Randomized Controlled Trial of Cognitive Behavioral Therapy vs Standard Treatment to Prevent Recurrent Cardiovascular Events in Patients With Coronary Heart Disease

Secondary Prevention in Uppsala Primary Health Care Project (SUPRIM)

Mats Gulliksson, MD, PhD; Gunilla Burell, PhD; Bengt Vessby, MD, PhD; Lennart Lundin, MD, PhD; Henrik Toss, MD, PhD; Kurt Svärdsudd, MD, PhD

Background: Psychosocial factors are independently associated with increased risk of cardiovascular disease (CVD) morbidity and mortality, but the effects of psychosocial factor intervention on CVD are uncertain. We performed a randomized controlled clinical trial of cognitive behavioral therapy (CBT) to measure its effects on CVD recurrence.

Methods: The study included 362 women and men 75 years or younger who were discharged from the hospital after a coronary heart disease event within the past 12 months. Patients were randomized to receive traditional care (reference group, 170 patients) or traditional care plus a CBT program (intervention group, 192 patients), focused on stress management, with 20 two-hour sessions during 1 year. Median attendance at each CBT session was 85%. Outcome variables were all-cause mortality, hospital admission for recurrent CVD, and recurrent acute myocardial infarction.

Results: During a mean 94 months of follow-up, the intervention group had a 41% lower rate of fatal and non-fatal first recurrent CVD events (hazard ratio [95% confidence interval], 0.59 [0.42-0.83]; \( P = .002 \)), 45% fewer recurrent acute myocardial infarctions (0.55 [0.36-0.85]; \( P = .007 \)), and a nonsignificant 28% lower all-cause mortality (0.72 [0.40-1.30]; \( P = .28 \)) than the reference group after adjustment for other outcome-affecting variables. In the CBT group there was a strong dose-response effect between intervention group attendance and outcome. During the first 2 years of follow-up, there were no significant group differences in traditional risk factors.

Conclusions: A CBT intervention program decreases the risk of recurrent CVD and recurrent acute myocardial infarction. This may have implications for secondary preventive programs in patients with coronary heart disease.

Trial Registration: clinicaltrials.gov Identifier: NCT00888485

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Despite decreasing trends in incidence and mortality, coronary heart disease (CHD) continues to be the main cause of death and disability in developed and developing countries.\(^1\,^2\) Moreover, a falling trend in recurrent acute myocardial infarction (AMI) risk has been shown.\(^3\,^4\) Recently, we presented evidence of a trend for decreasing risk of recurrent AMI during recent decades for both women and men, all age groups, and number of AMIs in Sweden.\(^7\)

There is evidence that psychosocial factors contribute independently to the risk of CHD even after adjustment for the effects of traditional risk factors.\(^8\,^9\) Psychosocial factors have been shown to account for approximately 30% of the attributable risk of AMI.\(^1\) Psychosocial factors that may promote atherosclerosis and cardiovascular disease (CVD) belong to 2 general categories: chronic stressors, including low socioeconomic status, low social support, marital distress, and work distress; and emotional factors, including major depression, hostility, anger, and anxiety.

The Secondary Prevention in Uppsala Primary Health Care project was set up as a randomized controlled clinical trial to test the effects of a cognitive behavioral therapy (CBT)—based intervention program, focused on stress management of emotional factors, on recurrent CVD.
STUDY POPULATION

The participants were recruited from among consecutive patients discharged from Uppsala University Hospital, Uppsala, Sweden, from May 1, 1996, until August 31, 2002; the follow-up data collection was completed in 2008. Inclusion criteria were being 75 years or younger; having been discharged from the hospital (index event) after an AMI, percutaneous coronary intervention, or coronary artery bypass grafting; living in the hospital primary catchment area; being healthy enough to be referred back to the general practitioner within 1 year after the hospital admission; not having participated in similar programs; being Swedish speaking; being willing to participate in the study; and accepting random group allocation. As soon as the participants were referred back to their general practitioner (at the earliest, 3 months after discharge in accordance with hospital standard procedure, and at the latest, 1 year after discharge according to inclusion criteria), all patients fulfilling the inclusion criteria were invited to participate, and verbal informed consent was obtained according to the standard requirement at the time. The study was approved on several occasions during the planning and data collection periods, first by the Research Ethics Committee at Uppsala University Hospital and later by the Regional Research Ethics Board.

