Original article

Serum total cholesterol: A mortality predictor in elderly hospitalized patients

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SUMMARY

Background & aims: Elevated serum total cholesterol levels are associated with increased risk of cardiovascular mortality among middle aged adults, but not the elderly. We therefore examined whether increased serum total cholesterol reduces mortality risk in the hospitalized elderly.
Methods: Of 1852 patients consecutively admitted to an acute geriatric department from 1/1/99–12/31/00, only 298 (49.6% males, mean age 81.36 ± 6.3 years) who had measured serum total cholesterol and albumin levels were included in the study and followed until August 31, 2004. Mortality data were extracted from their death certificates.
Results: During follow-up of 3.47 ± 1.87 years, 248 patients died. These patients had significantly lower levels of baseline serum total cholesterol (183.3 ± 45.4 vs. 200.2 ± 37.9, $p = 0.01$) and albumin (3.6 ± 0.5 vs. 3.8 ± 0.3 g/l, $p = 0.002$) than the survivors. In the Cox regression analysis, serum total cholesterol emerged as a significant, independent predictor of mortality in this cohort. Specifically, each 1 mg/dl increase in serum total cholesterol reduced risk of death by 0.4%. This association persisted even after controlling for serum creatinine, age, body mass index, dementia and congestive heart failure. These factors were also significantly, independently associated with mortality.
Conclusion: In very elderly hospitalized subjects, increased levels of serum total cholesterol and albumin may be associated with reduced mortality risk.

1. Introduction

It has been established that elevated serum total cholesterol (STC) is associated with increased all-cause and cardiovascular mortality in middle aged adults.[1,2] The National Cholesterol Education Program (NCEP) employs a modified Framingham risk function which includes STC in order to calculate the predicted 10-year risk of major coronary heart disease (CHD) events (mycoardial infarction or death) in adults aged 20–79 years.[2,3] However, this equation does not successfully predict CHD risk in individuals older than 79 years of age.[4] STC emerged as a significant, independent predictor of incident cardiovascular disease (CVD) in community-dwelling individuals aged 60 and older at baseline such that each 1 mmol/L increase in STC was associated with a relative 20% increase in odds of incident CVD at 5 and at 10 years post baseline.[4]

The value of STC as a predictor of CVD and all-cause mortality in elderly adults remains controversial.

The Honolulu Heart Program study reported that men aged 71–93 years in the lowest STC quartile, had a significant increase in relative risk of death (RR 1.64, 95% CI 1.13–2.36).[5] A study of home-dwelling Finish individuals aged 75 years and older identified a 22% relative decrease in a 6-year all-cause mortality for every 1 mmol/L increase in STC.[6]

It is possible that the inverse association between STC and mortality in elderly adults reflects nutritional status, as has been shown in other populations of patients with chronic diseases.[7] Elderly individuals undergoing acute hospitalization represent a population at increased risk of malnutrition and mortality.[8,9] If malnutrition contributes to mortality in elderly individuals, then mortality should also be inversely associated with serum albumin.

Only a few studies have addressed the association between STC and mortality among hospitalized elderly patients.[8,10] It is therefore instructive to examine the association between STC and CVD and all-cause mortality in a cohort of elderly individuals hospitalized in a geriatric unit at a large public hospital.

The aim of the present study was to assess the association between STC, serum albumin and mortality in a cohort of very old hospitalized individuals.

2. Methods

2.1. Study population

The present report is a historical-prospective study nested in a study designed to evaluate orthostatic hypotension in elderly hospitalized patients.[11]

Recruitment and inclusion criteria have been previously reported.[12] All patients consecutively admitted to an acute geriatric department from January 1, 1999 through December 31, 2000 were evaluated. Of the 1852 patients hospitalized during this period, 470 were eligible to be included in the orthostatic hypotension study. Subjects were followed until August 31 2004. Records on mortality were obtained from the day of admission until the end of the follow-up period.

Both serum albumin and serum total cholesterol were recorded for 377 of the original 470 patients. Seventy-nine patients died during the first 180 days. The remaining 298 patients were followed for a minimum of 180 days from day of admission.

The study was approved by the local ethics committee.

2.2. Data collection

Detailed medical history, standard physical examination, and routine blood chemistries were performed on all patients. Reason(s) for hospitalization and a prescribed medications list were recorded.

