates. Statistical analyses were performed using EZR version 1.61 [10], with a significance level set at 5%.

Results

At baseline, patients in the reduced renal function group were significantly older than those in the normal renal function group ($p = 0.03$). No other significant differences were observed in baseline characteristics aside from age and renal function (Table 1).

Table 1: Participants characteristics (n = 63).

	Overall (n = 63)	Normal renal function group (n = 28)	Reduced renal function group (n = 35)	p value
Age (years)	71.0 (62.5 – 78.0)	66.0 (58.5 – 73.0)	72.0 (67.5 – 78.0)	0.03b
Sex; Male (%)	34 (54.0)	13 (46.4)	21 (60.0)	0.32c
Weight (kg)	60.9 ± 14.3	62.4 ± 14.3	59.7 ± 14.4	0.46a
History of myocardial infarction	24 (38.1)	13 (46.4)	11 (31.4)	0.30c
Heart failure	24 (38.1)	10 (35.7)	14 (40.0)	0.80c
Angina pectoris	8 (12.7)	3 (10.7)	5 (14.3)	0.72c
Dissecting aortic aneurysm	3 (4.8)	1 (3.6)	2 (5.7)	1.00c
Valvular heart disease	1 (1.6)	1 (3.6)	0 (0)	0.44c
Unstable angina pectoris	2 (3.2)	0 (0)	2 (5.7)	0.50c
Peripheral arterial disease	1 (1.6)	0 (0)	1 (2.9)	1.00c
Rehabilitation session/ week	1.0 (0.5 – 1.0)	1.0 (0.5 – 1.0)	0.9 (0.6 – 1.2)	0.57b
LAD (mm)	37.3 ± 7.1	37.0 ± 6.7	37.6 ± 7.5	0.77a
LVDs (mm)	28.9 (25.9 – 34.6)	28.5 (26.2 – 33.3)	29.0 (25.6 – 36.5)	0.95b
LVDd (mm)	47.2 ± 8.1	47.5 ± 8.5	47.0 ± 7.9	0.83a
E/A	0.8 (0.7 – 1.2)	0.8 (0.7 – 1.0)	0.9 (0.7 – 1.2)	0.42b
E/e'	12.1 (9.9 – 15.9)	11.4 (9.6 – 13.8)	13.6 (10.5 – 16.3)	0.21b
BNP (pg/mL)	68.4 (35.6 – 139.7)	44.2 (28.4 – 64.0)	72.6 (26.6 – 136.9)	0.20b
Hb (g/dl)	13.1 (12.2 – 14.1)	13.4 (12.6 – 14.1)	13.0 (11.8 – 13.9)	0.44b
eGFR	59.3 ± 14.6	71.8 ± 9.1	49.4 ± 9.8	<0.01a
Cre (mg/dl)	0.9 (0.71 – 1.0)	0.7 (0.6 – 0.9)	1.0 (0.9 – 1.2)	<0.01b
K (mEq/l)	4.3 (4.0 – 4.7)	4.2 (4.1 – 4.4)	4.5 (4.1 – 4.9)	0.10b
ACE/ARB/ARNI	51 (81.0)	22 (78.6)	29 (82.6)	0.52c
β blocker	44 (69.8)	22 (78.6)	22 (62.9)	0.27c
MRA	17 (27.0)	7 (25.0)	10 (28.6)	0.79c
Loop diuretics	9 (14.3)	3 (10.7)	6 (17.1)	0.49c
Statin	34 (54.0)	16 (57.1)	18 (51.4)	0.77c
Anticoagulant	25 (39.7)	11 (39.9)	14 (40.0)	0.80c
SGLT2 inhibitor	13 (20.6)	5 (17.9)	8 (22.9)	0.57c

a non-paired t test, b Mann–Whitney U test, c Chi-squared test

Abbreviations: LAD, left atrial dimension; LVDs, left ventricular end-systolic diameter; LVDd, left ventricular end-diastolic dimension; E/A, early diastolic filling velocity/ atrial filling velocity; E/e', early diastolic left ventricular filling velocity/early diastolic transmitral flow velocity; BNP, brain natriuretic peptide; Hb, hemoglobin; eGFR, estimated glomerular filtration rate; Cre, creatinine; K, potassium; ACE, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium-glucose cotransporter 2.

