The Relationship of Biological and Psychological Risk Factors of Cardiovascular Disorders in a Large-scale National Representative Community Survey

György Purebl, MD; Emma Birkás; Csilla Csoboth, MD, PhD; Irena Szumska, PhD; Máriá S. Kopp, MD, PhD

A large-scale national representative community survey of 11,122 persons aged more than 35 years included the investigation of the coincidence of depressive symptoms, vital exhaustion, cardiovascular disorders, stroke, and myocardial infarction. A total of 20.3% of the survey participants reported having experienced a cardiovascular disorder (CVD). Of the subjects reporting a CVD, 52.1% exhibited depressive symptoms (22.0% subthreshold depressive symptoms, 30.1% clinical depression), and 69.7% exhibited vital exhaustion. The authors investigated 3 cardiovascular subgroups: (1) subjects having experienced a myocardial infarction (MI), (2) subjects having experienced stroke, and (3) subjects with a CVD but no experience of either an MI or a stroke. The frequency and severity of depressive symptoms did not differ significantly in the 3 subgroups. CVD subjects with no MI or stroke had almost as high frequencies of depressive symptoms and vital exhaustion as patients who experienced stroke or MI. The strength of relationships between these psychological variables and CVDs do not differ significantly from the relationships between hypertension or diabetes and CVDs. Depressive symptoms and increased vital exhaustion have exceptionally high comorbidity with CVDs. The authors detected the same high comorbidity among patients with a milder CVD and without stroke or MI. The assessment and management of depressive symptoms and vital exhaustion should be routine procedure in clinical cardiology.

Index Terms: CVD, depression, stroke, vital exhaustion

Cardiovascular disorders (CVDs) are major public health problems worldwide. Community-based prevention of CVDs is crucial in efforts to improve the morbidity status of populations. Community-based prevention requires a knowledge of behavioral and lifestyle variables as well as the underlying psychological mechanisms. Many psychological factors have been suspected as risk factors in CVDs, and there is a substantial body of research demonstrating the contribution of psychological factors to cardiovascular morbidity and mortality. Increasing evidence supports the possible role of negative emotional states, distress, and attitudes such as hostility.1,2 Depressive symptoms are the most consistently documented psychological factors in coronary artery disease (CAD).3-7 Coronary patients have an approximately three-
fold higher frequency of depression than the general population. Depressive symptoms are predictors of negative cardiac events in the presence of CVDs and increase the risk of future coronary heart disease among healthy individuals. Some studies have suggested that, as well as clinically significant major depression, mild to moderate depressive symptoms not fulfilling the diagnostic criteria of major depression may also carry increased risk of a cardiac event. In a series of studies, Frasure-Smith, Léspérance, and colleagues demonstrated that patients scoring 10 or more points on the Beck Depression Inventory (BDI), indicating mild to moderate subthreshold depression symptoms, have a higher rate of further negative cardiac events (e.g., non-fatal MI and cardiac death). One of their studies found that cardiac patients with 10 or more BDI points have almost as high a mortality rate as cardiac patients with clinical major depression. However, another study demonstrated the different nature of mild and more severe depressive symptoms. Although an improvement in mild depressive symptoms was associated with less cardiac mortality, high initial depression scores were associated with worse long-term outcome regardless of symptom changes. Other researchers found a positive correlation between severity of depressive symptoms and cardiovascular risk. Comorbidity between depressive symptoms and MI is very common. Some studies found major depression after MI of 16%-23% and subthreshold (“minor”) depressive symptoms of 15%-25%. A more recent study using the BDI found 23.5% with mild subthreshold depression (BDI 10–18) and only 8.8% with moderate or severe depression. However the majority of large-scale studies focus on MI, and there are few data on coronary artery disease (CAD) patients without histories of MI.

The investigation of depression and CVDs in an interactive framework is of major importance. According to the World Health Organization Global Burden of Disease Survey, these 2 disorders are estimated as the top underlying causes of disability-adjusted life years, and there is an emerging need for understanding all aspects of the relationship between depression and CAD.

