Angina Pectoris and Atherosclerotic Risk Factors in the Multisite Cardiac Lifestyle Intervention Program

Joanne Frattaroli, PhD, Gerdi Weidner, PhD*, Terri A. Merritt-Worden, MS, Steven Frenda, BA, and Dean Ornish, MD

Cardiovascular symptom relief is a major indicator for revascularization procedures. To examine the effects of intensive lifestyle modification on symptom relief, we investigated changes in angina pectoris, coronary risk factors, quality of life, and lifestyle behaviors in patients with stable coronary artery disease enrolled in the multisite cardiac lifestyle intervention program, an ongoing health insurance–covered lifestyle intervention conducted at 22 sites in the united states. Patients with coronary artery disease (nonsmokers; 757 men, 395 women; mean age 61 years) were asked to make changes in diet (10% calories from fat, plant based), engage in moderate exercise (3 hours/week), and practice stress management (1 hour/day). At baseline, 108 patients (43% women) reported mild angina and 174 patients (37% women) reported limiting angina. By 12 weeks, 74% of these patients were angina free, and an additional 9% moved from limiting to mild angina. This improvement in angina was significant for patients with mild and limiting angina at baseline regardless of gender (p <0.01). Significant improvements in cardiac risk factors, quality of life, and lifestyle behaviors were observed, and patients with angina who became angina free by 12 weeks showed the greatest improvements in exercise capacity, depression, and health-related quality of life (p <0.05). In conclusion, the observed improvements in angina in patients making intensive lifestyle changes could drastically reduce their need for revascularization procedures. **(Am J Cardiol 2008;101:911–918)**

Although the prognostic significance of angina pectoris in women was questioned,[1] a recent large-scale population study found that women aged <75 years with stable angina pectoris had higher 4-year cardiac mortality rates than their male counterparts.[2] It is important to examine angina reduction in both men and women who are making comprehensive lifestyle changes. In addition, it is unknown whether patients with limiting/severe angina show benefits from making lifestyle changes similar to those with mild angina. We examined angina symptoms, coronary risk factors, quality of life, and lifestyle behaviors in the Multisite Cardiac Lifestyle Intervention Program during a 12-week period.

Methods

The present study consisted of 1,152 patients with coronary artery disease (CAD; 757 men, 395 women) who enrolled in the Multisite Cardiac Lifestyle Intervention Program from September 1998 to June 2006. The Multisite Cardiac Lifestyle Intervention Program is an ongoing comprehensive lifestyle change program for primary and secondary prevention of CAD administered by insurance companies. All patients were individually prescribed exercise levels (typically walking) according to their baseline treadmill test results. Target training heart rates were calculated using the Karvonen formula at intensities of 45% to 80% of maximal heart rate achieved on the exercise test. If ischemia occurred, the upper training heart rate was limited to 10 beats/min lower than the heart rate at which 1-mm ST-segment depression was documented on the electrocardiogram. Patients were also trained to identify exertion levels using the Borg rate of perceived exertion scale, with intensity goals of 11 to 14 (fairly light to somewhat hard). Patients were asked to exercise for a minimum of 3 hours/week and spend a minimum of 30 minutes/session exercising within their target heart rates. In addition, patients were encouraged to eat a very low-fat plant-based diet, engage in strength-training activities at least twice per week, practice stress management for 1 hour/day, and attend group support sessions for 2 hours/week for 12 weeks (for details, see[9]). This study was approved by each site's institutional review board, and all patients gave informed consent.

Patients were eligible for the program if CAD had been diagnosed by a physician. CAD was defined as 1 of the following: (1) ischemia documented using noninvasive testing, such as exercise testing, nuclear imaging, echocardiogram, or other tests clearly showing ischemia; (2) cardiac catheterization showing CAD; (3) a history of percutaneous coronary intervention, coronary bypass surgery, or myocardial infarction; or (4) eligibility for percutaneous coronary intervention or coronary bypass surgery. Primary exclusion

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*Corresponding author: 415-332-2525; Fax: 415-332-5730.
E-mail address: gerdi.weidner@pmri.org (G. Weidner).

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Table 1
Patient characteristics by angina pectoris group and gender at baseline

