

Alcohol Consumption Before Myocardial Infarction

Results from the Kaiser-Permanente Epidemiologic Study of Myocardial Infarction

ARTHUR L. KLATSKY, M.D., F.A.C.P., GARY D. FRIEDMAN, M.D., M.S., F.A.C.P., and

ABRAHAM B. SIEGELAUB, M.S., Oakland, California

A statistically significant negative association between alcohol consumption and a subsequent first myocardial infarction in 464 patients was found in a study that was well controlled for cigarette smoking and five other established risk factors. There was a larger proportion of teetotalers among those who had a myocardial infarction ($P < 0.01$) as well as a smaller proportion of moderate (two or less drinks per day) and heavy (three or more drinks per day) consumers of alcoholic beverages. Alcohol consumption and cigarette smoking were strongly correlated habits. The lower consumption of alcohol by persons who subsequently had a myocardial infarction apparently was not the result of intake reduction because of known heart disease or risk-factor-related diseases such as hypertension and diabetes mellitus. Possible explanations include indirect association of drinking habits with ethnic origin, psychological traits or other unknown risk factors for myocardial infarction, or a protective effect of alcohol.

IN THE EARLY DECADES of this century, there were reports of an apparent negative association between heavy alcohol consumption and atherosclerotic disease, including coronary heart disease (1-3). In 1947 Wilens (4) discussed the concept that alcohol might prevent atherosclerosis by a solvent action on cholesterol deposits, but at the same time he suggested that the premature death of many heavy drinkers might preclude the development of vascular disease. Somewhat later, interest in the negative association shifted slightly to the relation of cirrhosis of the liver and arteriosclerosis. Several reports of a significant negative association between these conditions were explained as a statistical fallacy inherent in autopsy series and were considered not applicable to a living population (5, 6).

In the past decade the medical literature relevant to alcohol consumption and heart disease has been dominated by interest in primary myocardial disease related to alcohol consumption, usually called alcoholic cardiomyopathy or alcoholic heart disease. Most of these reports do not dis-

► From the Department of Medicine, Kaiser-Permanente Medical Center, and the Department of Medical Methods Research, Kaiser-Permanente Medical Care Program, Oakland, California.

294

cuss any relation, positive or negative, of alcohol consumption to coronary heart disease (7-10), although many studies of alcoholic heart disease include as a criterion for diagnosis the absence of evidence of coronary artery disease.

Prospective studies of coronary heart disease such as the Western Electric study (11) and the Framingham heart study (12) have not shown a relation between alcohol consumption and coronary heart disease.

We studied a wide range of variables recorded during multiphasic health checkups in a search for new predictors or risk factors for myocardial infarction (13). Here we report data from that study that show a negative association between alcohol consumption and a subsequent first myocardial infarction.

Patients and Methods

We studied 464 patients (408 [88%] white) who had undergone a multiphasic health checkup from 1964 to 1970 and who subsequently had a first myocardial infarction. The multiphasic examination was generally given as a routine medical checkup to Kaiser Foundation Health Plan subscribers. The procedure, which has been described in detail (14), included a self-administered medical history questionnaire involving over 500 yes-or-no answers. The questionnaire included the item, "In the past year did you drink any alcohol?" The next question was, "If yes, how many alcoholic drinks did you usually have (wine, beer, whisky, cocktails)?" and it included options to be checked: "nine or more a day, six to eight a day, three to five a day, two or less a day." Patients who did not answer or who answered no to the first question but checked a consumption category were not included in the tabulation. There were 420 patients (91%) whose responses were valid.

Other items on the questionnaire pertinent to alcohol consumption were [1] "Have you sometimes, in the past year, got drunk on workdays?" [2] "Have you sometimes, in the past year, had alcoholic drinks (wine, beer, whisky, or cocktails) in the morning?" and [3] "Before one year ago, at any time in the past, were you a heavy alcohol drinker?" The examinee was also asked, "Does your wife (husband) have a drinking problem?" A list of 31 items in the family history section of the questionnaire included "alcoholism."

Each patient was hospitalized for his first acute myocardial infarction at either the Oakland or San Francisco Kaiser Foundation Hospital. The interval between the multiphasic health checkup and the subsequent myocardial infarction averaged 16.8 months and was less than a year for 47% of

Annals of Internal Medicine 81:294-301, 1974

Klatsky, A.L.; Friedman, G.D.; and Siegelau, A.B. Alcohol consumption before myocardial infarction. Results from the Kaiser-Permanente epidemiologic study of myocardial infarction. *Annals of Internal Medicine* 81:294-301, 1974.

