Marital Stress Worsens Prognosis in Women With Coronary Heart Disease

The Stockholm Female Coronary Risk Study

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Context Psychosocial stress has been associated with incidence of coronary heart disease (CHD) in men, but the prognostic impact of such stress rarely has been studied in women.

Objective To investigate the prognostic impact of psychosocial work stress and marital stress among women with CHD.

Design and Setting Population-based, prospective follow-up study conducted in the city of Stockholm, Sweden.

Participants A total of 292 consecutive female patients aged 30 to 65 years (n=279 working or cohabiting with a male partner) who were hospitalized for acute myocardial infarction or unstable angina pectoris between February 1991 and February 1994. Patients were followed up from the date of clinical examination until August 1997 (median, 4.8 years).

Main Outcome Measures Recurrent coronary events, including cardiac death, acute myocardial infarction, and revascularization procedures, by marital stress (assessed using the Stockholm Marital Stress Scale, a structured interview) and by work stress (assessed using the ratio of work demand to work control).

Results Among women who were married or cohabiting with a male partner (n=187), marital stress was associated with a 2.9-fold (95% confidence interval [CI], 1.3-6.5) increased risk of recurrent events after adjustment for age, estrogen status, education level, smoking, diagnosis at index event, diabetes mellitus, systolic blood pressure, smoking, triglyceride level, high-density lipoprotein cholesterol level, and left ventricular dysfunction. Among working women (n=200), work stress did not significantly predict recurrent coronary events (hazard ratio, 1.6; 95% CI, 0.8-3.3).

Conclusions Our results indicate that marital stress but not work stress predicts poor prognosis in women aged 30 to 65 years with CHD. These findings differ from previous findings in men and suggest that specific preventive measures be tailored to the needs of women with CHD.

JAMA. 2000;284:3008-3014 www.jama.com

BEFORE 70 YEARS OF AGE, WOMEN have a worse prognosis than men following acute myocardial infarction (AMI),[1,2] but the causes are poorly understood. Studies in men suggest that psychosocial factors are important determinants of cardiovascular health.[3-7] In particular, work stress has been associated with increased coronary heart disease (CHD) incidence and poorer prognosis in men.[8-10] Among women in this age group, psychosocial stress in relation to CHD rarely has been studied,[11,12] and models of psychosocial influences are usually derived from studies in men.[5,13] Whereas marital stress has been shown to affect women's mental health,[13] to our knowledge, no studies have evaluated whether marital stress has adverse effects on CHD among women.

In the Stockholm Female Coronary Risk (FemCorRisk) Study, we have shown that low socioeconomic position and work stress increase CHD risk,[14,15] and that lack of social support and depression worsen prognosis[16] among women. The FemCorRisk Study is a community-based study of all women patients with CHD aged 30 to 65 years in Stockholm, Sweden, who were hospitalized during 1991-1994.[15-17] In this study we have prospectively investigated the effect of marital stress and work stress in women patients followed up for an average of 5 years after hospitalization for an acute coronary event. Marital stress was assessed by the Stockholm Marital Stress

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Scale (SMSS), previously developed and tested in healthy Stockholm women,[18,19] whereas work stress and traditional risk factors were assessed by standard measures.[15-17] A complete follow-up was obtained for the occurrence of cardiac death, hospitalization for recurrent AMI, and for revascularization procedures.

METHODS

Study Population

All women aged 30 to 65 years who were residents of Stockholm and hospitalized for an acute coronary event between February 1991 and February 1994 were asked for written informed consent to participate in the study, which was approved by the Karolinska Hospital Ethics Committee. The age limit of 65 years, the official retirement age in Sweden, was chosen to include all women who were actively employed outside the home. Because the Swedish health care system provides uniform care to all residents, regardless of income or insurance status, all patients who sought and received in-hospital care for an acute CHD event could be identified through the health care registry.[15,17] During the 3-year period, 335 women with CHD were identified, 43 (13%) of whom could not be included. Five women died during the 3 to 6 months between hospitalization and examination, 13 were too sick, and 2 could not get proper transportation to the research center. Two declined because of recruitment to other studies and another 21 for other reasons, including inability to speak Swedish.