Exhaustion could be another cardiovascular risk factor. Cole et al found exhaustion to be associated with a twofold increase in the risk of CAD. Vital exhaustion focuses on a triad of symptoms: (1) fatigue, (2) irritability, and (3) demoralized feelings. Some studies suggest that vital exhaustion is separate from depression as a cardiovascular risk factor. On the other hand, Wojciechowski et al demonstrated a strong (virtually identical) correlation between vital exhaustion and 2 different depression questionnaires and computed the separate conceptual identity of these entities. In an earlier Hungarian study, Kopp et al also found a highly significant correlation and a substantial common variance between depression and vital exhaustion, but also found important discriminating factors (level of disability, different behavioral factors, etc.). In the more recent study of Kudielka et al, vital exhaustion and depressive symptoms showed similar common variance to the previously mentioned study of Kopp et al, implying their interrelationship as well their differing entities. A large-scale study of depression and vital exhaustion in a common arrangement is needed to reveal the different roles of these entities. Research on exhaustion, depressive symptoms, and cardiovascular morbidity is especially important in the Central Eastern European countries, where there is a dramatic increase in reported cardiovascular morbidity and mortality.

Our aim in this study was to investigate the relationships between depressive symptomatology and vital exhaustion in their association with CVDs. Another aim was to establish whether patients with MI or stroke display any differences from those who have not experienced stroke or MI but have been treated for CVDs. This question was not addressed in the earlier Hungarian survey, and the majority of international studies focus on patients who have already had an MI.

**METHOD**

**Procedure**

We constructed the sample from a national representative stratified study (Hungarostudy 2002). The survey represented the Hungarian population by gender and age distribution (aged ≥ 18 years) and 150 geographical subregions. The subjects in the stratified sample were randomly selected from the database of Statistics Hungary 2001 (Ministry of Internal Affairs). A total of 12,643 participants completed a comprehensive questionnaire battery during a home interview by trained interviewers. The general aim of the Hungarostudy was to assess interrelationships between health, psychological factors, and socioeconomic background in a representative cross-sectional sample. The general refusal rate was 17.7%, although there were differences by settlement type; large cities and urban areas had higher refusal rates, the highest being in the capital, Budapest (30.0%). The highest estimated stratification error was 2.2% in men aged 18–39 years, within the limits of the permitted statistical deviation. The Hungarostudy researchers surveyed all settlements with a population greater than 10,000, and drew the rest of the sample from randomly selected smaller towns and villages. The age cohort selected for this analysis was 35 years and over (n = 11,122). The whole sample consisted of men and women aged ≥ 18 years.
years. We selected only those aged ≥ 35 years for our analysis. We measured the history of treatment for CVD, stroke, and MI. We also asked about treatment for hypertension and diabetes mellitus to compare the strength of association between coronary heart disease, depression, vital exhaustion, and these 2 traditional risk factors.

Instruments
We constructed a comprehensive 700-item test battery within the framework of the survey. We drew the questions for this study from the following scales and questionnaires:

  Shortened Beck Depression Inventory. This 9-item Hungarian adaptation of the BDI showed a strong correlation with the full 21-item version and proved a useful and beneficial device for screening depressive symptoms in former representative population surveys.

  Hungarian Adaptation of the Maastricht Vital Exhaustion Questionnaire. This shortened version of the original 21-item questionnaire developed by Appels et al comprises those 9 items that were most representative of the construct. This shortened version has excellent psychometric properties and was tested in a subsequent representative survey.

Identification of Individuals with CVD, Stroke, MI, Hypertension, and Diabetes
We asked the subjects to answer the following questions concerning cardiovascular and cerebrovascular morbidity:

1. Have you ever been treated because of cardiovascular disease?
2. Have you ever been treated for stroke?
3. Have you ever been treated for myocardial infarction?
4. Have you ever been treated for hypertension?
5. Have you ever been treated for diabetes mellitus?

The participants scored the answers according to a 4-point yes or no answer scale: 1 = never, 2 = once I was treated for ... 3 = I was involved in outpatient treatment within the past year, and 4 = I was hospitalized within the past year.

