The Association Between Metabolic Syndrome and its Components and Heart Failure in Patients Referred to a Primary Care Facility

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Summary

Background: Metabolic syndrome (MS) is characterized by a collection of risk factors that are associated with elevated rates of cardiovascular events and the risk of developing heart failure (HF). In our field, the association of MS in stable chronic HF patients has not been established.

Objective: To determine the prevalence of MS in relation to gender and HF type in patients treated at a Primary Care Facility.

Methods: Between January 2005 and August 2006, 144 patients were included in a cross sectional study. An echocardiogram, using the modified criteria of the EPICA study, was performed to determine whether or not the patient had HF, and of which type. Statistical analysis was conducted using the software SAS™ System, version 6.04, and statistical significance was established as 5%.

Results: MS was observed in 111 patients (77%), of which 73 (66%) were females: odds ratio (OR) 0.195 – (confidence interval - CI = 0.08 – 0.46) and p< 0.0001. HF was identified in 102 patients (71%) with a great correlation between females and the presence of MS: 51 patients (65%); OR 0.116 (CI = 0.36 – 0.37) and p < 0.0001. Among the HF patients, 61 (42%) presented HF with preserved systolic function and 41 (29%) with systolic dysfunction; p= ns. HF with preserved systolic function was associated with the presence of MS in 53 (87%) of the 61 patients, p = 0.022.

Conclusion: In our community, MS is closely related to HF with preserved systolic function and to the female gender. (Arq Bras Cardiol 2007; 89(1) : 37-45)

Key words: Metabolic syndrome; heart failure; cardiac output, low; primary health care; women.

Introduction

Metabolic Syndrome (MS) is characterized by a cluster of risk factors such as, elevated waist circumference, systemic hypertension (SH), hyperglycemia, insulin resistance and dyslipidemia (reduced HDL and elevated triglyceride levels). The presence of this cluster of factors is associated with elevated rates of cardiovascular events: sudden death, acute myocardial infarction (AMI) and encephalic stroke as well as a higher risk to develop diabetes mellitus (DM)[1-4].

In different adult populations, an elevated prevalence of MS is observed that ranges from 25 to 35%[5,6], and it is more common in women. Different criteria have been used to diagnose MS including those of WHO (World Health Organization)[7], NCEP-ATP III (National Cholesterol Education Program Panel III)[8] and more recently the criteria of IDF (International Diabetes Federation)[7-9].

Ever increasing amounts of solid epidemiological proof indicate an association between MS and the presence of cardiovascular alterations. Recently, a greater risk of the onset of heart failure (HF) was identified, particularly in middle aged and elderly men[1-4].

In our community, the prevalence of MS and its components in HF patients and differences in relation to gender have not yet been established.

Methods

Between January 2005 and August 2006, 150 patients were included in a cross sectional study involving patients with clinical suspicion of HF treated by the Family Medical Program (FMP). The patients were referred to a specialized HF outpatient clinic for diagnostic confirmation of HF by means of clinical criteria and echocardiography (ECHO). The population sample of HF patients was estimated at 100 patients based on the population of 100,000 patients treated by FMP and a HF prevalence of 1% to 2% for the overall population in accordance with data from the Framingham study[10].

Inclusion criteria - Patients with suspected HF – presence of dyspnea, fatigue or edema in the lower limbs or asymptomatic patients using digitalis and/or ACE inhibitors

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and/or diuretics. All patients had to be over the age of 18 and referred by the FMP.

Exclusion criteria - Lack of required data for analysis of the presence of MS (Laboratory tests) or HF (echocardiography) and other types of HF that did not include: HF with preserved systolic function or HF with systolic dysfunction. The M-mode or two dimensional transthoracic echocardiogram, in accordance with the modified criteria of the EPICA study for community HF patients[11], was used to determine whether or not the patient had HF and its type. The HF patients were identified according to the functional and structural alterations evaluated on the ECHO.

Structural alterations evaluated on the echocardiogram - 1) LV fractional shortening < 28%; 2) significant segment alterations associated with LV dilation; 3) LV mass index > 134 g/m² in males and > 110 g/m² in females; 4) hypertrophy of the interventricular septum and LV posterior wall according to the parameters for age and gender; 5) increased LA (left atrium) diameter according to the parameters for age and gender; 6) moderate to severe valve lesions of rheumatic origin; 7) moderate to severe pericardial hemorrhage; 8) RV dilation.

Structural alterations that determined HF type - 1) fractional shortening < 28% or the presence of significant segment alterations associated with LV dilation; - classified as HF with systolic dysfunction; 2) fractional shortening > 28% with no segment alteration, however with the presence of increased LA, or LV mass index (differentiated by gender), or hypertrophy of the interventricular septum or LV posterior wall; - classified as HF with preserved systolic function.

