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# Skipping breakfast is correlated with impaired fasting glucose in apparently healthy subjects

**Research Article**

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**Abstract:** Regular food consumption plays a critical role in normal glucose homeostasis. Today, a few studies have evaluated the level of fasting glucose in individuals who skip breakfast, which should theoretically lead to a lack of supplementary energy and thereby increase the risk for subsequent hypoglycemia. The prevalence of suspected habitual skipping breakfast (SHSB) (at least three times weekly) was evaluated with a simple question, along with measurement of fasting plasma glucose level and assessment of cardiovascular and lifestyle risk factors in a cross-sectional study of 2,331 asymptomatic adults who had never been treated with insulin or oral anti-diabetic drugs. The overall prevalence of SHSB was 16.3% (20.1% for men and 9.4% for women, $P<0.0001$, $\chi^2$-test). Compared with a normal fasting glucose level, an impaired fasting glucose (IFG) level (100–125 mg/dl), but not high fasting glucose (≥126 mg/dl), was significantly associated with SHSB, and this association remained after adjustment for relevant confounders [odds ratio (95% CI): 1.75 (1.33–2.30) and 2.10 (0.93-4.71), respectively]. Age (inversely), current smoker, late dinner just before sleeping, infrequent exercise, and high C-reactive protein (≥1.8 mg/L) were independently associated with SHSB. In a subgroup of subjects who underwent a 75g-oral glucose tolerance test (n = 1,315), isolated IFG (n = 272) was solely significantly associated with SHSB. Our results suggest that IFG, subtle inflammatory state, and high-risk lifestyle factors for diabetes and cardiovascular disease may have an association in asymptomatic adults who habitually skip breakfast.

**Keywords:** *Visceral leishmaniasis • Liposomal amphotericin B • Renal function • Uric acid • Tumor lysis syndrome*



## 1. Introduction

Regularly skipping breakfast is commonly observed among children and adolescents [1-3]. Skipping breakfast is also not rare among adults [4-6], although its prevalence is less frequent than in children and adolescents [2,4,5]. In adults, habitual skipping of breakfast was shown to be associated with other unfavorable lifestyle habits such as smoking, lack of exercise, alcohol abuse, and high energy intake and with cardiovascular risk factors such as obesity and impaired glucose metabolism [1-7].

Regular food intake plays a pivotal role in normal glucose homeostasis. In animal models, complex changes in insulin-dependent signalling mediated by two types of insulin receptor substrate (IRS) were shown before and after feeding [8-10]. However, the pathogenic feature of skipping breakfast, which theoretically aggravates the fasting condition in the morning, was addressed

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in a clinical study, particularly in terms of glucose metabolism. Furthermore, skipping breakfast theoretically means a lack of supplementary energy and increased risk for hypoglycemia, which, in turn, stimulates the desire to eat?

In this context, we examined whether skipping breakfast is associated with impaired glucose metabolism, along with cardiovascular risk factors including circulating C-reactive protein (CRP) for type 2 diabetes [11,12] and lifestyle risk factors, in a cross-sectional study of asymptomatic adults who underwent a detailed medical check-up. Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are involved in the pathophysiology of impaired glucose homeostasis and, hence, represent the pre-diabetic state [13-15]. We further investigated an association between skipping breakfast and these pre-diabetes conditions in a subgroup of subjects who underwent a 75-g oral glucose tolerance test (OGTT).

## 2. Material and Methods

This study was part of a federal research program focused on determination and quantitative evaluation of harmful environmental factors and conditions contributing to increased risk of metabolic and cardiovascular diseases among residents of the metropolitan area of Moscow, St. Petersburg, and other Russian cities whose population exceeds 1 million. The protocol was approved by the Ethics Committee of the Endocrinology Research Center. All subjects provided written informed consent.

