Commentary

Hepatitis Monthly 2007; 7(4): 243-244

Association between Fatty Liver and Coronary Artery Disease: Yet to Explore

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Emerging evidence suggests fatty liver (FL) as an important component of metabolic syndrome (MS), a major contributor to coronary artery disease (CAD) [1]. A few studies, however, have actually evaluated whether the association between FL and CAD is solely due to the presence of MS causing both disease or there is also an independent relationship between the two.

In a recent study published in Coronary Artery Disease [2], Arslan *et al.* attempted to answer the above question. Ninety-two patients without known CAD, who underwent elective coronary angiography (CAG), were studied. CAD was defined as the presence of at least 50% stenosis in at least one major coronary artery. Nonalcoholic fatty liver disease (NAFLD) was diagnosed based on the results of abdominal ultrasonography after exclusion of patients with viral hepatitis, chronic alcohol consumption, and those who used drugs known to improve NAFLD. MS was defined according to the Adult Treatment Panel-III (ATP-III) criteria [3]. 70.7% and 46.7% of patients turned out to have FL and CAD, respectively. In binary logistic regression analysis using the presence of CAD as the outcome variable and age, sex, body mass index, smoking history, waist circumference, blood pressure (cut-off: 130/85 mmHg), fasting blood sugar (FBS), total cholesterol, low- and high-density (HDL) lipoproteins, and triglycerides as independent variables, NAFLD [Odds Ratio (OR): 6.73; 95% confidence interval (CI): 1.14-39.61] was significantly correlated with the presence of CAD. Next, the authors considered ATP-III-defined MS *per se* (in stead of its components) as an independent variable in logistic regression. NAFLD (OR: 7.92; 95% CI: 1.57-40.04) turned out to be a significant predictor of CAD. The effect of MS, however, did not reach statistical significance. The authors concluded that there is a relationship between FL and CAD independent of MS. One limitation with this study was the exclusion of patients known to have dislipidemia.

In a similarly designed study, Mirbagheri *et al.* [4-6] evaluated 420 adult patients undergoing elective CAG based on the American College of Cardiology/American Heart Association class I indications for angiography [7]. A cut-off of 30% stenosis in at least one major coronary artery was used to define clinically significant CAD. Exclusion criteria were renal failure (plasma creatinine >2 mg/dL), positive markers for viral hepatitis, a history of other liver diseases, weight-reduction surgery in the past 1 year and use of drugs reported to cause steatosis (e.g. amiodarone, tamoxifen, steroids, valproic acid, methotrexate) within the past 3 months or greater than 6 months in the past 2 years. A liver ultrasonography was performed on the same day as CAG. 28.1% of patients were found to have CAD. In multivariate analysis, FL was a strong independent predictor of CAD (OR: 8.48, 95% CI: 4.39-16.40). When ATP-III-defined MS was used in stead of its components, both MS (OR: 1.94; 95% CI: 1.10-3.43) and FL (OR: 14.47; 95% CI:

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Received: *28 Jan 2008*
Accepted: *29 Jan 2008*

Hep Mon 2007; 7 (4): 243-244

7.89-26.54) were significantly correlated to CAD.

Given the above studies, among others, there seems to be little doubt that FL is at least a marker for CAD, independent of MS. But, is FL only a marker or is it also a mediator for CAD, independent of MS? The challenges we face are two-fold. First, the possibility of insulin resistance (IR) causing both NAFLD [8] and CAD [9, 10], and thus confounding the relationship between FL and CAD, has not been ruled out yet. Although IR is almost certainly the main causative factor for MS, which was statistically controlled in the above studies, more accurate indices for IR such as the homeostasis model assessment of insulin resistance (HOMA-IR) were not measured. Second, association is not equal to causation. The studies discussed here were cross-sectional, thus preventing one from drawing cause-and-effect conclusions. After an independent association between FL and CAD has been proven to exist, the next step would be to conduct a cohort study and evaluate the effect of FL on the risk of developing CAD.

References

1. Targher G, Arcaro G. Non-alcoholic fatty liver disease and increased risk of cardiovascular disease. *Atherosclerosis* 2007; **191**: 235-40.
2. Arslan U, Turkoglu S, Balcioglu S, Tavil Y, Karakan T, Cengel A. Association between nonalcoholic fatty liver disease and coronary artery disease. *Coron Artery Dis* 2007; **18**: 433-6.
3. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA* 2001; **285**: 2486-97.
4. Mirbagheri SA, Rashidi A, Abdi S, Saedi D, Abouzari M. Liver: an alarm for the heart? *Liver Int* 2007; **27**: 891-4.
5. Mirbagheri SA, Abouzari M, Rashidi A. Independent association between sonographic fatty liver and ischemic heart disease confirmed by coronary angiography: Preliminary results of an ongoing study. *Gastroenterology* 2007; **132**: A-814.
6. Mirbagheri SA, Rashidi A, Abouzari M. Reply. *Liver Int* 2008; **28**: 284-5.
7. Scanlon PJ, Faxon DP, Audet AM, Carabello B, Dehmer GJ, Eagle KA, *et al.* ACC/AHA guidelines for coronary angiography: executive summary and recommendations. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Coronary Angiography) developed in collaboration with the Society for Cardiac Angiography and Interventions. *Circulation* 1999; **99**: 2345-57.
8. Rector RS, Thyfault JP, Wei Y, Ibdah JA. Non-alcoholic fatty liver disease and the metabolic syndrome: An update. *World J Gastroenterol* 2008; **14**: 185-92.
9. Graner M, Syvanne M, Kahri J, Nieminen MS, Taskinen MR. Insulin resistance as predictor of the angiographic severity and extent of coronary artery disease. *Ann Med* 2007; **39**: 137-44.
10. Alavian SM. 'Liver: an alarm for the heart?' *Liver Int* 2008; **28**: 283.