Association between outpatient cardiac rehabilitation and all-cause mortality after cardiovascular surgery: A propensity score-matched analysis

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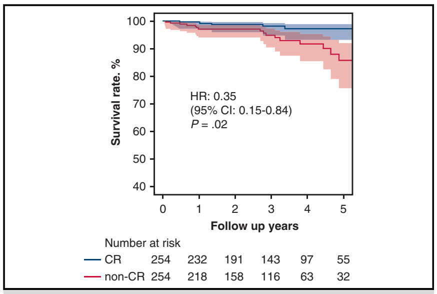
ABSTRACT

Objectives: Cardiac rehabilitation (CR) is a class I recommendation in the treatment guidelines for cardiovascular disease; however, its postoperative prognostic effects after surgery are not fully understood. Therefore, this study aimed to examine the effect of multidisciplinary outpatient CR on postdischarge all-cause mortality in patients who underwent cardiovascular surgery.

Methods: This retrospective cohort study included consecutive patients who underwent elective cardiovascular surgery between April 2015 and March 2021. Patients were categorized into CR and non-CR groups. The primary outcome measure was all-cause mortality. Propensity score-matching analysis was performed to minimize selection bias and differences in clinical characteristics. The propensity score for each patient was produced using logistic regression analysis, with the CR group and the subsequent 27 variables as the dependent and independent variables, respectively.

Results: In our cohort (n = 1095), 51 patients (4.7%) died during the follow-up period (mean, 1042 days). The CR group had a significantly lower mortality rate than the non-CR group (hazard ratio, 0.45; 95% CI, 0.21-0.95; *P* = .036). After propensity score matching adjusted for confounders, the association between CR and reduced risk of all-cause mortality remained (hazard ratio, 0.35; 95% CI, 0.14-0.85; *P* = .02).

Conclusions: Postdischarge multidisciplinary outpatient CR in patients who underwent cardiovascular surgery was associated with a substantial survival benefit, which persisted after adjusting for variables, including age, operative factors, physical and cognitive functions, and nutritional status. (JTCVS Open 2023;15:313-23)



Multidisciplinary outpatient cardiac rehabilitation reduces postoperative mortality.

CENTRAL MESSAGE

Multidisciplinary outpatient cardiac rehabilitation in patients undergoing cardiovascular surgery improves survival rates after adjusting for age and physical, cognitive, and nutritional status.

PERSPECTIVE

Patients are encouraged to participate in a multidisciplinary outpatient cardiac rehabilitation program after cardiovascular surgery; however, the background of the participants is skewed. Our study showed an improved prognostic effect even after adjusting for age, physical and cognitive functions, and nutritional status. These data suggest the usefulness of this program in improving survival.

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Institutional Review Board (IRB) Approval: This study was approved by the Research Ethics Committee of the Nagoya Heart Center (approval no. NHC2022-1004-08; approval date: October 4, 2022).

Informed Consent Statement: The requirement for written informed consent was waived because the study met the conditions outlined in the Japanese Ethical Guidelines for Medical and Biological Research Involving Human Subjects.

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Abbreviations and Acronyms
BNP = B-type natriuretic peptide
CR = cardiac rehabilitation
PS = propensity score

Cardiac rehabilitation (CR) is a comprehensive program that comprises exercise training, patient education and counseling, nutrition support, and optimal drug treatment by a multidisciplinary team. Previous meta-analyses have shown the effects of CR on health-related quality of life in patients with cardiovascular disease.[1-3] Therefore, CR is a key secondary prevention measure and a class I recommendation in the treatment guidelines for cardiovascular disease.[4] However, because the current recommendation is primarily based on evidence from coronary heart disease and heart failure, postcardiovascular surgery effects are yet to be established. Indeed, the prognostic effects of CR in patients who underwent cardiovascular surgery have been reported to be unknown in the previous meta-analysis.[1]

A meta-analysis reported that the early initiation of aerobic exercise after cardiovascular surgery improves functional and aerobic capacity.[5] Additionally, outpatient CR based on exercise training, patient education for disease management, and nutrition support reportedly improved exercise capacity in patients who underwent cardiovascular surgery.[6] Therefore, these results suggest that CR may improve long-term postoperative prognosis; however, as mentioned before, its postoperative prognostic effects remain unestablished. To date, only limited studies have reported the prognostic effects of outpatient CR after cardiovascular surgery. Previous studies have reported an association between CR participation and an approximately 30% to 50% reduction in all-cause mortality after cardiovascular surgery.[7-9] Although these studies were statistically adjusted for major clinical characteristics, clinically important confounders, such as physical function, cognitive function, and nutritional status, were not included in the multivariate model, possibly because they were retrospective analyses. This may overestimate the prognostic effects of CR because participants generally had better physical and cognitive status than nonparticipants.[10,11] Additionally, the implementation of inpatient CR, which is another factor associated with postoperative prognosis, was not considered when evaluating the effects of outpatient CR. Therefore, this study aimed to examine the effects of multidisciplinary outpatient CR on postdischarge all-cause mortality in patients who underwent cardiovascular surgery and participated in inpatient CR. We collected data on physical, cognitive, and nutritional status using standard methods and performed a propensity score (PS)-matched analysis.

METHODS

Study Design and Participants

This retrospective cohort study included consecutive patients who underwent elective cardiovascular surgery (eg, coronary artery bypass surgery, valve replacement or repair, coronary artery bypass surgery with concomitant valve replacement or repair, or aortic surgery) between April 2015 and March 2021 at Nagoya Heart Center, Japan. We excluded patients with chronic hemodialysis, thoracic aortic disease treated with endovascular aneurysm repair, abdominal aortic aneurysm, or hospital death.

