Serum Cholesterol Levels and In-Hospital Mortality in the Elderly

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PURPOSE: Although total cholesterol levels among middle-aged persons correlate with long-term mortality from all causes, this association remains controversial in older persons. We explored whether total cholesterol levels were independently associated with in-hospital mortality among elderly patients.

METHODS: We analyzed data from a large collaborative observational study, the Italian Group of Pharmacoepidemiology in the Elderly (GIFA), which collected data on hospitalized patients. A total of 6984 patients aged 65 years or older who had been admitted to 81 participating medical centers during four survey periods (from 1993 to 1998) were enrolled. Patients were divided into four groups based on total cholesterol levels at hospital admission: <160 mg/dL (n = 2115), 160 to 199 mg/dL (n = 2210), 200 to 239 mg/dL (n = 1719), and ≥240 mg/dL (n = 940).

RESULTS: Patients (mean [± SD] age, 78 ± 7 years) were hospitalized for an average of 15 ± 10 days. The mean total cholesterol level was 186 ± 49 mg/dL. A total of 202 patients died during hospitalization. Mortality was inversely related to cholesterol levels (<160 mg/dL: 5.2% [110/2115]; 160–199 mg/dL: 2.2% [49/2210]; 200–239 mg/dL: 1.6% [27/1719]; and ≥240 mg/dL: 1.7% [16/940]; *P* for linear trend <0.001). After adjustment for potential confounders (demographic characteristics, smoking, alcohol use, indicators of nutritional status, markers of frailty, and comorbid conditions), low cholesterol levels continued to be associated with in-hospital mortality. Compared with patients who had cholesterol levels <160 mg/dL, the odds ratios for in-hospital mortality were 0.49 (95% confidence interval [CI]: 0.34 to 0.70) for participants with cholesterol levels of 160 to 199 mg/dL, 0.41 (95% CI: 0.26 to 0.65) for those with cholesterol levels of 200 to 239 mg/dL, and 0.56 (95% CI: 0.32 to 0.98) for those with cholesterol levels ≥240 mg/dL. These estimates were similar after further adjustment for inflammatory markers and after excluding patients with liver disease.

CONCLUSION: Among older hospitalized adults, low serum cholesterol levels appear to be an independent predictor of short-term mortality. **Am J Med. 2003;115:265–271.** ©2003 by Excerpta Medica Inc.

Total cholesterol is an independent predictor of long-term mortality from all causes in middle-aged persons, but this association is controversial among the elderly (1–7). Several studies have suggested that high cholesterol levels provide a mortality advantage over lower levels among persons aged 65 years or older (2,4–6). In contrast, others have reported a direct (7) or a U-shaped relation (3) between total cholesterol levels and mortality.

A major difference between middle-aged and older adults is the greater prevalence of coexisting disease and poor health among the elderly (8). Older frail persons with a high burden of disease may have lower cholesterol levels and greater mortality than those with few (or no) medical problems who have low-to-normal cholesterol levels (9,10). Indeed, total cholesterol levels tend to decrease among older men and women, and this trend may correlate with the effects of poor health (11). Thus, frailty may confound the relation between cholesterol levels and long-term mortality in older patients. In previous studies, clinical parameters of malnutrition (low levels of serum albumin [12], lymphocytopenia [13], and low body mass index [14]) have independently predicted mortality among hospitalized older patients. In another study, markers of inflammation—which were associated with low levels of total cholesterol—predicted in-hospital mortality in the elderly (15).

We studied whether total cholesterol levels predict all-cause in-hospital mortality, independent of frailty and comorbidity, or whether it serves only as a marker of health status, among hospitalized elderly patients.

METHODS

The Gruppo Italiano di Farmacoepidemiologia nell'Anziano (GIFA), a group of investigators who are based in community and university hospitals throughout Italy, periodically surveys drug use, occurrence of adverse drug reactions, and quality of hospital care (16,17). Briefly, all patients admitted to 81 clinical centers in Italy were enrolled and followed until discharge. The study periods were May 1 to June 30 and September 1 to

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December 31, 1988; May 15 to June 15, 1991; and May 1 to June 30 and September 1 to October 31 in 1993, 1995, 1997, and 1998. For each patient, a questionnaire was completed at admission and updated daily by a study physician who had received specific training. Data collected included demographic characteristics, functional and cognitive status, medications taken before admission and during hospital stay, and admission and discharge diagnoses. We ascertained in-hospital mortality; data about cause of death or death after hospitalization were not gathered.

