Associations Between Alcohol Consumption and Insulin Sensitivity and Cardiovascular Disease Risk Factors

The Insulin Resistance and Atherosclerosis Study

RONNY A. BELL, PHD, MS
ELIZABETH J. MAYER-DAVIS, PHD
MICHELLE A. MARTIN, PHD
RALPH B. D'AGOSTINO JR., PHD
STEVE M. HAFFNER, MD, MPH

OBJECTIVE — Light-to-moderate alcohol consumption has been associated with reduced cardiovascular disease (CVD) mortality, which may be explained by increased insulin sensitivity (S_I) and an improved lipoprotein and blood pressure profile. Prior research has shown improved S_I with light-to-moderate alcohol intake even though somewhat imprecise measures of S_I were used.

RESEARCH DESIGN AND METHODS — Relationships between alcohol use and S_I and CVD risk factors were assessed in a cross-sectional analysis of 1,196 white, African-American, and Hispanic men and women from the Insulin Resistance and Atherosclerosis Study (IRAS). Five categories of previous-year alcohol use (never, <0.5 drinks/day, 0.5–0.99 drinks/day, 1–2.99 drinks/day, and ≥3 drinks/day) and log S_I + 1 (frequently sampled intravenous glucose tolerance test with Bergman minimal model analysis), log fasting insulin, log triglycerides, HDL cholesterol, and systolic/diastolic blood pressure were examined using analysis of variance.

RESULTS — Univariate analysis showed an inverse U-shaped relationship between S_I and alcohol intake, with a peak at the 0.5–0.99 drinks/day category. A U-shaped relationship was observed between fasting insulin and the lipid and blood pressure measures. After adjustment for demographic (clinic, sex, ethnicity, age), lifestyle (smoking, dietary energy/fat intake, physical activity), and physical (BMI, waist circumference) variables, the alcohol/insulin association was attenuated, but the association with lipids and blood pressure remained for high-intake categories.

CONCLUSIONS — These data suggest that the enhanced S_I associated with light-to-moderate alcohol consumption may be a function solely of a BMI and central adiposity profile more favorable to higher S_I.

Diabetes Care 23:1630–1636, 2000

A large body of cross-sectional and cohort data suggests that light-to-moderate consumption of alcoholic beverages (1–2 alcoholic drinks/day) is associated with a reduced risk of cardiovascular disease (CVD) morbidity and mortality compared with abstainers and heavy consumers (1–16). This U- or J-shaped relationship might be accounted for by nutritional components of alcoholic beverages or through alcohol's mediating of CVD risk factors, such as insulin sensitivity (S_I) (7,17–20), lipids (20, 21), clotting factors (22,23), blood pressure (24,25), or some combination of these factors.

Previous research has shown that light-to-moderate alcohol consumption is associated with an insulin profile favoring reduced CVD risk compared with nondrinkers and heavy drinkers (17–20,26,27). Prospective population-based data have shown an inverse association between light-to-moderate alcohol consumption and the development of type 2 diabetes (28–31). Three other prospective population-based studies show a positive association between alcohol intake and risk of type 2 diabetes in men but not in women (32–34). Despite these findings, there are some gaps in this current body of knowledge. A wide array of measures has been used to estimate S_I, such as fasting insulin only (19,20,27), or fasting or 2-h postload insulin and glucose to calculate a surrogate measure of S_I (17,18), or fasting and 1-, 2-, and 3-h postchallenge plasma insulin and glucose concentrations and a modified insulin suppression test (26), limiting to some degree the quality of this outcome measure.

Measurement of self-reported alcohol consumption can also prove to be problematic. Alcohol intake assessed in epidemiologic studies is typically derived from a food item listed on a food-frequency questionnaire (FFQ) and less frequently by a questionnaire designed specifically for alcohol intake. Issues that need to be addressed to adequately assess alcohol intake include patterns of alcohol use, types of beverages consumed, and history of alcohol use.

Other gaps in our understanding of the relationship between alcohol consumption and S_I include the influence of race/ethnicity, as well as diabetes status, on this association. This study aims to illustrate the relation between alcohol consumption and S_I in an ethnically diverse population using a sensitive measure of S_I and a rigorous standardized method of assessing alcohol intake. Relations between alcohol consumption and other CVD risk factors (lipids

From the Department of Public Health Sciences (R.A.B., R.B.D.), Wake Forest University School of Medicine, Winston-Salem, North Carolina; the Department of Epidemiology and Biostatistics (E.J.M.-D., M.A.M.), University of South Carolina School of Public Health, Columbia, South Carolina; and the Division of Clinical Epidemiology (S.M.H.), University of Texas at San Antonio, San Antonio, Texas.

Address correspondence and reprint requests to Ronny A. Bell, PhD, MS, Wake Forest University School of Medicine, Medical Center Blvd., Winston-Salem, NC 27157-1063. E-mail: rbell@wfubmc.edu.

Received for publication 9 October 1999 and accepted in revised form 18 July 2000.

