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## Menopause and Metabolic Syndrome in Obese Individuals with Binge Eating Disorder

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### Abstract

Menopausal transition has been associated with emergence of metabolic abnormalities, which may increase risk for chronic medical conditions in women. This study compared metabolic function between premenopausal women ( $n = 152$ ), postmenopausal women ( $n = 88$ ), and men ( $n = 98$ ) recruited for treatment studies for obesity co-occurring with binge eating disorder (BED), a high risk population for developing metabolic syndrome (MetS). Postmenopausal women were more likely than premenopausal women to show elevated total cholesterol (OR = 2.75; 95% CI = 1.56–4.80) and poor glycemic control (OR = 2.92; 95% CI = 1.32–6.33), but were more likely to have lower HDL levels (OR = 0.36; 95% CI = 0.19–0.68). These became non-significant after adjusting for age. Both pre- and postmenopausal women were less likely than age-matched men to show elevated levels of triglycerides (OR = 0.27; 95% CI = 0.13–0.53 [postmenopausal], OR = 0.29; 95% CI = 0.16–0.53 [premenopausal]), blood pressure (OR = 0.48; 95% CI = 0.25–0.91 [postmenopausal], OR = 0.40; 95% CI = 0.23–0.69 [premenopausal]), and less likely to have MetS (OR = 0.41; 95% CI = 0.21–0.78 [postmenopausal], OR = 0.46; 95% CI = 0.27–0.79 [premenopausal]). Premenopausal women were also less likely to have elevated fasting glucose level (OR = 0.50; 95% CI = 0.26–0.97) than age-matched men. Among obese women with BED, aging may have a more profound impact on metabolic abnormalities than menopause, suggesting the importance of early intervention of obesity and symptoms of BED. Active monitoring of metabolic function in obese men with BED may also be critical.

### Keywords

Menopause; Metabolic syndrome; Binge eating disorder; Obesity; Sex differences

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#### Contributors

All authors contributed in a significant way to development and/or writing of the manuscript. All authors have read and approved the final manuscript.

#### Conflict of interest

Dr. Grilo reports that he receives royalties from Guilford Press and Taylor and Francis Books (for academic books).

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## 1. Introduction

Metabolic syndrome (MetS) is a clustering of metabolic risk factors linked with cardiovascular disease, type-II diabetes, and other causes of mortality (Isomaa, et al., 2001; Trevisan, Liu, Bahsas, & Menotti, 1998; Wilson, D'Agostino, Parise, Sullivan, & Meigs, 2005). Maladaptive eating patterns similar to those reported in binge eating disorder (BED; e.g., gorging eating pattern, meal skipping, irregular meal consumption) have been associated with metabolic abnormalities and MetS (Kral, Buckley, Kissileff, & Schaffner, 2001; Roehrig, Masheb, White, & Grilo, 2009; Sierra-Johnson, et al., 2008). BED is characterized by recurrent binge eating (i.e., consumption of unusually large amount of food and feeling of loss of control) without inappropriate compensatory weight-control behaviors (American Psychiatric Association, 1994). BED occurs in a subset of obese individuals, and has been associated with the severity of obesity (Hudson, Hiripi, Pope, & Kessler, 2007). BED may also increase the risk for metabolic abnormalities and MetS beyond the risk attributable to obesity (Hudson, et al., 2010).

The prevalence of MetS is higher in women than men, although sex differences in abnormalities in each metabolic component appear to be complex (Razzouk & Muntner, 2009). In women, menopausal transition may be particularly vulnerable time to develop features of MetS, including increases in accumulation of central fat, worsening lipid profile, and insulin resistance (Carr, 2003; Lobo, 2008). Age-adjusted prevalence of MetS among women in the U.S. is 23.4% (Ford, Giles, & Dietz, 2002), but the rate increases with age, particularly after 50 years old in women (Ford, et al., 2002; Park, et al., 2003). Even after adjusting for age, postmenopausal women are also estimated to be 1.6 times more likely to have MetS than premenopausal women (Kim, Park, Ryu, & Kim, 2007). Menopause thus appears to make a unique contribution to development of MetS in women. Because MetS at postmenopausal has been strongly associated with various chronic medical conditions, such as cardiovascular disease (Carr, 2003; Ren & Kelley, 2009) and breast cancer (Agnoli, et al., 2010; Esposito, et al., 2013; Rosato, et al., 2011), emergence of metabolic abnormalities during the menopausal transition has been suggested as an important target of intervention for cardiac and other causes of mortality in women (Carr, 2003).