Upon admission to the study, the patients were clinically assessed and underwent PA and left lateral view chest x-rays, 12 lead ECG and the following biochemical tests: 1) fasting glucose; 2) triglycerides; 3) HDL cholesterol for composition of the MS criteria.

Determination of the MS components in accordance with the NCEP-ATP III criterium was performed using the following values: 1) Waist circumference > 102cm for males and 88cm for females; 2) Triglycerides ≥150mg/dl; 3) HDL-c < 40mg/dl for males and < 50mg/dl for females; 4) SBP ≥130X85mmHg and 5) blood glucose level ≥110mg/dl; and in accordance with the IDF criterium: 1) Waist circumference >94cm for males and 80cm for females; 2) Triglycerides ≥150mg/dl, 3) HDL-c < 40mg/dl for males and < 50mg/dl for females; 4) SBP ≥130X80mmHg and 5) blood glucose level ≥100mg/dl.

The use of hypoglycemic or antihypertensive medication was designated as a positive criterium. MS was confirmed by the NCEP ATP III criterium when three of the five possible components were present[7]. MS confirmation using the IDF components required an alteration in waist circumference along with two other alterations[8,9]. DM was determined by glucose levels ≥ 126 mg% and insulin resistance by glucose values between 100 and 125 mg%.

The variables evaluated in this model were: age, gender, blood pressure, waist circumference, blood glucose level, HDL, TG, BMI as well as the ECHO data to determine whether or not the patient had HF and of which type. The study was approved by the Research Ethics Committee at the Medical School of the Federal Fluminense University. All patients signed a free and informed consent form to participate in the study.

Statistical analysis - Mean value difference was calculated using the Student's t-test to estimate the association between the presence of HF with MS. Proportion differences and the prevalence odds ratio were calculated using the chi-square test ($\chi 2$). Statistical significance was established as 5%. Statistical analysis was performed using the software program SAS® System, version 6.04.

Results

The clinical and metabolic characteristics of the patients included in the study that were referred to the Primary Care Clinic with suspected HF are shown in table 1. From the sample of 150 patients, six were excluded due to moderate to severe valve disease. The study involved 144 patients of which 82 (57%) were females. No statistical differences were observed in relation to mean age or gender for this group.

A higher incidence of MS was observed using the IDF diagnostic criterium, and was diagnosed in 103 patients (72%), of which 69 (67%) were females; $p < 0.0001$. Using the NCEP-ATP III criterium, 65 patients (70%) were females; $p < 0.0001$.

HF was confirmed by the echocardigraphic criteria in 102 patients (71%) and there was a higher incidence of HF with preserved systolic functionin 61 patients (42%); p = ns.

No significant differences were found between the MS components and gender when the mean value of the measurements that determined the presence of MS was used. The only exception was BMI that was higher in the female group; $p = 0.032$; (Table 1).

No statistical significance was found in relation to age, gender, or incidence of MS components when analyzing whether or not the patients had HF. However, the HF patients had a greater incidence of insulin resistance syndrome; $p = 0.07$ and DM; $p = 0.09$; (Table 2).

Characterization of MS in relation to HF type revealed a greater incidence of HF with preserved systolic function; odds ratio (OR) 3.82 – confidence interval (CI) 1.4 to 10 and $p = 0.005$. The most prevalent MS components associated with HF with preserved systolic function were: SBP, DBP, waist circumference (IDF and NCEP ATP III criterium), triglycerides and BMI.

The presence of MS was determined using the mean values of the MS components. In relation to HF type, the greatest component association was found in the HF group with preserved systolic function with the presence of 3.6 ± 1.0 components (IDF criterium), $p = 0.009$ and 3.2 ± 1.1 components (NCEP-ATP III criterium), $p = 0.017$; (Table 3).

Evaluation of the prevalence of MS, using both criteria (NCEP and IDF), the presence of MS associated with HF was found in 79 patients (78%). A significant correlation was found in both groups between HF type, IDF and NCEP criteria, of which HF with preserved systolic function had greater prevalence with both the NCEP ($p = 0.020$) and IDF criteria ($p = 0.010$). The MS prevalence was 49 patients (80%) for HF with preserved systolic function and 22 patients (54%)

Table 1- Clinical characteristics of the population with suspected HF referred to a primary care facility