Patients qualified if they were hospitalized for AMI, defined by typical chest pain, enzyme patterns, and electrocardiographic changes, or unstable angina pectoris, defined as newly occurring severe angina pectoris that had deteriorated during the 4 weeks prior to admission, with an increase in pain intensity and pain duration, or with pain at rest or on low physical exertion.[20-22] The baseline examination included detailed medical history, lifestyle and demographic information, anthropometric measurements, and a full lipid and routine laboratory profile. Severity of heart failure symptoms (Killip classification)[23] at the time of the index event was abstracted from the medical record. The details of baseline characteristics and patient recruitment have been presented elsewhere.[15,17]

Measurement of Psychosocial Factors

Marital stress was measured by a structured interview developed in our research laboratory.[18,24] All interviews were carried out in a standardized procedure by trained behavioral scientists. The SMSS addressed marital stressors including quality of the emotional and sexual relationship with the spouse (TABLE 1). Questions were scored on a standardized coding template. A high score indicated severe marital stress. The SMSS has been previously examined for psychometric properties in 300 women who were representative of the normal female population of Stockholm. Internal consistency was adequate (Cronbach $\alpha = .77$), and construct validity, as assessed by other related scales, found to be satisfactory.[18,24] Marital stress was categorized as mild or absent (lowest quartile, scores 0-1), moderate (second quartile, scores 2-3), and severe (upper 2 quartiles, scores >3).

Work stress was measured using the Swedish version of the Karasek demand-control questionnaire,[25] which has been tested for consistency and reliability in the Swedish population.[26] Psychological work demands refer to work pace, deadlines, and time pressure. Control at work (decision latitude) refers to individual control and power over work and opportunity to master work activities and work situations. Work stress was computed as the ratio between psychological work demands and control and categorized as mild or absent (lowest quartile, scores 0-0.59), moderate (second quartile, scores 0.60-0.73), and severe (upper 2 quartiles, scores >0.73).

Ascertainment of Recurrent Coronary Events

Complete follow-up information for all patients regarding recurrent hospitalization and death was obtained by linkage of the unique 10-digit person identification numbers to the community health care registers.[27,28] Patients were followed up from the date of their examination until August 1997 (median, 4.8 years; range, 3.2-6.2 years).

Mortality was ascertained by linkage to the Swedish National Death Registry, which is maintained for all residents. All death certificates were collected. Death due to ischemic heart disease was considered when the primary cause of death was coded as *International Classification of Diseases, Ninth Revision (ICD-9)* codes 410-414.

Recurrent AMI was considered to have occurred on the date of admission for hospitalization with a discharge diagnosis of AMI (*ICD-9* code 410) in the hospital register. A previous validation of hospital registers of AMI found them to be highly reliable.[27,28] Revascularization proce-

Table 1. Questions Asked on the Stockholm Marital Stress Scale*

1. Is the relationship with your spouse loving?
2. Is the relationship with your spouse friendly?
3. Is the relationship with your spouse routine-like?
4. Is the relationship with your spouse problematic?
5. Do you engage in leisure activities together with your spouse?
6. Do you have your own private life outside the relationship with your spouse?
7. Is your spouse your closest confidant?
8. Does your spouse consider you his closest confidant?
9. Are there things you can't talk openly about with each other?
10. Have you had serious problems in the relationship with your spouse previously?
11. Have you had serious problems in the relationship with your spouse currently?
12. Have you had serious crises in your relationship?
13. Have you solved problems actively together?
14. Do you have a sexual relationship with your spouse?
15. Do you find the sexual relationship with your spouse satisfactory?
16. Has your sexual relationship been affected by your heart disease?
17. Has your sexual relationship ceased due to your heart disease?

