Published in final edited form as:

Mayo Clin Proc. 2008 December ; 83(12): 1350–1357.

Abnormal Cardiac Structure and Function in the Metabolic Syndrome: A Population-Based Study

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Abstract

OBJECTIVE—To measure the association between cardiac structure and function abnormalities and isolated metabolic syndrome (metabolic syndrome excluding established hypertension or diabetes mellitus).

PARTICIPANTS AND METHODS—We collected data prospectively on a population-based random sample of 2042 Olmsted County, Minnesota, residents aged 45 years or older who underwent echocardiography between January 1, 1997, and September 30, 2000. Metabolic syndrome was defined by National Cholesterol Education Program Adult Treatment Panel III criteria.

RESULTS—The prevalence of isolated metabolic syndrome was 21.7% (214/984) in men and 16.7% (177/1058) in women. Left ventricular (LV) mass index was greater (91.7 vs 87.9 g/m²; $P=.04$) and LV diastolic dysfunction more prevalent (28.2% [50/177] vs 14.9% [81/544]; $P<.001$) in women with isolated metabolic syndrome than in women without metabolic syndrome; no difference was found in men. When patients with hypertension or diabetes mellitus were included in the cohort, there was a stepwise increase in LV mass index and LV diastolic dysfunction from no metabolic syndrome to isolated metabolic syndrome to metabolic syndrome in women and men.

CONCLUSION—Isolated metabolic syndrome, which is associated with increased LV mass index and LV diastolic dysfunction in women, identifies women with evidence of early ventricular dysfunction.

Metabolic syndrome is associated with increased risk of cardiovascular disease (CVD) and mortality.^{1–6} The metabolic syndrome components of diabetes mellitus and hypertension are well known to be associated with abnormal cardiac structure and function, and reversal of these abnormalities is a goal of CVD prevention.^{7–13} However, whether isolated metabolic syndrome (patients fulfilling the hyperglycemia or elevated blood pressure criteria for metabolic syndrome but not the criteria for diabetes mellitus or hypertension) is also associated with abnormal cardiac structure and function is unknown. If isolated metabolic syndrome identifies persons who have already developed abnormal left ventricular (LV) structure and function, the importance of early recognition of isolated metabolic syndrome would be enhanced.

Population-based studies of cardiac structure and function abnormalities in metabolic syndrome are limited, and no studies have included quantitative assessment of LV diastolic

function. Few data are available on persons with isolated metabolic syndrome.¹⁴ Little is known about the association of sex and LV structure and function abnormalities in metabolic syndrome.^{6,15,16} Hence, the study goals were as follows: (1) to estimate the prevalence of cardiac structure and function abnormalities in a randomly selected cohort of community-dwelling adults with no metabolic syndrome, isolated metabolic syndrome, and metabolic syndrome including hypertension and diabetes and (2) to evaluate the effect of sex on cardiac structure and function in these groups.

PARTICIPANTS AND METHODS

The institutional review boards of Mayo Clinic and Olmsted Medical Center approved this study, and all patients gave written informed consent. Characteristics of this population have been described previously.¹⁷ Of the 106,470 residents of Olmsted County, Minnesota, 96% are white. A 7% random population sampling fraction was applied in each sex and 5-year age stratum of the population.¹⁷ Of the 4203 adults aged 45 years or older on January 1, 1997, who were invited to participate, 2042 (48.6%) completed the study and comprised the Olmsted County Heart Function Study (OCHFS) cohort. Participants were studied during a 3-year period, ending September 30, 2000. Data were collected prospectively according to a research protocol. Medical records were abstracted for previous cardiovascular events and risk factors by trained nurse abstractors, as previously described.¹⁷ The median medical record archive length was 36 years.

Participants underwent a physical examination. Waist circumference was measured at the top of the umbilicus and hip circumference at the greatest diameter.