### 2.1. Patients

We analyzed data collected from asymptomatic adults aged 27–69 years who voluntarily underwent a detailed regular medical check-up between May 2008 and March 2010. A total of 3,690 residents of Moscow and its suburban areas were requested to complete a standard questionnaire approved by an Expert Committee of the Russian Ministry of Health and Social Development. A total of 2,848 subjects responded (response rate 77.2%). Among those, 175 people did not mention age, gender, height, or weight, and their responses were excluded. Among the remaining 2,673 individuals, 137 were then excluded because they did not indicate eating behavior, smoking status, alcohol consumption, or physical activity. Of 2,536 people, 155 with self-reported use of insulin and/or oral anti-diabetic medications were then excluded from further consideration. Finally, 50 people with elevated circulating CRP ≥ 10.0 mg/L were also excluded due to latent inflammatory diseases. A total of 2,331 subjects (1,515 males and 816 females) with completed self-report questionnaires and biochemical/anthropometric data were finally selected for this study.

The questionnaire was developed in 2007 for the prevention of metabolic syndrome and cardiovascular diseases through better understanding of individual lifestyle risks. The questionnaire consisted of 22 questions related to eating behaviors (e.g., skipping breakfast and late dinner before bedtime), physical activities (e.g., regular, irregular or lack of exercise), smoking (non-smoker within the last 6 months or current smoker), habitual alcohol consumption (none, occasionally, daily), pharmacotherapy (e.g., for hypertension, hypercholesterolemia, or diabetes), and past medical history (e.g., cardiovascular disease and stroke). The suspected habitual skipping breakfast (SHSB) was determined with a positive response to a simple question, “Do you skip breakfast at least three times per week?” In the questionnaire, the late dinner and infrequent exercise were defined as follows: dinner within 2 hours before bedtime ≥ 3 times/week, and < 30 min exercise per session < 2 times/week, respectively. All questions were to be answered in a dichotomous manner, indicating presence or absence.

### 2.2. Laboratory measurements

All biochemical variables were measured in the same laboratory with standard enzymatic methods in samples obtained after an overnight fast. In this study, gastric emptying was confirmed by upper gastrointestinal fluoroscopy or endoscopy in the check-up. Fasting plasma glucose (FPG) levels were measured by the glucose oxidase method. HbA1c was measured by high-performance liquid chromatography.

### 2.3. Definition of pre-diabetes

Elevated blood pressure (≥130/85 mmHg), high cholesterol (≥200 mg/dL), high triglycerides (≥150 mg/dL), and low high-density lipoprotein cholesterol (HDL-C) (<40 mg/dL for men and <50 mg/dL for women) were defined according to the criteria of the National Cholesterol Education Program Expert Panel for the metabolic syndrome [16]. IFG (FPG 100–125 mg/dL) was defined according to the American Diabetes Association (ADA) [17]. After glucose metabolism was assessed by FPG, subjects were divided into three groups according to the degree of FPG (normal: FPG: <100 mg/dL; IFG: 100–125 mg/dL; high: FPG ≥126 mg/dL). After glucose metabolism was assessed by HbA1c, subjects were

divided into three groups according to the NGSP HbA1c (normal: <5.7%; borderline: 5.7–6.4%; diabetic: ≥6.5%).

Out of a total of 1,315 subjects (912 men and 403 women), 195 with suspected pre-diabetes (15% of 1,315), 102 with suspected diabetes (8% of 1,315), and 1,018 (77%) who wished to know their glucose metabolism in more detail underwent an OGTT. A total of 51 subjects with definite diabetes (under treatment consisting of diet and exercise) did not undergo an OGTT. ADA criteria was used to establish definitions of isolated IFG (I-IFG) (FPG 100–125 mg/d and 2-hour OGTT <140 mg/dL), isolated IGT (I-IGT) (FPG <100 mg/dL and 2-hour OGTT 140–199 mg/dL), combined IFG/IGT (FPG 100–125 mg/dL and 2-hour OGTT 140–199 mg/dL), diabetic (FPG ≥126 mg/dL or 2-hour OGTT ≥200 mg/dL), and normal glucose tolerance (NGT) (FPG <100 mg/dL and 2-hour OGTT <140 mg/dL) [13]. High and normal C-reactive protein (CRP) level was defined as levels >90$^{th}$ percentile (>1.8 mg/L) and <75$^{th}$ percentile (<0.8 mg/L), respectively.

