Use of total cholesterol/albumin ratio as an alternative to high density lipoprotein cholesterol measurement

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SUMMARY In a study of apparently healthy males, we noted a correlation between serum albumin and high density lipoprotein cholesterol (HDL-C) ($r = 0.32$, $p < 0.001$). We then correlated the total cholesterol:albumin ratio (TC:Alb) with the TC:HDL-C ratio ($r = 0.89$, $p < 0.001$). We used the TC:Alb ratio to determine whether this was better than TC by itself in predicting whether an individual had a TC:HDL-C ratio of $<$ or ≥ 5 . The ratio performed better than TC and correctly classified 89% of individuals (66% with TC) ($p < 0.001$). Since measurements of TC and Alb are routinely available on multichannel analysers, use of this ratio would provide a less expensive alternative to HDL-C measurement.

A wide variety of epidemiological data indicates that individual lipoproteins or combinations of lipids and lipoproteins are better predictors of risk for coronary heart disease (CHD) than are the levels of total plasma lipids alone.¹⁻³ However, the main concern to physicians are patients whose blood lipids do not place them in the category of hyperlipidaemia but rather in a group who have "high normal" blood lipids. Of the CHD in the general population, 75% come from this group of "high normals".⁴ Because persons with appreciably raised concentrations of high density lipoprotein (HDL) have mild hypercholesterolaemia,⁵ it is important to identify these subjects since they are in fact "protected" against atherosclerosis; and their hypercholesterolaemia should not be treated. Identification of these individuals requires determination of HDL cholesterol (HDL-C). Because HDL-C measurements are expensive, a cheaper alternative would considerably reduce medical costs. In a study of apparently healthy males, we noted a correlation between serum albumin and HDL-C concentrations ($r = 0.32$, $p < 0.001$). Because of this observation, we attempted to determine whether the total cholesterol: albumin (TC:Alb) ratio (a) correlated with the TC:HDL-C ratio and (b) could be useful clinically. An excellent correlation was obtained between TC:Alb and TC:HDL-C ($r = 0.89$,

$p < 0.001$). Using the TC:HDL-C as an index of cardiovascular risk, the TC:Alb ratio separated the patients with normal (< 5) and increased (≥ 5) TC:HDL-C ratio better than TC by itself.

Since measurement of TC and albumin are routinely available on multichannel analysers, use of the TC:Alb ratio could considerably reduce the number of HDL-C measurements necessary.

Patients and methods

Blood samples were obtained from 122 men (age range 42-59 yr) referred to the Metropolitan laboratory for a "health check-up." All were in apparently good health. Blood for analysis was drawn by venepuncture from the subjects after they had fasted for 12-14 h overnight. Patients with a chylomicron band seen on visual inspection of serum were excluded. Serum cholesterol and albumin were measured by an automated multiple analysis system (Technicon SMA-12 Analyser). HDL-cholesterol was measured after precipitation of lipoproteins containing apo B with heparin and manganese chloride.⁶ The range of values in the subjects for each parameter studied were: total cholesterol 101-329 mg/dl, HDL-cholesterol 29-86 mg/dl and albumin 3.4-5.6 g/dl. Separation of subjects with normal (< 5) and increased (≥ 5) TC:HDL-C ratio was done using (a) TC and (b) TC:Alb ratio. The overall percentage of patients correctly and incor-

Fig. 1 Correlation between total cholesterol and TC:HDL-C ratio.

Fig. 2 Correlation between cholesterol:albumin ratio and TC:HDL-C.

rectly classified was calculated. The statistical significance of the differences between percentages was calculated using the χ^2 test. Pearson's correlation coefficient r was used to identify associations.

Results

Figure 1 shows the correlation between plasma TC and TC:HDL-C ratio ($r = 0.52$, $p < 0.001$). Figure 2 shows the correlation between TC:Alb and TC:HDL-C ($r = 0.89$, $p < 0.001$).

Table 1 Comparison of total cholesterol (TC) and total cholesterol:albumin (TC:Alb) ratio in patients with normal and increased TC:HDL-C ratio

TC:HDL-C ratio	No of subjects with TC (mg/dl)		No of subjects with TC:Alb	
	<225	>225	<50	>50
<5 (n = 79)	43	36	69	10
>5 (n = 43)	7	36	4	39

Table 2 Comparison of sensitivity and specificity of cholesterol versus cholesterol: albumin ratio using TC:HDL-C as a standard

Parameter	Based on the TC:HDL-C ratio	
	Subjects correctly classified	Subjects incorrectly classified
Total cholesterol	79/122 (64.4%)	43/122 (35.6%)
Cholesterol: albumin ratio	108/122 (88.5%)	14/122 (11.5%)

Table 1 shows the TC and TC:Alb ratio compared in their abilities to differentiate subjects with normal (<5) and increased (>5) TC:HDL-C ratios. In the subjects with TC:HDL-C less than 5, 36/79 (43%) individuals had a TC of >225 mg/dl. This figure was reduced to 10/79 (12%) when the TC:Alb ratio was used. In subjects with a TC:HDL-C ratio of >5, the TC:Alb ratio is less useful since in most cases, the concentrations of serum TC are high. Table 2 shows the comparison of the overall sensitivity and specificity of TC versus TC:Alb. The TC:Alb ratio has better sensitivity and specificity than TC ($p < 0.001$). If one regards a TC:HDL-C of >5 as "disease", then using TC >225 mg/dl as a positive screening test result, this test has a sensitivity of 36/43 (0.837) and specificity of 43/79 (0.544). Using the alternate screen of TC:Alb with designation of TC:Alb >50 as a positive screening test, this test has a sensitivity of 39/43 (0.907) and specificity of 69/79 (0.873). Hence the TC:Alb ratio at the particular cut-off chosen has both better sensitivity and specificity.

Discussion

We are not aware of the correlation between serum albumin and HDL-C being previously documented, and serum albumin concentrations have never been shown to have a predictive value for coronary heart disease. Based on this relation between HDL-C and albumin, a total cholesterol:albumin ratio was used to discriminate between subjects with normal and increased TC:HDL-C. The TC:Alb ratio performed better than TC by itself. However, it is important to note that the high correlation between TC:Alb and

TC:HDL-C is partly due to the total cholesterol forming the numerator of both ratios. The TC:HDL-C ratio is most helpful in distinguishing patients with a modest hypercholesterolaemia due to increased HDL from patients whose hypercholesterolaemia is due to increased light density lipoprotein. HDL-C measurement is usually necessary to make this distinction. Because increased costs are incurred in HDL-C measurement, the use of the TC:Alb ratio would help in considerably reducing the number of HDL-C determinations necessary. Both TC and albumin are routinely available on multichannel analysers. We believe that the ratio is useful only in those subjects with modest hypercholesterolaemia since individuals with low or very high cholesterol concentrations are unlikely to have their risk of developing CHD altered either by HDL-C measurement or the calculation of the ratio.⁷

The explanation for the correlation between HDL-C and serum albumin may be related to the fact that lysolecithin, one of the products of the lecithin cholesterol acyltransferase (LCAT) reaction, is removed by binding to serum albumin.⁸ Since LCAT is implicated in the production of HDL cholesterol esters, increased amounts of albumin may be necessary to remove an increased amount of lysolecithin formed as a result of increased HDL and HDL-cholesterol ester formation.

Before our suggested ratio is applied, it is clear

that a large epidemiological study would be necessary to determine whether the TC:Alb ratio has a better predictive value in terms of morbidity and mortality than total cholesterol alone.

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