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ORIGINAL RESEARCH

Serum total cholesterol concentration and 10-year mortality in an 85-year-old population

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Abstract: Little is known about the association between total cholesterol (TC) and all-cause mortality in the elderly (especially the very elderly). Here we examined the association between TC and all-cause mortality in 207 very elderly (85-year-old) participants. In 2003, we performed a baseline laboratory blood examination, and blood pressure (BP) and body mass index (BMI) measurements, and lifestyle questionnaires were completed by the participants. The participants were followed for the subsequent 10 years. As of 2013, of the 207 participants in 2003, 70 participants had survived, 120 individuals had died, and 17 were lost to follow up. The TC values were divided into high-TC (≥209 mg/dL), intermediate-TC (176–208 mg/dL), and low-TC (≤175 mg/dL) categories. With the Kaplan–Meier method, we found that both the high-TC and intermediate-TC participants survived longer than the low-TC participants. The men with high TC survived longer than those with low TC, but no corresponding difference was found for the women. A multivariate Cox proportional hazards regression model, with adjustment for gender, smoking, alcohol intake, history of stroke or heart disease, serum albumin concentration, BMI, and systolic BP, revealed that the total mortality in the low-TC group was 1.7-fold higher than that in the high-TC group. Mortality, adjusted for the same factors, decreased 0.9% with each 1 mg/dL increase in the serum TC concentration and decreased 0.8% with each 1 mg/dL increase in the serum (low-density lipoprotein) LDL-cholesterol (LDL-C) concentration. Our results indicate an association between lower serum TC concentrations and increased all-cause mortality in a community-dwelling, very elderly population. Mortality decreased with the increases in both TC and LDL-C concentrations, after adjustment for various confounding factors. These findings suggest that low TC and low LDL-C may be independent predictors of high mortality in the very elderly.

Keyword: community-dwelling, very elderly, LDL-cholesterol, gender difference, prospective cohort

Introduction

There is a clear association between hypercholesterolemia and the increased incidence of ischemic heart disease.[1] For middle-aged populations[2] and younger men,[3] serum cholesterol has been consistently shown to be a risk factor for coronary heart disease (CHD). Similarly, in a middle-aged population aged 30–59 years, the risk of CHD deaths among the participants with cholesterol ≥8.0 mmol/L (309.4 mg/dL) was five-fold that of the participants with cholesterol <5.0 mmol/L (193.3 mg/dL).[4] In 6,063 healthy men aged 28–61 years with a mean follow-up interval of 18.7 years, hypercholesterolemia (≥6.5 mmol/L [251 mg/dL]) was also associated with an increased incidence of ischemic stroke and cardiac events and with a reduced incidence of

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intracerebral hemorrhage.[5] A meta-analysis of 61 prospective studies of 900,000 adults between the ages of 40–89 years found an association of 1 mmol/L (38.7 mg/dL) lower total cholesterol (TC) with about one-half, one-third, and one-sixth lower ischemic heart disease mortality at ages 40–49, 50–69, and 70–89 years, respectively, whereas no positive association was found between cholesterol and stroke mortality at older ages.[6] However, in men aged 65 years and older, although there was a positive association between serum TC and CHD morbidity/mortality, this association was not found for the very elderly (ie, aged ≥80 years).[7]

In a US National Heart, Lung, and Blood Institute (NHLBI) conference held in 1990, for populations with age ranges of 35–69 years, a U-shaped curve was described for the relation between all-cause mortality and blood TC, based on the data obtained from the positive relation of TC with CHD death and an inverse relation with deaths caused by some cancers, respiratory disease, digestive disease, trauma, and residual deaths.[8] In other studies, low TC was associated with increased all-cause mortality in the nondemented elderly aged 65–98 years (mean age 76.1 years),[9] in elderly aged 65–84,[10] and in elderly hospitalized patients with the mean age of 81.4 years.[11] In people older than 85 years, increases in TC were associated with longevity due to lower mortality from cancer and infection.[12] Thus, it seems likely that CHD morbidity and mortality may be related to high TC, but low TC may be related to all-cause mortality.