In Japan, an inpatient CR program generally begins the day after cardiovascular surgery and continues until discharge in Japan. The typical inpatient CR comprises an early postoperative mobilization program, exercise training, and disease management guidance toward hospital discharge. Preoperative patient education is also provided for patients undergoing elective surgery. Patients are referred for outpatient CR before discharge, and those who hope to start the outpatient CR program are usually at the hospital where the patient undergoes surgery. In contrast, some patients may be referred to a facility providing CR in the patient's neighborhood. All patients received inpatient CR during hospitalization in this study, which was provided according to the Japanese Circulation Society Guidelines for Rehabilitation in Patients with Cardiovascular Disease.[4] Briefly, the postoperative mobilization program began with active and passive movements in bed, where patients were trained to restore their activities of daily living skills. After a patient's condition is stable, exercise training, including aerobic exercise and resistance training, is performed in the rehabilitation room under the supervision of a physiotherapist to improve the patient's exercise tolerance. Rehabilitation was performed 5 to 6 times weekly for 60 minutes per day until the day before discharge.

This study was approved by the Research Ethics Committee of the Nagoya Heart Center (approval No. NHC2022-1004-08; approval date: October 4, 2022), and the protocol complied with the principles expressed in the Declaration of Helsinki. The requirement for written informed consent was waived because the study met the conditions outlined in the Japanese Ethical Guidelines for Medical and Biological Research Involving Human Subjects. All patients were informed of their participation in this study, and each was offered the opportunity to withdraw. Information regarding this study, including the inclusion criteria and withdrawal opportunity, was provided on the hospital's website. This consent procedure was approved by the ethics committees. No patient withdrew from the study at the time of the analysis.

Outpatient CR Program

The outpatient CR program was initiated approximately 1 week postdischarge and continued for 3 to 6 months. Patients were considered to have participated in CR if they attended at least one outpatient CR session within 3 months postdischarge.[7,8,12,13] The program included hospital-based supervised exercise sessions (1-3 times weekly; cycling with an ergometer, walking on a treadmill, and resistance training), educational classes, individual counseling, and home exercise. Exercise intensity was determined individually at the anaerobic threshold level obtained using metabolic gas exchange parameter via symptom-limited bicycle ergometry-assessed cardiopulmonary exercise testing or an intensity of 3 to 4 on the modified Borg scale. A resistance training program was conducted at each outpatient CR session. A 1-repetition maximum strength assessment was performed to adjust the load on the resistance training machines, and approximately 50% and 30% of the 1-repetition maximum intensities were adopted for the lower and upper muscles, respectively.[14] Resistance training of the upper muscles was initiated 2 months postoperatively in patients who underwent a median sternotomy.

Professional nurses educated patients on managing their heart failure symptoms, measuring their pulse, recognizing an arrhythmia or infection, monitoring their weight and surgical sites, and optimizing their cardioprotective medications. Additionally, information on smoking cessation, stress management, and daily exercise was provided. A registered dietitian provided education on fluid management, salt restriction, and daily alcohol intake and identified comorbidities, such as chronic kidney disease, obesity, hypertension, diabetes, and dyslipidemia.

At the study hospital, CR participants are encouraged to attend 1 to 3 sessions/week if possible. In this study, the frequency of CR participation for each patient was defined based on the planned frequency at starting the CR program and actual participation for 3 months postdischarge. We confirmed their participation frequency using medical records. If outpatient CR was interrupted a few times for any reason, including hospitalization or canceling a session for illness but quickly resumed, the patient was still considered as attending with the previous CR frequency.

Statistical Analysis

Continuous variables are expressed as mean ± SD and median with interquartile range. Patients were categorized into CR and non-CR groups, and between-group differences in clinical characteristics were compared using Student' *t* test or 1-way analysis of variance, χ^2 tests, or Fisher exact tests, as appropriate. PS matching was performed to reduce the risk of bias in treatment selection and potential confounding factors. The PS for each patient was produced using logistic regression analysis, with the CR group as the dependent variable and the subsequent 27 variables as independent variables (ie, age, sex, body mass index, left ventricular ejection fraction, diabetes mellitus, hypertension, chronic kidney disease, cancer, chronic heart failure, prior cardiovascular surgery, atrial fibrillation, NT-pro B-type natriuretic peptide (BNP), hemoglobin, coronary artery bypass grafting, duration of surgery time, postoperative ventilation time, Short Physical Performance Battery, knee extension isometric muscle strength, Mini-Mental State Examination, Geriatric Nutritional Risk Index),[15] currently working, living alone, prescriptions for an angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker and β-blocker, length of intensive care unit stay, length of hospital stay, and discharged home. Physical function, cognitive function, and nutritional status were evaluated preoperatively as a routine clinical assessment. We performed a 1:1 nearest available matching on the logit of the PS with a caliper value of 0.2 without replacement. We used the standardized mean difference to measure covariate balance, whereby an absolute standardized mean difference <0.1 represents a meaningful imbalance between groups.

This study's primary end point was all-cause mortality. Mortality incidence was a valid and reliable end point because it can be investigated by regular outpatient visits and telephone survival checks at the study hospital. Survival curves were estimated using the Kaplan-Meier method and compared using the log-rank test between the CR and non-CR groups before and after PS matching. The hazard ratio (HR) and 95% CI were calculated using a Cox proportional hazard model. The proportional hazards assumption was assessed using Schoenfeld residuals. Potential effect modification was assessed by subgroup analyses across operation year, age (stratified at the median), sex, NT-pro BNP (stratified at the median), smoking, and working status. Additionally, cumulative survival was compared with the frequency of outpatient CR participation during the first 3 months