**Table 1** Characteristics of subjects according to SHSB

| Characteristics | SHSB | Non-SHSB | P* |
|---|---|---|---|
| n | 381 | 1,950 | < 0.0001 |
| Age, y | 46.9 ± 10.0 | 54.7 ± 11.7 | < 0.0001 |
| Men, n (%) | 304 (79.8) | 1,211 (62.1) | 0.04 |
| Body mass index, kg/m2 | 23.7 ± 3.6 | 23.2 ± 3.1 | ns |
| Systolic blood pressure, mmHg | 119 ± 17.9 | 122 ± 19.3 | ns |
| Diastolic blood pressure, mmHg | 75.3 ± 12.8 | 75.7 ± 12.8 | ns |
| Total cholesterol, mg/dL | 206 ± 33.8 | 206 ± 35.9 | ns |
| Triglyceride, mg/dL | 109 (75–157) | 92.5 (66–134) | < 0.0001 |
| HDL-C, mg/dL | 59.1 ± 15.5 | 61.5 ± 14.8 | ns |
| Fasting plasma glucose, mg/dL | 101 ± 12.7 | 99.3 ± 15.7 | ns |
| HbA1c, % | 5.6 ± 0.4 | 5.7 ± 0.5 | ns |
| C-reactive protein, mg/L | 0.50 (0.30–1.00) | 0.40 (0.30–0.80) | ns |
| Prior history | | | |
| Cardiovascular diseases, n (%) | 6 (1.6) | 70 (3.6) | ns |
| Stroke, n (%) | 2 (0.5) | 37 (1.8) | ns |
| Medications | | | |
| Hypertension, n (%) | 35 (9.2) | 343 (17.6) | ns |
| Hypercholesterolemia, n (%) | 18 (4.7) | 207 (10.6) | ns |
| Current smoker, n (%) | 183 (48.0) | 429 (22.0) | < 0.0001 |
| Drinking alcohol every day, n (%) | 149 (39.1) | 585 (30.0) | < 0.0001 |
| Late dinner, n (%) | 224 (58.8) | 549 (28.2) | < 0.0001 |
| Infrequent exercise, n (%) | 321 (84.3) | 1,283 (65.8) | < 0.0001 |

*Data are expressed as means ± SD or n (%). Triglyceride and C-reactive protein are expressed as medians (interquartile range). *P-value was examined with ANCOVA controlling for age. Triglyceride and C-reactive protein were analyzed after log-transformation. P-values in prevalence of clinical factors were examined with ANCOVA after adjustment for age. SHSB, suspected habitual skipping breakfast; HDL-C, high-density lipoprotein cholesterol; ns, not significant*

## 2.4. Statistical analysis

Data were expressed as means ± SD. Triglyceride and CRP levels were expressed as medians (interquartile range). Multivariate logistic regression (ANCOVA analysis) was used to examine the associations between skipping breakfast and impaired glucose metabolism, lifestyle factors, and clinical variables, and to calculate odds ratios (OR) and 95% confidence intervals (95% CI) after adjustment for confounders. Statistical analysis was performed using IBM-SPSS version 18.0 (SPSS; Chicago, IL). Values of P<0.05 were considered statistically significant.

# 3. Results

Patients' characteristics according to the presence/absence SHSB are presented in Table 1. Overall, SHSB was found in 16.3% subjects (20.1% for men and 9.4% for women, $P$<0.0001, $\chi^2$-test). Subjects with SHSB were significantly younger (by approximately 8 years) than those without. The prevalence of men, current smokers, everyday alcohol consumption, late dinner, and infrequent exercise were significantly higher in those with SHSB, even after adjustment for age with logistic regression analysis (all $P$ < 0.0001). No significant difference in cardiovascular risk factors (except triglyceride levels) was found between subjects with SHSB and those without.

