Co-occurrence of Metabolic Syndrome With Depression and Anxiety in Young Adults: The Northern Finland 1966 Birth Cohort Study

Anne Herva, MD, Pirkko Rasanen, MD, PhD, Jouko Miettunen, PhD, Markku Timonen, MD, PhD, Kristian Laksy, MD, PhD, Juha Veijola, MD, PhD, Jaana Laitinen, PhD, Aimo Ruokonen, MD, PhD, and Matti Joukamaa, MD, PhD

Objective: Only a few studies have dealt with the association of metabolic syndrome with depression and anxiety. We studied whether metabolic syndrome and its components are associated with depressive and anxiety symptoms in a young adult population cohort. **Methods:** This study forms part of the Northern Finland 1966 Birth Cohort Study. The study sample consists of 5,698 members of the cohort who participated in the field study in 1997 to 1998. Metabolic syndrome was defined according to the five criteria of the National Cholesterol Education Program. Depressive and anxiety symptoms were defined by the Hopkins Symptom Checklist-25 questionnaire. **Results:** Metabolic syndrome was not associated with depression or anxiety. The correlations between the components of the metabolic syndrome and psychological distress as continuous measures were low. High waist circumference (>102 cm in males and >88 cm in females) associated with depression (odds ratio, 1.30; 95% confidence interval, 1.05–1.61), but this association vanished when adjusted for gender, smoking, alcohol consumption, marital status, level of education, and physical activity. **Conclusion:** No clear association was found between the metabolic syndrome and psychological distress. **Key words:** depression, HSCL-25, metabolic syndrome, cohort study.

ATP III = Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Cholesterol in Adults (Adult Treatment Panel III); CI =confidence interval; HSCL-25 = Hopkins Symptom Checklist-25, OR =odds ratio; HDL = high-density lipoprotein.

INTRODUCTION

Metabolic syndrome is a combination of several cardiovascular risk factors, including high fasting glucose and triglycerides, low HDL cholesterol, high blood pressure, and abdominal obesity (1). The estimated prevalence of the metabolic syndrome among US adults aged 20 through 70 years was 23% among women and 24% among men (2). The prevalence of the metabolic syndrome is increasing as the prevalence of obesity increases (3,4). The metabolic syndrome is a major risk factor for cardiovascular diseases (5) and type II diabetes mellitus (6). Cardiovascular diseases and disturbances in glucose metabolism have been shown to be associated with depression, which is a common public health problem (7–9).

Only a few studies have dealt with the association between affective or anxiety symptoms and the metabolic syndrome. Depressive symptoms have been shown to be associated with individual components of the metabolic syndrome in male twins with a mean age of 63 years (10). Among middle-aged women, depressive symptoms have been shown to be associated with an elevated risk of developing the metabolic syndrome 7 years later, as well as with the presence of the metabolic syndrome; meta-

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bolic syndrome at baseline also predicted increased anxiety 7 years later (11). As far as the present authors know, only one earlier study has dealt with young adults. According to that study, women with a history of a major depressive episode were twice as likely to have the metabolic syndrome compared with others. Depression in women was also associated with high blood pressure and high triglyceride level (12).

Our aim was to study whether metabolic syndrome and its different components are associated with depressive and anxiety symptoms, i.e., psychological distress. Access to a large, population-based birth cohort database enabled us to investigate this putative association in a young adult population aged 31 years.

METHODS

Participants

This study forms part of the prospective Northern Finland 1966 Birth Cohort Study. The original sample was collected from a geographically defined area of the two northernmost provinces of Finland. It consists of an unselected birth cohort of 12,058 live births, and covered 96.3% of all deliveries in Northern Finland in the year 1966. All the subjects are Caucasians (13). Data collection was begun in the antenatal phase, and it has been continued since then in several ways.