The impact of menopause on the risk for MetS has not been studied among obese individuals with BED. Interestingly, in obese individuals with BED, the rate of MetS has been found higher in men than women (Barnes, et al., 2011; Roehrig, et al., 2009). Yet, age-matched sex comparison of the risk for MetS has not been investigated in this population. An important question is whether menopause is an additional risk factor for MetS in women who are obese and have BED. It may also help inform development of targeted intervention strategies in relation to menopause in women who are already at risk for MetS. The present study compared the risk for metabolic abnormalities and MetS among postmenopausal women, premenopausal women, and age-matched men who were obese and sought treatment for BED.

## 2. Methods

### 2.1. Participants

Participants were 338 treatment-seeking obese adults (240 women, 98 men; mean age=46.4±10.7 years) with BED. Eighty-eight of the 240 women were categorized as being postmenopausal based on interview. All participants were obese (BMI ≥30 kg/m<sup>2</sup>) and had BED based on *DSM-5*. Exclusion criteria were: current anti-depressant therapy, severe psychiatric problems (lifetime bipolar disorders and schizophrenia, and current substance dependence), severe medical problems (cardiac and liver diseases), and uncontrolled hypertension, thyroid conditions, or diabetes. Ethnic/racial composition was: 62.3% Caucasian, 23.3% African-American, 8.7% Hispanic, and 5.8% Other. 94.8% of participants reported at least high-school education. All participants provided written informed consent and the research was approved by the Yale IRB.

### 2.2. Assessment and Measures

**2.2.1. Features of eating disorders**—Eating Disorder Examination (EDE) (Fairburn & Cooper, 1993) interview was used to assess the frequency of objective bulimic episodes in the past 28 days (OBE; i.e., binge eating defined as unusually large quantities of food with a subjective sense of loss of control). This EDE also includes four subscales (Restraint, Eating-Concern, Shape-Concern, and Weight-Concern) and a global total score. All items are rated on a 7-point scale (0–6 range) with higher scores reflecting greater severity/frequency.

**2.2.2. Metabolic measures**—Participants' weight was measured using a high-capacity digital scale. Height, waist circumference, heart rate, and blood pressure were measured by trained staff. Fasting lipid profile (total cholesterol, high-density-lipoprotein [HDL] cholesterol, low-density-lipoprotein [LDL] cholesterol, and triglycerides), glucose levels, and glycated hemoglobin 1Ac (HbA1c) were obtained through serum sample, and analyzed by Quest Diagnostics.

Clinically elevated total cholesterol level was defined as ≥200 mg/dL (%). Poor glycemic control was defined as an HbA1c value ≥5.45(%) which is demonstrated to predict MetS in non-diabetic samples (Sung & Rhee, 2007). For components of MetS, we followed clinical criteria outlined by the National Cholesterol Education Program's Adult Treatment Panel-III guidelines (Expert Panel, 2001): a) Central or abdominal obesity (> 40 inches for men, > 35 inches for women); b) Triglycerides ≥150 mg/dL; c) HDL cholesterol (< 40 mg/dL for men, < 50 mg/dL for women); d) Systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg; and e) Fasting glucose ≥110 mg/dL. Individuals were categorized as having MetS if they had three or more of the five criteria.

### 2.3. Analysis

Means and standard deviations, or proportions were calculated for demographic, eating/weight-related, and metabolic characteristics for four groups: premenopausal women, postmenopausal women, and two groups of age-matched men (20–58 years for premenopausal women, 42–65 years for postmenopausal women).

Odds ratios (ORs) for meeting clinical criteria for metabolic abnormalities were calculated by logistic regression with the following paired group comparison: post- vs. premenopausal (reference group), premenopausal vs. age-matched men (reference group), and postmenopausal women vs. age-matched men (reference group). Race (Caucasian [reference group], African American, other) was included as covariates in all analyses. For the comparison between pre- and postmenopausal women, we also completed age-adjusted analyses (age as a continuous variable) to examine whether the effect of menopause was beyond the effect of aging.

### 3. Results

#### 3.1. Participant characteristics

Table 1 summarizes participants' characteristics by four groups. Postmenopausal women were significantly older than respective age-matched men and premenopausal women. Majority of men and postmenopausal women were Caucasian, whereas only 50% of premenopausal women were Caucasian.