SUBGROUP DEFINITIONS

In accordance with the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria,¹⁸ metabolic syndrome was defined by the presence of 3 or more of the following criteria: (1) central obesity defined as a waist circumference greater than 102 cm in men and greater than 88 cm in women, (2) triglyceride level higher than 150 mg/dL (to convert to mmol/L, multiply by 0.0113), (3) high-density lipoprotein cholesterol level less than 40 mg/dL (to convert to mmol/L, multiply by 0.0259) in men and less than 50 mg/dL in women, (4) blood pressure of 130/85 mm Hg or higher, and (5) fasting glucose level of 110 mg/dL (to convert to mmol/L, multiply by 0.0555) or higher. To establish isolated metabolic syndrome, persons with elevated blood pressure or fasting blood glucose level who did not meet criteria for hypertension or diabetes mellitus were included. Hypertension was diagnosed using Joint National Committee VI criteria.¹⁹ A patient was determined to have diabetes mellitus if the condition was diagnosed by a staff physician and documented in the medical record.

ECHOCARDIOGRAPHIC EVALUATION

Patients underwent 2-dimensional, M-mode, and tissue Doppler echocardiography according to a standardized protocol, as previously described.^{17,20–22} A single echocardiologist (M.M.R.) independently interpreted all echocardiograms.

Ejection fraction was measured by M-mode echocardiography, by the quantitative 2-dimensional (biplane Simpson) method, and by the semiquantitative 2-dimensional visual estimate method.^{17,21,22} As previously described, final analyses used visual estimate ejection fraction because there was a high correlation among these 3 methods.¹⁷ Systolic dysfunction was defined as an ejection fraction of less than 50%.¹⁸ Left atrial volume index was measured as previously described.²² The LV mass was measured using standard formulas, based on M-mode measurement of diastolic dimension and wall thickness.

As previously described and validated, diastolic dys-function was assessed by pulsed-wave Doppler examination of mitral flow (before and during Valsalva maneuver) and pulmonary venous inflow, as well as by Doppler tissue imaging of the mitral annulus^{17,22,23} (Table 1). Diastolic dysfunction was graded on a 4-point ordinal scale: normal; mild diastolic dysfunction, defined as abnormal relaxation without increased LV end-diastolic filling pressure (peak early (E) to peak late [atrial] [A] diastolic filling velocity ratio <0.75); moderate or “pseudonormal” diastolic dysfunction, defined as abnormal relaxation with increased LV end-diastolic filling pressure (E/A ratio of 0.75 to 1.5, deceleration time >140 ms, and 2 other Doppler indices of elevated LV end-diastolic filling pressure); or severe diastolic dysfunction, defined as advanced reduction in compliance with restrictive filling (E/ A ratio >1.5, deceleration time <140 ms, and Doppler indices of elevated LV end-diastolic filling pressure). For patients in atrial fibrillation, diastolic function was classified as indeterminate unless restrictive physiologic factors (E/A ratio >1.5, deceleration time <140 ms) were present.

STATISTICAL ANALYSES

Categorical data are summarized as a percentage of the group total with corresponding 95% confidence intervals (CIS). Comparison among groups was made by the χ^2 test. Continuous variables are summarized as mean $\pm$ SD, and comparisons among groups were based on analysis of variance models. Post hoc analysis of variance comparisons of continuous variables were based on the *t* test, but no adjustments for multiple comparisons were made. Logistic regression analysis, stratified for sex, was performed for prevalence of echocardiographic abnormalities among patients with isolated metabolic syndrome and compared with those without metabolic syndrome. Echocardiographic variables were compared among the groups with no metabolic syndrome, isolated metabolic syndrome, and metabolic syndrome with hypertension and diabetes mellitus to assess for trend across groups. $P<.05$ was considered statistically significant. Analyses were performed with JMP statistical software, version 5 (SAS Institute, Cary, NC).

RESULTS

Of the 2042 persons in the cohort, 776 (38.0%) fulfilled NCEP ATP III metabolic syndrome criteria (Table 2). To identify persons with isolated metabolic syndrome, 673 persons (33.0%) with established diabetes mellitus or hypertension were excluded from the cohort. After this exclusion, 391 persons (19.1%) still fulfilled NCEP ATP III criteria and were considered to have isolated metabolic syndrome. The prevalence of isolated metabolic syndrome was 21.7% (214/984) in men and 16.7% (177/1058) in women. Among the 673 excluded persons with diabetes or hypertension, 385 (57.2%) also met NCEP ATP III metabolic syndrome criteria.

