53-8. (Japanese)
11. Kawakami N, Takao S, Kobayashi Y, Tsutsumi A. Effects of web-based supervisor training on job stressors and psychological distress among workers: a workplace-based randomized controlled trial. J Occup Health 2006; 48: 28-34.
12. Fukuhara S, Bito S, Green J, Hsiao A, Kurokawa K. Translation, adaptation, and validation of the SF-36 Health Survey for use in Japan. J Clin Epidemiol 1998; 51: 1037-44.
13. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983; 67: 361-70.
14. Abbas AE, Brodie B, Stone G, *et al*. Frequency of returning to work one and six months following percutaneous coronary intervention for acute myocardial infarction. Am J Cardiol 2004; 94: 1403-5.
15. Wenger NK, Hellerstein HK, Blackburn H, Castranova SJ. Uncomplicated myocardial infarction. Current physician practice in patient management. JAMA 1973; 224: 511-4.
16. European Commission. *Guidance on work-related stress, Spice of life or kiss of death? Executive Summary*. Luxembourg: Office for official publications of the European communities, 2002: 9-10.
17. Johnson JV, Hall EM. Job strain, work place social support, and cardiovascular disease: a cross-sectional study of a random sample of the Swedish working population. Am J Public Health 1988; 78: 1336-42.
18. Peterson M, Dunnagan T. Analysis of a worksite health promotion program's impact on job satisfaction. J Occup Environ Med 1998; 40: 973-9.
19. Huruki K. Availability of brief job stress questionnaire. In: Kato M, ed. *The Ministry of Labour sponsored grant for the prevention of work-related illness, The 1999 report*. Tokyo: Tokyo Medical College, 2000; 174-89. (Japanese)
20. Nijs J, Van de Putte K, Louckx F, Trujien S, De Meirleir K. Exercise performance and chronic pain in chronic fatigue syndrome: the role of pain catastrophizing. Pain Med 2008; 9: 1164-72.
21. Swenson JR. Quality of life in patients with coronary artery disease and the impact of depression. Curr Psychiatry Rep 2004; 6: 438-45. (Review)
22. Hare DL, Silverton M. Recovery from acute coronary syndromes. Hidden snares to resuming normality. Aust Fam Physician 2001; 30: 959-63. (Review)
23. Kallio V, Hämäläinen H, Hakkila J, Luurila OJ. Reduction in sudden death by a multifactorial intervention programme after acute myocardial infarction. Lancet 1979; 2: 1091-4.
24. Comparison of a rehabilitation programme, a counseling programme and usual care after an acute myocardial infarction: results of a long-term randomized trial. P.R.E. COR Group. Eur Heart J 1991; 12: 612-6.
25. Lamm G, Denolin H, Dorossiev D, Pisa Z. Rehabilitation and secondary prevention of patients after acute myocardial infarction. Adv Cardiol 1982; 31: 107-11.
26. Jackson L, Leclerc L, Erskine Y, Linden W. Getting the most out of cardiac rehabilitation: a review of referral and adherence predictors. Heart 2005; 91: 10-4. (Review)

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ORIGINAL ARTICLE
Cardiac Rehabilitation

Effects of Phase III Cardiac Rehabilitation on Mortality and Cardiovascular Events in Elderly Patients With Stable Coronary Artery Disease

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Background: Cardiac rehabilitation (CR) has numerous benefits, including reduction of mortality and cardiovascular events, in patients with coronary artery disease (CAD). However, the long-term effect of phase III CR in elderly patients with stable CAD is still unknown.

Methods and Results: The 111 elderly male CAD patients (≥65 years), including 37 subjects participating in supervised CR for 6 months and 74 age-matched controls, were analyzed. The patients were followed for up to 3,500 days, until the occurrence of death or 1 of the following major adverse cardiovascular events (MACE): cardiovascular death, acute coronary syndrome, refractory angina requiring revascularization, admission for congestive heart failure, or stroke. All-cause mortality tended to be lower in the CR group than in the Control group (14% vs 28%, P=0.081). The MACE incidence was significantly lower in the CR group than in the Control group (30% vs 62%, P=0.001). Multivariate Cox proportional hazard analysis showed that the MACE incidence was significantly lower in the CR group than in the Control group [adjusted hazard ratio 0.43 (95% confidence interval 0.20–0.91), P=0.027].