We considered individuals as having these disorders if they answered yes for the second, third, or fourth answers to these questions, because these diseases are chronic conditions. We did not examine age of onset and severity. We set up 3 CVD groups for analysis: (1) subjects with stroke, (2) subjects with MI, and (3) subjects who have CVD but neither stroke nor MI.

Statistical Analysis
We used the SPSS 8.0 statistical program package (SPSS, Inc, Chicago, IL) for analysis. To assess the interactions, we transformed continuous variables into categorical variables. For the shortened version of BDI, we used the cut-off values recommended by the literature of the Hungarian version (10-18 = mild subthreshold depressive symptoms, ≥ 19 = clinically significant depressive symptoms). For vital exhaustion, we constructed 2 categories with the cutoff of median (mean = 2.58, median = 2.0), as in a previous community survey. We considered p values ≤ .05 to be statistically significant. We administered the chi-square test to assess the odds ratio (OR) for CVDs associated with depressive symptoms. We used forward conditional logistic regression analysis with a .05 classification cutoff and .05-.1 probabilities for stepwise for assessing the strength of association among cardiovascular morbidity, depression, vital exhaustion, hypertension, and diabetes with the interpretation of Exp(B) with 95% confidence intervals (CI).

RESULTS

Total Sample
In the total sample, (n = 1,749) we found a prevalence rate of 20.3% for CVDs, as shown in Table 1.

Women had a significantly higher prevalence (OR = 1.44, 95% confidence interval [CI] = 1.30–1.59) of CVDs. The prevalence of stroke was equal for both sexes (5.8%, n = 501). The overall prevalence rate for MI was 4.5% percent (n = 386). Men demonstrated significantly higher frequencies of MI (OR = 1.93, CI = 1.57–2.37). The frequency of increased vital exhaustion was 49.1% (n = 3,969) with a significantly higher female contribution (OR = 1.76, CI = 1.63–1.90). The prevalence rate in both depression categories was 17.1% (subthreshold n = 1,487, clinical n = 1,489), slightly but significantly higher for women in both categories (subthreshold, OR = 1.26, CI = 1.10–1.40; clinical, OR = 1.31, CI = 1.18–1.47).

Depression and vital exhaustion as continuous variables show significant moderate correlation (Pearson's r = .567) and a substantial common variance (r² = .448). Depression and vital exhaustion categories demonstrate moderate correlation (Φ = .495, p = .000).

Cardiovascular Subgroup
The overall frequency of subthreshold depressive symptoms was 22.0% in the total cardiovascular subgroup, almost the same (22.3%) among the cardiovascular patients without MI or stroke, 20.5% among MI patients, and 22.6% among stroke patients. We did not find significant gender differences except among stroke patients (for women, OR = 1.78, CI = 1.10–2.93). The prevalence rates of depressive symptoms for men and women in the different CVD subgroups are presented in Table 2.
The frequency of clinical depression (moderate or severe depressive symptoms) was 30.1% in the cardiovascular subgroup as a whole, 27.4% for cardiovascular patients with no MI or stroke, 30.9% for MI patients, and 37.6% for stroke patients. We did not detect any significant gender differences in either the cardiovascular group as a whole or the 3 subgroups.

Increased vital exhaustion was frequent in the cardiovascular group (69.7%) and all subgroups (67.1% for the subgroup with no MI or stroke, 67.4% for MI patients, and 74.6% for stroke patients). We found significant gender differences in the cardiovascular group as a whole (OR = 1.41, CI = 1.13–1.76) and among patients with no consequences (OR = 1.55, CI = 1.22–1.97), appeared in the MI subgroup as a tendency (OR = 1.59, CI = 0.99–2.56, \( \Phi = 0.051 \)) and were insignificant in the stroke subgroup.

Interrelationship Among Psychological Risk Factors, Hypertension, and Diabetes

We examined the impact of depression and vital exhaustion on cardiovascular morbidity by logistic regression analysis and compared them with the impact of the well-documented traditional risk factors of hypertension and diabetes. The relationships among psychosocial variables, cardiovascular subgroups, hypertension, and diabetes are presented in Figure 1.