Variable	No Angina (class 0) at Baseline		Angina With Strenuous Exercise (class I) at Baseline		Limiting Angina (class II–IV) at Baseline		Sex p Value	Group p Value	Sex-by-Group p Value
	Men (n = 585)	Women (n = 285)	Men (n = 62)	Women (n = 46)	Men (n = 110)	Women (n = 64)			
Age	60.4 ± 8.8	61.7 ± 9.8	56.8 ± 10.5	58.7 ± 9.6	59.5 ± 10.6	60.4 ± 9.4	0.66	0.09	0.50
Education (college degree)	280 (51%)	80 (30%)	29 (52%)	13 (30%)	49 (48%)	17 (28%)	0.01*	0.69	0.88
Married or cohabitating	519 (89%)	172 (60%)	55 (89%)	28 (62%)	96 (87%)	42 (67%)	0.01*	0.89	0.30
Ethnicity (Caucasian)	544 (94%)	270 (95%)	56 (90%)	42 (91%)	104 (96%)	59 (95%)	0.59	0.18	0.49
Previous cigarette smoker	260 (50%)	106 (42%)	26 (51%)	16 (44%)	51 (57%)	19 (39%)	0.01*	0.72	0.28
Diabetes mellitus	144 (25%)	93 (33%)	19 (31%)	14 (30%)	29 (27%)	21 (33%)	0.01*	0.73	0.57
Systematic hypertension[†]	255 (44%)	133 (47%)	25 (40%)	18 (39%)	51 (46%)	23 (36%)	0.95	0.58	0.12
Hyperlipidemia[‡]	409 (71%)	180 (65%)	39 (63%)	28 (61%)	77 (71%)	39 (61%)	0.03*	0.39	0.47
Previous myocardial infarction	138 (46%)	61 (43%)	15 (50%)	10 (42%)	21 (47%)	13 (50%)	0.57	0.91	0.43
Previous percutaneous coronary intervention	336 (61%)	176 (65%)	41 (72%)	28 (62%)	79 (74%)	36 (59%)	0.89	0.20	0.02[§]
Previous coronary bypass	260 (49%)	94 (37%)	35 (64%)	12 (32%)	59 (59%)	15 (30%)	0.01*	0.34	0.08
Angina frequency (times/wk)							0.39	0.01[‖]	0.24
1–5	—	—	52 (84%)	38 (83%)	51 (46%)	33 (52%)			
6–10	—	—	5 (8%)	5 (11%)	20 (18%)	14 (22%)			
11–20	—	—	3 (5%)	1 (2%)	14 (13%)	8 (12%)			
>20 with exercise only	—	—	0 (0%)	0 (0%)	9 (8%)	4 (6%)			
>20 with exercise and at rest	—	—	1 (2%)	1 (2%)	6 (5%)	2 (3%)			
Constantly at rest or with exercise	—	—	1 (2%)	1 (2%)	10 (9%)	3 (5%)			
Nitrate use	81 (16%)	49 (20%)	20 (39%)	14 (39%)	52 (58%)	24 (49%)	0.34	0.01[¶]	0.11
β-Blocker use	351 (68%)	155 (62%)	36 (71%)	24 (67%)	64 (72%)	35 (71%)	0.14	0.44	0.60
ACE-inhibitor use	297 (40%)	93 (38%)	22 (43%)	18 (50%)	40 (45%)	17 (35%)	0.39	0.47	0.21
Lipid-lowering use	419 (29%)	203 (82%)	41 (80%)	27 (75%)	76 (85%)	42 (86%)	0.93	0.32	0.66
Anticoagulant use	432 (83%)	196 (79%)	41 (80%)	29 (80%)	76 (86%)	36 (73%)	0.05*	0.96	0.24
Body mass index (kg/m^2)	30.6 ± 5.5	31.6 ± 7.0	30.5 ± 6.0	32.3 ± 7.9	30.2 ± 4.9	32.5 ± 7.3	0.01*	0.84	0.42
Functional capacity (METs)	9.8 ± 3.1	7.5 ± 2.4	9.4 ± 2.9	7.3 ± 2.1	8.3 ± 2.8	7.0 ± 2.2	0.01*	0.01[¶]	0.15
Systolic blood pressure (mm Hg)	131 ± 18	132 ± 17	129 ± 18	128 ± 12	132 ± 17	128 ± 18	0.28	0.19	0.38
Diastolic blood pressure (mm Hg)	78 ± 11	77 ± 10	76 ± 11	77 ± 8	76 ± 10	74 ± 9	0.42	0.09	0.58
Total cholesterol (mg/dl)	167 ± 38	193 ± 47	165 ± 48	186 ± 43	161 ± 39	191 ± 49	0.01*	0.39	0.71
HDL cholesterol (mg/dl)	40 ± 11	49 ± 13	39 ± 11	50 ± 12	38 ± 11	50 ± 14	0.01*	0.88	0.23
LDL cholesterol (mg/dl)	94 ± 32	107 ± 39	96 ± 43	106 ± 36	87 ± 28	105 ± 34	0.01*	0.31	0.62
Triglycerides (mg/dl)	170 ± 106	194 ± 177	153 ± 84	147 ± 72	181 ± 119	178 ± 108	0.64	0.05	0.26
Total/HDL cholesterol ratio	4.4 ± 1.5	4.2 ± 1.5	4.5 ± 1.7	3.9 ± 1.3	4.4 ± 1.4	4.0 ± 1.3	0.01*	0.57	0.38
Hemoglobin A1c (%)[#]	7.1 ± 1.4	7.8 ± 1.8	7.0 ± 1.4	6.9 ± 1.2	7.9 ± 1.9	8.5 ± 2.2	0.16	0.01**	0.40
Depression (CES-D)	9.9 ± 8.1	12.6 ± 9.7	13.1 ± 8.5	13.9 ± 10.2	13.4 ± 8.9	15.3 ± 10.0	0.02*	0.01[††]	0.56
Hostility (Cook-Medley)	8.7 ± 4.9	7.1 ± 4.3	10.3 ± 4.9	6.2 ± 4.2	8.9 ± 4.7	8.3 ± 4.7	0.01*	0.28	0.01[‡‡]
Physical Component Score (MOS SF-36)	44.0 ± 10.6	40.4 ± 11.6	38.7 ± 10.9	39.7 ± 10.5	37.5 ± 11.4	33.5 ± 11.13	0.02*	0.01[††]	0.13