Conclusions: Phase III CR has the beneficial effect of reducing cardiovascular events even in elderly patients with stable CAD. (*Circ J* 2010; **74:** 709–714)

Key Words: Cardiovascular events; Cardiac rehabilitation; Coronary artery disease; Elderly patients; Prognosis

The elderly population has grown rapidly in Japan, resulting in a remarkable increase in the number of patients with coronary artery disease (CAD).[1,2] The elderly people have a 2- to 3-fold higher incidence of acute myocardial infarction (MI) than the younger population,[3–5] and they also tend to have more complications associated with prolonged hospital stays, low physical activity and hence, substantially higher fatality rates after a CAD event.[4,6] Because of these high rates of morbidity and mortality, primary and secondary prevention programs are important strategies not only for modifying cardiovascular risk factors, but also for improving the mortality and quality of life of elderly patients with CAD.[7,8]

Cardiac rehabilitation (CR) programs consist of exercise training, medical counseling, education about cardiovascular diseases, and psychosocial support. The comprehensive treatment has significant benefits on exercise capacity, coronary risk factors, and health-related quality of life (HRQOL).[4–12] In addition, CR reduces all-cause mortality and cardiovascular events; however, its use in patients with CAD is still low.[13–17] In general, CR programs consist of 3 stages: acute stage (phase I), subacute stage (phase II), and the chronic stage (phase III) at least 6 months after a major cardiovascular event. Most CR programs have been performed for phase I and phase II, however, phase III CR has not often been instituted in Japan, especially, because it was not covered by Japanese health insurance until March 2006. Moreover, most previous studies included very few older persons,[18–21] so limited data were available regarding the efficacy of phase III CR, especially in elderly patients with stable CAD.

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Table 1. Baseline Characteristics of the Study Subjects

	CR group (n=37)	Control group (n=74)	P value
Age (years)	69.6±3.4	70.1±4.2	NS
Body mass index (kg/m²)	23.8±2.8	23.2±2.6	NS
Hypertension (%)	19 (51)	50 (68)	NS
Diabetes mellitus (%)	16 (43)	31 (42)	NS
Dyslipidemia (%)	25 (66)	40 (54)	NS
Current smoker (%)	3 (8)	13 (18)	NS
Myocardial infarction (%)	21 (57)	44 (59)	NS
PCI (%)	15 (41)	30 (41)	NS
CABG (%)	15 (41)	32 (43)	NS
Diseased vessels			
1 (%)	14 (38)	20 (27)	NS
2 (%)	10 (27)	25 (34)	
3 (%)	11 (30)	28 (38)	
LMT (%)	2 (5)	6 (8)	NS
Ejection fraction (%)	64.9±13.5	65.2±13.8	NS
Time from last CVE	1,982±1,729	1,288±2,136	NS
Total cholesterol (mg/dl)	186.0±22.4	182.1±28.8	NS
Triglyceride (mg/dl)	132.4±74.3	136.6±79.4	NS
LDL-cholesterol (mg/dl)	109.3±21.8	108.5±27.8	NS
HDL-cholesterol (mg/dl)	50.2±10.8	46.2±10.5	NS
FBS (mg/dl)	104.0±31.1	104.3±22.0	NS
Hemoglobin A_{1c} (%)	6.0±1.0	5.9±1.1	NS
Medications			
Antiplatelets (%)	37 (100)	71 (96)	NS
CCB (%)	19 (51)	39 (53)	NS
β-blockers (%)	17 (46)	26 (35)	NS
ACEI/ARB (%)	12 (32)	24 (32)	NS
Statin (%)	9 (24)	20 (27)	NS
Sulfonylurea (%)	3 (8)	9 (12)	NS
Insulin (%)	2 (5)	3 (4)	NS

Values are mean value±SD or number and percentage in parentheses.
CR, cardiac rehabilitation; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CVE, cardiovascular event; LDL, low-density lipoprotein; HDL, high-density lipoproten; FBS, fasting blood glucose; CCB, calcium-channel blocker; ACEI/ARB, angiotensin converting enzyme inhibitor/angiotensin 1 receptor blocker.