Characteristics	Total group (n)	Females (n)	Males (n)	p value
Number of patients n (%)	144	82 (57)	62 (43)	ns
Mean age (years) (SD)	61±13	61±12	61±14	ns
Prevalence of MS n (%)				
MS present	111 (77.1)	73 (66)	38 (34)	< 0.0001
IDF	103 (71.5)	69 (67)	34 (33)	< 0.0001
NCEP	93 (64.6)	65 (70)	28 (30)	< 0.0001
Prevalence of HF n (%)				
HF present	102 (71)	55 (54)	47 (46)	
SHF	41 (29)	18 (44)	23 (56)	ns
DHF	61 (42)	37 (61)	24 (39)	
Criteria evaluated for MS diagnosis mean (SD)				
SBP (mmHg)	150.1±314	152±32	148±30	ns
DBP (mmHg)	90.3±16	90±17	91±15	ns
Waist circumference (cm)	96.1±13	96±14	96±12	ns
Blood glucose (mg%)	112±40	116±46	107±31	ns
HDL-cholesterol (mg%)	45.6±13.7	47±15	44±12	ns
Triglycerides (mg%)	158±88	164±93	152±81	ns
BMI (Kg/m²)	28.5±5.7	29.4±6.2	27.4±4.7	0.032
Mean of the MS components n (SD)				
IDF	3.2±1.2	3.5±1.0	2.8±1.2	< 0.001
NCEP-ATP III	2.9±1.2	3.2±1.0	2.4±1.0	< 0.001

IDF - International Diabetes Federation; NCEP-ATP III - National Cholesterol Education Program Panel III; HF - heart failure; MS - metabolic syndrome; SHF - systolic heart failure; DHF - diastolic heart failure; SBP - systolic blood pressure; DBP - diastolic blood pressure; HDL-cholesteral - high density cholesterol; BMI - body mass index.

for HF with systolic dysfunction in accordance with the IDF criterium. Using the NCEP-ATP III criterium, MS prevalence was 47 patients (77%) for HF with preserved systolic function and 21 patients (51%) for HF with systolic dysfunction; (Graphics 1, 2 and 3).

Evaluation of the association between HF and MS by gender indicated that women with HF are 8 times more likely to present MS than men in accordance with both the NCEP and/or IDF criteria; OR 0.116 - CI 0.36 – 0.37 and p< 0.0001, (Table 4).

Discussion

This study, the first to evaluate the presence of MS in stable chronic HF patients treated in Primary Care facilities in Brazil, identified an elevated prevalence of MS and HF in these patients. The presence of MS in this scenario was identified using the NCEP-ATP III criteria and the new determinations of IDF. We found a greater frequency of MS in females (70% and 67%, respectively), using the NCEP-ATP III and IDF criteria. HF with preserved systolic function had a greater association with MS and was also more prevalent in females.

The significant association between the presence of MS and the female gender, as demonstrated in earlier studies[12,13], could be indirectly correlated to the alterations presented, such as elevated triglycerides (53%), abdominal adiposity, SH (94%) and elevation of BMI (46%), that are inherent characteristics of females like hormonal alterations. Therefore, these factors could represent the decisive alterations in our case study to justify the presence of HF with preserved systolic function in females, determining the possible structural alterations presented on the ECHO; this was the link in the correlation found in our study between the presence of HF with preserved systolic function and the female gender.

Recently, MS has been identified as an independent risk factor for the onset of HF[1-4,14]. The possible mechanisms associated with MS that cause HF are still speculative. Nevertheless, evidence suggests that the damage to cardiac cellular integrity caused by MS can favor the development of HF. Just as the stimulating effect of insulin on the myocardium of mice leads to increased cardiac mass and consequent reduction of cardiac output[15], hyper stimulation of the sympathetic nervous system, caused by hyperinsulinemia, as well as its ability to promote fibroblast activation in

