Usefulness of left ventricular mass change to predict progression of renal dysfunction in Hispanics

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ABSTRACT

There is a strong relation between metabolic syndrome (MetS) and left ventricular (LV) mass in Hispanic patients. This population also tends to have a higher incidence of kidney disease, with progression to dialysis. We analyzed the change in LV mass in 982 Hispanic patients with MetS and used these data to anticipate the progression of renal dysfunction. Glomerular filtration rate (GFR) was calculated using the formula described by the Chronic Kidney Disease Epidemiology Collaboration. Echocardiographic data were collected using 2-dimensionally guided M-mode echocardiography measures. The data collected were then analyzed using linear regression analyses. Results showed a lower average GFR in individuals classified as having a severe change in LV mass in comparison to those with milder change in LV mass ($P < 0.0001$). This relation was also demonstrated when those with severe change in LV mass were compared with the control group ($P < 0.0001$). In those ≥ 54 years old, the presence of MetS and LV mass were negatively correlated with GFR (regression coefficient [RC] = 14.76, $P < 0.063$; RC = 0.11, $P < 0.0001$ respectively). In patients < 54 years old, no statistically significant association between the presence of MetS and GFR was seen. However, LV mass was once again negatively correlated with GFR (RC = 0.15, $P < 0.0001$). In conclusion, results demonstrated the association between the MetS, change in LV mass, and chronic kidney disease progression.

KEYWORDS Heart failure; metabolic syndrome; renal failure

In a recently published study, the relation between metabolic syndrome (MetS) and its components was investigated along with changes in left ventricular (LV) mass and LV mass index in Hispanics. Results of the study demonstrated a strong relation between MetS and LV mass. Furthermore, it was demonstrated that the MetS components along with advanced age had a strong influence on LV mass. These relations were particularly strong in the Hispanic population.¹ Hispanic patients who tend to have an increased prevalence of the MetS also tend to have a higher incidence of chronic kidney disease that is associated with increased LV mass. This study highlights an interesting association in a unique population and aims to determine whether LV mass change could be used to predict the progression of renal dysfunction in a predominantly Hispanic patient population.

METHODS

In a single-center retrospective controlled study at the University Medical Center of El Paso, Texas, data were collected from

Hispanic patients who underwent an echocardiogram during the period between January 1, 2012, and May 31, 2013. From this population, the study group had at least one component of MetS, whereas the control group had no component of MetS.

MetS was defined by the presence of at least 3 of the following characteristics according to the recently modified definition based on American Heart Association/National Heart, Lung and Blood Institute criteria:

- Triglycerides ≥ 150 mg/dL
- HDL C < 50 mg/dL for women and < 40 mg/dL for men
- BMI ≥ 30 kg/m² for men and ≥ 25 kg/m² for women
- Blood pressure $\geq 130/85$ mm Hg or on antihypertensive medications
- Fasting blood glucose ≥ 100 mg/dL or on medications for diabetes mellitus^{2,3}

The Institutional Review Board at the University Medical Center of El Paso and Texas Tech Health Sciences Center

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approved the study. Because this was a retrospective study, no informed consent was required.

The data collected after reviewing the medical records of the study population and control group consisted of demographic and risk factor measures including age, sex, ethnicity, fasting blood glucose, HDL C, triglycerides, systolic and diastolic blood pressures, height and weight measures (to calculate body mass index [BMI] and body surface area), and creatinine levels. Creatinine level was used to calculate glomerular filtration rate (GFR) based on the Chronic Kidney Disease Epidemiology Collaboration equation, which served as a marker of kidney function. Patients with incomplete data were excluded and data were collected from 2-dimensionally guided M-mode echocardiography measurements. Continuous data were described using appropriate measures such as mean, standard deviation, median, interquartile range, and range, and categorical data were described using frequency and proportion. Continuous data were compared according to MetS status using unpaired *t* test/Wilcoxon rank sum test. One-way analysis of variance/Kruskal-Wallis test was used for

comparing continuous data according to LV mass categories. All of the categorical variables were compared according to MetS status and LV mass categories using Fisher's exact test. Unadjusted and adjusted associations of continuous LV mass and MetS status on GFR were obtained using linear regression analyses. Unadjusted linear regression was used to determine the effect of each cofactor on GFR. All significant variables at a 10% level of significance were considered for multivariable linear regression analysis. First-order interactions were also explored for important variables. In the presence of significant interaction, we carried out stratified analysis. $P \leq 0.05$ was considered significant. Statistical analysis was conducted using SAS 9.3.

