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# Association between Increased Serum Cholesterol and Signs of Depressive Mood

**Maximilian Ledochowski[1], Christian Murr[2], Barbara Sperner-Unterweger[3], Gabriele Neurauter[2,4] and Dietmar Fuchs[2,4]***

[1] Department of Internal Medicine,
[2] Institute for Medical Chemistry and Biochemistry,
[3] Department of Psychiatry,
Leopold-Franzens University, Innsbruck, Austria
[4] Ludwig Boltzmann Institute of AIDS Research, Innsbruck, Austria

**Hypercholesterolemia is associated with an increased risk of atherosclerosis and coronary heart disease. Therefore, therapeutic lowering of cholesterol is an important preventive measure of cardiac morbidity and death. As one side effect, cholesterol-lowering drugs appear to increase the mortality due to suicides or violence, and low lipid concentrations were found to be associated with trait measures of depression. We compared serum cholesterol concentrations and the Beck Depression Rating Scale (Beck's score) in 604 otherwise healthy outpatients who visited the physician's office for a medical health check-up; 65.4% of individuals presented with serum cholesterol concentrations ≥5.2 mmol/l (>200 mg/dl) and 5.3% had elevated Beck's score (>19), indicative for depression. Beck's score was higher in patients with cholesterol concentrations above the 75th percentile (= 6.2 mmol/l; U = 31221, p<0.02, Mann-Whitney U-test), and Beck's score correlated with cholesterol concentrations and with age. Thus, in contrast to the widely accepted view, in our study, higher cholesterol concentrations were associated with signs of depressive mood. Hypercholesterolemia may not necessarily increase the risk of depressive mood, conversely, increased intake of fat and carbohydrates by individuals with depressive mood may increase cholesterol levels.** Clin Chem Lab Med 2003; 41(6):821–824

*Key words:* Cholesterol; Beck Depression Rating Scale; Depressive mood.

*Abbreviations:* Beck's score, Beck Depression Rating Scale; BMI, body mass index.

## Introduction

Cholesterol is synthesized ubiquitously in the human body as an essential component of cell membranes and lipoproteins and is a precursor of steroid hormones and bile acids. Hypercholesterolemia is associated with an increased risk of atherosclerosis and coronary heart disease. Dietary or therapeutic lowering of cholesterol is able to reduce the number of deaths due to coronary disease (1), but in several studies, a significant increase in mortality due to suicide or violence was observed (2–4). This observation suggests low cholesterol levels to be associated with psychiatric abnormalities, and recently, low lipid and lipoprotein concentrations were found to be inversely associated with trait measures of depression and anxiety in healthy young adult women (5). In contrast, depression is an independent risk factor of myocardial infarction (6). From this relationship one would deduce that increased blood cholesterol, rather than decreased, should be associated with an increased susceptibility for depression. However, there has been much dispute on the possible psychiatric risk of cholesterol-lowering drugs (7–12) and on the other hand, cholesterol lowering has also been found to, *e.g.*, improve depression in patients (7). In this study, we examined the possible relationship between serum cholesterol concentrations and depressive symptoms in a population of otherwise healthy outpatients.

## Materials and Methods

### *Patient selection*

Medical records were available from 1,000 sequential otherwise healthy outpatients who visited a physician's office in Innsbruck, Austria, for a medical health check-up. Of 604 patients (226 men and 378 women, age range: 15–85 years, median: 44 years), complete lipid status was available and data were used for retrospective statistical analyses. With the exception of contraceptives in some females, none of the patients were under medication at study entry. However, depending on a specific clinical or laboratory diagnosis, they were referred to adequate treatment immediately thereafter. According to their body mass indices (BMI) (8), 209 subjects (34.6%) were classified as overweight (BMI >25 kg/m$^2$) and 41 (6.8%) as underweight (BMI <19 kg/m$^2$). All patients performed the Beck self-rating scale to notice signs of depression (13).

