LIPOPROTEIN (a) ENZYME IMMUNOASSAY IN THE MANAGEMENT OF CARDIOVASCULAR DISEASE

MED207.123

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COVERAGE:

Measurement of lipoprotein (a) in the evaluation and management of cardiovascular disease is considered experimental or investigational

DESCRIPTION:

Lipoprotein (a) (lp[a]) is a lipid-rich particle similar to low density lipoprotein (LDL). Apolipoprotein B is the major apolipoprotein associated with LDL; in lp(a), however, there is an additional apolipoprotein A covalently linked to the apolipoprotein B. The apolipoprotein (a) molecule is structurally similar to plasminogen, suggesting that lp(a) may contribute to the thrombotic and atherogenic basis of cardiovascular disease. Levels of lp(a) are relatively stable in individuals over time, but vary up to 1000-fold between individuals, presumably on a genetic basis. In addition, the distribution of lp(a) varies among racial and ethnic groups. The similarity between apolipoprotein (a) and fibrinogen has stimulated intense interest in lp(a) as a link between atherosclerosis and thrombosis. Levels of lp(a) have been extensively studied as a cardiovascular risk factor in a variety of settings using a variety of study methodologies.

RATIONALE:

There have been numerous studies evaluating lp(a) as a cardiovascular risk factor. A large number of retrospective studies consistently suggested that elevated levels of lp(a) were associated with cardiovascular disease. However, they could not determine whether the elevation of lp(a) preceded the development of cardiovascular disease or was a result of cardiovascular disease. Prospective studies designed to answer this question have produced mixed results. The following are two representative prospective trials drawn from the extensive literature on this topic. Ridker and colleagues took advantage of stored serum samples from the 14,916 predominantly middle-aged white men participating in the Physicians’ Health Study. They measured initial lp(a) levels in the 296 participants who subsequently experienced a myocardial infarction, and compared these lp(a) levels with matched controls from the study group. The authors found that the distribution of lp(a) levels between the 2 groups was identical. Bostom and colleagues studied lp(a) levels of 2191 asymptomatic 20- to 54-year-old men who were members of the Framingham offspring cohort. In contrast to the previous study in which the lp(a) was assessed in frozen stored samples (which may falsely decrease lp(a) levels), in this study the lp(a) level was measured at the initiation of the study, albeit with a different technology than is commonly used now. After a mean follow up of 15 years, there were 129 coronary heart disease events, including
myocardial infarction, coronary insufficiency, angina, or sudden cardiac death. Comparing the lp(a) levels of these patients with the other participants, the authors concluded that elevated lp(a) was an independent risk factor for the development of premature coronary heart disease (i.e., before age 55).

Evaluation of lp(a) as a risk factor is complicated by the lack of a standardized assay, different study methodologies, the variation of lp(a) levels in different races and ethnic groups, and the complicated interplay of various lipid cardiovascular risk factors. For example, further studies have suggested that elevated lp(a) levels markedly affect the cardiovascular risk associated with other lipid parameters. For example, Cantin and colleagues reported on a 5-year prospective study of 2,156 French Canadian men without evidence of ischemic heart disease. During a 5-year follow-up, there were 116 first ischemic heart disease events. While elevated lp(a) was not found to be an independent risk factor for ischemic heart disease, the risk associated with an increased cholesterol, moderately increased LDL was further increased by the simultaneous presence of increased lp(a) levels. In addition, the protective effect of increased levels of HDL was diminished in the presence of increased lp(a). Another retrospective study found that a high lp(a) level was associated with increased cardiovascular risk, only if the total cholesterol/HDL ratio was at least mildly elevated.

The above discussion illustrates the complexity and uncertainty regarding the use of lp(a) levels as a cardiovascular risk factor, either as a general screening tool, or for further risk assessment in those with other cardiac risk factors. Adding to these factors is the uncertainty regarding its clinical role, specifically how knowledge of lp(a) levels can be used to beneficially alter the management of the patient. At the present time, with the exception of niacin, there is no therapy specifically to lower levels of lp(a), and it is unknown whether lowering serum levels of lp(a) would reduce the potential cardiovascular risk. It is not known whether patients with other cardiovascular risk factors in addition to elevated lp(a) would benefit from more aggressive treatment or whether compliance may be enhanced in informing the patient of the potential risk associated with lp(a).


The report states several studies report a strong association between Lp(a) levels and CHD risk. On the basis of these studies some
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authorities hold that an elevation of Lp(a) is an independent risk factor for CHD. It must be noted nonetheless that several prospective studies do not confirm independent predication. Thus the quantitative contribution of elevated Lp(a) to CHD risk beyond the major risk factors is uncertain. In addition, issues related to measurement of Lp(a) in clinical practice have not been fully resolved. Regardless of limitations some authorities believe Lp(a) measurement is a useful addition to the major risk factors for identifying persons at still higher risk than revealed by those factors. They believe this measurement is best reserved for patients with a strong family history of premature CHD or those with genetic causes of hypercholesterolemia, such as familial hypercholesterolemia. Thus, an elevated Lp(a) presents the option to raise a persons risk to a higher level. For example, if a person has a high LDL and only one other risk factor, the finding of a high Lp(a) could count as a second risk factor to justify a lower goal for LDL cholesterol. The ATP report did not find strong evidence to support this approach, but accepts it as an option for selected persons.

An additional search of literature was completed through the MEDLINE database for the period of April 2000 – April 2003. No additional information was found that would change the position of this policy.

PRICING:

None

REFERENCES:

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Blood Cholesterol in Adults (Adult Treatment Panel III) Executive Summary NCEP National Heart, Lung, and Blood Institute, National Institutes of Health, NIH Publication No. 01-3670, May 2001


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