Binge Drinking and Mortality After Acute Myocardial Infarction

Kenneth J. Mukamal, MD; Malcolm Maclure, ScD; James E. Muller, MD; Murray A. Mittleman, MD, DrPH

Background—Moderate drinkers have a lower risk of mortality after myocardial infarction (MI). Although binge drinking has been associated with a higher risk of MI in some studies, its relation to prognosis after MI is uncertain.

Methods and Results—In a prospective, inception cohort study conducted at 45 US hospitals, 1935 patients hospitalized with a confirmed MI between 1989 and 1994 underwent detailed personal interviews. Patients reported their usual frequency of binge drinking of beer, wine, and liquor, defined as intake of 3 or more drinks within 1 to 2 hours, and were followed up for mortality for a median of 3.8 years. Of 1919 eligible patients, 250 (94% men) reported binge drinking during the prior year, and a total of 318 patients died during follow-up. Binge drinkers had a 2-fold higher risk of mortality than drinkers who did not binge (hazard ratio, 2.0; 95% confidence interval, 1.3 to 3.0). A comparison of 192 binge drinkers and 192 other patients matched on propensity scores yielded a similar result. The association between binge drinking and total mortality tended to be similar among patients whose usual alcohol intake was light or heavier and for binge drinkers who consumed beer, wine, or liquor. Usual alcohol intake was inversely associated with mortality, but binge drinking completely attenuated this relation.

Conclusions—Our results suggest that alcohol consumption may be linked to potential hazards among patients who survive acute MI. Although moderate intake has been associated with lower mortality, binge drinking, even among light drinkers, appears to be associated with 2-fold higher mortality. (Circulation. 2005;112:3839-3845.)

Key Words: alcohol ■ epidemiology ■ myocardial infarction ■ prognosis
patients (601 women and 1334 men) were interviewed a median of 4 days after sustaining a confirmed MI. Trained research interviewers identified eligible patients by reviewing coronary care unit admission logs and patient charts. For inclusion, patients were required to have a creatine kinase level above the upper limit of normal, positive MB isoenzymes, an identifiable onset of symptoms of infarction, and the ability to complete a structured interview. For these analyses, we excluded patients with missing information about usual alcohol consumption or binge drinking (n = 16), leaving 1919 eligible patients for analysis. The institutional review board of each center approved this protocol, and each participant gave informed consent.

Interviewers used a structured data abstraction and questionnaire form. Participants reported their usual frequency of consumption (and corresponding numbers of drinks) during the preceding year of wine, beer, and liquor individually. As in previous analyses, we computed each patient’s average weekly intake of ethanol based on their reported consumption and the estimated ethanol content for a serving of each beverage (13.2 g for beer, 10.8 g for wine, and 15.1 g for liquor) and categorized usual weekly alcohol consumption as none, light (<105 g of ethanol; ≈7 drinks), or heavier (≥105 g of ethanol). In a validation analysis of 115 participants with measured levels of HDL cholesterol, alcohol intake was correlated with these levels to the expected degree (Pearson \( r = 0.21, P = 0.02 \)).

As a measure of binge drinking during the preceding year, patients reported the usual frequency with which they consumed “3 drinks or more (drinks) in 1 to 2 hours” for each of the beverage types. We summed the number of such episodes to determine the usual frequency of binge drinking. In beverage-specific analyses, we examined patients who reported heavy episodic intake of beer only, wine only, liquor only, or multiple beverages.

Other information collected from each interview and chart review included demographics, medical history, and medication use (prescription and nonprescription) at the time of hospitalization. During chart review, interviewers recorded complications of congestive heart failure (CHF) or ventricular arrhythmias based on clinical diagnoses documented in the medical record. Interviewers also collected initial blood pressure on admission and all creatine kinase levels to the expected degree (Pearson \( r = 0.30, P = 0.002 \)).

We defined initial hypertension as a presenting systolic blood pressure of <90 mm Hg, and current aspirin use, as reported use of any aspirin-containing product in the 4 days before the index MI; for other medications, regular use included active use up to the time of admission. We used 1990 US census data to derive median household income from US Postal Service zip codes (n = 1857). Participants reported their educational attainment and marital status during interviews. We derived body mass index from self-reported height and weight. We defined noncardiac comorbidity as any diagnosis of cancer, respiratory disease, renal failure, or stroke recorded in the medical record.