Elevated ratios of TC to high-density lipoprotein cholesterol (HDL-C) have been positively related to an increased total risk of mortality in older men aged 65 and over.[13] In another population aged 65 and older, the relationship of total mortality with low-density lipoprotein cholesterol (LDL-C) was J-shaped.[14] Hypocholesterolemia was not an independent risk factor for increased overall mortality in community-dwelling older persons with the average age of 74 years.[15] Since the association between TC and mortality in the elderly is not consistent and since little is known about this association, especially for the very elderly, we examined it in very old participants – aged 85 years. Additionally, as far as we know, no studies have been done on this topic in Japan. We hypothesized that in an 85-year-old population, TC might be inversely associated with total mortality.

Methods

This study commenced in 1998, with 827 participants who were 80 years old. The subjects were born in 1917 and lived in one of nine districts (Bunzen City, Munakata City, Yukuhashi City, Tobata Ward of Kitakyushu City, Kanda Town, Katsuyama Town, Toyotsu Town, Tsuiki Town, and Shinyoshitomi Village) in the Fukuoka Prefecture, Japan. Of the 827 persons, 410 declined to participate in the study, and 210 died in the following 5 years. Thus, 207 individuals who were 85 years old in 2003 (90 males, 117 females) participated in the present study, and at that time, each participant underwent a baseline laboratory blood examination, which included serum concentrations of TC, LDL-C, HDL-C, triglyceride (TG), albumin, and blood glycated hemoglobin (HbA_{1c}). Blood pressure (BP) and body mass index (BMI) were also measured in 2003, when all the participants were 85 years old. The serum TC, LDL-C, and TG were measured by an enzymatic method, while the HDL-C was measured by the precipitation method. All samples were shipped for analysis to the same laboratory (BML Inc, Tokyo, Japan). Further, questionnaires concerning the participants' smoking habit, alcohol intake, history of stroke, history of heart disease, and level of education were also completed by the participants in 2003. After the baseline examination, the 207 participants were followed up for 10 years. Confirmation of whether the individual was living or had died was obtained by asking the family via a telephone call or home visit.

The cause of death was classified according to the tenth version of the International Classification of Diseases (ICD-10).[16] This study was approved by the Human Investigations Committee of Kyushu Dental College and was conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki, as revised in 2002. Informed written consent was obtained from all participants, according to the principles mentioned above.

All the data were reported as means ± standard deviation (SD). The differences in mean values among three groups were examined using an analysis of variance (ANOVA) and those between two groups were evaluated using the unpaired *t*-test. The categorical variables were compared using the chi-squared test. The associations between the three TC groups (a high-TC group [n=69], with TC of ≥209 mg/dL; an intermediate-TC group [n=69], with TC of 176–208 mg/dL; and a low-TC group [n=67], with TC of ≤175 mg/dL) or serum concentrations of TC, LDL-C, HDL-C, or TG, and time with 10-year mortality were assessed using the multivariate Cox proportional hazards regression analysis, in which only gender was adjusted or both gender and other various confounding factors (smoking, alcohol intake, history of stroke or heart disease, serum albumin concentration, BMI, and systolic BP) were adjusted. A comparison of the survival rates among the three TC groups was also assessed by the Kaplan–Meier method, followed by a logrank test to assess

the significance between the survival curves. The results were considered to be significant at $P<0.05$.

Results

As of 2013, of the 207 participants aged 85 years in 2003 who participated in this study, 70 survived, 120 individuals had died, and 17 were lost to follow up. Of the 120 participants who died, 38 deaths were due to cardiovascular disease (CVD) (16 heart failures, eleven strokes, five myocardial infarctions, three aneurysms, one arrhythmia, one hypertension, and one unknown), 22 deaths were due to senility, 21 were due to respiratory tract diseases (18 pneumonias, one empyema, one respiratory failure, and one emphysema), 16 to cancers (four gastric, two lung, two hepatic, two colon, one gallbladder, one urinary tract, one laryngeal, one uterine, one esophageal, and one unknown), four to extrinsic causes, three to gastrointestinal disease, two to urinary tract disease, two to other diseases, and 12 deaths were due to unknown causes.

