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Impact of weight loss on waist circumference and the components of the metabolic syndrome

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ABSTRACT

Objective: Central adiposity is a component of the metabolic syndrome (MetS). Little is known about the impact of medical weight loss and decreased waist circumference (WC) on the MetS. Our objective was to assess the impact of changes in WC on blood pressure, lipids and glycemia.

Research design and methods: We studied 430 obese patients enrolled in a 2-year, intensive, behavioral, weight management program. We report results for participants who completed 6-month and 2-year follow-up.

Results: Participants were 49±9 years of age (mean ±SD), 56% were women and 85% were white. Baseline body mass index (BMI) was 41±6 kg/m^2 and baseline WC was 120±14 cm. At 6 months, BMI decreased by 6 ±3 kg/m^2 and WC by 14±9 cm. Relative change in WC was defined as the 6-month or 2-year WC minus the baseline WC divided by the baseline WC. Systolic blood pressure decreased by 8 mm Hg for the tertile of participants with the largest relative decrease in WC and by 2 mm Hg for those with the smallest relative decrease in WC (p=0.025). Similar patterns of improvement were observed in total cholesterol (−29 vs −12 mg/dL, p=0.017), low-density lipoprotein-cholesterol (−19 vs −4 mg/dL, p=0.033), and glycated hemoglobin (−1.2 vs −0.3%, p=0.006). At 2 years, BMI decreased by 5±4 kg/m^2 and WC by 11±11 cm and similar patterns of improvements were seen in components of the MetS. At both 6 months and 2 years, larger relative decreases in WC were associated with greater improvements in lipids and glycemia independent of sex.

Conclusions: In obese people, greater relative decreases in WC with medical weight loss are associated with greater improvements in components of the MetS independent of sex.

Key messages

- Central adiposity is a component of the metabolic syndrome, but little is known about the impact of intentional weight loss and decreased waist circumference on the metabolic syndrome.
- Among 430 obese patients enrolled in a 2-year, intensive, behavioral, weight management program, larger relative decreases in waist circumference were associated with greater improvements in components of the metabolic syndrome independent of sex.
- Monitoring changes in waist circumference during weight loss interventions may provide useful prognostic information for assessing the impact of weight loss on metabolic risk.

and within BMI categories, men and women with higher WC are at greater metabolic risk than those with lower WC.[4] It would seem to follow that greater reduction in WC with weight loss might lead to greater improvements in the components of the MetS. No studies, however, have described how changes in WC with medical weight loss are associated with changes in metabolic risk. The purpose of this study was to assess and compare the short-term and longer term impact of reductions in WC on the components of the MetS.

INTRODUCTION

Obesity contributes to the metabolic syndrome (MetS) and the MetS is associated with increased cardiovascular morbidity and mortality.[1–3] Body mass index (BMI) and waist circumference (WC) are both measures of obesity. Metabolic risk increases with BMI

RESEARCH DESIGN AND METHODS

The University of Michigan Weight Management Program (WMP) is a 2-year clinical program that employs intensive energy restriction for the first 3 to 6 months to promote 15% weight loss, followed by behavior change and physical activity counseling to promote weight loss maintenance. Initially, participants consume a very low energy diet (VLED, 800 kcal/day) in the form of total meal replacements and are asked to gradually increase low to moderate intensity physical activity to 40 min per day.

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After 3 to 6 months, participants are transitioned to regular food stuffs with total calorie intake of 1200–1500 kcal/day for women and 1500–1800 kcal/day for men. Participants are asked to record their food, beverage and calorie intake using a diary or an app (myfitnesspal.com, Calorieking.com, FatSecret.com or sparkpeople.com) that is downloaded for review by the dietitian. After 3 to 6 months, participants are asked to engage in 40 to 90 min of moderate to vigorous physical activity per day at least 4 days per week. The entire 2-year program involves 11 visits with a physician and 26 visits with a dietitian. Patients are seen by a physician for an initial assessment, at 1 month and quarterly thereafter. Patients are seen by a registered dietitian weekly during the first month and monthly thereafter. The program has been described in detail elsewhere.[5][6]

