Alcohol Intake, Insulin Resistance, and Abdominal Obesity in Elderly Men

Ulf Risérus and Erik Ingelsson**

Abstract

RISÉRUS, ULF AND ERIK INGELSSON. Alcohol intake, insulin resistance, and abdominal obesity in elderly men. *Obesity.* 2007;15:1766–1773.

Objective: Moderate and high alcohol intake have been associated with decreased and increased risk of type 2 diabetes, respectively. Insulin resistance, insulin secretion, and abdominal obesity are major predictors of diabetes, but the links with alcohol intake remain contradictory because of limited data.

Research Methods and Procedures: In a population-based cohort of 807 men (age, 70 years), we studied whether alcohol intake was related to insulin sensitivity, measured with the gold standard technique (euglycemic clamp), insulin secretion (early insulin response), or adiposity [BMI, waist circumference (WC), waist-to-hip ratio]. Alcohol intake was self-reported (questionnaire) and was assessed from a validated 7-day dietary record. The cross-sectional associations were evaluated using multivariable linear regression, adjusting for smoking, education level, physical activity, dietary total energy intake, hypertension, diabetes, triglycerides, and cholesterol.

Results: In multivariable models, self-estimated alcohol intake was not related to insulin sensitivity, early insulin response, or BMI, but was positively related to WC (β-coefficient, 0.77; 95% confidence interval, 0.15 to 1.39; $p = 0.02$) and waist-to-hip ratio (0.006 [0.002–0.009], $p = 0.003$). The association with WC and waist-to-hip ratio was most pronounced in men in the lowest tertile of BMI. The results using dietary records were similar.

Discussion: Evaluated in a large sample in elderly men, neither insulin sensitivity measured by clamp technique nor insulin secretion was significantly associated with alcohol intake. However, high alcohol intake was associated with abdominal obesity, which might explain the higher diabetes risk previously observed in high alcohol consumers.

Key words: alcohol, insulin sensitivity, abdominal obesity, insulin secretion, fat distribution

Introduction

Moderate alcohol intake has been associated with lower risk of type 2 diabetes, whereas high intake seems to increase the risk (1,2). It is unclear which factors might explain such associations.

Beneficial effects of moderate alcohol intake on insulin sensitivity has been proposed (3) and reported in some cross-sectional studies (4–6) but has not been consistently shown in intervention studies (7–12). Alcohol may also have acute effects on insulin secretion (12), which also questions the validity of previous studies on the influence of alcohol on insulin sensitivity, where insulin levels were used as a surrogate for insulin resistance. In addition, alcohol might affect body fat distribution, which in turn could modulate insulin sensitivity. The effect of alcohol on obesity and fat distribution is controversial, because it has been proposed that alcohol may not be as fattening as other nutrients (13).

Because insulin sensitivity and abdominal obesity are important predictors of diabetes, it is relevant to further study the links between these factors and alcohol intake. There are, however, few studies on alcohol intake and potential mediators of such relationships, i.e., directly measured insulin sensitivity, insulin secretion, and adiposity. We hypothesized that these mediators may be related to alcohol intake and, in particular, that moderate alcohol intake may be associated with increased insulin sensitivity or improved insulin secretion. Thus, we studied the association between alcohol intake and the three major factors preceding type 2 diabetes, i.e., decreased insulin sensitivity,

Received for review September 22, 2006.
Accepted in final form January 3, 2007.
The costs of publication of this article were defrayed, in part, by the payment of page charges. This article must, therefore, be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
Department of Public Health and Caring Sciences, Clinical Nutrition and Metabolism/Geriatrics, Uppsala University, Uppsala, Sweden.
*Both authors contributed equally to this publication.
Address correspondence to Ulf Risérus, Department of Public Health and Caring Sciences, Clinical Nutrition and Metabolism, Uppsala Science Park, 751 85 Uppsala, Sweden.
E-mail: ulf.riserus@pubcare.uu.se

deficient insulin secretion, and obesity, including body fat distribution in a large, community-based cohort with insulin sensitivity measured directly by the gold standard technique.

Research Methods and Procedures

The study is based on the Uppsala Longitudinal Study of Adult Men cohort (http://www.pubcare.uu.se/ULSAM/), a health study focusing on identifying metabolic risk factors for cardiovascular disease, to which all 50-year-old men living in Uppsala in 1970 to 1974 were invited. Of these, 82% (2322 men) participated in the original study (14). The cohort was restudied 20 years later (the baseline of this study; 1991 to 1995). Of the 1681 available 70-year-old men invited to the follow-up study, 73% (1221 men) attended. For this study, 414 participants were excluded because of the following reasons: unavailable clamp data (n = 61), unavailable oral glucose tolerance test data (n = 9), unavailable anthropometric data (n = 11), unavailable data on any of the clinical covariates (n = 140), missing data on self-estimated alcohol intake (n = 174), and missing data from 7-day diet registration (n = 19). Thus, 807 (age, 70 years) were eligible for this study. All subjects gave written consent, and the Ethics Committee of Uppsala University approved the study.

