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Low cholesterol concentrations and severe depressive symptoms in elderly people

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Abstract

Objective—To investigate the reported association between low serum cholesterol concentration and severe depressive symptoms in an elderly population.

Design—Cross sectional analysis of pooled data from three communities of the established populations for epidemiologic studies of the elderly. Participants who completed their interview, including the Centers for Epidemiologic Studies' depression scale and consented to measurement of their cholesterol concentration were included in the study.

Subjects—3939 men and women aged ≥ 71 .

Methods— χ^2 analysis, *t* tests, and multivariate regression analysis of the association between low cholesterol concentration and severe depressive symptoms. All analyses were stratified by sex, and multivariate analyses were adjusted for age, self reported health, physical function, number of drugs used, and weight loss.

Main outcome measure—Score of depressive symptoms on the Centers for Epidemiologic Studies' depression scale.

Results—Depressive symptoms, cholesterol concentration, weight, and use of drugs were all associated with age in men and women. The relative odds of severe depressive symptoms (score ≥ 16) for those with low cholesterol concentrations (< 4.14 mmol/l) were 1.9 (95% confidence interval, 1.1 to 3.3) for the older group of men and 1.8 (1.1 to 2.9) for the

older group of women. This association was also observed when depressive symptoms were analysed as a continuous rather than a categorical variable. In multivariate models that adjusted for age, self reported health, physical function, number of drugs used, and weight loss, the association was substantially weakened.

Conclusions—After several factors relating to health had been controlled for, no significant association between low cholesterol concentration and severe depressive symptoms was found.

Introduction

Although a high serum cholesterol concentration is a well established risk factor for heart disease,¹ an analysis of results of cholesterol lowering clinical trials has suggested that the benefits of reducing heart disease by reducing cholesterol concentration are offset by an increase in deaths from external causes such as suicide, accidents, and murder.²⁻⁴ This increase in deaths from causes unrelated to illness occurred regardless of whether the cholesterol lowering regimen was dietary or pharmacological, prompting the authors to suggest that lowering cholesterol concentration might have neurochemical consequences. One explanation for this may be that lowering cholesterol concentration causes changes in the cholesterol content of the synaptosomal membrane and a decrease in the number of serotonin receptors.⁵ Because a low serotonin concentration has been associated with suicidal depres-

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sion and impulsive behaviour^{6,7} some researchers have suggested that lowered serotonin concentration or perhaps fewer serotonin receptors may account for the increase in deaths from external causes in the treatment group in cholesterol lowering trials.⁵ Depression is a factor in a high proportion of suicides.⁸

On the basis of this argument, Morgan and colleagues investigated the association between low blood cholesterol concentration and an increase in depressive symptoms.^{9,10} They found an inverse association in men aged 70-89 but not in younger men, and they attributed this association to an effect of low cholesterol concentration. Evidence exists, however, for an alternative explanation. Poor or declining health has been associated with weight loss,^{11,12} and weight loss has been associated with lower serum cholesterol concentration.¹³ Poor or declining health is also associated with severe depressive symptoms or an increase in such symptoms among elderly people.¹⁴ Thus the inverse association between blood cholesterol concentration and depressive symptoms may result from their association with poor health.

Although Morgan *et al* considered health status to some degree in their analyses,⁹ their approach to adjusting for this factor may not have been adequate.¹⁵ Our study used data from the established populations for epidemiologic studies of the elderly to evaluate the association between low cholesterol concentration and severe depressive symptoms and adjusted for current illness, physical function, and weight loss as important potential confounders. We tried to replicate as closely as possible the variable and the types of analysis used by Morgan *et al*⁹ so that we could compare the main results.

Methods

The established populations for epidemiologic studies of the elderly were initiated by the National Institute on Aging in the United States to gather information on the health of people aged 65 and over.^{16,17} Baseline interviews were conducted between 1981 and 1983 in three communities—namely, east Boston, Massachusetts; Iowa and Washington counties, Iowa; and New Haven, Connecticut. During the participants' sixth annual follow ups, between 1987 and 1989, blood cholesterol concentrations were determined in those who consented. Participants, by then aged 71 or over, answered questions about their health, including questions about depressive symptoms as measured by the Centers for Epidemiologic Studies' depression scale.¹⁸ Participants were excluded from this analysis if they had not been able to answer the questions for themselves, if they had not been assessed with the depression scale, or if they had not had their cholesterol concentration tested. After exclusions 3939 (55%) participants remained in the study.