Abbreviations: CVD, cardiovascular disease; FFQ, food-frequency questionnaire; FSIGT, frequently sampled intravenous glucose tolerance test; IRAS, Insulin Resistance and Atherosclerosis Study; S_I, insulin sensitivity.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Characteristics of study participants according to daily alcohol consumption* (n = *1,196): IRAS, 1992–1994*

	Alcohol consumption				
	Never	<0.5 drinks/day	0.5–0.99 drinks/day	1–2.99 drinks/day	≥3 drinks/day
n	180	684	125	162	45
Female (%)	84.4	54.7	60.3	38.9	9.7
Non-white (%)	67.2	63.1	57.6	56.2	40.0
Alcohol consumption (g/day)	0	1.25	8.61	20.85	55.88
Current smoker (%)	5.6	17.0	16.0	26.5	31.1
Age (years)	58.4	54.9*	54.2*	54.6*	57.2*
Diabetes prevalence (%)	39.0	32.2	22.4	17.3	33.3
Energy expenditure (kcal · kg^{-1} · $year^{-1}$)	14,514	14,458	14,635	15,082	15,174
Dietary fat (% total calories)	35.8	35.4	34.5	33.0*	30.7*
Vigorous activity (%)	27.3	33.6	43.6	45.7	40.9
Waist circumference (cm)	91.8	93.8	90.4	92.8	97.3*
BMI (kg/m^2)	30.1	30.0	27.4*	27.9*	28.1*

*Significantly different ($P < 0.01$) compared with referent group (never-drinkers).

and lipoproteins, body composition, and blood pressure) were also examined.

RESEARCH DESIGN AND METHODS

Study population

The design and rationale of the Insulin Resistance and Atherosclerosis Study (IRAS) have been described in detail elsewhere (35). Briefly, the IRAS is a large epidemiological study designed to assess the association between S_I and measures of atherosclerosis and prevalent CVD. Participants in the IRAS were recruited from four sites: Los Angeles and Oakland, CA; San Antonio, TX; and the San Luis Valley, CO. The goal of the sampling strategy was to obtain equal numbers of participants according to sex, ethnicity, and glucose tolerance status (normal, impaired glucose tolerance, type 2 diabetes). Recruitment of white and non-Hispanic African-American subjects in California occurred through Kaiser Permanente, a nonprofit health maintenance organization. Recruitment of Hispanic subjects occurred primarily in the San Antonio and San Luis Valley clinics as part of two ongoing population-based studies (the San Antonio Heart Study [36] and the San Luis Valley Diabetes Study [37]). From the 3,416 potential participants contacted, 1,625 agreed to participate (48% recruitment rate).

The IRAS examinations involved two clinic visits at respective sites ~1 week apart. For the present secondary data analyses, variables assessed during clinic visits by IRAS participants were used. Variables were measured using the following standardized procedures.

Study outcome variables

S_I was assessed using an insulin-enhanced frequently sampled intravenous glucose tolerance test (FSIGT) (12 samples) (38) with minimal model analysis (39). FSIGTs were performed with an insulin (0.03 U/kg) and glucose (0.3 g/kg body wt) injection at 0 and 20 min, respectively. Insulin was used instead of tolbutamide to ensure accurate computation of S_I across ranges of glucose tolerance. Blood samples were collected at 0, 2, 4, 8, 19, 22, 30, 40, 50, 70, 100, and 180 min for determination of glucose and insulin levels. Blood levels of insulin and glucose were assessed in a central laboratory (University of Southern California, Los Angeles, CA); plasma glucose was measured using the glucose oxidase technique on an automated autoanalyzer (YSI, Yellow Springs, OH); and insulin was assessed by radioimmunoassay. These values were used to estimate the parameters of the minimal model, using the MINIMOD mathematical modeling method (39). This method of assessing S_I correlates well with the more difficult "gold standard" method—namely the euglycemic clamp (40).

Fasting lipids and lipoproteins were assessed by the quantification procedure in the laboratory of MedStar Research Institute (B.V. Howard, Washington, DC). Blood pressure was measured with a mercury sphygmomanometer with the subject seated for 5 min. The average of the second and third of three measurements was used.

Alcohol consumption

Current usual intake of alcohol over the previous month was assessed using a 10-item questionnaire, and alcohol intake in grams per day was calculated overall and by particular beverage type (beer, wine, or liquor). For this analysis, alcohol consumption was considered as a continuous variable (grams of alcohol per day) and as a categorical variable (drinks per day, assuming an average of 12 g/drink). Five categories of current alcohol intake were created for data analysis: never, <0.5 drinks/day, 0.5–0.99 drinks/day, 1.0–2.99 drinks/day, and ≥3 drinks/day. Never-drinkers were identified by a "no" response to the question "In your entire life, have you had at least 12 drinks of any kind of alcoholic beverage?" Ever-drinkers were identified by a "yes" response to the previous question and by a response of ">1 year ago" to the open-ended question "How long ago did you last drink any kind of alcoholic beverage?" Individuals classified as ex-drinkers (n = 254) were excluded from the analysis, since ex-drinkers represent a wide variety of health circumstances. Pattern of alcohol use was assessed using a single-item question that asked, "Do you typically drink: a) about the same every day; b) more on weekends; c) more during the week; or d) only on special occasions?"

