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ORIGINAL RESEARCH

Comparative Effectiveness of Interventional Therapy versus Exercise Rehabilitation in Stable Angina Patients with Severe Coronary Artery Stenosis

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Background: Management strategies for stable angina include pharmacotherapy, revascularization, and exercise-based cardiac rehabilitation (CR). The optimal treatment for stable angina patients with severe coronary artery stenosis remains unclear. This study aimed to compare interventional therapy with exercise rehabilitation in this population.
Methods: Fifty stable angina patients with severe coronary stenosis who underwent stent implantation were included in the optimal medical therapy (OMT) plus percutaneous coronary intervention (PCI) group, and 50 patients who did not undergo interventional treatment were included in OMT plus CR group receiving exercise rehabilitation guidance for one year. Cardiovascular composite endpoint events, cardiopulmonary fitness, and quality of life scale scores were assessed after one year.
Results: No significant difference in incidence of cardiovascular composite endpoint events was observed between OMT plus PCI group with OMT plus CR group (20.0% vs 14.6%) after one year. Cardiopulmonary fitness represented as peak VO_2 (19.2±3.5 vs 17.6 ±3.2 mL/kg/min), peak load (120±19 vs 108±20 W), and AT (13.5±1.5 vs 12.1±1.3 mL/kg/min) were significantly higher in the rehabilitation group than the intervention group after one year. Both groups showed improvement in their quality of life, but the rehabilitation group improved in more scales.
Conclusion: Interventional therapy did not reduce cardiovascular events compared to exercise-based rehabilitation in stable angina patients with severe coronary artery stenosis, but the rehabilitation can improve cardiovascular fitness and quality of life more.
Keywords: cardiac rehabilitation, stable angina, percutaneous coronary intervention, cardiopulmonary fitness

Introduction

Coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide, posing a significant burden on healthcare systems and individuals alike.[1] Among its manifestations, stable angina pectoris, characterized by episodic chest discomfort or pressure typically triggered by exertion or emotional stress, affects millions of individuals globally.[2]

Current guidelines recommend a multifaceted approach for the management of stable angina, including pharmacotherapy, exercise-based cardiac rehabilitation (CR), and in select cases, revascularization strategies such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).[3] The ISCHEMIA trial did not find evidence that an initial invasive strategy, as compared with an initial conservative strategy, reduced the risk of ischemic

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cardiovascular events or death from any cause among patients with stable coronary disease and moderate or severe ischemia.[4] Sang-Ho Jo et al found that PCI plus optimal medical therapy (OMT) was associated with higher rate of primary endpoint of myocardial infarction, stroke, cardiac death as compared with OMT alone in patients with pure stable angina.[5] However, for stable angina patients with severe coronary artery stenosis, the optimal treatment strategy remains a matter of debate.

This study aims to address this gap in knowledge by comparing two distinct treatment strategies for stable angina patients with severe coronary artery stenosis: OMT combined with interventional therapy versus OMT with exercise-based cardiac rehabilitation. Specifically, we seek to evaluate differences in cardiovascular outcomes, including angina recurrence, acute myocardial infarction, and cardiovascular mortality, between these two treatment arms. Additionally, we aim to assess changes in cardiorespiratory fitness and quality of life among participants in both groups before and after the intervention period.

Methods

Study Group

Stable angina patients with severe coronary stenosis at our hospital from September 2020 to March 2023 were selected. Patients who underwent interventional therapy were included in the OMT plus PCI group without exercise rehabilitation guidance. Medical treatment for coronary artery disease followed the 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guidelines for the management of patients with chronic coronary artery disease.[6] Patients who did not undergo interventional therapy and agreed to exercise rehabilitation were included in the OMT plus CR group. They received exercise rehabilitation guidance for one year according to the exercise prescription as follows: exercising for 30 minutes 3–4 times/week at home with moderate intensity such as jogging, brisk walking, aerobic exercise, and swimming with heart rate controlled at anaerobic levels. Supervision and encouragement of exercise rehabilitation were conducted regularly for patients in the rehabilitation group. Patients with poor compliance or who discontinued rehabilitation during follow-up were considered to have withdrawn.