Therefore, in the present study we assessed the effects of phase III comprehensive CR on the morbidity and mortality of cardiovascular diseases in elderly male Japanese patients with CAD.

Methods

Subjects

The study group consisted of 111 elderly male patients (≥65 years) with stable CAD attending the outpatient clinic at Juntendo University Hospital in 1999–2001: 37 patients underwent supervised phase III CR for 6 months as participants of the Juntendo Cardiac Rehabilitation Program (J-CARP), which has been described previously.[9,10] We recruited 39 subjects in the J-CARP study; however, 1 patient dropped out and 1 patient was lost to follow-up, so finally, 37 patients were enrolled as the CR group in this study. As the Control group, we randomly screened 120 stable CAD patients, using medical records, who were outpatients during the same period of the CR program. Patients with ongoing congestive heart failure (CHF), liver dysfunction (aspartate aminotransferase ≥40 IU/L), renal dysfunction (creatinine ≥2.0 mg/dl), or systemic disease, including malignancy and collagen disease, were excluded, so finally, 74 patients were selected as age-matched controls. All patients had been referred at least 6 months after a major coronary event such as acute coronary syndrome (ACS), coronary artery bypass grafting (CABG), or percutaneous coronary intervention (PCI). None of the subjects had previously undergone CR. Subjects received full verbal and written explanations of the nature and purpose of this study, and gave their written informed consent. The study was approved by the Ethical Committee of Juntendo University.

Rehabilitation Protocol

In the CR group, subjects participated in an outpatient phase III CR program once weekly for 6 months, as described previously.[9,10] Briefly, this program included exercise therapy and a dietary and education program. The supervised exercise session consisted of a 10-min warm-up of stretching, 40–60 min of intermittent aerobic exercise, and then resistance training such as sit-ups, squats, push-ups and back kicks and front raises using the patient's own weight. The exercise session was concluded with an approximately 10-min cool down. The intensity of exercise was prescribed individually at the anaerobic threshold (AT) as obtained by a treadmill test using expiratory gas analysis and a rating of 12–13 on the Borg's standard perceived exertion scale. Subjects were

Table 2. Changes in Body Mass Index, Lipid Profiles, Fasting Glucose, and Hemoglobin A_{1c} Levels

	CR group (n=37)		Control group (n=74)	
	At baseline	After 6 months	At baseline	After 6 months
Body mass index (kg/m²)	23.8±2.8	23.3±2.6*	23.2±2.6	23.4±2.3
Total cholesterol (mg/dl)	186.0±22.4	182.3±26.3	182.1±28.8	184.2±27.6
Triglyceride (mg/dl)	132.4±74.3	113.4±54.3#	136.6±79.4	143.7±61.0
LDL-cholesterol (mg/dl)	109.3±21.8	100.3±37.6	108.5±27.8	107.4±25.0
HDL-cholesterol (mg/dl)	50.2±10.8	50.4±11.9	46.2±10.5	46.6±10.9
FBS (mg/dl)	104.0±31.1	96.1±15.4#	104.3±22.0	105.7±17.3
Hemoglobin A_{1c} (%)	6.0±1.0	5.9±1.0	5.9±1.1	5.9±0.9

Values are mean value±SD. *P<0.05 compared with at baseline; #P<0.05 compared with the Control group after 6 months.
Abbreviations see in Table 1.

