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Alcohol Consumption and Prognosis in Patients With Left Ventricular Systolic Dysfunction After a Myocardial Infarction

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OBJECTIVES We assessed the influence of alcohol intake on the development of symptomatic heart failure (HF) in patients with left ventricular (LV) dysfunction after a myocardial infarction (MI).

BACKGROUND In contrast to protection from coronary heart disease, alcohol consumption has been linked to cardiodepressant effects and has been considered contraindicated in patients with HF.

METHODS The Survival And Ventricular Enlargement (SAVE) trial randomized 2,231 patients with a LV ejection fraction (EF) <40% following MI to an angiotensin-converting enzyme inhibitor or placebo. Patients were classified as nondrinkers, light-to-moderate drinkers (1 to 10 drinks/week), or heavy drinkers (>10 drinks/week) based on alcohol consumption reported at baseline. The primary outcome was hospitalization for HF or need for an open-label angiotensin-converting enzyme inhibitor. Analyses were repeated using alcohol consumption reported three months after MI.

RESULTS Nondrinkers were older and had more comorbidities than light-to-moderate and heavy drinkers. In univariate analyses, baseline light-to-moderate alcohol intake was associated with a lower incidence of HF compared with nondrinkers (hazard ratio [HR] 0.71; 95% confidence interval [CI] 0.57 to 0.87), whereas heavy drinking was not (HR 0.91; 95% CI 0.67 to 1.23). After adjustment for baseline differences, light-to-moderate baseline alcohol consumption no longer significantly influenced the development of HF (light-to-moderate drinkers HR 0.93; 95% CI 0.75 to 1.17; heavy drinkers HR 1.25; 95% CI 0.91 to 1.72). Alcohol consumption reported three months after the MI similarly did not modify the risk of adverse outcome.

CONCLUSIONS In patients with LV dysfunction after an MI, light-to-moderate alcohol intake either at baseline or following MI did not alter the risk for the development of HF requiring hospitalization or an open-label angiotensin-converting enzyme inhibitor. (J Am Coll Cardiol 2004;43:2015–21) © 2004 by the American College of Cardiology Foundation

Alcohol consumption appears to have both beneficial and adverse cardiac effects. Multiple observational studies have demonstrated a protective effect of light-to-moderate alcohol consumption on overall mortality, with a benefit largely derived from a reduction in fatal coronary heart disease (1–4). This benefit has also been demonstrated in studies of patients with known coronary artery disease (CAD) (5–7), although not all studies in this population have been positive (8).

In contrast, the consumption of excessive amounts of alcohol is a well-known cause of congestive cardiomyopathy (9), with some degree of cardiac dysfunction seen in up to one-third of patients with chronic alcoholism (10). In these patients with alcohol-induced cardiac dysfunction, reduction of alcohol intake is a crucial component of therapy, as several studies have shown that major clinical improvement and normalization of left ventricular (LV) function can be achieved after abstention (11,12).

Given the demonstrated risks and benefits of alcohol consumption, the effects of continued alcohol consumption in patients who have LV systolic dysfunction following an acute myocardial infarction (MI) are unclear. With the potential for CAD progression and possible re-infarction, these patients may derive a significant benefit from the protective effects of alcohol consumption; alternatively, patients with preexisting LV dysfunction may be more susceptible to the cardiotoxic effects of alcohol. Given this potential risk, the American College of Cardiology/American Heart Association Guidelines for the Evaluation and Management of Chronic Heart Failure (13) state that alcohol consumption should be avoided in patients at high risk for the development of chronic heart failure (HF). In a retrospective exploratory analysis, we used the Survival And Ventricular Enlargement (SAVE) trial to examine the influence of alcohol consumption in a cohort of patients

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Abbreviations and Acronyms

CAD = coronary artery disease
CI = confidence interval
CV = cardiovascular
HF = heart failure
HR = hazard ratio
LV = left ventricular
MI = myocardial infarction
NYHA = New York Heart Association
SAVE = Survival And Ventricular Enlargement trial
SOLVD = Studies Of Left Ventricular Dysfunction

who were at high risk for the development of chronic HF and its complications after sustaining an MI.