*A marital stress score of 1 was assigned if the respondent answered "no" to items 1, 2, 5, 7, 8, 13, 14, and 15, and "yes" to the remaining items. Another score of 1 was assigned for each problem (infidelity, substance use/abuse, economic problems, health problems, or other unspecified problems) as shown by answers to questions 10 and 11. Total scores were obtained by summing all scores.

dures were considered to have occurred on the date of operation and classified with *International Classification of Diseases, Ninth Revision, Clinical Modification* (Operations on the Cardiovascular System)[29] codes 36.1 for coronary artery bypass grafting, and 36.0 for percutaneous transluminal coronary angioplasty. Data on revascularization procedures were validated using cardiac procedure registries in the respective hospitals. If multiple events of cardiac death, AMI, and need for revascularization occurred during the follow-up period, only the first event for each woman was considered.

Data Analyses

Analyses of marital stress were based on cohabiting women (n=187), and that of work stress on women both working and cohabiting at the time of examination (n=130). Further analyses of work stress were conducted among all working women (n=200), excluding the 92 women who were disabled, sick, or receiving an early pension. Distributions of discrete and continuous variables in relation to recurrent events were examined using the χ^2 test and analysis of variance, respectively. None of these variables violated the assumption of the normal distribution. Age-adjusted and multivariate Cox proportional hazard regression models controlling for potential confounders were constructed. Hazard ratios (HRs) from the Cox models are presented with their 95% confidence intervals (CIs). Linear trend for the effect of stress was assessed by computing the *P* value for trend. We used STATA 5.0 for the statistical analyses.[30]

Table 2. Distribution of the Baseline Characteristics (Discrete) in Relation to the Presence of Recurrent Events

Factor	Patients With Recurrent Events, No. (%) (n = 81)	Patients Without Recurrent Events, No. (%) (n = 211)	*P* Value*
Marital status†			
Single	4 (5)	20 (9)	.35
Widowed	3 (4)	15 (7)	
Divorced or separated	17 (21)	35 (17)	
Cohabiting	57 (70)	141 (67)	
Out of work at the time of baseline examination‡			
Yes	27 (33)	65 (31)	.67
No	54 (67)	146 (69)	
Educational attainment			
Mandatory	28 (54)	82 (63)	.25
High school + college/university	24 (46)	48 (37)	
Estrogen status§			
Present	17 (33)	58 (43)	.13
Absent	35 (67)	77 (57)	
Cigarette smoking			
Nonsmokers	15 (29)	44 (33)	.82
Previous smokers	25 (49)	66 (49)	
Current smokers	11 (22)	24 (18)	
Sedentary lifestyle	11 (21)	31 (23)	.73
History of hypertension	26 (50)	60 (48)	.81
Diagnosis at index event			
Acute myocardial infarction	26 (50)	42 (31)	.02
Angina pectoris	26 (50)	93 (69)	
Symptoms of heart failure‖	8 (15)	9 (7)	.06
Family history of coronary heart disease	18 (35)	44 (33)	.24
Diabetes mellitus	8 (15)	12 (9)	.20
Severity of angina pectoris symptoms			
No angina	9 (18)	27 (22)	.72
Mild	13 (25)	37 (30)	
Moderately severe	22 (43)	47 (38)	
Very severe	7 (14)	12 (10)	

*Probability value from χ^2 test.
†Marital and work status data based on all women (N = 292); remaining categories based on cohabiting women (n = 187).
‡Not working due to sickness, disabilities, early retirement due to sickness, or temporarily out of work or in other studies.
§Premenopausal and postmenopausal with hormone replacement therapy vs postmenopausal without.
‖Killip classification of 2 or more at the time of the index event.

RESULTS

Clinical Characteristics

The mean (SD) age at baseline examination was 55.8 (7.2) years. Of the 292 women, 64% were married or cohabiting with a male partner and 70% of the latter were working at the time of examination. The observed scores for marital stress ranged from 0 to 14 (median=3) and for work stress from 0.28 to 1.4 (median=0.73). There was no statistically significant association between marital stress and work stress (*P*=.59).

Among cohabiting women, there were 8 deaths, 5 from ischemic heart disease, 1 from cancer, 1 from cerebral hemorrhage, and 1 from pulmonary fibrosis; 11 patients had a recurrent AMI, 24 had percutaneous transluminal coronary angioplasty; and 22 had coronary artery bypass grafting during the follow-up period. A total of 52 patients either died of ischemic heart disease, had a recurrent AMI or a revascularization procedure, or a combination of these.