ALCOHOL CONSUMPTION BEFORE MYOCARDIAL INFARCTION

Commentary by Michael H. Criqui, M.D., M.P.H.

KEY WORDS: AOD consumption; myocardial infarction; therapeutic dry effect; moderate AOD use

Klatsky and colleagues published their seminal article on alcohol's effects on the health of the heart more than 20 years ago (Klatsky et al. 1974). Although suggestions had been made in the early part of this century that alcohol might have some beneficial effect on the prevention of atherosclerotic diseases such as heart attacks, researchers in 1974 probably were cynical about such claims for at least two reasons. First, studies reporting that

patients with cirrhosis of the liver, a disease often associated with heavy alcohol consumption, showed lower-than-normal incidence of atherosclerotic disease had been dismissed as a statistical artifact. Second, two epidemiologic studies, one in Chicago, IL (1963), and one in Framingham, MA (1966), had reported no significant association between alcohol consumption and subsequent heart attacks.

Klatsky and colleagues found that among the group of 464 patients they studied, which included abstainers, moderate drinkers, and heavy drinkers, the abstainers had the highest proportion of heart attacks. This provocative finding apparently resulted from exploring a long list of risk factors in a search for "new predictors . . . for myocardial infarction" (i.e., heart attack). Having found strong statistical support for a theory discredited by the Chicago and Framingham studies, the authors were admirably cautious. Their discussion should serve as a model for other investigators. They addressed seven separate possible sources of bias in the data as well as the possibility that this result might be attributable to any single type of alcohol rather than all alcoholic beverages. Finally, they discussed the plausibility of a biological effect of alcohol on coronary circulation.

How could Klatsky and colleagues find a highly significant association between alcohol consumption and lower incidence of heart disease in a case-control study when two prospective studies had not? Apparently neither the Chicago nor the Framingham study had taken into consideration the strong correlation of alcohol consumption with cigarette smoking. Because cigarette

smoking is a powerful risk factor for heart attack, smokers present in the earlier studies would have caused any beneficial effect of alcohol to be underestimated. Complex statistical techniques such as multivariate risk models, which are routinely employed today to adjust for the potentially confounding affects of multiple variables (such as cigarette smoking), were still in their early development in 1974. Klatsky and colleagues clearly realized that these other variables could obscure alcohol's effects. Thus, for each case, they employed not only an "ordinary" control, but a "risk" control. Although by definition neither control had had a heart attack, only the risk control was matched with study patients for risk of heart attack on several factors, including the key variable of smoking, thus minimizing the potential for confounding.

The researchers' discussion of possible bias in the results seems prescient in retrospect. They presented data showing no

evidence that subjects at risk for heart disease had voluntarily reduced or stopped their alcohol consumption. A later study argued that such a bias was present (Shaper 1990). However, other studies, which carefully explored whether subjects who were at high risk of heart attack had voluntarily become abstainers, found little evidence to support Shaper's hypothesis and confirmed Klatsky and colleagues' earlier findings (Klatsky et al. 1986; Criqui 1990; Jackson et al. 1991; Rimm et al. 1991).

In 1974 it was unclear why alcohol might afford some protection against heart attack. The authors addressed the plausibility of a protective effect at the end of the discussion but had little to say on the subject. Their focus understandably was on cardiac physiology, and there was no clear evidence from cardiac physiology to explain alcohol's potentially beneficial effect on the heart. It was well known then, as now, that heavy alcohol consumption could damage the heart muscle and produce a specific condition called alcoholic cardiomyopathy.

The landmark paper by Klatsky and colleagues helped to stimulate careful evaluation of the association between alcohol consumption and heart disease in several large-scale, long-term epidemiological studies. We have learned much in the two decades since. We now know that the increase in high-density lipoprotein (HDL) cholesterol, which accompanies moderate alcohol consumption, may be responsible for one-half or more of moderate amounts of alcohol's beneficial effect on the incidence of heart disease (Criqui et al. 1987; Langer et al. 1992). We also know that moderate consumption may have an effect through reduced blood clotting (Meade et al. 1979; Renaud et al. 1992). However, we also have clearly learned the limit of any alcohol benefit to the heart. Only moderate drinkers (i.e., those who consume one to two drinks per day) gain any overall health advantage (Bofetta et al. 1990, Criqui 1994). Higher consumption levels may result in increases in stroke and other cardiovascular diseases, some cancers, cirrhosis, and accidents and violence. In fact, the optimal benefit against heart attack is achieved at one to five drinks per week, or less than one drink per day (Gronbaek et al. 1994).

