Psychological and Quality-of-Life Outcomes from a Comprehensive Stress Reduction and Lifestyle Program in Patients with Coronary Artery Disease: Results of a Randomized Trial

Andreas Michalsen[a]   Paul Grossman[b]   Nils Lehmann[c]
Nicola T.M. Knoblauch[a]   Anna Paul[a]   Susanne Moebus[c]
Thomas Budde[d]   Gustav J. Dobos[a]

[a]Kliniken Essen-Mitte, Chair of Complementary and Integrative Medicine of the University Duisburg-Essen, Department of Internal Medicine V and Integrative Medicine, Essen, Germany;
[b]University Hospital Basel, Department of Psychosomatic & Internal Medicine, Basel, Switzerland;
[c]University of Duisburg-Essen, Institute for Medical Informatics, Biometry and Epidemiology, and
[d]Alfried Krupp Krankenhaus, Department of Cardiology, Essen, Germany

Key Words

Coronary artery disease · Emotional distress · Lifestyle modification · Quality of life · Randomized trial · Stress reduction · Gender

Abstract

Background: Stress reduction and comprehensive lifestyle modification programs have improved atherosclerosis and cardiac risk factors in earlier trials. Little is known about the impact of such programs on quality-of-life (QoL) and psychological outcomes. Given recent significant improvements in cardiac care, we evaluated the current benefit of stress reduction/lifestyle modification on QoL and emotional distress in patients with coronary artery disease (CAD). *Methods:* 101 patients (59.4 ± 8.6 years, 23 female) with CAD were randomized to a 1-year lifestyle/stress management program (n = 48) or written advice (n = 53). QoL and psychological outcomes were assessed with the SF-36, Beck Depression, Spielberger State/Trait Anxiety, Spielberger State/Trait Anger and Perceived Stress Inventories. Group repeated-measures analyses of variance were performed for all measures. *Results:* Adherence to the program was excellent (daily relaxation practice 39 ± 5 vs. 5 ± 8 min, respectively; p < 0.001). Both groups improved comparably in most dimensions of QoL, and significantly greater improvements for the lifestyle group were found for physical function and physical sum score (p = 0.046 and p = 0.045). Depression, anxiety, anger and perceived stress were reduced similarly in both groups. However, intervention × gender interaction effects revealed greater benefits among women in the lifestyle intervention vs. advice group for depression and anger (p = 0.025 and p = 0.040), but no effects for men. *Conclusions:* A comprehensive lifestyle modification and stress management program did not improve psychological outcomes in medically stable CAD patients. The program did appear to confer psychological benefits for women but not men. Further trials should investigate gender-related differences in coronary patient responses to behavioral interventions.

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There are no conflicts of interest related to the study for all authors.

Andreas Michalsen, MD
Kliniken Essen-Mitte
Am Deimelsberg 34a
DE–45276 Essen (Germany)
Tel. +49 201 8054002, Fax +49 201 8054005, E-Mail andreas.michalsen@uni-essen.de

Introduction

Psychological distress (e.g. depression, anxiety or anger) has been associated with increased mortality in patients with [1–3] and without coronary artery disease (CAD) [4, 5], and this appears to be independent of biological risk factors. Most recently, the INTERHEART study estimated an attributable risk of 33% for combined psychosocial factors to acute myocardial infarction [6]. A substantial proportion of patients in cardiac rehabilitation suffer from psychological distress [7], and depression and anxiety are related to increased symptom severity and functional impairment in patients with CAD [8]. A recent review examining the role of psychological factors in CAD concluded that current findings establish an imperative for enhancing behavioral treatments among CAD-prone individuals [9]. However, it is unclear whether coronary patients substantially benefit from existing behavioral treatments. Data from recent randomized trials that employed psychosocial therapies, e.g. cognitive behavioral therapy (CBT), have yielded mixed results with respect to reduction of cardiac events or psychological outcomes [10–13].