We searched the National Death Index for deaths of Onset Study participants through January 1, 1996 and requested death certificates from state offices of vital records for all probable matches according to a previously validated algorithm. Three physicians independently verified the determination of each death. Two physicians categorized the cause of each death as due to cardiovascular disease or noncardiovascular disease. Disagreements among raters were resolved by discussion. All-cause mortality was the primary outcome in all analyses, with cardiovascular and noncardiovascular mortality as secondary outcomes.

Statistical Analysis
We used Cox proportional-hazards models to examine the relation of binge drinking to mortality after adjustment. We first adjusted for age, sex, and their interaction. In subsequent models, we further adjusted for race, body mass index (as linear and quadratic terms), marital status (married versus other), current smoking, previous smoking, usual frequency of exertion (in 3 categories), household income (in quartiles), educational attainment (in 3 categories), previous MI, previous CHF, diabetes mellitus, hypertension, noncardiac comorbidity, previous medication use (aspirin, \( \beta \)-adrenergic antagonists, calcium channel blockers, digoxin, diuretics, hypolipidemic agents, and angiotensin-converting-enzyme inhibitors individually), and receipt of thrombolytic therapy. We assigned indicator variables for patients with missing information on educational attainment (n = 58), household income (n = 56), smoking (n = 20), and marital status (n = 22) and set body mass index to the mean for 22 patients with missing information. Models that excluded individuals with any missing covariate information yielded similar results and are not shown here.

As a sensitivity analysis, we matched binge drinkers with an equal number of other patients by propensity scores. Each patient’s score is that individual’s probability that he or she would report binge drinking, based on demographic, behavioral, and clinical characteristics. To create propensity scores, we used multivariable logistic regression with a dependent variable of binge drinking, and the independent variables were all covariates used in the Cox models noted earlier, except for receipt of thrombolytic therapy and with the addition of linear and quadratic terms for age and alcohol use and interaction terms of sex with age and race. The area under the receiver operating characteristics curve was 0.90, indicating excellent discrimination for the logistic model. We then individually matched binge drinkers to unique non–binge-drinking patients with a nearest-available-pair greedy matching method.

We tested the proportionality of hazards by time-varying covariates and found no significant violations. We used standard methods to estimate the fraction of deaths attributable to binge drinking among current drinkers.

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We conducted statistical analyses with the SAS System for Windows, release 8.01 (SAS Institute, Inc.).

Results
Patient Characteristics
Table 1 shows the characteristics of the Onset Study participants according to their alcohol consumption. As expected, binge drinkers tended to be younger than other patients, had heavier usual alcohol consumption, and were more likely to be male, current smokers, and divorced or separated. Only 8 binge drinkers (3%) had a history of alcohol abuse documented in the medical record. Among binge drinkers, the median frequency of binge drinking episodes was 1 per week (interquartile range, 1/month to 5/week).

Binge Drinking and Mortality
A total of 318 patients died during a median of 3.8 years of follow-up. Table 2 shows HRs for mortality by comparing binge drinkers with other current drinkers. Binge drinking was associated with 2-fold greater total mortality among current drinkers, both in age- and sex-adjusted models and in more fully adjusted models. When compared with abstainers rather than other drinkers, binge drinking was associated with an HR of 1.4 (95% CI, 0.9 to 2.2; \( P = 0.09 \)). As shown in Table 2, binge drinking was associated with 2-fold greater post–acute MI mortality from both all causes and cardiovascular causes. In addition, the risk of noncardiovascular mortality was \( \approx80% \) higher but was not statistically significant. Given that 25% of current drinkers reported binge drinking and the 2-fold greater total mortality associated with it, we estimate that 20% of deaths (95% CI, 7% to 33%)
among current drinkers in this study were attributable to binge drinking.

Table 3 shows a series of factors that could alter the positive association between binge drinking and total mortality. As expected, adjustment for usual alcohol intake strengthened the association between binge drinking and mortality, because usual intake is inversely associated with mortality in the Onset Study. When stratified, there were similar associations between binge drinking and mortality among light and heavier drinkers (based on usual alcohol intake) and among patients who reported episodes up to once per week or more frequent episodes.
The risk associated with binge drinking was similar among patients who reported episodes of heavy drinking of beer, wine, liquor, or multiple beverages. Analyses that assessed the risk associated with binge drinking of any given beverage, simultaneously adjusting for binge intake of the other 2 beverages, yielded similar results ($P$ for interaction, 0.27).