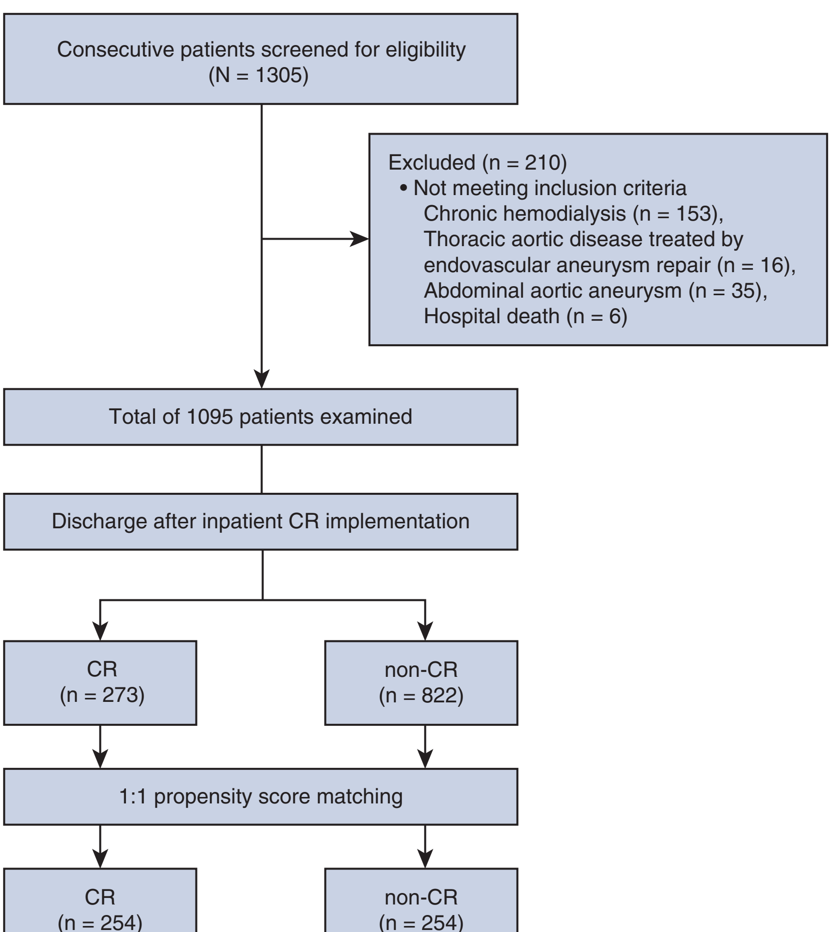


FIGURE 1. Study flow diagram. *CR*, Cardiac rehabilitation.

TABLE 1. Baseline characteristics of the entire cohort and matched-pair group stratified by participation in outpatient cardiac rehabilitation

	All study patients, (N = 1095)				(Propensity score-matched cohort) (n = 508)			
	CR (n = 273)	Non-CR, (n = 822)	SMD	*P* value	CR (n = 254)	Non-CR, (n = 254)	SMD	*P* value
Baseline clinical characteristics								
Age (y)	68.5 ± 11.7	68.5 ± 12.4	0.001	.99	68.8 ± 11.8	68.3 ± 12.6	0.04	.654
Male	160 (58.6)	550 (66.9)	0.172	.016	153 (60.2)	154 (60.6)	0.008	1.0
BMI	23.0 ± 3.5	23.1 ± 3.9	0.023	.745	23.1 ± 3.5	23.1 ± 3.6	0.002	.979
LVEF (%)	56.9 ± 13.1	55.4 ± 13.9	0.116	.102	57.0 ± 12.9	56.8 ± 12.6	0.016	.86
Comorbidities								
Diabetes mellitus	72 (26.4)	264 (32.1)	0.127	.082	68 (26.8)	63 (24.8)	0.045	.685
Hypertension	170 (62.3)	531 (64.6)	0.048	.513	163 (64.2)	154 (60.6)	0.073	.464
Chronic kidney disease	134 (49.1)	417 (50.7)	0.033	.675	124 (48.8)	124 (48.8)	<0.001	1.0
Cancer	26 (9.5)	106 (12.9)	0.107	.163	25 (9.8)	20 (7.9)	0.069	.533
Chronic heart failure	64 (23.4)	233 (28.3)	0.112	.117	58 (22.8)	53 (20.9)	0.048	.668
Prior cardiovascular surgery	12 (4.4)	25 (3.0)	0.072	.332	10 (3.9)	9 (3.5)	0.021	1.0
Atrial fibrillation	35 (12.8)	136 (16.5)	0.105	.15	32 (12.6)	31 (12.2)	0.012	1.0
Laboratory data								
NT-pro BNP (pg/mL)	291.0 (117.0-1215.0)	445.5 (115.5-1513.5)	0.167	.165	287.0 (117.0-1190.3)	348.0 (116.3-1095.3)	0.085	.86
Hemoglobin (g/dL)	13.5 ± 1.7	13.4 ± 1.8	0.038	.591	13.5 ± 1.7	13.5 ± 1.8	0.031	.728
Operative information								
Type of operation, n								
CABG	52 (19.0)	239 (29.1)	0.239	.021	51 (20.1)	52 (20.5)	0.075	.949
Valve	138 (50.6)	371 (45.1)			127 (50.0)	123 (48.4)		
Aortic	16 (5.9)	46 (5.6)			14 (5.5)	11 (4.3)		
Concomitant	55 (20.1)	136 (16.5)			52 (20.5)	57 (22.5)		
Other	12 (4.4)	30 (3.7)			10 (3.9)	11 (4.3)		
Duration of surgery, min	242.3 ± 83.2	248.2 ± 86.2	0.07	.32	242.6 ± 81.3	244.0 ± 84.8	0.017	.845
MICS approach	34 (12.5)	98 (11.9)	0.016	.83	33 (13.0)	42 (16.5)	0.10	.317
Postoperative ventilation time (h)	3.6 ± 7.8	3.7 ± 9.3	0.008	.913	3.6 ± 7.9	3.4 ± 4.9	0.03	.736
Physical function								
SPPB	12.0 (11.0-12.0)	12.0 (10.0-12.0)	0.304	.003	12.0 (11.0-12.0)	12.0 (11.0-12.0)	0.003	.874
KEIS (Nm/kg)	1.29 ± 0.4	1.27 ± 0.4	0.062	.39	1.29 ± 0.4	1.28 ± 0.4	0.016	.854
Cognitive function								
MMSE ≤27 (n = 1070)	98 (36.3)	351 (43.9)	0.155	.032	95 (37.4)	96 (37.8)	0.008	1.0
Nutritional status								
GNRI	100.7 ± 6.1	99.4 ± 67.5	0.192	.009	100.8 ± 6.0	101.1 ± 6.7	0.057	.521
Social data								
Currently working	127 (46.5)	358 (43.6)	0.06	.4	119 (46.9)	123 (48.4)	0.032	.79
Living alone	48 (17.6)	182 (22.1)	0.114	.123	47 (18.5)	51 (20.1)	0.04	.736
Medications								
β-blocker	112 (41.0)	318 (38.7)	0.048	.52	103 (40.6)	101 (39.8)	0.016	.928
ACE-i or ARB	118 (43.2)	410 (49.9)	0.134	.059	111 (43.7)	106 (41.7)	0.04	.72
Length of ICU stay, (d)	1.3 ± 1.1	1.5 ± 2.2	0.113	.157	1.2 ± 0.8	1.2 ± 0.6	0.034	.701
Length of hospital stay (d)	19.2 ± 12.8	19.7 ± 20.0	0.027	.73	19.1 ± 12.7	19.0 ± 23.9	0.005	.954
Discharged home	273 (100.0)	751 (91.4)	0.435	<.001	254 (100.0)	254 (100.0)	<0.001	–
No. of sessions within 3 mo	14 ± 8	–	–	–	14 ± 7	–	–	–
Frequency of CR			–	–			–	–
Nonparticipants	–	822 (100)			–	254 (100)		
<1 session/wk	8 (2.9)	–			7 (2.8)	–		
1 session/wk	155 (56.8)	–			145 (57.1)	–		
≥2 sessions/wk	110 (40.3)	–			102 (40.1)	–		