Comprehensive lifestyle programs combining stress management with dietary treatment or/and exercise have shown substantial benefits in earlier trials with coronary patients. Three angiographic trials, with one focusing on stress management, have demonstrated modest regression of coronary artery stenoses after 1–4 years of intensive lifestyle changes [14–17]. Several other lifestyle and stress-management trials have found clear beneficial effects on cardiac risk factors [18–21]. However, with one exception, these trials did not assess the impact of the intervention on quality of life (QoL) or psychological outcomes. Moreover, since standard medical cardiac care has changed dramatically in recent years with significant improvements through the widespread use of statins, angiotensin-converting enzyme (ACE) inhibitors and the introduction of coronary stents, existing data from earlier lifestyle and stress-management trials may not be generalizable or relevant to the current situation of coronary patients. Development of successful behavioral interventions that have impact on the psychosocial outcomes of coronary patients may be of particular significance given recent indications that interventions that fail to ameliorate distress also fail to lead to reduced mortality and morbidity of cardiovascular events [22].

The 'SAFE-LIFE' Essen Heart Program was a 1-year randomized controlled trial to evaluate the effectiveness of an optimized comprehensive lifestyle modification program that focused on stress management and relaxation practice, combined with a Mediterranean diet. The main cardiac outcomes of the study are the focus of a separate article, there we describe the interaction between genetic polymorphisms and lifestyle effects and report that the lifestyle program produced some improvement of markers of cardiac autonomic function but did not affect metabolic risk factors or 1-year indices of coronary atherosclerosis. In the present paper we report the prespecified secondary endpoints of QoL and psychological outcomes and a gender × intervention analysis. Our hypothesis was that participants randomized to the lifestyle program would show greater improvements on these outcomes than those in the control who merely received written advice.

Methods

Patients

Patients with documented CAD were enrolled from July 2001 to December 2001 in two hospitals after coronary angiography, percutaneous coronary intervention (PCI) or stationary treatment for CAD. Patients were excluded if they had had an acute coronary syndrome (ACS) or coronary artery bypass graft (CABG) during the previous 3 months, type 1 diabetes, a body mass index >33 kg/m^2, manifest cardiac arrhythmias, heart failure or a life-threatening co-morbid condition.

Study Design and Randomization

The study was a 1-year randomized controlled intervention trial. The follow-up ended in January 2003. The protocol of this study was approved by the Review Board of the University of Essen, and written informed consent was obtained from all patients. Randomization assignments were made centrally by a computer program. Assignments were stratified by age, sex and status of revascularization (previous PCI, stent, CABG). Eligible participants were assigned to a intensified 100 h/1-year comprehensive lifestyle therapy/stress reduction group (LTG) or to a written-advice-only group (AOG).

Evaluation of Psychological Outcomes and QoL

For the preplanned evaluation of psychological factors, stress and QoL, five self-rating questionnaires were used: the Spielberger State-Trait Anger Expression Inventory, (STAXI) [23], the Beck Depression Inventory (BDI) [24], the State and Trait Anxiety Inventory (STAI) [25], the Cohen Perceived Stress Scale (PSS) [26] and the MOS-Short Form-36 QoL Questionnaire (SF-36) [27]. Additionally, a single-item measure (Likert scale; 1 = not at all; 5 = very much) was used to evaluate the extent to which patients perceived 'general improvement in QoL' after treatment.

Statistical Analysis

Analysis included all patients for whom data were available at follow-up (per-protocol analysis). Group (Lifestyle vs. Advice) repeated-measures analyses of variance (ANOVA's) were performed

for all measures. Analyses of covariance of pre-to-post intervention change scores were performed, employing baseline value as covariate. No adjustments were made for multiple testing. All statistical computations were carried out with SAS version 8.2 statistical software.