The prevalences of heart failure, valvular heart disease, and coronary artery disease in the entire population were 2.5% (51/2042), 4.8% (98/2042), and 4.2% (86/2042), respectively. Use of medications that affect LV remodeling (β -blockers, angiotensin-converting enzyme inhibitors) did not differ considerably between those patients without metabolic syndrome and those with isolated metabolic syndrome but was significantly higher in those with metabolic syndrome ($P<.001$).

PREVALENCE OF METABOLIC SYNDROME COMPONENTS

In participants with isolated metabolic syndrome, a low level of high-density lipoprotein cholesterol was the most prevalent component of metabolic syndrome in both men and women (90.7% [194/214] and 84.2% [149/177], respectively), followed by elevated blood pressure (80.4% [172/214] and 82.5% [146/177], respectively). Women had a significantly higher prevalence of central obesity, defined by waist circumference, than men (74.6% [132/177] vs 60.7% [130/214], respectively; $P<.001$).

ECHOCARDIOGRAPHIC CHARACTERISTICS

Table 3 gives the echocardiographic data for men and women combined. A trend was seen toward an increased mild LV diastolic dysfunction in the transition from no metabolic syndrome to isolated metabolic syndrome (14.5% [183/1266] to 17.9% [70/391]). Greater changes in left atrial volume index, LV mass index, and LV systolic and diastolic dysfunction were observed in the transition from isolated metabolic syndrome to metabolic syndrome. As continuous variables, both blood pressure and serum glucose level had a significant positive correlation with LV mass index ($P<.001$ for both), LV enddiastolic dimension ($P=.004$ and $P<.001$, respectively), and diastolic dysfunction ($P<.001$ for both).

Cardiac structure and function data were then stratified by sex (Table 4 and Table 5). Among men, no substantial changes were found in the transition from no metabolic syndrome to isolated metabolic syndrome; however, in the transition from isolated metabolic syndrome to metabolic syndrome, increases in LV mass index, regional wall motion abnormalities, LV systolic dysfunction, and LV diastolic dysfunction were observed (Figure). In contrast, among women, LV mass index increased substantially from no metabolic syndrome to isolated metabolic syndrome (87.9 ± 19.0 to 91.7 ± 21.5 g/m²; $P=.04$). Increased LV mass index in women was associated with a doubling of the prevalence of mild LV diastolic dysfunction from 9.7% (53/544) to 20.9% (37/177). Among women, further significant increases in LV mass index ($P<.001$) and LV diastolic dysfunction ($P=.002$) were observed in moving from isolated metabolic syndrome to metabolic syndrome (Figure).

Among women, the risk of having LV diastolic dysfunction increased in the transition from no metabolic syndrome to isolated metabolic syndrome (unadjusted odds ratio, 2.38; 95% CI, 1.58–3.59; $P<.001$). After age adjustment, women with isolated metabolic syndrome still had higher odds of LV diastolic dysfunction than women without metabolic syndrome (age-adjusted odds ratio, 1.82; 95% CI, 1.13–2.93; $P=.01$).

DISCUSSION

The current study estimates the association between echocardiographic structure and function abnormalities and isolated metabolic syndrome in a randomly selected population-based cohort of adults 45 years or older. Mild LV diastolic dysfunction was more prevalent and LV mass index was greater in women with isolated metabolic syndrome than in women without metabolic syndrome. This finding was not seen in men. When patients with established hypertension or diabetes mellitus were reincluded in the analysis, an increase was seen in cardiac structure and function abnormality from isolated metabolic syndrome to metabolic syndrome (including hypertension and diabetes mellitus) in both women and men.