Laboratory Parameters

Clinical chemistry test results, including total serum cholesterol, were collected during the 1993, 1995, 1997, and 1998 survey periods. Total cholesterol level was part of a series of blood tests that were done routinely at admission. Levels of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol were not gathered. All routine laboratory tests were performed the morning after the first day of admission, following an overnight 12-hour fast. Samples were assayed in the central laboratory at each clinical center, using standardized enzymatic methods. Each laboratory fulfilled the requirements of a standard quality control program, thus ensuring the reliability and validity of all biochemical measures. For analytic purposes, four categories of total cholesterol levels were defined: $<$160 mg/dL (hypocholesterolemia), 160 to 199 mg/dL (normal cholesterol levels), 200 to 239 mg/dL (borderline hypercholesterolemia), and $\geq$240 mg/dL (hypercholesterolemia).

Serum albumin levels were measured using the colorimetric method, categorized as $<$35 g/L or $\geq$35 g/L. Erythrocyte sedimentation rate was measured by the Westergren method. Fibrinogen levels were determined by the prothrombin time–derived method.

Covariates

Functional impairment was defined as needing assistance to perform at least one of the following activities of daily living: eating, dressing, bathing, transferring, and toileting. Cognitive performance was assessed using the Hodkinson Abbreviated Mental Test (18); a score $<$7 was used to define cognitive impairment (19).

Drugs were coded according to the Anatomical Therapeutic and Chemical codes (20). Discharge diagnoses were coded according to the *International Classification of Diseases, Ninth Edition, Clinical Modification* (21). Comorbidity was quantified using the Charlson comorbidity index by adding scores assigned to specific discharge diagnoses (22).

Alcohol use was determined by asking patients to report the average daily number of drinks of any alcoholic beverage during the past year. The amount of alcohol was then expressed as mL of wine (one drink = 100 mL). A conversion table was used for other alcoholic beverages. Smoking habits were defined as current, former, and never smoker. Body mass index (kg/m^2) was calculated using objective measures and was coded as a three-level variable, using the cutpoints 18.5 kg/m^2 and 25 kg/m^2. Albumin level was coded as a dichotomous variable, based on the cutpoint of 35 g/L.

Data Analysis

From an initial sample of 12,757 patients in whom clinical chemistry data had been collected, we excluded those younger than 65 years (n = 3336) and those with cancer (n = 1035). We subsequently excluded 1402 patients for whom body mass index had not been collected. This resulted in a final sample of 6984 patients. In comparison with those who were excluded because of incomplete data, those included in the study were significantly younger (mean [$\pm$ SD] age, 78 $\pm$ 7 years vs. 80 $\pm$ 7 years, $P <0.001$), less likely to be functionally and cognitively impaired (need of assistance in one or more activities of daily living: 37% vs. 60%, $P <0.001$; and Hodkinson Abbreviated Mental Test $<$7: 32% vs. 52%, $P <0.001$), had higher mean cholesterol levels (186 $\pm$ 49 mg/dL vs. 178 $\pm$ 53 mg/dL, $P <0.001$), and were less likely to die during hospitalization (2.9% vs. 11.9%, $P <0.001$). Data on fibrinogen and erythrocyte sedimentation rate were not collected during the 1993 survey period; this information was available for 3080 patients. In comparison with this latter group, those for whom these data were not available were significantly older (78 $\pm$ 7 years vs. 77 $\pm$ 7 years, $P <0.001$), more likely to be functionally and cognitively impaired (need of assistance in one or more activities of daily living: 40% vs. 32%, $P <0.001$; and Hodkinson Abbreviated Mental Test $<$7: 34% vs. 30%, $P = 0.005$), and had a higher mortality (3.3% vs. 2.4%, $P = 0.04$); there was no difference in mean cholesterol levels (186 $\pm$ 49 mg/dL vs. 186 $\pm$ 50 mg/dL, $P = 0.67$).