Table 3. Prevalence of All-Cause Death and Cardiovascular Events

	CR group (n=37)	Control group (n=74)	P value
Death (%)	5 (14)	21 (28)	0.081
Cardiovascular death (%)	1 (3)	8 (11)	0.140
MACE* (%)	11 (30)	46 (62)	0.001
ACS (%)	5 (14)	16 (22)	0.304
PCI (%)	6 (16)	20 (27)	0.205
CABG (%)	1 (3)	7 (9)	0.194
CHF (%)	1 (3)	9 (12)	0.100
Stroke (%)	1 (3)	6 (8)	0.269
Cancer (%)	6 (16)	8 (11)	0.434

*Combined with cardiovascular death, ACS, PCI, CABG, CHF, and stroke.
MACE, major adverse cardiovascular events; ACS, acute coronary syndrome. Other abbreviations see in Table 1.

encouraged to perform home-based aerobic and resistance exercise twice weekly. In addition, subjects were instructed to follow the phase II diet of the American Heart Association at the beginning and every 2 months of the study. An education program was usually provided for each subject by physicians, nurses, and dietitians, regarding ischemic heart disease, risk factors, exercise and dietary instructions. In addition, individual counseling for physical and psychological conditions was provided every visit. The Control group received the standard outpatient care. Medical treatment was unchanged during the 6 months in both groups. After 6 months, the subjects were treated with a standard care protocol conducted by each physician in charge of the 2 groups.

Measurements

In both groups, we assessed body mass index (BMI), serum lipid profiles, glucose, and hemoglobin A_{1c} (HbA_{1c}) at baseline. Serum lipid profiles, including total cholesterol (TC), triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C) were determined by standard methods using an auto-analyzer after 12h of fasting at baseline and after 6 months. Levels of low-density lipoprotein cholesterol were calculated with Friedewald's equation using the concentrations of TC, HDL-C, and TG.

Follow-up

After the initial assessment, the subjects were followed for up to 3,500 days until the occurrence of 1 of the following events: all-cause death or major adverse cardiovascular events (MACE), including cardiovascular death, ACS, refractory ischemia requiring PCI or CABG, admission for CHF, and stroke.

Statistical Analysis

The results are expressed as the mean value±standard deviation. Baseline characteristics of the CR and Control groups were compared using Student's t-test for continuous variables and the chi-square test for categorical variables. Time-to-event data was estimated by the Kaplan-Meier method and analyzed with the log-rank test. The Cox proportional hazards method was used for the multivariate analysis. A value of P<0.05 was considered to be significant.

Results

Baseline Characteristics and Changes in BMI, Lipid Profiles, Fasting Glucose, and HbA_{1c} After 6 Months

The baseline characteristics at enrollment are shown in **Table 1**. There were no significant differences between the CR and Control groups in age, BMI, the rates of hypertension (HT), diabetes mellitus (DM), dyslipidemia or smoking history, or in the other clinical profiles. The concomitant use of medications was also identical between the 2 groups. After 6 months, BMI had significantly decreased in the CR group (from 23.8±2.8kg/m² to 23.3±2.6kg/m², P<0.05) (**Table 2**). The levels of TG (113.4±54.3mg/dl vs 143.7±61.0mg/dl, P<0.05) and fasting glucose (96.1±15.4mg/dl vs 105.7±17.3mg/dl, P<0.05) were significantly lower in the CR group than in the Control group (**Table 2**).

