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STATE-OF-THE-ART PAPER

Alcohol and Cardiovascular Health

The Razor-Sharp Double-Edged Sword

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An extensive body of data shows concordant J-shaped associations between alcohol intake and a variety of adverse health outcomes, including coronary heart disease, diabetes, hypertension, congestive heart failure, stroke, dementia, Raynaud's phenomenon, and all-cause mortality. Light to moderate alcohol consumption (up to 1 drink daily for women and 1 or 2 drinks daily for men) is associated with cardioprotective benefits, whereas increasingly excessive consumption results in proportional worsening of outcomes. Alcohol consumption confers cardiovascular protection predominately through improvements in insulin sensitivity and high-density lipoprotein cholesterol. The ethanol itself, rather than specific components of various alcoholic beverages, appears to be the major factor in conferring health benefits. Low-dose daily alcohol is associated with better health than less frequent consumption. Binge drinking, even among otherwise light drinkers, increases cardiovascular events and mortality. Alcohol should not be universally prescribed for health enhancement to nondrinking individuals owing to the lack of randomized outcome data and the potential for problem drinking. (J Am Coll Cardiol 2007;50: 1009–14) © 2007 by the American College of Cardiology Foundation

It has long been recognized that the problems with alcohol relate not to the use of a bad thing, but to the abuse of a good thing.
Abraham Lincoln (1)

Alcohol (ethanol) consumption is analogous to the proverbial double-edged sword, and perhaps no other factor in cardiovascular (CV) health is capable of cutting so deeply in either direction depending on how it is used. Accumulating scientific evidence indicates that light to moderate drinking done on a daily basis may significantly reduce the risks of coronary heart disease (CHD) and all-cause mortality. In contrast, excessive alcohol intake and binge drinking are toxic to both the heart and overall health and are the third leading cause of premature death among Americans.

The purpose of the present review is to: 1) outline the specific benefits and risks of alcohol, and the threshold of intake at which drinking becomes a health danger rather than an advantage; 2) detail the mechanisms whereby alcohol confers cardioprotection; and 3) discuss the ideal quantities, drinking patterns, and beverages, and which individuals are most likely to benefit.

Alcohol and Health: The J-Shaped Curve

The health effects of ethanol are dependent on the amount of alcohol consumed and the pattern of drinking. Most studies report J-shaped curves, whereby light to moderate drinkers have less risk than abstainers, and heavy drinkers are at the highest risk. A recent meta-analysis of over 1 million individuals showed that consumption of 1 drink daily by women and 1 or 2 drinks daily by men was associated with a reduction in total mortality of 18% (2). On the other hand, intakes of >2 drinks daily in women and 3 drinks daily in men were associated with increased mortality in a dose-dependent fashion (Fig. 1).

The possible CV benefits appear to be the most important health effects of light to moderate drinking, with most studies showing CHD risk reductions of approximately 30% to 35% (3,4). In the INTER-HEART study (5), involving 27,000 patients from 52 countries, regular alcohol consumption was associated with a reduced incidence of myocardial infarction (MI) in both genders, and in all adult age groups. Light to moderate drinking is associated with improved CV health in higher-risk individuals, such as those with known CHD and/or diabetes, but it also may reduce CV risk even in lower-risk individuals. A subgroup study taken from the total cohort of 51,000 men in the Health Professionals Follow-Up Study focused on the effects of alcohol in the 8,867 men (mean age 57 years) who followed all 4 of the major healthy lifestyle behaviors (abstention from smoking, maintaining a body mass index <25 kg/m^2, exercising at least 30 min daily, and eating a healthy diet). That study found that even in men who were already following a very healthy lifestyle, the consumption of 1 or 2 drinks per day was associated with a 40% to 50% decreased risk of MI (Fig. 2) (6). Patients with hypertension also appear to benefit from moderate alcohol consumption.

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Abbreviations and Acronyms

CHD = coronary heart disease
CV = cardiovascular
HDL = high-density lipoprotein
MI = myocardial infarction

In a recent 16-year longitudinal study of 11,711 hypertensive men, 1 drink per day reduced the risk of acute MI by approximately 30% (7). In contrast, alcohol increases blood pressure in a dose-dependent fashion at intakes above 2 drinks daily, and excessive ethanol intake is one of the most common reversible causes of hypertension (8). Acute ethanol exposure causes a negative inotropic effect on the myocardium, and heavy alcohol use has been associated with both declining ejection fraction and progressive left ventricular hypertrophy (9,10). Yet, light to moderate drinking has been associated with a substantially reduced risk of congestive heart failure, especially for those with CHD (11). Light to moderate alcohol intake is also associated with lower risks of both ischemic stroke (Fig. 3) (12,13) and dementia (14). Consistent J-shaped curves demonstrate increased risks for stroke, especially hemorrhagic stroke, (15) and dementia at heavier levels of alcohol consumption (12–15).