We used analysis of variance to compare baseline characteristics by cholesterol levels for normally distributed variables. Otherwise, the nonparametric Kruskal-Wallis H test was used. Chi-squared tests were used for dichotomous variables. The significance of the trend by cholesterol levels was assessed using the Mantel-Haenszel test for linear trend.

Crude and adjusted odds ratios and 95% confidence intervals for mortality by cholesterol levels were calculated using logistic regression models. Variables considered for adjustment were age, sex, body mass index, smoking, alcohol consumption, Charlson comorbidity index, functional impairment, cognitive impairment, and serum albumin levels. In these models, age was treated as a continuous variable; albumin and body mass index were coded as discrete variables, based on the cutpoints mentioned above. To address whether the associations between different levels of cholesterol and in-hospital mortality were similar among different age and sex

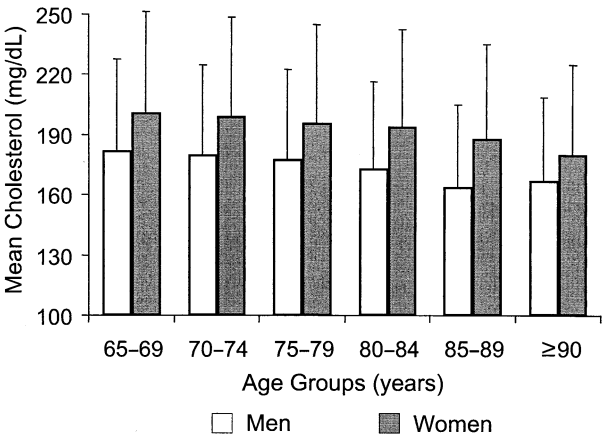

Figure 1. Mean (± SD) serum cholesterol level by sex and age. For both men and women, the *P* for trend for serum cholesterol level by age was <0.001.

groups, we performed logistic regression models that stratified the cohort by age and sex.

To assess whether the association between serum cholesterol and mortality could be explained by inflammation, we performed an additional logistic regression model that included the erythrocyte sedimentation rate and fibrinogen level. Because the use of statins or any other lipid-lowering agent was very low within the study sample (116 patients [1.7%]), it was not included in our analyses. Statistical analysis was performed using the SPSS 10.0 package (Chicago, Illinois).

RESULTS

The mean (± SD) age of the 6984 patients in the study was 78 ± 7 years, and 3279 (47%) were male. The mean length of hospital stay was 15 ± 10 days. The mean total cholesterol level was 186 ± 49 mg/dL (range, 50 to 492 mg/dL). Cholesterol declined with age, and at any age women had higher levels than men (Figure 1).

Demographic, clinical, and biochemical characteristics differed markedly by serum cholesterol level (Table 1). Increasing levels of total cholesterol were associated with a consistent reduction in the prevalence of several indicators of poor health, including body mass index, functional and cognitive impairment, and comorbid medical problems, as well as low albumin levels.

Cholesterol Levels and Mortality

A total of 202 deaths occurred during hospitalization. The mean cholesterol level was 162 ± 54 mg/dL among those who died, compared with 187 ± 49 mg/dL among survivors ($P < 0.001$). There was an inverse association between mortality and cholesterol levels (Table 2). In the unadjusted model, there was a significant and progressive decrease in mortality as cholesterol levels increased, particularly for patients with levels >200 mg/dL. Adjusting for potential confounders, including markers of frailty, somewhat reduced the strength of the association between total cholesterol level and mortality, but it remained statistically significant (Table 2). After exclusion of 382 patients with liver disease, the odds ratios (compared with cholesterol levels <160 mg/dL) for in-hospital mortality were 0.52 (95% confidence interval [CI]: 0.36 to 0.75) for participants with cholesterol levels of 160 to 199 mg/dL, 0.43 (95% CI: 0.27 to 0.68) for those with cholesterol levels of 200 to 239 mg/dL, and 0.56 (95% CI: 0.31 to 1.01) for patients with cholesterol levels ≥240 mg/dL in analysis that adjusted for age, sex, body mass index, smoking, alcohol consumption, Charlson comorbidity index, functional impairment, cognitive impairment, and serum albumin levels.