Potential confounds

Energy and dietary fat intake were assessed using a 1-year semiquantitative FFQ from the National Cancer Institute, modified at each center to capture regional and ethnic variation in dietary patterns. Height, weight, and waist-to-hip ratio were measured using protocol standardized across clinics. Weight and height were measured in duplicate and recorded to the nearest 0.1 kg and 0.5 cm, respectively. BMI was calculated as weight

Table 2—S_I *values according to alcohol consumption categories by sex, ethnicity, and diabetes status*

	Alcohol consumption				
	Never	<0.5 drinks/day	0.5–0.99 drinks/day	1–2.99 drinks/day	≥3 drinks/day
Sex					
Women	1.16	1.14	1.36	1.16	0.70
Men	1.16	1.16	1.10	1.16	1.12
Ethnicity					
Non-Hispanic white	1.39	1.23	1.39	1.27	1.14
African-American	1.03	1.05	0.92	0.99	1.44
Hispanic-American	0.97	1.08	1.23	1.12	0.88
Diabetes status					
Normoglycemic	2.06	2.25	2.49	2.16	2.10
Impaired glucose tolerance	1.14	0.95	0.84	1.14	1.03
Type 2 diabetes	0.42	0.45	0.46	0.45	0.31

(in kilograms) divided by height (in meters) squared. Waist circumference was measured in duplicate using a metal tape. Measurements were recorded to the nearest 0.5 cm. Waist circumference was measured at the indentation between the 10th rib and the iliac crest at mid-respiration. Physical activity was measured using two separate items. First, a single-item question on usual frequency of vigorous activity was assessed with fixed responses from "rarely to never" to "5 or more times per week." Data for this analysis are presented as the percentage of subjects who report having vigorous activity at least two times per week. Second, a structured interview was used to collect a 1-year recall of physical activities, from which an estimated energy expenditure was determined. These measures are described more clearly elsewhere (41).

Statistical analysis

Because of missing S_I values, 145 observations were excluded from the analysis. An additional 254 ex-drinkers were removed, along with 30 subjects who provided incomplete data or data with extreme values, leaving a total sample size of 1,196. Data were analyzed using the Statistical Analysis System (SAS) version 6.12 (SAS Institute, Cary, NC). Preliminary descriptive univariate analyses were performed on these data. Study characteristics were compared between categories of alcohol consumption using *t* tests for continuous variables and χ^2 analysis for dichotomous variables. Analysis of variance was performed to examine differences in means of six outcomes for five categories of alcohol consumption. Outcomes of interest included S_I, triglycerides, fasting insulin, HDL cholesterol, systolic blood pressure, and diastolic blood pressure (Table 1). For the primary outcome of interest (S_I) data were stratified by sex, ethnicity, and diabetes status (Table 2).

Based on previous research, it was hypothesized that the association between alcohol intake and S_I may be curvilinear. Therefore, to assess the linear or curvilinear relationship between alcohol consumption as a continuous variable and S_I, the continuous alcohol consumption variable was added to the model in an unadjusted regression analysis as a singular (linear) or squared (quadratic) interaction term. For a statistically significant quadratic term, a plot was ascertained to determine the highest point of S_I in the alcohol consumption continuum (Fig. 1).

Measures of S_I, triglycerides, and fasting insulin were $\log_e$-transformed to normalize distributions for analysis, and results were back-transformed for presentation in the tables. Two models were used for comparisons of each outcome variable among the alcohol consumption groups (Table 3). Model 1 adjusted for demographic (clinic, sex, ethnicity, age) and lifestyle (smoking, dietary energy/fat intake, physical activity) variables; model 2 adjusted for demographic and lifestyle variables (model 1), along with BMI and waist circumference.

To test whether diabetes status affected the association between alcohol consump-