Height is measured at the initial visit using a wall-mounted stadiometer (Easy-Glide Bearing Stadiometer, Perspective Enterprises, Portage, MI, USA) and all participants are weighed at each visit on a calibrated scale (Scale-Tronix Model 6002, White Plains, New York, USA). BMI is calculated as body weight in kilograms divided by height in meters squared. WC is measured in triplicate, at each visit midway between the ribs and iliac crests with a single-use nylon measuring tape with a length of 200 cm and the results are averaged. Blood pressure is measured once at each visit after 5 minutes of rest using a Carescape Dinamap V100 with the patient seated in a chair, back supported, and feet squarely planted on the floor. For any abnormal blood pressure value (>140/90 mm Hg), the blood pressure is rechecked after 10 min of rest with a wall-mounted mercury sphygmomanometer. Laboratory monitoring of serum chemistries, lipids, and glycated hemoglobin (HbA1c) is performed at baseline prior to dietary intervention, at 1 month during VLED in patients at high risk for metabolic derangements (eg, diabetes mellitus, chronic kidney disease, history of heart failure, etc) and every 3 to 6 months thereafter depending on the participant's comorbid health conditions. Hypertension was defined as systolic blood pressure (SBP) ≥140 mm Hg and/or diastolic blood pressure (DBP) ≥90 mm Hg. Diabetes was defined by American Diabetes Association criteria as fasting glucose ≥126 mg/dL (7.0 mmol/L) or HbA1c ≥6.5% (48 mmol/mol).

The study population included people with BMI ≥32 kg/m^2 and ≥1 comorbidity or BMI ≥35 kg/m^2 enrolled in the WMP between 1 January 2010 and 30 October 2013 who consented to participate in research. The study was reviewed and approved by the University of Michigan Institutional Review Board and all participants provided written informed consent. The trial is registered at Clinicaltrials.gov (NCT02043457). Four hundred and thirty patients made a first visit to the WMP and consented to participate in the research. Of the 430 patients, 344 (80%) made a 6-month follow-up visit (range 18–24 weeks) and had their WC measured. Of the 344 patients studied at 6 months, 170 (49%) made a 2-year follow-up visit (range 84–100 weeks) and had their WC measured.

In table 1, the demographic and clinical characteristics of the study population are described using means ±SD or number and percentage (%). Differences between 6-month and 2-year completers and non-completers were tested with t-tests for continuous variables and χ^2 tests for categorical variables. In table 2, participants are grouped into tertiles according to baseline WC. The first tertile had the smallest WC (<112 cm), the second tertile had an intermediate WC (112 to 124 cm), and the third tertile had the largest WC (≥124 cm). To examine the statistical significance of differences in the components of the MetS by tertile of WC at baseline, we used analysis of variance for continuous variables and χ^2 tests for categorical variables.

We then examined the change in WC for each participant between 6 months and baseline and between 2 years and baseline. The relative change in WC was defined as the 6-month or 2-year WC minus the baseline WC divided by the baseline WC. Initially, we stratified the population by sex to determine whether the association between relative change in WC and mean change in components of the MetS differed by sex. There was no consistent pattern (data not shown) so we grouped all participants into tertiles according to their relative change in WC at 6 months and 2 years (table 3). The first tertile had the largest relative decrease in WC and BMI at 6 months and 2 years (−9.0 and −9.1 kg/m^2, respectively) and the 3rd tertile had the smallest relative decrease in WC and BMI at 6 months and 2 years (−3.3 and −1.6 kg/m^2, respectively). For the groups with the largest and smallest relative decrease in WC, we assessed the mean change in each component of the MetS at 6 months and 2 years by calculating the difference in the component of the MetS between follow-up and baseline. We used t-tests to assess the statistical significance of the differences in the mean change in the outcome variables between individuals in the 1st versus the 3rd tertiles of change in WC.

We also used linear regression to assess change in the components of the MetS when relative change in WC was the primary predictor. To determine whether the association between relative change in WC and mean change in components of the MetS differed by sex, we included an interaction term for WC × sex. The interaction term did not enter any of the models, again suggesting that the associations between change in WC and change in components of the MetS did not differ by sex. We then assessed changes in the components of the MetS at 6 months and 2 years for the components of the MetS that were significant in bivariate analyses. Results were expressed as the unit change in the outcome variable associated with a 10% reduction in WC after adjusting for sex and BMI at 6 months and 2 years.

Analyses were performed using SAS V.9.3 (SAS Institute, Cary, North Carolina, USA). We used a p value <0.05 to define statistical significance.