The distributions of baseline characteristics in women with and without recurrent events are presented in TABLE 2 and TABLE 3. Among clinical predictors, history of AMI, symptoms of congestive heart failure, and low high-density lipoprotein cholesterol levels were associated with poor prognosis. Women who had a recurrent coronary event reported more severe marital stress (mean [SD]=4.5 [3.2]) than those who did not (mean

[SD] = 3.4 [3.4]) (P = .007). Work stress scores did not differ between the 2 groups (P = .72).

Marital Stress and Prognosis

Marital status in itself was not associated with an increased risk of recurrent events (P = .35) (Table 2). However, cohabiting women who reported severe marital stress had a lower probability of remaining free from recurrent events, with a Kaplan-Meier estimate of 65% (95% CI, 53%-74%) compared with cohabiting women who reported mild or absent marital stress (Kaplan-Meier estimate of 85% [95% CI, 71%-92%]).

The age-adjusted risk of recurrent events in women with severe compared with mild or absent marital stress was 3.02 (95% CI, 1.37-6.65). This risk persisted after simultaneous adjustment for age, estrogen status, educational level, diagnosis at index event, symptoms of heart failure, diabetes mellitus, systolic blood pressure, smoking, triglyceride level, and high-density lipoprotein cholesterol level (HR, 2.92; 95% CI, 1.30-6.54) (TABLE 4). Further adjustment for severity of angina pectoris symptoms, sedentary lifestyle, history of hypertension, family history of CHD, body mass index, and total cholesterol level did not substantially alter these results. In a subgroup of 144 patients, additional control for ventricular dysfunction (ejection fraction <30%) from catherization during left ventricular angiography did not substantially alter the risk ratios associated with severe marital stress (HR, 2.91; 95% CI, 1.32-6.84). Separate analyses for cardiac death or AMI (n = 14) showed nonsignificant trends in the same direction (HR, 1.69; 95% CI, 0.47-6.08) associated with severe marital stress.

Work Stress and Prognosis

The age-adjusted risk of recurrent coronary events associated with severe compared with mild work stress was 1.69 (95% CI, 0.72-3.98) in cohabiting women (Table 4). Repeating these analyses in all working women (n = 200) yielded similar results (HR, 1.63; 95% CI, 0.82-3.34). Analyses of separate dimensions of work stress suggested that lack of control had a stronger but nonsignificant effect (HR, 1.62; 95% CI, 0.84-3.01) than did work demand (HR, 1.21; 95% CI, 0.63-2.32). Separate analyses of cardiac death or AMI as end points yielded similar results.

Table 3. Distribution of the Baseline Characteristics (Continuous) in Relation to the Presence of Recurrent Events*

Factor	Patients With Recurrent Events (n = 52)	Patients Without Recurrent Events (n = 135)	*P* Value
Marital stress scores	4.5 (3.2)	3.4 (3.4)	.007
Work stress scores	0.74 (0.17)	0.73 (0.25)	.72
Age, y	55.5 (7.8)	55.9 (7.0)	.92
Systolic blood pressure, mm Hg	122.0 (18.4)	120.2 (16.3)	.70
Body mass index, kg/m^2	26.8 (3.9)	27.2 (4.6)	.81
Triglycerides, mmol/L	2.0 (1.7)	1.8 (2.3)	.33
Total cholesterol, mmol/L	6.7 (1.3)	6.5 (1.2)	.41
High-density lipoprotein cholesterol, mmol/L	1.3 (.39)	1.5 (.45)	.01

*Data are expressed as mean (SD). To convert triglycerides from mmol/L to mg/dL, divide by 0.0113; to convert total cholesterol and high-density lipoprotein cholesterol from mmol/L to mg/dL, divide by 0.0259.