The mean ± SD serum TC concentration was 194.1±37.1 mg/dL (180.4±29.4 mg/dL for the men, 204.6±39.0 mg/dL for the women) (P=0.000). The mean ± SD LDL-C was 118.0±29.1 mg/dL (110.5±22.7 mg/dL for the men, 123.8±32.1 mg/dL for the women) (P=0.001). The mean ± SD HDL-C was 51.6±13.4 mg/dL (47.5±12.7 mg/dL for the men, 54.7±13.0 mg/dL for the women) (P=0.000), and the mean ± SD TG was 122.4±55.9 mg/dL (112.1±51.9 mg/dL for the men, 130.3±57.8 mg/dL for the women) (P=0.019). The mean ± SD body height was 148.8±9.7 cm, body weight 50.4±9.9 kg, systolic BP 144.2±24.4 mmHg, diastolic BP 78.7±14.0 mmHg, pulse rate 69.5±11.6 beats/minute, hemoglobin 12.7±1.6 g/dL, and albumin 4.3±0.3 g/dL.

The baseline characteristics of the participants in 2003 are shown in Table 1 for three TC concentration groups. The serum TC values were classified into three categories: ≥209 mg/dL (high-TC group [n=69]); 176–208 mg/dL (intermediate-TC group [n=69]); and ≤175 mg/dL (low-TC group [n=67]). Men were more numerous in the low-TC group and there were fewer in the high-TC group compared with women. Alcohol drinking was more common in the intermediate-TC group. All-cause mortality was more prevalent in the low-TC group compared with the high-TC group, but no difference was found in mortality due to cardiovascular disease, cancer, respiratory disease, or senility among the TC groups. The serum albumin concentration was significantly higher in the high-TC group and lower in the low-TC group. Systolic BP was slightly lower in the intermediate-TC group. There was no difference in smoking, history of stroke, history of heart disease, BMI, HbA_{1c}, or level of education among the three TC groups.

The baseline characteristics of the group of participants who survived and the group who did not survive during the 10-year follow-up study period are shown in Table 2. The women survived significantly longer than the men. The serum TC concentration was significantly higher among the survivors compared with the nonsurvivors, and serum LDL-C and serum TG were also significantly higher in the former group than in the latter, whereas no difference was found for the serum HDL-C

Table 1 Baseline characteristics of the participants with different serum concentrations of TC

	High-TC group (≥209 mg/dL)	Intermediate-TC group (176–208 mg/dL)	Low-TC group (≤175 mg/dL)	*P*-value
n	69	69	67	
Gender (men/men+women)	21.7% (15/54)	49.3% (34/35)	59.7% (40/27)	0.000
Smoking (%)	4.4%	4.5%	6.1%	0.885
Alcohol drinking (%)	46.3%	68.7%	38.5%	0.001
History of stroke (%)	4.3%	10.1%	7.5%	0.425
History of heart disease (%)	24.6%	34.8%	29.9%	0.428
TC (mg/dL)	235.2±23.4	191.4±9.9	154.5±14.9	0.000
Mortality (%)	50.0%	62.5%	77.4%	0.007
Cardiovascular death (%)	16.1%	20.3%	24.2%	0.535
Cancer death (%)	3.2%	9.4%	12.9%	0.148
Respiratory death (%)	8.1%	10.9%	12.9%	0.680
Senility-related death (%)	11.3%	10.9%	12.9%	0.936
Serum albumin (mg/dL)	4.47±0.22	4.32±0.29	4.17±0.27	0.000
BMI (kg/m^2)	22.7±2.9	22.9±3.9	22.4±3.5	0.663
Systolic BP (mmHg)	147.8±20.9	138.2±24.7	146.3±26.7	0.047
HbA_{1c} (%)	5.55±0.66	5.48±0.54	5.51±0.77	0.800
Education (years)	9.5±2.2	9.5±2.5	9.3±3.0	0.887

Abbreviations: BMI, body mass index; BP, blood pressure; HbA_{1c}, glycated hemoglobin; TC, total cholesterol.