A power calculation based on a 5% difference in recurrent CVD rate during a minimum of 4 years of follow-up indicated that approximately 400 cases were needed for 80% statistical power. At the end of the recruitment period, 812 consecutive patients had been considered for inclusion, 302 of whom did not fulfill the inclusion criteria, and 148 patients declined to participate, in most cases because of distance from home to the hospital or lack of time. The remaining 362 patients (71.0% of eligible cases) were included; there were 85 women (23.5%) and 277 men (76.5%), of whom 185 (51.1%) had been admitted for an AMI, 122 (33.7%) for coronary artery bypass grafting, and 55 (15.2%) for a percutaneous coronary intervention. Seventy-one participants with AMI had had a percutaneous coronary intervention performed during the index admission and 3 had had coronary artery bypass grafting. There were no significant age, sex, or diagnosis differences between included and excluded patients and no diagnostic differences between women and men. At the time of the study, more than 95% of the Swedish population in these age groups were white and approximately 90% were of Swedish ethnic origin.

RANDOMIZATION PROCEDURE

The group allocation was based on the SAS “ranuni” function, providing random numbers with equal probability.10 The procedure resulted in pre-prepared sealed envelopes, kept in a safe, with a serial number on the outside and a sheet of paper inside with the group allocation on the front and a blinding print on the back to prevent reading the group allocation sheet from the outside. After inclusion of a participant, the study monitor, a secretary who managed data handling and follow-up appointments and who was the only person with access to the randomization envelopes, opened the next envelope in turn and noted the group allocation in the computerized monitoring logbook. Of those included, 192 were allocated to the behavioral intervention and 170 to the reference group. Participants were informed about the group allocation after the baseline measurement. The study flowchart is shown in Figure 1.

PATIENT VISITS AND MEASUREMENTS

The participants received a letter of invitation for a first (baseline) examination with a first postal questionnaire included. The procedure was repeated at the 6th, 12th, 18th, and 24th months after baseline. Weight was measured on a lever balance with indoor clothing to the nearest 0.1 kg. Height was measured without shoes on a wall-fixed measure to the nearest centimeter. Sagittal abdomen diameter was measured in the supine position to the nearest centimeter. Waist circumference was measured without clothes by means of a tape measure and recorded to the nearest centimeter. Systolic and diastolic blood pressure measurements were performed in duplicate in the supine position, on the right arm, after at least 5 minutes’ rest; systolic pressure was recorded at Korotkoff phase 1 and diastolic pressure at Korotkoff phase 5.

Blood was drawn in the morning, after an overnight fast, from an antecubital vein with minimal occlusion into evacuated glass tubes. After centrifugation, the blood lipid samples were assayed immediately. Total cholesterol and triglycerides in serum were assayed by enzymatic techniques with a centrifugal analyzer (Monarch 2000, Instrumentation Laboratories, Lexington, Massachusetts). High-density lipoprotein

Figure 1. Trial flowchart. CBT indicates cognitive behavioral therapy.
developed by Cantril15 and Andrews and Withey, 16 was used as an indicator of expected well-being 1 year later (credence score). The Mastery Subscale of the Ladder of Life measure, developed by Cantril13 and Andrews and Withey, 16 was used as an indicator of expected well-being 1 year later (credence score). The Mastery Subscale of the Ladder of Life measure, developed by Cantril13 and Andrews and Withey, 16 was used as an indicator of expected well-being 1 year later (credence score). The Mastery Subscale of the Ladder of Life measure, developed by Cantril13 and Andrews and Withey, 16 was used as an indicator of expected well-being 1 year later (credence score).