MEASURES OF HEALTH, CHRONIC ILLNESS, AND PHYSICAL FUNCTION

At each annual interview participants were asked whether certain serious medical conditions had been diagnosed by a doctor since their last interview—namely, diabetes; heart attack, stroke, or brain haemorrhage; cancer, malignancy, or tumour; or broken hip. Participants scored one for each condition, resulting in a score of 0-5. A summary of which of these conditions had been diagnosed between the first and sixth annual follow ups provided a history of chronic or serious illness. The number of drugs (both those prescribed and those bought over the counter) that the participant had taken in the previous two weeks was used to measure participants' health status at the time of interview.

In addition to answering questions about serious

medical conditions and use of drugs the participants answered questions about their ability to perform activities of daily living without the help of another person or equipment.¹⁹ Disability in any of six activities (walking across a small room, taking a bath, dressing, eating, transferring from a bed to a chair, and using the toilet, was summarised to give a physical function score of 0-6. Respondents self reported their health as excellent, good, fair, or poor.

Self reported weight was recorded at the sixth follow up, and the percentage change from the baseline weight was calculated. Participants were categorised according to whether they had lost more than 10% of their baseline weight over the six years of the study. More data were missing (6.6%) for this variable than for any other because either the baseline weight or the weight at the sixth follow up was missing. For all other variables <1% of values were missing.

BLOOD SPECIMENS

Non-fasting blood specimens were collected by a phlebotomist in the home of consenting participants and flown to Nichols Institute in San Juan Capistrano, California. The serum cholesterol concentrations were measured by the enzymatic method with an instrument (Technicon SMAC, Tarrytown, New York) calibrated according to the manufacturer's specifications. Cholesterol concentrations were categorised as low (<4.14 mmol/l), normal (4.14-5.16 mmol/l), borderline (5.17-6.20 mmol/l), or high (≥ 6.21 mmol/l).⁹

MEASUREMENT OF DEPRESSIVE SYMPTOMS

The Centers for Epidemiologic Studies' despression scale¹⁸ or a modification of it was used at each of the sites participating in the established populations for epidemiologic studies of the elderly. To minimise the burden on the participants a shorter version of the scale was used in east Boston and Iowa. The scores of these shorter versions were standardised against the first national health and nutrition examination survey, in 1974-5, by means of the equation $x_t = (sd_t/sd_s)(x_s - m_s) + m_t$, where x_t is the transformed score, x_s is the participant's score on the original scale, m_s and sd_s are the sex specific mean and standard deviation of scores from participants at the sixth follow up, and m_t and sd_t are the sex specific mean and standard deviation from the first national health and nutrition examination survey. An adjusted score of ≥ 16 indicated severe depression.^{18,20} Full details on the use of the modified scales, the methods for transforming the results to accord with the full scale, and the validity of these scales have been published.²⁰

STATISTICAL ANALYSIS

All analyses were performed with SAS software (SAS Institute, Cary, North Carolina). Analyses were stratified by sex. For comparison of variables by age group Student's *t* test was used for continuous data and the χ^2 test was used for categorical data. A Wilcoxon non-parametric test on ranks was used to assess the association between scores on the Centers for Epidemiologic Studies' depression scale and low cholesterol concentration. Pearson's correlation analysis of variables and depression scores was also performed. Multiple linear regression models with depression scores as the outcome were used to assess the relation between cholesterol concentration and depression, with potential confounders controlled for.