Values are presented as n (%), mean ± SD, or median (interquartile range). *CR*, Cardiac rehabilitation; *SMD*, standardized mean difference; *BMI*, body mass index; *LVEF*, left ventricle ejection fraction; *NT-pro BNP*, N-terminal pro-brain natriuretic peptide; *CABG*, coronary artery bypass grafting; *MICS*, minimally invasive cardiac surgery; *SPPB*, Short Physical Performance Battery; *KEIS*, knee extension isometric muscle strength; *MMSE*, Mini-Mental State Examination; *GNRI*, Geriatric Nutritional Risk Index; *ACE-i*, angiotensin-converting enzyme inhibitor; *ARB*, angiotensin II receptor blocker; *ICU*, intensive care unit.

TABLE 2. Reasons for nonparticipation in outpatient cardiac rehabilitation

	Overall (N = 858)
Distance from the hospital (%)	32.8
No desire to participate (%)	19.1
Return to work (%)	13.6
Lack of transportation (%)	10.6
Other (%)	23.9

in the entire cohort to examine the dose-response relationship. In this subanalysis, multivariate analysis was adjusted for age, gender, left ventricular ejection fraction, and NT-pro BNP. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University), which is a graphical user interface for R (R Foundation for Statistical Computing).[16]

RESULTS

Of the 1305 patients who underwent elective cardiovascular surgery during the study period, 1095 were included in the analysis (Figure 1). According to outpatient CR participation, patient characteristics are presented in Table 1. The mean age was 68.5 ± 12.2 years, and 273 patients (25%) participated in outpatient CR. The reasons for nonparticipation in outpatient CR in this study are listed in Table 2. For the entire cohort, the mean follow-up period was 1198.7 ± 645.7 and 990.3 ± 625.2 days for the CR and non-CR groups, respectively (1042.3 ± 636.5 days for all study patients). Overall, 51 patients (4.7%) died during the follow-up period. PS matching identified 254 pairs, and the *C* statistics of PS-predicting CR participation was 0.67 (95% CI, 0.64-0.71). The distributions of PS after matching were well-balanced between the groups (Figure 2). Additionally, the absolute standardized mean differences for all covariates were ≤0.1 (Table 1), indicating a sufficient balance. In the PS-matched cohort, the mean follow-up period was 1220.0 ± 647.9 and 1025.6 ± 623.3 days for the CR and non-CR groups, respectively (1122.8 ± 642.5 days overall). However, 23 patients died during the follow-up period.

Figure 3 shows the Kaplan–Meier survival curves before and after PS matching. For the entire cohort, the CR group had a lower risk of all-cause mortality before matching than the non-CR group (HR, 0.45; 95% CI, 0.21-0.95; $P = .036$). The association between CR and reduced risk of all-cause mortality remained after adjusting for confounders using PS matching (HR, 0.35; 95% CI, 0.14-0.85; $P = .02$). The proportional hazards assumption for a composite outcome was confirmed using the Schoenfeld residuals test ($P = .59$) and residuals plots (Figure E1). The results of the sensitivity analysis are presented in Figure 4. No variables were found showing the interactions with the CR effects.