Parameters Before and After Supervised CR

In the CR group, the values of peak $\dot{V}O_2$, peak heart rate (HR), peak speed, AT, AT-HR and AT-speed were 22.5±3.3ml·kg⁻¹·min⁻¹, 114±10beats/min, 6.3±0.9km/h, 12.2±2.1ml·kg⁻¹·min⁻¹, 87±10beats/min, and 3.5±0.8km/h, respec-

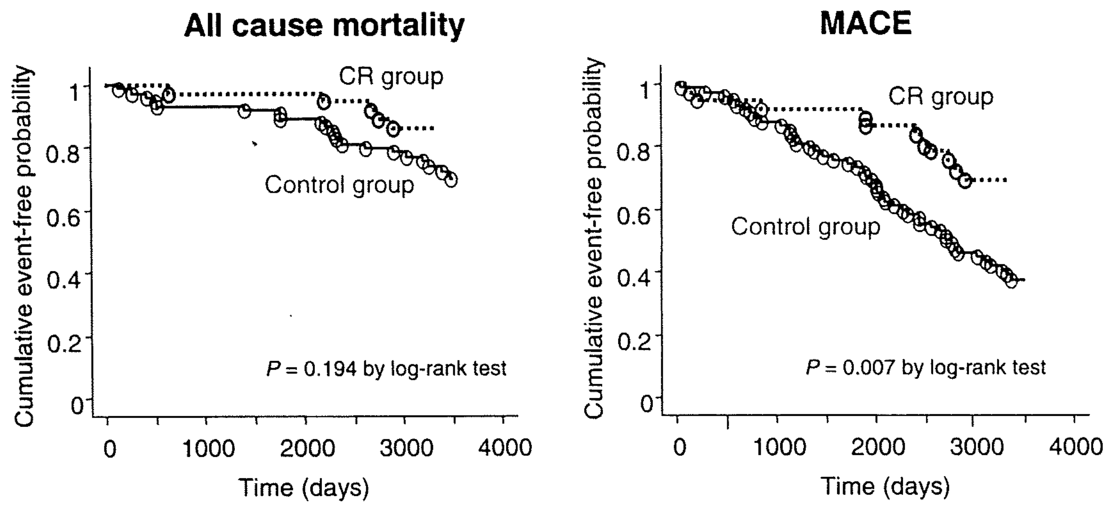

Figure. Kaplan-Meier curves for all-cause mortality and major cardiovascular events in the cardiac rehabilitation group and control group. CR, cardiac rehabilitation; MACE, major adsverse cardiovascular events combined with cardiovascular death, acute coronary syndrome, refractory ischemia requiring percutaneous coronary intervention or coronary artery bypass grafiting, congestive heart failure, and stroke.

Table 4. Relationships Between CR and Adjusted Risk of Total Mortality and MACE

	n	Total mortality			MACE		
		N (%)	HR (95%CI)	P value	N (%)	HR (95%CI)	P value
Control group	74	21 (28)	1.00		46 (62)	1.00	
CR group	37	5 (14)	0.65 (0.19–2.27)	0.505	11 (30)	0.43 (0.20–0.91)	0.027

Cox proportional hazard model adjusted for age, body mass index, hypertension, diabetes, dyslipidemia, smoking history, diseased vessels, and ejection fraction.
Combined with acute coronary events, PCI, CABG, CHF, and stroke.
HR, hazard ratio; CI, confidence interval. Other abbreviations see in Tables 1,3.

tively. In the CR group, all subjects completed the supervised program for 6 months, and 36 patients (97%) continued home exercise 3 times weekly during that period. After 6 months, the values of peak $\dot{V}O_2$, peak HR, peak speed, AT, AT-HR and AT-speed were 23.3±3.2 ml·kg^{-1}·min^{-1}, 121±16 beats/min (P<0.01 vs baseline), 7.0±0.8 km/h (P<0.01 vs baseline), 12.4±2.1 ml·kg^{-1}·min^{-1}, 88±10 beats/min, and 4.2±0.9 km/h (P<0.01 vs baseline), respectively.

Incidence of All-Cause Death and Cardiovascular Events

The incidence of all-cause mortality and of cardiovascular events in the CR and Control groups are presented in **Table 3**. All-cause death tended to be lower in the CR group than in the Control group (14% vs 28%, P=0.081). The MACE incidence was significantly lower in the CR group than in the Control group (30% vs 62%, P=0.001). The incidence of each of cardiovascular death, ACS, refractory ischemia requiring PCI or CABG, admission for CHF, stroke, and cancer did not significantly differ between the 2 groups.