The associations between cholesterol level and mortality were similar in those aged 65 to 79 years and those aged ≥80 years (Figure 2; *P* for interaction = 0.14). The associations between cholesterol level and mortality were also similar when patients were stratified by albumin level (Figure 3).

Erythrocyte sedimentation rate and fibrinogen levels were obtained from 3080 patients. When these inflammatory markers were added to the logistic regression model, the inverse association between total cholesterol level and mortality persisted. Compared with patients whose cholesterol levels were <160 mg/dL (mortality = 4.6% [43/932]), participants with higher cholesterol levels had lower mortality: 1.6% [15/967] among those with levels from 160 to 199 mg/dL (OR = 0.32; 95% CI: 0.17 to 0.61); 1.3% (10/772) among those with levels from 200 to 239 mg/dL (OR = 0.31; 95% CI: 0.15 to 0.65); and 1.7% (7/409) among those with levels ≥240 mg/dL (OR = 0.49; 95% CI: 0.20 to 1.18).

DISCUSSION

We found that among acutely ill hospitalized patients, low serum cholesterol level was associated with increased all-cause mortality during hospitalization, regardless of malnutrition, frailty, inflammation, and comorbidity. Mortality did not differ substantially among participants with high cholesterol levels (≥240 mg/dL) and those with intermediate cholesterol levels (160 to 199 mg/dL or 200 to 239 mg/dL), but was significantly higher among patients with cholesterol levels <160 mg/dL, suggesting a low-cholesterol threshold effect. Our results in this acutely ill sample are consistent with studies that have evaluated the effect of cholesterol on long-term mortality in community-dwelling older adults and in nursing home residents (2,4–6,23).

Table 1. Characteristics of the Sample, Stratified by Serum Cholesterol Levels

Characteristic	Cholesterol Level				
	<160 mg/dL (n = 2115)	160–199 mg/dL (n = 2210)	200–239 mg/dL (n = 1719)	≥240 mg/dL (n = 940)	*P* for Trend
	Number (%) or Mean ± SD				
Age					<0.001
65–79 years	1171 (55)	1287 (58)	1069 (62)	605 (64)	
≥80 years	944 (45)	923 (42)	650 (38)	335 (36)	
Male sex	1202 (57)	1087 (49)	715 (42)	275 (29)	<0.001
Alcohol use*	1072 (52)	1155 (53)	890 (53)	456 (50)	0.34
Smoking					<0.001
Never smoker	1049 (50)	1202 (55)	998 (58)	629 (67)	
Current smoker	213 (10)	222 (10)	142 (8)	91 (10)	
Former smoker	839 (40)	775 (35)	569 (33)	215 (23)	
Functional impairment†	882 (42)	833 (38)	562 (33)	271 (29)	<0.001
Cognitive impairment‡	749 (36)	704 (33)	487 (29)	255 (27)	<0.001
Comorbidity index§	1.5 ± 1.4	1.5 ± 1.4	1.4 ± 1.3	1.4 ± 1.3	0.03
Hypertension	564 (27)	804 (36)	691 (40)	470 (50)	<0.001
Ischemic heart disease	554 (26)	648 (29)	537 (31)	261 (28)	0.04
Heart failure	501 (24)	402 (18)	266 (16)	125 (13)	<0.001
Diabetes	463 (22)	418 (19)	371 (22)	218 (23)	0.36
Liver disease	252 (12)	78 (4)	38 (2)	14 (2)	<0.001
Number of medications	8.1 ± 5.8	7.3 ± 4.8	7.2 ± 5.0	6.9 ± 4.3	<0.001
Use of lipid-lowering drug	7 (0)	22 (1)	26 (2)	61 (7)	<0.001
Serum albumin level <35 g/L	1151 (54)	813 (37)	507 (30)	191 (20)	<0.001
Erythrocyte sedimentation rate (mm/h)‖	39 ± 33	32 ± 28	30 ± 27	31 ± 23	<0.001
Fibrinogen (mg/dL)‖	424 ± 181	430 ± 163	416 ± 146	411 ± 122	0.15
Body mass index					<0.001
<18.5 kg/m^2	172 (8)	119 (5)	84 (5)	29 (3)	
18.5–24.9 kg/m^2	1045 (49)	1054 (48)	736 (43)	435 (46)	
≥25 kg/m^2	898 (43)	1037 (47)	899 (52)	476 (51)	

* Users of any amount of alcohol before hospital admission.
† Need for assistance in one or more of the following activities of daily living: eating, dressing, bathing, transferring, and toileting.
‡ Hodkinson Abbreviated Mental Test <7.
§ Charlson comorbidity index.
‖ Data were collected among 3080 participants.