Table 2 – Heart failure odds ratio as per metabolic syndrome components

		General heart failure						
		Present		Absent				
Variable	Category	n	%	n	%	p value	Odds ratio	Confidence interval
Age	≥ 61	56	55	20	48	0.43	1.34	0.65 - 2.75
	≤ 60	46	45	22	52			
Gender	female	55	54	27	64	0.25	1.54	0.73 - 3.22
	male	47	46	15	36			
MS	yes	79	78	32	76	0.87	1.07	0.46 - 2.51
	no	23	22	10	24			
IDF	yes	71	70	32	76	0.43	0.72	0.31 - 1.64
	no	31	30	10	24			
NCEP	yes	68	67	25	59	0.41	1.36	0.65 - 2.85
	no	34	33	17	41			
SBP (mmHg)	> 130	70	64	27	68			
	≤ 130	32	36	15	31	0.61	1.21	0.57 - 2.59
DBP (mmHg)	≤ 80	67	66	27	64			
	> 80	35	34	15	36	0.87	1.06	0.50 - 2.25
DBP (mmHg)	> 85	63	62	26	62			
	≤ 85	39	38	16	38	0.98	0.99	0.47 - 2.08
WC – IDF (cm)	IDF altered	73	72	35	17			
	normal	29	28	7	57	0.2	0.5	0.21 - 1.26
WC – NCEP (cm)	NCEP altered	54	53	23	55			
	normal	48	47	19	45	0.84	0.93	0.45 - 1.91
HDL (mg%)	altered	53	52	22	52			
	normal	49	48	20	48	0.96	0.98	0.48 - 2.02
Triglycerides (mg%)	> 149	43	42	19	45			
	≤ 149	59	58	23	55	0.73	0.88	0.43 - 1.81
Glucose (mg%)	> 99	58	57	20	48			
	≤ 99	44	43	22	52	0.31	1.45	0.70 - 2.98
Glucose (mg%)	> 109	35	34	8	19			
	≤ 109	67	66	34	81	0.07	2.22	0.92 - 5.31
Glucose (mg%)	> 126	23	23	4	9			
	≤ 126	79	77	38	91	0.09	2.77	0.89 - 8.56
BMI (Kg/m^2)	> 30	37	36	14	33			
	≤ 30	65	64	28	67	0.73	1.14	0.53 - 2.43

MS - metabolic syndrome; IDF - International Diabetes Federation; NCEP-ATP III - National Cholesterol Education Program Panel III; SBP - systolic blood pressure; DBP - diastolic blood pressure; WC – IDF - waist circumference > 94 cm for Men and > 80 cm for Women; WC-NCEP ATP III - waist circumference > 102 cm for Men and > 88 cm for Women; HDL-cholesterol - high density cholesterol; BMI - body mass index.

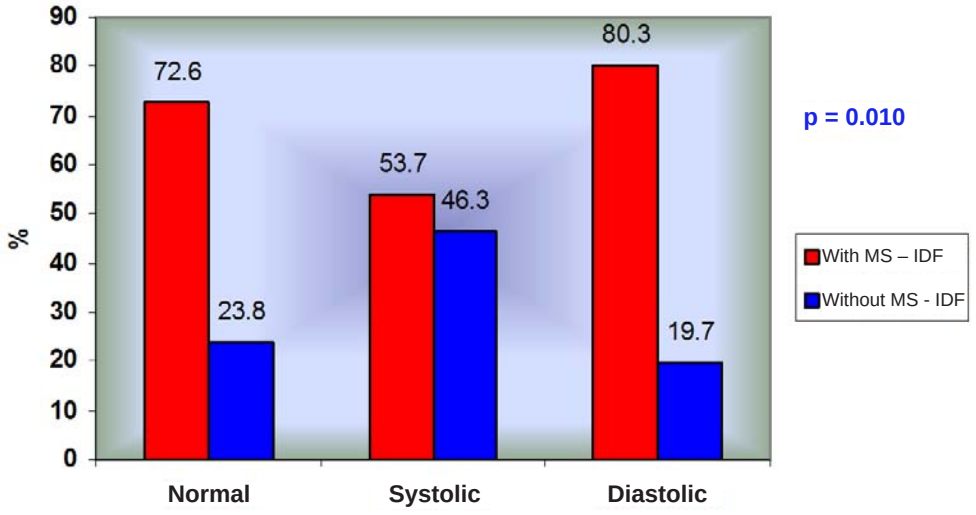
hypertensive patients, causing LV hypertrophy, increases the production of collagen and fibrosis[16]. This collection of actions causes disease progression and greater mortality.

HF is regarded as an emerging cardiovascular epidemic whose increase is directly related to population growth as well as the alarming increase in conditions that favor its onset, in particular the MS components - DM, SH, Dyslipidemia and Obesity[17]. Therefore, it is of utmost importance to identify HF risk factors that can be modified in order to enable adequate intervention.