RESULTS

A total of 989 Hispanic patients were included in the study. Of those, 834 were determined to have MetS and 155 were used as a control group. An association was found between MetS status and age, ethnicity, proteinuria, categorized GFR, actual GFR, LV mass, and LV mass index. Average

Table 1. Comparison of variables according to MetS status

Variables	Total (n = 989)	MetS (n = 834)	Non-MetS (n = 155)	P value
Age (mean, SD)	52.2 ± 11.1	54.7 ± 8.6	38.4 ± 13	<0.0001
Gender				0.93
Male	529 (53.5%)	447 (53.6%)	82 (52.9%)	
Female	460 (46.5%)	387 (46.4%)	73 (47.1%)	
Ethnicity				
Hispanic	989 (100%)	834 (84.3%)	155 (15.7%)	
Proteinuria				<0.0001
0	611 (61.8%)	484 (58%)	127 (81.9%)	
1	202 (20.4%)	182 (21.8%)	20 (12.9%)	
2	76 (7.7%)	69 (8.3%)	7 (4.5%)	
3	47 (4.8%)	46 (5.5%)	1 (0.7%)	
4	53 (5.4%)	53 (6.4%)	0 (0.0%)	
GFR categorized (mL/min/1.73 m ²)				<0.0001
(>90)	577 (58.3%)	469 (56.2%)	108 (69.7%)	
(60–90)	195 (19.7%)	159 (19.1%)	36 (23.2%)	
(30–60)	107 (10.8%)	97 (11.6%)	10 (6.5%)	
(15–30)	34 (3.4%)	33 (4%)	1 (0.7%)	
(<15)	76 (7.7%)	76 (9.1%)	0 (0.0%)	
GFR (mean, SD)	86.8 ± 36.8	83.5 ± 37.2	104.8 ± 29	<0.0001
Creatinine (median, interquartile range)	0.82 (0.62, 1.09)	0.82 (0.61, 1.17)	0.81 (0.66, 0.94)	0.117 ^a
LV mass (mean, SD)	184.57 ± 82.3	195.8 ± 84.7	124.3 ± 32.3	<0.0001
LV mass index (mean, SD)	95.75 ± 40.82	101.2 ± 41.5	66.6 ± 18.8	<0.0001
Relative wall thickness, cm (mean, SD)	0.43 ± 0.11	0.43 ± 0.12	0.44 ± 0.06	0.312

LV indicates left ventricular; MetS, metabolic syndrome; GFR, glomerular filtration rate.

^aP value was extracted from Wilcoxon rank sum test.

LV mass was found to be higher in patients with MetS compared to the non-MetS group ($P < 0.0001$). Average GFR was lower in individuals with MetS when compared to the non-MetS group ($P < 0.0001$). A comparison of all of the variables is provided in *Table 1*. The presence of MetS as well as associated variables were separately analyzed according to the severity of changes in LV mass. The presence of MetS was associated

with an increase in the LV mass ($P < 0.0001$). All of the variables analyzed are presented in *Table 2*. A direct correlation was observed with severity of proteinuria and severity of LV mass category ($P < 0.0001$). The average GFR was higher in individuals classified as having a severe change in LV mass compared to milder categories and compared to the control group ($P < 0.0001$).

