ORIGINAL ARTICLE

Gender-specific association of psychological distress with cardiovascular risk scores

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Abstract

Objective. To examine the gender differences in the association of psychological distress with cardiovascular disease (CVD) risk scores using two different CVD risk assessment models. **Design and setting.** A cross-sectional, population-based study from 1997 to 1998 in Pieksämäki, Finland. **Subjects.** A population sample of 899 (399 male and 500 female) middle-aged subjects. **Main outcome measures.** The 10-year risk for CVD events was calculated using the European SCORE model and the Framingham CVD risk prediction model. Psychological distress was measured using the 12-item General Health Questionnaire (GHQ-12). Study subjects were allocated into three groups according to their global GHQ-12 -scores: 0 points, 1–2 points, and 3–12 points. **Results.** Psychological distress was associated with higher mean CVD risk scores in men. Men in the highest GHQ group (3–12 points) had significantly higher mean European CVD risk score (3.6 [SD 3.3]) compared with men in the lowest group (0 points) (2.5 [SD 2.6]), the difference being 1.1 (95% CI 0.4 to 1.9). The p-value for linearity between the three GHQ groups was 0.003. The Framingham CVD risk prediction model yielded similar results: 15.7 (SD 10.2) vs. 12.3 (SD 9.6), the difference 3.4 (95% CI 1.0 to 6.0) and p-value for linearity 0.008. No significant association was observed in women. **Conclusion.** A gender-specific association was found between psychological distress and cardiovascular risk scores. These results highlight the importance of identifying men with psychological distress when assessing CVD risk.

Key Words: Cardiovascular disease, Framingham, gender difference, general health questionnaire, psychological distress, SCORE

Cardiovascular disease (CVD) is the leading cause of death worldwide, and global cardiovascular deaths are projected to increase from 16.7 million in 2002 to 23.3 million in 2030 [1], although several cardiovascular risk factors have improved at population level, at least in some Western countries [2]. The relationship between various psychological factors and CVD has been investigated extensively in the last decade [3–5]. In a review by Everson-Rose et al. [4], negative emotional states, chronic psychosocial stressors, and social factors were all associated with an increased risk of cardiovascular morbidity and mortality. There are, however, a limited number of studies among women in this field:

Denollet et al. [6] reported a significant association of CVD with anxiety and Rosengren et al. [7] with stress, locus of control and depression. The General Health Questionnaire (GHQ) [8,9] is one of the most widely used and studied indicators of psychological distress. The shortest 12-item version (GHQ-12) has gained acceptance as a screening instrument because of its space-saving properties and good validity [10–12]. The questionnaire includes questions regarding the general level of happiness, experience of depressive and anxiety symptoms, and sleep disturbance over the last four weeks. Several studies have shown the association of psychological distress with cardiovascular mortality using

Psychological distress is associated with cardiovascular risk, but this association seems to be weaker and less studied among women.

- Men with high psychological distress had 28–44% higher cardiovascular risk scores compared to men with low distress.
- Among women, psychological distress was not associated with cardiovascular risk scores.
- GPs should consider screening for psychological distress when using CVD risk assessment tools in men.

the GHQ-12 [13,14] and GHQ-30 [15–18]. Some of these studies, however, did not include women [16–18], or men and women were analysed as one group [13]. Stansfeld et al. [15] reported a significant association in women between psychological distress (GHQ-30) and self-reported coronary heart disease. Using the GHQ-12, Hamer et al. [14] reported similar effects of distress on CVD among men and women, but the statistical significance was not reported. Thus, the existence of a possible gender difference is yet to be fully elucidated.

The total risk for CVD events can be assessed by using multivariable risk prediction algorithms. Two of the most widely used risk assessment tools are the European SCORE model [19], which assesses the 10-year risk for fatal cardiovascular events, and the Framingham CVD risk prediction model [20], which assesses the 10-year risk for any CVD events (fatal or non-fatal). To our knowledge, no research has been done thus far on the association between GHQ-12 and CVD risk scores. The aim of this study was to establish whether such an association exists in both men and women.

Material and methods

Subjects

The study population consisted of middle-aged, Caucasian subjects ($n = 1294$) born in 1942, 1947, 1952, 1957, and 1962 in Pieksämäki, Finland. The age groups were recruited from the local population records. No exclusion criteria were applied. Altogether, 923 (411 men and 512 women) of 1294 subjects (71.3%) participated in a cross-sectional study from 1997 to 1998, which included clinical and laboratory measurements performed by two trained nurses, and completing a standard questionnaire with questions regarding any chronic diseases, medication, smoking, and psychological distress. Of the

original 923 subjects, 21 were excluded from the analyses because of incomplete measurements for calculating the CVD risk and additional three because of lacking data on psychological distress. Thus, the actual study sample consisted of 899 subjects.