Inclusion and Exclusion Criteria

Inclusion criteria: (1) Age ≥ 18 years old; (2) Clinical diagnosis of stable angina; (3) Coronary angiography indicating severe coronary stenosis which was defined as a narrowing of more than 75% in the lumen of any one or more of the left anterior descending artery, left circumflex artery, or right coronary artery, regardless of whether the stenosis is located in the proximal or distal segment; (4) Completion of cardiopulmonary exercise testing. Exclusion criteria: (1) Left main coronary artery stenosis; (2) Acute coronary syndrome; (3) Uncontrolled malignant arrhythmias; (4) Chronic obstructive pulmonary disease and respiratory failure; (5) Bone or joint diseases severely affecting exercise; (6) Mental illness such as schizophrenia, mania, paranoia, anxiety and depression.

Parameters Assessed and Assessment Methods

Baseline characteristics of all patients were collected, including general information, comorbidities, medications, coronary angiography results, laboratory testing, cardiac structure and function, cardiopulmonary fitness indicators (peak VO_2, peak load, and anaerobic threshold), and quality of life scores. Quality of life was assessed by 36-Item Short Form Survey (SF-36)[7] which contained physical and mental component scales. Definition of comorbidities such as hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, atrial fibrillation, chronic heart failure, and chronic obstructive pulmonary disease followed the 9th edition of "Internal Medicine" published by People's Health Press.[8] Cerebrovascular accident was defined as cerebral infarction and cerebral hemorrhage.

Cardiopulmonary exercise testing (CPET) was performed to assess cardiopulmonary fitness using the Master Screen-CPX cardiopulmonary exercise testing system (JAEGER, Germany), with a ramp protocol and cycling mode.[9] Electrocardiography, blood pressure, and cardiopulmonary function-related indicators were monitored during exercise, which included warm-up, preparation, exercise, and rest stages. Exercise termination criteria and criteria for a positive cardiopulmonary exercise test were referenced from the Chinese expert consensus on standardized clinical application of cardiopulmonary exercise testing.[10] CPET was conducted by a professional cardiac rehabilitation team (comprising three physicians and one therapist), and no major cardiovascular adverse events occurred in any patient during testing.

Coronary angiography was performed using the FD20 angiography system (PHILIPS), conducted by the cardiology catheterization team, with imaging of the left and right coronary arteries and multiple projections.[11] Quantitative coronary angiography (QCA) software was used to determine the degree of coronary artery stenosis.[12]

One-year follow-up was conducted to compare the incidence of cardiovascular composite endpoint events between the two groups. Endpoint events included emergency visits or rehospitalizations due to angina, myocardial infarction, and cardiovascular death. Cardiopulmonary fitness (peak VO_2, peak load, and anaerobic threshold) and quality of life scores were reassessed for both groups at the 1-year follow-up.

Ethical Issues

This study was approved by the Ethics Committee of the affiliated Taizhou People's Hospital of Nanjing Medical University (KT 2020–073-01) which complied with the Declaration of Helsinki. All participants voluntarily joined the study and signed informed consent forms.

Statistical Analysis

The sample size was estimated using the EZR statistical software (The R Foundation, Ames, Iowa, United States), based on a significance level of 0.05 and a power of 0.80. Considering the loss of visits, the sample size for each group was set to 50. Continuous data are presented as mean ± standard deviation (SD). Baseline characteristics of patients and the incidence of cardiovascular endpoint events were analyzed using Student's *t*-test or Fisher's exact test, as appropriate. A two-way analysis of variance (ANOVA) was employed to compare parameters for exercise capacity and quality of life (QoL) measured at baseline and follow-up between the groups. If the F ratio was found to be significant, a Bonferroni post-hoc test was conducted, and statistical significance was set at $P < 0.05$. All statistical analyses were performed using SPSS 19.0 for Windows (SPSS Statistics).

Results

From September 2020 to March 2023, a total of 100 patients with coronary artery stenosis greater than 75% based on angiographic results at our center were initially selected for inclusion in this study. Among them, 50 patients who underwent stent implantation and 50 patients who did not undergo interventional treatment but agreed to participate in exercise rehabilitation were included, representing the OMT plus PCI and OMT plus CR groups, respectively. Two patients in the rehabilitation group dropped out of the study due to discontinuation of exercise rehabilitation. Baseline characteristics of the patients are summarized in Table 1, and no significant differences were observed between the two groups except the use of aspirin. The main reasons for non-intervention included patient refusal, inability to open chronic occlusions, and technical challenges such as vessel tortuosity or small vessel size, precluding stent implantation.