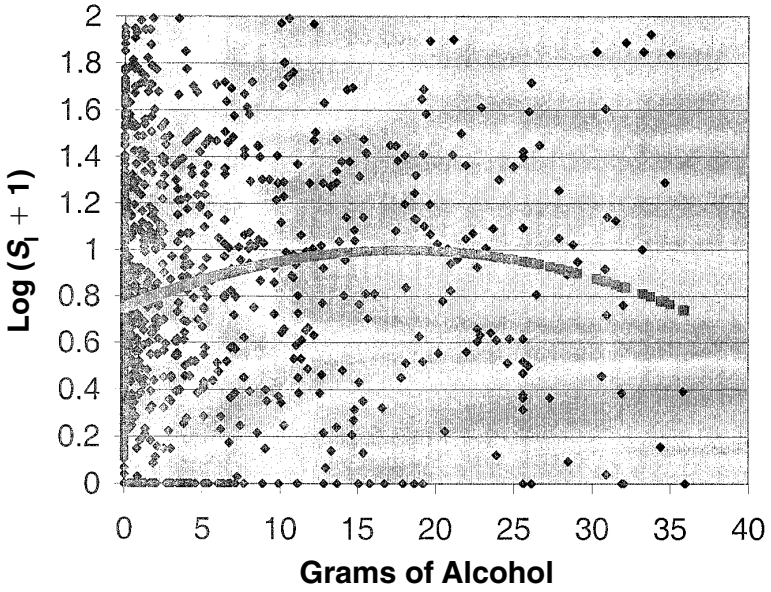

Figure 1—*Grams of alcohol per day by log (S_I + 1). ◆, Log (S_I + 1); ■, fitted log (S_I + 1).*

Table 3—*Adjusted mean values for S_I, fasting insulin, triglycerides, HDL cholesterol, and systolic and diastolic blood pressure for five levels of alcohol consumption*

	Alcohol consumption				
	Never	<0.5 drinks/day	0.5–0.99 drinks/day	1–2.99 drinks/day	≥3 drinks/day
n	180	685	126	173	45
S_I					
Model 1	1.08	1.22	1.65*	1.49*	1.24
Model 2	1.22	1.29	1.42	1.37	1.21
Fasting insulin (pmol/l)					
Model 1	96.7	101.1	82.1*	92.3	88.4
Model 2	90.9	94.7	83.7	88.8	84.0
Triglycerides (mmol/l)					
Model 1	3.53	3.47	3.42	3.13*	3.07
Model 2	3.30	3.28	3.30	2.99	3.03
HDL cholesterol (mmol/l)					
Model 1	1.01	1.06*	1.15†	1.23†	1.36†
Model 2	1.03	1.08	1.16*	1.25*	1.39*
Systolic blood pressure (mmHg)					
Model 1	125.9	123.2	123.7	128.1	128.4
Model 2	125.8	122.7	124.1	127.7	128.8
Diastolic blood pressure (mmHg)					
Model 1	77.8	77.6	75.9	79.5	80.7
Model 2	77.7	77.4	76.3	79.7	80.7

Model 1 is adjusted for demographic (clinic, sex, ethnicity, age) and lifestyle (smoking, dietary energy/fat intake, physical activity) variables; model 2 is adjusted for demographic and lifestyle variables (model 1) and for BMI and waist circumference. *Significantly different ($P < 0.05$) compared with referent group (never-drinkers); †significantly different ($P < 0.01$) compared with referent group (never-drinkers).

tion and the outcomes of interest, diabetes status was included as a main effect term and as an interaction term using diabetes status (normal, impaired glucose tolerance, type 2 diabetes) and the categorical alcohol consumption variable, which allowed for eight degrees of freedom. A similar strategy was used to test the effect of sex and ethnicity (non-Hispanic white, African-American, Hispanic) on the relationship between alcohol consumption and S_I.

RESULTS — Table 1 shows demographic and lifestyle characteristics of study participants according to alcohol consumption categories. The percentages of female and non-white subjects in each category decreased with increasing alcohol consumption, whereas mean age decreased with increasing alcohol consumption, up to the highest alcohol category. Dietary fat as a percent of total calories decreased with increasing alcohol consumption, while energy expenditure and vigorous activity indicators increased. Current smoking prevalence increased greatly with incremental increases in alcohol consumption. BMI declined with increasing alcohol intake, whereas waist circumference was lowest among the 0.5–0.99 drinks/day group and peaked at the highest drinking category. Diabetes prevalence was lowest for the 0.5–0.99 drinks/day (22.4%) and 1–2.99 drinks/day (17.3%) categories.

Using the continuous alcohol consumption variable, a quadratic inverted U-shaped relationship was observed with S_I ($P = 0.0007$ for quadratic term) (Fig. 1). The peak of the line was observed to be ~18.6 g/day, which translates to ~1.5 drinks/day. An inverted U-shaped relationship was also observed among S_I measurements ($\times 10^{-4}$ min^{-1} · μu^{-1} · ml^{-1}) using the categorical values of alcohol consumption, with a peak in the 0.5–0.99 drinks/day category after adjustment for demographic and lifestyle characteristics (Table 3, model 1). The log-transformed value of S_I was significantly greater for this category ($P < 0.01$) than for every other category except the 1–2.99 drinks/day category. Log-transformed values of S_I for the 1–2.99 drinks/day category were significantly higher ($P < 0.01$) than the value for never-drinkers. Conversely, a U-shaped relationship was observed for fasting insulin and alcohol intake, with a low mark in the 0.5–0.99 drinks/day category. Log-transformed values for fasting insulin were significantly lower ($P < 0.01$) for this category compared with all other categories except the 1–2.99 drinks/day category.