Clinical and laboratory methods

The anthropometric and laboratory sampling was carried out as described previously [21]. The risk for CVD events was calculated using (1) the European SCORE model [19] with gender, age, smoking, systolic blood pressure, and total cholesterol as variables, and (2) the Framingham CVD risk prediction model by using the direct application of the Cox model [20]. This model includes gender, age, total cholesterol, HDL cholesterol, systolic blood pressure, anti-hypertensive medication, smoking, and diabetes as variables.

Psychological distress was measured using the 12-item version of the General Health Questionnaire (GHQ-12). The rating method of the four-point response scale was 0–0–1–1 (presence of symptom: not at all = 0, same as usual = 0, more than usual = 1, much more than usual = 1) as in many previous studies [10,13,14]. The points were summed to a global score ranging from 0 to 12. For illustrative purposes, study subjects were in further analysis allocated into three groups according to their scores (0 points, 1–2 points, and 3–12 points) in order to get as equal-sized groups as possible.

Statistical analyses

Results are expressed as mean with standard deviation (SD). The 95% confidence intervals (95% CI) were obtained by bias-corrected bootstrapping (5000 replications). Statistical comparison between the genders was performed by t-test, bootstrap-type t-test (5000 replications), permutation test, or chi-squared test, when appropriate. Statistical significance for the hypotheses of linearity was evaluated by a bootstrap-type ANCOVA. Correlation coefficients were calculated by the Pearson method with bias-corrected bootstrap confidence intervals.

Results

Table I gives the baseline characteristics of the 899 (399 male and 500 female) subjects. Age and BMI distributions were similar in both genders. There were more current smokers among men than women and men had higher systolic and diastolic blood pressure. The levels of total cholesterol, triglycerides, and fasting plasma glucose were significantly lower in

Table I. Demographic, clinical and biochemical characteristics and use of medication of the study subjects.

Characteristics	Male (n=399)	Female (n=500)	p-value
Demographic:			
Age, mean (SD), years	46 (6)	46 (6)	0.61
Body mass index, mean (SD), kg/m ²	26.6 (3.7)	26.4 (5.2)	0.42
Smoking, n (%)	136 (34)	112 (22)	<0.001
Clinical:			
Blood pressure, mean (SD), mmHg:			
Systolic	137 (17)	131 (18)	<0.001
Diastolic	84 (10)	80 (10)	<0.001
Biochemical:			
Total cholesterol, mean (SD), mmol/l	5.8 (1.1)	5.7 (1.0)	0.02
HDL cholesterol, mean (SD), mmol/l	1.3 (0.3)	1.5 (0.3)	<0.001
Total triglycerides, mean (SD), mmol/l	1.7 (1.3)	1.2 (0.6)	<0.001
Fasting plasma glucose, mean (SD), mmol/l	6.0 (0.9)	5.7 (0.6)	<0.001
Medication, n (%)			
Anti-hypertensive medication	41 (10)	43 (9)	0.39
Cholesterol-lowering medication	12 (3)	6 (1)	0.06
Anti-diabetic medication	32 (8)	26 (5)	0.09

women, whereas mean HDL cholesterol level was higher. There was no gender difference in the use of medication.

Initial analyses of psychological distress were calculated using the GHQ score as a continuous variable. The mean GHQ score for women was 1.9 (SD 3.1) and for men 1.5 (SD 2.5), the difference was 0.5 (95% CI: 0.1 to 0.8) ($p = 0.014$; after age-adjustment $p = 0.011$). An interaction effect between gender and psychological distress was identified regarding both European CVD score ($p < 0.001$) and Framingham CVD risk ($p = 0.013$), justifying a further subgroup analysis by gender. In men, a significant correlation was identified between GHQ and both European CVD score (0.19 [95% CI 0.08 to 0.32]) and Framingham CVD risk (0.15 [CI 0.05 to 0.26]). In women, correlations were not significant (0.09 [95% CI -0.01 to 0.20] and 0.06 [CI -0.05 to 0.18], respectively).

For illustrative purposes, the study subjects were further allocated into three groups according to their GHQ score: 224 (56%) men and 273 (55%) women scored 0 points, 92 (23%) men and 96 (19%) women scored 1–2 points, and 83 (21%) men and 131 (26%) women scored 3–12 points.

The association of GHQ with both the European CVD risk score and the Framingham CVD risk divided by gender is illustrated in Figure 1. We identified a relationship of psychological distress with cardiovascular risk scores in men. Those in the highest group (3–12 points) had significantly higher mean European CVD risk score (3.6 [SD 3.3]) compared with men in the lowest group (0 points) (2.5 [SD 2.6]). The difference between the groups was 1.1 (95% CI 0.4 to 1.9). The p -value for linearity between the three GHQ groups was 0.003. The Framingham CVD risk prediction model yielded similar results:

15.7 (SD 10.2) for the highest and 12.3 (SD 9.6) for the lowest GHQ group, the difference being 3.4 (95% CI 1.0 to 6.0). The p -value for linearity was 0.008.

