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EDITORIAL COMMENT

Alcohol and Cardiac Structure

Less Is Better*

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Alcohol consumption of any beverage type is a significant cause of nonischemic dilated cardiomyopathy (DCM), known as alcoholic cardiomyopathy (ACM). Alcohol drinking is linked to DCM because ethanol acts as a toxin that directly weakens the heart muscle (1,2). ACM may be caused by both ethanol (pure alcohol) and acetaldehyde, the first metabolite of ethanol, and it can be worsened by interaction with other toxins, such as heavy metals, or by lack of nutrients (3). In a worldwide analysis in 2015, it was estimated that 6.3% of all global deaths from cardiomyopathy were caused by alcohol (4). However, there were large regional variations with regard to ACM mortality burden, which seems heavily concentrated on a few countries from Eastern Europe and Central Asia. These variations may partly be the result of a lack of detection or underdeclaration of the condition. ACM incidence has been mainly linked to very heavy alcohol consumption over an extended period of time (5). However, the relationship between alcohol intake and cardiac function does not seem unequivocal.

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In the CARDIA (Coronary Artery Risk Development in Young Adults) study cohort, the authors studied the associations between drinking habits and echocardiographic evaluation in 2,368 subjects from a cohort of young adults with mild to moderate alcohol consumption (6). Greater alcohol intake had an independent adverse association with ventricular structure (greater indexed left ventricular [LV] mass and left ventricular end-diastolic volume [LVEDV]) after 20 years of follow-up. By contrast, alcohol consumption was not significantly associated with systolic dysfunction measured by left ventricular ejection fraction (LVEF). These results are relevant because CARDIA studied the largest cohort with this level of characterization for alcohol consumption, and included a very long follow-up. Because long-term randomized trials assessing the effect of alcohol consumption on LV function are impossible and unethical, such a large longitudinal study is the best option to assess the cardiac effect of alcohol intake in populations. Beyond the findings of changes limited to LV mass and LVEDV (but not LVEF), the absolute changes in echocardiographic parameters were small, and overall, the values generally remained within normal limits; this conclusion is relatively similar to a previous transversal analysis performed in the ARIC (Atherosclerosis Risk In Communities Study) (7). Therefore, the results reinforce the opinion that mild alcohol consumption is not associated with a major cardiovascular risk in healthy subjects.

The findings on type of drinks (wine, beer, or liquor) and cardiac measures are also interesting, because they are regularly discussed elsewhere with low level of evidence. Wine has been reported to be associated with less coronary events (8) but very few studies have examined the association between beverage types and the risk of heart failure (HF). Abramson et al. (9) analyzed associations between beer, wine, and spirits drinking and HF risk among older patients, and none of the specific beverage types showed a significant association with HF after controlling for total alcohol consumption (9). Other evidence from the published data did not support a major role for nonethanol components of beverages on the risk of HF (10). The new results from the

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CARDIA study suggest that drinking predominantly wine may be associated with less deleterious effects in cardiac structure, although these results may be confounded without the consideration of other dietary factors.

In the CARDIA study, presenting the results with LVEDV and LVEF as continuous variables might not optimally identify patients with a possible ACM. Thus, the authors also analyzed in a simple manner whether the percentages of subjects with abnormal LVEDV or LVEF at the end of follow-up were different in the several subgroups of drinks per week, to identify a higher risk of ACM with a "yes" or "no" profile, and results were similar.

Genetic factors may play a role in the so-called ACM. A latent cardiomyopathy specifically worsened by alcohol in some patients seems conceivable, because some other patients have very high alcohol consumption and major extracardiac disorders with a fully normal heart. A study recently examined mutations in 9 genes known to be associated with DCM in patients with ACM or DCM and in healthy control subjects. The prevalence of variants in ACM subjects was significantly higher than in healthy control subjects, but was similar to that in the DCM cohort (11). Mutations in the titin gene particularly represented a genetic predisposition and increased vulnerability to ACM. The lack of information on genetics in the CARDIA study is a limitation of the study, because it would be highly relevant to study whether a similar dose-effect relationship exists between alcohol intake and the altered cardiac structure for all or only some mutations in specific genes.

