Evaluation of the ratios T-C/HDL-C and LDL-C/HDL-C as useful summary estimates of coronary heart disease risk in Enugu, Nigeria

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ABSTRACT

Summary estimates result in convenient expressions relating cholesterols to coronary heart disease (CHD) risk. Recent data from a population based cohort study noted that a summary estimate is the most powerful predictor of future CHD. In a randomized population based study, summary estimates involving the ratio T-C to HDL-C and LDL-C to HDL-C in healthy volunteers were examined alone or in the presence of joint information on individual levels of cholesterols. Standardized logistic regression model was applied in data analysis. Results revealed that the regression co-efficients for HDL-C, the ratios T-C/HDL-C and LDL-C/HDL-C were statistically significant (P<0.05); whereas the reverse is the case for T-C and LDL-C (P>0.05). Thus, summary estimates are strong predictors of CHD and very necessary in prompt identification of subjects at high risk of developing CHD who may benefit from lipid lowering drug therapy.

Key words: Coronary heart disease, high and low density lipoprotein cholesterols, summary estimate, total cholesterol

INTRODUCTION

Summary estimates of cholesterols and lipoprotein fractions are convenient measures of disease risk as they provide a single value that quantifies the potential for developing CHD that can be compared to easily remembered scale1. It should be noted, however, that summary estimates are not intended to replace the need to jointly consider individual pieces of information concerning lipid profiles. It is pertinent to note that combining cholesterol levels into one summary estimate might eliminate important information available when individual cholesterol values are considered together. Attempts to reduce the complex explanations of causality among the lipoprotein density classes have resulted in the derivation of summary estimates, which combine information contained in more than one cholesterol value2-6. The study emphasized the need to consider the value of using measures of several lipids rather than rely on the measure of a single lipid for the purpose of assessing the risk of CHD in the population. The summary estimates examined in this paper include the ratio of T-C to HDL-C and LDL-C to HDL-C and verifying their effects in predicting risk of CHD when considered alone or in the presence of joint information on individual levels of cholesterols.

METHODS

Subjects who presented in this study (n=120) were within the age range 35 to 85 (mean,
RESULTS

The regressions co-efficients for T-C and LDL-C are not statistically significant (P>0.05) in both male and female subjects. However, the regression co-efficients for HDL-C and both summary estimates, that is, LDL-C/HDL-C and T-C/HDL-C ratios are statistically significant for both sexes as (P<0.05). The signs of the co-efficients, however, indicate that HDL-C is inversely related to CHD risk whereas the summary estimates are directly and positively related to CHD in both sexes.

The standardized logistic regression co-efficients for the various lipid measures and ratios are presented in tables 1 and 2 for the male and female subjects respectively.

DISCUSSION

Cardiovascular risk is severally believed to be a function of cholesterol concentration\(^{10}\). This study attempted to explore how well summary estimates of cholesterols predict the development of CHD when considered alone or in the presence of joint information on individual levels of cholesterols. The two ratios have shown strong associations with CHD for both sexes. In the male subjects, information from both ratios used to predict CHD is not significantly improved by considering