In women, no significant association was observed. The mean European CVD risk scores for the highest and the lowest GHQ groups were 0.7 (SD 0.8) and 0.5 (SD 0.6), respectively. The difference between the groups was 0.1 (95% CI -0.1 to 0.3) and the p -value for linearity between the three GHQ groups was 0.64. The mean Framingham CVD risk scores for women were 6.7 (SD 6.4) vs. 6.2 (SD 5.4), the difference being 0.5 (95% CI -1.0 to 1.8). The p -value for linearity was 0.45.

Figure 1. Gender-specific association of GHQ with European CVD score and Framingham CVD risk. Whiskers show 95% confidence intervals.

Discussion

The novel finding in this study was the gender-specific association of psychological distress with the CVD risk scores. Among men, significant psychological distress was associated with increased mean European and Framingham CVD risk scores. No such association was observed in women.

Previous literature on psychological factors and CVD among women is rather limited. Denollet et al. [6] reported a significant association of CVD with anxiety and Rosengren et al. [7] with stress, locus of control, and depression. However, the existence of a possible gender difference in CVD risk, when measuring general psychological distress, has not been properly studied. Robinson et al. [13] reported that high levels of psychological distress (GHQ-12) almost doubled the risk of death for ischaemic heart disease, but men and women were analysed as one group. Some other studies linking GHQ with CVD mortality included only men as study subjects [16–18]. Only two studies have reported results stratified by gender. Stansfeld et al. [15] reported also in women a significant association of psychological distress (GHQ-30) with self-reported coronary heart disease. Using the GHQ-12, Hamer et al. [14] reported similar effects of psychological distress on CVD among men and women, but the statistical significance was not reported.

In this study, the risk scores among women were rather low and showed only little variance as compared with men. As a consequence, correlations as strong as those found among men may not be expected. However, we find it unlikely that this could fully explain the observed gender-specific association of GHQ-12 with CVD. The number of female participants in the sample was higher, which should provide enough statistical strength to detect a significant association also among women if there were one.

Why does the association between psychological distress and CVD risk appear to be more consistent in men than in women? There is an exponential increase in cardiac incidents in women around the age of 55–60 years [22,23]. In the current study, subjects were between the ages of 35 and 55 years, making it possible that the association reported in men becomes significant later in women. Alternatively, women may cope better with psychological distress. Further research is needed to elucidate whether psychological distress causes gender-specific changes in health behavior, e.g. smoking initiation or lack of physical activity.

The relationship between psychological distress and CVD risk is multi-factorial, as biological, envi-

ronmental, social, and behavioural pathways all play important roles. The relative contribution of different mediating variables has been studied to some extent [14,15,24]. Considering biologic pathways, Everson-Rose et al. [4] suggested four main mechanisms through which psychological factors may cause CVD mortality in their review: (1) activation of the hypothalamic-pituitary-adrenal axis and the autonomic nervous system, (2) serotonergic dysfunction, (3) secretion of pro-inflammatory cytokines, and (4) platelet activation. Further research is needed to determine the roles of different environmental, social, behavioural, and biologic pathways in explaining the gender-specific association of psychological distress with CVD risk scores observed in the current study.

Although GHQ-12 has wide acceptance as a screening instrument [10,12], there is debate about the efficacy of screening and case detection for psychological factors in general practice. When compared with normal circumstances without screening, GHQ-12 used in an ordinary general practice environment was able to detect one additional patient with a real diagnostic psychological problem for every five patients screened, when used with infrequently seen patients, but screening of well-known patients provided fewer additional cases [25]. This implies that routine screening for psychological distress should be carefully targeted. The results of our study have also some important implications in this respect. Psychological distress is strongly associated with cardiovascular risk scores in men and should be taken into account (e.g. by using the GHQ-12) when using CVD risk assessment tools. In addition, new CVD risk evaluation tools for GPs, which would also assess psychological factors, may be worth developing in the future.

The strength of this study is a broad, population-based sampling from five age groups in a geographically defined area. Some limitations of the present study warrant consideration. The study group was relative small and genetically homogeneous, which limits the possibility to generalize the results. Additionally, the present study was cross-sectional and lacked actual mortality and morbidity data. Thus, the direction of causation between psychological distress and CVD risk remains unclear: various biological and behavioural factors associated with psychological distress may increase CVD risk, but variables included in the CVD risk scores – such as age, smoking, and diabetes – may also be causally related to future psychological distress. Gender-stratified prospective studies on psychological distress and CVD are needed before interpreting further the gender specificity observed in this study.

Ethical approval

The ethics committee of Kuopio University approved this study, and participants provided informed written consent.

Source of funding and conflict of interests

There was no external source of funding. The authors have no conflicts of interests to declare related to this paper.

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