Cholesterol levels may be associated inversely with the onset and outcomes of specific diseases. Previous studies have shown a graded negative relation between serum cholesterol levels and the risk of nosocomial infections, and in-hospital mortality related to infectious diseases has been associated with low cholesterol levels (24,25). Higher cholesterol levels have been associated with better short-term health outcomes after acute strokes (26). Another study found that cholesterol levels were related inversely to mortality after surgery (27). Finally, although elevated serum cholesterol levels increase coronary heart disease incidence, morbidity, and mortality, they do not affect in-hospital outcomes among patients with acute myocardial infarction (28).

One possible explanation for the lower mortality among patients with elevated cholesterol could be selective survival, if those who are susceptible to the biological effects of high cholesterol levels tend to die before reaching an advanced age. The remaining survivors would represent a selected group with lower cholesterol levels and with favorable genetic factors or other characteristics that protected them from the harmful effects of high cholesterol levels. In addition, although we adjusted all analyses for several indicators of frailty, nutritional status, and comorbidity, it is possible that low cholesterol levels are simply an indicator of poor health status, and that its association with mortality is due to inadequate adjustment for other confounding factors, such as disease severity. In some patients, low cholesterol levels may be a result of an illness that is ultimately fatal, leading to higher mortality among those with lower cholesterol levels. Also, the exclusion of patients with missing data may have led to the selection of a healthier sample, thus affecting the generalizability of our results; for example, inflammatory markers (erythrocyte sedimentation rate and fibrinogen) were measured in less than half of the sample,

Table 2. Association between Serum Cholesterol Levels and All-Cause Mortality, after Adjustment for Various Confounders

Cholesterol level	Mortality during Hospitalization	Unadjusted	Adjusted for Age* and Sex	Also Adjusted for Body Mass Index†, Smoking, and Alcohol Consumption	Also Adjusted for Frailty Indicators‡§
	Number (%)	Odds Ratio (95% Confidence Interval)			
All					
<160 mg/dL (n = 2115)	110 (5.2)	–	–	–	–
160–199 mg/dL (n = 2210)	49 (2.2)	0.41 (0.29–0.58)	0.43 (0.31–0.61)	0.45 (0.32–0.64)	0.49 (0.34–0.70)
200–239 mg/dL (n = 1719)	27 (1.6)	0.29 (0.19–0.45)	0.33 (0.21–0.50)	0.34 (0.22–0.53)	0.41 (0.26–0.65)
≥240 mg/dL (n = 940)	16 (1.7)	0.32 (0.19–0.54)	0.38 (0.22–0.65)	0.41 (0.24–0.71)	0.56 (0.32–0.98)
Men					
<160 mg/dL (n = 1202)	62 (5.2)	–	–	–	–
160–199 mg/dL (n = 1087)	24 (2.2)	0.42 (0.26–0.67)	0.43 (0.27–0.70)	0.47 (0.29–0.76)	0.56 (0.34–0.93)
200–239 mg/dL (n = 715)	14 (2.0)	0.37 (0.20–0.66)	0.41 (0.23–0.74)	0.43 (0.24–0.79)	0.59 (0.32–1.10)
≥240 mg/dL (n = 275)	6 (2.2)	0.41 (0.18–0.96)	0.47 (0.20–1.11)	0.51 (0.22–1.22)	0.80 (0.33–1.96)
Women					
<160 mg/dL (n = 913)	48 (5.3)	–	–	–	–
160–199 mg/dL (n = 1123)	25 (2.2)	0.41 (0.25–0.67)	0.42 (0.26–0.69)	0.42 (0.26–0.69)	0.41 (0.25–0.68)
200–239 mg/dL (n = 1004)	13 (1.3)	0.24 (0.13–0.44)	0.26 (0.14–0.48)	0.26 (0.14–0.49)	0.28 (0.15–0.54)
≥240 mg/dL (n = 665)	10 (1.5)	0.28 (0.14–0.55)	0.34 (0.17–0.67)	0.35 (0.17–0.70)	0.42 (0.20–0.88)