Table 2 Baseline characteristics of participants who survived or did not survive during the 10-year follow-up period

	Survivors (n=70)	Nonsurvivors (n=120)	*P*-value
Gender (men/women)	30.0% (21/49)	54.2% (65/55)	0.001
Smoking (%)	1.4% (1/68)	7.8% (9/107)	0.093
Alcohol drinking (%)	44.8% (30/37)	48.3% (56/60)	0.759
History of stroke (%)	4/66 (5.7%)	10/110 (8.3%)	0.578
History of heart disease (%)	19/51 (27.1%)	34/86 (28.3%)	1.000
TC (mg/dL)	205.9±33.3	186.2±37.0	0.000
LDL-C (mg/dL)	124.8±26.8	112.9±29.2	0.005
HDL-C (mg/dL)	53.6±11.5	50.3±14.3	0.080
TG (mg/dL)	137.3±65.5	114.8±50.6	0.015
Serum albumin (mg/dL)	4.38±0.29	4.28±0.29	0.023
BMI (kg/m^2)	23.1±2.9	22.3±3.7	0.105
Systolic BP (mmHg)	146.0±23.3	142.2±24.5	0.283
HbA_{1c} (%)	5.48±0.61	5.53±0.71	0.626
Education (years)	9.5±2.4	9.4±2.8	0.793

Abbreviations: BMI, body mass index; BP, blood pressure; HbA_{1c}, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

concentration. The serum albumin concentration was also significantly higher in the survivor group. There was no difference in the prevalence of smoking, alcohol intake, or histories of stroke or heart disease between the survivors and nonsurvivors. Finally, BMI, systolic BP, HbA_{1c}, and level of education did not differ between the survivors and nonsurvivors.

Figure 1 shows the survival curves of the participants among the three TC groups who survived during the 10-year follow-up period. The average survival period was 85.3 months for all participants and was 97.6 months for the high-TC group, 86.5 months for the intermediate-TC group, and 71.2 months for the low-TC group. The high-TC group survived significantly longer than did the low-TC group (*P*=0.000), and the intermediate-TC group also survived significantly longer than the low-TC group (*P*=0.024), whereas no difference was found between the high-TC group and the intermediate-TC group. Among the men, the average survival period was 73.4 months for all men, 95.5 months for the high-TC group, 76.2 months for the intermediate-TC group, and 61.6 months for the low-TC group. The men with high serum TC concentrations survived longer than did those with low TC concentrations (*P*=0.004). There was no difference in survival period between the high-TC group and the intermediate-TC group or between the intermediate-TC group and the low-TC group. Among the women, the survival period was 94.9 months for all women, 98.3 months for the high-TC women, 96.8 months for the intermediate-TC women, and 85.7 months for the low-TC

