

SECTION ON LONGITUDINAL STUDIES

Combined measurement of serum albumin and high-density lipoprotein cholesterol strongly predicts mortality in frail older nursing-home residents

Giovanni Zuliani¹, Stefano Volpato¹, Franco Romagnoni², Lucia Soattin², Cristina Bollini², Vincenzo Leoci², and Renato Fellin¹

¹Section of Internal Medicine, Gerontology and Geriatrics, Department of Clinical and Experimental Medicine, University of Ferrara, ²Istituto di Riposo per Anziani (I.R.A.), Padova, Italy

ABSTRACT. Background and aims: The aim of this study was to verify the hypothesis that a combined measurement of albumin and HDL-C might predict total mortality in institutionalized frail older residents. **Methods:** Participants were 344 older subjects (272 F, 72 M), living in the "Istituto Riposo Anziani" (I.R.A.), a nursing-home located in Padova, North-east Italy. Functional status, comorbidity, and clinical chemistry parameters were evaluated at entry. All-cause mortality was evaluated after 2 and 4 years. The sample was divided into 4 groups by using the 50th percentile of albumin and HDL-C as cut-off value. The mortality odds ratio (OR) was estimated by multivariate logistic regression analysis. **Results:** Total mortality was 36.8% after 2 years and 51.8% after four years. A trend toward an increase in mortality from group 1 to 4 was observed (*p* for trend: 0.01). The OR for 2 and 4 years mortality was 3.83 (95% CI 1.86-7.58) and 2.66 (95% CI 1.37-5.17), respectively, in group 4 compared with group 1, after adjustment for age, gender, number of chronic diseases, functional status, BMI, diabetes, dementia, stroke, CHD, CHF, hypertension, depression, COPD, and total cholesterol levels. **Conclusions:** Among frail older nursing-home residents, simple measurement of serum albumin and HDL-C levels may be useful in identifying varying degrees of frailty. (Aging Clin Exp Res 2004; 16: 472-475)

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INTRODUCTION

A number of studies have demonstrated that low serum total cholesterol (TC) levels are associated with an increased risk of all-cause mortality in older subjects (1-3);

indeed, low TC is more frequent among frail elderly subjects affected by chronic illness and disability (4). Several studies have also shown a close association between reduced levels of serum albumin and poor health status or all-cause mortality in the elderly (5, 6).

We have previously found that severe functional impairment is closely associated with low levels of high-density lipoprotein cholesterol (HDL-C) in institutionalized older individuals (7), and proposed that low HDL-C represents a marker for "ongoing" disability in these subjects (8). More recently, we have shown that, in community-dwelling older subjects with low cholesterol, serum albumin and HDL-C may be very useful in distinguishing different subgroups with different mortality rates (9). It has been proposed that these two simple quantitative indices may be useful to clinicians in estimating the individual risk of frailty (10).

In the present study, we tested the hypothesis that the combined measurement of serum albumin and HDL-C levels is helpful in predicting all-cause mortality in a different setting, made up of a large sample of frail older nursing-home residents, since the awareness of the predictors of mortality is necessary for correct definition of the goals of care, and for prognosis.

METHODS

Subjects

This study was carried out at the I.R.A. (Istituto di Riposo per Anziani), a nursing-home located in Padova, North-east Italy, as previously described (8). Briefly, from a total population of 410 individuals living in the Institute, all eligible subjects (*n*=344: 272 females, 72 males) were recruited at baseline using the following criteria: 1) age ≥65 years; 2) residence in the Institute for

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Correspondence: G. Zuliani, MD, PhD, 2nd Department of Internal Medicine, University of Ferrara, via Savonarola 9, 44100 Ferrara, Italy. E-mail: gzuliani@hotmail.com

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at least one month; 3) no evidence of acute illness either at the time of observation or in the previous 30 days. Terminal patients affected by cancer or severe liver/kidney diseases were excluded.

Clinical chemistry parameters

All determinations were performed at baseline in the central laboratory of the Geriatric Hospital of Padova, as previously described (8). Total cholesterol (TC) was assayed by the Trinder method, and serum albumin by nephelometry. HDL-C was determined after selective precipitation of apoprotein B-containing lipoproteins with $MgCl_2$ -phosphotungstic acid.

Health and functional status

Age, gender, functional status, body mass index (BMI), number of pathologies and number of drugs currently used were recorded at baseline (directly from patient records). ADLs were evaluated by the Katz index (11) with reference to independence in feeding, continence, moving about, going to the toilet, dressing, and bathing. The principal symptomatic diseases (heart disease [including coronary heart disease (CHD) and congestive heart failure (CHF)], hypertension, stroke, diabetes, chronic obstructive pulmonary disease (COPD), dementia, depression, Parkinson's disease, and claudication) were recorded.

The more frequent diseases were: stroke (29%), hypertension (28%), dementia (25%), CHF (24%), depression (15%), CHD (15%), COPD (14%), and diabetes mellitus (12%).