PREVALENCE

Studies from the Third National Health and Nutrition Examination Survey (age >20 years) report the prevalence of metabolic syndrome (including established diabetes mellitus and hypertension) to be between 17% and 27%.^{2,24} In our cohort, 774 (37.9%) of the 2042 persons fulfilled the NCEP ATP III criteria, likely because of the older age range in the OCHFS cohort (<45 years). Indeed, patients older than 60 years in the Third National Health and Nutrition Examination Survey had a metabolic syndrome prevalence of 42% to 43%.^{2,24,25}

LV MASS

Increased LV mass is associated with coronary heart disease, stroke, and heart failure.^{26–29} Metabolic syndrome has been associated with prevalent CVD in most studies, including the population-based Strong Heart Study.^{7,14,15,30–32} This observation is of clinical importance because treatment leading to regression in LV mass can improve cardiovascular prognosis.

^{33,34} In the OCHFS cohort, women with isolated metabolic syndrome had a greater LV mass index than women without metabolic syndrome, demonstrating that women with isolated metabolic syndrome already manifest measurable abnormalities in LV structure. The use of medications known to affect LV mass index was not notably different between the no metabolic syndrome and isolated metabolic syndrome groups.

LV DIASTOLIC DYSFUNCTION

The prevalence of LV diastolic dysfunction was higher in women with isolated metabolic syndrome than in women without metabolic syndrome, a difference predominantly explained by an increase in mild LV diastolic dysfunction. In 2 previous studies of patients with established hypertension, the prevalence of LV diastolic dysfunction in metabolic syndrome was slightly increased (defined by Doppler flow and tissue Doppler imaging) or no different (defined by transmitral E/A velocity ratio only).^{30,32} Data from the Strong Heart Study did not show deterioration in diastolic function in patients with metabolic syndrome.¹⁴ The OCHFS cohort was larger and older than these other cohorts. Our criteria for LV diastolic dysfunction were more comprehensive and perhaps better suited to identify mild LV diastolic dysfunction.

Because blood pressure and serum glucose level both positively correlated with LV mass index and LV diastolic dysfunction in this study, the modest magnitude of the increase in LV diastolic dysfunction among persons with isolated metabolic syndrome was likely due to the exclusion of patients with diabetes mellitus and hypertension. When those patients were included in the analysis, a progression was seen in LV diastolic dysfunction from no metabolic syndrome to isolated metabolic syndrome to metabolic syndrome that included hypertension and diabetes. This progressive increase in LV mass index and LV diastolic dysfunction is consistent with the concept that isolated metabolic syndrome is an early stage in the evolution of a risk factor complex, which is reflected in progressive adverse remodeling and LV diastolic dysfunction.^{22,34–36}

The pathophysiologic mechanisms for the increased prevalence of LV diastolic dysfunction in women with isolated metabolic syndrome are uncertain. Growing evidence highlights the different effect of CVD risk factors, including metabolic syndrome, on future CVD and mortality in men and women.^{37,38} Possible mechanisms may relate to different pathophysiologic roles of inflammation, insulin resistance, and adipokines in women.^{37,39} Women have increased LV systolic and diastolic stiffness and increased aortic vascular stiffness compared with men.²⁰ This finding may be an important mechanism for development of subsequent heart failure, especially in elderly women. Similarly, current evidence suggests that women are more sensitive to the development of advanced glycation end products, which are known to increase the risk of CVD in persons with insulin resistance and metabolic syndrome.^{40,41} Erdogan et al⁴² showed that fasting hypertriglyceridemia, a surrogate marker of insulin resistance, correlates with carotid intima media thickness only in women.