The design and methods of the Uppsala Longitudinal Study of Adult Men cohort has been described in detail previously (15). Briefly, insulin sensitivity was determined by hyperinsulinemic euglycemic clamp, according to DeFronzo (16), which was slightly modified [insulin was infused at a constant rate of 56 mU/(min · m^2) to achieve nearly total suppression of hepatic glucose output]. Insulin sensitivity (M-value) was calculated as glucose infusion rate (milligram per minute times kilograms of body weight) during the last 60 minutes of the 2-hour clamp. Insulin secretion was assessed as the early insulin response (EIR)[1] during an oral glucose tolerance test (30-minute-increment of insulin/30-minute-increment of glucose). BMI was calculated as the ratio of the weight to height squared. The waist circumference (WC) was measured in the supine position midway between the lowest rib and the iliac crest, and the hip circumference was measured over the widest part (17). All subjects completed a standardized questionnaire including five questions regarding alcohol intake. The questions were formulated as follows: How much light beer/cider (number of bottles) do you usually drink per week?; How much medium alcohol beer (number of bottles) do you usually drink per week?; How much high alcohol beer (number of bottles) do you usually drink per week?; How much wine (number of glasses) do you usually drink per week?; and How much liquor (number of milliliters) do you usually drink per week? The answers were transformed into grams of alcohol per week. In addition, a dietitian instructed all subjects to record their daily energy and alcohol intake using a validated 7-day precoded dietary record, previously used by the National Food Administration in a food survey of 3000 households in 1989 (18). Daily alcohol and energy intakes were calculated using a computerized program (MATs; Rudans Lättdata, Västerås, Sweden) and the National Food Administration database. Smoking status was assessed from interview questions and a self-administered questionnaire (19), and the participants were classified as never-smokers, ex-smokers, or current smokers. Leisure-time physical activity (sedentary, moderate, regular, athletic) and education level (elementary school, high school, upper secondary school, college/university) was assessed using a self-administered questionnaire as previously described (15). Blood pressure was measured in the supine position after a 10-minute rest (20), and hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or use of anti-hypertensive treatment (20). Serum triglycerides, cholesterol, and plasma glucose were analyzed from blood samples drawn after an overnight fast (20). Diabetes was defined as fasting plasma glucose ≥7.0 mM or use of oral hypoglycemic agents or insulin (21).

Data are given as means ± standard deviation (SD) and percentage. Self-reported alcohol intake was modeled as a continuous (with natural logarithmic transformation to normalize the skewed distribution) and as a categorical variable, split in tertiles. Multivariable linear regression models were used to assess the relations of self-reported alcohol intake to insulin sensitivity, EIR, BMI, WC, and waist-to-hip ratio, each in separate models. Non-linear associations were excluded by plotting means of insulin sensitivity and anthropometric measures against decentiles of alcohol intake. Multivariable models were adjusted for smoking status (never-smoker, ex-smoker, current smoker), education level, leisure time physical activity, total energy intake, hypertension prevalence, diabetes prevalence, triglycerides, and total cholesterol, and adjusted means from the multivariable linear regression models were reported. To validate the findings, the relationships of alcohol intake derived from 7-day dietary record and measures of insulin sensitivity, insulin secretion, and obesity were examined using the same models. To obtain an easily understood clinical measure of alcohol intake, we also transformed the self-reported alcohol intake in grams into number of drinks per week (1 drink = 15 grams alcohol). In secondary analyses, we examined whether different types of alcohol (grams of alcohol derived from beer, wine, and liquor; modeled in tertiles) differed in their association to insulin sensitivity, EIR, BMI, WC, and waist-to-hip ratio using multivariable linear regressions, adjusted for the same covariates as in the

[1] Nonstandard abbreviations: EIR, early insulin response; WC, waist circumference; SD, standard deviation; CI, confidence interval.