The relationship between alcohol consumption and S_I was not affected by diabetes status ($P = 0.4726$ for interaction term) or sex ($P = 0.3001$ for interaction term). The relationship between alcohol consumption and S_I differed slightly by ethnic status, although not significantly so ($P = 0.1192$ for interaction term). S_I was greatest for non-Hispanic white and Hispanic subjects in the 0.5–0.99 drinks/day category, whereas for African-American subjects, S_I was greatest in the ≥3 drinks/day category (Table 2).

The relationship between alcohol consumption and S_I did not vary according to type of alcohol consumed, but typical pattern of use did independently predict S_I. S_I was greater for subjects who drank the same each day (1.78), followed by those who drank more on the weekends (1.56). The lowest S_I value among drinkers was found for those who drank only on special occasions (1.14), but was slightly higher than that found for nondrinkers (1.06). Nondrinkers had a significantly lower S_I compared with those who drank more on the weekend ($P < 0.001$) and those who drank the same each day ($P < 0.0001$).

Table 4—*Review of previous studies and the present study examining the association between insulin function and alcohol consumption*

Reference	Insulin function assessment	Potential confounders	Highest alcohol category	Alcohol category with highest insulin function
Kiechl et al. (18)	Homeostasis model assessment to estimate insulin resistance and β-cell activity	Age, sex, smoking status, BMI, physical activity, social status	≥100 g/day	≥100 g/day
Razay and Heaton (27)	Fasting insulin	Age, BMI, smoking status, use of hypertensive drugs	>40 g/day	21–30 g/day
Facchini et al. (26)	Steady-state plasma insulin and glucose	None	10–30 g/day (nondrinkers compared with light-to-moderate drinkers	10–30 g/day
Lazarus et al. (19)	Fasting insulin	Body weight, BMI, waist-to-hip ratio, age, physical activity, saturated fat intake, daily energy intake	≥30 g/day	10–30 g/day
Mayer et al. (17)	Fasting insulin, 2-h insulin	Age, weight, height, waist circumference, hip circumference, total daily caloric intake, family history of diabetes	≥10 g/day (1.5 drinks/day)	2.0–9.9 g/day (3 drinks/week) for fasting insulin; ≥10 g/day (1.5 drinks/day) for 2-h insulin
Manolio et al. (20)	Fasting insulin	Age, sex, race, BMI	Alcohol intake considered as a continuous variable (ml/week)	Inverse association in unadjusted (−0.09) and adjusted (−0.04) models between fasting insulin and alcohol intake
Bell et al. (current study)	S_I (FSIGT using Bergman minimal model analyses)	Clinic, sex, ethnicity, age, smoking status, dietary energy, dietary fat, physical activity, BMI, waist circumference	≥3 drinks/day	0.5–1.0 drinks/day (nonsignificant in multivariate analyses)

When adjusting for demographic and lifestyle characteristics, BMI and waist circumference altered the relationship between alcohol consumption and S_I and fasting insulin (Table 3, model 2). Whereas the pattern was similar, the significant differences in S_I between nondrinkers and moderate drinkers dissipated, as did the difference in fasting insulin between nondrinkers and subjects in the 0.5–0.99 drinks/day category, indicating that BMI and central adiposity mediated the U-shaped association observed in the univariate analysis.

When adjusting for demographic and lifestyle characteristics, triglycerides, diastolic blood pressure, and systolic blood pressure levels showed a U-shaped relationship with alcohol intake, with the lowest values seen in the 1–2.99 drinks/day category (triglycerides) or the 0.5–0.99 drinks/day category (systolic and diastolic blood pressure). Triglyceride levels were statistically significantly higher ($P < 0.01$) for consumers of 1–2.99 drinks/day compared with nondrinkers, whereas blood pressure values were not significantly different across alcohol categories. HDL cholesterol gradually increased with increasing alcohol intake, with significantly greater ($P < 0.01$) levels for each of the three highest alcohol consumption categories.

CONCLUSIONS — These data indicate that our primary hypothesis, that light-to-moderate alcohol intake is associated with S_I, could not be completely confirmed after adjustment for BMI and central adiposity; that is, light-to-moderate alcohol consumers no longer have a significantly better S_I profile once indexes of body composition are considered. This finding parallels that of the Nurses' Health Study, which showed that the protective effect of moderate alcohol consumption on risk of diabetes was attenuated when body weight was considered (42). Regarding our secondary outcomes, these data also support prior research showing that increasing alcohol consumption improves lipid profiles while increasing blood pressure (20,21,24,25).

Previous research has shown a correlation between alcohol intake and various indicators of S_I (17–20,26,27). As shown in Table 4, these studies vary greatly in the assessment of insulin function and in the heterogeneity of alcohol consumption within the populations studied. It is likely that the variability shown in the outcomes of these studies are the result of these differences. Nonetheless, the effects of alcohol intake on S_I should be considered.