The nonstroke, non-MI cardiovascular subgroup showed a significant relationship to all variables included in the analysis. Hypertension, \( \text{exp}(B) = 1.82, \text{CI} = 1.60–2.07 \), and vital exhaustion, \( \text{exp}(B) = 1.75, \text{CI} = 1.52–2.03 \), demonstrated the strongest associations and diabetes the weakest, \( \text{exp}(B) = 1.27, \text{CI} = 1.04–1.54 \), but there were no significant differences in strength of association.

### TABLE 1. Gender-Related Prevalence Rates for Cardiovascular Disorders, Depression, and Vital Exhaustion

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Women</th>
<th></th>
<th>Men</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Cardiovascular disease total</td>
<td>1,093</td>
<td>22.4</td>
<td>654</td>
<td>17.5</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>151</td>
<td>3.1</td>
<td>233</td>
<td>6.3</td>
</tr>
<tr>
<td>Stroke</td>
<td>285</td>
<td>5.8</td>
<td>216</td>
<td>5.8</td>
</tr>
<tr>
<td>Subthreshold depressive symptoms</td>
<td>885</td>
<td>18.0</td>
<td>602</td>
<td>15.9</td>
</tr>
<tr>
<td>Clinical depression</td>
<td>905</td>
<td>18.4</td>
<td>581</td>
<td>15.3</td>
</tr>
<tr>
<td>Vital exhaustion</td>
<td>2,512</td>
<td>55.0</td>
<td>1,452</td>
<td>41.4</td>
</tr>
</tbody>
</table>

### TABLE 2. Prevalence of Depressive Symptoms and Vital Exhaustion in Cardiovascular Disorders (CVDs)

<table>
<thead>
<tr>
<th>CVDs</th>
<th>Women</th>
<th></th>
<th>Men</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subthreshold depression</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Total</td>
<td>241</td>
<td>22.7</td>
<td>327</td>
<td>30.8</td>
</tr>
<tr>
<td>CVDs with no consequences</td>
<td>206</td>
<td>22.9</td>
<td>253</td>
<td>28.1</td>
</tr>
<tr>
<td>MI</td>
<td>25</td>
<td>17.4</td>
<td>48</td>
<td>33.3</td>
</tr>
<tr>
<td>Stroke</td>
<td>69</td>
<td>25.6</td>
<td>106</td>
<td>39.3</td>
</tr>
<tr>
<td></td>
<td>Clinical depression</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Total</td>
<td>133</td>
<td>20.9</td>
<td>183</td>
<td>28.8</td>
</tr>
<tr>
<td>CVDs with no consequences</td>
<td>104</td>
<td>21.2</td>
<td>127</td>
<td>25.9</td>
</tr>
<tr>
<td>MI</td>
<td>52</td>
<td>22.4</td>
<td>68</td>
<td>29.3</td>
</tr>
<tr>
<td>Stroke</td>
<td>38</td>
<td>18.6</td>
<td>72</td>
<td>35.3</td>
</tr>
</tbody>
</table>

*Note.* Total = all persons with cardiovascular disorders; CVDs with no consequences = persons with cardiovascular disorders but not stroke or myocardial infarction; MI = persons with myocardial infarction.
We found similar results in the subgroup of patients who had experienced MI. All variables demonstrated significant association with the subgroup except subthreshold depression, exp(B) = 1.23, CI = 0.90–1.67. We found the weakest relationship with vital exhaustion, exp(B) = 1.51, CI = 1.15–1.98, and the strongest with hypertension, exp(B) = 1.84, CI = 1.46–2.31, but the differences in the strength of associations were not significant.

The picture was little different in the stroke subgroup. In our study diabetes did not display significant association with stroke. The strongest relationship was with hypertension, exp(B) = 3.16, OR = 2.57–3.89, and was significantly stronger than those with vital exhaustion and subthreshold depression, but not significantly stronger than that with clinical depression, exp(B) = 2.2, CI = 1.71–2.86. The strength of associations among depression categories and vital exhaustion did not differ significantly.