After 1 year of follow-up, a total of 10 patients in the intervention group experienced cardiovascular composite endpoint events. Among them, 7 patients were admitted to the emergency department or readmitted due to angina, 3 patients experienced myocardial infarction, and no patient suffered cardiovascular death. In the rehabilitation group, 7 patients experienced cardiovascular composite endpoint events. Specifically, 5 patients were admitted to the emergency department or readmitted due to angina, 2 patient experienced myocardial infarction, and no patient suffered cardiovascular death. There was no statistically significant difference in the incidence of cardiovascular composite endpoint events (20.0% vs 14.6%, P = 0.479) between the two groups during the 1-year follow-up, nor the emergency or readmission due to angina (14.0% vs 10.4%, P = 0.760) and myocardial infarction (6.0% vs 4.2%, P = 1.000), as shown in Figure 1.

The changes in cardiopulmonary fitness between baseline and follow-up for both groups are illustrated in Figure 2. Significant interactions were observed between the groups from follow-up to baseline in peak VO_2, peak load, and anaerobic threshold (AT) (P = 0.004, P = 0.034, and P <0.001, respectively). At the follow-up, in the OMT plus CR group, the peak VO_2 (19.2±3.5 vs 17.6±3.2 mL/kg/min), peak load (120±19 vs 108±20 W), and AT (13.5±1.5 vs 12.1±1.3 mL/kg/min) were higher compared to the OMT plus PCI group (all P < 0.05). Specifically, in the rehabilitation group, there were significant increases

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Table 1 Comparison of Baseline Characteristics Between Two Groups

	OMT + PCI (n= 50)	OMT + CR (n= 48)	P
Male sex [n (%)]	28 (56.0)	26 (54.2)	0.855
Age, yr	64 ± 11	65 ± 9	0.624
Body mass index, kg/m^2	23.1 ± 3.7	23.8 ± 4.1	0.377
Current smoking [n (%)]	21 (42.0)	19 (39.6)	0.808
Comorbidities [n (%)]			
Hypertension	35 (70.0)	30 (62.5)	0.432
Diabetes mellitus	10 (20.0)	12 (25.0)	0.553
Dyslipidemia	18 (36.0)	20 (41.7)	0.565
Chronic kidney disease	7 (14.0)	6 (12.5)	0.827
Atrial fibrillation	8 (16.0)	6 (12.5)	0.621
Chronic heart failure	7 (14.0)	6 (12.5)	0.827
COPD	5 (10.0)	3 (6.3)	0.498
Cerebrovascular accident	6 (12.0)	4 (8.3)	0.549
Medications [n (%)]			
Aspirin	50 (100.0)	30 (62.5)	<0.001
Clopidogrel	35 (70.0)	36 (75.0)	0.580
Ticagrelor	15 (30.0)	7 (14.6)	0.067
Statin	50 (100.0)	48 (100.0)	–
Beta-blocker	44 (88.0)	39 (81.3)	0.354
ARB or ACEI	26 (52.0)	23 (47.9)	0.686
ARNI	13 (26.0)	14 (29.2)	0.726
SGLT-2i	16 (32.0)	18 (37.5)	0.567
Nitrates	11 (22.0)	13 (27.1)	0.559
Coronary angiography (n)			
Single-vessel/Multi-vessel	28/22	25/23	0.697
Proximal/Middle/Distal	18/13/19	10/15/23	0.250
Stenosis of 75–80%/81–90%/91–100%	16/25/9	22/19/7	0.372
Laboratory testing			
Triglyceride, mmol/L	2.1 ± 0.7	2.3 ± 0.9	0.221
LDL-C, mmol/L	3.57 ± 0.9	3.69 ± 0.8	0.488
FBG, mmol/L	6.8 ± 1.6	7.3 ± 1.5	0.144
hs-CRP, mg/L	3.8 ± 1.7	4.3 ± 1.8	0.161
NT-proBNP, ng/L	405 ± 78	387 ± 63	0.213
Echocardiography			
LVEF, %	61.2 ± 5.1	59.6 ± 4.4	0.100
LVDd, mm	46.3 ± 4.2	47.7 ± 4.1	0.098
LVDs, mm	30.7 ± 4.1	32.1 ± 5.7	0.165
LAD, mm	37.7 ± 4.5	39.1 ± 4.5	0.127
Cardiopulmonary fitness			
Peak VO_2, mL/kg/min	17.4 ± 3.5	16.4 ±3.3	0.149
Peak load, W	106 ± 18	107 ± 21	0.800
Anaerobic threshold, mL/kg/min	11.7 ± 2.4	11.2 ± 2.2	0.286