Information on social background, lifestyle factors, and current medication was obtained from the questionnaires at each measurement occasion. For this report, marital status was classified as single (including never married, divorced, or widowed) or married/cohabiting. Educational level was measured on a 4-point scale ranging from mandatory education only to university education. Smoking habits, regardless of type of tobacco used, were classified as never smoked, ex-smoker, smoking 1 to 14 g/d, 15 to 24 g/d, or 25 g/d or more. Snuff taking was classified accordingly. The participants were asked to indicate whether they had a job, had retired at normal retirement age (65 years at the time), or were receiving a disability pension.

The psychosocial data questionnaire has been described in detail previously. 13 Briefly, vital exhaustion was measured with the Maastricht Questionnaire. 14 The Ladder of Life measure, developed by Cantril13 and Andrews and Withey, 16 was used as an indicator of expected well-being 1 year later (credence score) on a ladderlike scale. The Mastery Subscale of Factor Items Measuring Coping Resources 17 was used to measure coping capability.

Information on medical history before the baseline measurement regarding angina pectoris, hyperlipemia, hypertension, heart failure, diabetes mellitus, asthma/chronic obstructive pulmonary disease, stroke, and peripheral artery disease (yes or no) was obtained from the baseline questionnaire and used as comorbidity variables, a proxy for disease severity.

OUTCOME DATA

The primary outcome of the study was recurrent CVD, fatal as well as nonfatal. Because AMI is the major component of CVD, recurrent AMI was also analyzed, as was all-cause mortality. Secondary outcomes were quality-of-life measures. Hospital admission data from January 1, 1971, until December 31, 2006, were obtained by record linkage with the National Hospital Discharge Registry, covering all hospital admissions in Sweden. The variables date of admission and discharge and all diagnoses were used.

Mortality data were obtained by record linkage with the National Cause of Death Registry for all deaths in the study population until December 31, 2006. The variables used were date of death, underlying and all contributing causes of death, and data on postmortem examinations, including autopsies. The overall autopsy rate was 22.8%, and the autopsy rate among those who had a first fatal CVD outcome was 50.0%. Hospital discharge diagnoses and causes of death were coded according to the International Classification of Diseases (ICD), revisions 8 to 10. 18 Cardiovascular disease was defined as ICD-8 codes (until 1986) and ICD-9 codes (1987-1996) 401 to 449, and ICD-10 codes (from 1997 on) I10 to I19. Acute myocardial infarction was defined as ICD-8 and ICD-9 code 410 and ICD-10 codes I21 and I22. On the basis of these data, the number of AMIs per participant since 1971 and before baseline and all deaths irrespective of their cause, the first CVD (fatal or nonfatal), and the first AMI (fatal or nonfatal) after baseline were identified.

INTERVENTIONS

The intervention group and the reference group both received traditional care, defined as traditional risk factor optimization efforts during follow-up. In addition, the intervention group consisted of the CBT intervention program as soon as they were included in the trial. A detailed description of the intervention program is available in the eAppendix (available at http://www.archinternmed.com). The program has 3 key components with specific goals—education, self-monitoring, skills training, cognitive restructuring, and spiritual development—and is focused on stress management, coping with stress, and reducing experience of daily stress, time urgency, and hostility. It is highly structured and standardized, and it follows a treatment manual developed and evaluated in previous studies.

The program was performed in 20 two-hour sessions during 1 year with 5 to 9 participants per group, with separate groups for men and women. Each session had a specific theme, working material, and homework assignment. Simple diaries were used for self-monitoring of behaviors and reactions. Behavioral exercises (“drills”) were introduced early and were monitored and discussed in every session.

The session format was as follows: brief relaxation, reflections on the previous session, follow-up of homework assignment, introduction of new themes, and preparation of homework. The communication style of the therapist was oriented toward motivational interviewing rather than educational. No other intervention was allowed or provided.

A team of experienced clinical psychologists and nurses, experts in and working with patients with CHD at Uppsala University Hospital, was used. They performed the CBT sessions under the supervision of the team leader (G.B.), who had developed the program. To secure continuity, each group had the same group leader throughout the program. Attendance rate was monitored. Individual median attendance rate was 85% per session. All group members participated at least once, and only 8 (4.2%) attended fewer than 50% of the sessions.