In 1997, a 31-year follow-up study was conducted by postal inquiry and clinical examination to the cohort members. At the time, 8,465 cohort members who were living in Northern Finland or in the capital area of Helsinki were invited to a clinical examination; 5,999 (70.9%) of them participated. The study protocol was approved by the ethical committee of Oulu University, Faculty of Medicine. A written informed consent was obtained from all participants. The material consisted of 5,698 subjects (2,832 men and 2,866 women) with data on depression, anxiety, and metabolic syndrome.

Measures

The Metabolic Syndrome

The metabolic syndrome and metabolic risk factors were defined according to the National Cholesterol Education Program (Adult Treatment Panel III or ATP III) (1). Subjects having three or more of the following criteria were defined as having the metabolic syndrome: (1) abdominal obesity: waist circumference >102 cm in men and >88 cm in women; (2) high triglycerides: \geq 1.69 mmol/l (\geq 150 mg/dl); (3) low high-density lipoprotein (HDL) cholesterol: <1.04 mmol/l (<40 mg/dl) in men and <1.29 mmol/l (<50 mg/l) in women; (4) high blood pressure: \geq 130/85 mm Hg; (5) high fasting glucose: \geq 6.1 mmol/l (\geq 110 mg/dl).

Waist circumference was measured in the clinical examination as centimeters at the level midway between the lowest rib margin and the iliac crest. Blood samples were drawn after overnight fasting from 10:00 PM until 8:00 to 11:00 AM. Enzymatic determinations of serum triglycerides (Boehringer

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From the Oulu University Hospital, Department of Psychiatry, Oulu, Finland (A.H., P.R., J.M., K.L.); Department of Public Health, Science and General Practice, University of Oulu, Oulu, Finland (M.T., J.L.); Oulu Health Center, City of Oulu, Finland (M.T.); Academy of Finland and Department of Psychiatry, University of Oulu, Oulu, Finland (J.V.); Oulu Regional Institute of Occupational Health, Oulu, Finland (J.L.); Department of Clinical Chemistry, University of Oulu, Oulu, Finland (A.R.); Department of Social Psychiatry, Tampere School of Public Health, University of Tampere and Department of Psychiatry, Tampere University Hospital, Tampere, Finland (M.J.); Department of Psychiatry, University of Oulu, Oulu, Finland (P.R.).

Address correspondence and reprint requests to Anne Herva, MD, Department of Psychiatry, University Hospital of Oulu, PL 26, FIN-90029 OYS, Finland. E-mail: anne.herva@oulu.fi

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Mannheim, Germany) were done using Hitachi 911 automatic analyzer. HDL cholesterol was determined using the same analyzer and the method published before (14). Blood pressure was also taken during the clinical examination. Two blood pressure readings were obtained, and the average of the systolic and diastolic blood pressure readings was used in the analysis. Serum glucose was measured by a glucose dehydrogenase method (Granutest 250, Diagnostica Merck, Darmstadt, Germany).

Depression and Anxiety

Depressiveness and anxiousness were defined by the Hopkins Symptom Checklist-25 (HSCL-25 questionnaire), which is a 25-item shortened version of an originally 90-item questionnaire designed by Derogatis et al. (15). The HSCL has been used in several versions of different lengths (16-90 items), all of which have been shown to have satisfactory validity and reliability as a measure of mental symptoms (16,17). The HSCL-25 includes the depression and anxiety subscales of the HSCL-90. The HSCL-25 questionnaire contains a 13-item depression and a 10-item anxiety subscale (18,19). In this subscale, the subject assesses the presence and intensity of depressive and anxiety symptoms over the previous week. The answers are scored on a scale from 1 (not bothered) to 4 (extremely bothered). The HSCL-score is the sum of items divided by the number of items answered. Different cutoff points have been used to define depression and anxiety (16,20). In this study, a cutoff point of 1.74/1.75 or over was used as an indicator of depression or anxiety. Subjects were excluded from the sample if more than five items of the whole HSCL-25 were missing. Additionally, depression was not measured if four or more depression items were lacking; correspondingly, anxiety was not measured if three or more anxiety items were lacking. Missing data were not replaced. The HSCL-25 has previously been found to be a valid instrument for screening psychiatric cases in the Nordic countries, including Finland (21,22).