Results

The mean scores for depressive symptoms and proportion of participants categorised as being severely depressed were both significantly higher in the older age group (≥ 80) than the younger age group

TABLE I—Association between age group and cholesterol, depression, weight, and use of drugs in 3939 participants in established populations for epidemiologic studies of the elderly

	Men			Women		
	Aged 70-79 (n=966)	Aged ≥80 (n=448)	Significance*	Aged 70-79 (n=1536)	Aged ≥80 (n=989)	Significance*
Depressive symptoms: Mean (SD) score†	6.17 (6.70)	8.40 (7.61)	t=-5.3 P<0.0001	9.84 (9.01)	10.80 (9.24)	t=-2.6 P=0.01
No (%) severely depressed (score† ≥16)	88 (9.1)	71 (15.9)	χ²=13.9 P<0.001	354 (23.0%)	268 (27.1)	χ²=5.3 P=0.02
Cholesterol Mean (SD) (mmol/l)	5.34 (0.98)	5.01 (1.09)	t=5.5 P<0.0001	5.91 (1.08)	5.68 (1.10)	t=5.2 P<0.001
No (%) with low cholesterol	92 (9.5)	90 (20.1)	χ²=30.5 P<0.0001	67 (4.4)	70 (7.1)	χ²=8.6 P=0.003
Drugs: Mean (SD) No used	3.07 (2.43)	3.41 (2.86)	t=2 P=0.02	3.64 (2.58)	3.79 (2.57)	t=-1.4 P=0.16
Weight: Mean (SD) (kg)	78.8 (12.7) n=957	74.3 (12.7) n=438	t=6.7 P<0.0001	66.6 (12.7) n=1494	62.1 (11.8) n=928	t=9.2 P<0.001
Mean (SD) change (%)	-0.82 (7.4) n=922	-3.26 (8.5) n=421	t=-5.1 P<0.0001	-1.99 (9.34) n=1444	-4.08 (9.14) n=893	t=5.3 P<0.001
No (%) who lost >10%	80 (8.7)	74 (17.6)	χ²=22.5 P<0.001	251 (17.4)	214 (24.0)	χ²=16.7 P<0.01

*Student's *t* test and χ² test with 1 df were used.

†Centers for Epidemiologic Studies' depression scale.

TABLE II—Relation between severe depressive symptoms* and cholesterol concentration in 3939 participants in established populations for epidemiologic studies of the elderly, by cholesterol concentration and age group. Values are numbers (percentages) of participants with severe depressive symptoms/numbers of participants with low cholesterol concentration

Cholesterol (mmol/l)	Severely depressed men		Severely depressed women	
	70-79 years	≥80 years	70-79 years	≥80 years
Low (<4.14)	9/92 (9.8)	21/90 (23.3)	18/67 (26.9)	27/70 (38.6)
Normal (4.14-5.16)	35/346 (10.1)	29/172 (16.9)	60/299 (20.1)	78/261 (29.9)
Borderline (5.17-6.20)	33/361 (9.1)	13/126 (10.3)	143/586 (24.4)	98/369 (26.6)
High (≥6.21)	11/167 (6.6)	8/60 (13.3)	133/584 (22.8)	65/289 (22.5)
Significance†	χ²=0.06 P=0.81	χ²=4.73 P=0.03	χ²=0.58 P=0.45	χ²=5.02 P=0.03
Odds ratio (95% confidence interval)	1.1 (0.5 to 2.3)	1.9 (1.1 to 3.3)	1.2 (0.7 to 2.2)	1.8 (1.1 to 2.9)

*Scores of ≥16 on Centers for Epidemiologic Studies' depression scale.

†Low cholesterol group v all other cholesterol groups.

TABLE III—Age group specific depression scores* by cholesterol group in 3939 participants in established populations for epidemiologic studies of the elderly. Values are means (SD)

Cholesterol (mmol/l)	Men		Women	
	70-79 years	≥80 years	70-79 years	≥80 years
Low (<4.14)	7.1 (6.7) n=92	9.9 (8.1) n=90	11.0 (9.9) n=67	13.4 (9.9) n=70
Normal (4.14-5.16)	6.3 (6.6) n=346	8.5 (7.4) n=172	9.8 (9.1) n=299	11.4 (9.1) n=261
Borderline (5.17-6.20)	6.1 (7.0) n=361	7.4 (7.5) n=126	9.8 (8.9) n=586	11.0 (9.8) n=369
High (≥6.21)	5.6 (6.3) n=167	7.9 (7.6) n=60	9.7 (9.1) n=584	9.3 (8.1) n=289
Wilcoxon non-parametric test on ranks†	z=1.95 P=0.05	z=2.08 P=0.04	z=1.39 P=0.16	z=2.40 P=0.02

*Scores on Centers for Epidemiologic Studies' depression scale.