### *Blood collection and measurements*

Blood samples were drawn after an overnight fast. The blood was allowed to clot at room temperature and serum was obtained by centrifugation at 1500 × *g* for 15 minutes. All analyses were performed within 1 day after blood collection. Serum cholesterol and triglycerides were measured by commercially available enzymatic methods, CHOD-PAP and GPO-PAP, respectively, with a Hitachi 711 auto-analyzer (Boehringer Mannheim, Vienna, Austria), the laboratory's reference range

*E-mail of the corresponding author:
dietmar.fuchs@uibk.ac.at

being < 5.2 mmol/l (200 mg/dl) for cholesterol and < 2.3 mmol/l (200 mg/dl) for triglycerides.

*Statistical analysis*

Differences of distributions of laboratory variables among subgroups of patients were tested for by the non-parametric Mann-Whitney U-test since the distributions of observed values were generally non-Gaussian. Correlations between variables were assessed by the non-parametric Spearman's rank correlation technique. The effect of the three parameters Beck Depression Rating Scale (Beck's score), serum triglycerides, and age on serum cholesterol concentrations was assessed by a three-way analysis of variance (ANOVA). Thereby Beck's score, serum triglycerides, and age were dichotomized by the third quartile point of the observed distribution (for values see Table 1). Since variances in the eight resulting subgroups formed on the basis of Beck's score, serum triglycerides, and age were different, a logarithmic transformation of cholesterol concentration was done before analysis. The success of transformation was confirmed by Bartlett's test for equal variances (test statistics = 9.616; p > 0.05) as implemented in the program GraphPad Prism (GraphPad Software, Inc., San Diego, CA, USA). To determine whether the response of cholesterol concentrations to one factor depends on the level of the second factor or third factor, the interaction terms were also tested for significance. ANOVA was calculated by the program BMDP2V (BMDP Statistical Software, 1990 edition, University of California Press).

## Results

Table 1 lists characteristics of the study subjects. Notably, 65.4% of the studied individuals had cholesterol concentrations above 5.2 mmol/l (200 mg/dl) and 32 (5.3%) of them presented with a Beck's score above 19, indicative for signs of depressive mood. There were strong correlations between age, BMI, and concentrations of cholesterol and triglycerides (all $p < 0.0001$; Table 2). A weaker association was found between Beck's score and age ($p = 0.0084$) and cholesterol concentrations ($p = 0.01$). As shown in Figure 1, there was also a statistically significant increase in Beck's score in individuals with higher cholesterol concentrations ($U = 31221$, $p < 0.02$; Mann-Whitney U-test) indicated by increasing median values.

A possible interrelationship between serum cholesterol and triglyceride concentrations, Beck's score, and age was tested for by three-way ANOVA. Untrans-

**Table 1** Baseline characteristics of the study subjects (n = 604: 226 males and 378 females).

| Characteristics | First quartile | Median value | Third quartile | Range | Out of reference range[a] | |
|---|---|---|---|---|---|---|
| | | | | | below n (%) | above n (%) |
| Age (years) | 35 | 44 | 55 | 15–85 | | |
| BMI (kg/m$^2$) | 21.1 | 23.3 | 26.4 | 16.0–50.6 | 41 (6.8) | 209 (34.6) |
| Beck Depression Rating Scale (BS) | 2 | 5 | 9 | 0–47 | | 32 (5.3) |
| Serum cholesterol, mmol/l (mg/dl) | 4.9 (191) | 5.6 (218) | 6.2 (241) | 2.9–10.4 (112–401) | | 395 (65.4) |
| Serum LDL-cholesterol, mmol/l (mg/dl) | 2.7 (104) | 3.4 (130) | 4.0 (153) | 0.9–8.3 (33–321) | | |
| Serum HDL-cholesterol, mmol/l (mg/dl) | 1.2 (47) | 1.5 (56) | 1.8 (68) | 0.5–3.2 (19–125) | | |
| Serum triglycerides (mmol/l) | 0.95 (83) | 1.39 (122) | 2.06 (181) | 0.42–10.94 (37–960) | | 120 (19.9) |

n, number of observations; BMI, body mass index; LDL, low densitiy lipoprotein; HDL, high density lipoprotein; [a] reference ranges: BMI, 19–25 kg/m$^2$; Beck Depression Rating Scale, ≤19; cholesterol, ≤5.2 mmol/l (200 mg/dl); triglycerides, ≤2.3 mmol/l (200mg/dl).