We also performed additional sensitivity analyses. To minimize possible overfitting, we performed stepwise models (with entry and stay criteria of $P/0.20$) that gave very similar results, as did a model adjusted for propensity score with no other covariates. Models that excluded patients who died during hospitalization did not materially change our results, nor did further adjustment for tea intake, measures of infarct size and severity (initial hypotension, complications of CHF or ventricular arrhythmias during hospitalization, and peak creatine kinase levels), the timing of last alcohol consumption before the index MI ($<6$, $6$ to $<24$, or $\geq24$ hours), or current smoking in 4 categories ($\leq70$, $71$ to $140$, $141$ to $280$, and $\geq280$ cigarettes/week). We also repeated our analyses, further adjusting for use of coffee, marijuana, and cocaine or heroin among the 1857 participants with complete information on these covariates; the HR associated with binge drinking was 1.8 (95% CI, 1.2 to 2.8). Finally, we explored the dose-response relation between frequency of binge episodes and risk. Although a positive trend among all binge drinkers was not statistically significant ($P$ for trend, 0.15),

### TABLE 2. HRs and 95% CIs for All-Cause, Cardiovascular, and Noncardiovascular Mortality After Acute MI According to Drinking Among Onset Study Participants

<table>
<thead>
<tr>
<th>Current Drinkers</th>
<th>Binge</th>
<th>Other</th>
<th>Abstainers</th>
<th>$P^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>33</td>
<td>88</td>
<td>197</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular deaths</td>
<td>23</td>
<td>62</td>
<td>153</td>
<td></td>
</tr>
<tr>
<td>Person-years</td>
<td>913</td>
<td>3029</td>
<td>3132</td>
<td></td>
</tr>
<tr>
<td>Mortality rate, per 100 person-years†</td>
<td>7.2</td>
<td>3.1</td>
<td>5.8</td>
<td></td>
</tr>
<tr>
<td>Age and sex adjusted</td>
<td>2.0 (1.3–3.1)</td>
<td>1.0=reference</td>
<td>1.8 (1.4–2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted model‡</td>
<td>2.0 (1.3–3.0)</td>
<td>1.0=reference</td>
<td>1.4 (1.1–1.8)</td>
<td>0.002</td>
</tr>
<tr>
<td>Cardiovascular mortality§</td>
<td>2.1 (1.2–3.4)</td>
<td>1.0=reference</td>
<td>1.5 (1.1–2.0)</td>
<td>0.005</td>
</tr>
<tr>
<td>Noncardiovascular mortality</td>
<td></td>
<td>1.8 (0.8–4.0)</td>
<td>1.0=reference</td>
<td>1.2 (0.7–2.0)</td>
</tr>
</tbody>
</table>

* $P$ values derive from comparison of binge and other drinkers.
†Mortality rate was standardized to age distribution of the full Onset Study population.
‡The adjusted model included age, sex, body-mass index, marital status, race, income, education, physical activity, current smoking, former smoking, medical history (previous acute MI, CHF, diabetes, hypertension, and noncardiac comorbidity), receipt of thrombolytic therapy, and medication use (aspirin, β-blockers, calcium channel antagonists, angiotensin-converting-enzyme inhibitors, digoxin, diuretics, and hypolipidemic agents).
§These models show HRs for death from cardiovascular or noncardiovascular causes with the same covariates as the adjusted model.

### TABLE 3. Additional Adjusted Analyses of Binge Drinking and Total Mortality Among Onset Study participants.

<table>
<thead>
<tr>
<th>HR vs Abstainers and Other Drinkers*</th>
<th>$P^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any binge drinking</td>
<td>1.7 (1.1–2.5)</td>
</tr>
<tr>
<td>Further adjusted for usual alcohol intake</td>
<td>2.1 (1.4–3.4)</td>
</tr>
<tr>
<td>No. of binge episodes</td>
<td></td>
</tr>
<tr>
<td>$\leq$1/wk</td>
<td>1.6 (0.9–2.8)</td>
</tr>
<tr>
<td>$&gt;1$/wk</td>
<td>1.8 (1.1–3.0)</td>
</tr>
<tr>
<td>Usual alcohol intake</td>
<td></td>
</tr>
<tr>
<td>Light ($\leq$15 g/d)</td>
<td>1.7 (0.9–3.2)</td>
</tr>
<tr>
<td>Heavier ($\geq$15 g/d)</td>
<td>1.5 (0.6–3.7)</td>
</tr>
<tr>
<td>Beverage type used in binges</td>
<td></td>
</tr>
<tr>
<td>Beer</td>
<td>1.6 (0.9–2.9)</td>
</tr>
<tr>
<td>Wine</td>
<td>2.7 (1.3–5.6)</td>
</tr>
<tr>
<td>Liquor</td>
<td>1.1 (0.5–2.7)</td>
</tr>
<tr>
<td>Mixed</td>
<td>1.9 (0.9–3.9)</td>
</tr>
</tbody>
</table>