The prognostic differences by frequency of outpatient CR participation in the entire cohort are shown in Figure 5. Patients who attended ≥2 sessions/week had better prognoses (HR, 0.15; 95% CI, 0.02-1.08; $P = .06$) than nonparticipants, although the association was not statistically significant. CR attendance of ≤1 session/week was not associated with a significantly reduced risk of all-cause mortality (HR, 0.72; 95% CI, 0.32-1.62; $P = .43$). The distribution of the number of participating sessions during the first 3 months in the entire cohort CR group is

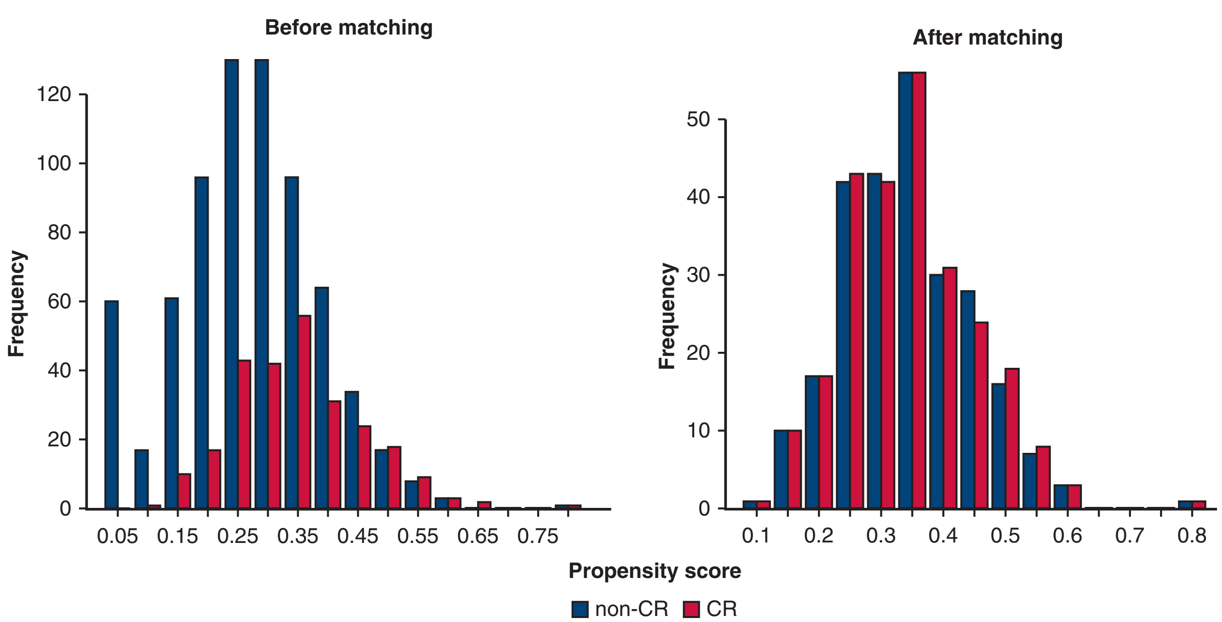


FIGURE 2. Comparison of propensity score distributions before and after matching between the outpatient cardiac rehabilitation (*CR*) and nonparticipating CR groups.

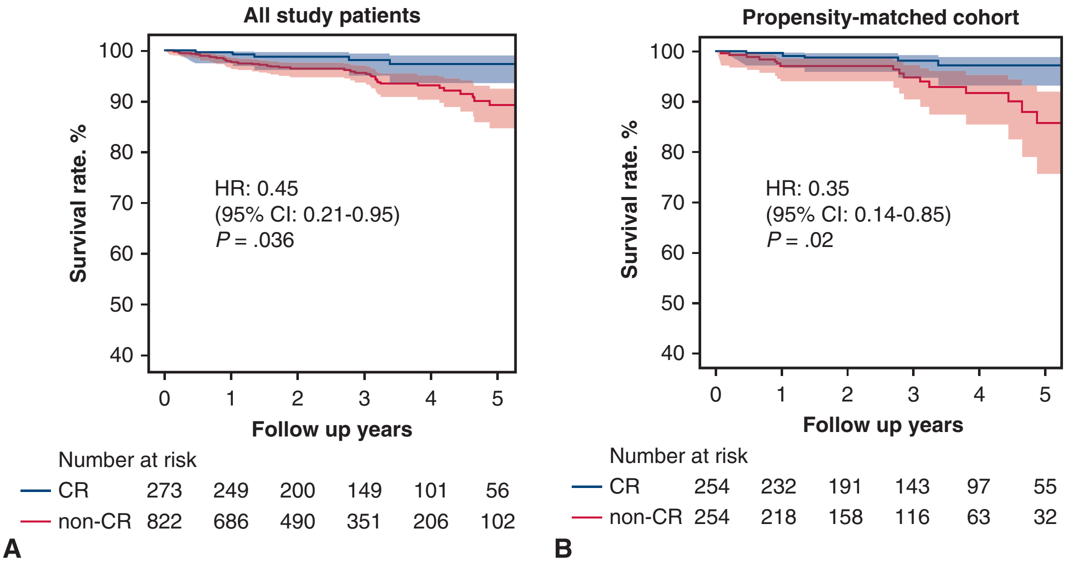


FIGURE 3. Kaplan-Meier survival curves for cumulative mortality postcardiovascular surgery between the cardiac rehabilitation (*CR*) (*blue line*) and non-CR (*red line*) groups in the entire (A) and propensity score-matched (B) cohorts. The incidence of mortality in the CR group was significantly lower than that in the non-CR group. The *shaded areas* represent 95% CI. *HR*, Hazard ratio; *CI*, confidence interval.