Figure shows the survival curves for all-cause mortality and MACE between the CR and Control groups. Kaplan-Meier analysis demonstrated that the CR group had a significantly lower rate of MACE, but not of all-cause death, during the entire follow-up period (P=0.007, P=0.194, respectively). Multivariate Cox proportional analysis adjusted for age, BMI, HT, DM, dyslipidemia, smoking history, diseased vessels, and ejection fraction, showed that the MACE incidence was significantly lower in the CR group than in the Control group (adjusted hazard ratio 0.43, 95% confidence interval 0.20–0.91, P=0.027) (**Table 4**).

Discussion

In this study, the MACE incidence was significantly lower in the CR group than in the Control group for long-term follow-up of ≤3,500 days even in elderly patients with stable CAD. To the best of our knowledge, this is the first report to demonstrate the efficacy of phase III CR for reducing cardiovascular events in elderly and stable CAD patients.

Comprehensive CR has numerous beneficial effects, including not only improvement of exercise capacity, muscle strength, cardiac risk factors, and HRQOL, but also reducing mortality in CAD patients. We and other groups have shown that these benefits of CR even affect elderly patients with CAD.[9,10,22–24] However, most of the previous studies were observational and assessed the phase II period.[22–24] Naylor et al[25,26] and Clark et al[27] showed that comprehensive discharge planning and home follow-up intervention improved clinical outcomes in elderly patients with CAD, but their reports were based on educational programs without a structured exercise component in the phase II period. Recently, Suaya et al reported that CR participants decreased their 5-year mortality, among elderly patients of US Medicare beneficiaries who were hospitalized for coronary conditions or cardiac revascularization procedures.[21] Most of the subjects were thought to be recruited during the phase II period, such as after acute MI and coronary revascularization. In addition, detailed clinical conditions, such as lipid profiles, data of glucose tolerance, ejection fraction, severity of coronary lesions, and medical treatment, were not clarified, because the origin of the data was the Medicare database.[21] Therefore, we believe that the present study is important, because we investigated the effects of CR on mortality and cardiovascular events in elderly patients in the phase III period.

The precise mechanisms by which CR improves the clinical outcome, even in elderly patients with stable CAD, have not fully been elucidated. Exercise-based training has direct effects on the cardiovascular system, including improvement of oxygen demand, endothelial function, autonomic nerve balance, coagulation system, and inflammatory state.[20] Moreover, comprehensive CR may have indirect effects, such as improvements in the risk factors for atherosclerotic disease.[20] In the present study, BMI significantly decreased in the CR group, and the levels of TG and fasting glucose were significantly lower in the CR group than in the Control group. Indeed, we have already demonstrated in a study of randomized design that CR reduced fat weight without a reduction in lean body weight, as well as the levels of TC in older patients with CAD.[10] The CR group maintained exercise capacity, although peak $\dot{V}O_2$ significantly decreased in the Control group.[10] In addition, the CR group significantly improved muscle strength, flexibility and HRQOL scores calculated by SF-36.[9,10] These direct and indirect effects may have lead to the reduction in cardiovascular events in the subjects of this study.

Although this study reported that the MACE incidence was significantly lower in the CR group than in the Control group, all-cause mortality and cardiovascular death were not significantly different between the 2 groups. This result may be caused by the small sample size. Indeed, a recent study demonstrated that the mortality rate was 34% lower in CR users than nonusers in propensity-based matching of 70,040 subjects.[21] In the present study, the adjusted hazard ratio by multivariate Cox proportional method was 0.65, which was not statistically significant for total mortality in the CR group, compared with the Control group, which suggests that the impact of CR on reducing mortality might be identical in this different cohort. Another possibility is the short period of follow-up. The prognosis for these study subjects may be relatively better than in a previous study, which demonstrated 24.6% mortality at 5 years, even in the non-CR group.[21]