At baseline, both AT and Peak VO₂ were significantly lower in the reduced renal function group (AT: p = 0.03; Peak VO₂: p < 0.01; Table 2). After one year of outpatient CR, this trend persisted, with significantly lower AT and Peak VO₂ in the reduced renal function group (AT: p = 0.02; Peak VO₂: p = 0.02; Table 3). No significant differences were observed between groups in any other measured variables at either time point.

ANCOVA, using the change in AT and Peak VO₂ as dependent variables and adjusting for baseline renal function, age, sex, and weekly CR frequency, revealed that the reduced renal function group demonstrated significantly smaller improvements compared to the normal renal function group (AT: [95% CI, 2.1 to -0.1; adjusted R² = 0.14; p = 0.04]; Peak VO₂: [95% CI, 2.1 to 5.2; adjusted R² = 0.27; p < 0.01]).

Discussion

At the initiation of outpatient CR, exercise capacity was significantly lower in the reduced renal function group. However, no significant differences were observed in grip strength, isometric knee extension strength, or skeletal muscle index (SMI), and this pattern remained unchanged after one year of outpatient CR.

Moon et al. [11] reported that the risk of sarcopenia increased in males with CKD stages 3–5, though no significant association was found in females. Song et al. [12] suggested that sarcopenia in CKD results from increased protein catabolism due to the disease itself, as well as decreased energy and protein intake, and emphasized the need to consider factors beyond disease severity, including sex.

In the present study, bioelectrical impedance analysis (BIA) was used to assess muscle mass. However, in patients with CKD, obesity or

Table 2: Comparison of clinical evaluation between groups at baseline.

	Normal renal function group (n = 28)	Reduced renal function group (n = 35)	p Value
Grip strength (kg)	27.8 (21.4 – 37.4)	28.6 (20.5 – 35.3)	0.56b
Knee extension strength (kgf)	34.5 ± 11.9	28.8 ± 10.2	0.74a
SMI (kg/m ²)	7.4 ± 1.0	7.3 ± 1.2	0.66a
HADS-A (point)	4.7 ± 2.3	4.5 ± 2.7	0.29a
HADS-D (point)	5.5 (3.8 – 7.0)	4.0 (2.0 – 6.0)	0.26b
AT (ml/kg/min)	11.4 (10.3 – 12.0)	10.3 (9.4 – 11.4)	0.03b
Peak VO ₂ (ml/kg/min)	17.7 ± 3.9	15.1 ± 3.5	<0.01a
a non-paired t test, b Mann–Whitney U test			
Abbreviations: SMI, skeletal muscle index; HADS, Hospital Anxiety and Depression Scale; AT, anaerobic threshold; VO ₂ , oxygen consumption			

Table 3: Comparison of clinical evaluation between groups follow-up.

	Normal renal function group (n = 28)	Reduced renal function group (n = 35)	p Value
Grip strength (kg)	27.2 (22.8 – 36.7)	31.7 (21.0 – 36.3)	0.84b
Knee extension strength (kgf)	33.0 ± 14.3	35.4 ± 13.1	0.52a
SMI (kg/m ²)	7.5 ± 1.0	7.3 ± 1.1	0.59a
HADS-A (point)	4.8 ± 3.0	4.1 ± 2.6	0.41a
HADS-D (point)	4.0 (2.0 – 5.8)	4.0 (2.0 – 7.0)	0.61b
AT (ml/kg/min)	11.7 (10.9 – 13.1)	10.6 (9.1 – 12.3)	0.02b
Peak VO ₂ (ml/kg/min)	19.7 ± 2.9	16.5 ± 4.5	0.02a
a non-paired t test, b Mann–Whitney U test			
Abbreviations: SMI, skeletal muscle index; HADS, Hospital Anxiety and Depression Scale; AT, anaerobic threshold; VO ₂ , oxygen consumption			

fluid retention may have led to inaccurate estimations of true muscle mass. Additionally, given that approximately half of the participants were female, and that muscle strength is influenced by factors such as cortical excitability [13], these variables may have contributed to the observed outcomes. The use of standardized outpatient CR across both groups may explain why muscle-related metrics remained unchanged after 1 year.