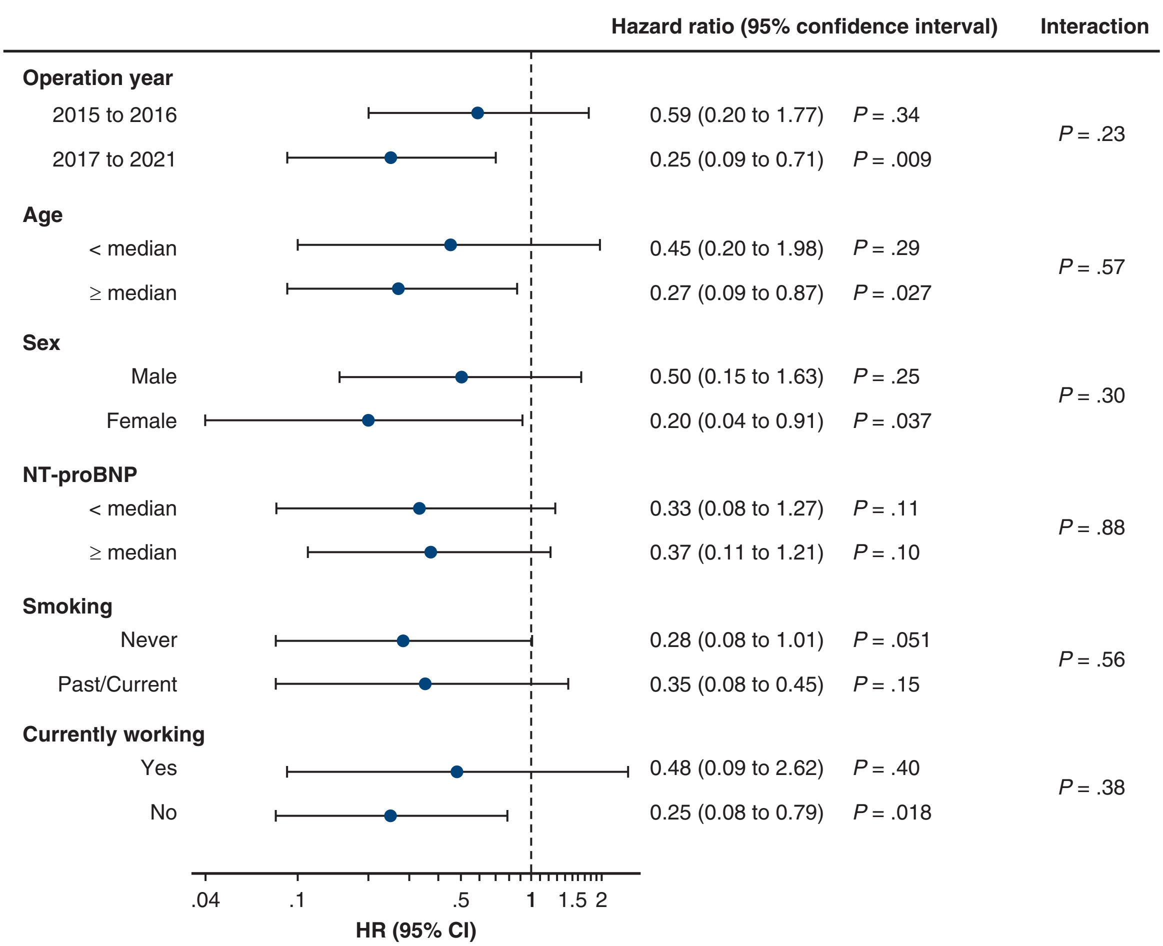
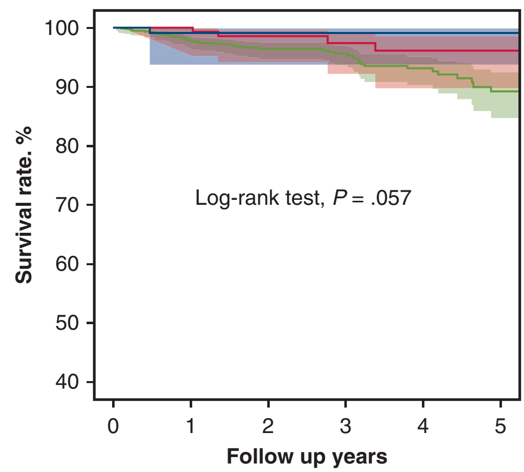


FIGURE 4. Forest plot of the hazard ratio for association of outpatient cardiac rehabilitation (CR) with all-cause mortality. *NT-pro BNP*, N-terminal pro-brain natriuretic peptide; *HR*, hazard ratio; *CI*, confidence interval.



Number at risk	0	1	2	3	4	5
≥ 2/week CR	110	100	82	60	38	16
≤ 1/week CR	163	149	118	89	63	40
non-CR	822	686	490	351	206	102

Age-, gender-, LVEF-, NT-proBNP- adjusted HR [95% CI]	
non-CR participants	1 (Reference)
≤ 1/week	0.72 [0.32-1.62], *P* = .43
≥ 2/week	0.15 [0.02-1.08], *P* = .06

FIGURE 5. Kaplan-Meier survival curves for cumulative mortality by frequency of outpatient cardiac rehabilitation (*CR*) participation in the entire cohort. Patients who attended ≥2 sessions/week (*blue line*) had better prognoses than the nonparticipants (*green line*), although the association was not statistically significant. CR attendance of ≤1 session/week (*red line*) was not associated with a significantly reduced risk of all-cause mortality. The *shaded areas* represent 95% CI. *LVEF*, Left ventricle ejection fraction; *NT-pro BNP*, N-terminal pro-brain natriuretic peptide; *HR*, hazard ratio; *CI*, confidence interval.

presented in Figure E2. In the multivariate Cox regression analysis, the number of sessions was not statistically associated with the study outcome (HR in reference to non-CR group: lowest tertile, 0.36 (95% CI, 0.09-1.48; $P = .16$); middle tertile, 0.73 (95% CI, 0.26-2.04;, $P = .54$); and highest tertile, 0.38 (95% CI, 0.09-1.56; $P = .18$)).

DISCUSSION

This study demonstrated that outpatient CR participation was independently associated with a significant reduction in postoperative mortality after adjusting for potential confounders. The PS-matched analysis in this study included physical and cognitive functions and nutritional status, which have recently been reported as postoperative prognostic factors. Additionally, the prognostic effects of outpatient CR in patients who receive standard inpatient CR in Japan have been suggested. This study is clinically significant because it suggests the effectiveness of outpatient CR in controlling for important confounding factors that have not been previously considered (Figure 6).