STATISTICAL CONSIDERATIONS

Data were analyzed with SAS software, version 9.1. 10 All analyses were based on the intention-to-treat approach. As shown in Figure 1, most individuals participated in all follow-up examinations, with a small group coming and going. The largest number of permanent dropouts from the study were attributable to death. In case of missed appointments among survivors, data from the most recent previous appointment were used until new values were available.

The outcome analyses were performed in 2 steps. First, a bivariate Cox proportional hazards regression analysis of the group effect on the cumulative mortality rate, the rate of first recurrent CVD, and the rate of first recurrent AMI was performed. To adjust for possible outcome-affecting variables other than the CBT program, the analyses were repeated with adjustment for the effects of age, sex, marital status, education, smoking habits, and medical history or comorbidity (number of previous AMIs, angina pectoris, hypertension, hyperlipidemia, heart failure, stroke, peripheral artery disease, diabetes mellitus, and asthma/chronic obstructive pulmonary disease) used as proxies for disease severity. Moreover, mean systolic blood pressure, serum cholesterol level, serum triglyceride level, vital exhaustion score, coping score, and credence in the future were scored across the first 24 months or until new values were available.

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Follow-up time was calculated as the number of days from baseline to the time of outcome or end of follow-up. Censoring events in the analyses of recurrent CVD and recurrent AMI were death from other causes during follow-up and no
new event by the end of follow-up. Mean follow-up time in the intervention group was 96 months (median, 95 months; range, 14-128 months) vs 91 months (median, 94 months; range, 15-127 months) in the reference group. The numbers of person-months of observation were 18,402 and 15,547, respectively.

In the analyses, individual follow-up time was right-truncated because there were few remaining exposed participants. Numbers needed to treat was calculated as the inverted difference between group-specific successful outcomes. Program participation and outcome dose-response was tested with logistic regression. Only 2-tailed tests were used. P values less than .05 were regarded as statistically significant.

## RESULTS

### CHARACTERISTICS OF THE STUDY POPULATION

There were no significant baseline differences between the intervention and reference groups in the characteristics shown in Table 1 and no significant differences in the medical history variables (Table 2).

During the first 24 months of follow-up, there were small and shifting nonsignificant differences in alcohol use between the groups and small but systematic differences in smoking habits, blood pressure and blood lipid levels, vital exhaustion, coping abilities, and credence in the future, some favoring one group and some the other, with a magnitude similar to the baseline levels shown in Table 2. There were no significant differences in use of aspirin, diuretics, β-blockers, calcium-channel block-

### EFFECTS OF INTERVENTION ON RECURRENT EVENTS AND SURVIVAL

During follow-up, 23 participants in the intervention group and 25 in reference group died (Table 3). In a bivariate Cox proportional hazards regression analysis, the intervention group had a nonsignificant 24% lower cumulative all-cause mortality than the reference group. After adjustments for other outcome-affecting variables (covariates), the corresponding measure was 28% (adjusted hazard ratio, 0.72; 95% confidence interval, 0.40-1.30; P = .28).

In the intervention group, 69 participants (35.9%) had a nonfatal CVD and 1 (0.5%) a fatal CVD. The corresponding numbers in the reference group were 77 (45.3%) and 3 (1.8%). In a bivariate Cox analysis, the intervention group had 33% fewer fatal or nonfatal CVD events than the reference group (P = .01). In a multivariate Cox