Table 1. Baseline characteristics ($n = 807$), according to tertiles of self-estimated alcohol intake

	Lowest tertile ($n = 269$) of alcohol intake (<28 g/wk)	Middle tertile ($n = 269$) of alcohol intake (28 to 81 g/wk)	Highest tertile ($n = 269$) of alcohol intake (>81 g/wk)
Self-estimated alcohol intake (g/wk)	15 ± 7	50 ± 14	158 ± 86
Self-estimated beer intake (g alcohol/wk)	12 ± 7	24 ± 16	42 ± 34
Self-estimated wine intake (g alcohol/wk)	1 ± 4	13 ± 17	49 ± 68
Self-estimated liquor intake (g alcohol/wk)	1 ± 4	13 ± 15	66 ± 58
7-day dietary registration alcohol intake (g/d)	3.3 ± 3.6	6.5 ± 5.4	13.3 ± 9.7
Insulin sensitivity (mg/kg body weight/min)	5.3 ± 2.1	5.0 ± 2.1	5.4 ± 2.0
EIR (pM/mM)	6.4 ± 4.0	6.3 ± 4.4	6.0 ± 3.7
BMI (kg/m^2)	25.9 ± 3.5	26.4 ± 3.3	26.2 ± 3.4
WC (cm)	93 ± 9	95 ± 9	95 ± 9
Waist-to-hip ratio	0.94 ± 0.05	0.94 ± 0.05	0.95 ± 0.05
Current smoker (%)	47 (17)	48 (18)	70 (26)
Ex-smoker (%)	121 (45)	147 (55)	148 (55)
Education level (%)			
Elementary school	171 (64)	165 (61)	130 (48)
High school	37 (14)	29 (11)	41 (15)
Upper secondary school	20 (7)	27 (10)	41 (15)
College/university	41 (15)	48 (18)	57 (21)
Leisure time physical activity (%)			
Sedentary	6 (2)	8 (3)	14 (5)
Moderate	80 (30)	107 (40)	80 (30)
Regular	167 (62)	139 (52)	157 (58)
Athletic	16 (6)	15 (6)	18 (7)
Dietary total energy intake (kcal/d)	1830 ± 466	1710 ± 394	1715 ± 472
Systolic blood pressure (mm Hg)	146 ± 19	147 ± 20	148 ± 18
Diastolic blood pressure (mm Hg)	83 ± 10	83 ± 10	85 ± 9
Hypertension prevalence (%)	195 (72)	199 (74)	210 (78)
Fasting plasma glucose (mM/L)	5.7 ± 1.4	5.9 ± 1.7	5.7 ± 1.4
Diabetes prevalence (%)	28 (10)	36 (13)	23 (9)
Serum total cholesterol (mM/L)	5.8 ± 1.0	5.8 ± 1.0	6.0 ± 1.0
Serum triglycerides (mM/L)	1.4 ± 0.7	1.4 ± 0.7	1.4 ± 0.7

EIR, early insulin response; WC, waist circumference. Values are means ± standard deviation for continuous variables and counts (percentages) for categorical variables.

primary analyses. In further secondary analyses, to examine whether alcohol intake was associated with abdominal obesity regardless of generalized obesity, we examined interaction terms between BMI and alcohol intake in multivariable linear regressions with WC and waist-to-hip ratio as dependent variables. Because the interaction terms were significant ($p < 0.001$ for both), we examined the associations between self-estimated alcohol intake and WC and waist-to-hip ratio in BMI tertiles separately (tertile 1, 16.7 to <24.6 kg/m^2; tertile 2, 24.6 to <27.3 kg/m^2; tertile 3, 27.3 to 46.3 kg/m^2). Two-tailed 95% confidence intervals (CIs) and p values are given, with $p < 0.05$ regarded as significant. Statistical software package STATA 8.2 (Stata Corp LP., College Station, TX) was used.

Results

The baseline characteristics are shown in Table 1. In multivariable models adjusting for potential confounders,

Table 2. Alcohol intake as assessed by self-estimation and 7-day dietary record and associations with insulin sensitivity and obesity