The mechanism of action of alcohol on S_I has been studied extensively. Biologically, acute alcohol consumption has been shown to affect insulin action. Some studies have shown that relatively large doses of alcohol acutely impair insulin-mediated glucose uptake (44,45), whereas others have shown an enhanced effect on glucose-stimulated insulin secretion (46). Some studies have also reported that acute alcohol consumption results in an initial hyperinsulinemic effect followed by a hypoinsulinemic and/or hypoglycemic effect (47,48). Acute consumption of two alcoholic drinks resulted in a more favorable insulin resistance profile

measured by a hyperinsulinemic clamp compared with a larger dose of six drinks (49), indicating that dose of administration is an important factor in the impact on insulin response. The results of studies attempting to assess the association between chronic alcohol consumption and S_I have been fairly consistent in showing that heavy alcohol consumers are more insulin resistant, although there is little to indicate from these studies that pattern of use was assessed. It is likely that the results of this study, which show that light-to-moderate chronic consumption and consistent versus inconsistent typical consumption, reflect the optimal profile from a biologic standpoint.

The finding in the present study that body composition, i.e., BMI and central adiposity, negatively influenced the association between light-to-moderate alcohol consumption and enhanced S_I deserves some consideration. Biologically, ethanol metabolism is favored over fat metabolism in the body, which reduces lipid oxidation and enhances lipid storage (50). In the absence of alcohol calories replacing dietary calories, it is assumed that alcohol consumption would promote weight gain. However, there is no clear consensus in epidemiologic data on the relationship between alcohol intake and body weight (51). For example, Sakurai et al. (52) showed that alcohol intake was very strongly and positively associated with waist-to-hip ratio but not with BMI, whereas Liu et al. (53) showed that alcohol does not prospectively increase the risk of obesity. Previous studies of the relationship between alcohol intake and S_I have considered BMI only (18,20,27) or both BMI and some measure of central adiposity (17,19) as a potential confounder.

The present study is hampered by at least two limitations that affect the generalizability of these findings. First, the study included a small number of heavy drinkers. Only 45 of 1,196 (4.2%) participants were classified in the highest category of ≥3 drinks/day. Other studies, however, have had difficulty in identifying large numbers of heavy drinkers (17). Second, this study, as well as other studies, relies on self-report of alcohol consumption, which may result in both random error and systematic bias in alcohol classification.

Nonetheless, this study has a number of strengths that add to the current body of literature on this topic: *1*) the measure of S_I is more comprehensive than surrogate measures previously used; *2*) the study uses a validated assessment of alcohol intake and takes into consideration current and previous consumption of alcohol; *3*) the study includes individuals with normal and impaired glucose tolerance and previously diagnosed diabetes; and *4*) the study examines this relationship in a large multiethnic sample from across the U.S.

In summary, this study contradicts previous research (17,19,26,27) showing a positive effect of light-to-moderate chronic alcohol consumption on S_I in that the relationship was shown in this analysis to be attenuated by body composition—a known CVD risk factor. Further investigation of longitudinal data from the IRAS cohort will provide more definitive answers to this complex issue.

Acknowledgments— This study was supported by the following grants from the National Institutes of Health: R29-HL53798, U01-HL47887, U01-HL47889, U01-HL47890, U01-HL47892, U01-HL47902, and DK-29867.

Parts of this study were presented at the 58th Annual Meeting and Scientific Sessions of the American Diabetes Association, Chicago, Illinois, 13–16 June 1998.