Table 1
(*continued*)

Variable	No Angina (class 0) at Baseline		Angina With Strenuous Exercise (class I) at Baseline		Limiting Angina (class II–IV) at Baseline		Sex p Value	Group p Value	Sex-by-Group p Value
	Men (n = 585)	Women (n = 285)	Men (n = 62)	Women (n = 46)	Men (n = 110)	Women (n = 64)			
Mental Component Score (MOS SF-36)	46.5 ± 14.3	44.8 ± 14.3	44.0 ± 14.4	45.7 ± 14.7	41.2 ± 15.6	43.3 ± 15.5	0.59	0.03¶	0.22
Dietary fat intake (% total calories)	24.8 ± 11.4	26.6 ± 10.8	25.5 ± 10.6	25.3 ± 10.7	22.3 ± 11.6	25.3 ± 11.9	0.13	0.17	0.56
Exercise (min/wk)	120.0 ± 138.0	75.4 ± 86.8	96.5 ± 88.2	82.9 ± 101.3	106.7 ± 121.6	70.0 ± 104.9	0.01*	0.59	0.46
Stress management (min/wk)	19.7 ± 69.1	25.4 ± 73.5	9.4 ± 32.9	32.3 ± 98.9	25.5 ± 73.9	19.9 ± 56.9	0.21	0.97	0.27

Data presented as mean ± SD for continuous variables and frequency (percent) for dichotomous variables.

* Overall, men were more likely to be married, be employed, have a history of tobacco use, have hyperlipidemia, have undergone a coronary artery bypass graft, have higher exercise capacity, have higher total/HDL cholesterol ratio, have greater hostility, have higher SF-36 Physical Component Summary scores, and exercise more, whereas women were significantly more likely to have diabetes mellitus, have higher body mass index, have higher total cholesterol, have higher HDL and LDL cholesterol, have higher hemoglobin A1c, consumer a higher fat diet, and practice more stress management.

† Systematic hypertension defined as blood pressure >140/90 mm Hg or >130/80 mm Hg for patients with diabetes.[27]

‡ Hyperlipidemia defined as LDL cholesterol ≥100 mg/dl, HDL cholesterol ≤40 mg/dl, or triglycerides ≥150 mg/dl.[28]

§ Men were more likely than women to have undergone previous percutaneous coronary intervention in patients who had limiting angina at baseline, but this gender difference was not found among patients who had class I or no angina at baseline.

‖ Overall, patients with class I angina at baseline were more likely to experience angina 1 to 5 times/week, whereas patients with limiting angina were more likely to experience angina at least 6 times/week.

¶ Overall, patients with limiting angina at baseline were more likely to use nitrates and have significantly poorer functional capacity and psychosocial-related quality of life than patients with no angina at baseline.

\# This analysis included patients with diabetes only.

** Overall, patients with limiting angina at baseline had higher hemoglobin A1c than patients with class I or no angina at baseline.

†† Overall, patients with limiting or class I angina at baseline had higher depression and poorer health-related quality of life than patients with no angina at baseline.

‡‡ Men had higher hostility scores than women in patients with no or class I angina at baseline, but this gender difference was not found in patients who have limiting angina at baseline.

ACE = angiotensin-converting enzyme; CES-D = Center for Epidemiological Studies Depression Scale; HDL = high-density lipoprotein; LDL = low-density lipoprotein; MOS SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

Table 2
Number of patients by angina pectoris group at baseline and 3 months

	Angina Pectoris	Total	Angina Severity at 12 Weeks		
			None at 12 Weeks (Level 0)	Mild at 12 Weeks (Level I)	Limiting at 12 Weeks (Levels II–IV)
Angina Severity at Baseline	None at baseline (level 0)	538 men, 261 women	525 men, 250 women	9 men, 6 women	4 men, 5 women
	Mild at baseline (level I)	50 men, 40 women	38 men, 35 women	12 men, 4 women	0 men, 1 woman
	Limiting at baseline (level II–IV)	103 men, 55 women	73 men, 40 women	19 men, 4 women	11 men, 11 women
	Total	691 men, 356 women	636 men, 325 women	40 men, 14 women	15 men, 17 women

McNemar-Boker test, $p < 0.01$, with significant improvements in angina severity during the 12-week period. Twelve-week data for angina severity were missing for 66 men and 39 women (47 men and 24 women with no angina at baseline, 12 men and 6 women with mild angina at baseline, and 7 men and 9 women with limiting angina at baseline).