**Table 2** Spearman correlations of investigated characteristics (n = 604).

| | Spearman's rank correlation coefficient | | | | |
|---|---|---|---|---|---|
| | Value | 95% Confidence interval | | | p-Value |
| BS *vs.* age | 0.107 | 0.025 | – | 0.188 | 0.0084 |
| BS *vs.* cholesterol | 0.101 | 0.019 | – | 0.181 | 0.0134 |
| BS *vs.* BMI | −0.012 | −0.009 | – | 0.070 | n.s. |
| BS *vs.* triglycerides | 0.013 | −0.069 | – | 0.095 | n.s. |
| Cholesterol *vs.* age | 0.363 | 0.289 | – | 0.432 | <0.0001 |
| Cholesterol *vs.* triglycerides | 0.351 | 0.277 | – | 0.921 | <0.0001 |
| Triglycerides *vs.* age | 0.241 | 0.162 | – | 0.317 | <0.0001 |
| BMI *vs.* age | 0.324 | 0.248 | – | 0.396 | <0.0001 |
| BMI *vs.* cholesterol | 0.236 | 0.157 | – | 0.312 | <0.0001 |
| BMI *vs.* triglycerides | 0.319 | 0.243 | – | 0.391 | <0.0001 |

n, number of pairs; BS, Beck Depression Rating Scale; BMI, body mass index; n.s., not significant.

formed mean values and standard deviations of the subgroups resulting from dichotomization at the third quartiles of the observed distributions are shown in Figure 2. All the three factors, namely triglyceride concentrations ($F = 23.96$; $p < 0.0001$), Beck's score ($F = 7.08$; $p < 0.01$), and age ($F = 16.43$; $p = 0.0001$) showed a significant effect on serum cholesterol concentrations, whereas all the interaction terms (age *vs.* Beck's score, triglycerides *vs.* age, Beck's score *vs.* age, triglycerides *vs.* Beck's score *vs.* age) were statistically not significant ($p > 0.1$), indicating interactions being negligible.

## Discussion

In our study, we found a significant positive correlation of cholesterol levels with Beck's score. This result contrasts with earlier findings of an inverse association between depression scores and total cholesterol (5). The discrepancy might be due to different study populations. In the earlier study, the association between low cholesterol and depression scores (5) derived from women presenting with total cholesterol concentrations below 4.14 mmol/l (160 mg/dl). When restricting our study population to those 30 individuals with a serum cholesterol concentration below 4.14 mmol/l, the positive correlation of cholesterol levels with Beck's score no longer existed (data not shown). On the other hand, the average age of our study population was much higher (average age: 45 years) than that, *e.g.*, in the study of Suarez (5) (average age: 21 years). Troisi *et al.* reported a relationship between lower cholesterol levels and negative mood in obese women, which was limited to a group of people older than 60 years (14). Nevertheless, our study demonstrates that high cholesterol concentrations are also associated with a higher susceptibility for depressive mood and our data thus adds to the existing controversy about an increased risk of suicide and violence in individuals with lower cholesterol or under cholesterol-lowering treatment (15). The results of our study may support the notion of a U-shaped curve for risk associated with cholesterol levels (16).