Study Limitations

There are several potential limitations to the present study. First, as described, this study had a small sample. Second, all subjects were male. Third, the supervised exercise session at the clinic was performed only once weekly with at least two home exercise sessions. Therefore, the protocol of this study might not be sufficient to improve the incidence of clinical events such as cardiovascular death, development of new lesions, and admission for CHF. Fourth, the CR group consisted only of subjects who accepted to participate in a formal CR program. Therefore, there may be some selection bias and the study group may not be representative of all elderly patients with CAD. However, the baseline characteristics were identical, including age, BMI, frequency of coronary risk factors, ejection fraction, severity of diseased vessel, and concomitant use of medications, between the 2 groups in this study. In the CR group, 21 patients (57%) undertook habitual exercise, including walking, golf, tennis, and stretching. We did not have precise data of prevalence of regular exercise in the Control group; however, 29 patients (58%) undertook habitual exercise among 50 consecutive elderly patients with CAD who were admitted to our division. Therefore, the prevalence of habitual exercise between the 2 groups may be identical. We believe that the present study is a pioneering and valuable report promoting further investigations. In addition, we did not evaluate physical activity in detail. We assessed the continuance of home-based exercise in the CR group after 1 year of the CR program. Nearly 70% of subjects had continued home exercise, including walking and stretching (data not shown). This high prevalence of continuing home-based exercise may be an explanation for the reduction in cardiovascular events in the CR group. We need to clarify this point in the next step.

Conclusion

A phase III comprehensive CR program significantly improved clinical prognosis, even in elderly patients with stable CAD. Further large sample studies of then elderly population are required to confirm these findings.

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References

1. The Japanese Coronary Artery Disease (JCAD) Study Investigators. Current status of the background of patients with coronary artery disease in Japan: The Japanese Coronary Artery Disease Study (The JCAD Study). *Circ J* 2006; **70:** 1256–1262.
2. Sawabe M, Hamamatsu A, Chida K, Arai T, Harada K, Ozawa T, et al. Elderly patients with minimal common carotid atherosclerosis not infrequently have severe coronary atherosclerosis and myocardial infarction. *Circ J* 2008; **72:** 1946–1952.
3. Lavie CJ, Milani RV, Littman AB. Benefits of cardiac rehabilitation and exercise training in secondary coronary prevention in the elderly. *J Am Coll Cardiol* 1993; **22:** 678–683.
4. Lavie CJ, Milani RV. Effects of cardiac rehabilitation programs on exercise capacity, coronary risk factors, behavioral characteristics, and quality of life in a large elderly cohort. *Am J Cardiol* 1995; **76:** 177–179.
5. Lavie CJ, Milani RV. Effects of cardiac rehabilitation and exercise training programs in patients > or = 75 years of age. *Am J Cardiol* 1996; **78:** 675–677.
6. Lavie CJ, Milani RV. Factors predicting improvements in lipid values following cardiac rehabilitation and exercise training. *Arch Intern Med* 1993; **153:** 982–988.
7. Ades PA, Waldmann ML, McCann WJ, Weaver SO. Predictors of cardiac rehabilitation participation in older coronary patients. *Arch Intern Med* 1992; **152:** 1033–1035.
8. Pasquali SK, Alexander KP, Peterson ED. Cardiac rehabilitation in the elderly. *Am Heart J* 2001; **142:** 748–755.
9. Seki E, Watanabe Y, Sunayama S, Iwama Y, Shimada K, Kawakami K, et al. Effects of phase III cardiac rehabilitation programs on health-related quality of life in elderly patients with coronary artery disease: Juntendo Cardiac Rehabilitation Program (J-CARP). *Circ J* 2003; **67:** 73–77.
10. Seki E, Watanabe Y, Shimada K, Sunayama S, Onishi T, Kawakami K, et al. Effects of a phase III cardiac rehabilitation program on physical status and lipid profiles in elderly patients with coronary artery disease: Juntendo Cardiac Rehabilitation Program (J-CARP). *Circ J* 2008; **72:** 1230–1234.