Mortality follow-up

Vital status was ascertained through chart records of the nursing-home or follow-up interviews with proxies ($n=9$) for subjects who had moved from the nursing-home. Up to four years of follow-up data for mortality were available. Information on vital status at the end of the study was obtained for all participants.

Statistical analysis

Mean values were compared by the unpaired *t*-test. The χ^2 test was used to compare categorical variables.

The odds ratio (OR), estimated by means of multivariate logistic regression analysis, was used to compare the 2 and 4 years all-cause mortality risk by levels of combined measurement of serum albumin and HDL-C.

The sample was thus divided into 4 groups by using the 50° percentile of albumin and HDL-C as cut-off value:

- Group 1: albumin >4.2 g/dL and HDL-C >42 mg/dL (frequency: 29.1%)
- Group 2: albumin >4.2 g/dL and HDL-C ≤42 mg/dL (frequency: 20.3%)
- Group 3: albumin ≤4.2 g/dL and HDL-C >42 mg/dL (frequency: 14.7%)

- Group 4: albumin ≤4.2 g/dL and HDL-C ≤42 mg/dL (frequency: 35.9%)

The logistic models included the following covariates: age, gender, number of chronic diseases, functional status (Katz group), BMI, diabetes, dementia, stroke, CHD, CHF, hypertension, depression, COPD, and total cholesterol level.

The SPSS for Windows version 7.0 statistical package was used.

RESULTS

Table 1 lists the principal characteristics of the 344 institutionalized elderly individuals, divided by the two-year outcome. Deceased subjects were older, and had a higher number of chronic pathologies and lost ADLs compared with survivors. BMI, HDL-C, and albumin levels, but not TC levels, were lower in deceased individuals compared with survivors. Among the diseases considered, only the prevalence of congestive heart failure was significantly different in deceased subjects compared with survivors (32.8 vs 18.5%).

On the whole, total mortality was 36.8% after 2 years and 51.8% after 4 years.

Interestingly, no statistical association emerged between TC levels and mortality when different cut-off values were applied (160, 180, 200 mg/dL). For example, 2-year mortality was 35.5% in subjects with TC ≤200 mg/dL, and 39% in subjects with TC >200 mg/dL ($p=0.29$).

Table 1 - Baseline principal characteristics of 344 frail older nursing-home residents, divided by 2-year outcome [means (SD)].

Parameter	2-year survivors (N=216)	2-year deceased (N=128)	p
Age (years)	81.1 (7.2)	83.8 (7.0)	0.001
Gender (females %)	81.5	75.0	0.09
Number of pathologies	3.4 (1.0)	3.8 (1.5)	0.01
Number of drugs	4.0 (2.1)	4.4 (2.0)	0.06
No. of lost ADLs	4.6 (2.2)	5.6 (1.8)	0.001
Body mass index (kg/m ²)	24.6 (4.5)	23.1 (4.6)	0.02
Total cholesterol (mg/dL)	205 (44)	200 (51)	0.30
Albumin (g/dL)	4.25 (0.36)	4.05 (0.38)	0.001
HDL-cholesterol (mg/dL)	45.6 (12.6)	42.3 (12.2)	0.01
Dementia (%)	20	31	0.15
Coronary heart disease (%)	14	18	0.31
Congestive heart failure (%)	18.5	32.8	0.03
Stroke (%)	26.4	32.8	0.20
Hypertension (%)	26.4	30.5	0.40
Depression (%)	15.7	15.6	0.97
COPD (%)	12.5	15.6	0.41
Liver disease (%)	3.8	6.2	0.30
Diabetes (%)	14.4	8.6	0.11