As additional research on alcohol and heart disease continues to unfold, Klatsky and his colleagues are not resting on their laurels. They continue to publish careful, reasoned contributions on this topic from studies conducted with the Northern California Kaiser health maintenance organization population. Such studies include the differential effects of age, ethnicity, and beverage preference as well as the overall effects of alcohol consumption on alcohol-related disease and death (Klatsky et al. 1992; Klatsky et al. 1993). ■

MICHAEL H. CRIQUI, M.D., M.P.H., is a professor in the Departments of Family and Preventive Medicine and director, Preventive Cardiology Academic Award, University of California at San Diego, San Diego, California.

REFERENCES

- BOFETTA, P., AND GARFINKEL, L. Alcohol drinking and mortality among men enrolled in an American Cancer Society prospective study. *Epidemiology* 1:342-348, 1990.
- CRIQUE, M.H. The reduction of coronary heart disease with light to moderate alcohol consumption: Effect or artifact? *British Journal of Addiction* 85:854-857, 1990.
- CRIQUE, M.H. Alcohol and the heart: Implications of present epidemiologic knowledge. *Contemporary Drug Problems* 21:125-142, 1994.
- CRIQUE, M.H.; COWAN, L.D.; TYROLER, H.A.; BANGDIWALA, S.; HEISS, G.; WALLACE, R.B.; AND COHN, R. Lipoproteins as mediators for the effects of alcohol consumption and cigarette smoking on cardiovascular mortality: Results from the Lipid Research Clinics Follow-up Study. *American Journal of Epidemiology* 126(4):629-637, 1987.
- GRONBAEK, M.; DEIS, A.; SORENSEN, T.I.A.; BECKER, U.; BORCH-JOHNSEN, K.; MULLER, C.; SCHNOHR, P.; AND JENSEN, G. Influence of sex, age, body mass index, and smoking on alcohol intake and mortality. *British Medical Journal* 308(6924):302-306, 1994.
- JACKSON, R.; SCRAGG, R.; AND BEAGLEHOLE, R. Alcohol consumption and risk of coronary heart disease. *British Medical Journal* 303:211-216, 1991.
- KLATSKY, A.L., AND ARMSTRONG, M.A. Alcoholic beverage choice and risk of coronary artery disease mortality: Do red wine drinkers fare best? *American Journal of Cardiology* 71:467-469, 1993.
- KLATSKY, A.L.; FRIEDMAN, G.D.; AND SIEGELAUB, A.B. Alcohol consumption before myocardial infarction. *Annals of Internal Medicine* 81:294-301, 1974.
- KLATSKY, A.L.; ARMSTRONG, M.A.; AND FRIEDMAN, G.D. Relations of alcoholic beverage use to subsequent coronary artery disease hospitalization. *American Journal of Cardiology* 58:710-714, 1986.
- KLATSKY, A.L.; ARMSTRONG, M.A.; AND FRIEDMAN, G.D. Alcohol and mortality. *Annals of Internal Medicine* 117:646-654, 1992.
- LANGER, R.D.; CRIQUI, M.H.; AND REED, D.M. Lipoproteins and blood pressure as biologic pathways for the effect of moderate alcohol consumption on coronary heart disease. *Circulation* 85:910-915, 1992.
- MEADE, T.W.; CHAKRABARTI, R.; AND HAINES, A. Characteristics affecting fibrinolytic activity and plasma fibrinogen concentrations. *British Medical Journal* 1:153-156, 1979.
- RENAUD, S.C.; BESWICK, A.D.; FEHILY, A.M.; SHARP, D.E.; AND ELWOOD, P.C. Alcohol and platelet aggregation: The Caerphilly Prospective Heart Disease Study. *American Journal of Clinical Nutrition* 55(5):1012-1017, 1992.
- RIMM, E.B.; GIOVANNUCCI, E.L.; WILLETT, W.C.; COLDITZ, G.A.; ASCHERIO, A.; ROSNER, B.; AND STAMPFER, M.J. Prospective study of alcohol consumption and risk of coronary disease in men. *Lancet* 338(8765):464-468, 1991.
- SHAPER, A.G. Alcohol and mortality: A review of prospective studies. *British Journal of Addiction* 85:837-847, 1990.