†Low cholesterol group v all other groups.

(70-79) in both men and women (table I). The mean cholesterol concentration was significantly lower in the older age group. Low cholesterol concentrations were found in a higher proportion of the older participants (table I). A significantly lower mean weight and a significantly greater mean change from baseline weight were found in the older age group, and a significantly higher proportion of these participants had lost more than 10% of their baseline weight (table I).

Because Morgan *et al*⁸ had observed a significant association between low cholesterol concentration and severe depressive symptoms classified as a categorical variable, we analysed the data to determine if the proportion of severely depressed participants was higher in the group with low cholesterol concentration than in the other groups in the established populations for epidemiologic studies of the elderly (table II). For both men and women aged ≥80 a significant association was found between low cholesterol concentration and severe depression. No significant asso-

ciation between cholesterol concentration and severe depression was found in the younger age group.

The Wilcoxon rank test of the depression scores of the participants with low cholesterol concentration compared with all other participants indicated that in both age groups of men low cholesterol concentration was associated with severe depressive symptoms (table III). This was also true in the older group of women.

Pearson's correlation coefficients indicated that the log depression score was inversely associated with cholesterol concentration (table IV). Weight loss, number of drugs taken in the previous two weeks, and other factors related to health were associated with both the log depression score and cholesterol concentration in both men and women (table IV).

Because the relation between low cholesterol concentration and depression might be confounded by the effects of advancing age and subsequent illness and weight loss, we analysed multiple regression models with log depression scores as the dependent variable. In the simplest model age, self reported health, physical function, and a low cholesterol variable (low v all others) were analysed for both men and women. The results of this analysis indicated that the association between low cholesterol concentration and higher depression scores was not significant in either men or women (table V, model A).

The model that included weight loss and number of drugs used diminished the association between low cholesterol concentration and severe depressive symptoms (table V, model B). This model only slightly improved the explanatory power in the models for both men and women. For women, however, the coefficient for cholesterol concentration was halved when weight loss and number of drugs used were included in the model. The effect on the model for men was less drastic. Neither a six year history of chronic conditions nor the development of new chronic conditions was significant in these regression models. A logistic model that used severe depressive symptoms as the dependent variable yielded similar results (data not shown).

Discussion

An association between low cholesterol concentration and severe depressive symptoms was observed in elderly men and women in the established populations for epidemiologic studies of the elderly. This confirms the findings of a report by Morgan *et al* on men from Rancho Bernardo, California.⁸ In contrast to their study, however, no significant association was

found after we had controlled for self reported health and physical functioning. In a multivariate model that adjusted for weight loss and the number of drugs used as an indication of current illness no significant association was found between low cholesterol concentration and severe depressive symptoms.

Several possible explanations exist for the differences between our findings and those of Morgan *et al.*⁹ In both studies respondents were asked to rate their own health, including their psychological well-being.²¹ This partly accounts for the association between self reported health and depressive symptoms measured with the Beck depression inventory or the Centers for Epidemiologic Studies' depression scale. The other variable in the regression model was the level of physical function. In the study of men in Rancho Bernardo physical function was assessed by participants being asked to rate their current physical function against that 10 years earlier. In the established populations for epidemiologic studies of the elderly it was assessed by participants being asked to identify difficulties in performing activities of daily living. This is a more direct and stronger measure of restrictions in physical function. The regression model used in the study of men in Rancho Bernardo explained 10% of the variance in depressive symptoms whereas the model in this study explained 13-15% of the variance (table V).