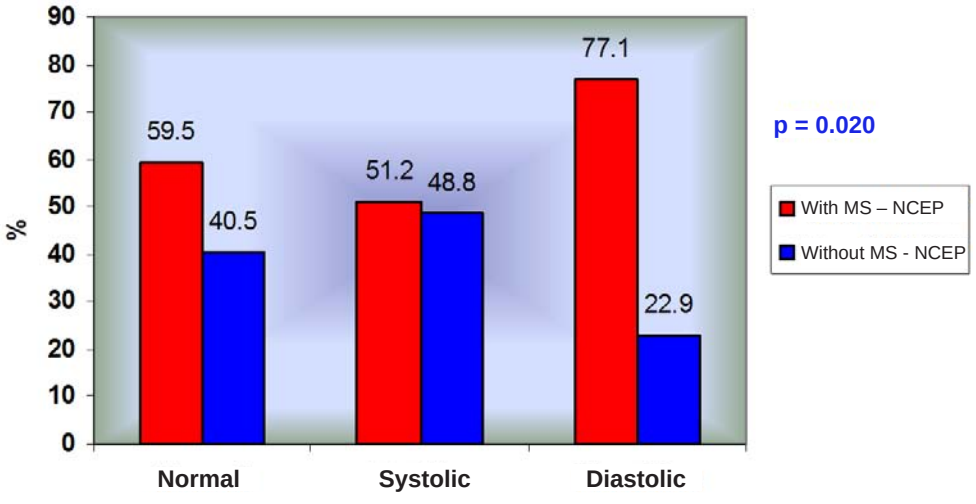
Table 3 – DHF odds ratio (in relation to SHF) according to the metabolic syndrome components

		Heart failure						
		DHF		SHF				
Variable	Category	n	%	n	%	p value	Odds ratio	Confidence interval
Age	≥ 61	34	56	22	54			
	≤ 60	27	44	19	46	0.84	1.09	0.49 - 2.40
Gender	female	37	61	18	44			
	male	24	39	23	56	0.09	0.51	0.23 - 1.13
MS	yes	53	87	26	63			
	no	8	13	15	37	0.005	3.82	1.44 - 10.2
IDF	yes	49	80	22	54			
	no	12	20	19	46	0.004	3.53	1.47 - 8.51
NCEP	yes	47	77	21	51			
	no	14	23	20	49	0.007	3.2	1.36 - 7.52
SBP (mmHg)	> 130	47	77	23	56			
	≤ 130	14	23	18	44	0.025	2.63	1.11 - 6.19
DBP (mmHg)	≤ 80	46	75	21	51			
	> 80	15	25	20	49	0.012	2.92	1.25 - 6.80
DBP (mmHg)	> 85	44	72	19	46			
	≤ 85	17	28	22	54	0.009	3	1.31 - 6.90
WC - IDF (cm)	IDF altered	51	84	22	54			
	normal	10	16	19	46	0.001	4.4	1.76 - 11
WC – NCEP (cm)	NCEPaltered	39	64	15	37			
	normal	22	36	26	63	0.007	3.07	1.35 - 6.99
HDL (mg%).	altered	33	54	20	49			
	normal	28	46	21	51	0.59	1.24	0.56 - 2.73
Triglycerides (mg%)	> 149	32	53	11	27			
	≤ 149	29	47	30	73	0.01	3.009	1.28 - 7.07
Glucose (mg%)	> 99	38	62	20	49			
	≤ 99	23	38	21	51	0.18	1.73	0.78 - 3.87
Glucose	> 109	21	34	14	34			
	≤ 109	40	66	27	66	0.97	1.01	0.44 - 2.33
Glucose	> 126	14	23	9	22			
	≤ 126	47	77	32	78	0.91	1.05	0.41 - 2.74
BMI (Kg/m²)	> 30	28	46	9	22			
	≤ 30	33	54	32	78	0.014	3.02	1.23 - 7.38
Mean of components present for the different HF types								
IDF		3.6 ± 1.0		2.8 ± 1.3		0.009		
NCEP-ATP III		3.2 ± 1.1		2.5 ± 1.3		0.017		

MS - metabolic syndrome; IDF - International Diabetes Federation; NCEP-ATP III - National Cholesterol Education Program Panel III; SBP - systolic blood pressure; DBP - diastolic blood pressure; WC – IDF - waist circumference > 94 cm for Men and > 80 cm for Women; WC-NCEP ATP III - waist circumference > 102 cm for Men and > 88 cm for Women; HDL-cholesterol - high density cholesterol; BMI - body mass index.