Multiple logistic analyses showed that IFG, age (inversely), smoking, late dinner, infrequent exercise, and high CRP were significantly and independently associated with SHSB, even after adjustment for residual confounders (Table 2). Further adjustment for continuous HbA1c strengthened the association between IFG and SHSB (Model 5). However, body mass index (BMI), elevated blood pressure, and dyslipidemia were not significantly associated with SHSB after adjustment for confounders including age and sex (data not shown).

When impaired glucose metabolism was evaluated with HbA1c (Table 3), borderline and diabetic HbA1c levels were not significantly associated with SHSB after adjustment for covariates, although overall FPG was highly correlated with HbA1c in this study, as generally expected (r=0.77, P<0.0001, Pearson correlation, data not shown).

SHSB showed significant association only with the I-IFG, not with any other category of OGTT results, even after adjustment for residual confounders (Table 4)

**Table 2.** Associations between the degree of fasting plasma glucose and confounding factors with SHSB

| | Model 1 | Model 2 | Model 3 | Model 4 | Model 5 |
|---|---|---|---|---|---|
| FPG | | | | | |
| Normal FPG (<100 mg/dL) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) |
| IFG (100–125 mg/dL) | 1.38 (1.10–1.73) ** | 1.70 (1.32–2.18)*** | 1.64 (1.27–2.13)** | 1.63 (1.25–2.12)** | 1.75 (1.33–2.30)*** |
| High FPG (≥126 mg/dL) | 1.05 (0.58–1.89) | 1.38 (0.75–2.54) | 1.26 (0.67–2.36) | 1.18 (0.61–2.25) | 2.10 (0.93–4.71) |
| Confounding factors | | | | | |
| Age (continuous value) | | 0.94 (0.93–0.95)*** | 0.95 (0.94–0.96)*** | 0.95 (0.94–0.96)*** | 0.95 (0.94–0.97)*** |
| Men | | 1.89 (1.43–2.49)*** | 1.18 (0.87–1.61) | 1.16 (0.84–1.59) | 1.13 (0.82–1.56) |
| Current smoker | | | 2.11 (1.64–2.71)*** | 2.03 (1.57–2.62)*** | 2.07 (1.60–2.68)*** |
| Late dinner | | | 2.15 (1.67–2.76)*** | 2.20 (1.71–2.83)*** | 2.20 (1.70–2.83)*** |
| Infrequent exercise | | | 1.65 (1.21–2.26)** | 1.62 (1.18–2.23)** | 1.63 (1.19–2.24)** |
| Drinking alcohol | | | 1.20 (0.93–1.56) | 1.24 (0.95–1.62) | 1.21 (0.92–1.57) |
| BMI (continuous value) | | | | 0.97 (0.93–1.01) | 0.97 (0.93–1.01) |
| Elevated blood pressure | | | | 0.93 (0.71–1.22) | 0.94 (0.71–1.23) |
| High triglyceride | | | | 1.23 (0.91–1.66) | 1.24 (0.92–1.67) |
| Low HDL-C | | | | 0.96 (0.57–1.61) | 0.99 (0.59–1.67) |
| High CRP | | | | 1.72 (1.18–2.50)** | 1.76 (1.21–2.57) ** |
| HbA1c (continuous value) | | | | | 0.68 (0.48–0.97) * |

*The normal FPG, IFG, and high FPG involve 1,425, 815, and 91 subjects, respectively. Model 1: unadjusted; Model 2: adjusted for age and sex (men); Model 3: Model 2 plus adjustment for current smoking (versus non-smokers), late dinner (versus non late dinner), infrequent exercise (versus frequent exercise), drinking alcohol every day (versus infrequent/no alcohol consumption); Model 4: Model 3 plus adjustment for BMI, elevated blood pressure, dyslipidemia, and high CRP (>90th percentile [>1.8 mg/L] versus <75th percentile [<0.8 mg/L]); Model 5: Model 4 plus adjustment for HbA1c. SHSB, suspected habitual skipping breakfast; FPG, fasting plasma glucose; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; CRP, C-reactive protein. *P<0.05, **P<0.01, ***P<0.0001.*