	Log self-estimated alcohol intake (g/wk)		Tertile 1 (n = 269) (<28 g/wk)	Tertile 2 (n = 269) (28 to 81 g/wk)	Tertile 3 (n = 269) (>81 g/wk)	Test for linear trend
Alcohol intake according to self-administered questionnaire						
	β* (95% CI)	p	[mean (95% CI)]	[mean (95% CI)]	[mean (95% CI)]	(p)
Insulin sensitivity	0.01 (−0.11 to 0.13)	0.90	5.2 (5.0–5.4)	5.2 (5.0–5.4)	5.3 (5.1–5.5)	0.54
EIR	−0.01 (−0.05 to 0.03)	0.67	5.3 (4.9 to 5.7)	5.2 (4.8 to 5.5)	5.0 (4.7 to 5.4)	0.29
BMI	0.20 (−0.02 to 0.43)	0.07	25.9 (25.5 to 26.2)	26.3 (25.9 to 26.6)	26.3 (26.0 to 26.7)	0.09
WC	0.77 (0.15 to 1.39)	0.02	93.4 (92.3 to 94.4)	94.6 (93.6 to 95.6)	95.2 (94.1 to 96.2)†	0.02
Waist-to-hip ratio	0.006 (0.002 to 0.009)	0.003	0.94 (0.93 to 0.94)	0.94 (0.94 to 0.95)	0.95 (0.95 to 0.96)‡	0.002
Alcohol intake according to 7-day dietary record						
	Log 7-day dietary registration alcohol intake (g/d)		Tertile 1 (n = 269) (<3.2 g/d)	Tertile 2 (n = 269) (3.2 to <8.8 g/d)	Tertile 3 (n = 269) (≥8.8 g/d)	Test for linear trend
	β* (95% CI)	p	[mean (95% CI)]	[mean (95% CI)]	[mean (95% CI)]	(p)
Insulin sensitivity	−0.03 (−0.16 to 0.10)	0.64	5.3 (5.1 to 5.5)	5.3 (5.1 to 5.5)	5.1 (4.9 to 5.3)	0.38
EIR	−0.02 (−0.06 to 0.03)	0.50	5.3 (4.9 to 5.7)	5.2 (4.8 to 5.5)	5.0 (4.7 to 5.4)	0.31
BMI	0.19 (−0.04 to 0.43)	0.10	26.1 (25.7 to 26.5)	25.9 (25.5 to 26.2)	26.5 (26.1 to 26.9)	0.10
WC	0.97 (0.32 to 1.63)	0.003	93.7 (92.6 to 94.7)	93.7 (92.7 to 94.8)	95.7 (94.7 to 96.8)‡	0.008
Waist-to-hip ratio	0.007 (0.003 to 0.010)	0.001	0.94 (0.93 to 0.94)	0.94 (0.94 to 0.95)	0.95 (0.95 to 0.96)§	0.001

CI, confidence interval; EIR, early insulin response; WC, waist circumference. Values are means (95% CI), adjusted for smoking status (never-smoker, ex-smoker, current smoker), education level, leisure time physical activity, dietary total energy intake, hypertension prevalence, diabetes prevalence, triglycerides, and total cholesterol.

* Regression coefficient (β) is the increase in insulin sensitivity or obesity variable per standard deviation increment in log alcohol intake adjusting for covariates. Standard deviations for log self-estimated alcohol intake, 1.04, and for log 7-day dietary registration alcohol intake, 1.01.

† $p < 0.05$ for comparisons using tertile 1 as referent.

‡ $p < 0.01$ for comparisons using tertile 1 as referent.

§ $p < 0.001$ for comparisons using tertile 1 as referent.

self-estimated alcohol intake was positively related to WC and waist-to-hip ratio but not to insulin sensitivity, EIR, or BMI (Table 2, top). There was a statistically significant trend of increasing WC and waist-to-hip ratio across tertiles of self-estimated alcohol intake (Table 2). Furthermore, in analyses examining the relation of number of drinks per week to WC, each additional drink per week was associated with an increased WC of 0.12 cm in multivariable regression models.

In validating analyses using data from a 7-day dietary registration, alcohol intake was positively related to WC and waist-to-hip ratio but not to insulin sensitivity, EIR, or BMI (Table 2, bottom). There was a statistically significant trend of increasing WC and waist-to-hip ratio across tertiles of 7-day dietary registration alcohol intake.

In analyses of the associations between different types of alcohol (beer, wine, and liquor) and insulin sensitivity and obesity measures, we found higher liquor intake to be significantly associated with increased BMI, WC, and waist-to-hip ratio (Table 3). Neither beer nor wine intake was significantly associated with insulin sensitivity, EIR, BMI, WC, or waist-to-hip ratio.

In secondary analyses relating self-estimated alcohol intake to WC and waist-to-hip ratio in tertiles of BMI, alcohol intake was positively related to WC (β, 0.82; 95% CI, 0.15 to 1.50; $p = 0.02$ for a 1-SD increase of log alcohol intake) and waist-to-hip ratio (β, 0.006; 95% CI, 0.0001 to 0.012; $p = 0.03$ for a 1-SD increase of log self-estimated alcohol intake) in the lowest tertile but not in the two highest tertiles of BMI. There was a statistically significant trend of in-

Table 3. Self-estimated intake of beer, wine, and liquor and associations with insulin sensitivity and obesity