*HRs are shown with 95% CIs and were adjusted for the same covariates as in Table 2.
†$P$ values derive from comparison of binge drinkers with both abstainers and other drinkers, except for analyses stratified by usual intake.
‡$P$ values derive from comparison of HRs in each subgroup.
this appeared disproportionately influenced by the 20 individuals at the extreme of binge frequency. Among the other 92% of binge drinkers, there appeared to be a positive relation between binge frequency and mortality (P for trend, 0.03).

**Stratified Analyses**

We conducted analyses of participants in subgroups of age and sex to assess the homogeneity of our findings further. Although few women reported binge drinking, the risks associated with binge drinking among current drinkers appeared to be similar among men (HR, 1.7; 95% CI, 1.1 to 2.7) and women (HR 1.9, 95% CI, 0.2 to 15.1). The HR associated with binge drinking was 1.5 (95% CI, 0.8 to 2.6) among participants younger than 65 years of age and 2.1 (95% CI, 1.1 to 4.1) among participants aged 65 years and older.

**Matched-Pair Analysis**

Figure 1 shows the estimated survival of 192 binge drinkers and 192 other patients matched on propensity scores. These groups were similar in baseline characteristics, including mean age (52.9 versus 53.1 years), mean body mass index (27.4 versus 27.8 kg/m²), and the proportions of women (6% versus 7%), nonwhites (11% versus 10%), and current smokers (45% versus 42%). Clinical characteristics of the index infarction were comparable, with similar proportions receiving thrombolytic therapy (45% versus 41%) and peak creatine kinase levels (1730 versus 1745 IU/L). Among these 384 matched patients, binge drinkers had significantly worse survival than other patients (P=0.05); the unadjusted HR was 1.8 (95% CI, 1.0 to 3.3). When we excluded 36 abstainers and their matched binge drinkers, the corresponding HR was 2.1 (95% CI, 1.0 to 4.2).

**Usual Drinking, Binge Drinking, and Mortality**

To illustrate the joint effects of usual alcohol intake and binge drinking, we examined the risks among light and heavier drinkers who did and did not report binge drinking (Figure 2). Alcohol intake was inversely associated with mortality among patients who did not report binge drinking (P for trend, 0.009), with HRs of 0.75 (95% CI, 0.57 to 1.00) among nonbinging light drinkers and of 0.59 (95% CI, 0.33 to 1.04) among nonbinging heavier drinkers. Binge drinking completely attenuated this relation (P for trend, 0.83), with HRs of 1.58 (95% CI, 0.91 to 2.75) among binging light drinkers and 1.30 (95% CI, 0.76 to 2.22) among binging heavier drinkers.

**Discussion**

In this inception cohort study of early survivors of acute MI, binge drinking, measured at the time of hospitalization, was associated with 2-fold higher subsequent mortality. The magnitude of this association was similar for total, cardiovascular, and noncardiovascular mortality and among light and heavier drinkers.

Although several reports,7–9 including one from the Onset Study,12 have suggested that light to moderate alcohol intake may be associated with a better prognosis than abstention among patients with CHD, our findings suggest that any potential benefits of moderate drinking must be weighed against the risks of even occasional binge drinking. Three fourths of all Americans who report at least occasional binge drinking are otherwise light or moderate drinkers.23 In our analyses, the apparent benefit associated with otherwise light drinking among patients with acute MI was completely eliminated by episodes of binge drinking.

One difficulty in generalizing our results is that no single uniform measure of binge drinking exists.4,5,24–28 Some studies have used measures of regular heavy drinking,29 whereas others have used episodic heavy drinking.5 Even previous definitions of episodic heavy drinking show considerable heterogeneity, with variability in the quantity of alcohol that defines a binge and the time period during which such
drinking occurs. It seems likely that all of these measures capture some portion of the same underlying construct, but no specific measure has an unequivocal advantage over others. In support of their similarity, the Onset Study definition (3 drinks within 2 hours) was correlated with the same sociodemographic characteristics linked to binge drinking according to other definitions, including age, sex, smoking, marital status, and usual alcohol consumption. However, in the absence of studies with multiple assessment methods, we cannot determine the magnitude and speed of drinking that is most strongly associated with postinfarction mortality. Given the relatively conservative nature of the Onset Study definition, our results highlight the serious potential risks of drinking to excess or intoxication.

