LOW CHOLESTEROL AND LOW ALBUMIN LEVELS: ALERTS TO HIDDEN MORTALITY RISK

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Executive Summary *Total cholesterol (TC) ≤130 mg/dL for women and ≤140 mg/dL for men was present in a small percentage of life insurance applicants and identified substantially increased mortality risk. For albumin, the comparable low values were ≤3.9 g/dL for women and ≤4.1 g/dL for men. Still lower cut-off levels of TC and albumin were also identified where risk remained even if other laboratory studies, BP and build were unremarkable.*

Introduction

Low levels of total cholesterol (TC) and albumin may be associated with excess mortality in insurance applicants.[1,2] Diseases or conditions potentially responsible for both findings include cirrhosis, poor nutrition, inflammatory conditions, advanced malignancy and congestive heart failure, all of which may be symptomatically silent or at least unknown to the underwriter. Low TC may also be caused by aggressive lipid therapy for cardiovascular disease. But low TC may also simply be the result of favorable heredity and low albumin the result of 2nd or 3rd trimester pregnancy, neither of which has excess risk. The degree of risk can be better defined by review of demographic, medical history, physical measurements and other laboratory results, but some risk may potentially remain even if such review is unremarkable.

We conducted a study to determine what low levels of total TC or albumin suggest that further underwriting review is needed, and what low levels suggest increased risk even if no other findings are apparent after review.

How the Study Was Done

Applicants tested at CRL from 1991 to 2007 with both blood chemistry and urine cotinine results were matched to the Social Security Death Master File to obtain vital status in September 2011, and then were de-identified prior to the study. This provided 7,582,518 applicants with 144,725 deaths. We performed a survival analysis utilizing Cox regression (IBM SPSS 22) splitting applicants by sex and by age 20-59 and 60-89, with age and smoking status (cotinine ≥200 ng/mL) included as covariates. Relative mortality curves by TC or albumin levels were constructed for all applicants and for only those applicants who had unremarkable values for other tests, BP and build. "Unremarkable" was defined by an overall lab score (CRL Smart Score) <50, which includes the 71% of applicants with the lowest mortality risk based on lab results, BP and build.

What the Study Found

Figures 1 and 2 (page 66) show relative mortality for men age <60 and 60+ based on TC level, with those having values ≥211 mg/dL comprising the reference band. Relative mortality increased by >25% at TC values ≤140 mg/dL (3.8% of all men in the study). Based on the pool when the composite of other test results, build and BP was unremarkable, relative risk increased >25% when total TC was ≤120 mg/dL (0.5% of all men in the study).

Figures 3 and 4 (page 67) show comparable findings for women based on total TC. Relative mortality is increased by >25% at values ≤130 mg/dL (2.1% of all women in the study). Based on the pool when the composite of other test results, build and BP was unremarkable, risk increased >25% when total TC reached ≤120 mg/dL for age <60 (0.6% of all younger women in the study), but showed little increase in risk at older ages.