Table 2. Comparison of variables according to LV mass categories

Variables	Normal (n = 124)	Mild (n = 88)	Moderate (n = 93)	Severe (n = 684)	P value
Age, in years (mean, SD)	47.3 ± 12.8	44.5 ± 13.6	51.9 ± 11.5	54.1 ± 9.6	<0.0001
MetS					<0.0001
Case	79 (63.7%)	51 (58%)	70 (75.3%)	634 (92.7%)	
Control	45 (36.3%)	37 (42.1%)	23 (24.7%)	50 (7.3%)	
Triglycerides (mg/dL)					<0.0001
≥150	30 (24.2%)	17 (19.3%)	35 (37.6%)	285 (41.7%)	
<150	94 (75.8%)	71 (80.7%)	58 (62.4%)	399 (58.3%)	
Glucose (mg/dL)					<0.0001
≥100	56 (45.2%)	37 (42.1%)	52 (55.9%)	490 (71.6%)	
<100	68 (54.8%)	51 (58%)	41 (44.1%)	194 (28.4%)	
HDL (mg/dL)					<0.0001
Male (<40), female (<50)	42 (33.9%)	31 (35.2%)	43 (46.2%)	445 (65.1%)	
Male (≥40), female (≥50)	82 (66.1%)	57 (64.8%)	50 (53.8%)	239 (34.9%)	
BMI (kg/m ²)					0.0002
Male (≥30), female (≥25)	57 (46%)	49 (55.7%)	53 (57%)	450 (66%)	
Male (<40), female (<50)	67 (54%)	39 (44.3%)	40 (43%)	234 (34.2%)	
Blood pressure (mm Hg)					<0.0001
Systolic ≥ 130 or diastolic ≥ 80	60 (48.4%)	46 (52.3%)	60 (64.5%)	601 (87.9%)	
Systolic < 130 or diastolic < 80	64 (51.6%)	42 (47.7%)	33 (35.5%)	83 (12.1%)	
Proteinuria					<0.0001
0	102 (82.3%)	60 (68.2%)	67 (72.0%)	382 (55.9%)	
1	13 (10.5%)	21 (23.9%)	13 (14%)	155 (22.7%)	
2	5 (4.0%)	6 (6.8%)	9 (9.7%)	56 (8.2%)	
3	1 (0.8%)	1 (1.1%)	3 (3.2%)	42 (6.1%)	
4	3 (2.4%)	0 (0.0%)	1 (1.1%)	49 (7.2%)	
GFR categorized (mL/min/1.73 m ²)					<0.0001
>90	95 (76.6%)	69 (78.4%)	64 (68.8%)	349 (51.0%)	
60–90	18 (14.5%)	13 (14.8%)	18 (19.4%)	146 (21.4%)	
30–60	7 (5.7%)	6 (6.8%)	7 (7.5%)	87 (12.7%)	
15–30	0 (0.0%)	0 (0.0%)	2 (2.2%)	32 (4.7%)	
<15	4 (3.2%)	0 (0.0%)	2 (2.2%)	70 (10.2%)	
GFR (mean, SD)	105.3 ± 32.2	102.5 ± 24.7	96.2 ± 30.4	80.2 ± 37.7	<0.0001
Creatinine (median, interquartile range)	0.75 (0.6, 0.9)	0.74 (0.6, 0.9)	0.74 (0.6, 0.9)	0.87 (0.7, 1.2)	<0.0001 ^a
Relative wall thickness, cm (mean, SD)	0.42 ± 0.09	0.43 ± 0.09	0.44 ± 0.1	0.44 ± 0.12	0.137

BMI indicates body mass index; GFR, glomerular filtration rate; HDL, high-density lipoprotein cholesterol; LV, left ventricular; MetS, metabolic syndrome.

^aP value was extracted from Wilcoxon rank sum test.