Previous studies have reported an association between CR participation and an approximately 30% to 50% reduction in all-cause mortality after cardiovascular surgery.[7-9] In this study, the incidence of all-cause mortality during the follow-up period was 4.7%, and the PS-matched analysis showed a 65% reduction in the mortality risk in the CR group. These results were consistent with previous findings, supporting the current recommendation for CR postoperatively. This study contributes additional evidence to the literature by demonstrating the effects of outpatient CR on postdischarge outcomes among patients participating in inpatient CR. Although inpatient CR has been reported to affect prognosis postcardiovascular surgery,[9] previous studies that examined the effects of outpatient CR did not adjust for inpatient CR participation as a confounder. In Japan, inpatient CR has become the standard intervention after cardiovascular surgery, with an implementation rate of approximately three-quarters.[17] All patients in the study hospital received standard inpatient CR care. The clinical significance of this study is that outpatient CR improved postdischarge prognosis even after standardized inpatient CR.

Moreover, CR was associated with reduced all-cause mortality, even after adjusting for physical and cognitive functions and nutritional status. In this study's entire cohort, the non-CR group had significantly lower Short Physical Performance Battery, higher prevalence of Mini-Mental State Examination score of ≤27 points,[18,19] and lower

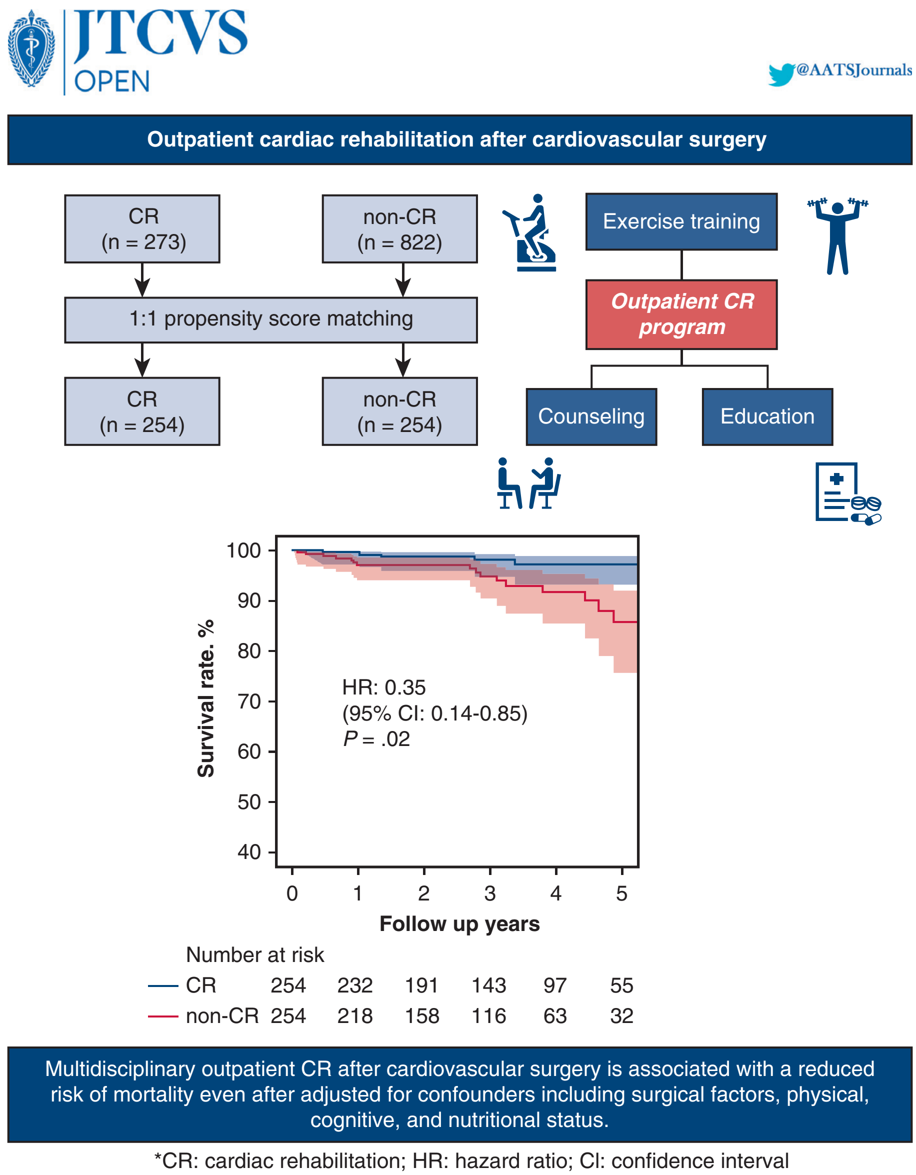


FIGURE 6. Outpatient cardiac rehabilitation after cardiovascular surgery. *CR*, Cardiac rehabilitation; *HR*, hazard ratio; *CI*, confidence interval.

Geriatric Nutritional Risk Index than the CR group, indicating that these were important confounding factors.

Several possible mechanisms underlie the relationship between outpatient CR and reduced mortality risk. One possible explanation was the effect of CR on physical function. Systemic inflammation postcardiovascular surgery induces a catabolic state that results in decreased muscle mass[20] and subsequent functional decline.[21] Moreover, recent studies have also reported the prognostic impact of hospital-acquired functional decline. Because increased physical activity has anti-inflammatory effects[22] and improves exercise tolerance,[6] facility-based exercise training and physical activity may be major determinants of the prognostic effects of CR. Another explanation was improved disease management through patient education, including nutrition guidance. A recent systematic review demonstrated the effects of educational interventions postcardiovascular surgery on patients' knowledge, lifestyle modification, and quality of life.[23] Although the direct effect on survival benefit was not shown, the educational intervention helped to reduce mortality risk via improving the above surrogate indicators. Malnutrition has been reportedly associated with a poor prognosis postcardiovascular surgery.[24] In this study hospital, patients with malnutrition received periodical nutrition assessment and dietary guidance from a registered dietitian, and the improved nutritional status may have contributed to the improved prognosis. Furthermore, preoperative cognitive dysfunction is a known poor prognostic factor for vascular surgery.[18] Previous meta-analyses have demonstrated the effects of physical activity and resistance training on reducing cognitive decline,[25,26] and outpatient CR may effectively improve cognitive function. In this study, most participants undergoing CR attended at least 1 session weekly for 3 months, which was considered a sufficient frequency to obtain the above effects. Although data supporting the above mechanisms were not obtained in this study, comprehensive multidisciplinary CR was considered effective in improving prognosis postcardiovascular surgery.