Figure 1. Mortality ratio by TC level for men age <60

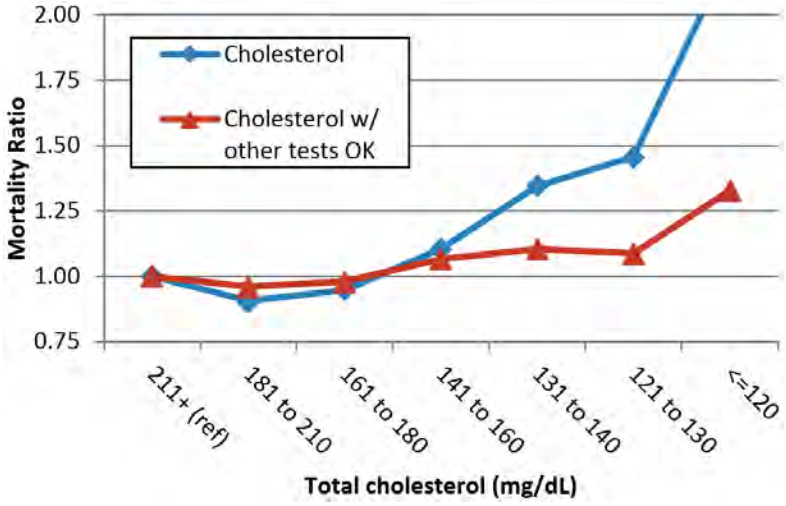
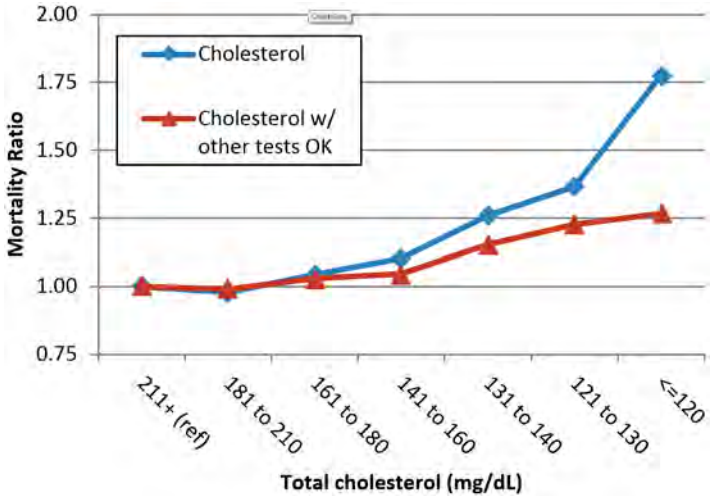


Figure 2. Mortality ratio by TC level for men age 60+



Figures 5 and 6 (page 68) show relative mortality for men age <60 and 60+ based on albumin level, with those having values >4.2 g/dL comprising the reference band. Relative mortality increased by >25% at values ≤4.1 g/dL (7% of all men age <60 in the study and 23% of age 60+). Based on the pool when the composite of other test results, build and BP was unremarkable, risk increased >50% when albumin was ≤3.9 g/dL (0.3% all men age <60 in the study and 1.7% of men age 60+).

Figures 7 and 8 (page 69) show comparable albumin findings for women. Relative mortality increased by >50% at values ≤3.9 g/dL (7% of all women in the study). Based on the pool when the composite of other test results, build and BP was unremarkable, risk increased >25% when albumin fell to ≤3.7 g/dL (1.7% all women age <60 in the study [many being pregnant, at low risk not requiring further evaluation] and 0.75% of women age 60+).

What Do the Study Results Contribute to Risk Assessment?

The results indicate the point where mortality risk begins to increase for low albumin and TC (see blue line in figures) and where that risk exceeds 125% (see text and figures) regardless of other laboratory or physical measurement findings. This data suggests points where additional underwriting review may be needed, and identifies, by age and sex, the percentage of applicants impacted. Some applicants, such as pregnant women (low albumin but not low TC) can quickly be excluded from further review.

The results also indicate potential points where underwriting action may be needed, even when additional review of laboratory and physical measurements is unremarkable (see red line in figures for total cholesterol and purple line in figures for albumin). The percentage of applicants impacted at specific cut-off values is provided in the text of the results section; knowing this as well as relative risk is needed in implementing such action.