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### Table 1. Baseline Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Intervention (n=192)</th>
<th>Reference (n=170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at baseline, mean (SD), y</td>
<td>62.0 (7.94)</td>
<td>61.0 (8.28)</td>
</tr>
<tr>
<td>Sex, No. (%)</td>
<td>43 (22.4)</td>
<td>42 (24.7)</td>
</tr>
<tr>
<td>Marital status, No. (%) married</td>
<td>150 (78.1)</td>
<td>132 (77.6)</td>
</tr>
<tr>
<td>Highest educational level, No. (%)</td>
<td>(n=189)</td>
<td>(n=161)</td>
</tr>
<tr>
<td>Compulsory education</td>
<td>67 (35.4)</td>
<td>62 (38.5)</td>
</tr>
<tr>
<td>Vocational training</td>
<td>62 (32.8)</td>
<td>57 (35.4)</td>
</tr>
<tr>
<td>High school</td>
<td>22 (11.6)</td>
<td>10 (6.2)</td>
</tr>
<tr>
<td>College or university education</td>
<td>38 (20.1)</td>
<td>32 (19.9)</td>
</tr>
<tr>
<td>Disability pensioner, No. (%)</td>
<td>33 (17.2)</td>
<td>15 (8.8)</td>
</tr>
<tr>
<td>Old-age pensioner, No. (%)</td>
<td>96 (50.0)</td>
<td>76 (44.7)</td>
</tr>
<tr>
<td>Tobacco use, No. (%)</td>
<td>(n=191)</td>
<td>(n=160)</td>
</tr>
<tr>
<td>Ex-smokers</td>
<td>112 (59.3)</td>
<td>92 (57.7)</td>
</tr>
<tr>
<td>Current smokers</td>
<td>24 (12.7)</td>
<td>24 (15.0)</td>
</tr>
<tr>
<td>Ex-snuff takers</td>
<td>15 (7.9)</td>
<td>20 (12.5)</td>
</tr>
<tr>
<td>Current snuff takers</td>
<td>15 (8.0)</td>
<td>13 (3.7)</td>
</tr>
<tr>
<td>Alcohol intake in past week, mean (SD), g</td>
<td>(n=186)</td>
<td>(n=162)</td>
</tr>
<tr>
<td>Beer</td>
<td>37.6 (11.6)</td>
<td>37.3 (52.9)</td>
</tr>
<tr>
<td>Wine</td>
<td>36.4 (62.6)</td>
<td>39.5 (68.5)</td>
</tr>
<tr>
<td>Hard liquor</td>
<td>17.8 (37.3)</td>
<td>17.5 (32.4)</td>
</tr>
<tr>
<td>Leisure-time physical activity, No. (%)</td>
<td>(n=189)</td>
<td>(n=160)</td>
</tr>
<tr>
<td>Sedentary</td>
<td>20 (10.6)</td>
<td>22 (13.8)</td>
</tr>
<tr>
<td>Moderately active</td>
<td>137 (72.5)</td>
<td>118 (73.8)</td>
</tr>
<tr>
<td>Vigorously active</td>
<td>32 (16.9)</td>
<td>20 (12.5)</td>
</tr>
<tr>
<td>Follow-up, mean (SD), mo</td>
<td>95.6 (19.2)</td>
<td>91.5 (23.1)</td>
</tr>
<tr>
<td>Person-months of observation</td>
<td>18402</td>
<td>15 547</td>
</tr>
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</table>

### Table 2. Medical History and Risk Factor Measurements at Baseline

<table>
<thead>
<tr>
<th>Medical History</th>
<th>Intervention (n=192)</th>
<th>Reference (n=170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical history, No. (%)</td>
<td>60 (31.3)</td>
<td>60 (35.3)</td>
</tr>
<tr>
<td>Previous myocardial infarctions</td>
<td>0.4 (0.7)</td>
<td>0.5 (0.9)</td>
</tr>
<tr>
<td>No. of previous myocardial infarctions, mean (SD)</td>
<td>114 (60.6)</td>
<td>87 (54.7)</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>105 (56.8)</td>
<td>89 (55.6)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>96 (51.3)</td>
<td>69 (43.1)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>45 (24.6)</td>
<td>42 (26.8)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>24 (12.7)</td>
<td>25 (15.6)</td>
</tr>
<tr>
<td>Asthma</td>
<td>7 (3.7)</td>
<td>9 (5.6)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>4 (2.1)</td>
<td>4 (2.5)</td>
</tr>
<tr>
<td>Stroke</td>
<td>4 (2.1)</td>
<td>5 (3.1)</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>7 (3.7)</td>
<td>8 (4.7)</td>
</tr>
</tbody>
</table>