The significantly lower exercise capacity in the reduced renal function group may be attributed to findings by Gamboa et al. [13], who examined mitochondrial function in patients with CKD. They categorized 63 participants into three groups: 21 controls, 20 patients with non-dialysis CKD stages 3–5, and 22 patients undergoing maintenance hemodialysis. Mitochondrial function in knee extensors was assessed using the phosphocreatine (PCr) recovery time constant, along with performance on the 6-minute walk test, levels of intermuscular fat, and markers of inflammation and oxidative stress.

Their findings demonstrated that PCr recovery time was significantly prolonged in patients with CKD, indicating mitochondrial dysfunction. This was correlated with reduced 6-minute walking distance ($r = 0.62$, $p = 0.001$), increased intermuscular fat ($r = 0.44$, $p = 0.001$), and elevated levels of inflammation and oxidative stress ($r = 0.60$, $p = 0.001$). Mitochondrial dysfunction may also have been present in the reduced renal function group in the present study, potentially contributing to the decreased AT and Peak VO₂.

Even after adjusting for baseline renal function, age, sex, and weekly outpatient CR frequency, the changes in AT and Peak VO₂ were

significantly smaller in the reduced renal function group compared to the normal renal function group. Although previous studies have demonstrated that exercise capacity can improve in patients with reduced renal function through outpatient CR [4], the magnitude of improvement observed in our study was significantly lower in this group.

The progression of renal disease is influenced by several factors, including sympathetic nervous system activity, inflammation, hypertension, dyslipidemia, and diabetes [6], all of which may have contributed to the limited improvements in exercise tolerance. Persistent mitochondrial dysfunction [14] may also have affected exercise capacity, even after 1 year of outpatient CR.

This study has several limitations. First, it was a retrospective, single-center study, which limited the generalizability of the findings. Consequently, it was not possible to fully investigate the mechanisms by which differences in renal function influenced the effects of exercise tolerance improvement. Moreover, the sample size was relatively small. Future research should include a larger number of participants to further examine the impact of impaired renal function on exercise capacity in the context of outpatient CR.

Second, although the findings suggest that patients with reduced renal function may show only limited improvement in exercise tolerance at the start of outpatient CR, it remains unclear which type of exercise intervention may be more effective. Further investigation is needed to determine whether a long-term program, such as the one used in this study, is preferable, or whether increased intensity or frequency of exercise therapy would produce superior outcomes.

Additionally, all participants in this study completed one year of outpatient CR, indicating that the sample consisted of individuals who were capable of maintaining a certain level of motivation. Therefore, the potential for selection bias cannot be excluded.

Conclusions

Patients with reduced renal function demonstrated lower exercise capacity at the start of outpatient CR, and this trend persisted after one year. Furthermore, the degree of improvement in exercise tolerance was smaller compared to those with normal renal function, potentially due to skeletal muscle abnormalities associated with renal disease.

List of Abbreviations

AMI: Acute Myocardial Infarction
ANCOVA: Analysis of Covariance
AT: Anaerobic Threshold
BIA: Bioelectrical Impedance Analysis
CKD: Chronic Kidney Disease
CPET: Cardiopulmonary Exercise Testing
CR: Cardiac Rehabilitation
CVD: Cardiovascular Disease
eGFR: Estimated Glomerular Filtration Rate
HADS-A: Hospital Anxiety and Depression Scale-Anxiety
HADS-D: Hospital Anxiety and Depression Scale-Depression
PCr: Phosphocreatine
SMI: Skeletal Muscle Index
VE: Ventilation
VO₂: Oxygen Uptake
VCO₂: Carbon Dioxide Output

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Seijoh University (Approval No.: 2024C0019).

Availability of Data and Materials

No datasets were generated or analyzed during the current study.

Competing Interests

The authors declare no competing interests.

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Author Contributions

M.T. and K.I. conceived the study concept. K.I. developed the statistical analysis plan and performed the statistical analyses. M.T., K.S., S.N., K.I., and Y.K. contributed to the interpretation of the results. M.T., K.S., and S.N. were responsible for data acquisition. Y.K. supervised the execution of the study. All authors reviewed and critically revised the manuscript for intellectual content and approved the final version for publication.

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