The association of LV diastolic dysfunction with metabolic syndrome in women was most strongly influenced by waist circumference and elevated blood pressure. Metabolic syndrome is characterized by insulin resistance, which is strongly associated with central obesity. Indeed, central obesity has been proposed to be an important underlying pathophysiologic factor in metabolic syndrome.^{40,41}

CLINICAL IMPORTANCE OF METABOLIC SYNDROME

The value of the diagnosis of metabolic syndrome has been challenged because it includes persons with established hypertension and diabetes mellitus, components already known to be CVD risk factors. Because persons with established hypertension or diabetes mellitus are already candidates for primary and secondary CVD prevention, it has been suggested that the

additional classification of metabolic syndrome does not add to the already established need for risk factor management.^{43–48} However, metabolic syndrome also includes persons with mild hyperglycemia, but not diabetes, who are at an increased risk of developing overt diabetes.^{45–49} Established hypertension is a powerful risk factor for CVD, but those with prehypertension may already manifest detrimental changes in cardiac structure and function. The current study shows that, at least in women, isolated metabolic syndrome is already associated with abnormal LV structure and function. The increase in LV mass index is physiologically consistent with an increase in LV diastolic dysfunction. The identification of isolated metabolic syndrome in women may be an indication that aggressive preventive measures should not be postponed until overt hypertension or diabetes mellitus has developed.

STUDY STRENGTHS AND LIMITATIONS

The strengths of this study include its randomly selected population-based sample, the availability of medical records with a 36-year median length of archive, uniform prospective data collection, and standardized echocardiographic measurements. The concern for participation bias (48.6% participation rate) has been diminished by demonstration of a similar prevalence of CVD in participants and nonparticipants.⁵⁰ Our cohort includes only persons aged 45 years or older, and conclusions cannot be generalized to younger cohorts. Another potential limitation is lack of ethnic diversity; if groups of races other than white have a higher prevalence of metabolic syndrome, the OCHFS estimates may underestimate the prevalence of metabolic syndrome in the overall US population. These data are cross-sectional and cannot demonstrate longitudinal progression or establish causation.

CONCLUSION

Isolated metabolic syndrome is associated with an increase in LV mass index and diastolic dysfunction in women but not in men. This finding suggests that isolated metabolic syndrome in women, absent established diabetes mellitus or hypertension, is already associated with early signs of ventricular remodeling and dysfunction that may increase the risk of CVD.

Glossary

CI, confidence interval; CVD, cardiovascular disease; LV, left ventricular; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; OCHFS, Olmsted County Heart Function Study.

Acknowledgments

This study was supported by Public Health Service, National Institutes of Health grants HL55902 (R.J.R.) and AR30582 (S.J.J.).

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Figure 1. Prevalence of left ventricular diastolic dysfunction (LVDD) (left) and left ventricular mass index (LVMI) values (right) in men and women with no metabolic syndrome, isolated metabolic syndrome, and metabolic syndrome (including hypertension and diabetes mellitus).

TABLE 1

Doppler Criteria for Classification of Diastolic Dysfunction^a

	Normal diastolic function	Mild DD (impaired relaxation)	Moderate DD (pseudonormal)	Severe DD (reversible restrictive)	Severe DD (fixed restrictive)
Mitral inflow	0.75 < E/A < 1.5 DT > 140 ms ΔE/A < 0.5	E/A ≤ 0.75 ΔE/A < 0.5	0.75 < E/A < 1.5 DT > 140 ms ΔE/A ≥ 0.5	E/A > 1.5 DT < 140 ms ΔE/A < 0.5	E/A > 1.5 DT < 140 ms ΔE/A < 0.5
Mitral inflow at peak Valsalva maneuver					
Doppler tissue imaging of mitral annular motion	E/e' < 10	E/e' < 10	E/e' ≥ 10	E/e' ≥ 10	E/e' ≥ 10
Pulmonary venous flow	S ≥ D ARdur < Adur	S > D ARdur < Adur	S < D or ARdur > Adur + 30 ms Impaired	S < D or ARdur > Adur + 30 ms Impaired	S < D or ARdur > Adur + 30 ms Impaired
LV relaxation	Normal	Impaired	Impaired	Impaired	Impaired
LV compliance ^b	Normal	Normal to ↓	↓	↓	↓↓↓
Atrial pressure ^b	Normal	Normal	↑↑	↑↑↑	↑↑↑↑

^a A = peak late (atrial) diastolic filling velocity; Adur = duration of mitral A wave; ARdur = pulmonary venous atrial reversal flow duration; D = diastolic forward flow; DD = diastolic dysfunction; DT = mitral peak early filling velocity deceleration time; E = peak early diastolic filling velocity; e' = early diastolic mitral annular velocity; LV = left ventricular; S = systolic forward flow.