Intervention

The intervention for the LTG consisted of an intensive, group-based intervention that focused on stress reduction and stress management, combined with a recommendation for a Mediterranean-type diet. Regular exercise and increased daily activity were strongly recommended but were not part of training. The stress management program was adopted according to the Mind/Body Program of the Mind-Body Medical Institute of the Harvard Medical School [28], and included additionally elements from the Mindfulness-Based Stress-Reduction (MBSR) program of the University of Massachusetts [29]. Programs were delivered by personnel who had undergone training via staff of the above two institutions and who had experience teaching these programs for at least 2 years.

Patients practised various relaxation techniques according to personal choice. Techniques taught included mindfulness meditation, guided imagery, yoga breathing techniques and body scan. Further elements included CBT (cognitive restructuring) and psychoeducational approaches (coping skills training). Patients were taught that emotions and behavior are largely determined by the individual's processing of perceptions and cognitions. CBTs included monitoring irrational automatic thoughts and generating alternative interpretations of situations. The program also included practical exercises aimed at developing attitudes of non-judging, acceptance, and patience.

The 1-year intervention was carried out in small groups of 10–12 participants in order to ensure group support. The program started with a 3-day retreat followed by weekly 3-hour sessions for 10 weeks and thereafter by biweekly 2-hour meetings. Each session included educational lectures about stress reduction, stress management and nutritional therapy, followed by training and practice of yoga, mindfulness meditation, body scan, and visualizations. Patients in the AOG received written information about stress management and diet by means of a booklet sent by mail after randomization.

Assessment of Adherence

Patients completed detailed protocols for practice of stress management and relaxation techniques that were cross-checked by interviews (to control for overreporting) at baseline and after 1 year. Dietary adherence was assessed with Likert scales and cross-checked with a validated prospective 7-day Food Record and focused on key features of the recommended diet. Physical activity was determined by the 4-week retrospective modified Minnesota Leisure Time Physical Activity (LTPA) questionnaire [30]. A summarized, predefined adherence score was calculated with 100% adherence defined as at least 30 min daily relaxation training, full adherence to the dietary key nutrients, and >1,500 kcal energy expenditure/week from exercise.

Results

Of 235 screened individuals, 105 fulfilled all study criteria and underwent randomization. Of these, 3 patients in the study course declined to return for further visits to the study center and withdrew from the study (LTG: 2; 1 female; AOG: 1), 1 more male patient of the LTG dropped out due to severe co-morbidity. Results are presented for the 101 patients who completed follow-up. Baseline characteristics were well balanced between groups (all p values for group dependence >0.1, except a trend (p = 0.06) for patients in the AOG to have a higher body mass index (table 1). Most patients in both groups were currently treated with statins, β-blockers and aspirin or coumadin. Only a minor proportion currently smoked. Two patients in each group had a diagnosis of depression, as established by a psychiatrist. One patient in each group was treated with antidepressants (imipramine) at baseline, and antidepressant medication was unchanged on study. No patient reported any other psychiatric disorder.

Adherence with the Study Intervention

Adherence to the treatment program in the LTG was excellent, with only 3 patients attending less than 90% of the group sessions. At baseline, no patients in either group reported prior experience with stress reduction or relaxation training. After 1 year, only patients in the LTG reported regular stress-reduction practice with a mean of 39 ± 5 min daily, compared to 5 ± 8 min in the AOG (p < 0.001). The majority of patients in the LTG practised body scan and yoga breathing techniques, followed by meditation. Both groups improved their diet moderately; significant group differences in favor of the LTG were related to the intake of saturated fats, long-chain ω–3 fatty acids and daily fruit consumption. Mean caloric energy expenditure from exercise at follow-up was 1,270 kcal/week in the LTG and 920 kcal/week in the AOG. The adherence score amounted to 97% in the LTG and 46% in the AOG (p < 0.001). The number of active smokers was only slightly reduced from 8 to 6 in the LTG and from 4 to 3 in the AOG.

Medical Treatment

The proportion of patients treated with β-blockers, ACE inhibitors and other antihypertensives did not change during the study in both groups. However, dosages of β-blocker, ACE and calcium antagonists were more frequently reduced in LTG vs. AOG patients (p = 0.004).