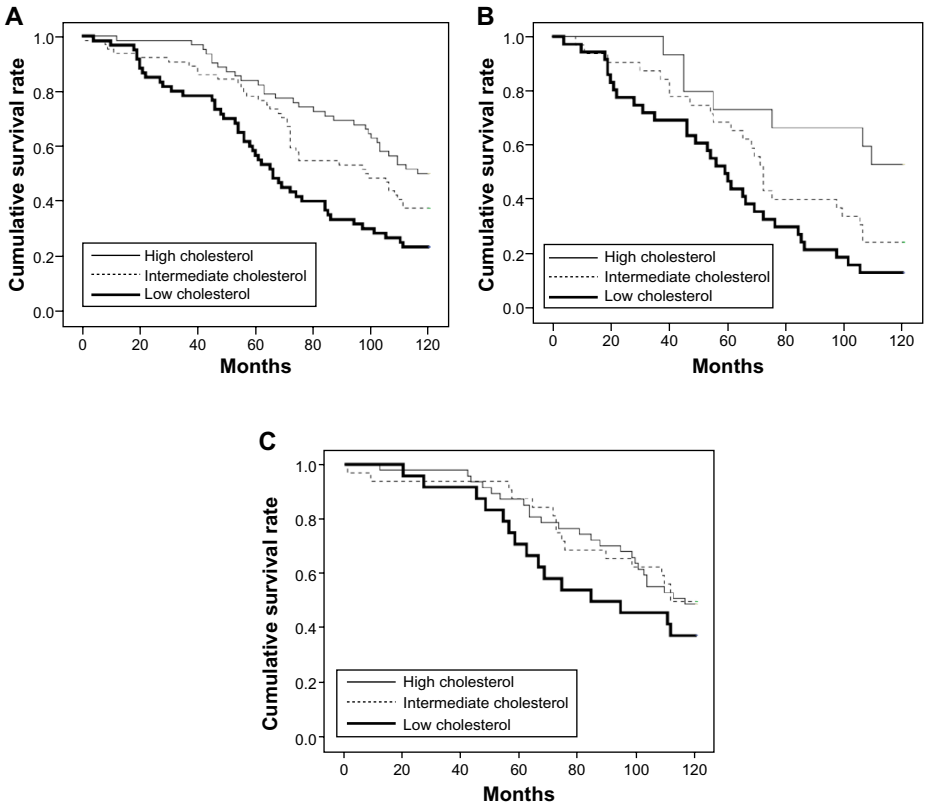

Figure 1 Survival curves of the participants who survived during the 10-year follow-up period among the three total cholesterol (TC) groups: for all participants (**A**), for men (**B**), and for women (**C**).

women. There was no difference in survival period among the female TC groups.

The hazard ratios (HRs), with a 95% confidence interval (CI), assessed by the multivariate Cox proportional hazards regression model for total mortality are shown in Table 3, without adjustment, with adjustment only for gender, and with adjustment for gender, smoking, alcohol intake, history of stroke or heart disease, serum albumin concentration, BMI, and systolic BP. The total mortality without adjustment was 2.4-fold higher in the low-TC group than in the high-TC group, whereas no difference in mortality was found between the high-TC group and the intermediate-TC group.

With adjustment only for gender, the total mortality was twofold higher in the low-TC group than in the high-TC group, and there was no difference between the intermediate- and high-TC groups. The mortality for all men was 1.8-fold higher than the mortality for the women. The total mortality in the low-TC group was still 1.7-fold higher than that in the high-TC group, even with adjustment for the confounding factors of gender, smoking, alcohol intake, history of stroke or heart disease, serum albumin concentration, BMI, and systolic BP. The women and participants with higher BMIs were less likely to die than were men and those with lower BMIs.

Table 3 Multivariate Cox analyses of the high-TC, intermediate-TC, and low-TC groups for total mortality without adjustment; with adjustment only for gender; and with adjustment for gender, smoking, alcohol intake, history of stroke or heart disease, serum albumin concentration, BMI, and systolic BP

	Hazard ratio	95% CI	*P*-value
Not adjusted			
High TC	1.000		
Intermediate TC	1.445	0.904–2.311	0.124
Low TC	2.361	1.494–3.732	0.000
Adjusted only for gender			
High TC	1.000		
Intermediate TC	1.298	0.807–2.087	0.283
Low TC	2.042	1.278–3.262	0.003
Men	1.786	1.229–2.596	0.002
Women	1.000		
Adjusted for gender, smoking, alcohol intake, history of stroke and heart disease, serum albumin concentration, BMI, and systolic BP			
High TC	1.000		
Intermediate TC	1.133	0.670–1.914	0.642
Low TC	1.718	1.016–2.906	0.044
Men	1.672	1.110–2.520	0.014
Women	1.000		
Nonsmoker	1.000		
Smoker	1.304	0.606–2.806	0.498
Nondrinker	1.000		
Drinker	0.877	0.597–1.288	0.504
History of stroke (+)	1.240	0.586–2.627	0.574
History of stroke (–)	1.000		
History of heart disease (+)	1.177	0.754–1.837	0.472
History of heart disease (–)	1.000		
Albumin concentration (g/dL)	0.491	0.232–1.041	0.064
BMI (kg/m^2)	0.939	0.883–0.998	0.044
Systolic BP (mmHg)	0.997	0.989–1.004	0.389

Note: The TC group was divided into three groups (high ≥209 mg/dL; intermediate 176–208 mg/dL; low ≤175 mg/dL), in relation to serum TC concentration.
Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; TC, total cholesterol.