<table>
<thead>
<tr>
<th>S No.</th>
<th>Lipid Measures /Ratios</th>
<th>Regression Co-efficients</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>T-C</td>
<td>0.124</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>2.</td>
<td>HDL-C</td>
<td>-0.468</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>3.</td>
<td>LDL-C</td>
<td>0.219</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>4.</td>
<td>LDL-C/ HDL-C</td>
<td>0.387</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>5.</td>
<td>T-C/ HDL-C</td>
<td>0.368</td>
<td>&lt; 0.05</td>
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<th>S No.</th>
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<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>T-C</td>
<td>0.149</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>2.</td>
<td>HDL-C</td>
<td>-0.431</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>3.</td>
<td>LDL-C</td>
<td>0.204</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>4.</td>
<td>LDL-C/ HDL-C</td>
<td>0.372</td>
<td>&lt; 0.05</td>
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<td>5.</td>
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specific levels of cholesterol that make up the ratios. This is also applicable to the female subjects for both ratios. The above corroborates findings in other lipid surveys\textsuperscript{2,4-6}. Indeed, other investigators have utilized lipoprotein summary statistics to show an association with CHD. It has been documented that results similar to those for TC/HDL-C ratio were obtained when LDL-C/HDL-C ratio was used\textsuperscript{5}. It should be noted that the significance of the coefficient for HDL-C and both summary estimates indicate a strong association between these variables and CHD for both sexes (P<0.05). Substantive evidence is in support of the fact that HDL-C is inversely related to total cholesterol\textsuperscript{11}. It has been shown that significantly reduced level of HDL-C is closely related to CHD\textsuperscript{12}. It has been postulated that the mechanism of action may involve transport of cholesterol back to the liver, the only organ which can catabolize and excrete quantitatively important amounts of cholesterol\textsuperscript{13}. HDL-C alters the balance of unesterified cholesterol between plasma and cells by increasing its utilization in the lecithin/cholesterol acyltransferase (LCAT) system to form cholesterol ester which would move less slowly back to the cells\textsuperscript{14}. On the other hand, HDL-C may interfere with cellular uptake of cholesterol\textsuperscript{15}. It has been documented that serum lipoprotein abnormalities especially elevated LDL-C is a major risk factor in CHD\textsuperscript{16}. Conclusive evidence from available data suggest that oxidized LDL-C may be more avidly bound and taken up by macrophages and thus more atherogenic than unmodified LDL-C\textsuperscript{17}. Furthermore, given values of T-C/HDL-C, the additional predictive information contributed by HDL-C and T-C is not significant for either sex. This is true when HDL-C and T-C are considered jointly or separately in the logistic model. However, data from a Chinese population based cohort study noted that the TC/HDL-C ratio or its inverse is the most powerful lipoprotein predictor of future coronary heart disease\textsuperscript{18}. It should be noted that the TC/HDL-C is not just a ratio but has the advantage of summarizing complex associations into a single numerical approximation. In the Framingham study, it was reported that the ratios TC/HDL-C and LDL-C/HDL-C emerged as strong predictors of coronary heart disease risk in multiple regression analysis\textsuperscript{1,18}. However, additional information on HDL–C and the ratio LDL-C/HDL-C contribute significantly to the prediction of CHD given knowledge of LDL-C (P< 0.05). In the presence of information on HDL–C for males, when LDL-C/HDL-C ratio is considered as a separate piece of information, it improves the prediction of CHD significantly (P< 0.05). However, when LDL-C and LDL-C/HDL-C are considered jointly among males, as additional information; given information about HDL–C, the contribution is not significant (P>0.05). In the female subjects, given information about HDL-C, the LDL-C does not provide significant additional information for the prediction of CHD. This is also true when LDL- C is considered jointly with LDL-C/HDL-C. Interestingly, these ratios are considered relevant because the higher the ratio, the greater the risk of developing CHD. This further highlights the convenience of the summary estimates because high values of the ratio are of greatest interest and are not necessarily bounded, enabling the ratio to readily emphasize extreme combinations of cholesterol. However, it must be stressed that the information given by the summary estimate is only as good as the measurements of T-C, HDL-C and LDL-C that go into the ratio computation. Thus, any quantification of disease risk, be it in relative or absolute terms, should be undertaken with specific attention to the laboratory procedures used in these determinations\textsuperscript{1,18}. It is therefore pertinent for clinicians using summary estimates for screening purposes to realize that limitations of the estimates may emerge in future studies with improvements in the precision of laboratory procedures. In conclusion, both ratios are useful expressions for combining cholesterol information and remain useful as quick summary for assessing CHD risk and identifying subjects at high risk of developing CHD who may benefit from lipid lowering drug therapy.
REFERENCES


