Lipoprotein a (LPa), Fibrinogen and Homocysteine in Patients with Coronary Artery Disease and without Major Risk Factors

Ahmad A. Yousefi MD, Nozar Givtaj* PhD, Abbas Zavarehee PhD*,
Navid Sabourizadeh MD and Mohammad R. Chizaree, MD

Abstract

Background- Coronary artery disease (CAD) is the major cause of death in the world today.[1] Many factors are responsible for causing CAD, but some patients have none of the known major risk factors, i.e. hypertension, diabetes, smoking, hyperlipidemia and family history of CAD.[2] Recent studies suggest other factors such as lipoprotein a (LPa), fibrinogen and homocysteine as risk factors for CAD.[1] The present study tries to establish the relationship between these three factors with CAD in patients with no other major known risk factor(s).

Methods- Sixty-four patients without any known major risk factors whose angiographies showed significant disease in their coronary arteries were selected. Their blood samples were obtained, and their serum homocysteine, fibrinogen and LPa levels were determined.

Results- 9.4% of the cases investigated had elevated fibrinogen levels above normal. This was also true for 42.2% and 87.5% of the cases in terms of homocysteine and LPa, respectively. Therefore, of these three factors, LPa seems to have the strongest and fibrinogen the weakest relation with CAD.

Conclusion- The results of this study and similar studies indicate that these three factors, particularly homocysteine and LPa, could be considered as independent risk factors for CAD and that controlling them would be a significant step toward preventing cardiovascular diseases ***(Iranian Heart Journal 2006; 7 (1): 37-39)***.

Key words: Lipoprotein a ■ fibrinogen ■ homocysteine ■ CAD

Despite significant and notable advances in the diagnosis and treatment of cardiovascular diseases, they still remain the main cause of death among men and women, and it has been predicted that it will remain so until 2020.[1]

Long-term programs and planning for prevention should, therefore, be considered.

Although there is no doubt as to the role of genetic background in CAD, external factors are also known to play a particularly important part.

As a result, those clinical manifestations of CAD that usually occur in later years could be prevented to a large extent.[2]

Some of the risk factors for CAD such as age, sex and family background cannot be

Received March 6, 2005; Accepted for publication April 4, 2006.
From the Dept. of Cardiology and* Research Laboratory, Shaheed Rajaee Cardiovascular Medical Center, Iran University of Medical Sciences, Tehran, Iran.
Address Correspondence to: N. Givtaj, PhD, Research Laboratory, Shadeed Rajaee Cardiovascular Medical Center, Iran University of Medical Sciences, Tehran Iran. Tel : 021-23922546

altered, but others such as arterial hypertension, diabetes, smoking and hyperlipidemia could be controlled.[2] It is notable that 5 to 10 percent of CAD patients have none of the known risk factors.[2]

Recent studies have suggested other factors such as fibrinogen, homocysteine, LPa, CRP, PAI-1, D-dimer and coagulation factor VII as risk factors for CAD.[1] A number of studies have indicated fibrinogen, homocysteine and LPa as independent risk factors for CAD and cerebrovascular diseases.[4,5,6] The present study investigates both the relationship between fibrinogen, homocysteine and LPa levels with CAD in patients with none of the known major risk factors and the relationship between these factors with the number of diseased coronary arteries.

Methods

Sixty-four patients admitted to our department were selected if that they showed significant (more than 50%) stenosis of their coronaries in coronary angiography and did not have any of the risk factors listed below:

1- Age over 45 for men and 55 for women
2- Systolic blood pressure ≥ 140 mmHg
3-Total cholesterol ≥ 200 mg/dl
4-Triglycerides ≥ 200 mg/dl
5- LDL ≥ 130 mg/dl
6-HDL ≤ 35 mg/dl
7-FBS ≥ 126 mg/dl
8-Smoking

Patients receiving medication to lower their glucose level were also excluded. Blood samples were obtained, and measurements of fibrinogen, homocysteine and LPa were performed employing spectrometry, ELISA (enzyme-linked immunosorbant assay) and immunoturbidometric procedures, respectively. Possible interference of an unnatural rise in fibrinogen, homocysteine and LPa levels was avoided by excluding those patients who had been admitted because of severe ischemic attack.

Results

Of the 64 selected patients, 37 were men and 27 were women. The fibrinogen level was higher than normal in 6 patients (9.4%), 3 male and 3 female. It must be noted that fibrinogen measurement was not performed in 5 cases. The homocysteine level was over normal in 27 patients (42.2%), 19 male and 8 female. The LPa level was found to be higher than normal in 56 patients (87.5%), 33 male and 23 female. This clearly demonstrates the importance of LPa as a risk factor for CAD in this group of patients.