We also assessed the association of mortality due to cardiovascular disease with the three TC groups, LDL-C, HDL-C, and TG, using the multivariate Cox proportional hazards regression model, with adjustment for gender, smoking, alcohol intake, history of stroke or heart disease, serum albumin concentration, BMI, and systolic BP. No associations were found between cardiovascular mortality and the three TC groups or LDL-C, HDL-C, and TG (data not shown).

The results of the multivariate Cox analyses of serum concentrations (mg/dL) of TC, LDL-C, HDL-C, and TG for total mortality are shown in Table 4. Mortality without adjustment decreased by 1.2% with each 1 mg/dL increase in the serum TC concentration, 1.1% with each 1 mg/dL increase in the LDL-C concentration, 1.7% with each 1 mg/dL increase in the HDL-C concentration, and 0.5% with each 1 mg/dL increase in the TG concentration.

With the adjustment only for gender, the total mortality decreased 1.1% with each 1 mg/dL increase in the TC concentration, and it decreased by 1.0% with each 1 mg/dL increase of LDL-C. It decreased by 0.4% with each 1 mg/dL increase in the TG concentration. No relation was found between mortality and the HDL-C.

Mortality, when adjusted for gender, smoking, alcohol intake, history of stroke and heart disease, serum albumin concentration, BMI, and systolic BP, also decreased 0.9% with each 1 mg/dL increase in the serum TC concentration, and it decreased 0.8% with each 1 mg/dL increase in the serum LDL-C concentration. There was no relation between mortality and the serum concentrations of HDL-C or of TG. Even with adjustment for various factors, no association was found between mortality from cardiovascular disease and 1 mg/dL changes in TC, LDL-C, HDL-C, or TG (data not shown).

Discussion

We found an association between lower serum concentration of TC and increased all-cause mortality in a community-dwelling population of 85-year-olds. During the 10-year study follow-up period, the mean survival of the individuals

Table 4 Multivariate Cox analyses of serum concentrations (mg/dL) of TC, LDL-C, HDL-C, and TG for total mortality, without adjustment; with adjustment for gender; and with adjustment for gender, smoking, alcohol intake, history of stroke or heart disease, serum albumin concentration, BMI, and systolic BP