criteria included (1) ischemic left main CAD with an obstruction >50% and (2) significant (>70%) proximal left anterior descending artery and proximal left circumflex artery disease and an ejection fraction <50%. These patients were excluded because some evidence indicated that this small subset of patients may benefit from coronary bypass surgery.[3]

At baseline, demographic information, medical history, and currently prescribed medications were documented. At baseline and 12 weeks, patients reported the frequency and severity of their angina symptoms in the last 7 days. Angina severity was assessed using the Canadian Cardiovascular Society guidelines for grading angina: no angina (level 0); angina with strenuous, rapid, or prolonged exertion at work or recreation—ordinary physical activity does not cause angina, such as walking and climbing stairs (level I); slight limitations of ordinary activity—walking or stair climbing rapidly, walking uphill, in cold, in wind, under emotional stress, or only during the few hours after awakening (level II); marked limitation of ordinary physical activity—walking 1 to 2 blocks on the level and climbing 1 flight of stairs in normal conditions and at normal pace (level III); and inability to carry on any physical activity without discomfort, anginal syndrome may be present at rest (level IV).[4]

Height, weight, and blood pressure were measured by trained health professionals. Fasting blood samples were collected and analyzed for total, high-density lipoprotein, and low-density lipoprotein cholesterol; triglycerides; and glycated hemoglobin (for diabetic patients). Functional capacity was assessed using maximal treadmill or bicycle ergometry testing. In addition, a battery of instruments was administered to patients measuring depression,[5] hostility,[6] and quality of life.[7] Finally, patients completed assessments of exercise and stress management,[8,9] as well as 3-day food diaries.[10] Food diaries were analyzed by each study site using nationally recognized software (Food Processor; ESHA Research, Inc., Salem, Oregon) to assess the daily percentage of total calories from fat, daily milligrams of dietary cholesterol, and daily grams of dietary fiber. All exercise testing and all other risk-factor, quality-of-life, and lifestyle behavior measurements were made at baseline and 12 weeks (see[9] for more details).

Patients were categorized into 1 of the 3 angina groups according to their initial Canadian Cardiovascular Society level of no angina (level 0), mild angina (level I), and limiting angina (levels II to IV). This revised grouping was also used by other researchers.[11] Changes in angina were assessed using the McNemar-Boker test. Baseline group differences were tested using chi-square analyses and multiway frequency analyses (for categorical variables) and independent samples *t* tests and factorial analysis of variance (for continuous variables). Group effects, time effects, and group-by-time interactions for risk factors, quality of life, and/or lifestyle behaviors were tested using repeated-measures analysis of variance and Bonferroni adjustments.

Results

Baseline characteristics are listed in Table 1. Patients with limiting angina ($n = 174$) had poorer health (e.g., angina frequency, functional capacity) and poorer quality of life than those with mild ($n = 108$) or no angina ($n = 870$). Women (as a group) had significantly poorer functional capacity, health-related quality of life, and depression scores than men. Also, women with limiting angina were less likely than men with limiting angina to have undergone a previous percutaneous coronary intervention, and men with no or mild angina had higher hostility scores than women in these groups.

Follow-up data were available for 1,047 of 1,152 patients (91%). As listed in Table 2, at baseline, 799 (76%) of these patients had no angina, 90 (9%) had mild angina, and 158 (15%) had limiting angina. At 12 weeks, 186 patients (74%) with angina at baseline became angina free, and an additional 23 (9%) reduced their angina severity from limiting to mild. Twenty-four patients (3%) who were angina free at baseline reported symptoms of angina at 3 months. Overall, there was significantly more improvement in angina than worsening of angina ($p < 0.01$). There was no significant relation between gender and angina change (men and women improved equally) or between baseline angina severity and angina change (those with mild angina and limiting angina improved equally). (Categorizing "mild" angina as levels I and II and "limiting" angina as levels III and IV showed the same pattern of findings. That is, 27 of 42 patients [64%] with limiting angina and 159 of 206 patients [77%] with mild angina were symptom free by the end of 3 months, and there were no differences in gender or symptom severity.) During the 12 weeks of the intervention, 18 patients underwent a revascularization procedure. Removing data for these 18 patients from the analysis did not alter the findings.