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Table 1. Baseline characteristics

Characteristics	Lifestyle therapy	Advice-only	Difference p value
Subjects	48	53	
Age, years	59.0 ± 8.7	59.8 ± 8.6	0.65
Male, %	79.2	75.5	0.66
Body mass index, kg/m^2	26.1 ± 3.2	27 ± 2.8	0.06
Seated SBP/DBP, mm Hg	145/85 ± 19/4	145/83 ± 18/2	0.95
Current smoker, %	16.7	7.5	0.15
Total cholesterol, mmol/l	4.84 ± 1.2	5.00 ± 1.0.2	0.28
LDL cholesterol, mmol/l	3.17 ± 1.0	3.28 ± 0.8	0.18
HDL cholesterol, mmol/l	1.40 ± 0.3	1.39 ± 0.3	0.91
History of MI, %	45.8	54.7	0.37
Years since last MI	4.8 ± 4.5	6.1 ± 4.7	0.91
Coronary bypass, %	33.3	30.1	0.73
PCI, %	56.2	52.8	0.73
Implanted stent, %	43.7	39.6	0.68
Three-vessel disease	41.7	39.6	0.43
Medication, %			
Statins	85.4	79.2	0.42
Aspirin, coumadin	97.9	98.1	0.94
β-Blockers	75.0	77.3	0.79
ACE inhibitors	50.0	45.3	0.64

Means ± SD if not indicated otherwise. SBP = Systolic blood pressure, DBP = diastolic blood pressure, PCI = percutaneous coronary intervention.

Table 2. Mean SF-36 scores at baseline, after 1 year and mean change on study

SF-36 dimension	Lifestyle therapy (n = 48)			Advice-only (n = 53)			Group difference	
	baseline	1 year	change	baseline	1 year	change	change (95% CI)	p value[1]
GHP	52.1 ± 14.9	63.1 ± 15.5	10.9 ± 14.8[c]	53.5 ± 17.7	59.6 ± 19.7	6.1 ± 15.4[b]	4.9 (–1.1; 10.8)	0.123
Physical function	75.8 ± 21.3	83.8 ± 15.1	7.9 ± 13.4[c]	75.2 ± 20.1	78.8 ± 18.4	3.6 ± 14.8	4.3 (–1.2; 9.9)	0.046
Physical role	53.6 ± 44.0	76.6 ± 36.2	22.9 ± 45.5[b]	53.3 ± 40.1	64.1 ± 39.7	10.8 ± 41.2	12.0 (–5.0; 29.1)	0.079
Emotional role	63.9 ± 45.0	74.3 ± 37.2	10.4 ± 52.4	59.1 ± 40.6	69.8 ± 38.5	10.1 ± 45.1	0.4 (–18.9; 19.6)	0.589
Social function	74.5 ± 20.4	82.6 ± 20.6	8.1 ± 19.3[b]	73.8 ± 22.3	81.6 ± 18.6	7.8 ± 20.1[b]	0.3 (–7.5; 8.1)	0.850
Mental health	69.6 ± 13.6	75.8 ± 15.7	6.1 ± 13.8[b]	67.0 ± 17.3	74.6 ± 16.1	7.5 ± 18.9[b]	–1.4 (–7.9; 5.2)	0.990
Energy, vitality	56.4 ± 15.8	63.8 ± 15.8	7.31 ± 13.1[c]	53.7 ± 16.2	60.0 ± 16.6	6.3 ± 18.2[a]	1.0 (–5.2; 7.4)	0.410
Pain	64.4 ± 23.6	77.8 ± 24.7	13.3 ± 22.8[c]	60.4 ± 25	73.5 ± 24.9	13.1 ± 27.5[b]	0.2 (–9.8; 10.2)	0.595
Physical sum score	43.2 ± 9.2	48.9 ± 8.7	5.7 ± 7.5[c]	43.2 ± 10.0	46.1 ± 9.3	2.9 ± 8.5[a]	2.9 (–0.3; 6.0)	0.045
Mental sum score	47.2 ± 9.2	49.7 ± 9.5	2.5 ± 8.9[a]	45.7 ± 9.8	49.3 ± 10.0	3.6 ± 10.1[a]	–1.1 (–4.9; 2.7)	0.813

GHP = General health perception; CI = confidence interval.
Difference within group: [a] p < 0.05; [b] p < 0.01; [c] p < 0.001.
[1] Differences adjusted for baseline value.