The difference may be further explained by the fact that the populations studied were not alike with respect to age and health: the age of the cohort in Rancho Bernardo ranged from 50 to 89 while in this study the age of male participants ranged from 71 to 100. Also, participants with severe depressive symptoms differed in profile: whereas in Rancho Bernardo the highest rate of severe depression was 5.4%, in the 80-89 year old age group, in the established populations for epidemiologic studies of the elderly the lowest rate was 9.1%, in the youngest age group of men. These distinctions could be due to differences in the two models but are

Clinical implications

- High cholesterol concentration is a well established risk factor for heart disease
- Low cholesterol concentration in elderly people is thought to cause severe depressive symptoms, which could increase mortality from external causes such as suicide, murder, and accidents
- In this study men and women aged ≥ 80 with a low cholesterol concentration were nearly twice as likely to have severe depressive symptoms as those with a normal or high concentration
- After factors relating to health had been controlled for, however, low cholesterol concentration was not associated with severe depressive symptoms in this age group
- This finding is important for the management of elderly patients with high cholesterol concentrations

probably due to characteristics of these populations, such as health status. In Morgan *et al.*'s study the number of drugs used was not entered into the final regression model because it did not reach the level of $P \leq 0.05$ in the regression model; this may have been because the younger participants were taking fewer drugs or because the older participants were healthier than those in the established populations for epidemiologic studies of the elderly. Use of drugs was positively correlated with the score on the Centers for Epidemiologic Studies' depression scale in this study. These differences in the study populations and in the variables examined may explain why the conclusions differ.

Our findings do not support the hypothesis that increased mortality from external causes in people with a lower cholesterol concentration is due to their having more severe depressive symptoms, which might lead to suicide or violence. Cholesterol concentration is influenced by dietary and genetic factors and by health.¹¹⁻¹³ This study showed that after the confounding effects of poor health had been controlled for by adjustment for self reported health, physical function, recent weight loss, and the number of drugs used in the previous two weeks, no association between low cholesterol concentration and severe depressive symptoms in either elderly men or elderly women was observed. Doctors should not be deterred, therefore, from seeking to lower cholesterol concentration in elderly patients whose concentrations are high.

TABLE IV—Correlations between log depression score, cholesterol concentration, and measures of health status in 3939 participants in established populations for epidemiologic studies of the elderly

	Men		Women	
	Log score†	Total cholesterol	Log score†	Total cholesterol
Log depression score†	1.00		1.00	
Total cholesterol	-0.08**	1.00	-0.05**	1.00
Current weight	-0.05*	0.05	-0.01	0.03
Lost > 10% of baseline weight	0.10***	-0.15***	0.11***	-0.13***
Age	0.15***	-0.19***	0.07***	-0.13***
No of new diseases:				
In previous five years	0.11***	-0.04	0.09***	-0.04*
Since last annual follow up	0.08**	-0.04	0.10***	-0.02
No of drugs	0.22***	-0.06*	0.18***	-0.04*
Physical function	0.16***	-0.12***	0.14***	-0.10***
Self reported health	0.36***	-0.04	0.36***	-0.05**

P* < .05, **P < .01, ***P < .001.

†Scores on Centers for Epidemiologic Studies' depression scale.

TABLE V—Regression model of log depression score* for 3939 participants in established populations for epidemiologic studies of the elderly

	Men		Women	
	Coefficient (SE)	P value	Coefficient (SE)	P value
Model A: Adjusted for self reported health and physical function				
Age	0.01 (0.003)	0.0001	0.01 (0.002)	0.02
Self reported health	0.33 (0.02)	0.0001	0.31 (0.02)	0.0001
Physical function (0-6)	0.09 (0.03)	0.002	0.05 (0.02)	0.003
Low cholesterol	-0.09 (0.05)	0.11	-0.06 (0.06)	0.20
Adjusted r ²	0.15		0.13	
Model B: Adjusted for self reported health, physical function, weight loss, and No of drugs				
Age	0.01 (0.003)	0.0001	0.004 (0.002)	0.08
Self reported health	0.29 (0.02)	0.0001	0.29 (0.02)	0.0001
No of drugs	0.25 (0.01)	0.001	0.02 (0.005)	0.0009
Physical function	0.06 (0.03)	0.03	0.04 (0.02)	0.02
Weight loss > 10% of baseline value	0.05 (0.06)	0.34	0.06 (0.03)	0.07
Cholesterol	-0.09 (0.05)	0.12	-0.03 (0.06)	0.61
Adjusted r ²	0.15		0.14	

*Scores on Centers for Epidemiologic Studies' depression scale.