Other Variables

Data on smoking, alcohol consumption, marital status, and physical activity were obtained from the postal questionnaire. Smoking was treated as a dichotomous variable: yes or no. The amount of alcohol consumed per day was converted to grams of absolute alcohol, and subjects were divided into light <15 g/day, moderate 15 to 40 g/day, and heavy >40 g/day, drinkers. Marital status was defined as married or cohabiting/unmarried, widowed, divorced. Physical activity was defined as regular versus nonregular. Regular physical activity was defined as consisting of exercise at least two to three times a month or more often that makes the subject become breathless and sweat at least mildly. Data on level of education was obtained from the registers of Statistic Finland at the end of the year 1997 and divided into three groups: basic/secondary/tertiary level. Subjects were also asked in the questionnaire of the 31-year follow-up whether they had ever been diagnosed by a physician as having angina pectoris or diabetes mellitus.

Statistical Analyses

The statistical analyses were performed using the SPSS system version 11.5 for Windows (23). The intercorrelations between HSCL-depression and

HSCL-anxiety were determined by Spearman's correlation coefficients. Spearman's partial correlation coefficients were used to examine the relationships between the components of metabolic syndrome and psychological distress adjusting for gender. As a preliminary method to study the association between variables, we used cross-tabulation, using Pearson's χ^2 test for independence to evaluate statistical significance. Multivariate binary logistic regression analyses were used to explore the associations between the metabolic syndrome, depression and anxiety, controlling for the confounding variables to get adjusted odds ratios (ORs). As possible confounding variables affecting the metabolic abnormalities, we used gender, smoking, alcohol consumption, marital status, level of education, and physical activity. The analyses were performed also excluding subjects with angina pectoris and diabetes mellitus. The number of subjects used in the statistical analyses varies due to some missing data.

Subjects were not included in the analyses if they (1) had no data available on depression and anxiety; (2) did not have data available on more than two components of the metabolic syndrome; (3) had not fasted overnight before the blood samples were taken; (4) were pregnant.

RESULTS

The prevalence of the metabolic syndrome was 5.8% in the whole sample (6.8% in males and 4.8% in females). The prevalence of depression was 13.5% (10.4% in males and 16.5% in females), and the prevalence of anxiety 8.1% (6.7% and 9.5%). The mean HSCL-depression score was 1.36, SD \pm 0.37 (1.31, SD \pm 0.33 in males and 1.41, SD \pm 0.39 in females) and the mean HSCL-anxiety score 1.31, SD \pm 0.31 (1.28, SD \pm 0.29 in males and 1.34, SD \pm 0.33 in females). The intercorrelation between depressive and anxiety symptoms was 0.668 (0.663 in males and 0.662 in females).

The components of metabolic syndrome, HSCL-depression and HSCL-anxiety, were first analyzed as continuous measures. As seen in Table 1, Spearman's partial correlation coefficients between the components of the metabolic syndrome and psychological distress as continuous measures were low, varying from -0.062 to 0.041 for depression and from -0.033 to 0.046 for anxiety. The positive correlation between glucose level and psychological distress vanished when subjects with angina pectoris or diabetes mellitus were excluded from the analyses.