Table 3. Unadjusted association of variables with average GFR

Variable	RC	95% Confidence interval		P value
Age	−1.02	−1.22	0.83	<0.0001
Male	4.71	0.11	9.31	0.044
Triglycerides (mg/dL) ≥ 150	−4.87	−9.62	−0.12	0.044
Glucose (mg/dL) ≥ 100	−16.04	−20.73	−11.35	<0.0001
HDL (mg/dL); male < 40, female < 50	−8.84	−13.45	−4.23	0.0002
BMI (kg/m ²); male ≥ 30, female ≥ 25	0.09	−4.63	4.82	0.969
Blood pressure (mm Hg); systolic ≥ 130 or diastolic ≥ 80	−20.57	−25.92	−15.21	<0.0001
MetS	−21.3	−27.48	−15.12	<0.0001
Number of MetS disorders (reference of 0)				
1	−6.25	−16.52	4.02	0.232
2	−21.93	−31.8	−12.07	<0.0001
3	−25.53	−34.92	−16.14	<0.0001
4	−22.9	−32.1	−13.7	<0.0001
5	−25.81	−35.46	−16.16	<0.0001
LV mass	−0.13	−0.16	−0.1	<0.0001
LV mass index	−0.3	−0.35	−0.25	<0.0001
Relative wall thickness (cm)	−32.24	−53.07	−11.41	0.002

BMI indicates body mass index; GFR, glomerular filtration rate; HDL, high-density lipoprotein cholesterol; LV, left ventricular; MetS, metabolic syndrome.

Each variable was individually analyzed to determine its effect on GFR. It was determined that per unit increase in age, a reduction in average GFR by 0.92 mL/min/1.73 m² occurred. Average GFR was found to be higher in male patients. Further analysis of the association of GFR with the individual components of MetS revealed that all components of MetS were associated with GFR except BMI. Elevated blood pressure had the greatest inverse correlation with GFR (regression coefficient [RC] = 20.57, $P < 0.0001$), suggesting that elevated blood pressure led to the greatest decrease in GFR. Triglycerides had the lowest inverse correlation with GFR (RC = 4.87, $P < 0.044$). GFR was found to be negatively associated with

Table 4. Adjusted analysis of cofactors with GFR

Variable	RC	95% Confidence interval		P value
Age	−0.18	−0.58	0.22	0.375
Male	9.42	5.07	13.77	<0.0001
MetS (yes)	42.19	20.07	64.31	0.0002
LV mass	−0.12	−0.15	−0.1	<0.0001
Age * MetS	−0.94	−1.42	−0.45	0.0002

GFR indicates glomerular filtration rate; LV, left ventricular; MetS, metabolic syndrome; RC, regression coefficient.

LV mass (RC = 0.13, $P < 0.0001$), suggesting that lower LV mass was associated with higher GFR and therefore a lower risk of progression to end-stage renal disease requiring renal replacement therapy (Table 3).

Multivariable analysis was used to establish a relationship between gender, MetS status, LV mass, and GFR. A significant interaction was observed between age and MetS status on GFR (Table 4). To further explore the relationship, patients were stratified into 2 categories based on age. In individuals ≥ 54 years old, the presence of MetS and LV mass was negatively correlated with GFR (RC = 14.76, $P < 0.063$; RC = 0.11, $P < 0.0001$, respectively). In patients < 54 years old, no statistically significant association between the presence of MetS and GFR was found. However, LV mass was once again negatively correlated with GFR (RC = 0.15, $P < 0.0001$). Male gender was positively correlated with GFR regardless of age (Table 5).

DISCUSSION

In the initial phase of the study, the association between MetS components and LV mass was investigated. It was found that LV mass is higher in patients with 3 or more components of MetS and that higher LV mass is associated with lower high-density lipoprotein, higher blood pressure, higher fasting serum glucose, and obesity. These findings were used to conclude that there is, in fact, an association between components of MetS and LV mass in a predominantly Hispanic study population. In addition, our study showed a higher incidence of chronic kidney disease that is associated with increased LV mass among Hispanics who also tend to have an increased prevalence of MetS. This association suggests

Table 5. Effects of MetS status and LV mass on GFR according to different age categories

Variable	Age ≥ 54 (n = 531)				Age < 54 (n = 458)			
	RC	95% Confidence interval		P value	RC	95% Confidence interval		P value
Male	11.34	5.42	17.26	0.0002	7.95	1.37	14.52	0.018
MetS	−14.76	−30.33	0.8	0.063	−0.79	−8.42	6.83	0.838
LV mass	−0.11	−0.15	−0.07	<0.0001	−0.15	−0.19	−0.11	>0.0001

GFR indicates glomerular filtration rate; LF, left ventricular; MetS, metabolic syndrome; RC, regression coefficient.

that a change in LV mass could be used to predict the progression of renal dysfunction among Hispanics. Age, ethnicity, proteinuria, GFR, LV mass, and LV mass index were all associated with MetS status. The presence of MetS was associated with higher LV mass and lower average GFR. To further characterize the association between MetS and GFR, each component of MetS was analyzed with regard to its effect on GFR; all components of MetS except BMI were associated with changes in GFR. Blood pressure was found to have the largest inverse relationship with GFR, whereas elevations in triglycerides were found to have the lowest inverse relationship with GFR.