11. Izawa K, Hirano Y, Yamada S, Oka K, Omiya K, Iijima S. Improvement in physiological outcomes and health-related quality of life following cardiac rehabilitation in patients with acute myocardial infarction. *Circ J* 2004; **68:** 315–320.
12. Maines TY, Lavie CJ, Milani RV, Cassidy MM, Gilliland YE, Murgo JP. Effects of cardiac rehabilitation and exercise programs on exercise capacity, coronary risk factors, behavior, and quality of life in patients with coronary artery disease. *South Med J* 1997; **90:** 43–49.
13. Lavie CJ, Milani RV. Effects of cardiac rehabilitation, exercise training, and weight reduction on exercise capacity, coronary risk factors, behavioral characteristics, and quality of life in obese coronary patients. *Am J Cardiol* 1997; **79:** 397–401.
14. Lavie CJ, Milani RV. Disparate effects of improving aerobic exercise capacity and quality of life after cardiac rehabilitation in young and elderly coronary patients. *J Cardiopulm Rehabil* 2000; **20:** 235–240.
15. Lavie CJ, Milani RV. Benefits of cardiac rehabilitation and exercise training programs in elderly coronary patients. *Am J Geriatr Cardiol* 2001; **10:** 323–327.
16. Goto Y, Itoh H, Adachi H, Ueshima K, Nohara R. Use of exercise cardiac rehabilitation after acute myocardial infarction. *Circ J* 2003; **67:** 411–415.
17. Goto Y, Saito M, Iwasaka T, Daida H, Kohzuki M, Ueshima K, et al; Japanese Cardiac Rehabilitation Survey Investigators. Poor implementation of cardiac rehabilitation despite broad dissemination of coronary interventions for acute myocardial infarction in Japan: A nationwide survey. *Circ J* 2007; **71:** 173–179.
18. Shaw LW. Effects of a prescribed supervised exercise program on mortality and cardiovascular morbidity in patients after myocardial infarction: The National Exercise and Heart Disease Project. *Am J Cardiol* 1981; **48:** 39–46.
19. Vermeulen A, Lie KI, Durrer D. Effects of cardiac rehabilitation after myocardial infarction: Changes in coronary risk factors and long-term prognosis. *Am Heart J* 1983; **105:** 798–801.
20. Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K, et al. Exercise-based rehabilitation for patients with coronary heart disease: Systematic review and meta-analysis of randomized controlled trials. *Am J Med* 2004; **116:** 682–692.
21. Suaya JA, Stason WB, Ades PA, Normand SL, Shepard DS. Cardiac rehabilitation and survival in older coronary patients. *J Am Coll Cardiol* 2009; **54:** 25–33.
22. Lavie CJ, Milani R. Benefits of cardiac rehabilitation in the elderly. *Chest* 2004; **126:** 1010–1012.
23. Ståhle A, Mattsson E, Rydén L, Unden A, Nordlander R. Improved physical fitness and quality of life following training of elderly patients after acute coronary events: A 1 year follow-up randomized controlled study. *Eur Heart J* 1999; **20:** 1475–1484.
24. Pasquali SK, Alexander KP, Peterson ED. Cardiac rehabilitation in the elderly. *Am Heart J* 2001; **142:** 748–755.
25. Naylor M, Brooten D, Jones R, Lavizzo-Mourey R, Mezey M, Pauly M. Comprehensive discharge planning for the hospitalized elderly: A randomized clinical trial. *Ann Intern Med* 1994; **120:** 999–1006.
26. Naylor MD, Brooten D, Campbell R, Jacobsen BS, Mezey MD, Pauly MV, et al. Comprehensive discharge planning and home follow-up of hospitalized elders: A randomized clinical trial. *JAMA* 1999; **281:** 613–620.
27. Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: Secondary prevention programs for patients with coronary artery disease. *Ann Intern Med* 2005; **143:** 659–672.