METHODS

Enrollment and data collection. The database used for this investigation was that of the SAVE trial, whose design (14) and primary analysis (15) have been described in detail. Briefly, SAVE was a randomized, multicenter double-blind placebo controlled trial in 2,231 patients conducted in 45 centers in the U.S. and Canada between 1987 and 1992. This trial was designed to test the hypothesis that the long-term administration of an angiotensin-converting enzyme inhibitor (captopril) to survivors of acute MI with reduced systolic function would lessen deterioration in cardiac performance and thereby improve both mortality and other clinical outcomes. Patients 21 to 80 years of age with a LV ejection fraction of 40% or less, as measured by radionuclide ventriculography, who survived a minimum of three days after a confirmed acute MI were eligible for enrollment. All patients provided informed consent.

Upon entry into the SAVE trial, participants were asked to classify their pattern of alcohol use three weeks before MI into five categories: 0, 1 to 4, 5 to 10, 11 to 20, and >20 drinks/week. Outpatient visits were then scheduled two weeks after randomization, at intervals of three months during the first year, and at intervals of four months during the remainder of the trial. At these visits, participants were again asked to classify their pattern of alcohol use since their last visit. For the purpose of our study, patients were classified as nondrinkers (0 drinks/week), light-to-moderate drinkers (1 to 10 drinks/week), and heavy drinkers (>10 drinks/week).

In addition to analyses using the level of alcohol consumption reported at baseline, we performed analyses using alcohol consumption reported three months after the index MI in order to determine the association of continued alcohol consumption on the development of HF. There was a moderate correlation between individual alcohol consumption reported at three months and the level reported at 6 and 12 months (Spearman coefficient 0.67 and 0.58, respectively, $p < 0.001$ for both). This correlation was slightly stronger than the correlation between alcohol consumption at baseline and at 6 and 12 months (Spearman coefficient 0.55 and 0.58, respectively, $p < 0.001$ for both).

In addition to drinking status, other baseline variables were assessed, including age, gender, hypertension, body mass index (calculated from self-reported weight and height), and LV ejection fraction as measured by radionuclide ventriculography. Patients were also classified into groups based on smoking status, New York Heart Association (NYHA) functional classification (I to IV), Killip class, history of diabetes mellitus, baseline medication use, and treatment (captopril) assignment.

Definition of end points. The primary outcome of this analysis was the development of chronic HF, defined as the occurrence of HF requiring hospitalization or requiring the use of open-label angiotensin-converting enzyme inhibitors for symptomatic treatment. Additional outcomes included total mortality, combined HF and total mortality, recurrent MI, and cardiovascular (CV) mortality. Myocardial infarction was identified by the primary investigator or the Mortality Classification Committee and was independently reviewed to confirm elevated creatine kinase levels, which were considered positive if the levels were two times the upper limit of normal in the absence of positive results for the myocardial isoform or 1.5 times the upper limit in the presence of the myocardial isoform. Cardiovascular mortality included death from atherosclerotic heart disease (death resulting from LV dysfunction, acute MI, sudden death, and cardiac procedures) and other vascular causes. The Mortality Classification Committee assigned the causes of death based on blinded review.

Statistical analysis. Age, LV ejection fraction, and body mass index were analyzed as continuous variables and are presented as mean ± SD. Global differences in baseline demographics among the three alcohol usage subgroups were ascertained using chi-square tests for ordinal data and one-way analysis of variance for continuous variables. The differences in the crude incidence of cardiovascular outcomes were also compared with chi-square tests. Two-sided values of $p < 0.05$ were considered significant.

Cox proportional hazards models were used to assess the association between alcohol consumption and the outcome of interest. A univariate and a multivariate model were created to identify both the unadjusted and adjusted risk of the outcome of interest. The multivariate model included age, gender, LV ejection fraction, prior MI, history of hypertension, history of diabetes mellitus, body mass index, prior tobacco use, NYHA functional classification, Killip class, beta-blocker use at time of randomization, thrombolytic therapy with qualifying MI, and treatment (captopril) assignment. As described earlier, analyses were performed using alcohol consumption at baseline and repeated using alcohol consumption reported 3 months following the index MI. In the model using self-reported alcohol consumption at 3 months, only end points of interest that occurred after 90 days from enrollment (after the ascertainment of alcohol consumption information) were included. Patients who had