Binge drinking may have adverse consequences both on cardiovascular physiology and thrombosis/fibrinolysis. Canine models show acute coronary vasoconstriction with alcohol exposure. Single episodes of heavy drinking increase both blood pressure and heart rate, and trials with stress tests have confirmed greater ischemia after short-term heavy alcohol intake. Large amounts of alcohol given to nonalcoholic men increase platelet reactivity, thromboxane B₂ formation, and plasminogen activator inhibitor-1 activity. In one controlled trial, heavy but not moderate drinking increased plasminogen activator inhibitor-1 activity, decreased tissue plasminogen activator activity, and prolonged clot lysis time, in some cases for >12 hours. These effects could clearly interact to trigger recurrent MI and thus, to increase mortality among those with a recent MI.

Binge alcohol use could also contribute to sudden cardiac death (SCD) related to ventricular arrhythmias. Heavy episodic consumption appears to lower the ventricular fibrillation threshold in response to both electric and mechanical provocation and increases the risk of SCD. This is likely to be a particularly important factor for MI survivors, who have a 4- to 6-fold increased baseline risk of SCD.

Although the ethanol content of a typical serving of beer, wine, or liquor is relatively similar, the amount of ethanol in a standard serving can vary substantially between countries. For example, standard drinks (12 oz of beer, 5 oz of wine, or 1.5 oz of liquor) contain 13 to 14 g in the United States, but 1 unit of alcohol in the United Kingdom contains 8 g; despite this discrepancy, recommended limits for drinking (in grams of ethanol) are similar in the 2 regions. However, discrepancies such as these complicate cross-national comparisons of binge drinking. The definition used here (3 drinks in 1 to 2 hours) represents 40 to 45 g of ethanol, but appropriate scaling would be needed to replicate our findings elsewhere. The Onset Study is subject to limitations. As with any observational study, we cannot prove cause-and-effect relations, and there may be unmeasured aspects of lifestyle that are responsible in part for our findings. For example, we adjusted for educational attainment and income associated with zip code of residence (a measure at the community level), but we did not have information on current personal income. Comparisons of binge drinkers with other drinkers, rather than abstainers, may be somewhat less susceptible to confounding because of the greater comparability of these groups in sociodemographic features.

Participants reported their usual drinking habits during the year before hospitalization, and we do not have information on posthospitalization drinking patterns. Limited evidence suggests that preinfarction and postinfarction alcohol consumption patterns are strongly correlated. If some binge drinkers cease such drinking after hospitalization, we may have underestimated the true effect of postinfarction binge drinking on survival, but variation over time appears unlikely to have produced an overestimate of risk. On the other hand, by determining each patient’s usual alcohol consumption before hospitalization and the onset of follow-up, we minimized the possibility of differential misclassification caused by sicker patients giving up binge drinking more often than healthier patients during the follow-up period. For the most accurate results, future studies will need to assess both pre-MI and post-MI drinking patterns and correct for changes in intake among sicker patients.

We do not have information on how Onset Study participants changed their lifestyle or complied with medical therapy after hospitalization. Numerous studies suggest that heavier alcohol consumption directly affects smoking cessation, likelihood of relapse among ex-smokers, and medication compliance. Because binge drinking is likely to affect these factors directly, lack of adjustment for differences in posthospitalization behaviors is appropriate to estimate the full effect of binge drinking. However, this limitation precludes determination of whether our findings may relate to cardiovascular or neurobehavioral effects of alcohol.

Our patients were hospitalized during the thrombolytic era, before widespread use of primary angioplasty and coronary stenting. Additional studies are needed to determine whether current treatment approaches modify the hazards associated with binge drinking.

Despite the size of the Onset Study, the power of our analyses was limited in some cases, particularly in analyses of subgroups and interactions. Larger studies with different measures of binge drinking will be needed to describe possible dose-response relations in the quantity of alcohol consumed per binge and the consistency of the association among women and across beverage types and usual levels of intake.

In conclusion, binge drinking appears to be associated with 2-fold greater mortality after acute MI in the Onset Study. Because binge drinking occurs frequently even in otherwise light drinkers, this finding highlights the potential hazards of inappropriate alcohol consumption at all levels of usual intake. Although determination of the risks and benefits of regular drinking for an individual requires consideration of numerous personal, clinical, and social factors best addressed by a physician, we encourage physicians and patients to consider the detrimental consequences that accompany alcohol use when not consumed with care.

Acknowledgments

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Disclosures

None.
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