### Baseline Measurements, mean (SD)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Intervention (n=192)</th>
<th>Reference (n=170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>139.3 (21.4)</td>
<td>135.5 (18.9)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>78.9 (10.0)</td>
<td>77.3 (9.0)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>82.5 (14.4)</td>
<td>80.6 (12.6)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>173.4 (8.8)</td>
<td>172.5 (8.5)</td>
</tr>
<tr>
<td>BMI</td>
<td>27.4 (3.8)</td>
<td>27.0 (3.4)</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>93.8 (10.3)</td>
<td>92.8 (9.6)</td>
</tr>
<tr>
<td>Sagittal diameter, cm</td>
<td>24.3 (2.9)</td>
<td>24.1 (2.7)</td>
</tr>
<tr>
<td>Serum cholesterol, mg/dL</td>
<td>196.3 (38.6)</td>
<td>193.1 (34.7)</td>
</tr>
<tr>
<td>LDL-C, mg/dL</td>
<td>119.7 (34.7)</td>
<td>115.8 (34.7)</td>
</tr>
<tr>
<td>HDL-C, mg/dL</td>
<td>46.3 (11.6)</td>
<td>46.3 (11.6)</td>
</tr>
<tr>
<td>Serum triglycerides, mg/dL</td>
<td>159.3 (97.3)</td>
<td>150.4 (70.8)</td>
</tr>
<tr>
<td>LDL-C/HDL-C ratio</td>
<td>2.6 (0.9)</td>
<td>2.6 (1.0)</td>
</tr>
</tbody>
</table>

### Psychosocial data, mean (SD) score

<table>
<thead>
<tr>
<th>Psychosocial data</th>
<th>Intervention (n=192)</th>
<th>Reference (n=170)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vital exhaustion</td>
<td>13.2 (8.4)</td>
<td>13.4 (8.0)</td>
</tr>
<tr>
<td>Coping</td>
<td>15.3 (2.9)</td>
<td>15.5 (3.3)</td>
</tr>
<tr>
<td>Credence in the future</td>
<td>6.6 (1.7)</td>
<td>6.9 (1.6)</td>
</tr>
</tbody>
</table>

**Abbreviations:** BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

**SI conversion factors:** To convert serum cholesterol, HDL-C, and LDL-C to millimoles per liter, multiply by 0.0259; triglycerides to millimoles per liter, multiply by 0.0113.

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ers, angiotensin-converting enzyme inhibitors, other blood pressure–lowering drugs, lipid-lowering drugs, or antidepressants.

**EFFECTS OF INTERVENTION ON RECURRENT EVENTS AND SURVIVAL**

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The CBT intervention program based on stress management improved outcome on hard cardiovascular endpoints during a mean follow-up time of 94 months, and there was a nonsignificant tendency toward less all-cause mortality. A strong dose-response relationship between attendance rate at the intervention program sessions and risk of recurrent CVD or recurrent AMI was observed: the higher the attendance rates, the lower the risk.

# Table 3. Morbidity and Mortality Outcome During Follow-up in Cox Proportional Hazards Regression Analyses

<table>
<thead>
<tr>
<th>Outcome Event</th>
<th>Bivariate Cox Regression</th>
<th>Multivariate Cox Regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>All-cause mortality (23/25)</td>
<td>0.76 (0.43-1.33)</td>
<td>.34</td>
</tr>
<tr>
<td>Smoking score</td>
<td>1.09 (1.04-1.14)</td>
<td>.001</td>
</tr>
<tr>
<td>Age, y</td>
<td>1.03 (1.01-1.06)</td>
<td>.006</td>
</tr>
<tr>
<td>Hypertension, yes/no</td>
<td>1.33 (1.07-1.64)</td>
<td>.009</td>
</tr>
<tr>
<td>No. of previous AMIs</td>
<td>0.67 (0.48-0.92)</td>
<td>.01</td>
</tr>
<tr>
<td>First recurrent AMI event (70/80)</td>
<td>0.62 (0.41-0.93)</td>
<td>.02</td>
</tr>
<tr>
<td>First recurrent cardiovascular disease event (21.4%)</td>
<td>0.59 (0.42-0.83)</td>
<td>.007</td>
</tr>
</tbody>
</table>

Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; HR, hazard ratio.