^b The number of arrows indicates relative increase (↑) or decrease (↓) without any quantitative value.

TABLE 2

Characteristics of Patients With No Metabolic Syndrome, Isolated Metabolic Syndrome, and Metabolic Syndrome, Stratified by Sex^{a,b}

Characteristic	Men				Women			
	No metabolic syndrome (n=434)	Isolated metabolic syndrome (n=214)	metabolic syndrome (n=197) ^c	P value for trend	No metabolic syndrome (n=544)	Isolate metabolic syndrome (n=177)	metabolic syndrome (n=188) ^c	P value for trend
Age (y)	60.0±10.0	59.4±9.3	65.6±9.6 ^d	<.001	60.6±10.4 ^e	64.2±10.4	67.7±10.5 ^d	<.001
Current smokers	55 (12.7)	24 (11.2)	16 (8.1)	.11	40 (7.4)	19 (10.7)	10 (5.3)	.67
HDL-C (mg/dL) ^{f,g}	43.0±11.0 ^e	32.3±7.0	33.3±7.0	<.001	56.8±13.1 ^e	42.4±9.5	42.3±10.2	<.001
Fasting glucose (mg/dL) ^{f,g}	93.1±7.7 ^e	103.2±24.2	119.0±43.0 ^d	<.001	90.4±6.8 ^e	97.6±15.4	109±27.5 ^d	<.001
Triglycerides (mg/dL) ^{f,g}	117.9±63.4 ^e	204.0±93.4	204.5±138.2	<.001	116.9±52.0 ^e	191.7±83.8	192.6±81.6	<.001
Total cholesterol (mg/dL)	198.7±35.2	200.6±35.5	190.1±36.1 ^d	.02	208.8±33.0 ^e	215.6±40.0	208.9±34.7	.57
BNP (pg/mL)	34.1±59.8	25.5±52.4	78.2±162.5	<.001	47.5±59.3	46.3±51.5	61.5±72.1	.02
Weight (kg)	83.7±12.4 ^e	98.5±16.7	96.3±17.5	<.001	67.4±12.6 ^e	81.2±15.9	83.5±17.7	<.001
Waist circumference (cm) ^f	94.2±9.0 ^e	105.8±11.2	105.4±12.1	<.001	78.5±10.0 ^e	94.5±12.5	96.2±12.5	<.001
Height (cm)	175.2±7.1	177.2±7.2	174.8±6.4 ^d	.42	161.4±6.4	160.6±6.6	160.3±6.7	.03
Hip circumference (cm)	101.0±6.6 ^e	108.0±9.2	107.1±9.8	<.001	100.5±10.0 ^e	110.8±12.9	111.3±12.6	<.001
Body mass index (kg/m ²)	27.0±3.4 ^e	31.3±4.7	31.5±5.1	<.001	25.9±4.6 ^e	31.2±5.7	32.5±6.2	<.001
Edema	12 (2.8)	12 (5.6)	28 (14.2) ^d	<.001	42 (7.7) ^e	31 (17.5)	40 (21.3)	<.001
Systolic BP (mm Hg) ^f	126.2±16.5 ^e	137.1±14.9	145.3±18.5 ^d	<.001	123.6±18.4 ^e	139.2±16.9	147.1±19.5 ^d	<.001
Diastolic BP (mm Hg) ^f	76.2±9.1 ^e	81.6±9.0	81.7±10.0	<.001	71.4±9.3 ^e	78.1±10.7	77.3±10.9	<.001
Sitting HR (beats/min)	68.6±11.2 ^e	72.7±11.6	70.9±12.5	<.001	70.5±9.9 ^e	72.9±9.4	72.2±12.6	.01

^a BNP = brain natriuretic peptide; BP = blood pressure; HDL-C = high-density lipoprotein cholesterol; HR = heart rate.