Graphic 1 - *MS according to the IDF criterium and HF type.*



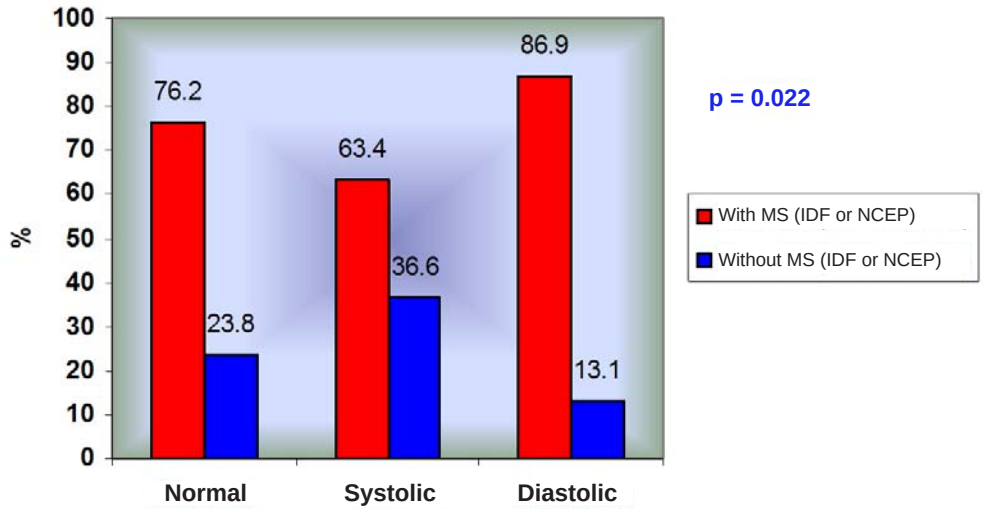
Graphic 2 - *MS according to the NCEP ATP III criterium and HF type.*

Visceral obesity, another factor correlated to MS, develops its aggressive role on the myocardium through the production of substances with cardiovascular and systemic actions,such as leptin, inflammatory cytokines (interleukins and tumor necrosis factor), plasminogen activator inhibitor-1 (PAI-1) and free fatty acids in addition to promoting a reduction of adiponectin[18]. Therefore, the loss of the protective vascular action generated by the reduction of the adiponectin levels[19,20], in conjunction with the inflammatory and prothrombotic action determines the substrate that will jeopardize the cardiovascular system.

Current concepts confirm that the physiopathlogy of HF is distinct in relation to gender and HF type[12,13]. In these studies, it is confirmed that HF with preserved systolic function is predominately associated with females, advanced age and a lower incidence of ischemic heart disease[21]. This fact correlates with data throughout the world as demonstrated by Rodrigues-Artalejo et al[22] where the number of female deaths increased between 1980-2000. This is an important fact that demonstrates nonconformity in relation to HF treatment for females.

Data from the EPICA study[11], that evaluated HF patients in a community, confirmed that HF in females occurs at a more advanced age and heart failure with preserved systolic function is more predominant.

Kenchaiah et al[23] demonstrated that the HF risk when related to an increase of one BMI unit is 5% for men and 7% for women and that when comparing the incidence of HF between obese and non-obese individuals this same increase doubles the risk which is higher for women – 2.12 (females) / 1.90 (males). Other studies[24] suggest that the female hormones affect heart function by means of estrogen-induced



Graphic 3 - *MS according to IDF or NCEP criteria and HF type.*

Table 4 - MS prevalence odds ratio by different criteria, according to gender

		HF present				
Characteristic		**Females**	**Males**	**p value**	**Odds ratio**	**Confidence interval**
MS	MS yes	51 (64.6)	28 (35.4)			
	MS no	4 (17.4)	19 (82.6)	< 0.0001*	0.116	0.36 – 0.37
IDF	MS yes	47 (66.2)	24 (33.8)			
	MS no	8 (25.8)	23 (74.2)	< 0.0001*	0.178	0.46 – 0.69
NCEP	MS yes	46 (66.7)	22 (32.4)			
	MS no	9 (26.5)	25 (73.5)	< 0.0001*	0.172	0.43 – 0.69

HF - heart failure; IDF - Internatinal Diabetes Federation; NCEP-ATP III - National Cholesterol Education Program Panel III; MS - metabolic syndrome present. NCEP-ATP III or IDF criteria HF in females with MS was associated with a greater prevalence in comparison to HF patients without MS.*

vasodilatation that in conjunction with SH could reduce rennin action and consequently reduce myocardial fibrosis.

A sub-study of Framingham[25], conducted between 1950 and 1999, determined that in a population of white individuals, there is a greater prevalence of HF in males, which can be explained by the higher incidence of atherosclerosis in males when compared to females. Barker et al[26] demonstrated that the HF epidemic increase occurred in the elderly male population (> 65 years), where the increased prevalence was directly associated to the increased incidence and therefore directly related to its greater survival rate. Other relevant data were demonstrated by Levy et al[27] where the association between HF and hypertension was more common in females; also, the risk to develop HF for individuals with SH was two-fold for males and three-fold for females.

In our study, a substantial under usage of hypoglycemia-inducing medication was confirmed, where in a population of 78 patients (54%) with blood glucose levels > 100mg/dl, only 37 patients (47%) used some type of oral hypoglycemia-inducing medication. Another significant correlation was the strong trend of the presence of HF in DM and insulin resistance syndrome patients, with respective p values of 0.07 and 0.09, odds ratio of 2.22 for the insulin resistant patients and 2.77 for the diabetic group (Table 3).