Figure 3. Mortality ratio by TC level for women age <60

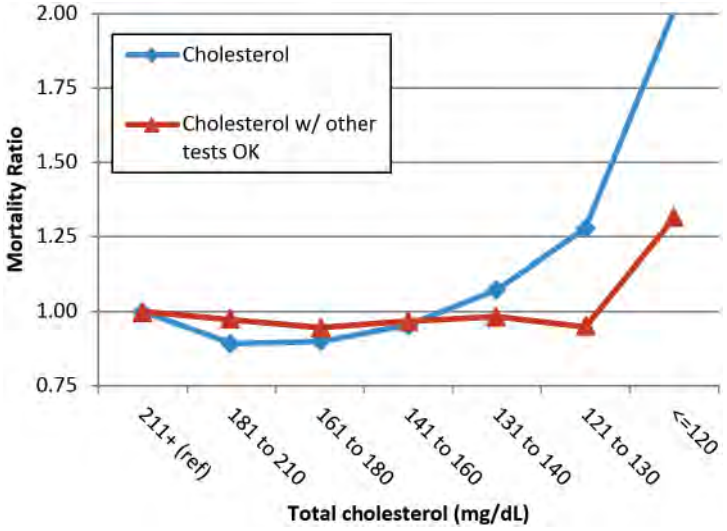
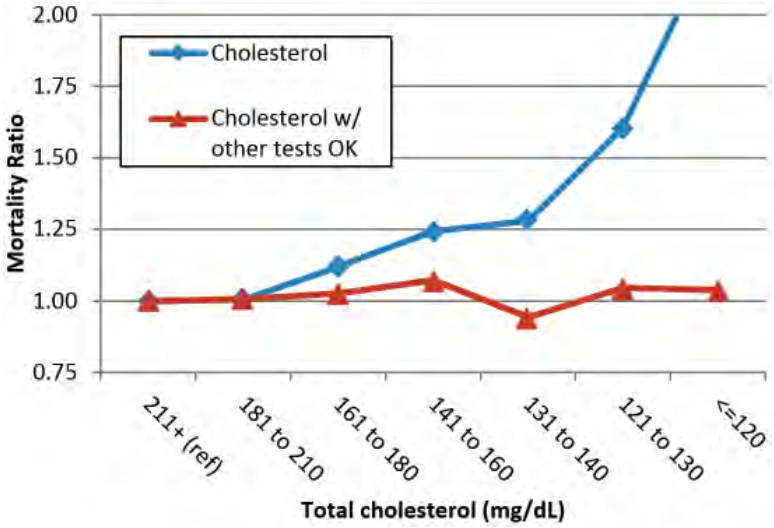


Figure 4. Mortality ratio by TC level for women age 60+



References

1. Fulks M, Stout RL, Dolan VF. Albumin and All-Cause Mortality Risk in Insurance Applicants. *J. Insurance Medicine*. 2010;42:11-17.
2. Fulks M, Stout RL, Dolan VF. Association of Cholesterol, LDL, HDL, Cholesterol/HDL and Triglyceride with All-Cause Mortality in Life Insurance Applicants. *J. Insurance Medicine*. 2009;41:244-53.

About the Authors

Michael Fulks, MD, Consulting Medical Director, is board-certified in internal and insurance medicine. After leaving practice, he served as a medical director, creating or editing several underwriting manuals and preferred programs. For the past 8 years, Dr. Fulks has consulted for CRL, participating in its mortality research on individual tests and all laboratory test results, BP and build in combination. He is also involved in the development and implementation of automated screening tools for non-laboratory data.

Robert L. Stout, PhD, is Chief Science Officer, Associate Laboratory Director and board member of the Clinical Reference Laboratory based in Lenexa, KS. He completed undergraduate studies at California State University (Fullerton) and obtained a PhD in Biological Chemistry from UCLA School of Medicine. Since 1978 he has been directly responsible for introducing many of the new tests and procedures used in risk assessment such as urine and saliva HIV. Dr. Stout has produced nine US patents and numerous papers on the relationship between laboratory testing and insurance applicant mortality.