^b Data are expressed as mean ± SD for continuous variables and number (percentage) of participants for categorical variables.

^c Includes hypertension and diabetes mellitus.

^d $P < .05$ for comparison of isolated metabolic syndrome and metabolic syndrome that includes hypertension and diabetes.

^e $P < .001$ for comparison of no metabolic syndrome and isolated metabolic syndrome.

^fComponents of the metabolic syndrome definition.

^gSI conversion factors: To convert cholesterol values (HDL-C, total) to mmol/L, multiply by 0.0259; to convert fasting glucose values to mmol/L, multiply by 0.0555; to convert triglyceride values to mmol/L, multiply by 0.0113; to convert BNP values to ng/L, multiply by 1.0.

TABLE 3

Comparison of Cardiac Structure and Function in Patients With No Metabolic Syndrome, Isolated Metabolic Syndrome, and Metabolic Syndrome^{a,b}

	No metabolic syndrome (n=1266)	Isolated metabolic syndrome (n=391)	Metabolic syndrome (n=385) ^c	P value for trend
Men	573 (45.3)	214 (54.7)	197 (51.2)	
LAV index (cm/m ²)	24.8±11.5	23.6±6.1	27.5±10.1	.001
LVEDD (cm)	4.9±0.5	4.9±0.5	5.0±0.6	.003
LVMI (g/m ²)	94.9±21.5	96.1±20.7	106.0±26.5	<.001
EF (%)	62.8±6.8	63.1±6.6	62.6±8.8	.98
RWMA	57 (4.5)	13 (3.3)	26 (6.8)	.15
EF <50%	64 (5.1)	19 (4.9)	40 (10.4)	<.001
EF <40%	21 (1.7)	5 (1.3)	14 (3.6)	.04
Mild LVDD	183 (14.5)	70 (17.9)	112 (29.1)	<.001
Moderate-severe LVDD	81 (6.4)	18 (4.6)	38 (9.9)	<.001

^a EF = ejection fraction; LAV = left atrial volume; LVDD = left ventricular diastolic dysfunction; LVEDD = left ventricular end-diastolic dimension; LVMI = left ventricular mass index; RWMA = regional wall motion abnormality.

^b Data are expressed as mean ± SD for continuous variables and number (percentage) of participants for categorical variables.

^c Includes hypertension and diabetes mellitus.

Table 4

Cardiac Structure and Function in Patients With No Metabolic Syndrome, Isolated Metabolic Syndrome, and Metabolic Syndrome, Stratified by Sex^{a,b}

	Men			Women				
	No metabolic syndrome (n=434)	Isolated metabolic syndrome (n=214)	Metabolic syndrome (n=197) ^c	P value for trend	No Metabolic syndrome (n=544)	Isolated Metabolic syndrome (n=177)	Metabolic syndrome (n=188) ^c	P value for trend
LAV index (cm/ms)	24.9±8.3	23.7±6.3	29.0±11.1 ^d	<.001	23.0±7.7	23.5±5.8	26.0±8.7 ^d	<.001
LVEDD (cm)	5.1±0.5	5.2±0.5	5.3±0.6	.02	4.7±0.4	4.7±0.4	4.8±0.5	.44
LVMi (g/m ²)	98.9±18.8	100.5±18.8	110.8±26.9 ^d	<.001	87.9±19.0 ^e	91.7±21.5	101.6±25.5 ^d	<.001
EF (%)	60.8±6.8	61.1±6.7	59.8±9.3	.17	64.3±5.5 ^e	65.5±5.6	65.6±7.0	.003
RWMA	24 (5.5)	11 (5.1)	22 (11.2) ^d	.02	6 (1.1)	2 (1.1)	4 (2.1)	.33
EF <50%	25 (5.8)	15 (7.0)	32 (16.2) ^d	<.001	14 (2.6)	4 (2.3)	8 (4.3)	.30
EF <40%	11 (2.5)	3 (1.4)	12 (6.1) ^d	.04	2 (0.4)	2 (1.1)	2 (1.1)	.25

^aEF = ejection fraction; LAV = left atrial volume; LVEDD = left ventricular end-diastolic dimension; LVMI = left ventricular mass index; RWMA = regional wall motion abnormality.