Clinical Outcome and QoL

There were no deaths during the study. During the intervention period, 2 patients in the AOG received PCI after an ACS, whereas 2 patients in the LTG underwent CABG due to symptom progression. Three control patients had hospitalizations due to angina pectoris with diagnosis of ACS in 2 of them.

Post-treatment perception of mean general improvement of QoL was 2.8 in the LTG vs. 2.2 in the AOG (p < 0.001 for group difference). Patients in the LTG showed

Table 3. Mean anger scores at baseline, after 1 year and mean change on study

	Lifestyle therapy (n = 48)			Advice-only (n = 53)			Group difference	
	baseline	1 year	change	baseline	1 year	change	change (95% CI)	p value[1]
State anger	11.3±2.9	10.9±2.3	−0.4±2.8	11.7±3.7	11.1±2.6	−0.7±4.2	0.2 (−1.2; 1.7)	0.851
Trait anger	19.4±5.4	17.4±4.2	−2.0±4.1[b]	19.0±4.8	18.0±4.8	−1.0±3.3[a]	−1.0 (−2.5; 0.5)	0.178
Anger in	18.7±5.3	17.1±4.7	−1.6±4.3[a]	18.1±5.1	16.8±4.9	−1.2±3.8[a]	−0.4 (−2.0; 1.2)	0.831
Anger out	12.4±3.3	11.6±2.7	−0.8±2.2[a]	12.0±3.2	11.5±3.1	−0.4±2.7	−0.4 (−1.3; 0.6)	0.614
Anger control	23.9±4.2	24.5±4.2	0.6±3.7	24.6±4.6	24.4±4.5	−0.2±4.5	0.8 (−0.8; 2.5)	0.501

CI = Confidence interval.
Difference within group: [a] $p < 0.05$; [b] $p < 0.01$.
[1] Differences adjusted for baseline value.

Table 4. Mean anxiety, depression and stress scores at baseline, after 1 year and change on study

	Lifestyle therapy (n = 48)			Advice-only (n = 53)			Group difference	
	baseline	1 year	change	baseline	1 year	change	change (95% CI)	p value[1]
State anxiety	36.5±7.6	36.5±8.8	0.0±8.1	39.3±10.4	36.2±7.6	−3.1±8.8[a]	3.1 (−0.2; 6.5)	0.240
Trait anxiety	40.3±11.0	35.7±8.3	−4.5±8.2[c]	40.7±10.0	37.5±10.0	−3.3±7.6[b]	−1.3 (−4.4; 1.9)	0.295
Beck score	9.3±6.3	6.4±4.2	−2.9±4.7[c]	9.8±5.8	7.6±4.7	−2.2±5.5[b]	−0.7 (−2.8; 1.3)	0.186
Cohen perceived stress score	22.6±8.6	19.1±7.6	−3.5±7.1[b]	23.7±7.6	21.7±7.7	−2.0±6.6[a]	−1.5 (−4.2; 1.2)	0.117

CI = Confidence interval.
Difference within group: [a] $p < 0.05$; [b] $p < 0.01$; [c] $p < 0.001$.
[1] Differences adjusted for baseline value.

significant post-intervention improvements in seven of eight subscales of the SF-36 QoL inventory, whereas control patients showed significant improvements in four subscales. Mean improvement of QoL was higher for the LTG in seven of eight subscales. However, group differences for change were only significant for physical function. Correspondingly, the physical component sum score increased more in the lifestyle group (p = 0.45; table 2).