Table 1 Baseline characteristics of the study population by follow-up status (N (%) or mean±SD)

	Total population	6-month completers	6-month non-completer	p Value	2-year completers	2-year non-completers	p Value
N	430	344	86		170	174	
Age (years)	49±9	50±9	47±10	0.006	51±8	48±9	0.005
Sex				0.808			0.166
Female	240 (56%)	191 (56%)	49 (57%)		88 (52%)	103 (59%)	
Race/ethnicity				0.204			0.066
White	364 (85%)	288 (84%)	76 (88%)		151 (89%)	137 (80%)	
Marital status				0.714			0.002
Married or life partner	356 (83%)	286 (83%)	70 (81%)		152 (89%)	134 (77%)	
Education				0.084			0.853
College degree or higher	320 (74%)	265 (77%)	55 (64%)		133 (78%)	132 (76%)	
Diabetes mellitus	114 (27%)	94 (27%)	20 (23%)	0.444	48 (28%)	46 (26%)	0.708
Baseline BMI (kg/m^2)	41±6	40±6	42±7	0.035	40±5	41±6	0.103
Baseline WC (cm)	120±14	119±14	123±16	0.063	119±13	120±15	0.459

BMI, body mass index; WC, waist circumference.

Table 2 Associations between tertile of WC at baseline and components of MetS

	1st tertile of WC (WC <112 cm) N=106	2nd tertile of WC (WC ≥112 and <124 cm) N=120	3rd tertile of WC (WC ≥124 cm) N=118	p Value
BMI (kg/m^2)	37±3	39±4	45±6	<0.001
Hypertension (%)	40%	50%	66%	<0.001
SBP (mm Hg)	127±12	133±15	132±16	0.002
DBP (mm Hg)	65±8	69±8	68±9	0.008
Dyslipidemia (%)	42%	54%	57%	0.077
Tot chol (mg/dL)	181±37	184±33	178±33	0.563
Triglycerides (mg/dL)	140±79	161±187	175±96	0.244
HDL (mg/dL)	53±16	46±12	42±8	0.001
LDL (mg/dL)	103±34	108±28	101±28	0.282
Tot chol/HDL	3.9±1.0	4.2±1.3	4.3±0.8	0.021
Diabetes (%)	23%	28%	31%	0.343
Fasting glucose (mg/dL)	105±20	104±15	110±25	0.158
HbA1c (%)	6.5±1.0	6.7±1.4	6.9±1.5	0.373

BMI, body mass index; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein-cholesterol; SBP, systolic blood pressure; Tot chol, total cholesterol; Tot chol/HDL, total cholesterol to HDL-cholesterol ratio; WC, waist circumference.

RESULTS

Table 1 shows the baseline characteristics of the study population (n=430) and the 6-month program completers (n=344) and non-completers (n=86). At baseline, mean age was 49±9 years, 56% were women, and 85% were non-Hispanic white. In general, the population was married and highly educated. At baseline, 114 participants (27%) had diabetes mellitus. Of the 114 participants with diabetes, 22 (19%) were treated with insulin, 70 (61%) were treated with non-insulin pharmacological therapies, and 22 (19%) were receiving no antihyperglycemic pharmacological therapies. Baseline BMI was 41 ±6 kg/m^2 and WC was 120±14 cm. Six month completers were older and had lower baseline BMIs than non-completers. They did not differ with respect to sex, race, marital status, education, diabetes status, or WC. Table 1 also shows the baseline characteristics of 2-year program

completers and non-completers. Compared to program non-completers (n=174), 2-year program completers (n=170) were older and were more likely to be married (table 1). They did not differ with respect to sex, race, education, diabetes status, BMI or WC.

Table 2 shows BMI and the components of the MetS for 6-month program completers by tertile of WC at baseline. At baseline, higher tertile of WC was significantly associated with higher BMI, history of hypertension, higher SBP and DBP, lower high-density lipoprotein (HDL)-cholesterol, and higher total cholesterol to HDL-cholesterol ratio.