	Tertile 1 (n = 285) (<12 g/wk) [mean (95% CI)]	Tertile 2 (n = 278) (12 to 30 g/wk) [mean (95% CI)]	Tertile 3 (n = 244) (>30 g/wk) [mean (95% CI)]	Test for linear trend (p)
Intake of beer (g alcohol/wk) according to self-administered questionnaire				
Insulin sensitivity	5.1 (4.9 to 5.3)	5.4 (5.2 to 5.6)	5.2 (5.0 to 5.4)	0.58
EIR	5.2 (4.9 to 5.6)	5.1 (4.7 to 5.4)	5.2 (4.8 to 5.5)	0.88
BMI	26.1 (25.8 to 26.5)	26.0 (25.6 to 26.4)	26.4 (26.0 to 26.8)	0.40
WC	94.0 (93.0 to 95.0)	93.9 (92.9 to 94.9)	95.4 (94.3 to 96.5)	0.09
Waist-to-hip ratio	0.94 (0.94 to 0.95)	0.94 (0.93 to 0.94)	0.95 (0.95 to 0.96)	0.09
Intake of wine (g alcohol/wk) according to self-administered questionnaire				
	Tertile 1 (n = 456) (<7 g/wk) [mean (95% CI)]	Tertile 2 (n = 104) (8 to 16 g/wk) [mean (95% CI)]	Tertile 3 (n = 247) (>16 g/wk) [mean (95% CI)]	Test for linear trend (p)
Insulin sensitivity	5.1 (5.0 to 5.3)	5.4 (5.1 to 5.7)	5.3 (5.1 to 5.6)	0.13
EIR	5.2 (5.0 to 5.5)	5.0 (4.5 to 5.6)	5.0 (4.7 to 5.4)	0.32
BMI	26.2 (25.9 to 26.5)	25.8 (25.2 to 26.4)	26.2 (25.8 to 26.6)	0.99
WC	94.7 (93.9 to 95.5)	93.2 (91.5 to 94.9)	94.3 (93.2 to 95.4)	0.48
Waist-to-hip ratio	0.94 (0.94 to 0.95)	0.94 (0.93 to 0.95)	0.95 (0.94 to 0.95)	0.86
Intake of liquor (g alcohol/wk) according to self-administered questionnaire				
	Tertile 1 (n = 390) (<1.6 g/wk) [mean (95% CI)]	Tertile 2 (n = 151) (1.6 to 25.6 g/wk) [mean (95% CI)]	Tertile 3 (n = 266) (>25.6 g/wk) [mean (95% CI)]	Test for linear trend (p)
Insulin sensitivity	5.3 (5.1 to 5.5)	5.2 (5.0 to 5.5)	5.2 (4.9 to 5.4)	0.34
EIR	5.1 (4.8 to 5.4)	5.4 (4.9 to 5.9)	5.1 (4.7 to 5.5)	0.99
BMI	25.9 (25.6 to 26.2)	26.3 (25.8 to 26.8)	26.4 (26.0 to 26.8)*	0.04
WC	93.4 (92.6 to 94.3)	94.6 (93.2 to 96.0)	95.6 (94.6 to 96.7)†	0.002
Waist-to-hip ratio	0.94 (0.93 to 0.94)	0.95 (0.94 to 0.96)	0.95 (0.95 to 0.96)‡	<0.001

CI, confidence interval; EIR, early insulin response; WC, waist circumference. Values are means (95% CI), adjusted for smoking status (never-smoker, ex-smoker, current smoker), education level, leisure time physical activity, dietary total energy intake, hypertension prevalence, diabetes prevalence, triglycerides, and total cholesterol. The reasons for the unbalanced numbers of participants in the tertiles are the nature of the questions asked (no. of glasses; smallest unit being half a glass/wk of a specific alcohol type) and that a large number of participants did not drink a specific alcohol type at all (i.e., preferring one sort of alcohol).

* $p < 0.05$ for comparisons using tertile 1 as referent.

† $p < 0.01$ for comparisons using tertile 1 as referent.

‡ $p < 0.001$ for comparisons using tertile 1 as referent.

creasing WC and waist-to-hip ratio across tertiles of self-estimated alcohol intake in the lowest tertile of BMI (p = 0.02 and 0.04, respectively). Also in the validating analyses using data from the 7-day dietary registration, alcohol intake was positively related to WC and waist-to-hip ratio (β, 1.21; 95% CI, 0.41 to 2.01; p = 0.003; and β, 0.008; 95% CI, 0.001 to 0.014; p = 0.02; for a 1-SD increase of log alcohol intake) in the lowest tertile of BMI. There were no signif-

icant associations between alcohol intake and WC or waist-to-hip ratio in the two highest tertiles of BMI.

To assess the potential selection bias resulting from exclusion of participants with missing data, we compared the clinical features in participants excluded from our study and those included in our sample. Participants who were excluded because of missing data had significantly lower insulin sensitivity, higher WC, and higher serum triglycerides; although the differences were moderate (see Appendix, available on the *Obesity* website, www.obesityresearch.org).

Discussion

Principal Findings

This study provides several interesting findings that add to the present knowledge. First, neither insulin sensitivity nor insulin secretion was significantly associated with alcohol intake. This negative finding is of interest because this study is, to our knowledge, the largest study sample with gold standard measurements (euglycemic clamp) of insulin sensitivity and data on alcohol consumption. Second, high alcohol intake was associated with increased abdominal obesity, measured as WC or waist-to-hip ratio, after adjusting for relevant confounders. This association was robust, although in absolute terms, the effect was moderate, i.e., each additional drink per day corresponded to an increased WC of by ~1 cm. Because the associations between alcohol intake and BMI were non-significant apart from a weak association between liquor intake and BMI, our findings support an effect of alcohol on abdominal fat accumulation per se. Third, the link between high alcohol intake and abdominal obesity was only evident in subjects in the lowest tertile of BMI, further indicating that high alcohol intake is associated with abdominal, rather than generalized, obesity. Fourth, the association between total alcohol intake and abdominal obesity seemed to be mainly driven by liquor intake rather than by beer or wine intake.