**Table 3.** Associations between the degree of HbA1c and confounding factors with SHSB

| | Model 1 | Model 2 | Model 3 | Model 4 | Model 5 |
|---|---|---|---|---|---|
| HbA1c | | | | | |
| Normal <5.7% | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) |
| Borderline 5.7–6.4% | 0.58 (0.46–0.74) *** | 0.99 (0.76–1.28) | 0.95 (0.73–1.24) | 0.89 (0.67–1.17) | 0.81 (0.61–1.08) |
| Diabetic ≥6.5% | 0.66 (0.36–1.20) | 1.03 (0.55–1.92) | 0.96 (0.50–1.83) | 0.82 (0.42–1.62) | 0.38 (0.15–1.00) |
| Confounding factors | | | | | |
| Age (continuous value) | | 0.94 (0.93–0.96) *** | 0.96 (0.95–0.97) *** | 0.96 (0.95–0.97) *** | 0.96 (0.94–0.97) *** |
| Men | | 2.08 (1.58–2.73) *** | 1.29 (0.95–1.74) | 1.22 (0.89–1.68) | 1.17 (0.85–1.61) |
| Current smoker | | | 2.07 (1.61–2.67) *** | 1.99 (1.54–2.57) *** | 2.00 (1.54–2.58) *** |
| Late dinner | | | 2.17 (1.69–2.78) *** | 2.22 (1.72–2.85) *** | 2.21 (1.71–2.84) *** |
| Infrequent exercise | | | 1.67 (1.22–2.28) ** | 1.63 (1.19–2.23) ** | 1.61 (1.17–2.21) ** |
| Drinking alcohol | | | 1.24 (0.96–1.61) | 1.29 (0.99–1.68) | 1.26 (0.96–1.64) |
| BMI (continuous value) | | | | 0.98 (0.94–1.02) | 0.97 (0.93–1.02) |
| Elevated blood pressure | | | | 0.98 (0.75–1.29) | 0.96 (0.73–1.26) |
| High triglyceride | | | | 1.27 (0.94–1.72) | 1.27 (0.94–1.71) |
| Low HDL-C | | | | 0.95 (0.56–1.60) | 0.98 (0.58–1.66) |
| High CRP | | | | 1.76 (1.21–2.57) ** | 1.75 (1.20–2.55) ** |
| FPG (continuous value) | | | | | 1.01 (1.00–1.02) * |

*The normal HbA1c, borderline HbA1c, and diabetic HbA1c involve 1,239, 997, and 94 subjects, respectively. Models 1–4 are the same as those used in Table 2, Model 5: Model 4 plus adjustment for FPG. SHSB, suspected habitual skipping breakfast; FPG, fasting plasma glucose; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; CRP: C-reactive protein. *P < 0.05, **P < 0.01, ***P < 0.0001.*

It is noteworthy that after exclusion of subjects with past history of heart disease and stroke or those treated with medications and reanalysis of data, similar results were obtained. SHSB was significantly associated with IFG (n=1,793, OR=1.69, 95%CI=1.27-2.24, P=0.0003), but not IGT (OR=1.25, 95%CI =0.58-2.69, P=0.57), even after adjustment for the same confounders shown in Table 2.