	Hazard ratio	95% CI	*P*-value
Without adjustment			
TC concentration (mg/dL)	0.988	0.982–0.993	0.000
LDL-C concentration (mg/dL)	0.989	0.983–0.996	0.002
HDL-C concentration (mg/dL)	0.983	0.969–0.997	0.020
TG concentration (mg/dL)	0.995	0.991–0.999	0.007
With adjustment only for gender			
Serum concentrations of TC			
TC concentration (mg/dL)	0.989	0.984–0.995	0.000
Men	1.696	1.167–2.464	0.006
Women	1.000		
Serum concentrations of LDL-C			
LDL-C concentration (mg/dL)	0.990	0.983–0.997	0.006
Men	1.886	1.308–2.720	0.001
Women	1.000		
Serum concentrations of HDL-C			
HDL-C concentration (mg/dL)	0.990	0.975–1.005	0.179
Men	1.854	1.266–2.714	0.002
Women	1.000		
Serum concentrations of TG			
TG concentration (mg/dL)	0.996	0.992–0.999	0.019
Men	1.903	1.318–2.746	
Women	1.000		
With adjustment for gender, smoking, alcohol intake, history of stroke or heart disease, serum albumin concentration, BMI, and systolic BP			
Serum concentrations of TC			
TC concentration (mg/dL)	0.991	0.985–0.998	0.010
Men	1.625	1.080–2.447	0.020
Women	1.000		
Nonsmoker	1.000		
Smoker	0.854	0.395–1.848	0.688
Nondrinker	1.000		
Drinker	0.874	0.599–1.277	0.488
History of stroke (+)	1.214	0.578–2.552	0.608
History of stroke (–)	1.000		
History of heart disease (+)	1.172	0.757–1.816	0.476
History of heart disease (–)	1.000		
Albumin concentration (g/dL)	0.580	0.270–1.248	0.163
BMI (kg/m^2)	0.935	0.879–0.995	0.034
Systolic BP (mmHg)	0.998	0.990–1.005	0.552
Serum concentrations of LDL-C			
LDL-C concentration (mg/dL)	0.992	0.984–1.000	0.037
Men	1.748	1.169–2.612	0.006
Women	1.000		
Nonsmoker	1.000		
Smoker	0.830	0.384–1.794	0.636
Nondrinker	1.000		
Drinker	0.826	0.566–1.205	0.322
History of stroke (+)	1.300	0.617–2.741	0.490
History of stroke (–)	1		
History of heart disease (+)	1.180	0.760–1.833	0.461
History of heart disease (–)	1.000		
Albumin concentration (g/dL)	0.489	0.234–1.022	0.057
BMI (kg/m^2)	0.935	0.879–0.995	0.035
Systolic BP (mmHg)	0.997	0.990–1.005	0.512
Serum concentrations of HDL-C			
HDL-C concentration (mg/dL)	0.990	0.975–1.006	0.240
Men	1.725	1.135–2.623	0.011
Women	1.000		
Nonsmoker	1.000		
Smoker	0.733	0.340–1.581	0.428
Nondrinker	1.000		
Drinker	0.869	0.593–1.273	0.470
History of stroke (+)	1.122	0.529–2.379	0.764
History of stroke (–)	1.000		
History of heart disease (+)	1.341	0.866–2.076	0.189
History of heart disease (–)	1.000		
Albumin concentration (g/dL)	0.409	0.202–0.828	0.013
BMI (kg/m^2)	0.928	0.870–0.990	0.024
Systolic BP (mmHg)	0.998	0.991–1.006	0.652
Serum concentrations of TG			
TG concentration (mg/dL)	0.997	0.994–1.001	0.195
Men	1.803	1.205–2.698	0.004
Women	1		
Nonsmoker	1		
Smoker	0.801	0.371–1.730	0.572
Nondrinker	1		
Drinker	0.866	0.592–1.266	0.457
History of stroke (+)	1.186	0.563–2.498	0.654
History of stroke (–)	1.000		
History of heart disease (+)	1.223	0.787–1.900	0.370
History of heart disease (–)	1.000		
Albumin concentration (g/dL)	0.430	0.209–0.885	0.022
BMI (kg/m^2)	0.944	0.886–1.006	0.076
Systolic BP (mmHg)	0.998	0.990–1.005	0.560

Abbreviations: CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

with lower TC was 71.2 months, which was shorter than the mean survival of those with higher TC (97.6 months). The mortality of the individuals with lower TC was 1.7-fold higher than that of the participants with higher TC, after an adjustment for various confounding factors. After adjustment for gender, smoking, alcohol intake, history of stroke and heart disease, serum albumin concentration, BMI, and systolic BP, the mortality decreased by 0.9% with each 1 mg/dL increase in TC. These findings are similar to those found in other studies of elderly populations (aged 65 years and older),[9,10] suggesting that the association of high mortality with low-TC could be extended to the very elderly population in the present study.