References

1. McElduff P, Dobson AJ: How much alcohol and how often? Population based case-control study of alcohol consumption and risk of major coronary event. *BMJ* 314:1159–1164, 1997
2. Jackson R, Scragg R, Beaglehole R: Alcohol consumption and risk of coronary heart disease. *BMJ* 303:211–216, 1991
3. Woodward M, Tunstall-Pedoe H: Alcohol consumption, diet, coronary risk factors, and prevalent coronary heart disease in men and women in the Scottish Heart Health Study. *J Epidemiol Community Health* 49:354–362, 1995
4. Cullen KJ, Knuiman MW, Ward NJ: Alcohol and mortality in Busselton, Western Australia. *Am J Epidemiol* 137:242–248, 1993
5. Rimm EB, Giovannucci EL, Willett WC, Colditz GA, Ascherio A, Rosner B, Stampfer MJ: Prospective study of alcohol consumption and risk of coronary disease in men. *Lancet* 338:464–468, 1991
6. Kaufman DW, Rosenberg L, Helmrich SP, Shapiro S: Alcoholic beverages and myocardial infarction in young men. *Am J Epidemiol* 121:548–554, 1985
7. Kitamura A, Iso H, Sankai T, Naito Y, Sato S, Kiyama M, Okamura T, Nakagawa Y, Iida M, Shimamoto T, Komachi Y: Alcohol intake and premature coronary heart disease in urban Japanese men. *Am J Epidemiol* 147:59–65, 1998
8. Renaud SC, Gueguen R, Schenker J, d'Houtaud A: Alcohol and mortality in middle-aged men from Eastern France. *Epidemiology* 9:184–188, 1998
9. Camargo CA Jr, Stampfer MJ, Glynn RJ, Grodstein F, Gaziano JM, Manson J, Buring J, Hennekens CH: Moderate alcohol consumption and risk for angina pectoris or myocardial infarction in U.S. male physicians. *Ann Intern Med* 126:372–375, 1997
10. Keil U, Chambless LE, Doring A, Filipiak B, Steiber J: The relation of alcohol intake to coronary heart disease and all-cause mortality in a beer-drinking population. *Epidemiology* 8:150–156, 1997
11. Coate D: Moderate drinking and coronary heart disease mortality: evidence from NHANES I and the NHANES I follow-up. *Am J Public Health* 83:888–890, 1993
12. Goldberg RJ, Burchfiel CM, Reed DM, Wergowske G, Chiu D: A prospective study of the health effects of alcohol consumption in middle-aged and elderly men: the Honolulu Heart Program. *Circulation* 89:651–659, 1994
13. Steinberg D, Pearson TA, Kuller KH: Alcohol and atherosclerosis. *Ann Intern Med* 114:967–976, 1991
14. Sacco RL, Elkind M, Boden-Albala B, Lin I, Kargman DE, Hauser WA, Shea S, Paik MC: The protective effect of moderate alcohol consumption on ischemic stroke. *JAMA* 281:53–60, 1999
15. Grønbaek M, Deis A, Becker U, Hein HO, Schnohr P, Jensen G, Borch-Johnsen K, Sørensen TIA: Alcohol and mortality: is there a U-shaped relation in elderly people? *Age Ageing* 27:739–744, 1998
16. Valmadrid CT, Klein R, Moss SE, Klein BEK, Cruickshanks KJ: Alcohol intake and the risk of coronary heart disease mortality in persons with older-onset diabetes mellitus. *JAMA* 282:239–246, 1999
17. Mayer EJ, Newman B, Quesenberry CP Jr, Friedman GD, Selby JV: Alcohol consumption and insulin concentrations: Role of insulin in associations of alcohol intake with high-density lipoprotein cholesterol and triglycerides. *Circulation* 88:2190–2197, 1993
18. Kiechl S, Willeit J, Poewe W, Egger G, Oberhollenzer F, Muggeo M, Bonora E: Insulin sensitivity and regular alcohol consumption: large, prospective, cross sectional population study (Bruneck study). *BMJ* 313:1040–1044, 1996
19. Lazarus R, Sparrow D, Weiss ST: Alcohol intake and insulin levels. *Am J Epidemiol* 145:909–916, 1997
20. Manolio TA, Savage PJ, Burke GL, Liu K, Wagenknecht LE, Sidney S, Jacobs DR Jr, Roseman JM, Donahue RP, Oberman A: Association of fasting insulin with blood pressure and lipids in young adults: the CARDIA Study. *Arteriosclerosis* 10:430–