Alcohol Intake and Insulin Sensitivity and Secretion

In this large study sample with clamp-derived insulin sensitivity, there was no association between alcohol intake and insulin sensitivity. This result is in contrast to some previous cross-sectional studies, where beneficial effects of moderate alcohol intake on insulin sensitivity was reported (4–6). However, only one of those studies measured insulin sensitivity using the clamp technique, and that was in a considerably smaller study sample of 104 individuals (6). In experimental studies investigating acute effects of alcohol, the results were inconclusive (7–12).

Similarly, there was no association between alcohol intake and insulin secretion. We are not aware of any epidemiologic study that has assessed alcohol consumption and early insulin response as an indicator of insulin secretion. Consequently, our findings need confirmation in future studies. However, our negative findings are in concordance with an experimental study that did not observe any acute effect on insulin secretion after alcohol intake (22).

Alcohol Intake and Measures of Adiposity

Notably, high alcohol intake was associated with abdominal, rather than generalized, obesity in this study. Because abdominal obesity is one of the few factors proposed to cause insulin resistance and consequently type 2 diabetes (23,24), increased abdominal fat accumulation might contribute to the increased diabetes risk previously reported in subjects with high alcohol intake (1,25–27). Our results accord with cross-sectional data in French men (28), Italian men (29), Swedish women (30), and young Finnish men (31), where high alcohol intake was associated with elevated WC or waist-to-hip ratio. However, there are also conflicting data. Two prospective studies have failed to show an association between high intake of alcohol and increased WC in men but found such associations in women (32,33). Furthermore, a recent 4-week controlled trial could not show any effect of alcohol on abdominal fat content in healthy men (8). However, the duration of that study may have been too short to show a potential effect. Cross-sectional data, on the other hand, probably represent a chronic alcohol intake pattern, fairly stable over time.

It has been proposed that high alcohol intake contributes to abdominal fat storage (34), although the mechanism is still not clear. Considering that alcohol provides a significant amount of calories (~6% to 10% of energy intake in the U.S.) (35), an increased energy intake through high alcohol intake is one reasonable explanation. However, high alcohol intake was only significant in the lowest tertile of BMI, which argues against such explanations. If alcohol promotes abdominal obesity mainly through excess energy intake, one would expect a stronger association with BMI. Indeed, high alcohol intake has not consistently been related to obesity when measured as BMI (13), in agreement with our findings. Alternatively, alcohol may contribute to abdominal obesity through non-caloric mechanisms, such as alterations of steroid hormones that subsequently could favor central fat storage (34). High alcohol intake has, for example, been shown to acutely decrease blood testosterone concentrations in men (36), and a lower secretion of lipid mobilizing sex steroid hormones promotes visceral fat accumulation (34). Whether this is a mechanism by which high alcohol intake promotes abdominal obesity requires further study. These findings with low BMI and a concomitantly high WC and waist-to-hip ratio in high alcohol consumers might also reflect lower muscle mass, suggesting a catabolic effect of alcohol, possibly also mediated through reduced anabolic sex and growth hormones needed to preserve muscle mass. In addition, men with excessive alcohol

intake may have poor overall nutrient intake, promoting a catabolic state with decreased muscle mass and increased abdominal fat mass (37).

Strengths and Limitations

The strengths of our study include the large study sample with euglycemic clamp tests and oral glucose tolerance tests to assess insulin sensitivity and secretion and the availability of several relevant confounders. Also, our results from the self-estimated alcohol intake and the independent validated 7-day dietary records were consistent and should be considered as an internal validation. There are several limitations of our study. First, the cross-sectional design does not allow assumptions of cause and effect. Second, because our sample consisted of elderly white men, the generalization of our findings to women, other ethnicities, or other age groups is unknown. Third, the exclusion of participants with lack of data on alcohol intake might have introduced a selection bias. However, we addressed this possibility by comparing the clinical characteristics (all variables listed in Table 1) in the study sample with those excluded because of missing data on alcohol intake, using Student's t tests and χ^2 tests. The only variable that significantly differed between the two groups was education level (those with missing data on alcohol consumption had a lower education level; $p = 0.02$). Fourth, there were no available data on past alcohol history (e.g., alcoholism) and prior or present patterns of alcohol consumption (e.g., binge drinking), which are potential confounders for which we, unfortunately, could not adjust. For example, our finding that liquor, rather than beer or wine, was associated with abdominal obesity, might well suggest that there were particular drinking patterns involved that might partly explain these results. Intake of liquor might be associated with a more unhealthy drinking behavior (for instance, binge drinking) compared with wine and beer intake, which is more often consumed with evening meals in moderate amounts, and perhaps, by individuals with a higher socioeconomic status. However, because these findings originated from secondary analyses, further studies with complete data on drinking patterns will be needed to confirm them.