When multivariate binary logistic regression analyses were used, metabolic syndrome did not associate with depression or anxiety. Of the components of the metabolic syndrome, high waist circumference (>102 cm in males and >88 cm in females) associated with depression (OR 1.30, 95% confi-

 TABLE 1.
 Spearman's Partial Correlations of the Components of the Metabolic Syndrome With Psychological Distress as Continuous Measures

Mariah la q		60	HSCL-Dep	ression	HSCL-Anxiety		
Variable ^a	Mean	SD	Correlation ^b	р	Correlation ^b	р	
Waist (cm)	83.81	12.13	0.024	.071	0.017	.20	
Triglycerides (mmol/L)	1.17	0.72	0.022	.11	0.035	.011	
HDL-cholesterol (mmol/L)	1.55	0.38	0.015	.28	-0.005	.71	
Glucose (mmol/L)	5.05	0.38	0.041	.003	0.046	.00	
Systolic blood pressure (mm Hg)	125.17	13.50	-0.062	<.001	-0.033	.013	
Diastolic blood pressure (mm Hg)	77.65	11.65	-0.033	.013	-0.009	.48	

a n = 5287 to 5691.

^bAdjusted by gender.

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dence interval [CI], 1.05–1.61), but the association vanished when adjusted for gender, smoking, alcohol consumption, marital status, level of education, and physical activity. On the other hand, high blood pressure associated inversely with depression (adjusted OR = 0.80, 95% CI 0.66–0.97). The results regarding Table 2 did not change substantially if subjects with angina pectoris or diabetes mellitus were excluded from the analyses.

DISCUSSION

The main finding of this study, based on a populationbased database of young, 31-year-old adults, was that no clear association was found between the metabolic syndrome and psychological distress, when ATP III-criteria of the metabolic syndrome were used. Our results were to some extent controversial compared with earlier studies on this topic. Kinder et al. (12) found in a cross-sectional study of 3186 males and 3003 females aged 17 to 39 that the prevalence of the metabolic syndrome was elevated among women with a lifetime history of depression as assessed by the Diagnostic Interview Schedule. It must, however, be remembered that the definition of depression was different compared with our definition. In men, Kinder et al. (12) found no association between metabolic syndrome and depression, which is in line with our findings. Further, our findings also disagree with those of a study concerning middle-aged women, in which depressive symptoms were associated with the co-occurring metabolic syndrome; in addition, metabolic syndrome at baseline predicted increased anxiety 7 years later (11). However, the latter study was based on middle-aged subjects, among which the presence of other physical disorders, such as coronary artery disease, might have affected the relationship between metabolic syndrome and psychological distress.

In the present study, of the components of the metabolic syndrome, blood pressure associated inversely with depression when analyzed as continuous measure and in logistic regression models even after adjusting for confounders. A growing body of earlier research has reported the independent role of depression in predicting the onset of cardiovascular disease (24,25). Because cardiovascular disease is a hypertension-related condition, it is reasonable to hypothesize that depression would also be associated with hypertension. However, the findings regarding the relationship between depression and hypertension have been controversial (26-28), albeit recent follow-up studies indicate that preceding depression predicts later hypertension (27,29,30). Possible explanations for our findings might be the young age of the cohort members among whom the prevalence of hypertension is relatively low. In addition, our research frame was a crosssectional in its nature, and as hypertension develops over the course of years, the strongest connection between depression and hypertension may come out in later life. For example, the follow-up time in earlier studies showing a positive association between antecedent depression and later hypertension was 5 to 16 years (27,29,30).

In the present study, there was a positive correlation between glucose level and depression. With regard to anxiety, a positive correlation was found concerning triglyceride and glucose levels and a negative correlation, regarding systolic blood pressure. Albeit being statistically significant, it must, however, be emphasized that these correlations were very small per se. In addition, the correlations of glucose level between depression and anxiety vanished when subjects with angina pectoris and diabetes mellitus were excluded from the analyses, which is not surprising, taking into account that the association between diabetes and depression is already well established (9). Thus, our findings are inconsistent with those of male twin data showing an association between the individual components of the metabolic syndrome and depression (10). However, the study subjects in the twin data were middle-aged, which may have affected the result.