*Adjusted for the effect of age, sex, marital status, education, smoking habits, comorbidity, and 2-year mean systolic blood pressure, serum cholesterol level, triglyceride level, and scores for vital exhaustion, coping, and credence in the future.

**Non-significant covariates:** sex, marital status, education, smoking habits, number of previous AMIs, angina pectoris, hypertension, hyperlipidemia, heart failure, stroke, peripheral artery disease, diabetes mellitus, asthma/chronic obstructive pulmonary disease, and 2-year mean systolic blood pressure, serum cholesterol level, triglyceride level, and scores for vital exhaustion, coping, and credence in the future.

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The randomization procedure produced fairly equal groups in terms of background variables. In the analyses, the intention-to-treat approach was used regardless of attendance rate. Because outcome data were complete, all randomized participants could be included in the analyses. For obvious reasons, no complete blinding could be done. However, all “hard” outcome data were obtained from official registries, and the follow-up was complete until death or end of follow-up, minimizing the bias risk. The study population size was large enough to provide sufficient power (90% given 360 participants and 15% outcome difference). The intervention program was constructed so that patients would be involved, which kept adherence to the program high, and the monitoring of the trial was intense. The follow-up time was long enough to avoid conclusions being based on temporary group differences.

We were able to adjust for a large number of outcome-affecting variables other than the CBT program, such as traditional risk factors, which increased analysis and conclusion-drawing precision. Even though the analysis model contained a large number of variables, the stability of the model was maintained by backward elimination of nonsignificant variables. Baseline rates of cardiac and other disease, except previous AMIs, were based on self-reports because most diseases are treated in an outpatient setting and we had no access to that type of patient record information. We had no attention or contact control group, which is a limitation of the study. However, we have no reason to believe that the data are affected by selection or biased to such an extent that the conclusions have been affected.

A number of psychologically oriented treatment programs for patients with CHD have been reported in the literature. Reports from small randomized controlled trials testing rehabilitation programs after AMI have shown conflicting results. Jones and West found no effects of stress management intervention on mortality, clinical sequel, or clinical complications. In contrast to the Recurrent Coronary Prevention Project, the Enhancing Recovery in Coronary Heart Disease Patients study, and the Montreal Heart Attack Readjustment Trial, no beneficial effects on mortality or recurrent events were found. In the analysis of subgroups, the group component of the Enhancing Recovery in Coronary Heart Disease program demonstrated positive effects. Rahe et al found reduced coronary mortality and recurrent events. In the Recurrent Coronary Prevention Project, a reduced cardiac recurrence rate and a reduction in cardiac morbidity and mortality in participants after AMI was found with type A counseling. In both the Recurrent Coronary Prevention Project and the Secondary Prevention in Uppsala Primary Health Care studies, there was a focus on behavioral skills training. Also, the treatment period of these 2 programs was considerably longer. These results imply that, to affect CVD or CHD end points, the interventions need to be long-term (possibly 6-12 months), be conducted in groups, and include specific techniques for altering behavior. A possible mechanism is decreased behavioral and emotional reactivity, which would lead to less psychophysiologic burden on the cardiovascular system.

In 2 meta-analyses of psychosocial educational programs (health education and stress management) for patients with coronary disease, a 34% reduction in cardiac mortality and a 29% reduction in recurrent AMI were reported, as well as a reduction in mortality and morbidity during the first 2 years. The number-needed-to-treat measure in this trial was low, 9 to 10, indicating a high efficacy of the therapy given. In secondary prevention drug trials, numbers need to treat usually are in the range 10 to 145.

In conclusion, the group exposed to the 1-year CBT intervention program, focusing on stress management in patients with CHD, had a significantly more favorable outcome regarding fatal and nonfatal recurrent CVD and fatal and nonfatal recurrent AMI than the reference group during 94 months of follow-up. The results indicate not only statistical but also clinical significance. A dose-response relationship between attendance rate in the program and outcome was demonstrated. The benefit was equal for women and men. This demonstrates the potential efficacy of adding CBT to secondary preventive programs after AMI for better patient adherence to treatment and better outcome.

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