Table 4. Work Stress and Marital Stress in Relation to Prognosis in Women With Coronary Heart Disease

Factor	No. of Women	No. of Events	No. of Person-Years	Age-Adjusted Hazard Ratio (95% Confidence Interval)	Multivariate-Adjusted Hazard Ratio (95% Confidence Interval)*
Marital stress†					
Mild or absent	59	8	273.17	1	1
Moderate	51	17	210.28	2.68 (1.15-6.20)	2.79 (1.18-6.60)
Severe	77	27	300.08	3.02 (1.37-6.65)	2.92 (1.30-6.54)
P value				.007	.01
Work stress‡					
Mild or absent	32	7	150.88	1	1
Moderate	33	10	135.85	1.53 (0.58-4.02)	1.33 (0.43-4.10)
Severe	65	21	251.87	1.69 (0.72-3.98)	1.67 (0.64-4.32)
P value				.24	.27

*Adjusted for age, estrogen status, educational level, diagnosis at index event, symptoms of heart failure, systolic blood pressure, diabetes mellitus, smoking, trigylceride level, and high-density lipoprotein cholesterol level.
†Marital stress was defined as mild or absent (lowest quartile, scores 0-1), moderate (second quartile, scores 2-3), and severe (upper 2 quartiles, scores >3).
‡Work stress was defined as mild or absent (lowest quartile, scores 0-0.59), moderate (second quartile, scores 0.60-0.73), and severe (upper 2 quartiles, scores >0.73).

COMMENT

Marital Stress and Prognosis

In this 5-year prospective follow-up of women patients aged 30 to 65 years and admitted for an acute coronary event in Stockholm, we found the self-reported experience of marital stress at baseline to worsen prognosis, as manifested by cardiac death, AMI, or revascularization. Women with severe marital stress had a 3-fold increased risk of a new coronary event compared with women without marital stress. This association remained largely unchanged when controlling for possible confounders, including left ventricular dysfunction, poor health habits, and standard coronary risk factors. We have previously demonstrated a history of AMI and diabetes and a low high-density lipoprotein cholesterol level to be strong predictors of poor prognosis in the entire study group.[31]

Work Stress and Prognosis

In contrast to the findings for marital stress, there was no statistical evidence of work stress effect on recurrent coronary events for either cohabiting women or those living alone. Caution is needed in the interpretation as statistical power in the follow-up of cohabiting working

women patients (n=130) was diminished. However, analyses of all working women (n=200), including those living alone, did not alter the results. Among men, harmful effects of work stress on both incident and recurrent CHD have been systematically demonstrated.[8] Returning to a stressful work environment after AMI increased mortality risk in young males by a factor of 6.[9] Although work stress is a moderate predictor of incident CHD in women,[11,14,32,33] its prognostic impact has not been previously examined. Overall, the effects of family and work stress in combination, as well as women's multiple roles and role conflicts in relation to cardiovascular health, need further investigation.[32,34-39]

Marital Relations and Social Support

Women seem to perceive their relationships with their spouses as less supportive than men do. In a population-based study, men were more than twice as likely as women to name their spouse or partner as their primary provider of social support, whereas women were most likely to name a relative, usually female, as their primary supporter.[25] In addition, women were more likely to report that they give more than they receive in dyadic relationships.[19,40] In this study, 89% of the women said they were their spouse's closest confidant, whereas only 75% of the women patients named the spouse as their closest confidant. In fact, being married or cohabiting in itself did not provide any extra protection, but strain from a problematic spousal relationship significantly contributed to a poor prognosis over and above the effect of clinical predictors.

To our knowledge, the marital stress concept has not been applied in men, but a Swedish report suggests that men's mental stress is experienced at work and rarely in the family situation.[41]

Putative Mediators Between Marital Stress and CHD

That marital stress worsens prognosis in women with CHD is consistent with previous findings that lack of perceived social support in women is associated with increased risk of both first[42] and recurrent AMI.[16,43] It is also consistent with reports of an adverse effect on lipid levels and glucose metabolism in women.[44] Emotional strain and lack of social support in women patients may affect prognosis through 2 potential pathways. The first involves lack of adherence to healthier lifestyles and medical therapy.[45] The second pathway implicates the potentially damaging effects of negative emotional states and/or stress on neuroendocrine and physiological regulatory mechanisms.[46] In this regard, the link between social isolation and hostility[47,48] deserves mention as well as the links to hypercortisolemia[49] and high levels of circulating catecholamines,[50] β-adrenergic dysfunction,[51] decreased cardiac vagal tone,[52,53] and increased platelet reactivity.[54] Additionally, perceptions of dominance from a spouse during marital interactions have been associated with increased blood pressure reactivity.[55]