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Attitudes among NHS doctors to requests for euthanasia

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Abstract

Objectives—To explore NHS doctors' attitudes to competent patients' requests for euthanasia and to estimate the proportion of doctors who have taken active steps to hasten a patient's death.

Design—Anonymous postal questionnaire, with no possibility of follow up. The survey was conducted from December 1992 to March 1993.

Subjects—All (221) general practitioners and 203 hospital consultants in one area of England.

Results—273 doctors responded to a question on whether a patient had ever asked them to hasten death. Of these, 163 had been asked to; 124 of these had been asked to take active steps to hasten death; 38 of 119 (32%) of these had complied with such a request (95% confidence interval 23% to 40%). This proportion represented 12% of all those who returned a completed questionnaire and 9% of all those who had been sent a questionnaire (95% confidence interval 6.3% to 11.7%). A larger proportion of the respondents (142/307 (46%)), however, would consider taking active steps to bring about the death of a patient if it was legal to do so.

Conclusions—Many doctors face difficult decisions about euthanasia. For the benefit of both patients and doctors euthanasia should be discussed more openly.

Introduction

Euthanasia evokes strong feelings in everyone, including doctors. Although doctors in Britain are known to practise euthanasia, few data exist either on doctors' attitudes to euthanasia or on its incidence. Euthanasia can be classified as active or passive: active euthanasia occurs when a doctor takes active steps to end a patient's life, and passive euthanasia occurs when he or she allows a patient to die through deliberate inaction. We aimed to explore doctors' attitudes to requests for euthanasia from competent patients and to estimate the proportion of doctors who have practised active euthanasia.

Methods

We conducted our survey from December 1992 to March 1993. We sent a questionnaire about euthanasia to all general practitioners (n=221) and to a similar number of hospital consultants (n=203) in one area of England. The questions were worded to elicit response about hastening death in competent patients only.

Not all respondents were required to answer all the questions: respondents who denied ever having been requested to hasten a patient's death (question 1) were

directed to bypass question 2 (about complying with requests) and to proceed to the remaining questions. All respondents were asked about their age, sex, and religious beliefs. Respondents were assured of anonymity but were told that the results of the survey might be published.

All statistics were calculated with the program SPSS 4.0 and Pearson's χ^2 test.

Results

In all, 318 of the 424 questionnaires were returned, but only 312 had been completed. This represents a return rate of 73.6%.

In question 1 the doctors were asked whether a patient had ever asked them to hasten his or her death. They were given a choice of three responses: "Yes, by asking for treatment to be withdrawn or withheld" (passive euthanasia); "Yes, by seeking active steps to hasten death" (active euthanasia); or "No." Table I shows the responses. In all, 163 of the 273 doctors who responded to this question had been asked at some stage to hasten a patient's death; 124 had been asked to hasten death with active euthanasia, 71 of whom had also been asked for passive euthanasia. A higher proportion of general practitioners (109/169 (64%)) than consultants (54/104 (52%)) had received such a request.

In question 2 the doctors were asked whether they had ever complied with a patient's request for active euthanasia; 119 of the 124 doctors who had ever been asked for such help answered this question. Table II shows their responses. In all, 38 had taken active steps to end a patient's life, which represents 12% of all doctors who returned a completed questionnaire and 9.0% (95% confidence interval 6.3% to 11.7%) of all those who had been sent a questionnaire. No significant associations existed between the respondents' age, sex, or religious beliefs and answers to question 2.

TABLE I—Responses of 273 doctors to question 1, which asked "In the course of your medical practice, has a patient ever asked you to hasten his or her death?" Values are numbers (percentages) of doctors

Response	General practitioners (n=169)	Consultants (n=104)	Total (n=273)
Had been asked to hasten death	109 (64)	54 (52)	163 (60)
Had been asked for:			
Passive euthanasia only	22 (13)	17 (16)	39 (14)
Active euthanasia only	42 (25)	11 (11)	53 (19)
Both passive and active euthanasia	45 (27)	26 (25)	71 (26)
Total who had been asked for active euthanasia	87 (51)	37 (36)	124 (45)
Had not been asked to hasten death	60 (36)	50 (48)	110 (40)

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