Studies indicate that alcohol, when used in moderation, has an antiatherosclerotic effect. Investigators have reported that moderate alcohol use is associated with a decreased atherosclerotic burden as assessed by coronary angiography (16), computerized tomography-detected coronary calcium (Fig. 4) (17), and carotid ultrasound (18). Moderate alcohol intake has also been associated with a decreased incidence of peripheral arterial disease (10). Recent Data from the Framingham study indicate that a J-shaped relationship even exists between alcohol intake and Raynaud's phenomenon, whereby light to moderate drinkers have a lower incidence of Raynaud's compared with abstainers or heavier drinkers (19).

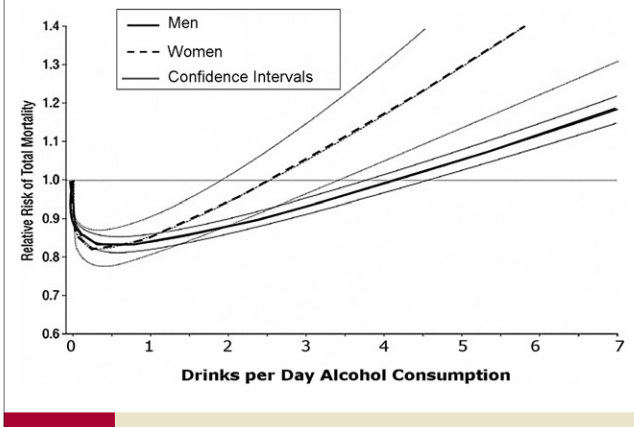

Figure 1 Alcohol and All-Cause Mortality

The relationship of daily alcohol consumption to the relative risk of all-cause mortality in men and women. Reproduced with permission from DiCastelnuovo et al. (2).

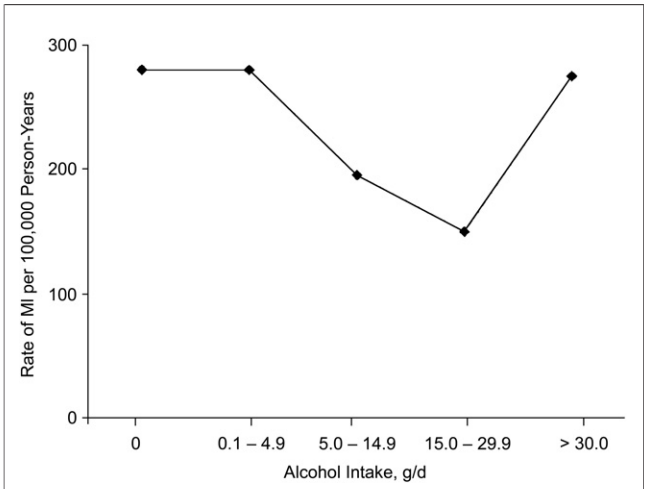

Figure 2 Alcohol Intake and Risk of MI in Men Following a Healthy Lifestyle

Moderate alcohol intake (1 to 2 drinks per day) reduced the rate of myocardial infarction (MI) in this group of 8,867 middle-aged males already following healthy lifestyle recommendations (**6**).

How Alcohol Confers Cardioprotection

Existing data suggest that light to moderate alcohol consumption confers CV protection predominantly through enhancement of insulin sensitivity, and elevation of high-density lipoprotein (HDL) cholesterol; however, improvements in inflammation and abdominal obesity may also be playing lesser roles in the apparent alcohol-related cardioprotection (20). Because these parameters are interrelated via complex metabolic pathways, the exact contribution of each is difficult to tease out statistically (4,21). Alcohol intake increases HDL levels in a dose-dependent fashion.