Figure 5. Mortality ratio by albumin level for men age <60

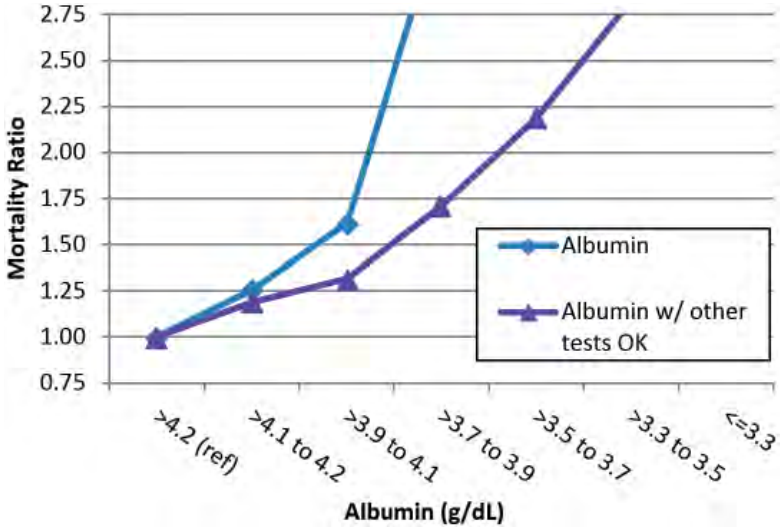


Figure 6. Mortality ratio by albumin level for men age 60+

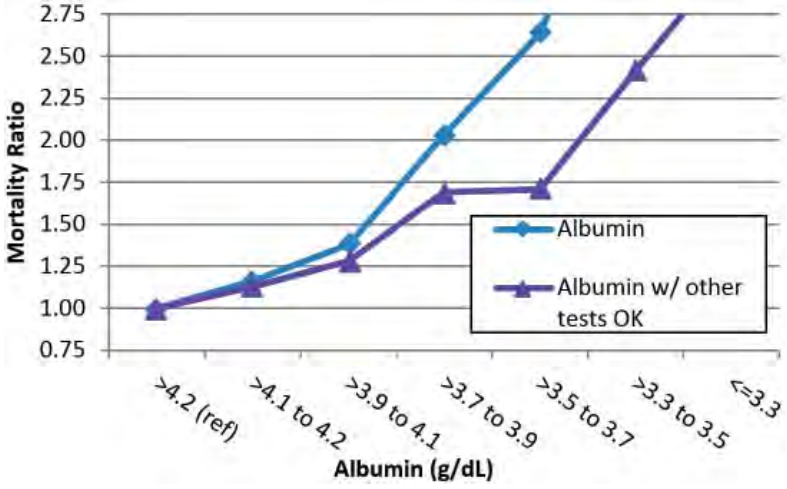


Figure 7. Mortality ratio by albumin level for women age <60

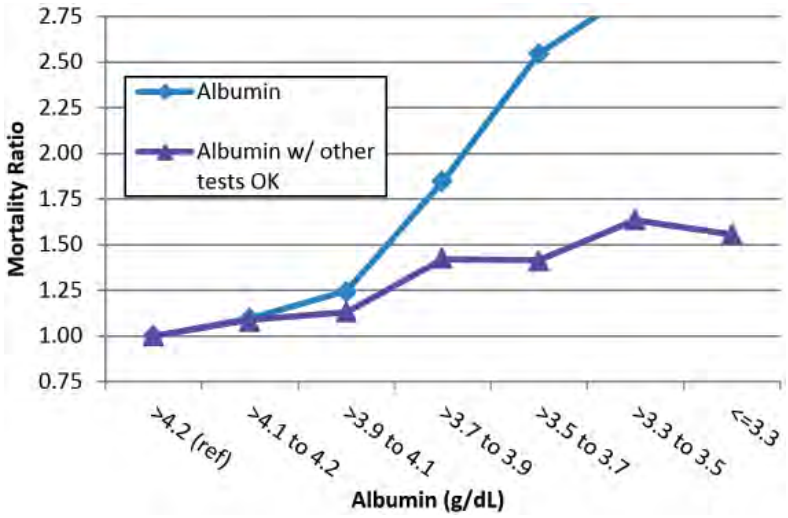


Figure 8. Mortality ratio by albumin level for women age 60+