The US Health Maintenance Organization Study, demonstrated that a 1% increase in the level of glycosylated hemoglobin correlated to an increased risk of 15% to develop HF, demonstrating the important relationship between

dysglycemia and HF. Another significant correlation is that MS patients are two times more likely to develop atherosclerotic cardiovascular disease and five times more likely to develop DM[28]. It has also been demonstrated that LV wall thickness and mass are directly altered in relation to glucose intolerance; this is higher for the female gender[29].

A small observational and prospective study[30] demonstrated that patients treated with glitazones, had higher survival rates and lower HF risk, whereas another study[31] demonstrated that glitazones worsen survival rates and increase HF prevalence. These variances are probably related to the different study populations analyzed, where the first group could be a population with a better controlled heart disease. The PROACTIVE study demonstrated a greater number of hospital admissions but a stable mortality rate[32].

The under usage of medications related to MS and HF treatment was also confirmed in the dyslipidemia patients. The use of oral hypolipemia-inducing medication was only confirmed in 18 (12.5%) of the 111 (77.1%) MS patients in the study. For chronic HF patients, large studies involving the use of statins have systematically excluded HF patients. Therefore, the use of statins in chronic HF patients remains a topic for further discussion[33].

Prospective studies, such as the one by Node et al[34], demonstrated a functional capacity improvement in HF patients that received statins in comparison to those that received placebo, where a reduction in the levels of TNF-a, IL-6 and BNP were significantly greater in the sinvastatin group. Another prospective, double blind, randomized study used cerivastatin in patients with nonischemic dilated cardiomyopathy, confirming an improvement in quality of live, physical capacity and endothelial function[35]. Recently, the study called the TNT-study (Treating to New Targets) involved 10,001 patients with CAD and ejection fractions > 30% to evaluate the incidence of hospital admissions as a primary HF event. The study concluded that patients taking 80mg of artorvastatin, presented a reduction of 26% in hospital admission rates for HF[36]. Therefore, the study concluded that statins could reduce the incidence of new HF cases. The answers to these questions will probably come to light when two large placebo-controlled studies, that are currently in progress, called CORONA, (The Controlled Rosuvastatin Multinational Trial) involving HF patients with chronic systolic dysfunction and GISSI (GISSI heart failure trial) involving ischemic and nonischemic patients are concluded[33].

Conclusion

There is a high incidence of MS in our community; this condition has a significant association with HF with preserved systolic function and also with females.

References

1. Lakka HM, Laaksonnen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilento J, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA. 2002; 288 (21): 2709-16.
2. Poirier P, Eckel RH. Obesity and cardiovascular disease. Curr Atheroscler Rep. 2002; 4: 448-53.
3. Wilson PW, D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. Arch Intern Med. 2002; 162: 1867-72.
4. Ingelsson E, Ärnlöv J, Lind L, Sundström J. Metabolic syndrome and risk for heart failure in middle-aged men. Heart. 2006; 92: 1409-13.
5. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care. 1998; 21: 1414-31.
6. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey. JAMA. 2002; 287: 356-9.
7. Alberti KG, Zimmet PZ. Definition, diagnosis, and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med. 1998; 15: 539-53.
8. National Cholesterol Education Program: Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 2001; 285: 2486-97.
9. I Diretriz Brasileira de Diagnóstico e Tratamento da Síndrome Metabólica. Arq Bras Cardiol. 2005; 84 (supl 1): 3-28.
10. Ho KK, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: the Framingham study. J Am Coll Cardiol. 1993; 22: 6A-13A.
11. Ceia F, Fonseca C, Mota T, Morais H, Matias F, de Sousa A, et al., on behalf of the EPICA Investigators. Prevalence of chronic heart failure in Southwestern Europe: the EPICA study. Eur J Heart Fail. 2002; 4: 531-9.
12. Leiro MGC, Martín MJP. Insuficiencia cardiaca. ¿Son diferentes las mujeres? Rev Esp Cardiol. 2006; 59: 725-35.
13. Ghali JK, Krause-Steinrauf HJ, Adams KF, Khan SS, Rosenberg YD, Yancy CW, et al. Gender differences in advanced heart failure: insights from the BEST study. J Am Coll Cardiol. 2003; 42 (12): 2128-34.
14. Butler J, Rodondi N, Zhu Y, Figaro K, Fazio S, Vaughan DE, et al., Health ABC Study. Metabolic syndrome and the risk of cardiovascular disease in older adults. J Am Coll Cardiol. 2006; 47 (8): 1595-602.
15. Holmang A, Yoshida N, Jennische E, Waldenstrom A, Bjorntorp P. The effects of hyperinsulinaemia on myocardial mass, blood pressure regulation and central haemodynamics in rats. Eur J Clin Invest. 1996; 26: 973-8.
16. Anderson EA, Hoffman RP, Balon TW, Sinkey CA, Mark AL. Hyperinsulinaemia produces both sympathetic neural activation and vasodilation in normal humans. J Clin Invest. 1991; 87 (6): 2246-52.
17. Wong CY, O'Moore-Sullivan T, Fang ZY, Haluska B, Leano R, Marwick TH. Myocardial and vascular dysfunction and exercise capacity in the metabolic syndrome. Am J Cardiol. 2005; 96 (12): 1686-91.
18. Berg AH, Scherer PE. Adipose tissue, inflammation, and cardiovascular disease. Circ Res. 2005;96:939-49.
19. Kistorp C, Faber J, Galatius S, Gustafsson F, Frystyk J, Flyvbjerg A, et al. Plasma adiponectin, body mass index, and mortality in patients with chronic heart failure. Circulation. 2005; 112: 1756-62.
20. Ingelsson E, Risérus NEF, Berne C, Frystyk JM, Flyberg A, Alexander T, et al. Adiponectin and risk of congestive heart failure. JAMA. 2006; 295 (15): 1772-4.
21. Gustafsson F, Torp-Pedersen C, Burchardt H, Buch P, Seibaek M, Kjoller E, et al. Female sex is associated with a better long-term survival in patients