Psychological Outcomes

Anger as assessed with the STAXI was significantly reduced in the LTG after 1 year. However, patients in the AOG also improved substantially, resulting in non-significant group differences in the five dimensions of the STAXI (table 3). Table 4 presents the mean values for anxiety, depression and perceived stress before and after treatment for each group and the between-group differences for change on study. Both groups improved significantly with regards to trait anxiety, depression and perceived stress during the 1-year study period. Compared

to the AOG, improvements in the LTG were only slightly greater, resulting each in a non-significant group difference. State Anxiety was non-significantly more reduced in the AOG. Therefore, there were no main effects for the intervention.

Group × gender interactions, however, did indicate favorable responses to the lifestyle program for women (mean age 58.8 ± 9.3 years) but not for men (mean age 59.6 ± 8.4 years): three-way interactions were significant for depression and trait anger (F(1,97) = 6.02; p < 0.02, depression; F(1,96) = 6.76; p < 0.02, trait anger). Women were significantly more psychologically distressed at baseline than men on a number of different inventories, including depression, anxiety and perceived stress, with a similar tendency for anger measures (table 5). Separate analyses of females alone were, therefore, performed in order to overcome violations of homogeneity of variance between cells, and to further explore specific female effects. Women in the LTG (n = 10), compared to women in the AOG (n = 13), showed clear improvements in

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Fig. 1. a Mean change of Beck Depression score with 95% CI for women in the LTG (n = 10) and in the AOG (n = 13). p = 0.025 for between-group difference of change on study, adjusted for baseline value. **b** Mean change of Beck Depression score with 95% CI for men in the LTG (n = 38) and in the AOG (n = 38). p = 0.82 for between-group difference of change on study, adjusted for baseline value.
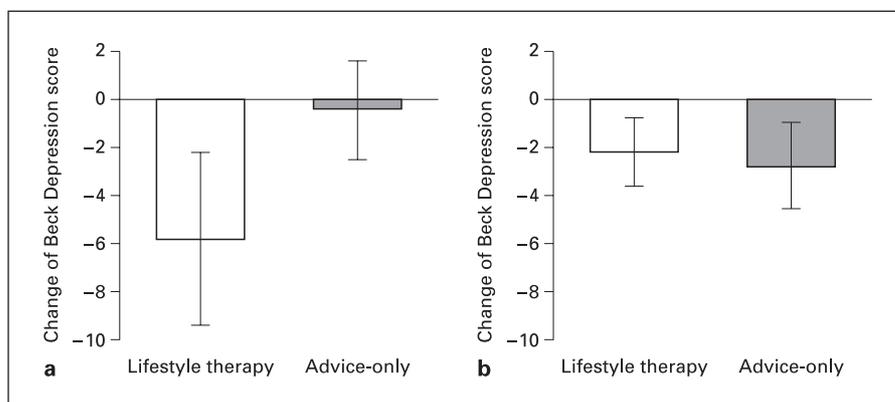
Table 5. Baseline gender differences in psychological variables significant or tending to significance across both groups

Psychological variable	Males (mean ± SD)	Females (mean ± SD)	p value
Depression	8.7 ± 5.7	12.6 ± 6.2	<0.006
Perceived stress	20.3 ± 7.9	26.0 ± 8.3	0.050
State anxiety	37.0 ± 9.3	41.1 ± 8.9	<0.069
Trait anxiety	39.6 ± 10.5	43.6 ± 10.0	0.100
Anger control	24.9 ± 3.9	22.2 ± 5.4	<0.009

depression scores (mean between-group difference of change = –5.3; $F_{(1,21)} = 8.98$; $p < 0.007$; 95% confidence interval (CI) –9.0 to –1.6; $p < 0.03$) (fig. 1). Additionally, trait anger decreased for women in the LTG (mean –3.4 (–6.4 to –0.34)) but increased in the AOG (mean 0.4 (–0.9 to 1.7)) resulting in a significant between-group difference for change of –3.8 ($F_{(1,21)} = 7.21$; $p < 0.02$; 95% CI –6.6 to –0.9; $p < 0.04$). A similar trend was found for trait anxiety and QoL but did not reach significance.

