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**File: ■ Alcohol and Red Wine (from grapes [*Vitis vinifera*, Vitaceae])
■ Fruits, Vegetables, Dairy Products, and Fish
■ Cardiovascular Disease Risk**

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RE: Consumption of Alcohol and Red Wine, but Not of Fruits, Vegetables, Fish, or Dairy Products, Decreases Biomarkers of Cardiovascular Disease

van Bussel BCT, Henry RMA, Schalkwijk CG, et al. Alcohol and red wine consumption, but not fruit, vegetables, fish or dairy products, are associated with less endothelial dysfunction and less low-grade inflammation: the Hoorn Study. *Eur J Nutr.* March 27, 2017; [epub ahead of print]. doi: 10.1007/s00394-017-1420-4.

Endothelial dysfunction and low-grade inflammation are involved in the development of cardiovascular disease (CVD). Because a healthy diet—rich in fruit, vegetables, and fish; low in dairy products; and with moderate alcohol and red wine (from grapes [*Vitis vinifera*, Vitaceae]) consumption—is associated with a reduced risk for CVD, these authors investigated the associations between the consumption of fruits, vegetables, fish, dairy products, and alcohol and red wine and biomarkers of endothelial dysfunction, flow-mediated vasodilation (FMD), and low-grade inflammation. They also investigated whether any such associations were specific to any foods of a healthy diet and lifestyle factors.

The authors used data from the 2000 Hoorn Study follow-up examination. The objective of the Hoorn Study, a population-based cohort study of glucose metabolism that started in 1989, was to determine the prevalence of type 2 diabetes mellitus and associated risk factors in Hoorn, The Netherlands. Of the 822 surviving participants of the original Hoorn Study who gave permission to be contacted again, 801 had sufficient data to be included in the study, full data on diet and biomarkers were available for 738 participants, and full data on diet and FMD were available for 643 participants.

A validated self-administered food frequency questionnaire (FFQ) was used to assess the participants' consumption (g/d) of fruits, vegetables, fish, dairy products, alcohol in general (categorized as nonconsumers, moderate consumers, or high consumers), and red wine specifically (categorized as consumers or nonconsumers) during the previous year.

Measured biomarkers of endothelial dysfunction included soluble intercellular adhesion molecule 1 (sICAM-1), vascular cell adhesion molecule 1, endothelial selectin,

thrombomodulin, and von Willebrand factor. Biomarkers of low-grade inflammation included C-reactive protein, serum amyloid A, interleukin (IL)-6, IL-8, tumor necrosis factor-alpha, and sICAM-1.

FMD was measured to determine the peak arterial vasodilatory response, or maximum diameter, after the cuff was released from the forearm. Measured at four post-cuff release time points, the brachial diameter was not available for 70 participants at one of the time points, for 21 participants at two time points, and for 10 participants at three time points. Using a longitudinal regression method, the authors assigned a value for the missing diameters.

Other assessments included health status, medical history, glucose metabolism status, medication use, educational level, physical activity, and smoking habits. Height, weight, serum creatinine, albuminuria, total cholesterol and high-density lipoprotein cholesterol, blood pressure, body mass index (BMI), and any prior CVD were recorded.

Of the 801 participants selected for the study, 91% were older than 60 years. Regarding alcohol consumption, 139 were nonconsumers, 414 were moderate consumers, and 248 were high consumers.

Compared to the participants with full data, the 63 participants without biomarker data and the 158 participants without FMD data had a higher BMI, a lower educational level, and used antihypertensive medications more frequently ($P < 0.05$ for all). Those without biomarker data were younger and more likely to have type 2 diabetes mellitus. Those without FMD data were older and less physically active, had a lower estimated glomerular filtration rate (eGFR) indicating a risk for kidney disease, and consumed alcohol and red wine less often ($P < 0.05$ for all). Clinical disease was reported in 70% of participants with all data.

First among this study's major findings was that both alcohol and red wine consumption were associated with a lower endothelial dysfunction biomarker score and a greater FMD, although the associations for FMD were not significant. Specifically, after adjusting for sex, age, glucose metabolism status, and energy intake, the authors found that moderate and high consumers of alcohol had a lower endothelial dysfunction biomarker score compared with nonconsumers, showing a trend toward significance (P for trend=0.051). A significantly lower endothelial dysfunction biomarker score was seen in red wine consumers compared with nonconsumers of red wine after making the same adjustments ($P=0.004$).

The study's second major finding was that the consumption of all other food groups was not associated with the low-grade inflammation biomarker score after adjustment for potential confounders. The consumption of vegetables, fruits, fish, and dairy products did not affect endothelial dysfunction or low-grade inflammation.

The study's limitations may have influenced the results, however. The variation in consumption among participants was too small to reveal any associations between foods and endothelial dysfunction and low-grade inflammation; the effects of foods may be seen primarily in younger individuals. Participants following an unhealthy diet and with worse endothelial dysfunction and low-grade inflammation may have died before the follow-up examination, leading to an underestimation of the reported associations. The use of an overall biomarker score was also a possible limitation, as it assumes that

each biomarker carries similar weight, which may not be true in the relationship between food intake and CVD biomarkers.

The authors conclude that "alcohol and red wine consumption were associated with lower biomarkers of endothelial dysfunction and red wine consumption was associated with lower biomarkers of low-grade inflammation, whereas results for vegetable, fruit, fish and dairy product consumption were less clear."

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—*Shari Henson*

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