Notes: Data are presented as mean ± SD or n (%).

Abbreviations: ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin 2 receptor blocker; ARNI, Angiotensin receptor neprilysin inhibitor; COPD, chronic obstructive pulmonary disease; CR, cardiac rehabilitation; OMT, optimal medical therapy; PCI, percutaneous coronary intervention; LAD, left atrial diameter; LVEF, left ventricular ejection fraction; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; LDL-C, low density lipoprotein cholesterol; FBG, fasting blood glucose; hs-CRP, hypersensitive C-reactive protein; SGLT-2i, sodium-glucose cotransporter-2 inhibitors.

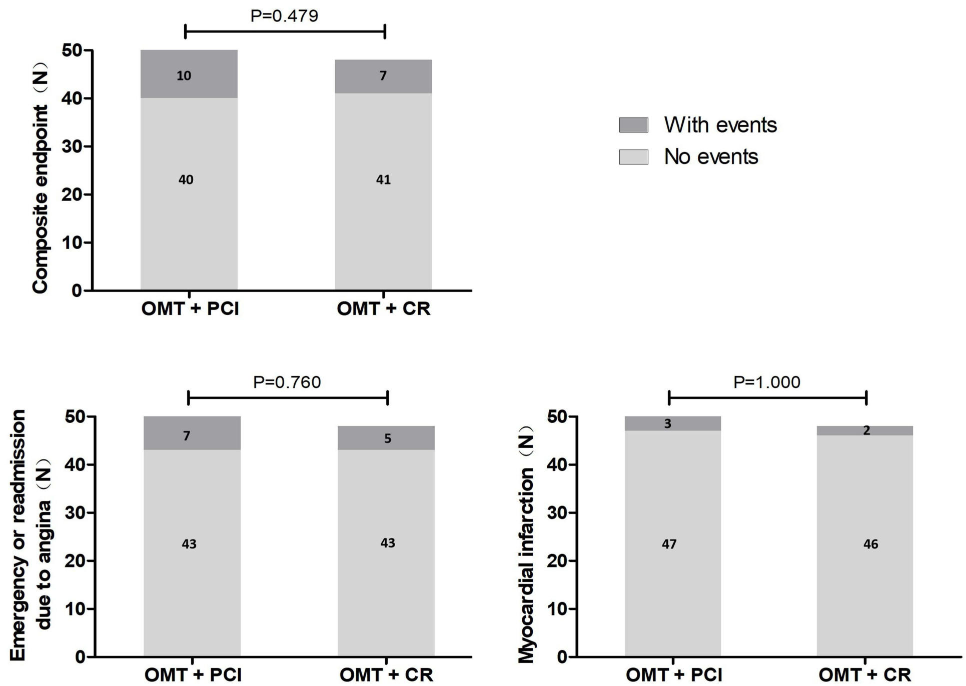

Figure 1 Comparison of cardiovascular events between two groups from baseline to follow-up.
Abbreviations: CR, cardiac rehabilitation; OMT, optimal medical therapy; PCI, percutaneous coronary intervention.