Table 3
Mean values for quality of life, adherence, and risk factor scores at baseline and 12 weeks

Variable	Became Angina Free		Remained Angina Free		Angina Remained or Appeared	
	Men (n = 111)	Women (n = 75)	Men (n = 525)	Women (n = 250)	Men (n = 55)	Women (n = 31)
Risk factors Weight (lbs)*†‡						
Baseline	210.8 ± 43.7	186.4 ± 42.7	210.4 ± 40.3	181.9 ± 40.9	202.7 ± 43.2	186.6 ± 43.5
12 wk	198.2 ± 39.5	176.4 ± 40.1	197.8 ± 36.3	172.8 ± 38.3	192.2 ± 39.9	178.7 ± 41.9
Exercise capacity (METs)*†‡§‖						
Baseline	9.0 ± 2.9	7.2 ± 2.1	9.9 ± 3.1	7.6 ± 2.5	7.9 ± 2.7	7.3 ± 2.4
12 wk	11.2 ± 2.9	9.2 ± 2.5	11.6 ± 3.2	9.2 ± 2.6	9.5 ± 2.8	8.0 ± 2.7
Systolic blood pressure (mm Hg)†‡§						
Baseline	132 ± 17	128 ± 15	131 ± 18	132 ± 17	126 ± 18	127 ± 14
12 wk	119 ± 15	121 ± 12	120 ± 15	123 ± 16	115 ± 12	119 ± 17
Diastolic blood pressure (mm Hg)†‡§						
Baseline	77 ± 10	76 ± 9	77 ± 11	77 ± 10	75 ± 12	73 ± 9
12 wk	70 ± 10	71 ± 8	71 ± 9	71 ± 9	67 ± 9	69 ± 8
Total cholesterol (mg/dl)*†						
Baseline	163 ± 41	189 ± 42	166 ± 39	193 ± 48	159 ± 36	188 ± 41
12 wk	142 ± 38	170 ± 42	141 ± 33	173 ± 43	136 ± 27	166 ± 41
HDL cholesterol (mg/dl)*†‡						
Baseline	40 ± 11	51 ± 13	40 ± 11	49 ± 13	38 ± 11	49 ± 11
12 wk	35 ± 9	45 ± 12	36 ± 10	43 ± 11	35 ± 7	44 ± 10
LDL cholesterol (mg/dl)*†						
Baseline	91 ± 35	105 ± 31	94 ± 32	107 ± 40	86 ± 31	104 ± 32
12 wk	77 ± 31	92 ± 35	77 ± 27	94 ± 34	73 ± 24	89 ± 37
Triglycerides (mg/dl)*†						
Baseline	159 ± 84	161 ± 86	170 ± 108	1961 ± 187	180 ± 101	188 ± 111
12 wk	151 ± 66	166 ± 85	148 ± 78	185 ± 109	153 ± 76	175 ± 76
Total/HDL cholesterol ratio†‡						
Baseline	4.4 ± 1.5	3.9 ± 1.1	4.4 ± 1.6	4.2 ± 1.5	4.3 ± 1.1	4.0 ± 1.5
12 wk	4.2 ± 1.2	3.9 ± 1.0	4.1 ± 1.3	4.2 ± 1.4	4.0 ± 0.9	4.0 ± 1.1
Hemoglobin A1c (%)†#						
Baseline	7.2 ± 1.0	7.6 ± 1.9	7.1 ± 1.5	7.9 ± 1.7	7.9 ± 1.6	8.5 ± 1.9
12 wk	6.6 ± 0.8	6.8 ± 1.1	6.3 ± 0.9	7.7 ± 1.1	6.9 ± 1.5	7.9 ± 1.4
Depression (CES-D)†‡§‖						
Baseline	13.6 ± 9.0	13.5 ± 8.8	9.7 ± 8.1	12.8 ± 9.7	12.2 ± 7.9	13.9 ± 10.5
12 wk	7.2 ± 7.3	6.3 ± 6.9	6.4 ± 6.0	7.0 ± 6.3	9.2 ± 7.8	9.0 ± 8.1
Hostility (Cook-Medley)*†§						
Baseline	8.8 ± 4.4	6.7 ± 4.4	8.7 ± 4.9	7.3 ± 4.3	10.2 ± 5.5	8.5 ± 4.8
12 wk	7.2 ± 4.5	6.0 ± 4.5	7.2 ± 4.6	6.0 ± 4.0	8.7 ± 5.4	6.8 ± 5.0
Physical Component Summary score*†§‖						
Baseline	38.3 ± 11.2	35.9 ± 11.6	44.3 ± 10.5	40.3 ± 11.5	37.8 ± 10.5	38.1 ± 12.0
12 wk	45.8 ± 10.8	43.1 ± 10.9	49.4 ± 9.6	46.6 ± 10.2	41.2 ± 10.9	42.1 ± 10.9
Mental Component Summary score†**						
Baseline	42.7 ± 14.9	46.1 ± 14.2	46.9 ± 14.0	44.5 ± 14.3	44.4 ± 14.5	44.5 ± 15.0
12 wk	53.0 ± 11.9	52.6 ± 13.3	52.3 ± 11.8	53.1 ± 11.2	49.5 ± 14.0	52.2 ± 12.8
Dietary fat (% total calories)*†						
Baseline	24.7 ± 11.3	25.3 ± 11.4	25.1 ± 11.4	26.3 ± 10.6	21.0 ± 9.6	28.1 ± 9.1
12 wk	9.2 ± 2.9	9.7 ± 2.8	8.9 ± 2.5	9.4 ± 2.6	8.9 ± 2.3	10.4 ± 5.8
Dietary fiber (g/d)*†						
Baseline	25.6 ± 12.3	21.3 ± 10.3	26.1 ± 15.4	22.3 ± 14.2	25.3 ± 12.4	17.0 ± 7.4
12 wk	43.2 ± 16.3	33.3 ± 11.1	44.4 ± 18.0	35.4 ± 12.1	40.3 ± 12.6	32.7 ± 11.2
Dietary cholesterol (mg/d)†						
Baseline	180.9 ± 171.5	144.4 ± 133.6	194.5 ± 155.4	160.5 ± 155.4	135.6 ± 157.6	172.0 ± 100.7
12 wk	9.0 ± 14.5	8.6 ± 11.5	8.8 ± 13.9	11.9 ± 43.9	9.8 ± 12.3	12.8 ± 23.2
Exercise (min/wk)*†						
Baseline	100.7 ± 104.7	64.6 ± 98.6	120.0 ± 138.0	77.6 ± 86.5	116.5 ± 126.1	101.0 ± 122.2
12 wk	236.3 ± 128.1	211.3 ± 80.6	236.6 ± 93.3	211.6 ± 79.5	234.6 ± 99.3	228.9 ± 95.8