Discussion

The present study shows that among patients with CAD a comprehensive lifestyle modification and stress reduction program achieved excellent adherence including daily relaxation practice. Physical components of QoL improved in the intervention group, and there was a reduced need of anti-ischemic medication. Surprisingly, however, the lifestyle intervention did not provide specific psychological benefits for males, although women manifested reductions in depression and trait anger.

When both genders were pooled, improvement at 12 months was substantial but non-specific, generally occurring for participants of both the lifestyle modification program and the written-advice group. This may suggest that mere advice, alone, may be sufficient to effect a broad range of psychological and QoL dimensions, or it may merely indicate that time itself – even a 1-year period – may ameliorate physical and psychological symptoms associated with CAD.

Our results contrast to the findings of a recent randomized trial that evaluated a stress management program in patients 3 months after myocardial infarction or CABG [31]. In that study, significant improvements in psychological outcomes over an untreated waiting list group were found. However, no information was provided regarding medications, the follow-up period was only 6 months, and the waiting list group was provided with no intervention whatsoever. Other stress reduction programs have failed to produce psychological improvements, despite substantial interventional efforts [32, 33]. Several trials evaluating comprehensive lifestyle modification combined with stress management have shown beneficial effects on coronary atherosclerosis and cardiac risk factors [16, 18, 20, 34]; nevertheless, QoL and psychological outcomes were not assessed in these studies. Investigations that evaluated psychosocial therapies, e.g. CBT, have yielded mixed results: in a meta-analysis of controlled trials of psychosocial therapies, evidence for a beneficial effect in CAD was found [35]. However, no reduction in psychological distress was observed in two recent CBT trials [12, 13].

Few recent investigations have evaluated the complex mechanisms that may link stress reduction to improved cardiovascular outcomes. Among many possible factors, hypercoagulability, impaired autonomic and endothelial

function, and exaggerated hemodynamic responses to stress have been related to cardiovascular outcomes and enhanced atherosclerosis [9, 36]. Accordingly, daily relaxation and stress reduction have been associated with reduced carotid atherosclerosis [37]. In patients with mental stress-induced coronary ischemia, Blumenthal et al. [10] showed improved reduced coronary ischemia and improved clinical outcome with a CBT-based stress management program. These investigators also found improvements in general health perception and hostility, but not in anxiety or depression. Most recently, the impact of the ENRICHD trial on depression scores was modest, resulting in unexpectedly small effect sizes for CBT in psychological outcomes and no reduction of cardiovascular events [11].

The modest level of psychological benefits of our comprehensive lifestyle modification program, particularly among men, should be addressed, especially given the elaborate and intensive expenditure of effort entailed. One possible explanation is that the recent substantial improvements in cardiac care have generally reduced cardiovascular symptoms and morbidity, thus minimizing emotional distress and overshadowing any additional benefit of stress reduction interventions. Compared to prior studies in this field [10, 14, 15, 17], a very high proportion of patients in the present study was treated with β-blockers and statins and had undergone previous PCI.

Secondly, the similar improvements among males in both groups may reflect the natural course of psychological outcomes in CAD. Emotional distress commonly improves over time, and mild to moderate forms of depression and anxiety disorders frequently abate in the first weeks to months after an ACS [38, 39]. We only included patients who were already in a stable post-treatment phase and who had no ACS or CABG during the preceding 3 months. The median duration since the last myocardial infarction was over 3 years. Furthermore, about half of the patients were enrolled in our study during a mostly elective hospital stay for diagnostic or therapeutic reasons, but only 7 patients had a rehospitalization during the subsequent 1-year study period. Thus, for the majority of studied patients, absence of hospital stay during the intervention may have also positively influenced their psychological adjustment independent of intervention.