After adjustment, not only TC, but also, LDL-C was negatively associated with mortality in this population of 85-year-olds; this finding is also similar to the data observed in the nondemented elderly aged 65 years and older.[9] Elsewhere, Whites and African-Americans with TC and LDL-C in the lowest quartiles were also found to be twice as likely to die as those with values in the highest quartile.[17] Among 85-year-old persons, both low LDL-C and low TC concentrations have been associated with an increased mortality risk due to infections, such as pneumonia and sepsis.[18] In the "oldest old," with a mean age of 89 years, each 1 mmol/L (38.7 mg/dL) increase in TC corresponded to a 15% decrease in total mortality, this being due to the decrease in mortality from cancer and infection.[12]

A report presented at the NHLBI conference[8] indicated that noncardiovascular causes of death, such as respiratory mortality, digestive mortality, traumatic mortality, and residual mortality, were more prevalent in the lowest TC group (<160 mg/dL) than in the higher TC groups. We also found a tendency of higher mortality due to cancer or respiratory disease in the low-TC group compared with the high-TC group (Table 1), although the difference was not significant.

In the present study, it is likely that relatively high TC and LDL-C levels in elderly people benefits their longevity. The high-TC group had a tendency of lower mortality from cancer or respiratory disease, this finding being similar to the findings of Weverling-Rijnsburger et al.[12] These researchers concluded that in people older than 85 years, high-TC is associated with longevity owing to lower mortality from cancer and infection. In hospitalized elderly patients with an average age of 81.5 years, other investigators concluded that increased TC may be associated with reduced mortality risk from malnutrition or inflammation.[11] We additionally found a positive association between TC and albumin concentration. Therefore, high TC and LDL-C may be a marker of better nutrition, which is related to a lower risk of cancer and infection, such as pneumonia.

In the present study, the survival rate in the men was lower in the low-TC group compared with the high-TC group, but no corresponding difference was found in the women. This finding is also in agreement with the NHLBI conference report,[8] indicating that many findings for women were discrepant from those for men. The relation of TC to total mortality is usually flat.[8] Similarly, in a Japanese cohort study with participants aged 30 years or older, the men with the lowest TC (<4.14 mmol/L [160.1 mg/dL]) showed an increase in all-cause mortality; no significant association was found between lowest TC and all-cause mortality in the women in that study.[19] However, there were two limitations in our study. First, the number of men participants was lower than women. Second, more men participants were in the low-TC group (40/27), while more women were in the high-TC group (54/15). These differences between men and women could have affected the conclusion that the inverse association between TC and mortality was found in the men but not in the women.

In our very elderly population of 85-year-olds, we found no association between the serum levels of TC, LDL-C, HDL-C, or TG and mortality from cardiovascular disease. However, cardiovascular mortality has been shown to be greater in individuals with higher serum TC levels, in young men,[3] in healthy men 28–61 years of age,[5] in 900,000 adults between ages of 40–89 years,[6] in 19 cohort studies,[8] and in 7,735 men aged 40–59.[20] However, a meta-analysis found that in elderly women aged 65 years and older, an association between TC and CHD mortality was not significant.[7] In 3,120 older people aged 65 and older, the age-adjusted death rate in relation to serum LDL-C showed a U-shaped pattern for cardiovascular mortality.[14] In another study, the mortality due to CVD was similar among three strata of TC and of LDL-C, in 85-year-old persons.[17] Therefore, it is likely that in an older population, the positive association between cardiovascular mortality and serum TC or LDL-C found in a younger adult population may disappear. Our findings extended this association to 85-year-olds. Since not even a tendency of positive association between TC and CVD mortality was found in our very elderly population, the lack of association may not be due to the small number of subjects. Malnutrition-related inflammation of arteries might increase CVD morbidity and mortality. The reason for the lack of association between TC and CVD mortality remains obscure. Further studies into this association are needed.

Our study had some limitations. The number of participants was small. The participation rate was not high. The causes of death and times of death were obtained by asking the family via telephone or a home visit. We did not consider dietary information, although saturated fat and trans fat are known to affect TC levels. Further studies with a larger sample size and a longer follow-up period are needed to further examine the association between TC and all-cause or cause-specific mortality in the very elderly.

In conclusion, in an 85-year-old Japanese population, decreased TC was associated with an increased mortality, after adjustment for various confounding factors, suggesting

that low TC concentration may be an independent predictor of shorter survival periods among the very elderly.

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Disclosure

The authors report no conflicts of interest in this work.

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