* In these models, age was treated as a continuous variable.
† Body mass index (kg/m^2) was coded as a three-level variable, using the cutpoints 18.5 kg/m^2 and 25 kg/m^2.
‡ Frailty indicators include Charlson comorbidity index, functional impairment, cognitive impairment, serum albumin level. Albumin level was coded as a dichotomous variable, based on the cutpoint of 35 g/L.
§ *P* for interaction between serum cholesterol level and sex in the fully adjusted model = 0.30.

who were younger and had lower rates of functional and cognitive impairment and mortality than the remaining sample.

Because we did not measure cholesterol fractions, we could not investigate whether HDL or LDL cholesterol levels affect the association between total cholesterol levels and mortality. However, Krumholz et al did not detect an association between the ratio of total to HDL cholesterol and all-cause mortality among persons older than 70 years (29). Finally, because we did not ascertain the causes of death in the sample, we were unable to assess the association between cholesterol levels and disease-specific mortality.

Our study provides preliminary evidence that high cholesterol levels are associated with better outcomes among older patients admitted to acute care hospitals.

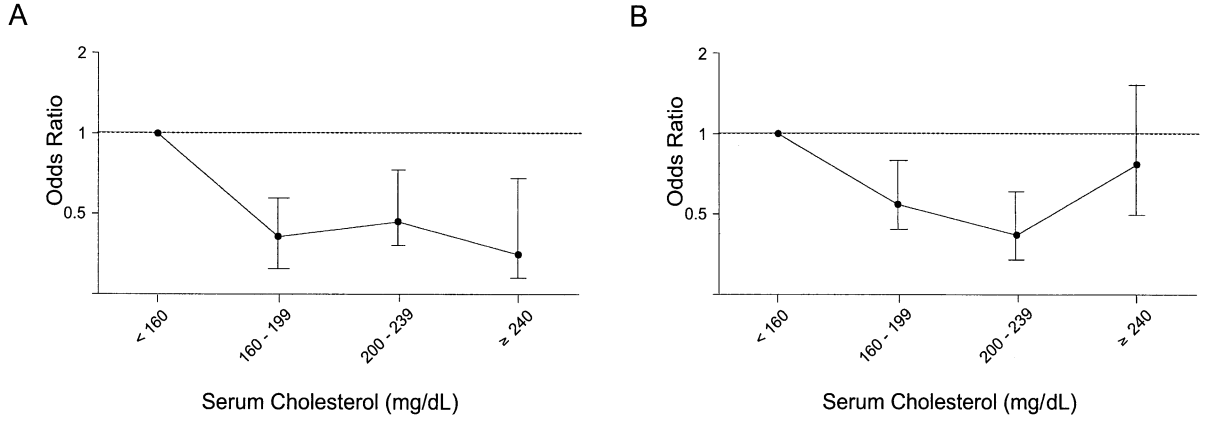

Figure 2. Association between all-cause mortality and serum cholesterol level among participants aged (A) 65–79 years (n = 4132, deaths = 72) and (B) ≥80 years (n = 2852, deaths = 130). Analyses are adjusted for age as a continuous variable, sex, body mass index, smoking, alcohol consumption, Charlson comorbidity index, functional impairment, cognitive impairment, and serum albumin level.