**Table 4.** Associations between FPG/2 h OGTT profiles and SHSB

| | Model 1 | Model 2 | Model 3 | Model 4 |
|---|---|---|---|---|
| FPG/2-h OGTT profile | | | | |
| NTG | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) |
| I-IFG | 1.62 (1.15–2.28) * | 1.96 (1.35–2.84) ** | 1.94 (1.32–2.85) ** | 1.87 (1.26–2.77) * |
| I-IGT | 0.61 (0.33–1.13) | 0.76 (0.41–1.43) | 0.77 (0.40–1.48) | 0.68 (0.35–1.33) |
| Combined I-IFG/I-IGT | 1.01 (0.63–1.62) | 1.37 (0.83–2.26) | 1.53 (0.91–2.57) | 1.37 (0.80–2.35) |
| Diabetic | 0.96 (0.57–1.62) | 1.41 (0.81–2.46) | 1.41 (0.79–2.49) | 1.34 (0.73–2.48) |

*Numbers of subjects included in each profile group are 649, 272, 118, 153, and 123 for NTG, IFG, IGT, combined I-IFG/I-IGT, and diabetic groups, respectively. Mean levels of HbA1c in NTG, IFG, IGT, combined I-IFG/I-IGT, and diabetic groups were 5.5%, 5.6%, 5.6%, 5.8%, and 6.7%, respectively. Models 1–4 are the same as those used in Table 3. SHSB, suspected habitual skipping breakfast; FPG, fasting plasma glucose; OGTT, 75-g oral glucose tolerance test. *P<0.01, **P<0.001.*

# 4. Discussion

This pilot study was primarily designed to verify whether habitual skipping breakfast roughly assessed by a simple question is associated with IFG in asymptomatic adults who were mostly non-obese and were not known to be diabetic. According to the Ural Regional Health and Nutrition Survey performed in Ekaterinburg in 2009, the prevalence of skipping breakfast was 11.6 % in total population and over 20% in people aged 20-39 years old [18], which is consistent with current results.

In addition, elevated circulating CRP and some lifestyle factors predisposing to diabetes and cardiovascular disease were also independently associated with SHSB. In contrast, none of the metabolic syndrome constituents was associated with skipping breakfast. Notably, among pre-diabetes conditions, SHSB was solely associated with I-IFG.

A significant association between SHSB and late dinner suggests that those persons skipping breakfast habitually, rather than intentionally as part of a diet, possibly have a nocturnal lifestyle [19,20]. Indeed, a late dinner just before sleeping may impair postprandial glucose metabolism and food digestion, and it may lead to prolonged elevated FPG and poor appetite in the morning. Therefore, in some breakfast skippers, the physical condition in the early morning might be close to a prolonged postprandial state, rather than a distinct fasting state. However, late dinner is unlikely to be a major factor related to IFG, because it was not associated with IFG after controlling for alcohol consumption and other confounders.

Alternatively, significant association of SHSB with IFG, but not with high FPG, may possibly be explained by reverse causality, because subjects with a past history of heart disease and stroke, as well as those treated with medications, are likely to change their dietary habits to improve their health. However, when these subjects were excluded from the data analysis, similar results were obtained, suggesting the unlikelihood of reverse causality.

In a recent prospective study, Smith et al. [7] reported that people who regularly skipped breakfast in childhood and adulthood had significantly higher fasting glucose and higher fasting insulin levels over a 20-year period compared with those who did not skip breakfast, and their findings appear to be consistent with our results. However, further evaluation of associations with features of impaired glucose metabolism such as elevated HbA1c and IGT was not performed in their study.

The peripheral (muscle) insulin resistance was found to represent a major pathogenic feature in individuals with isolated IGT [15]. For isolated IFG, Kim et al. [21] showed that peripheral insulin resistance varies considerably in individuals with IFG, concluding that most individuals with IFG are insulin-resistant and the remainder are insulin-sensitive. This, therefore, suggests heterogeneity in insulin sensitivity in IFG. However, several studies have shown that IFG is less strongly associated with future risk of type 2 diabetes [22], peripheral insulin resistance [23,24], and cardiovascular diseases [13-15] compared with IGT.