Table 3 compares the mean change in each component of the MetS at 6 months follow-up (top panel) and 2 years follow-up (bottom panel) for participants who had the largest relative decrease in WC (first tertile) versus the smallest relative decrease in WC (third

Table 3 Change in Components of the MetS by tertile of change in WC between baseline and 6-month follow-up and baseline and 2-year follow-up

	(N)	Change in outcome in the tertile with the greatest relative decrease in WC	(N)	Change in outcome in the tertile with the smallest relative decrease in WC	p Value
6-month f/u (n=344)					
Δ BMI	114	−9	116	−3	<0.001
Δ SBP	109	−8	104	−2	0.025
Δ DBP	109	−2	104	−1	0.283
Δ Total cholesterol	61	−29	36	−12	0.017
Δ Triglycerides	61	−58	36	−60	0.959
Δ HDL-cholesterol	61	0	36	1	0.700
Δ LDL-cholesterol	61	−19	34	−4	0.033
Δ Tot chol/HDL	61	−0.8	36	−0.4	0.107
Δ Fasting glucose	60	−11	20	−10	0.835
Δ HbA1c	27	−1.2	40	−0.3	0.006
2-year f/u (n=170)					
Δ BMI	57	−9	57	−2	<0.001
Δ SBP	57	−8	57	−2	0.027
Δ DBP	57	−2	57	−1	0.492
Δ Total cholesterol	21	−7	13	8	0.236
Δ Triglycerides	21	−59	13	11	0.025
Δ HDL-cholesterol	21	17	13	3	<0.001
Δ LDL-cholesterol	21	−12	13	8	0.128
Δ Totchol/HDL	21	−1.1	13	−0.2	<0.001
Δ Fasting glucose	20	−9	13	6	0.005
Δ HbA1c	10	−0.8	12	−0.4	0.208

BMI, body mass index; DBP, diastolic blood pressure; f/u, follow-up; HbA1c, glycated hemoglobin; LDL, low-density lipoprotein-cholesterol; SBP, systolic blood pressure; Tot chol/HDL, total cholesterol to HDL-cholesterol ratio; WC, waist circumference.

tertile). At 6 months, with a mean decrease in BMI of 6 $\pm$3 kg/m^2 and a mean decrease in WC of 14$\pm$9 cm, and at 2 years with a mean decrease in BMI of 5$\pm$4 kg/m^2 and a mean decrease in WC of 11$\pm$11 cm, there were significant differences in the changes in BMI, blood pressure, lipids and measures of glycemia between the groups. At 6 months, BMI decreased by 9 kg/m^2 in the tertile of participants with the largest relative decrease in WC and by 3 kg/m^2 for the tertile of participants with the smallest relative decrease in WC (p<0.001). SBP decreased by 8 mm Hg in the tertile of participants with the largest relative decrease in WC and by 2 mm Hg for the tertile of participants with the smallest relative decrease in WC (p=0.025). At 6 months follow-up, significant differences were also observed in total cholesterol (−29 vs −12 mg/dL, p=0.017), low-density lipoprotein (LDL)-cholesterol (−19 vs −4 mg/dL, p=0.033), and HbA1c (−1.2 vs −0.3% p=0.006) in participants with the largest relative decrease in WC compared to participants with the smallest relative decrease in WC.

At 2 years of follow-up, BMI decreased by 9 kg/m^2 for those in the tertile with the largest relative decrease in WC and by 2 kg/m^2 for those in the tertile with the smallest relative decrease in WC (p<0.001). At 2 years of follow-up, greater improvements were also seen in SBP (−8 vs −2 mm Hg, p=0.027), triglycerides (−59 vs +11 mg/dL, p=0.025), HDL-cholesterol (+17 vs +3 mg/dL, p<0.001), the ratio of total cholesterol to

HDL-cholesterol (−1.1 vs −0.2, p<0.001), and fasting glucose (−9 vs +6 mg/dL, p=0.005) for participants in the tertile with the largest relative decrease in WC compared to the tertile with the smallest relative decrease in WC.

In bivariate analyses stratified by sex and in multivariate analyses in which we included an interaction term for WC×sex, we found no consistent evidence that the association between change in WC and change in the components of the MetS differed by sex (data not shown). To further assess whether relative decrease in WC was associated with improvement in the components of the MetS independent of sex, we performed linear regression analyses adjusting for sex and BMI at 6 months and 2 years. At 6 months follow-up, a 10% relative decrease in WC was independently associated with a 10 mg/dL decrease in LDL-cholesterol (p=0.017) and a 0.7% decrease in HbA1c (p=0.002). At 2 years follow-up, a 10% relative decrease in WC was independently associated with a 7 mg/dL increase in HDL-cholesterol (p=0.001), a 0.4 unit decrease in total cholesterol to HDL-cholesterol ratio (p=0.015), and a 10 mg/dL decrease in fasting glucose (p=0.012).