In summary, in a large, community-based cohort of elderly men, we found no associations between alcohol intake and insulin sensitivity or insulin secretion. Thus, we did not observe any beneficial metabolic effects of moderate alcohol intake, as reported in some studies. Instead, there was a strong association between high alcohol intake and increased abdominal fat distribution. This was primarily evident in subjects with a normal BMI. Given that abdominal obesity is an independent risk factor of diabetes and might precede insulin resistance (23), these results are in line with data indicating increased diabetes risk in subjects with excessive alcohol intake. Considering the increasing prevalence of abdominal obesity, these results support current dietary recommendations for type 2 diabetes, i.e., to limit excess alcohol intake (38). However, our results do need confirmation in other studies to better clarify the link between alcohol intake and adiposity, including body fat distribution.

Acknowledgments

This work was supported by the Swedish Society for Medical Research (to U.R.) and the Swedish Heart Lung Foundation (to E.I.). The funding source had no involvement in the work with the article.

References

1. **Howard AA, Arnsten JH, Gourevitch MN.** Effect of alcohol consumption on diabetes mellitus: a systematic review. *Ann Intern Med.* 2004;140:211–9.
2. **Carlsson S, Hammar N, Grill V.** Alcohol consumption and type 2 diabetes Meta-analysis of epidemiological studies indicates a U-shaped relationship. *Diabetologia.* 2005;48: 1051–4.
3. **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.* 1995;310:555–9.
4. **Kiechl S, Willeit J, Poewe W, et al.** Insulin sensitivity and regular alcohol consumption: large, prospective, cross sectional population study (Bruneck study). *BMJ.* 1996;313: 1040–4.
5. **Bell RA, Mayer-Davis EJ, Martin MA, D'Agostino RB Jr, Haffner SM.** Associations between alcohol consumption and insulin sensitivity and cardiovascular disease risk factors: the Insulin Resistance and Atherosclerosis Study. *Diabetes Care.* 2000;23:1630–6.
6. **Goude D, Fagerberg B, Hulthe J.** Alcohol consumption, the metabolic syndrome and insulin resistance in 58-year-old clinically healthy men (AIR study). *Clin Sci.* 2002;102:345–52.
7. **Davies MJ, Baer DJ, Judd JT, Brown ED, Campbell WS, Taylor PR.** Effects of moderate alcohol intake on fasting insulin and glucose concentrations and insulin sensitivity in postmenopausal women: a randomized controlled trial. *JAMA.* 2002;287:2559–62.
8. **Beulens JW, van Beers RM, Stolk RP, Schaafsma G, Hendriks HF.** The effect of moderate alcohol consumption on fat distribution and adipocytokines. *Obesity.* 2006;14:60–6.
9. **Cordain L, Bryan ED, Melby CL, Smith MJ.** Influence of moderate daily wine consumption on body weight regulation and metabolism in healthy free-living males. *J Am Coll Nutr.* 1997;16:134–9.
10. **Cordain L, Melby CL, Hamamoto AE, et al.** Influence of moderate chronic wine consumption on insulin sensitivity and other correlates of syndrome X in moderately obese women. *Metabolism.* 2000;49:1473–8.
11. **Sierksma A, Patel H, Ouchi N, et al.** Effect of moderate alcohol consumption on adiponectin, tumor necrosis factor-alpha, and insulin sensitivity. *Diabetes Care.* 2004;27:184–9.
12. **Flanagan DE, Pratt E, Murphy J, et al.** Alcohol consumption alters insulin secretion and cardiac autonomic activity. *Eur J Clin Invest.* 2002;32:187–92.