Sex differences in relation to physiological reactions as a result of marital discord, however, have been demonstrated.[35,56-58] For example, in one study, marital conflict was associated with higher levels of catecholamines, corticotropin, and growth hormone in women, but not in men.[56] In another study, increased cardiovascular reactivity was associated with hostility among men under conditions of high evaluative threat during marital interactions, while women showed such a reactivity only when disagreeing with hostile husbands.[48] Additionally, among women and men middle managers with identical job positions at the Volvo automobile company, a diurnal peak in urinary norepinephrine excretion rates occurred at about midday in both sexes, whereas women had an additional but higher peak in the evening, which was absent in men.[35]

Although this study did not examine acute trigger effects, emotional stressors are known to precipitate the onset of AMI in men and women.[57] As has been shown in men,[58] acute psychophysiological responses to stressors may also be exaggerated in chronically adapted women who are burdened with prolonged exposure to marital stress. It is conceivable that marital stress both triggers the acute onset of AMI and promotes enhanced progression of atherosclerosis, endothelial dysfunction, and plaque instability.

Limitations

The FemCorRisk Study was designed to evaluate effects of work- and family-related factors, and therefore included only women aged 65 years or younger. The results cannot be generalized to older women or to men. However, younger women are often underrepresented, particularly in studies of psychosocial factors and CHD, and recent findings suggest a poorer prognosis in this group of patients.[2]

The use of a composite end point (cardiac death, AMI, and revascularization) may impose problems of interpretation. Marital stress experiences could have increased the likelihood of revascularization, eg, stressed patients may have overemphasized their anginal symptoms. Due to the small numbers (n=14), separate analyses of recurrent MI and cardiac death were not conclusive, but trends were in the same direction as for composite end points.

A widely used measure of severe marital stress was not available in the Swedish language,[59] so we used a structured interview procedure that was previously examined for psychometric properties in Swedish women.[18,24] Marital stressors were generally major, concrete, and of a chronic nature. Infidelity, alcohol abuse, and physical and psychiatric illness of the spouse were the most commonly reported stressors.

Applying an interview method for marital stress and a survey method for work stress could produce spurious differences in effects. Patients could overemphasize their stress experiences in a personal interview compared with a written test. In a previous article, work stress based on a structured interview showed a similar effect on CHD risk as work stress assessed by the Karasek survey.[18] Furthermore, expert ratings and

self-reports of work stress have been shown to be highly correlated and to have similar effects on CHD in men and women.[26]

Studying work stress is often hampered by the selection of healthier or socially and economically better equipped women into the labor force. In the United States about two thirds of eligible women are working outside the home,[60,61] whereas in Sweden practically all women are employed outside the home and to the same extent as men.[62] In our total study group of 600 women from Stockholm, the capital of Sweden, only 2 full-time women homemakers were found. Thus, a comparison of work stress and marital stress was particularly relevant in these women.

Finally, our results may be biased because return to work may have been delayed by the onset of CHD. However, the proportion of women who were out of work due to disabilities or early retirement at the time of examination (3-6 months after hospitalization) did not differ between patients (32%) and controls (28%).[31] Furthermore, about 90% of these women had been in their current positions for more than 10 years and consequently returned to the same job after AMI.

In conclusion, our results suggest that stressful experience from marital relationships may seriously affect prognosis in women with CHD, whereas living alone without a partner had no effect. Further research is needed to examine the reproducibility and the pathogenic pathways of these novel findings.

Funding/Support: This work was supported by grant HL45785 from the US National Institutes of Health, by grant 98-0336 from the Swedish Council for Work Life Research, by grants from the Swedish Medical Research Council and the Swedish Labor Market Insurance Company, and the Swedish Heart and Lung Foundation.

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Medicine is not merely a science but an art. The character of the physician may act more powerfully upon the patient than the drugs employed.

—Philippus Aureolus Paracelsus (c 1493-1541)