Alcohol consumption and incident cardiovascular disease: not just one unifying hypothesis

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This editorial refers to ‘Alcohol consumption and risk of heart failure: the Atherosclerosis Risk in Communities Study’, by A. Gonçalves et al., on page 939.

The occurrence of cardiovascular disease (CVD) events remains the number one cause of death worldwide.1,2 Therefore, the definition of potentially modifiable targets to reduce the incidence of CVD remains a key public health priority. While excessive alcohol consumption is a major contributor to the occurrence of non-cardiovascular morbidity and mortality, a large body of evidence suggests that individuals consuming low to moderate amounts of alcohol have a lower risk of suffering from some, but not all CVD outcomes. For example, previous studies found a linear inverse relationship between alcohol consumption and the occurrence of ischaemic heart disease or myocardial infarction,3,4 and a U-shaped association of alcohol consumption with the occurrence of sudden cardiac death.5 In contrast, low to moderate amounts of alcohol intake have not been found to be protective for the incidence of atrial fibrillation or stroke.6,9

In this context, some previous studies have also suggested that low to moderate amounts of alcohol consumption are associated with a reduced risk of developing congestive heart failure.8,9 Gonçalves et al. now present a large additional study on this potentially important relationship.10 The authors took advantage of the Atherosclerosis Risk in Communities (ARIC) study, where the type and amount of alcohol consumed was assessed by questionnaires at four time points over the course of the study. Incident heart failure during an impressive mean follow-up of 24 years was defined as heart failure hospitalization or heart failure death, using retrospective surveillance of hospital discharges and not differentiating between heart failure with reduced and preserved ejection fraction. In multivariable Cox proportional hazards models adjusting for a large number of potential confounders and taking into account changes in alcohol consumption and other risk factors over time, the authors found a U-shaped association between alcohol consumption and incident heart failure, with a significant 21% and 22% lower risk of heart failure among men and women consuming < 7 alcoholic beverages per week compared with abstainers. The authors found no evidence that the heart failure risk differed according to gender or race. These results are consistent with previous studies on the association between alcohol consumption and incident heart failure.8,9

On the other hand, the authors found no association between elevated alcohol intake defined as consuming at least 21 drinks per week and incident heart failure (hazard ratio 0.86, 95% confidence interval 0.62–1.18 among men; 1.01, 0.32–3.16 among women). This finding is somewhat unexpected because of the known occurrence of alcoholic cardiomyopathy among individuals consuming excessive amounts of alcohol over a long period of time.11 However, it has to be emphasized that in the ARIC study the absolute number of participants consuming at least 21 alcoholic drinks per week was small, and therefore this study had limited power to find such an association. In addition, much higher amounts than 21 drinks per week over a long period of time may be needed to induce clinically overt cardiotoxicity,11 further reducing the number of ARIC participants who fulfilled this condition.

An important strength of the study of Gonçalves et al. is the differentiation between individuals voluntarily abstaining from alcohol and former drinkers who stopped consuming alcohol in the past. As shown in Supplementary table S1 of the study manuscript, there are important differences in the baseline characteristics between abstainers and former drinkers, the latter clearly showing a higher risk profile. These different risk profiles highlight the potential that current non-drinkers may have stopped drinking alcohol for an adverse health issue, thereby confounding the relationship between alcohol intake and incident heart failure. By updating over time the number of alcoholic beverages consumed and several important co-morbidities, the authors further reduced the risk of residual confounding.

However, despite the large sample size and the large number of events, the study was unable to assess in detail the risk associated with elevated alcohol consumption, as explained in detail above. The same is true for the detailed assessment of sex- and/or race-related differences. In addition, the low number of individuals consuming only a single type of alcohol reduced the ability to assess the risk of heart failure associated with a single type of
Alcohol consumption suggests that alcohol may have a direct arrhythmic effect on incident heart failure with reduced compared with preserved ejection fraction.

Heart failure and atrial fibrillation are closely inter-related and frequently co-occur in the same individual. Interestingly, the shape of the relationship between alcohol intake and heart failure differs from that between alcohol intake and atrial fibrillation. Earlier studies on the effects of alcohol consumption on the occurrence of atrial fibrillation suggested that only elevated levels of alcohol consumption were associated with an increased risk of atrial fibrillation and that the level of risk may differ between men and women. However, a recent meta-analysis showed that there seems to be a linear association between alcohol and atrial fibrillation, with an 8–10% increased risk of atrial fibrillation for every alcoholic beverage consumed per day, without any apparent gender differences. In the context of the current study, these results suggest that the frequently cited alcoholic cardiomyopathy should not be a driver of atrial fibrillation at low to moderate levels of alcohol consumption. The meta-analysis also highlights the strengths of a well-performed systematic review, providing enough power to assess in detail the complex relationships of alcohol intake to CVD outcomes. Similar systematic reviews on the association between alcohol consumption and incident heart failure may also be helpful to obtain further insights into this important link.

In summary, the currently known relationships between alcohol intake and CVD occurrence are complex. The shape of these associations differs across most major CVD entities, as shown in Figure 1. If at least some causality is assumed, a single unifying hypothesis on how to explain these differing relationships seems impossible, and several potential mechanisms have to be relied on. For example, the reduced risk of heart failure among individuals consuming small to moderate amounts of alcohol may be explained by a reduced incidence of coronary heart disease, which by itself may be due to the effects of alcohol on HDL cholesterol, insulin sensitivity, thrombotic activity, and inflammation. On the other hand, the greater susceptibility to develop atrial fibrillation at lower levels of alcohol consumption suggests that alcohol may have a direct arrhythmic effect on the left atrium. The increased risk of stroke at higher levels of alcohol intake may be mediated by a higher risk of hypertension and/or atrial fibrillation in these individuals. In the end, too little is known about these mediating factors, and future studies should focus on interventional studies to elucidate whether and how alcohol intake really influences the occurrence of CVD. Until then, the overall evidence clearly should not discourage individuals from consuming and enjoying low amounts of alcohol.

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**References**