436, 1990
21. Criqui MH, Cowan LD, Tyroler HA, Bangdiwala S, Heiss G, Wallace RB, 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. *Am J Epidemiol* 126:629–637, 1987
22. Renaud S, De-Lorgeril M: Wine, alcohol, platelets and the French paradox for coronary heart disease. *Lancet* 339:1523–1526, 1992
23. Renaud SC, Deswick AD, Fehily AM, Sharp DS, Elwood PC: Alcohol and platelet aggregation: the Caerphilly Prospective Heart Disease Study. *Am J Clin Nutr* 55:1012–1017, 1992
24. MacMahon SW: Alcohol consumption and hypertension. *Hypertension* 9:111–121, 1987
25. Friedman GD, Selby JV, Quesenberry CP, Armstrong MA, Klatsky AL: Precursors of essential hypertension: body weight, alcohol and salt use, and parental history of hypertension. *Prev Med* 17:387–402, 1988
26. Facchini F, Chen YD, Reaven GM: Light-to-moderate alcohol intake is associated with enhanced insulin sensitivity. *Diabetes Care* 17:115–119, 1994
27. Razay G, Heaton KW: Moderate alcohol consumption has been shown previously to improve insulin sensitivity in men. *BMJ* 314:443–444, 1997
28. Rimm EB, Chan J, Stampfer MJ, Colditz GA, Willett WC: Prospective study of cigarette smoking, alcohol use, and the risk of diabetes in men. *BMJ* 310:555–559, 1995
29. Perry IJ, Wannamethee SG, Walker MK, Thomson AG, Whincup PH, Shaper AG: Prospective study of risk factors for development of non-insulin dependent diabetes in middle aged British men. *BMJ* 310:560–564, 1995
30. Tsumura K, Hayashi T, Suematsu C, Endo G, Fujii S, Okada K: Daily alcohol consumption and the risk of type 2 diabetes in Japanese men. *Diabetes Care* 22:1432–1437, 1999
31. Wei M, Gibbons LW, Mitchell TL, Kampert JB, Blair SN: Alcohol intake and incidence of type 2 diabetes in men. *Diabetes Care* 23: 18–22, 2000
32. Holbrook TL, Barrett-Connor E, Wingard DL: A prospective population-based study of alcohol use and non-insulin dependent diabetes mellitus. *Am J Epidemiol* 132:902–909, 1990
33. Monterrosa AE, Haffner SM, Stern MP, Hazuda HP: Sex differences in lifestyle factors predictive of diabetes in Mexican-Americans. *Diabetes Care* 18:448–456, 1995
34. Ajani UA, Hennekens CH, Spelsberg A, Manson JE: Alcohol consumption and risk of type 2 diabetes mellitus among US male physicians. *Arch Intern Med* 160:1025–1030, 2000
35. Wagenknecht LE, Mayer EJ, Rewers M, Haffner S, Selby J, Borok GM, Henkin L, Howard G, Savage PJ, Saad MF: The Insulin Resistance and Atherosclerosis Study (IRAS): objectives, design, and recruitment results. *Ann Epidemiol* 5:464–472, 1995
36. Stern MP, Rosenthal M, Haffner SM, Hazuda HP, Franco LJ: Sex difference in the effects of sociocultural status on diabetes and cardiovascular risk factors in Mexican Americans: the San Antonio Heart Study. *Am J Epidemiol* 120:834–851, 1984
37. Hamman RF, Marshall JA, Baxter J, Kahn LB, Mayer EJ, Orleans M, Murphy JR, Lezotte DC: Methods and prevalence of non-insulin dependent diabetes mellitus in a biethnic Colorado population: the San Luis Valley Diabetes Study. *Am J Epidemiol* 129:296–311, 1989
38. Bergman RN, Finegood DT, Ader M: Assessment of insulin sensitivity in vivo. *Endocr Rev* 6:45–86, 1985
39. Pacini G, Bergman RN: MINMOD: a computer program to calculate insulin sensitivity and pancreatic responsivity from the frequently sampled intravenous glucose tolerance test. *Comput Methods Programs Biomed* 23:113–122, 1986
40. Saad MF, Anderson RL, Laws A, Watanabe RM, Kades WW, Chen YDI: A comparison between the minimal model and the glucose clamp in the assessment of insulin sensitivity across the spectrum of glucose tolerance. *Diabetes* 43:1114–1121, 1994
41. Mayer-Davis EJ, D'Agostino R Jr, Karter AJ, Haffner SM, Rewers MJ, Saad M, Bergman RN, for the IRAS Investigators: Intensity and amount of physical activity in relation to insulin sensitivity: the Insulin Resistance Atherosclerosis Study (IRAS). *JAMA* 279: 669–674, 1998
42. Stampfer MJ, Colditz GA, Willett WC, Manson JE, Arky RA, Hennekens CH, Speizer FE: A prospective study of moderate alcohol drinking and risk of diabetes in women. *Am J Epidemiol* 128:549–558, 1988
44. Shah J: Alcohol decreases insulin sensitivity in healthy subjects. *Alcohol Alcohol* 23:103–109, 1988
45. Avogaro A, Fontana P, Valerio A: Alcohol impairs insulin sensitivity in normal subjects. *Diabetes Res* 5:23–27, 1987
46. Metz R, Berger S, Mako R: Potentiation of the plasma insulin response to glucose by prior administration of alcohol: an apparent islet-priming effect. *Diabetes* 18:517–522, 1969
47. Puhakainen I, Koivisto VA, Yki-Jarvinen H: No reduction in total hepatic glucose output by inhibition of gluconeogenesis with ethanol in NIDDM patients. *Diabetes* 40: 1319–1327, 1991
48. Taskinen M, Nikkila EA: Nocturnal hypertriglyceridemia and hyperinsulinemia following moderate evening intake of alcohol. *Acta Med Scand* 202:173–177, 1977
49. Yki-Jarvinen H, Koivisto VA, Ylikahui R, Taskinen M: Acute effects of ethanol and acetate on glucose kinetics in normal subjects. *Am J Physiol* 254:E175–E180, 1988
50. Suter PM, Schutz Y, Jequier E: The effect of ethanol on fat storage in healthy subjects. *N Engl J Med* 326:983–987, 1992
51. Jequier E: Alcohol intake and body weight: a paradox. *Am J Clin Nutr* 69:173–174, 1999
52. Sakurai Y, Umeda T, Shinchi K, Honjo S, Wakabayashi K, Todoroki I, Nishikawa H, Ogawa S, Katsurada M: Relation of total and beverage-specific alcohol intake to body mass index and waist-to-hip ratio: a study of self-defense officials in Japan. *Eur J Epidemiol* 13:893–898, 1997
53. Liu S, Serdula MK, Williamson DF, Mokdad AH, Byers T: A prospective study of alcohol intake and change in body weight among US adults. *Am J Epidemiol* 140:912–920, 1994