All baseline and 12-week measurements are listed in Table 3. Time effects for all variables were significant regardless of the baseline angina group. Patients with no, mild, or limiting angina at baseline improved on all coronary risk factors from baseline to 12 weeks (except for high-density lipoprotein cholesterol, which significantly decreased, as expected in the context of a low-fat diet).[12] Results are listed for all 3 severity categories combined.

Table 3
(*continued*)

Variable	Became Angina Free		Remained Angina Free		Angina Remained or Appeared	
	Men (n = 111)	Women (n = 75)	Men (n = 525)	Women (n = 250)	Men (n = 55)	Women (n = 31)
Stress management (min/wk)†						
Baseline	19.4 ± 67.3	27.0 ± 85.1	18.5 ± 66.7	26.2 ± 74.1	27.1 ± 77.5	15.0 ± 43.3
12 wk	371.3 ± 112.5	298.8 ± 92.5	379.2 ± 131.9	384.3 ± 114.0	385.4 ± 98.8	378.8 ± 129.2

* Significant gender effect. Overall, men were more likely to weigh more, have higher exercise capacity, have greater hostility, have higher SF-36 Physical Component Summary scores, consume a higher fiber diet, and exercise more, whereas women were significantly more likely to have higher total cholesterol, have higher HDL and LDL cholesterol, have higher triglycerides, and consume a higher fat diet (all $p < 0.001$). For all other gender effects, all $p > 0.07$.

† Significant time effect. All variables improved over time, except for HDL cholesterol, which decreased ($p < 0.01$).

‡ Significant gender-by-time interaction. Overall, men lost more weight ($p < 0.001$), showed greater improvements in exercise capacity ($p < 0.04$), and decreased their blood pressure ($p < 0.02$) and total/HDL cholesterol ratio ($p < 0.01$) more than women, whereas women decreased their cholesterol ($p < 0.02$) and depression scores ($p < 0.02$) more than men. For all other gender-by-time interactions, all $p > 0.05$.

§ Significant group effect. Overall, patients who remained angina free had the highest exercise capacity, followed by those who became angina free, followed by those whose angina remained or appeared ($p < 0.001$). Patients whose angina remained or appeared had lower diastolic blood pressure ($p < 0.01$) and higher hostility scores ($p < 0.05$) than patients who remained or became angina free, and they had lower systolic blood pressure ($p < 0.05$) than patients who remained angina free. Patients who remained angina free had lower depression scores ($p < 0.01$) and higher SF-36 Physical Component Summary scores ($p < 0.001$) than the other 2 groups. For all other group effects, all $p > 0.07$.

‖ Significant time-by-group interaction. Patients who became angina free showed greater improvements in exercise capacity than patients whose angina remained or appeared ($p < 0.01$), and their depression scores ($p < 0.01$) and SF-36 Physical Component Summary scores ($p < 0.05$) improved more than patients whose angina remained or appeared and patients who remained angina free. For all other time-by-group interactions, all $p > 0.06$.

\# This analysis includes patients with diabetes only.

** Significant gender-by-time-by-group interaction. For SF-36 Mental Component Summary scores, there was a group-by-time interaction for men (patients who became angina free showed greater improvement than those remained angina free; $p < 0.01$), but there was no group-by-time interaction with women (all 3 groups improve equally). For all other gender-by-time-by group interactions, all $p > 0.13$.

Abbreviations as in Table 1. SF-36 = 36-Item Short Form Health Survey.

Patients who became angina free evidenced the greatest improvements in exercise capacity, depression, and health-related quality of life compared with the other patients. For psychosocial-related quality of life, men (but not women) who became angina free showed greater improvements than men who remained angina free. It should be noted that the 25 patients with angina that worsened during the course of the 12 weeks reported similar diet, exercise, and stress management improvements as the other patients (not shown).