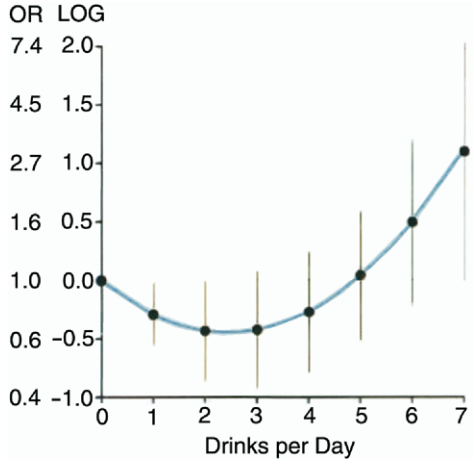

Figure 3 Alcohol and Stroke Risk

Relationship between daily alcohol and ischemic stroke. This was fully adjusted for the usual stroke factors. OR = odds ratio. Reproduced with permission from Sacco et al. (12).

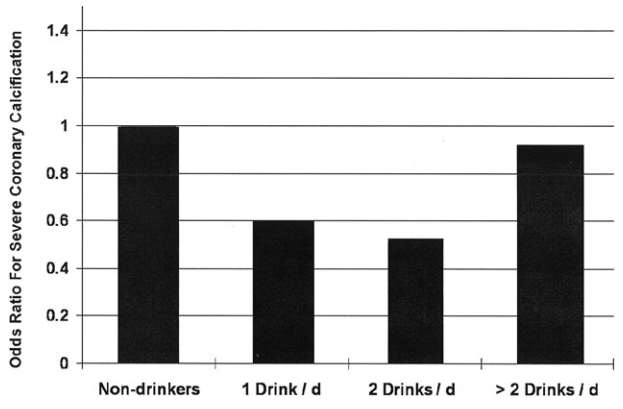

Figure 4 **Alcohol and Coronary Calcium**

The likelihood of having extensive coronary calcification on computerized tomography scanning was reduced in those who consumed 1 to 2 drinks daily. Data from Vliegenthart et al. (17).

For example, HDL will rise about 5% with 1 drink per day and 10% with 2 to 3 drinks per day (4,22–24). The dose-dependent effect of alcohol on HDL contrasts with the J-shaped relationship between alcohol and adverse health outcomes. A recent cross-sectional study of 3,700 Russian individuals between the ages of 18 and 75 years reported that 75% of male and 47% of female Russians chronically consume excessive amounts of alcohol (25). Consequently, adults in Russia have significantly higher mean levels of HDL cholesterol compared with other countries (26). Despite higher HDL levels, Russia has higher age-adjusted rates of CV disease and all-cause mortality than Western Europe or the U.S. (25,26).

The 2007 American Diabetic Association guidelines state, "In individuals with diabetes, light to moderate alcohol intake (1 or 2 drinks per day; 15 to 30 g alcohol) is associated with a decreased risk of CV disease, which does not appear to be due to an increase in HDL cholesterol" (27). Consuming a moderate amount of alcohol, like exercising aerobically, will increase insulin sensitivity and glucose metabolism for the ensuing 12 to 24 h (22,28). Randomized placebo-controlled trials in nondiabetic individuals showed that 2 drinks per day will significantly lower fasting insulin and postprandial insulin levels and increase insulin sensitivity (23,24). Ethanol, when consumed by diabetic patients in small to moderate quantities with or immediately before the evening meal, has been shown to substantially reduce the glucose excursion following the meal (Fig. 5) (22,28). The biologic mechanism whereby alcohol improves insulin sensitivity appears to involve suppression of fatty acid release from adipose tissue (29). This reduction in fatty acids decreases substrate competition in the Krebs cycle of skeletal muscles, thereby facilitating glucose metabolism (29).

One or 2 drinks per day lowers triglycerides modestly (7% to 10%), but alcohol consumption above 2 drinks per day increases triglycerides in a dose-dependent fashion (23,24). Individuals who consume light to moderate amounts of alcohol on a daily basis have less abdominal obesity than do nondrinkers, but those who consume more than 2 drinks per day have increased abdominal obesity that rises in proportion to the amount of alcohol consumed (29,30). Intra-abdominal fat is strongly linked with low HDL levels, insulin resistance, and inflammation, suggesting that alcohol's health effects may in part be mediated by its influence on abdominal obesity (29).

The anti-inflammatory effects of light to moderate alcohol intake were documented by reductions in C-reactive protein in a small randomized controlled trial and a large observational study (31,32), and in tumor necrosis factor alpha, interleukin-6, and fibrinogen in other studies (Fig. 6) (10,33).

Consumption of wine, more so than beer or spirits, has been independently associated with improvements in heart rate variability, a marker of autonomic balance (34). This augmentation of the vagal tone could be a factor in improving CHD prognosis (35).