**COMMENT**

The exceptionally high prevalence rates of CVD—approximately one fifth of the Hungarian population over the age of 35 have been treated for CVDs—are similar to the results of previous Hungarian studies and other data from Central Eastern Europe. Approximately half of the population with cardiovascular problems exhibit depressive symptoms. In the cardiovascular subgroup without MI or stroke, the proportion of mild subthreshold and clinical depressive states are approximately equal, and in the MI subgroup the overall frequency of depressive symptoms was similar, with a slightly higher proportion of clinically depressive cases. In the stroke subgroup, women have a higher frequency of overall depressive symptoms (64.9%), made up mostly of clinical depression (39.3%). The overall frequency of depressive symptoms among men in this subgroup is 53.9%, made up mostly of clinical depression (35.3%).

Gender differences emerged for both depression categories in the total sample, but not significantly among cardiovascular patients except for mild subthreshold depressive symptoms in the stroke subgroup.

Our findings indicate exceptionally high comorbidity between depressive symptoms and cardiovascular disorders. It is surprising that the comorbidity among cardiovascular cases with no MI or stroke was as high as in the subgroups with MI or stroke. This may suggest that there are factors other than disease severity and negative consequences affecting the strength of the relationship between depressive symptomatology and CVDs. Other complex connections involving the psychophysiological mechanisms of stress response and depressive symptomatology could produce circular interactions with cardiovascular pathophysiology. Further research is needed to clarify the nature of CVD

![Figure 1. Relationships among psychological variables. CVD = Cardiovascular disease.](image)
RISK FACTORS OF CARDIOVASCULAR DISORDER

and the functional elements of these interactions and their impact on the course of CVDs and depression.

The majority of cardiovascular patients suffer from vital exhaustion (76.1%-74.6% in the different subgroups). Gender differences are significant but decrease with severity: they show up clearly in the non-MI–nonstroke subgroup, but are only a tendency in the MI group, and are not significant at all in the stroke subgroup.

Depression and vital exhaustion showed moderate correlation. We found the gender differences significantly higher in the total sample than in the depression categories. The investigation of depression categories and vital exhaustion in the same multivariate arrangement revealed that both depression and vital exhaustion have significant independent associations with cardiovascular morbidity. Although these results lend support to the concept of vital exhaustion as an independent factor, they still show that it has a substantial common variance with depression. Further investigations are needed to reveal the nature of the relationship between vital exhaustion and depressive symptoms.

In all the cardiovascular subgroups, cardiovascular morbidity appeared to have a similarly strong association with the psychological variables as with hypertension and diabetes. The associations were of similar strength throughout, except for hypertension in the stroke subgroup. The psychological characteristics are thus equally associated with cardiovascular morbidity as the 2 traditionally examined risk factors.

Limitations

Our survey has some important limitations. First, cross-sectional sampling could not reveal the directions of the interactions and imposed severe limitations concerning causality. Second, disease categories are based on self-reports, and no information was available about the onset and severity of disease.

Our data clearly demonstrate that depressive symptoms and vital exhaustion are very common problems among cardiovascular patients. In view of the high prevalence of CVDs and the increasing importance of both depression and cardiovascular problems projected for the near future, we suggest that the screening and treatment of depression could be equally important in clinical cardiology as the management of hypertension, lipid and cholesterol abnormalities, and behavioral factors, such as diet and exercise.

ACKNOWLEDGMENTS

The national representative study reported in this article is supported by the United Nations Development Program (UNDP) project No. HUN/00/002/A/01/99, the National Research Fund (OTKA) projects OTKA TS-40889(2002), and TS 049785(2004) Scientific School Grants NKFP 1/002/2001 and NKFP 16/020/2004.

NOTE

For comment or further information, please address correspondence to György Purebl, MD, Institute of Behavioural Sciences, Semmelweis University, Nagyvárad tér 4, H-1089 Budapest, Hungary (e-mail: purgyor@net.sote.hu).

REFERENCES