Results of angiography showed that out of 64 patients, 18 had SVD (single vessel diseases), 25 had 2VD and 21 had 3VD. However, the correlation between the number of diseased vessels and the levels of investigated factors was not statistically meaningful.

Conclusion

The results of the present study indicate that a meaningful correlation between CAD and high level of fibrinogen does not exist. This does not correspond with the results of a study by Maresca et al.[7] Maresca et al. and Heinrich et al.[8,9] reported that later episodes such as death and myocardial infarction did show a significant correlation with high levels of fibrinogen. According to our results, raised serum homocysteine could be considered as a risk factor for the occurrence of CAD. These results are in accordance with the results of a study by Folsome et al.[10] which was carried out on 15,792 patients. The study of Boushey el al.[11] also demonstrated that high levels of

plasma homocysteine could be a risk factor for CAD. Our results also indicate that high levels of LPa have a more pronounced relation with CAD in comparison to the other investigated factors. The results of this study correspond with those of a study by Alfthan et al[12] and also reports by other investigators such as Sunayama et al.[13], Ridker et al.[3] and Weiss et al[14].

Considering the present results and results reported by other investigators, one can suggest that homocysteine and LPa measurements should be performed as a routine check-up procedure, because the assessment of these factors could be an important step toward the prevention of CAD. These measurements can be very informative, particularly in those patients without other known major risk factor(s). Consequently, when the levels are higher than normal, preventive measures could be taken to stop the further advance of the condition and possibly work toward the treatment of disease.

References

1. Braunwald E, Zipes DP, Libby P: A Textbook of Cardiovascular Medicine, 6th edition, W.B. Saunders Co, USA, 2001; pp. 1010-1031.

2. Maron DJ, Ridker PM, Pearson TA, Grundy SM: Hurst's the Heart, 10th ed. McGraw-Hill, USA, 2001; pp 1131-1153.

3. Ridker PM, Hennekens CH, Stampfer MJ: A prospective study of LP (a) and the risk of myocardial infarction. JAMA 1993; 270: 2195-99.

4. Ernst E, Resch KL. Fibrinogen as a cardiovascular risk factor: A meta-analysis and review of the literature. Ann Intern Med 1993; 118: 956-63.

5. Wald NJ, Watt HC, Law MR, Sakurai H. Homocysteine and ischemic heart disease: Results of a prospective study with implications regarding prevention. Arch Intern Med 1998; 158: 862-65.

6. Moliterno DJ, Jokinen EV, Miserez AR. No association between plasma LP (a) concentrations and the presence or absence of coronary atherosclerosis. Arterioscler Thromb Vasc Biol 1995; 15: 850-55.

7. Ma J, Hennekens CH, Ridker PM, Stampfer MJ. A prospective study of fibrinogen and risk of myocardial infarction in the physicians health study. J Am Coll Cardiol 1999; 33: 1347-52.

8. Maresca G, Di Blasio A, Marchioli R. Measuring plasma fibrinogen to predict stroke and myocardial infarction. Arterioscler Thromb Vasc Biol 1990; 19: 1368-77.

9. Heinrich J, Balleisen L, Schulte H. Fibrinogen and factor VII in the prediction of coronary risk: Results from the PROCAM study in healthy men. Arterioscler Thromb 1994; 14: 54-59.

10. Folsom AR, Wu KK, Rosamond WD, Sharrett AR, Chombless LE. Prospective study of hemostatic factors and incidence of coronary heart disease. Circulation 1997; 96: 1102-1108.

11. Boushey CJ, Beresford SA, Omenn GS, Motulsky AG. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. JAMA 1995; 274: 1046-1051.

12. Alfthan G, Pekkanen J, Jauhianen M. Relation of serum homocysteine and LP (a) concentrations to atherosclerotic disease in a prospective Finnish population based study. Atherosclerosis 1994; 106: 9-19.

13. Sunayama S, Daida H, Mokuno H, Miyano H, Yokoi H, Leey J: Lack of increased CAD risk due to elevated LP (a) in woman greater than or equal to 55 years of age. Circulation 1996; 94: 1263-68.

14. Wesis SR, Bachorik PS, Becker LC. LP (a) and coronary heart disease risk factors in a racially mixed population: The Johns Hopkins sibling study. Ethn Dis 1998; 8: 60-72.