Sixty-six men and 39 women (9% of original sample) did not complete the 12-week follow-up. These patients had higher depression scores than those who completed the study ($p < 0.05$). There were no other statistically significant differences. When performing a worst-case scenario analysis in which these missing patients were assumed to show no change from baseline, all main effects for time (e.g., changes in angina, changes in risk factors) remained significant at $p < 0.05$.

Discussion

Significant improvements in angina were found during the 12-week period, with 74% of angina patients becoming angina free and an additional 9% moving from the limiting to mild angina category. Angina improvements in this multisite study with >1,000 patients were similar to those observed in smaller randomized controlled clinical trials evaluating the same lifestyle change program.[8,13] In addition, the observed decreases were similar to those reported in studies of coronary artery bypass graft or percutaneous coronary intervention.[14–17] Improvements in angina were significant regardless of gender and initial angina severity, with significant improvements in all subgroups. All patient groups improved in risk factors, quality of life, and lifestyle behaviors during the 12 weeks, with patients who became angina free showing the greatest improvements in exercise capacity, depression, and health-related quality of life. Although it was surprising that these patients did not also report greater improvements in lifestyle behaviors compared with the other 2 groups, it is conceivable that they improved in other aspects of health behaviors that were not measured by us (e.g., exercise intensity).

The finding that angina reduction was equally strong for patients with limiting angina as for patients with mild angina was particularly important because patients with limiting angina were more likely than those with mild angina to undergo percutaneous coronary intervention.[18] A recent comparison of optimal medical therapy (i.e., medications plus American Heart Association–recommended lifestyle changes) with percutaneous coronary intervention plus optimal medical therapy showed no significant difference in benefit with respect to mortality or cardiac-related events during a 5-year period.[14] Although angina symptoms decreased for patients in that study, angina reduction at 1 year (i.e., 66% angina free for percutaneous coronary intervention plus optimal medical therapy and 58% angina-free for optimal medical therapy) was still lower than angina reduction at 12 weeks for our angina patients (74% angina free). Given the dramatic decrease in angina symptoms observed in the present study, comprehensive changes in lifestyle may be a viable alternative to more conventional therapies, especially considering the questionable benefit of such procedures in patients with stable CAD.[19] In an earlier study of patients eligible to undergo revascularization but who instead opted for the lifestyle program used in the present study showed that almost 80% of patients were able to safely avoid invasive procedures for ≥3 years by making comprehensive lifestyle changes without increasing cardiac morbidity and mortality.[20] Interestingly, decreases in angina in the intervention group of that study were similar to those achieved using revascularization.[20]

One limitation of the present study was that angina symptoms were measured using self-report and did not include objective measures of myocardial ischemia. However, the Canadian Cardiovascular Society angina classification used in our study correlated highly with more objective measures (e.g., angiographic findings), showing its validity.[18] Also, improvements in objectively measured functional capacity were particularly strong for patients with angina that resolved by follow-up, further supporting the validity of this self-report measure. A second limitation is that patients willing to participate in a multicomponent comprehensive lifestyle program may represent a "unique" group of patients for whom results may not be generalizable to a wider population. However, characteristics of our patients were very similar to those of patients enrolled in more traditional cardiac interventions, at least with respect to medical variables (e.g., age, diabetes status, and total cholesterol).[21,22] Furthermore, the pattern of gender differences observed in our sample (e.g., men were more likely to have a history of tobacco use) were similar to those reported in the literature.[23] Finally, without a randomized control group, we cannot conclude that participation in the lifestyle program was directly responsible for the observed improvements in coronary risk and psychosocial factors. However, the efficacy of this lifestyle intervention was already shown in earlier randomized controlled trials.[8,13,24] The purpose of the present study was to compare the feasibility of this intervention for subgroups of patients (men vs women and patients with mild vs limiting angina). Our findings take on added significance considering the substantial economic burden of angina caused by the management of symptoms, lost productivity, and risk of myocardial infarction and other major cardiac events. It was estimated that direct health care costs of angina reach an average of $33,695 per person per year[25] and cost up to $1,051,302 per person during a lifetime.[26]