Premenopausal women reported significantly younger age onset of binge eating than age-matched men and postmenopausal women. Pre- and postmenopausal women both reported significantly earlier age onset of dieting, compared with their respective age-matched men. Postmenopausal women reported a significantly greater number of times on a diet than age-matched men and premenopausal women. Regardless of menopausal status, women reported higher scores on EDE subscales than their respective age-matched men, except for restraint eating. Postmenopausal women reported significantly higher scores on restraint eating than age-matched men and premenopausal women.

Waist circumferences, systolic and diastolic blood pressure, fasting glucose level, and triglycerides were significantly elevated in age-matched men, regardless of menopausal status. HbA1c was significantly lower in premenopausal women, compared with age-matched men and postmenopausal women. Postmenopausal women showed significantly higher HDL cholesterol level than age-matched men or premenopausal women; HDL cholesterol was also significantly lower in premenopausal women than age-matched men. Total and LDL cholesterol levels were significantly higher in postmenopausal women, compared with age-matched men and premenopausal women. Regardless of menopausal status, a smaller proportion of women had MetS than their respective age-matched men.

#### 3.2. Odds ratios for meeting clinical criteria for metabolic abnormalities

Adjusting for race, compared with premenopausal women, postmenopausal women were significantly more likely to show clinically elevated total cholesterol and poor glycemic control, but less likely to have a clinically low level of HDL cholesterol (Table 2). After adjusting for age, however, all significant odds ratios became non-significant. Compared with age-matched men, postmenopausal women were significantly more likely to show clinically elevated total cholesterol level, but significantly less likely to show clinically elevated triglycerides and blood pressure. Compared with age-matched men, premenopausal women were significantly less likely to have clinically low level of HDL cholesterol,

elevated blood pressure, and elevated fasting glucose level. Men were more likely have MetS than both pre- and postmenopausal women.

## 4. Discussion

We found that among obese individuals with BED postmenopausal women were more likely than premenopausal women to have a clinically elevated level of total cholesterol and poor glycemic control. However, these significant differences disappeared after adjusting for age, suggesting that aging rather than menopause may add risk for metabolic abnormalities in obese women with BED. While controversial, an independent effect of menopause on metabolic abnormalities above and beyond the effect of aging has been demonstrated (Dasgupta, et al., 2012; Ford, et al., 2002; Janssen, et al., 2008; Kim, et al., 2007; Sowers, et al., 2007). Significantly earlier age of binge-eating onset might have contributed to earlier emergence of metabolic abnormalities in premenopausal women. The prevalence of MetS in our female sample (34.8% [premenopausal] and 31.8% [postmenopausal], respectively) was higher than age-adjusted rate in a U.S. general population (23.4%) (Ford et al., 2002). Alternatively, in an already at risk population such as obese individuals with BED, menopause may not be a significant additional risk for MetS. Treatment of obesity and binge eating prior to menopause may be critical for prevention of MetS in this population.

In comparison with respective age-matched men, both pre- and postmenopausal women were less likely to meet clinical criteria for elevated triglycerides and blood pressure, and MetS. Premenopausal women were also less likely to show clinically elevated glucose level. Thus, obese men with BED may be at increased risk for MetS, which is consistent with our previous studies with treatment-seeking individuals with BED (Barnes, et al., 2011; Roehrig, et al., 2009). In our study, women overall reported significantly earlier onset of dieting than men. Furthermore, although men represent a substantial proportion of individuals with BED (Hudson, et al., 2007), they have been underrepresented in treatment studies (Franko, et al., 2012), suggesting that men may be less likely than women to seek treatment for their binge eating problems. Thus, higher prevalence of MetS in our male samples than females may be a result of lack of active coping with BED until the negative consequences of BED becomes severe.

There are several limitations to consider. First, we relied on self-report to determine menopausal status in women. Furthermore, the study was unable to control the effect of hormone replacement therapy (HRT) on metabolic function. HRT has been associated with reduced risk for MetS, but the results vary by the types of HRT (Kim, et al., 2011; Salpeter, et al., 2006). Finally, the present study focused on treatment-seeking individuals and findings may not generalize to community samples (Grilo, Lozano, & Masheb, 2005; Wilfley, Pike et al., 2001). Further, since our participants enrolled without major or uncontrolled health problems, our findings may not generalize to individuals with advanced metabolic issues.