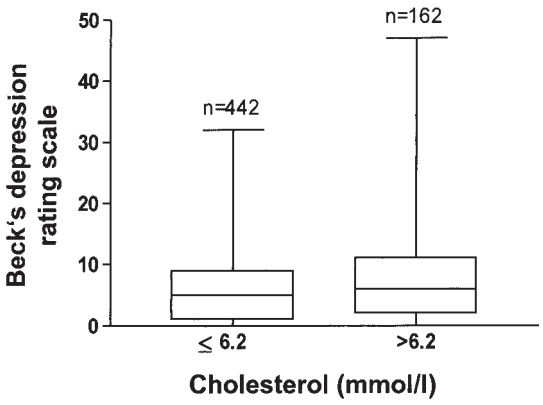


**Figure 1** Box and Whiskers plots of Beck Depression Rating Scale (Beck's score) of patients with different cholesterol concentrations. The box extends from the 25th percentile to the 75th percentile, with a horizontal line at the median (50th percentile), bars showing the range of the data. The median Beck's score of the group with serum cholesterol above 6.2 mmol/l (241 mg/dl = third quartile of cholesterol concentrations) is significantly higher ($p < 0.02$) compared to the group with cholesterol concentrations <6.2 mmol/l (241 mg/dl).

The data also fit to the observation that cholesterol lowering may not only increase the risk of psychiatric illness (2–4, 15) but also was found to improve depression (7). Similarly, hypercholesterolemia (1) is an independent risk factor for myocardial infarction as is depression (6), which suggests that increased cholesterol might coincide with an increased susceptibility for depression. Certainly, an increased Beck's score cannot be used as a diagnostic tool to detect major depression, since increased scores can also be seen in other psychiatric and organic conditions. However, higher Beck's scores indicate signs of depressive mood in the individuals with hypercholesterolemia.

In our study, age positively correlated with total cholesterol, serum triglycerides, BMI, and Beck's score. It is therefore tempting to speculate that age would play a crucial role for explaining the results of our study. Depressive mood may be related to disturbed metabolism of 5-hydroxytryptamine, serotonin

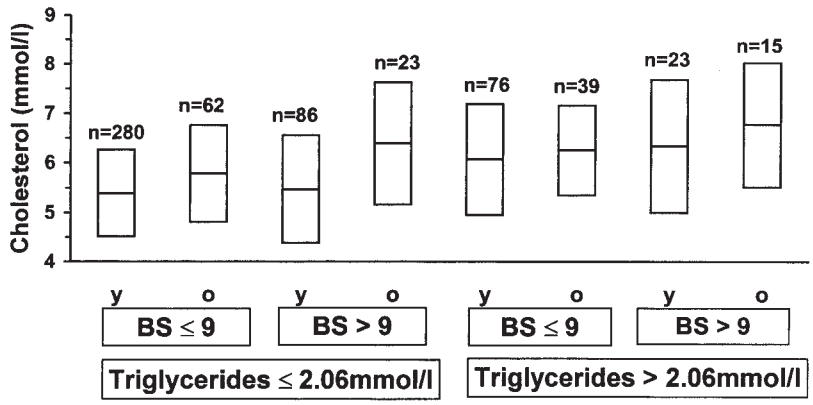


**Figure 2** Box and Whiskers plots of serum cholesterol concentrations (boxes extending from the mean ± standard deviations, with a horizontal line at the mean) of patients with different serum triglycerides concentrations, Beck Depression Rating Scale (Beck's score) and age ("y" indicates < 55 years, "o" indicates > 55 years).

(17). Thus, individuals with depressive mood may increase their intake of dietary fat and of carbohydrates (18), and consequently, cholesterol concentrations would increase.

We conclude that not only lower, but also higher, cholesterol concentrations are associated with signs of depressive mood. Older age might contribute to the development of depressive symptoms, which is associated with increased cholesterol levels probably resulting from an increased dietary food intake.

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Corresponding author: Dr. D. Fuchs, Institute for Medical Chemistry and Biochemistry, Leopold-Franzens University, Fritz Pregl Strasse 3, 6020 Innsbruck, Austria
Phone: +43 512 507 3519, Fax: +43 512 507 2865,
E-mail: dietmar.fuchs@uibk.ac.at