There are several limitations in our study. One major limitation is that self-report questionnaires, such as HSCL-25, give limited data on depression or anxiety. It gives information of depressive and anxiety symptoms at one time point but no information on lifetime psychological health. In addition, by using the HSCL-questionnaire as a measure of depression

		HSCL-Depression (Cutoff 1.75)					HSCL-Anxiety (Cutoff 1.75)					
	Subjects ^{b, c}	Number of Cases,	Crude Odds Ratio		Adjusted Odds Ratio		Subjects ^{b,c}	Number of Cases,	Crude Odds Ratio		Adjusted Odds Ratio	
		n (%)	OR	95% CI	OR	95% CI		n (%)	OR	95% CI	OR	95% CI
Waist >88/102	736/5648	120 (16.3)	1.30	1.05–1.61	1.06	0.85–1.33	736/5648	65 (8.8)	1.12	0.85–1.47	0.82	0.61–1.10
Trigly. ≥1.69	916/5341	121 (13.2)	1.01	0.82-1.25	0.98	0.78–1.23	916/5341	80 (8.7)	1.15	0.89–1.48	1.03	0.78–1.36
HDL <1.04/1.29	609/5402	77 (12.6)	0.94	0.73–1.22	0.87	0.67–1.13	609/5402	45 (7.4)	0.92	0.67–1.26	0.87	0.63–1.21
BP ≥135/85	1762/5667	197 (11.2)	0.74	0.63–0.88	0.80	0.66–0.97	1762/5667	124 (7.0)	0.82	0.66–1.01	0.82	0.65-1.04
Gluc. ≥6.1	151/5322	24 (15.9)	1.26	0.81–1.97	1.17	0.73–1.89	151/5322	10 (6.6)	0.82	0.43–1.58	0.60	0.29–1.26
MS ^d	325/5691	39 (12.0)	0.87	0.62–1.23	0.76	0.53–1.09	325/5691	23 (7.1)	0.86	0.56–1.32	0.71	0.45–1.12

TABLE 2. The Crude and Adjusted" Odds Ratios of Depression and Anxiety in Subjects With Metabolic Risk Factors and Metabolic Syndrome

^a Adjusted by gender, smoking, alcohol consumption, marital status, level of education and physical activity.

^b Metabolic syndrome, ATP III criteria, 3 of the risk factors.

^c Total number of subjects who fulfill the criteria.

^d Number of subjects whose data were available.

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and anxiety, comorbidity of other mental disorders could not be assessed, and the results were not adjusted by other mental disorders. Although HSCL-25 has previously been found to be a valid instrument for screening psychiatric cases (21,22), a diagnostic interview would be better for measuring depression and anxiety. Also, we did not have the possibility to explore the associations longitudinally. Finally, because the analyses were cross-sectional, the directionality of associations cannot be truly determined.

The strength in this study is that it is based on a populationbased database. Additionally, all the subjects were young 31-year-old adults, the age at which the prevalence of cardiovascular diseases is low. Furthermore, the HSCL-25 has previously been found to be a valid instrument for screening psychiatric cases in the Nordic countries including Finland and also in this database (21,22); the HSCL-25 has been found to be moderately reliable in a two-stage field study with structured interview for DSM-III-R as a diagnostic instrument (22). In addition, comparison with the General Health Questionnaire (GHQ) has shown comparable sensitivity and specificity (31), and compared with the Montgomery-Åsberg-Depression Rating Scale, as well as with the diagnostic criteria of depression HSCL-25, was found to be a sensitive case-finder of depressive disorders (32).

In conclusion, we did not find an association between the metabolic syndrome and psychological distress in a sample of 31-year-old young adults. Also, all the correlations between the components of the metabolic syndrome and psychological distress were very small; hypertension, however, associated inversely with depression in the logistic regression analysis. We suggest that in future studies it would be important to study these associations in large longitudinal population-based cohorts in order to better highlight the putative association of metabolic syndrome with depression and anxiety. In addition, an important topic would be to assess mental disorders by more specific diagnostic criteria, and to take into consideration the comorbidity of mental disorders in different age cohorts.

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