### 4.1. Conclusions

To our knowledge, this is the first study to directly compare, in obese persons with BED, metabolic abnormalities between pre- and postmenopausal women and with age-matched

men. Development of MetS during menopausal transition has been linked with chronic disease conditions and mortality in women (Lin, et al., 2010). Therefore, understanding the impact of menopause on metabolic function has been emphasized as an important venue of research for prevention of chronic disease conditions in women. Our findings suggest that among treatment-seeking obese individuals with BED, menopause does not appear to increase risk for metabolic abnormalities when accounting for the effect of age. We also found that being male gender was associated with elevated rates of MetS in our study. Clinically, the observed findings suggest the importance of assessing for metabolic problems in obese patients with BED and, if present, considering interventions to address the metabolic disturbances in addition to addressing the excess weight and binge eating.

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### Highlights

- We compared metabolic abnormalities between pre- and postmenopausal women, and men
- We included treatment-seeking obese individuals with binge eating disorders (BED)
- Aging may have stronger influence on metabolic abnormalities than menopause
- Men showed greater risk for metabolic abnormalities than women in general
- Actively assessing for metabolic problems is important in obese patients with BED

Table 1

## Participant characteristics

	Postmenopausal women ( <i>n</i> = 88)	Age-matched men <i>I</i> (42–65 years old; <i>n</i> = 74)	Premanopausal women ( <i>n</i> = 152)	Age-matched men <i>I</i> (20–58 years old; <i>n</i> = 88)
Age	55.8 (4.6) <i>a,b</i>	51.7 (5.9)	39.6 (9.2) <i>a</i>	45.9 (8.7)
Race				
White	69.3 <i>b</i>	74.3	50.0 <i>a</i>	70.4
African American	23.9	14.9	29.0	15.9
Other	6.8	10.8	21.0	13.6
Education (% completed at least high school/GED)	96.6	97.3	91.5	97.7
BMI	38.2 (5.7)	38.9 (4.9)	38.6 (5.9)	39.2 (5.5)
Age of first time overweight	20.8 (12.7)	22.0 (12.8)	17.8 (9.3)	20.5 (11.6)
Age of binge eating onset	27.8 (24.6) <i>b</i>	30.4 (13.6)	22.0 (10.8) <i>a</i>	28.4 (12.5)
Age of dieting onset	21.7 (10.4) <i>a</i>	30.6 (11.0)	20.2 (8.6) <i>a</i>	28.2 (10.9)
Number of times on a diet <sup>2</sup>	69.6 (200.5) <i>a,b</i>	26.9 (55.3)	30.0 (57.6)	22.7 (51.0)
Global	2.8 (0.8) <i>a</i>	2.3 (0.9)	2.7 (1.0) <i>a</i>	2.3 (0.8)
Restraint	2.0 (1.3) <i>a,b</i>	1.5 (1.2)	1.6 (1.4)	1.4 (1.2)
Eating concern	2.2 (1.3)	1.8 (1.3)	2.2 (1.3) <i>a</i>	1.7 (1.3)
Shape concern	3.7 (1.1) <i>a</i>	3.2 (1.2)	3.6 (1.2) <i>a</i>	3.2 (1.2)
Weight concern	3.2 (1.1) <i>a</i>	2.8 (1.1)	3.3 (1.1) <i>a</i>	2.7 (1.0)
Binge eating frequency (OBE) <sup>2</sup>	18.1 (11.2)	19.9 (17.9)	19.3 (15.7)	19.6 (17.5)
Waist (inches)	45.4 (5.6) <i>a</i>	49.4 (4.8)	44.9 (5.5) <i>a</i>	49.6 (5.3)
Heart rate (bpm)	74.6 (11.6)	77.0 (12.0)	75.4 (11.0)	77.2 (12.7)
Systolic BP (mmHg)	128.0 (15.4) <i>a</i>	132.6 (13.2)	125.6 (14.9) <i>a</i>	132.5 (13.0)
Diastolic BP (mmHg)	78.8 (8.8) <i>a</i>	82.3 (10.5)	79.1 (10.8) <i>a</i>	82.3 (9.3)
Fasting glucose level <sup>2</sup>	105.4 (33.0) <i>a</i>	115.1 (38.9)	99.2 (25.9) <i>a</i>	112.2 (38.0)
HbA1c <sup>2</sup>	6.0 (0.9) <i>b</i>	6.3 (1.2)	5.8 (5.7) <i>a</i>	6.1 (1.2)
Total cholesterol	210.8 (36.8) <i>a,b</i>	184.5 (35.9)	186.3 (33.9)	186.5 (38.6)