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1. DeVon HA, Johnson Zerwic J. Symptoms of acute coronary syndromes: are there gender differences? A review of the literature. *Heart Lung* 2002;31:235–245.
2. Hemingway H, McCallum A, Shipley M, Manderbacka K, Martikainen P, Keskimaki I. Incidence and prognostic implications of stable angina pectoris among women and men. *JAMA* 2006;22:1404–1411.
3. Caracciolo EA, Davis KB, Sopko G, Kaiser GC, Corley SD, Schaff H, Taylor HA, Chaitman BR. Comparison of surgical and medical group survival in patients with left main coronary artery disease. Long-term CASS experience. *Circulation* 1995;91:2325–2334.
4. Campeau L. Letter: Grading of angina pectoris. *Circulation* 1976;54:522–523.
5. Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1977;1:385–401.
6. Barefoot JC, Dodge KA, Peterson BL, Dahlstrom WG, Williams RB Jr. The Cook-Medley hostility scale: item content and ability to predict survival. *Psychosom Med* 1989;51:46–57.
7. Ware JE, Snow KK, Kosinski M, Gandek B. SF-36 Health Survey Manual and Interpretation Guide. Boston, MA: The Health Institute, New England Medical Center; 1993.
8. Ornish D, Sherwitz LW, Billings JH, Brown SE, Gould KL, Merritt TA. Intensive lifestyle changes for reversal of coronary heart disease. *JAMA* 1998;280:2001–2007.
9. Daubenmier JJ, Weidner G, Sumner M, Mendell N, Merritt-Worden T, Studley J, Ornish D. The contribution of changes in diet, exercise, and stress management to changes in coronary risk in women and men in the Multisite Cardiac Lifestyle Intervention Program. *Ann Behav Med* 2007;33:57–68.
10. Stuff JE, Garza C, Smith EO, Nichols BL, Montandon CM. A comparison of dietary methods in nutritional studies. *Am J Clin Nutr* 1983;37:300–306.
11. Lawson WE, Hui JCK, Lang G. Treatment benefit in the enhanced external counterpulsation consortium. *Cardiology* 2000;94:31–35.
12. Brinton EA, Eisenberg S, Breslow JL. A low-fat diet decreases high density lipoprotein (HDL) cholesterol by decreasing HDL apolipoprotein transport rates. *J Clin Invest* 1990;85:144–151.
13. Ornish D, Sherwitz LW, Doody RS, Kesten D, McLanahan SM, Brown SE, DePuey E, Sonnemaker R, Haynes C, Lester J, et al. Effects of stress management training and dietary changes in treating ischemic heart disease. *JAMA* 1983;249:54–59.
14. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, Knudtson M, Dada M, Casperson P, Harris CL, et al. Optimal medical therapy with or without percutaneous coronary intervention for stable coronary disease. *N Engl J Med* 2007;356:1503–1516.
15. Hasdai D, Lerman A, Grill DE, Rihal CS, Holmes DR. Medical therapy after successful percutaneous coronary revascularization. *Ann Intern Med* 1999;130:108–115.
16. Serruys PW, Ong ATL, van Herwerden LA, Sousa JE, Jatene A, Bonnier JJ, Schönberger JP, Buller N, Bonser R, Disco C, et al. Five-year outcomes after coronary stenting versus bypass surgery for the treatment of multivessel disease. *J Am Coll Cardiol* 2005;46:575–581.
17. RITA-2 Trial Participants. Coronary angioplasty versus medical therapy for angina: the Second Randomized Intervention Treatment of Angina (RITA-2). *Lancet* 1997;350:461–468.
18. Hemingway H, Fitzpatrick NK, Gnani S, Feder G, Walker N, Crook AM, Magee P, Timmis A. Prospective validity of measuring angina severity with Canadian Cardiovascular Society Class: the ACRE study. *Can J Cardiol* 2004;20:204–209.

19. Grace LA, Dudley A, Redberg RF. Cardiologists' use of percutaneous coronary interventions for stable coronary artery disease. *Arch Intern Med* 2007;167:1604–1609.
20. Ornish D. Avoiding revascularization with lifestyle changes: the Multicenter Lifestyle Demonstration Project. *Am J Cardiol* 1998; 82(suppl):72T–76T.
21. Todaro JF, Shen BJ, Niaura R, Tilkemier PL. Prevalence of depressive disorders in men and women enrolled in cardiac rehabilitation. *J Cardiopulm Rehabil* 2005;25:71–75.
22. Mercado N, Wijns W, Serruys PW, Sigwart U, Flather MD, Stables RH. One year outcomes of coronary artery bypass graft versus percutaneous coronary intervention with multiple stenting for multi-system disease: a meta-analysis of individual patient data from randomized clinical trials. *J Thorac Cardiovasc Surg* 2005;130:512–519.
23. Eastwood JA, Doering LV. Gender differences in coronary artery disease. *J Cardiovasc Nurs* 2005;20:340–351.
24. Pischke CR, Scherwitz L, Weidner G, Ornish D. Long term effects of lifestyle changes on well-being and cardiac variables among coronary heart disease patients. Health Psychology. 2008 In press.
25. Reynolds MW, Frame D, Cheye R, Rose ME, George S, Watson JB, Hlatky MA. A systematic review of the economic burden of chronic angina. *Am J Manag Care* 2004;10:347–357.
26. Shaw LJ, Bairey Merz CN, Pepine CJ, Reis SE, Bittner V, Kip KE, Kelsey SF, Olson M, Johnson BD, Mankad S, et al. Women's Ischemia Syndrome Evaluation (WISE) Investigators. The economic burden of angina in women with suspected ischemic heart disease: results from the National Institutes of Health–National Heart, Lung, and Blood Institute–sponsored Women's Ischemia Syndrome Evaluation. *Circulation* 2006;114:894–904.
27. Chobanian AV, Bakris GL, Black HR, Cushman WV, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report on the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003;42:1206–1252.
28. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) JAMA 2001;285:2486–2497.