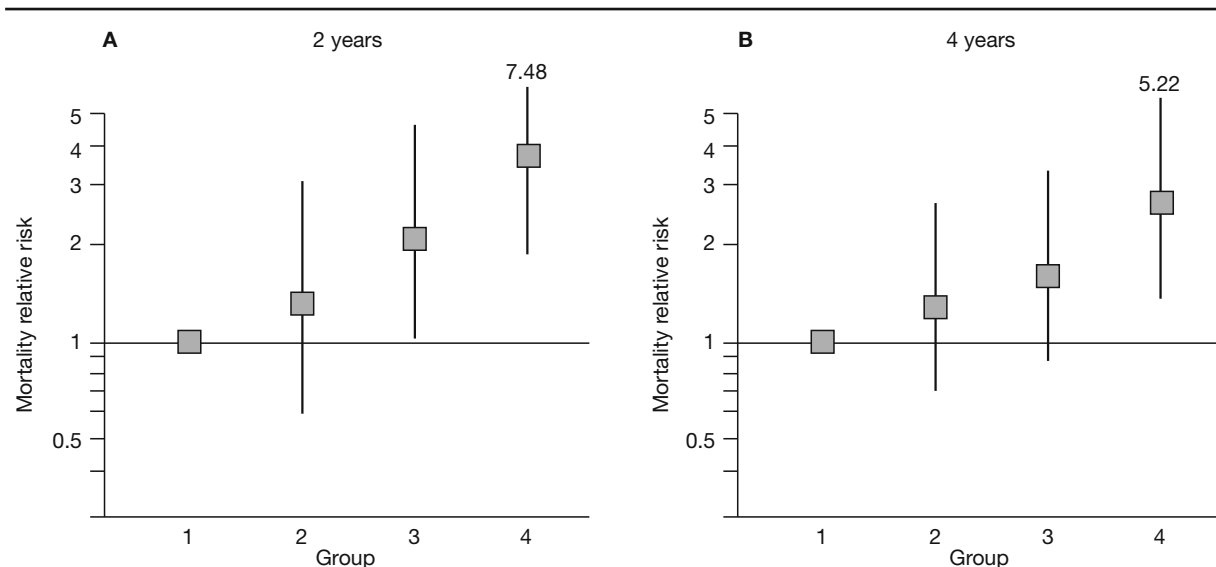


Figure 1 - Relative risk of mortality in 344 frail older nursing-home residents by decreasing levels of serum albumin and HDL-C. Group 1: albumin >4.2 g/dL and HDL-C >42 mg/dL; Group 2: albumin >4.2 g/dL and HDL-C ≤ 42 mg/dL; Group 3: albumin ≤ 4.2 g/dL and HDL-C >42 mg/dL; Group 4: albumin ≤ 4.2 g/dL and HDL-C ≤ 42 mg/dL.

The 2-year mortality rate was 19.2% in group 1, 26.0% in group 2, 39.1% in group 3, and 54.1% in group 4 ($p=0.001$). The 4-year mortality rate was 34.3% in group 1, 44.0% in group 2, 55.1% in group 3, and 67.2% in group 4 ($p=0.001$). These results did not change after stratification for TC levels (cut-offs: 160, 180, and 200 mg/dL) (data not shown).

The results of multivariate logistic regression analysis are shown in Figure 1.

A significant trend toward an increase in total mortality from group 1 to group 4 was observed. The OR for 2-year mortality (panel A) was 1.40 (95% CI 0.58-3.41) in group 2, 2.21 (1.01-4.84) in group 3, and 3.83 (1.86-7.58) in group 4 (p for trend: 0.01; correct classification: 74%) after full adjustment. The OR for 4-year mortality (panel B) was 1.27 (0.58-2.77) in group 2, 1.68 (0.81-3.49) in group 3, and 2.66 (1.37-5.17) in group 4 (p for trend: 0.01; correct classification: 70%) after full adjustment.

DISCUSSION

In this study, we found that, in a large sample of institutionalized frail older subjects, combined measurement of albumin and HDL-C was associated with 2- and 4-year mortality. The association was close and independent of the effect of important predictors such as age, gender, comorbidity, functional status, BMI, diabetes, dementia, and TC levels.

A number of studies have focused on the association between low albumin and TC and poor health in the el-

derly. It has been shown that both low albumin and TC are common among frail older individuals, and are good predictors of total mortality. Reuben et al. have demonstrated that the combination of hypoalbuminemia and hypocholesterolemia is particularly useful in identifying older healthy people at risk of mortality and disability (12).

The explanation for this association is not known. Several conditions have been associated with a reduction in albumin and/or TC levels, including chronic illnesses, and malnutrition (13). Serum cytokines can modulate both albumin levels and lipoprotein metabolism (14), and both albumin and TC may be considered as negative acute phase reactants (15). Interestingly, during the acute phase reaction, the reduction of the HDL fraction contributes greatly to the reduction of TC levels; Volpato et al. showed that among hospitalized older subjects, the biomarkers of the acute phase are associated with low TC and HDL-C, but not with low LDL-C (16). Zuliani et al. have also shown that severe disability is closely associated with low HDL-C, independently of TC, and proposed that low HDL-C may be considered as a marker for "ongoing" disability in ADLs (8). More recently, Volpato et al. have demonstrated that, among community-dwelling older subjects with hypocholesterolemia, low albumin and HDL-C levels identify several groups of individuals with different mortality rates (9). In the dedicated editorial, Hazzard suggested that these two parameters may be useful, in the clinical setting, in estimating the individual risk of frailty (10).

The results of the present study confirm our previous observations and, especially, further extend those findings to suggest that, among institutionalized frail older residents, albumin and HDL-C do identify various degrees of frailty, independently of total cholesterol levels.

Lastly, one major limitation of this study is that in order to be validated, our results must be confirmed in other similar settings: clinicians should therefore use cut-off values defined by medians in their reference populations.

In conclusion, we suggest that simple measurement of albumin and HDL-C levels may provide important information for geriatricians working in nursing-homes, and contribute to more precise prognoses.

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