Age and MetS were found to have a significant effect on GFR. In individuals ≥ 54 years of age, the presence of MetS and LV mass was negatively correlated with GFR, whereas in individuals < 54 years of age, there was no statistically significant relationship. However, in this age group, LV mass was inversely correlated with GFR, suggesting the presence of an independent negative correlation between LV mass and GFR. Male gender was positively correlated with GFR regardless of age. Proteinuria, as measured by urine dipstick, was also compared in patients with and without components of MetS. The presence of any degree of proteinuria was found to be higher in subjects with MetS than in those without MetS (43% vs 18%). Subjects with MetS were also found to have higher degrees of proteinuria. Although urine dipstick is poorly sensitive to exact measurements of proteinuria, the consistency of the association between MetS components and the qualitative assessment of proteinuria suggests a true relationship between chronic kidney disease and MetS as measured by increased urinary protein.

The association between cardiovascular risk and chronic kidney disease has long been established; however, causality is yet to be definitively determined. We hypothesize that MetS is likely a key component in this puzzle given its strong association with the development of cardiovascular disease. A literature review revealed 2 studies from 2004 and 2015 that investigated the relationship between MetS and chronic kidney disease. In a cross-sectional study designed to compare the presence of components of MetS and chronic kidney disease in the United States, participants with 2 or more components of MetS were found to have an increased risk of developing chronic kidney disease.⁵ A more recent study examining the association between MetS and proteinuria was a population-based, cross-sectional study of Korean adults that revealed that MetS was associated with an increased risk of microalbuminuria.⁶ All components of MetS showed an increased risk of microalbuminuria, with the greatest risk seen with elevated blood pressure. This increased risk was seen in a dose-dependent manner, with the highest risk observed in subjects with all components of MetS. A recent observation noting increased cardiovascular mortality in living kidney donors prompted the investigation of the cardiac complications of the decrease in GFR noted in living donors. LV mass change was compared in a multicenter,

parallel-group, blinded end point study of living kidney donors and healthy controls.⁷ It was noted that in donors compared to controls, there were significant increases in LV mass ($+7 \pm 10$ vs -3 ± 8 g; $P < 0.001$) and mass:volume ratio ($+0.06 \pm 0.12$ vs -0.01 ± 0.09 g/mL; $P < 0.01$) with a simultaneous decrease in GFR of -30 ± 12 mL/min/ 1.73 m². These changes in GFR were independently associated with increases in LV mass and therefore suggest that GFR should be regarded as an independent cardiovascular risk factor. This association between reduction in GFR and increases in LV mass in kidney donors can be easily translated in nondonors with reduced GFR. Along with our findings, these associations provide a potential means of predicting progression of renal dysfunction in high-risk patients.

The hallmark limitation of the study is replacing abdominal waist circumference with BMI; however, this was done in accordance with the International Diabetes Federation guidelines that use BMI > 25 kg/m² in females and BMI > 30 kg/m² in males to determine central obesity.⁴ In addition, had we used a more direct measure of intra-abdominal obesity rather than BMI, a stronger impact of obesity might have been evident. The discrepancy in size between the control group and the study sample could limit the results derived from the control group. Another limitation we acknowledge is the retrospective nature of the study. Among the population studied, the occurrence of LV hypertrophy as a binary variable was not determined. Finally, this study was conducted in a predominantly Hispanic population to investigate the relationship between MetS and kidney function in this ethnic group; it is uncertain whether our conclusions could be generalized for other ethnic groups.

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