The authors also present intraindividual variations in LV remodeling comparing years 25 and 5 and their association with total alcohol intake, which was actually not significant. However, alcohol intake may vary over 20 years (it is actually very likely). Previous reports suggested that alcohol abstinence is usually associated with improved prognosis in patients with ACM (12,13). A patient with ACM and a high level of alcohol drinking from years 8 to 18 would theoretically have most cardiac remodeling at year 15, and might recover at year 25. Unfortunately, the authors were not able to perform an analysis with intraindividual association of alcohol intake and echocardiographic measures at each point for years 5, 15, and 25, which would provide a more definite answer on this important question.

Some data suggest that drinking patterns play an important role in the association between alcohol consumption and cardiovascular disease, particularly in men (14). Specifically, binge-drinking (a consumption of 3 or more alcoholic drinks within 1 to 2 h) seems to have deleterious effects (15), whereas a similar light-to-moderate alcohol consumption spread over the week may produce rather beneficial health effects. Subjects with binge-drinking in the CARDIA study also had adverse cardiac remodeling in the crude analysis, which was not significant after adjustment. Beyond the limited number of participants with binge-drinking habits, the lack of an intraindividual variation analysis is again a significant limitation, because a steady-state of binge-drinking over 25 years may hardly be conceived.

Although many studies have been published about how and why moderately drinking alcohol may be associated with reduced mortality due to heart disease in some populations, it should systematically be repeated that drinking more alcohol increases the risk of alcoholism, high blood pressure, obesity, cardiomyopathy, stroke, cancer, suicide, and accidents. Overall, there are still considerable knowledge gaps about how alcohol in combination with other factors may affect incidence of ACM and prognosis in HF patients. Both observational real-life analyses and interventional trials are still needed to improve the clinical management in these patients.

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REFERENCES

1. Urbano-Marquez A, Estruch R, Navarro-Lopez F, Grau JM, Mont L, Rubin E. The effects of alcoholism on skeletal and cardiac muscle. N Engl J Med 1989;320:409–15.

2. Piano MR. Alcoholic cardiomyopathy: incidence, clinical characteristics, and pathophysiology. Chest 2002;121:1638–50.

3. Klatsky AL. Alcohol and cardiovascular diseases: where do we stand today? J Intern Med 2015;278:238–50.

4. Manthey J, Probst C, Rylett M, Rehm J. National, regional and global mortality due to alcoholic cardiomyopathy in 2015. Heart 2018 Mar 13 [E-pub ahead of print].

5. Lazarević AM, Nakatani S, Nesković AN, et al. Early changes in left ventricular function in chronic asymptomatic alcoholics: relation to the duration of heavy drinking. J Am Coll Cardiol 2000;35:1599–606.

6. Rodrigues P, Santos-Ribeiro S, Teodoro T, et al. Association between alcohol intake and cardiac remodeling. J Am Coll Cardiol 2018;72:1452–62.

7. Gonçalves A, Jhund PS, Claggett B, et al. Relationship between alcohol consumption and cardiac structure and function in the elderly: the Atherosclerosis Risk In Communities Study. Circ Cardiovasc Imaging 2015;8:e002846.

8. Grønbaek M, Becker U, Johansen D, et al. Type of alcohol consumed and mortality from all causes, coronary heart disease, and cancer. Ann Intern Med 2000;133:411–9.

9. Abramson JL, Williams SA, Krumholz HM, Vaccarino V. Moderate alcohol consumption and risk of heart failure among older persons. JAMA 2001;285:1971–7.

10. Klatsky AL, Chartier D, Udaltsova N, et al. Alcohol drinking and risk of hospitalization for heart failure with and without associated coronary artery disease. Am J Cardiol 2005;96:346–51.

11. Ware JS, Amor-Salamanca A, Tayal U, et al. Genetic etiology for alcohol-induced cardiac toxicity. J Am Coll Cardiol 2018;71:2293–302.

12. Fauchier L, Babuty D, Poret P, et al. Comparison of long-term outcome of alcoholic and idiopathic dilated cardiomyopathy. Eur Heart J 2000;21:306–14.

13. Fauchier L. Alcoholic cardiomyopathy and ventricular arrhythmias. Chest 2003;123:1320.

14. Tolstrup J, Jensen MK, Tjønneland A, Overvad K, Mukamal KJ, Grønbaek M. Prospective study of alcohol drinking patterns and coronary heart disease in women and men. BMJ 2006;332:1244–8.

15. Mukamal KJ, Maclure M, Muller JE, Mittleman MA. Binge drinking and mortality after acute myocardial infarction. Circulation 2005;112:3839–45.

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