Another explanation for lack of specific psychological improvements of the lifestyle modification therapy may be simply that the intervention itself was not effective for male patients. The stress-management and stress-reduction procedures delivered in this trial were based on well-established concepts that have been successful with other diagnoses or in trials assessing cardiac risks [20, 40, 41]. However, as mentioned earlier, most earlier lifestyle trials did not assess QoL and psychological outcomes, and studies with CBT have yielded mixed results. Therefore, it may be that this type of intervention may not ameliorate psychological symptoms among male coronary patients or that the intervention has to be better targeted to individual symptoms and patterns of distress [42], implying also a more individual assessment with improved clinical measurement tools, as has been recently suggested [43, 44].

It is noteworthy that women in the lifestyle intervention of our study showed clear reductions of depression and trait anger, in contrast to the control group. These results may indicate gender-specific benefits of lifestyle modification interventions for CAD, with women potentially more responsive than men to the various behavioral components of this type of program. Alternatively, the elevated initial levels of psychological distress among female patients in our study, coupled with the specific benefits apparently received by women undergoing the lifestyle modification program, could suggest that such treatments are most likely to benefit patients of either gender who are more severely distressed and, conversely, may be less likely to provide improvement among patients more in the normal range of psychological functioning at baseline (as the male patients seemed, based on the psychological scales).

Recent research indicates that gender differences may be important in cardiac disease in that women show higher levels of anxiety and distress and reduced QoL, compared to men [45, 46]. It has also been suggested that women manifest lower self-efficacy related to health behavior change [47]. Unfortunately, lifestyle modification studies in CAD have only rarely included women or have not performed analysis of gender differences. Regarding cardiac rehabilitation, only one uncontrolled study has reported the effects of the intervention on symptoms of depression and anger separately for men and women, and results indicated that women were less likely to experience reductions in depressive symptom [48].

It appears that in most studies on CAD with mixed populations, women are older and likelier to present with more severe co-morbid medical conditions than males. In our study, however, age and medical baseline variables were well balanced between men and women. In two other investigations specifically addressing the effectiveness of lifestyle modification and comprehensive cardiac rehabilitation in women, the intervention improved some

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psychosocial endpoints and QoL [49, 50]. In the M-HART trial the individually tailored program was only marginally significant in reducing symptoms of anxiety and depression for men and had no impact on psychological symptoms in women. Furthermore, cardiac mortality was marginally greater in women in the treatment group than in controls [13], and also the ENRICHD trial found an adverse treatment group × gender interaction for women [11]. Thus, it may be that efforts to provide individualized stress management interventions may be less effective for women, whereas group-based lifestyle support groups may facilitate a sense of belonging and confer benefit. To the extent that our investigation was a carefully controlled, randomized trial, the findings of gender differences in response to lifestyle modification are potentially of major relevance. Nevertheless, these results, although interesting, should be regarded with caution, due to the relatively small number of women studied. In any case, our findings certainly underline the need for further research in this area.

A principal limitation of our study relates to the moderately sized study sample. The sample size calculations in this study were based on medical endpoints, for which the lifestyle modification program was slightly superior compared to advice-only. It is possible that a larger study would have resulted in a greater number of significant group differences in favor of the lifestyle therapy, although the clinical value of such small differences between groups might remain questionable. An additional limitation relates to the restriction of analysis to patients with complete available data (per-protocol analysis), i.e. we did not perform 'intention-to-treat' analysis. However, due to the very low number of dropouts, a bias associated with non-random loss of participants is unlikely. Another methodological constraint of our study is that our patient population was primarily medically stable and not overtly psychologically distressed; thus, generalization of findings to other populations would be premature.

In conclusion, our study indicated that comprehensive lifestyle modification, with a focus on stress reduction, improved QoL only slightly more than written advice when gender was pooled and did not confer psychological benefits for the larger male subsample. In this era of improved cardiac care for CAD, the value of such programs requires further evaluation in randomized trials. Given the observed benefits of lifestyle modification among women, our findings may serve to warrant further exploration of the impact of gender upon lifestyle and psychosocial interventions for cardiac disease.

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