Favorable Effects on Diabetes and Metabolic Syndrome

Alcohol, with its favorable effects on HDL, insulin action, and inflammation, may be particularly beneficial for individuals with abnormal glucose metabolism and/or insulin resistance. Recent studies indicate that diabetes, prediabetes, or the metabolic syndrome is present in approximately 1 of every 3 American adults (36) and 2 of 3 patients who present with symptomatic CHD (37). Light to moderate alcohol intake is associated with reductions in both the prevalence and incidence of diabetes. A large meta-analysis of 370,000 individuals followed for 12 years showed a 30%

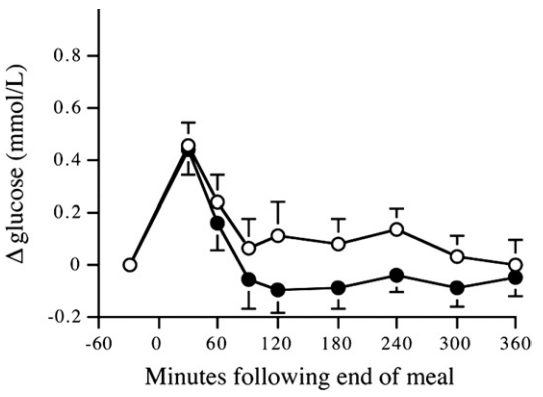

Figure 5 **Wine With Meal Reduced Postprandial Glucose**

In this group of type 2 diabetic patients, wine with the meal **(solid circles)** substantially reduced postprandial glucose for the subsequent 6 h compared with subjects who drank a wine placebo **(open circles)**. Reproduced with permission from Greenfield et al. (22).

reduction in new diabetes in people who consumed 1 to 2 drinks per day (Fig. 7) (38).

Moderate alcohol consumption is also associated with lower rates of the metabolic syndrome. In a recent study of 1,966 men followed for 13 years, alcohol intake of approximately 1 drink daily was associated with a 40% decreased risk of having the metabolic syndrome (39). That same study demonstrated a 39% risk-adjusted decrease in risk of CHD events that was more apparent in those with the metabolic syndrome than in those without it. Moderate alcohol intake is associated with similar reductions in relative risk of CHD in diabetic and nondiabetic cohorts; although superior reductions in absolute risk of CHD are seen in diabetic patients owing to their higher overall event rates (40).

Drinking Patterns, Beverage Choices

The ethanol itself, rather than a specific component of wine, beer, or spirits, appears to be the major factor in conferring the health benefits (4,21), and most studies show equal protection from all types of alcohol. Red wine, however, has been shown to have higher levels of bioflavonoids (with antioxidant, antiplatelet, and antiendothelin-1 effects) compared with white wine and other forms of alcohol (41). Nevertheless, the developing consensus suggests that the specific alcoholic beverage is less important than the quantity and pattern of the alcohol intake (42).

Studies of both men and women have shown that daily alcohol intake provides superior health benefits compared with less frequent consumption (4,21,43–45). In one large study, a 37% decrease in CHD risk was present for those who drank 5 to 7 days per week compared with those who drank less than once per week (4). This may be due to the fact that the alcohol-induced favorable changes in insulin sensitivity, HDL cholesterol, and inflammation are transient, reverting back to baseline within 24 h (43). Some studies show that alcohol is most cardioprotective when consumed before or during a meal

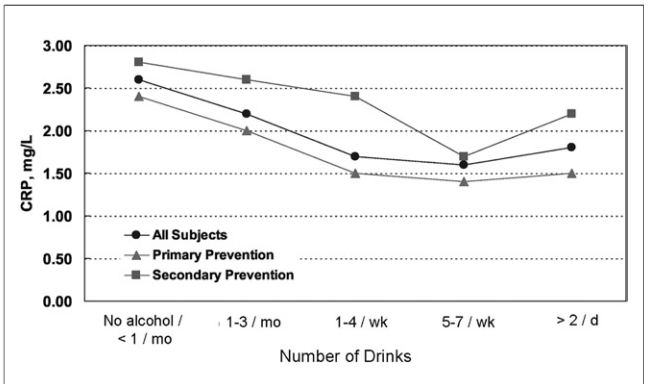

Figure 6 Alcohol and CRP Levels

Alcohol was associated with a reduction in C-reactive protein (CRP), particularly at 5 to 7 drinks per week. Reproduced with permission from Albert et al. (31).