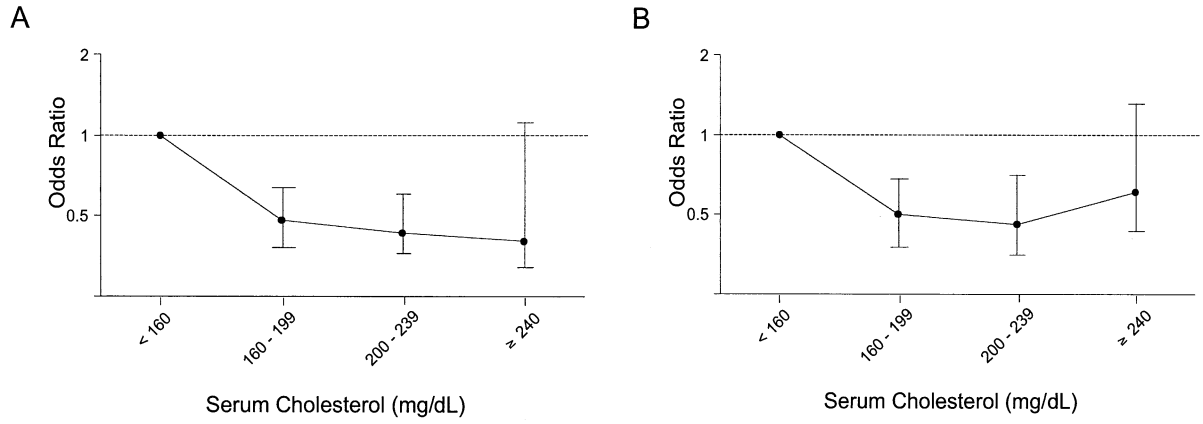

Figure 3. Association between all-cause mortality and serum cholesterol level among participants with (A) serum albumin level <35 g/L (n = 2662, deaths = 116) and (B) serum albumin level ≥35 g/L (n = 4322, deaths = 86). Analyses are adjusted for age as a continuous variable, sex, body mass index, smoking, alcohol consumption, Charlson comorbidity index, functional impairment, and cognitive impairment.

These results should not be misinterpreted as indicating that elevated cholesterol levels confer long-term survival benefit for older adults, which would question the utility of cholesterol-lowering therapy in the elderly (30,31). However, results from the Heart Protection Study, conducted in patients who were not considered ideal candidates in previous studies, indicate that statins provide benefit for elderly persons at risk of vascular disease, regardless of age, sex, or baseline cholesterol levels (32). Similarly, the Prospective Study of Pravastatin in the Elderly at Risk trial, which included many subjects aged 70 years or older, showed a significant benefit of pravastatin on the composite outcome of coronary death, nonfatal myocardial infarction, or stroke, although no effect was seen on all-cause mortality (33).

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REFERENCES

1. Anderson KM, Castelli WP, Levy D. Cholesterol and mortality: 30 years of follow-up from the Framingham study. *JAMA.* 1987;257: 2176–2180.
2. Staessen J, Amery A, Birkenhager W, et al. Is a high serum cholesterol level associated with longer survival in elderly hypertensives? *J Hypertens.* 1990;8:755–761.
3. Jacobs DR Jr. Why is low blood cholesterol associated with risk of nonatherosclerotic disease death? *Annu Rev Public Health.* 1993;14: 95–114.
4. Fagard R. Serum cholesterol levels and survival in elderly hypertensive patients: analysis of data from the European Working Party on High Blood Pressure in the Elderly. *Am J Med.* 1991;90(suppl):62S–63S.
5. Schatz IJ, Masaki K, Yano K, et al. Cholesterol and all-cause mortality in elderly people from the Honolulu Heart Program: a cohort study. *Lancet.* 2001;358:351–355.
6. Weverling-Rijnsburger AW, Blauw GJ, Lagaay AM, et al. Total cholesterol and risk of mortality in the oldest old. *Lancet.* 1997;350: 1119–1123.
7. Corti MC, Guralnik JM, Salive ME, et al. Clarifying the direct relation between total cholesterol levels and death from coronary heart disease in older persons. *Ann Intern Med.* 1997;126: 753–760.
8. Fried LP, Guralnik JM. Disability in older adults: evidence regarding significance, etiology, and risk. *J Am Geriatr Soc.* 1997;45:92–100.
9. Pekkanen J, Nissinen A, Vartiainen E, et al. Changes in serum cholesterol level and mortality: a 30-year follow-up. *Am J Epidemiol.* 1994;139:155–165.
10. Ettinger WH Jr, Harris T, Verdery RB, et al. Evidence of inflammation as a cause of hypocholesterolemia in older people. *J Am Geriatr Soc.* 1995;43:264–266.
11. Volpato S, Zuliani G, Guralnik JM, et al. The inverse association between age and cholesterol level among older patients: the role of poor health status. *Gerontology.* 2001;47:36–45.
12. Antonelli Incalzi R, Landi F, Cipriani L, et al. Nutritional assessment: a primary component of multidimensional geriatric assessment in the acute care setting. *J Am Geriatr Soc.* 1996;44:166–174.
13. Incalzi RA, Capparella O, Gemma A, et al. The interaction between age and comorbidity contributes to predicting the mortality of geriatric patients in the acute-care hospital. *J Intern Med.* 1997;242: 291–298.
14. Landi F, Onder G, Gambassi G, et al. Body mass index and mortality among hospitalized patients. *Arch Intern Med.* 2000;160:2641–2644.
15. Volpato S, Palmieri E, Fellin R, Zuliani G. Acute phase markers are associated with reduced plasma lipid levels in a population of hospitalized elderly patients. *Gerontology.* 2000;46:22–27.
16. Onder G, Pedone C, Gambassi G, et al. Temporal patterns in medical treatment of osteoporosis among elderly patients in Italy. *Eur J Clin Pharmacol.* 2001;57:599–604.
17. Onder G, Pedone C, Landi F, et al. Adverse drug reactions as cause of hospital admissions: results from the Italian Group of Pharmaco-