As highlighted, there is an increasing implementation rate of inpatient CR in Japan; however, outpatient CR postcardiovascular surgery remains underutilized, with only a 9% implementation rate,[17,27] which is lower than that in Western countries. This low participation rate may be attributed to the differences in health care systems among countries[27]; however, low CR referral rates by healthcare providers is another important factor for the CR implementation rate.[28] Previous studies have shown a relationship between strong recommendations from health care providers and the CR participation rate.[29] The subanalysis explored the dose–effect relationship; however, the association between the frequency of outpatient CR participation and all-cause mortality was not statistically significant in this study. The insufficient statistical power may have resulted in this because of the limited number of outcome onsets since HRs appeared to be lowered with increased CR attendance. Additionally, the number of patients who participated in CR less than once per week was relatively small, and the influence of low CR frequency could not be examined in this study. From the above, further large-scale studies are required to confirm the dose–effect relationship of outpatient CR in this population. However, we believe that this study's results provide fundamental evidence for recommending outpatient CR regardless of a patient's physical or cognitive function. In this study, physical barriers, including distance from the hospital (32.8%), return to work (13.6%), and lack of transportation (10.6%), accounted for approximately 60% of non-CR participation. Overall, 25% of the CR participation rate in this study was higher than the nationwide data of Japan[17]; however, there is room for improving the implementation rate. In addition to motivating patients, we believe different approaches are required, such as remote CR programs and flexible time settings.

Study Limitations

This study had some limitations. First, it was based on a single center, and the generalizability of the findings should be confirmed using large samples in multiple facilities. Second, the study population was a homogeneous Japanese cohort with relatively high physical function. For instance, although the average length of hospitalization of 19 days was similar to the nationwide data of Japan, this was longer than in other countries, and the generalizability of the findings may not be limited to populations with shorter durations of hospitalization. Third, this study did not assess several confounding factors, including perioperative complications such as pneumonia, stroke, and renal failure. Socioeconomic status, including economic status and educational background, was another important confounder not assessed in this study. Fourth, the difference in prognosis was more pronounced in the longer follow-up period, and the number of patients followed-up for >3 years was relatively small, possibly leading to the reduced accuracy of survival rates of both groups. Finally, our results may not be generalizable to patients who choose not to enroll in CR programs. Nevertheless, this study showed an improved prognosis after adjusting for various variables, including physical or cognitive functions, nutritional status, age, and gender, which is an important finding for recommending outpatient CR.

CONCLUSIONS

Postdischarge multidisciplinary outpatient CR in patients who underwent cardiovascular surgery was associated with a substantial survival benefit, which remained after adjusting for variables, including age, operative factor, physical and cognitive functions, and nutritional status in a PS-matched analysis.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: cardiac rehabilitation, cardiovascular surgery, all-cause mortality, Japan, propensity score

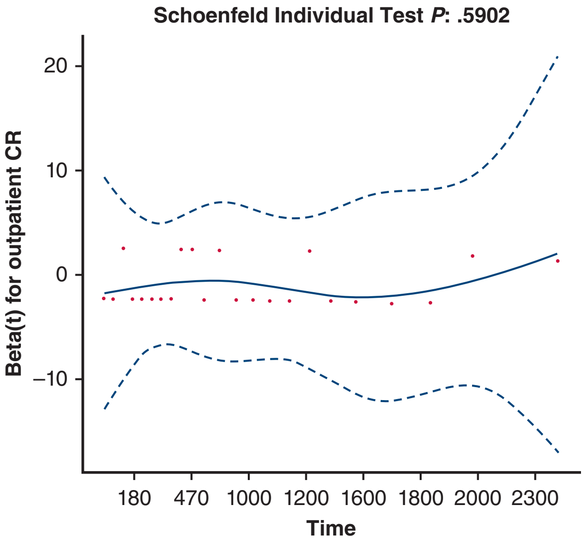

FIGURE E1. Schoenfeld residual plot. *CR*, Cardiac rehabilitation.

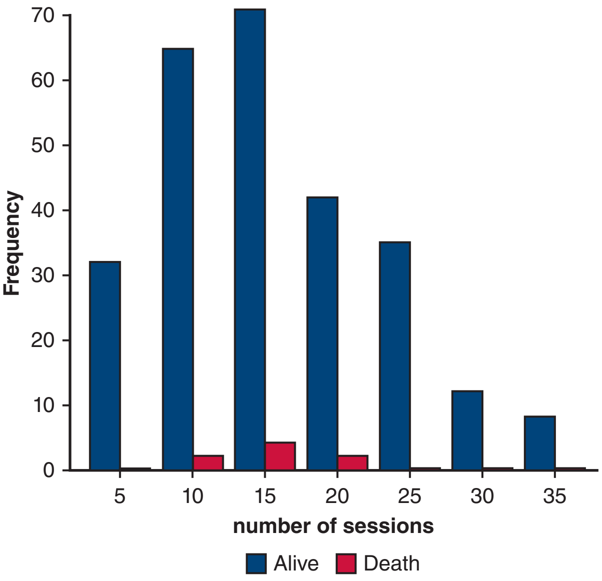

FIGURE E2. The distribution of the number of participating sessions during the first 3 months in the cardiac rehabilitation (CR) group.