Meanwhile, people with IFG predominantly exhibit hepatic insulin resistance [15,23-25], which increases fasting hepatic glucose production and may account for elevated FPG in the morning and for skipping breakfast due to the absence of hunger. Bock et al. [25] reported that individuals with IFG had hepatic insulin resistance because of impaired insulin-mediated suppression of endogenous glucose production during the fasting state. However, endogenous glucose production is rapidly suppressed by rising insulin concentration immediately after eating because the second-phase insulin response is not attenuated [25,26]. From the results of the study by Kubota et al. [8] using Irs knockout mice, the authors proposed the existence of a functional relay between IRS-1 and IRS-2 in hepatic insulin action during fasting and refeeding. Briefly, IRS-1 functions primarily after refeeding, whereas IRS-2 functions mainly during fasting and immediately after the start of refeeding. Considering that fasting glucose levels were slightly increased in Irs2 knockout mice in the study by Dong et al. [9], it is possible that IRS-2 might be attenuated in individuals

with IFG. Thus, as Haeusler et al. [10] suggested, IFG should be re-examined in terms of emerging findings concerning insulin signaling via IRS. In this regard, IFG should also be considered in terms of skipping breakfast, because skipping breakfast theoretically aggravates the fasting state.

Meanwhile, social factors may also influence correlations observed here. For example, the meal times for individuals are often determined by social factors rather than biological need [3,6,27], indicating that such skipping breakfast may be an unintentional unfavorable lifestyle factor for diabetes and cardiovascular disease related to individual circumstances. To fully address the underlying mechanisms, future studies should examine the associations between social factors and food intake.

Many previous studies [1-3,6], but not all [4,5,7,28], reported that skipping breakfast predisposes toward overweight and obesity. Indeed, in this study, SHSB was significantly associated with overweight/obesity (BMI ≥ 25.0kg/m$^2$) before controlling for confounders (OR=1.42, 95%CI=1.12–1.80, p=0.004). However, this association disappeared after adjustment for sex (OR=1.23, 95%CI=0.96–1.57, p=0.1) and after full adjustment for all confounders described in Table 2. In the analysis of NHANES III data [29], an inverse association between breakfast consumption and BMI was observed in women, but not in men. This is partially consistent with our results, because the proportion of men was larger (65%) than that of women in this study. Alternatively, a small portion of obese subjects (BMI ≥ 30kg/m$^2$, 3.3% of total subjects) may explain the inconsistency with previous studies [4,28].

Some limitations should be discussed. First, because of the cross-sectional design of this study, we cannot determine causality and whether SHSB is a consequence (unintentional) or a cause (intentional) of the factors identified in regression models. Some subjects with SHSB are likely to skip breakfast for the purpose of weight loss through a diet. Well designed prospective studies are needed to confirm the current findings and to elucidate the underlying mechanism in more detail. Second, the quantity, type, and timing of food intake were not recorded in this study, because the current study was not originally designed to explore the relationship between skipping breakfast and metabolic abnormalities. Thus, we could not take into account the amount or the content of meals consumed each day. Detailed assessment of food intake by food-frequency questionnaires, for example, will help us to further explore the interactions between skipping breakfast and impaired glucose metabolism. Third, SHSB was defined as a dichotomous (binary) variable as ≥ 3 times/week using a standard questionnaire. Thus, we were unable to examine linear associations. To achieve this, the questionnaires should record intermediate categories, such as occasionally skipping breakfast. However, adjustment for late dinner, a similar undesirable eating behavior, and other lifestyle factors may attenuate the bias provided by the binary assessment. Finally, because this study is comprised mostly of non-obese persons without diabetes, the findings may not be applicable to those with diabetes or cardiovascular disease.

In conclusion, our findings suggest a possible association between SHSB and IFG, but not with any component of the metabolic syndrome, in asymptomatic adults. Furthermore, subtle inflammatory state (high CRP) and some unfavorable lifestyle factors (e.g., smoking), which are potent risk factors for cardiovascular disease and a pre-diabetic state, were also associated with SHSB. These findings, the causality, and the clinical relevance need to be further confirmed, particularly in prospective studies.

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