^bThis table excludes participants with hypertension or diabetes who do not meet criteria for metabolic syndrome. Data are expressed as mean ± SD for continuous variables and number (percentage) of participants for categorical variables.

^cIncludes hypertension and diabetes mellitus.

^d $P < .05$ for comparison between isolated metabolic syndrome and metabolic syndrome (including hypertension and diabetes).

^e $P < .05$ for comparison of no metabolic syndrome and isolated metabolic syndrome.

TABLE 5
Prevalence of Diastolic Dysfunction in Patients With No Metabolic Syndrome, Isolated Metabolic Syndrome, and Metabolic Syndrome, Stratified by Sex^{a,b}

	Men				Women			
	No metabolic syndrome (n=434)	Isolated metabolic syndrome (n=214)	Metabolic syndrome (n=197) ^c	P value for trend	No metabolic syndrome (n=544)	Isolated metabolic syndrome (n=177)	Metabolic syndrome (n=188) ^c	P value for trend
Normal diastolic function	298 (68.7)	150 (70.1)	80 (40.6) ^d	<.001	420 (77.2) ^e	109 (61.6)	80 (42.6) ^d	<.001
Abnormal diastol function (%)	75 (17.3)	38 (17.8)	75 (38.1) ^d	<.001	81 (14.9) ^e	50 (28.2)	75 (39.9) ^d	<.001
Mild LVDD (%)	58 (13.4)	33 (15.4)	54 (27.4) ^d	.005	53 (9.7) ^e	37 (20.9)	58 (30.9) ^d	<.001
Moderate-severe LVDD (%)	17 (3.9)	5 (2.3)	21 (10.7) ^d	.26	28 (5.1)	13 (7.3)	17 (9.0)	.02
Indeterminate diastolic function ^f	61 (14.1)	26 (12.1)	39 (19.8) ^d	.08	43 (7.9)	18 (10.2)	33 (17.6) ^d	<.001
Abnormal diastolic function subgroup classification								
Abnormal relaxation (mild)	58 (13.4)	33 (15.4)	54 (27.4) ^d	<.001	53 (9.7) ^e	37 (20.9)	58 (30.9) ^d	<.001
Abnormal relaxation; increased LVEDP (moderate)	0 (0.0)	0 (0.0)	2 (1.0)	NA	1 (0.2)	1 (0.6)	1 (0.5)	.31
Pseudonormal (moderate)	16 (3.7)	5 (2.3)	17 (8.6) ^d	.43	25 (4.6)	11 (6.2)	15 (8.0)	.15
Restrictive, reversible (severe)	0 (0.0)	0 (0.0)	1 (.05)	NA	0 (0.0)	1 (0.6)	0 (0.0)	NA
Restrictive, fixed (severe)	1 (0.2)	0 (0.0)	1 (.05)	NA	2 (0.4)	0 (0.0)	0 (0.0)	NA

^a LVDD = left ventricular diastolic dysfunction; LVEDP = left ventricular end-diastolic pressure; NA = not applicable (values not calculated because of small numbers of patients).

^b Data are expressed as number (percentage) of participants.

^c Includes hypertension and diabetes mellitus.

^d $P < .05$ for comparison of isolated metabolic syndrome and metabolic syndrome that includes hypertension and diabetes.

^e $P < .001$ for comparison of no metabolic syndrome and isolated metabolic syndrome.

^f Participants with atrial fibrillation with deceleration time >140 ms, other arrhythmia, and fusion of peak early filling velocity and peak late (atrial) filling velocity, those in whom diastolic parameters were not obtained, those who had only 1 criterion suggesting moderate or severe diastolic dysfunction, and those in whom diastolic parameters were borderline and suggestive of but not diagnostic of abnormality were classified as having indeterminate diastolic function.