	Postmenopausal women ( <i>n</i> = 88)	Age-matched men <sup>1</sup> (42–65 years old; <i>n</i> = 74)	Premenopausal women ( <i>n</i> = 152)	Age-matched men <sup>1</sup> (20–58 years old; <i>n</i> = 88)
HDL	60.0 (13.5) <i>a,b</i>	43.7 (10.2)	54.7 (14.3) <sup>a</sup>	42.7 (10.2)
LDL	125.4 (32.5) <i>a,b</i>	108.2 (32.0)	108.6 (29.7)	111.8 (34.2)
Triglycerides <sup>2</sup>	127.4 (53.5) <i>a,b</i>	162.5 (66.1)	115.4 (66.5) <sup>a</sup>	159.2 (72.1)
Meeting criteria for MetS (%) <sup>3</sup>	31.8 <sup>a</sup>	52.7	34.9 <sup>a</sup>	55.7

Notes. Numbers in parentheses indicate standard deviations. BP = blood pressure; HbA1c = glycated hemoglobin 1Ac.

<sup>1</sup> Two groups of age-matched men are not mutually exclusive;

<sup>2</sup> Statistics are based on log-transformed values, but presented means and standard deviations are raw values;

<sup>3</sup> Criteria for MetS was based on the National Cholesterol Education Program's Adult Treatment Panel III guidelines (Expert Panel on Detection, 2001). Participants were categorized as having metabolic syndrome if they report 3 or more of the 5 criteria.

<sup>†</sup> *p* < .05;

<sup>‡</sup> *p* < .01.

<sup>a</sup> significantly different from respective age-matched men;

<sup>b</sup> significantly different from premenopausal women.

Table 2

Adjusted odds ratios (95% confidence intervals) for meeting clinical criteria for each metabolic measure and MetS

	Postmenopausal women vs. premenopausal women*	Postmenopausal women vs. premenopausal women* (age-adjusted)	Postmenopausal women vs. age-matched men*	Premenopausal women vs. age-matched men*
Elevated total cholesterol	2.75 (1.56–4.80) ‡	1.43 (0.66–3.10)	3.59 (1.84–7.00) ‡	0.94 (0.53–1.67)
Poor glycemic control	2.92 (1.32–6.33) ‡	1.13 (0.40–3.18)	0.73 (0.26–2.05)	0.55 (0.27–1.09)
Central or abdominal obesity	1.01 (0.17–5.91)	0.82 (0.07–10.17)	0.65 (0.06–7.47)	1.09 (0.19–6.37)
Elevated triglycerides	1.12 (0.57–2.21)	1.06 (0.42–2.67)	0.27 (0.13–0.53) ‡	0.29 (0.16–0.53) ‡
Low HDL cholesterol	0.36 (0.19–0.68) ‡	0.78 (0.34–1.83)	0.53 (0.25–1.11)	1.16 (0.67–2.01)
Elevated blood pressure	1.24 (0.71–2.16)	0.69 (0.32–1.50)	0.48 (0.25–0.91) †	0.40 (0.23–0.69) ‡
Elevated fasting glucose	1.76 (0.89–3.49)	0.80 (0.31–2.07)	0.68 (0.34–1.38)	0.50 (0.26–0.97) †
Meeting criteria for MetS (%) <sup>1</sup>	0.86 (0.49–1.53)	0.97 (0.44–2.13)	0.41 (0.21–0.78) ‡	0.46 (0.27–0.79) ‡

Notes. All analyses are adjusted for race (Caucasian [reference group], African American, and Other). Numbers in parentheses are 95% confidence interval. Age ranges for age-matched men were 20–58 years old for premenopausal women ( $n = 88$ ), and 42–65 years old for postmenopausal women ( $n = 74$ ). Elevated total cholesterol = total cholesterol  $\geq 200$  mg/dL; Poor glycemic control = an HbA1c value  $\geq 5.45\%$  (Sung & Rhee, 2007); Central or abdominal obesity =  $> 40$  inches for men,  $> 35$  inches for women; Elevated triglyceride = triglycerides  $\geq 150$  mg/dL; Low HDL cholesterol =  $< 40$  mg/dL for men,  $< 50$  mg/dL for women; Elevated blood pressure = systolic BP  $\geq 130$  mmHg or diastolic BP  $\geq 85$  mmHg; Elevated fasting glucose level = fasting glucose  $\geq 110$  mg/dL;

\* reference group.

<sup>1</sup> Criteria for MetS was based on the National Cholesterol Education Program's Adult Treatment Panel III guidelines (Expert Panel on Detection, 2001). Participants were categorized as having metabolic syndrome if they report 3 or more of the 5 criteria.

†  $p < .05$ ;

‡  $p < .01$