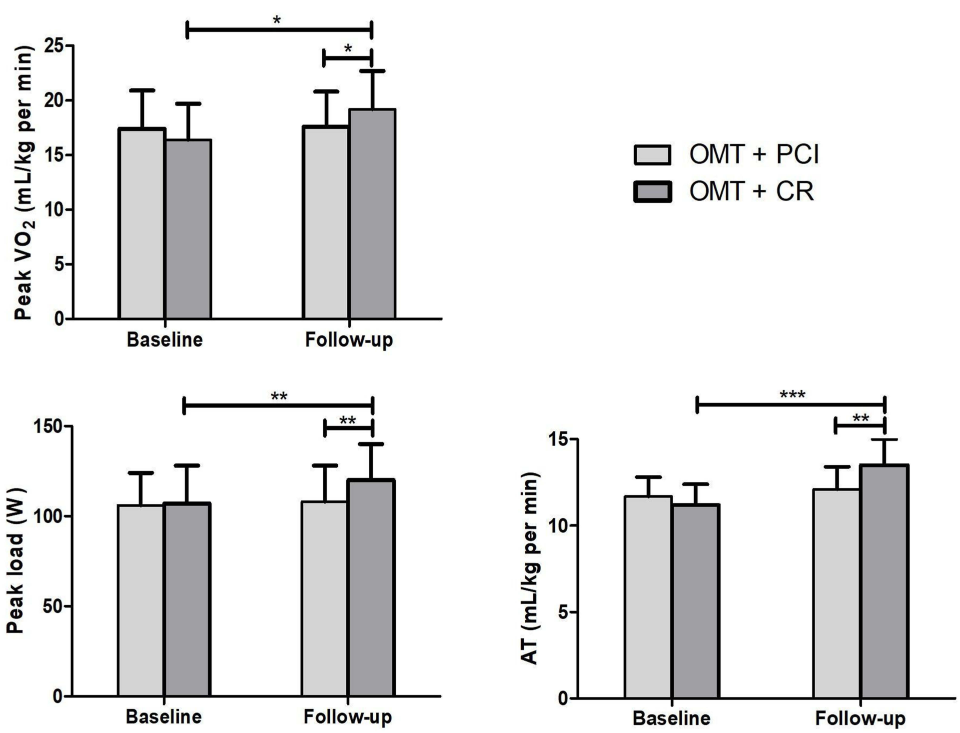

Figure 2 Comparison of cardiopulmonary fitness between two groups from baseline to follow-up.
Notes: *, P<0.05; **, P<0.01; ***, P<0.001.
Abbreviations: AT, anaerobic threshold; CR, cardiac rehabilitation; OMT, optimal medical therapy; PCI, percutaneous coronary intervention; VO_2, oxygen uptake.

Table 2 Comparison of Quality of Life Between Two Groups

	OMT + PCI (n= 50)		OMT + CR (n= 48)		P of Interaction[d]
	Baseline	Follow-Up	Baseline	Follow-Up	
Bodily pain index	78.1 ± 7.4	82.4 ± 6.3[b]	72.4 ± 5.2	82.1 ± 6.5[c]	0.004
General health perception	65.3 ± 4.3	64.6 ± 4.3	61.7 ± 4.6	70.2 ± 6.2[c]	<0.001
Mental health index	68.1 ± 4.2	71.2 ± 5.2[a]	68.2 ± 6.3	82.1 ± 6.4[c]	<0.001
Physical functioning index	81.3 ± 6.3	82.6 ± 5.2	80.1 ± 5.2	86.7 ± 4.8[c]	<0.001
Role emotional index	65.3 ± 6.3	73.2 ± 5.3[c]	67.3 ± 5.2	82.5 ± 6.2[c]	<0.001
Role physical index	52.3 ± 5.4	53.8 ± 4.7	49.3 ± 4.2	67.3 ± 7.1[c]	<0.001
Social functioning index	76.4 ± 6.3	82.2 ± 6.5[c]	74.5 ± 6.3	86.5 ± 6.7[c]	<0.001
Vitality index	50.5 ± 5.3	53.4 ± 5.6[a]	52.4 ± 5.6	64.2 ± 6.5[c]	<0.001
Physical Component Scale	44.5 ± 5.1	45.3 ± 5.8	46.5 ± 4.7	52.9 ± 4.1[c]	<0.001
Mental Component Scale	46.7 ± 4.5	47.3 ± 5.4	45.4 ± 5.3	52.3 ± 5.4[c]	<0.001

Notes: Data are presented as mean ± SD. Change from follow-up to baseline in each group: a, P < 0.05; b, P < 0.01; c, P < 0.001; d, P of interaction between groups and time.
Abbreviations: CR, cardiac rehabilitation; OMT, optimal medical therapy; PCI, percutaneous coronary intervention.

after the study period in peak VO_2 (19.2±3.5 vs 16.4±3.3 mL/kg/min), peak load (120±19 vs 107±21 W), and AT (13.5±1.5 vs 11.2±2.2 mL/kg/min) compared to baseline (all P < 0.05).