DISCUSSION

The National Heart, Lung, and Blood Institute has suggested that in individuals with BMI≥35 kg/m^2, WC adds

little to BMI in predicting cardiometabolic risk, and therefore, WC need not be assessed.[7] In contrast, we found that in a population with mean BMI of 41 kg/m^2, larger baseline WC identified individuals who were at greater risk for having hypertension, higher SBP and DBP, lower HDL-cholesterol and higher total-cholesterol to HDL-cholesterol ratios. We further demonstrated that greater relative decrease in WC with an intensive behavioral weight management intervention was associated with greater improvements in the components of the MetS including measures of blood pressure, lipids, and glycemia at both 6 months and 2 years. Some of the improvements in lipid measures and measures of glycemia that occurred with the greater relative decrease in WC occurred independently of sex. The reasons for the differential effects of decrease in WC on the individual components of the metabolic syndrome at 6 months and at 2 years are not clear but may be due to the magnitude, duration, and persistence of the decrease in WC and to a legacy effect.

Many of the complications of obesity arise from lipotoxicity. Adipocytes store excess free fatty acids (FFA) in the cytosol and release adipokines that are inflammatory and associated with the development of MetS and atherosclerosis.[8] Non-adipose cells have a limited capacity to store FFA and with exposure to excess FFA, undergo metabolic derangements, cellular dysfunction, or cell death.[9] Weight loss that preferentially reduces metabolically active visceral adipose tissue may have a salutary effect on the components of the MetS. Moderate weight loss (5–10%) has been associated with disproportionate mobilization of visceral adipose tissue with concomitant decrease in risk.[10]

A recent study examining 15 184 adults from the National Health and Nutrition Examination Survey reported that individuals with higher WC had higher long-term mortality across BMI categories between 20 and 50 kg/m^2, even after adjusting for other risk factors.[11] Janssen and colleagues[4] found that when both BMI and WC are examined as continuous variables, WC but not BMI explained obesity-related health risks. For a given WC value, overweight and obese persons and normal-weight persons have comparable health risks.[4] In a meta-regression analysis of pooled results from 15 prospective studies in which WC (and/or waist-hip ratio) were measured, de Koning et al[12] found that a 1 cm increase in WC increased the relative risk of incident cardiovascular events by 2%.

We found only one previous study that assessed changes in components of the MetS associated with change in WC and none that described how changes in WC with medical weight loss are associated with changes in metabolic risk. In a report from the Data from an Epidemiological Study on the Insulin Resistance syndrome (DESIR), a prospective observational study, Balkau et al[13] examined the effects of changes in abdominal obesity on components of the MetS in 1868 men and 1939 women 30–64 years of age over 9 years.

Increasing WC ≥7 cm was associated with increased cardiometabolic risk in both sexes, but a decrease in WC ≥3 cm did not have a large effect on individual cardiometabolic risk factors or their aggregation in the MetS.[13] Of note, only 19% of men and 10% of women who were abdominally obese at baseline decreased their WC by ≥3 cm over 9 years.[13] The failure to observe a beneficial effect of reduced WC on components of the MetS may have been due to limited power to observe an effect due to the small proportion of participants who lost weight and the modest weight loss achieved.

The strengths of this study were the well-characterized study population, the substantial weight loss achieved, and the serial measures of anthropometry and components of the MetS. Limitations include a 50% loss to follow-up between baseline and 2 years and missing data on components of the MetS at both 6-month and 2-year follow-up. To the extent that loss to follow-up occurred independently of changes in WC and to the extent that missing data occurred at random, these limitations would not be expected to affect the observed associations between change in WC and the components of the MetS. Longer follow-up would, however, be important to demonstrate that the improvements in the components MetS associated with greater relative decrease in WC translate into reduced cardiovascular morbidity and mortality. Findings from this population of predominantly non-Hispanic white participants may not be generalizable to the general population. Similarly, these results may not apply to other subgroups such as patients with diabetes although ~30% of the participants carried this diagnosis. Visceral fat was not directly measured and therefore, it is not possible to attribute the metabolic changes observed directly to changes in visceral adipose tissue.

CONCLUSIONS

In patients enrolled in an intensive, behavioral, weight management program, greater relative decrease in WC is associated with greater improvements in components of the MetS. A greater relative decrease in WC is also associated with greater improvements in lipid measures and measures of glycemia independent of sex. Monitoring changes in WC during weight loss interventions may provide useful prognostic information for assessing the impact of weight loss on metabolic risk.

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