Title

HEART FAILURE INCIDENCE ACCORDING TO PRESENCE OF METABOLICALLY HEALTHY/UNHEALTHY NORMAL WEIGHT AND OVERWEIGHT/OBESITY IN POSTMENOPAUSAL WOMEN: THE WOMEN'S HEALTH INITIATIVE (WHI)

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128*
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Background/Synopsis: Obesity increases risk of heart failure (HF), but it is not clear whether those who are metabolically unhealthy normal weight or healthy overweight/obesity are also at increased risk.

Objective/Purpose: To evaluate whether metabolically healthy/ unhealthy normal weight and overweight/obesity are associated with greater HF hospitalizations in postmenopausal women.

Methods: WHI enrolled 161,808 postmenopausal women ages 50-79. We included those who had cardiovascular disease (CVD) biomarkers (n=19,516) without CVD at baseline and were followed for HF for a mean of 11.3 years. We defined normal weight as body mass index (BMI) (≥18.5 and <25 kg/m^2) or waist circumference (WC) (<88 cm) and overweight/obesity as a BMI ≥25 kg/m^2 or WC

≥88 cm. Metabolically healthy included <2 and metabolically unhealthy ≥2 of the following: triglycerides ≥150 mg/dl or niacin or fibrates, systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or antihypertensive drugs, fasting glucose ≥100 mg/dl or antidiabetic therapy or HDL cholesterol <50 mg/dl or niacin or fibrates. Cox regression examined the HF hospitalizations risk (with and without diabetes at baseline) among those who were metabolically healthy normal weight (MHNW), metabolically unhealthy normal weight (MUHNW), metabolically healthy obese (MHO), and metabolically unhealthy overweight/obese (MUHO), compared to those who were MHNW as the reference group.

Results: The table shows HR's for incident HF, according to each group overall and by diabetes (DM) status. As compared to those with MHNW, those with MHO had a modest increased risk of experiencing incident HF hospitalization events among those without DM at baseline. Incident HF was also greater in those with MUHO both among those with and without DM. Among all participants, the MHO group experienced a modest increased risk of incident HF, with those with MUHO having a 2-fold greater risk. An interaction term of metabolic weight groups with prevalent DM status was not significant (p=0.24), indicating similar risks conferred by metabolic weight groups for HF in those with vs. without DM.

Table Cox proportional hazard ratios risk of incident heart failure hospitalizations with risk factors in WHI postmenopausal women with and without prevalent diabetes and all participants at baseline

	Prevalent Diabetes (n=2,394)		No Prevalent Diabetes (n=17,122)		All Participants (n=19,516)	
	Incident HF (n=141)		Incident HF (n=315)		Incident HF (n=456)	
Risk Factor	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
MUHNW vs MHNW	4.48 (0.59-33.90)	0.15	1.29 (0.87-1.91)	0.20	1.35 (0.94-1.93)	0.10
MHO vs MHNW	2.45 (0.27-21.89)	0.42	1.49 (1.04-2.14)	0.03	1.45 (1.02-2.06)	0.04
MUHO vs MHNW	7.79 (1.09-55.83)	0.04	2.22 (1.63-3.04)	<.0001	2.37 (1.76-3.18)	<.0001

HF = heart failure, HR = hazard ratio, CI = confidence intervals, MHNW = metabolically healthy normal weight, MUHNW = metabolically unhealthy normal weight, MHO = metabolically healthy overweight/obese, and MUHO = metabolically unhealthy overweight/obese. Models adjusted for: age, education, income, smoking, and minutes of moderate/strenuous activity/week. Also, the all participants group was adjusted for prevalent diabetes. $p < 0.05$.

Conclusions: MUHO, in particular, and MHO to a lesser extent showed an increased risk for incident HF. Our results show among postmenopausal women that a healthy cardiometabolic status in the presence of obesity does not protect against HF.