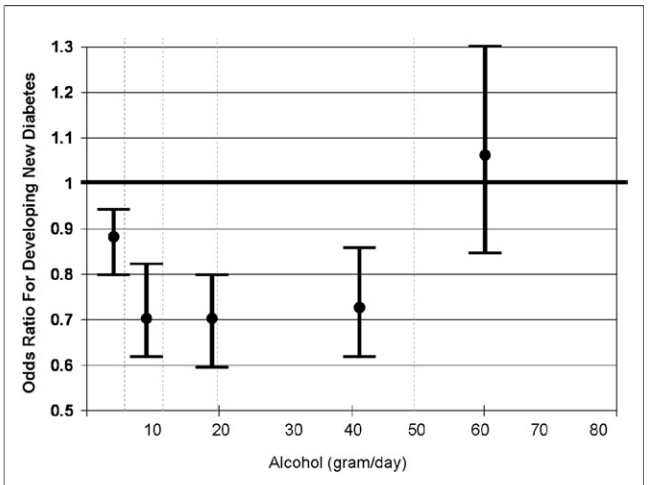

Figure 7 Alcohol and Risk of Diabetes

Alcohol intake and incidence of new type 2 diabetes. Data from Koppes et al. (38).

(44); the improvements in postprandial glucose metabolism noted with light to moderate drinking lend biologic plausibility to this finding (22).

Although Mark Twain once quipped, "Everything in moderation, including moderation," studies indicate that even occasional immoderate drinking presents a health risk. Binge drinking increases risk of MI, all-cause mortality, and other adverse outcomes even among otherwise light drinkers (4,44–46). In the MONICA (Monitoring of Trends and Determinants in Cardiovascular Disease) project, men who consumed ≥5 drinks per drinking day had a 2-fold increased risk for acute MI and all-cause mortality compared with those who did not drink at all (47). In that same study, men who consumed 1 or 2 drinks daily had a 50% reduction in risk of acute MI compared with abstainers.

Cardioprotective alcohol intake is generally defined as 1 or 2 drinks per day for men and 1 drink per day for women (2,4,27). A drink is considered to be 12 oz beer, 5 oz wine, 1.5 oz 80-proof spirits, or 1 oz 100-proof spirits, all of which contain approximately 13 g to 15 g ethanol.

Summary and Recommendations

The cumulative scientific evidence demonstrates concordant J-shaped associations between alcohol intake and a variety of adverse health outcomes. These data suggest that alcohol consumption, like exercise, is most cardioprotective when done daily and in moderation (29). It is tempting, based on the current wealth of evidence, to recommend small daily doses of alcohol (e.g., 1 drink per day) to nondrinkers with or at high risk for CV disease. Guidelines for sensible drinking developed in the United Kingdom state, "Middle-aged or elderly men and postmenopausal women who drink infrequently or not at all may wish to consider the possibility that light drinking may benefit their health" (42). We occasionally make this recommendation to patients well

known to us who have no personal or family history of substance abuse, have no history of depression or bipolar disorder, and are nonsmokers. However, light to moderate drinking cannot be universally recommended to the general public or even patients with CV disease.

Despite convincing observational data and randomized trials using surrogate end points suggesting that hormone replacement therapy in women and antioxidant vitamins improved cardiovascular outcomes, subsequent large randomized outcomes trials showed the opposite (48). Randomized trials of alcohol for improving clinical outcomes have not been done, and residual unmeasured confounding factors could be playing a role in the benefits associated with light to moderate drinking in observational studies (49–51).

Sobering statistics warn that moderate daily drinking is a slippery slope that many individuals cannot safely navigate. Heavy drinking is the source of much individual and societal suffering and morbidity; and some studies suggest that alcohol abuse and binge drinking have been on the rise over the past 15 years (52). Alcohol abuse, the third largest preventable cause of death, is responsible for killing more than 100,000 Americans annually (52). Excessive alcohol intake increases the risks of motor vehicle accidents, stroke, cardiomyopathy, cardiac dysrhythmia, sudden cardiac arrest, suicide, cancer (most notably of the breast and gastrointestinal tract), cirrhosis, fetal alcohol syndrome, sleep apnea, and all-cause mortality (44–46,52). The latest American Heart Association guidelines caution people not to start drinking if they do not already drink alcohol, because it is not possible to predict in which people alcohol abuse will become a problem (10). Until we have more randomized outcome data, and tools for predicting susceptibility to problem drinking, it would seem prudent to encourage physicians and patients to focus on more innocuous interventions to prevent CHD.

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