hospitalized with congestive heart failure. Eur Heart J. 2004; 25: 129-35.

22. Rodríguez-Artalejo F, Banegas Banegas J, Guallar-Castillón P. Epidemiología de la insuficiencia cardiaca. Rev Esp Cardiol. 2004; 57: 163-70.

23. Kenchaiah S, Evans J, Levy D, Wilson P, Benjamin E, Larson M, et al. Obesity and the risk of heart failure. N Engl J Med. 2002; 347: 305-13.

24. Fischer M, Baessler A, Schunkert H. Renin angiotensin system and gender differences in the cardiovascular system. Cardiovasc Res. 2002; 53: 672-7.

25. Levy D, Kenchaiah S, Larson M, Benjamin E, Kupka M, Ho K, et al. Long-term trends in the incidence of and survival with heart failure. N Engl J Med. 2002; 347: 1397-402.

26. Barker W, Mullooly J, Getchell W. Changing incidence and survival for heart failure in a well-defined older population, 1970-1974 and 1990-1994. Circulation. 2006; 113: 799-805.

27. Levy D, Larson M, Vasan R, Kannel W, Ho K. The progression from hypertension to congestive heart failure. JAMA. 1996; 275: 1557-62.

28. Grundy SM. Drug therapy of the metabolic syndrome: minimizing the emerging crisis in polypharmacy. Nat Rev Drug Discov. 2006; 5 (4): 295-309.

29. Rutter M, Parise H, Benjamin E, Levy D, Larson M, Meigs J, et al. Impact of glucose intolerance and insulin resistance on cardiac structure and function: sex-related differences in the Framingham Heart Study. Circulation. 2003; 107: 448-54.

30. Masoudi FA, Inzucchi SE, Wang Y, Havranek EP, Foody JAM, Krumholz HM. Thiazolidinediones, metformin, and outcomes in older patients with diabetes and heart failure: an observational study. Circulation. 2005; 111 (5): 583-90.

31. Delea TE, Edelsberg JS, Hagiwara M, Oster G, Phillips LS. Use of thiazolidinediones and risk of heart failure in people with type 2 diabetes: a retrospective cohort study. Diabetes Care. 2003; 26 (11): 2983-9.

32. Cleland JGF, Freemantle N, Coletta AP, Clark AL. Clinical trials update from the American Heart Association: REPAIR-AMI, ASTAMI, JELIS, MEGA, REVIVE-II, SURVIVE, and PROACTIVE. Eur J Heart Fail. 2006; 8 (1): 105-10.

33. Van der Harst P, Voors AA, Van Gilst WH, Böhm M, Van Veldhuisen DJ. Statins in the treatment of chronic heart failure: biological and clinical considerations. Cardiovasc Res. 2006; 71 (3): 443-54.

34. Node K, Fujita M, Kitakaze M, Hori M, Liao JK. Short-term statin therapy improves cardiac function and symptoms in patients with idiopathic dilated cardiomyopathy. Circulation. 2003; 108: 839-43.

35. Laufs U, Wassmann S, Schackmann S, Heeschen C, Bohm M, Nickenig G. Beneficial effects of statins in patients with non-ischemic heart failure. Z Kardiol. 2004; 93: 103-8.

36. LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. N Engl J Med. 2005; 352: 1425-35.