epidemiology in the Elderly (GIFA). *J Am Geriatr Soc.* 2002;50: 1962–1968.
18. Hodkinson HM. Evaluation of a mental test score for assessment of mental impairment in the elderly. *Age Ageing.* 1972;1:233–238.
19. Rocca WA, Bonaiuto S, Lippi A, et al. Validation of the Hodkinson abbreviated mental test as a screening instrument for dementia in an Italian population. *Neuroepidemiology.* 1992;11:288–295.
20. Pahor M, Chrischilles EA, Guralnik JM, et al. Drug data coding and analysis in epidemiological studies. *Eur J Epidemiol.* 1994;10:405–411.
21. *International Classification of Diseases.* 9th rev. Washington, DC: Public Health Service–Health Care Financing Administration; 1980.
22. Charlson ME, Pompei P, Ales KL, Mackenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40:373–383.
23. Forette B, Tortrat D, Wolmark Y. Cholesterol as risk factor for mortality in elderly women. *Lancet.* 1989;1:868–870.
24. Iribarren C, Jacobs DR Jr, Sidney S, et al. Cohort study of serum total cholesterol and in-hospital incidence of infectious diseases. *Epidemiol Infect.* 1998;121:335–347.
25. Pacelli F, Doglietto GB, Alfieri S, et al. Prognosis in intra-abdominal infections. Multivariate analysis on 604 patients. *Arch Surg.* 1996; 131:641–645.
26. Dyker AG, Weir CJ, Lees KR. Influence of cholesterol on survival after stroke: retrospective study. *BMJ.* 1997;314:1584–1588.
27. Delgado-Rodriguez M, Medina-Cuadros M, Gomez-Ortega A, et al. Cholesterol and serum albumin levels as predictors of cross infection, death, and length of hospital stay. *Arch Surg.* 2002;137:805–812.
28. Becker RC, Corrao JM, Lew R, et al. Relationship between serum total cholesterol, infarct size, and early clinical outcome following acute myocardial infarction. *Cardiology.* 1992;80:65–70.
29. Krumholz HM, Seeman TE, Merrill SS, et al. Lack of association between cholesterol and coronary heart disease mortality and morbidity and all-cause mortality in persons older than 70 years. *JAMA.* 1994;272:1335–1340.
30. Jacobson TA. "The lower the better" in hypercholesterolemia therapy: a reliable clinical guideline? *Ann Intern Med.* 2000;133: 549–554.
31. Smith SC Jr. Lessons from cholesterol-lowering trials. *Am J Med.* 1998;104(suppl):28S–32S.
32. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360:7-22.
33. Shepherd J, Blauw GJ, Murphy MB, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. *Lancet.* 2002;360:1623–1630.