In addition to age, height and weight were recorded to the nearest 0.5 cm and kg, respectively. Body Mass index (BMI) was calculated as weight (kg) divided by height (m^2).

Comorbidities abstracted from the patient history included hypertension: defined as taking prescribed antihypertensive medications, systolic blood pressure >140 mm Hg, or diastolic blood pressure >90 mm Hg; dyslipidemia: defined as serum total cholesterol levels of ≥200 mg/dl; diabetes mellitus: defined when hypoglycemic agents prescribed or fasting blood glucose of ≥126 mg/dl on at least two occasions; renal failure: when repeated serum creatinine ≥ 1.5 mg/dl; coronary heart disease; ischemic heart disease: according to a history of angina pectoris, myocardial infarction, coronary catheterization with balloon dilatation or coronary artery bypass graft operation; atrial fibrillation; chronic obstructive pulmonary disease; and dementia.

Relevant blood measures studied included urea (mg/dl), creatinine (mg/dl) and hemoglobin (g/dl) and lipid profile. Prescribed medications were categorized as diuretics, angiotensin converting enzyme inhibitor/angiotensin receptor blocker, calcium channel blockers, aspirin, beta blockers, and hypoglycemic agents.

Mortality data throughout follow-up (January 1, 1999–August 31, 2004) were extracted from the Ministry of Interior Affairs registry. Cause of death was recorded from death certificates and the patients' medical record.

2.3. Data analysis

Data were analyzed using SPSS 19.0 statistical analysis software (IBM Inc., USA). The primary independent variable was TSC, the secondary independent variables were age, sex, comorbidities, prescribed medications, and biochemical variables and the primary outcome variable was survival. Distributions of continuous data were assessed for normality using the Kolmogorov–Smirnov test (cut-off $p < 0.01$).

Continuous variables are described as mean ± SD and were compared by vital status using the t-test for independent samples or the Mann–Whitney U as appropriate. Categorical variables are described as (%) of indicator value and compared by vital status using the chi square test. Subjects were compared by STC quartile using one-way analysis of variance (ANOVA) followed post hoc by Bonferroni's test to evaluate pairwise differences. Survival was modeled using the Cox proportional hazard regression model, adjusting for variables identified as associated with mortality in univariate analysis. These variables were entered into the model and the final parsimonious model was arrived at using a backward, stepwise approach with the Log Ranks test. Additionally, STC was categorized into quartiles and survival curves were calculated for each quartile. All tests were two-sided and considered significant at $p < 0.05$.

3. Results

3.1. Patient dispensation

Of the 470 patients participating in the original study on orthostatic hypotension, 377 had values for both albumin and STC
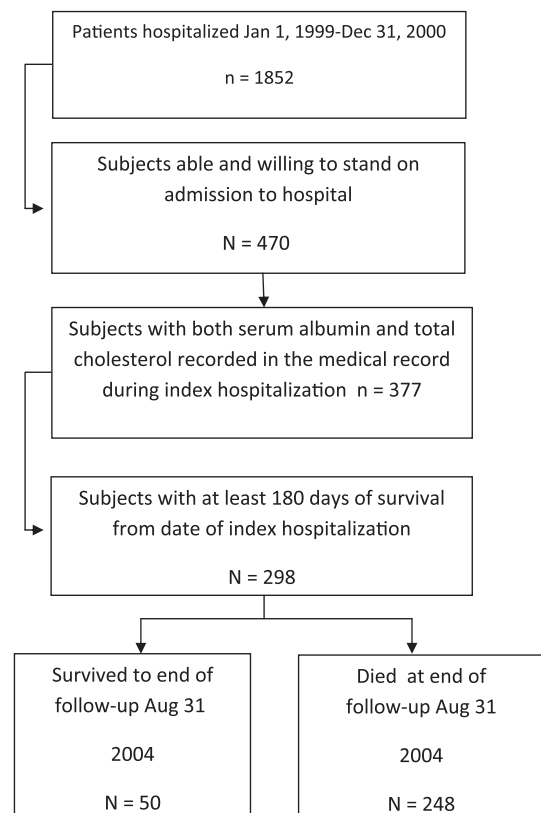

Fig. 1. Patient dispensation.