13. **Suter PM.** Is alcohol consumption a risk factor for weight gain and obesity? *Crit Rev Clin Lab Sci.* 2005;42:197–227.
14. **Hedstrand H.** A study of middle-aged men with particular reference to risk factors for cardiovascular disease. *Ups J Med Sci.* 1975;19:1–6.
15. **Byberg L, Zethelius B, McKeigue PM, Lithell HO.** Changes in physical activity are associated with changes in metabolic cardiovascular risk factors. *Diabetologia.* 2001; 44:2134–9.
16. **DeFronzo RA, Tobin JD, Andres R.** Glucose clamp technique: a method for quantifying insulin secretion and resistance. *Am J Physiol.* 1979;237:E214–23.
17. **Sjöström L, Larsson B, Backman L, et al.** Swedish obese subjects (SOS). Recruitment for an intervention study and a selected description of the obese state. *Int J Obes Relat Metab Disord.* 1992;16:465–79.
18. **Becker W.** *Dietary Habits and Nutrient Intake in Sweden 1989. Methods and Analysis.* Uppsala, Sweden: Nutritional Unit, Swedish National Food Administration; 1994.
19. **Olofsson H, Byberg L, Mohsen R, Melhus H, Lithell H, Michaelsson K.** Smoking and the risk of fracture in older men. *J Bone Miner Res.* 2005;20:1208–15.
20. **Bjorklund K, Lind L, Zethelius B, Andren B, Lithell H.** Isolated ambulatory hypertension predicts cardiovascular morbidity in elderly men. *Circulation.* 2003;107:1297–302.
21. **Expert Committee on the Diagnosis and Classification of Diabetes Mellitus.** Report of the Expert Committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2003;26(Suppl 1):S5–20.
22. **Avogaro A, Watanabe RM, Dall'Arche A, De Kreutzenberg SV, Tiengo A, Pacini G.** Acute alcohol consumption improves insulin action without affecting insulin secretion in type 2 diabetic subjects. *Diabetes Care.* 2004;27:1369–74.
23. **Banerji MA, Chaiken RL, Gordon D, Kral JG, Lebovitz HE.** Does intra-abdominal adipose tissue in black men determine whether NIDDM is insulin-resistant or insulin-sensitive? *Diabetes.* 1995;44:141–6.
24. **Bosello O, Zamboni M.** Visceral obesity and metabolic syndrome. *Obes Rev.* 2000;1:47–56.
25. **Carlsson S, Hammar N, Grill V, Kaprio J.** Alcohol consumption and the incidence of type 2 diabetes: a 20-year follow-up of the Finnish twin cohort study. *Diabetes Care.* 2003;26:2785–90.
26. **Kao WH, Puddey IB, Boland LL, Watson RL, Brancati FL.** Alcohol consumption and the risk of type 2 diabetes mellitus: atherosclerosis risk in communities study. *Am J Epidemiol.* 2001;154:748–57.
27. **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: the Osaka Health Survey. *Diabetes Care.* 1999;22:1432–7.
28. **Dallongeville J, Marecaux N, Ducimetiere P, et al.** Influence of alcohol consumption and various beverages on waist girth and waist-to-hip ratio in a sample of French men and women. *Int J Obes Relat Metab Disord.* 1998;22:1178–83.
29. **Leite ML, Nicolosi A.** Lifestyle correlates of anthropometric estimates of body adiposity in an Italian middle-aged and elderly population: a covariance analysis. *Int J Obes Relat Metab Disord.* 2006;30:926–34.
30. **Lapidus L, Bengtsson C, Bergfors E, Bjorkelund C, Spak F, Lissner L.** Alcohol intake among women and its relationship to diabetes incidence and all-cause mortality: the 32-year follow-up of a population study of women in Gothenburg, Sweden. *Diabetes Care.* 2005;28:2230–5.
31. **Laitinen J, Pietilainen K, Wadsworth M, Sovio U, Jarvelin MR.** Predictors of abdominal obesity among 31-y-old men and women born in Northern Finland in 1966. *Eur J Clin Nutr.* 2004;58:180–90.
32. **Halkjaer J, Sorensen TI, Tjonneland A, Togo P, Holst C, Heitmann BL.** Food and drinking patterns as predictors of 6-year BMI-adjusted changes in waist circumference. *Br J Nutr.* 2004;92:735–48.
33. **Fan AZ, Russell M, Dorn J, et al.** Lifetime alcohol drinking pattern is related to the prevalence of metabolic syndrome. The Western New York Health Study (WNYHS). *Eur J Epidemiol.* 2006;21:129–38.
34. **Björntorp P.** Endocrine abnormalities of obesity. *Metabolism.* 1995;44:21–3.
35. **Block G, Dresser CM, Hartman AM, Carroll MD.** Nutrient sources in the American diet: quantitative data from the NHANES II survey. II. Macronutrients and fats. *Am J Epidemiol.* 1985;122:27–40.
36. **Emanuele MA, Emanuele NV.** Alcohol's effects on male reproduction. *Alcohol Health Res World.* 1998;22:195–201.
37. **Kvist H, Hallgren P, Jonsson L, et al.** Distribution of adipose tissue and muscle mass in alcoholic men. *Metabolism.* 1993;42:569–73.
38. **Mann JI, De Leeuw I, Hermansen K, et al.** Evidence-based nutritional approaches to the treatment and prevention of diabetes mellitus. *Nutr Metab Cardiovasc Dis.* 2004;14:373–94.