The effect of rehabilitation on quality of life (QoL) is detailed in Table 2. All QoL scales in the cardiac rehabilitation group showed significant improvement at follow-up compared to baseline (all P < 0.05). In contrast, improvements were observed only in the bodily pain index, mental health index, role emotional index, social functioning index, and vitality index in the OMT plus PCI group.

Discussion

The findings of this study shed light on the optimal management strategy for stable angina patients with severe coronary artery stenosis, providing valuable insights into the comparative effectiveness of interventional therapy versus exercise-based cardiac rehabilitation based on optimized medical treatment.

Contrary to initial expectations, our results indicate that among stable angina patients with severe coronary artery stenosis, adjunctive interventional therapy following optimization of medical treatment does not confer a reduction in cardiovascular endpoint events compared to exercise-based cardiac rehabilitation. This unexpected outcome challenges conventional wisdom regarding the superiority of revascularization strategies in this patient population.[13] It prompts a reevaluation of treatment paradigms and underscores the importance of evidence-based medicine in guiding clinical decision-making.

One possible explanation for the lack of cardiovascular benefit associated with interventional therapy in our study cohort could be attributed to the high efficacy of contemporary pharmacological regimens in achieving symptom control and risk factor modification. Optimal medical therapy, including antiplatelet agents, beta-blockers, statins, and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, has been shown to significantly reduce ischemic events and improve outcomes in stable angina patients.[14] Furthermore, our findings highlight the potential drawbacks of interventional therapy in terms of its impact on cardiorespiratory fitness and quality of life compared to exercise-based cardiac rehabilitation. While revascularization procedures may alleviate ischemic symptoms by restoring coronary blood flow, they do not necessarily address the underlying physiological deconditioning and functional impairment characteristic of stable angina patients. In contrast, exercise-based cardiac rehabilitation offers a comprehensive approach to cardiovascular health, promoting physical conditioning, symptom relief, and psychosocial well-being through structured exercise training, education, and counseling.[15]

Cardiac rehabilitation plays a pivotal role in improving the prognosis of patients with coronary heart disease (CHD). Numerous studies have demonstrated significant benefits in terms of both morbidity and mortality reduction following participation in cardiac rehabilitation programs. A meta-analysis by Anderson et al encompassing 63 randomized controlled trials concluded that cardiac rehabilitation reduces all-cause mortality by 26% and cardiovascular mortality by 31% in patients with CHD.[16] Moreover, it significantly decreases the risk of hospital readmissions due to cardiac causes. A study by Keteyian et al observed a substantial increase in VO_2 peak among participants undergoing cardiac rehabilitation, which correlated with enhanced functional capacity and reduced cardiovascular events.[17] Additionally, improvements in other clinical parameters such as lipid profile, blood pressure control, and glycemic control have been consistently reported in the literature. A study by Taylor et al demonstrated significant reductions in LDL cholesterol and systolic blood pressure following participation in a cardiac rehabilitation program.[18] Furthermore, cardiac rehabilitation has been associated with enhanced psychological well-being and quality of life among CHD patients. Research by Oldridge et al indicated improvements in depression, anxiety, and overall health-related quality of life post-rehabilitation.[19]

It is important to acknowledge the limitations of our study, including its unblind and non-random design, relatively small sample size, and potential confounding factors such as patient adherence to prescribed interventions and variations in healthcare delivery. Future prospective, randomized controlled trials with larger cohorts and longer follow-up periods are warranted to validate our findings and elucidate the underlying mechanisms driving treatment outcomes in this patient population.

In conclusion, invasive interventional therapy did not reduce cardiovascular events compared to exercise-based rehabilitation in stable angina patients with severe coronary artery stenosis, but the rehabilitation can improve cardio-vascular fitness and quality of life more, which could offer tangible benefits in terms of cardiovascular health, functional capacity, and quality of life.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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