Prevalence of Diastolic Dysfunction in Non Diabetic Patients of Metabolic Syndrome

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Research

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Abstract

Background : The purpose of the present study was to study the prevalence of metabolic syndrome in non diabetic patients of metabolic syndrome

Materials and Methods: 100 patients of non diabetic metabolic syndrome were screened using 2-D Echocardiogram.

Results: 34% of non diabetic patients of metabolic syndrome had diastolic dysfunction, with no association found between the components of metabolic syndrome and diastolic dysfunction. There was a strong correlation between a past history of hypertension and dyslipidemia with diastolic dysfunction.

Conclusion: Our findings suggest that long standing metabolic syndrome is a risk factor for diastolic dysfunction, rather than short term elevation of the metabolic syndrome parameters. Also it is likely that Diabetes and Prediabetes itself is responsible for most of the diastolic dysfunction that is seen in metabolic syndrome

Introduction

The term metabolic syndrome was coined by Haller in1977.Also known as Syndrome X its main features are central obesity, dyslipidemia, hypertension and hyperglycemia. The cardiovascular risk factors comprising the metabolic syndrome are now considered the driving force behind the new cardiovascular disease (CVD) epidemic (1).

Presence of diastolic dysfunction (DD) in metabolic syndrome (MS) has been seen in several studies. Its incidence appear to range between 20-40% in the western population (1,2).However, several south east Asian studies show a much higher percentage of DD in MS, up to 73%(1,3,4).

These alarming numbers maybe due to the higher risk that Asian Indians have for coronary artery disease (CAD) because of their unique lipid profile. The dyslipidemia in South Asians is most importantly characterized by elevated levels of triglycerides, low levels of HDL-C, elevated Lp(a) levels, and a higher atherogenic particle burden despite relatively normal LDL-C levels. HDL particles appear to be smaller, dysfunctional, and proatherogenic in South Asians, thus leading to earlier CAD independent of other metabolic risk actors (5). Diastolic dysfunction occurs early in the ischemic cascade.(6). Thus it appears reasonable to postulate that the higher incidence of DD in MS in this region might be due to the higher incidence of early CAD in South Asians. In this context it is interesting to note that low HDL is the only variable not significantly associated with DD in a study from Serbia (7) while Khan et al, reporting on a similar study from Pakistan, showed a very strong association between low HDL and DD (4).

DD is characterized by left ventricular (LV) stiffness and impaired relaxation due to LV myocardial fibrosis. Several mechanisms are responsible for the same, from the cardiac remodeling seen in advanced hypertensive and diabetic patients to the insulin resistance and inflammation seen in

asymptomatic patients of metabolic syndrome (8).DD accounts for 50% of all admissions for acute heart failure (9) and has a cardiovascular mortality similar to systolic heart failure (10).For the asymptomatic patient, impaired exercise capacity limits activities of daily life.(11). Grade 1 DD causes 2 fold increase in all cause and cardiac mortality (12,13).It is now imperitive,from a medical and economic perspective to identify the patients of DD

While studies have been performed which show association between various components of MS with DD, with clear evidence that worsening grades of diastolic dysfunction are associated with increasing burden of metabolic syndrome(4,8), the contribution of each variable towards DD is not clear.

To assess the effect of individual components of MS on DD, it would require studies in which each of the three components; Diabetes, Hypertension and Dyslipidemia is excluded and the effect of the rest is evaluated on DD. W Dinh et al in 2010 showed that presence of diabetes and prediabetes leads to increased prevalence of DD in MS (14). However, to the best of our knowledge, such studies do not exist in the Asian context. Thus as a step towards determining the contribution and association of the various components of MS on DD, we present a study of the prevalence of DD in non-diabetic patients of MS from a tertiary care center in India

Methods

This study was conducted in Mangalore, a coastal city in Karnataka, South India. The period of study was from July 2013 to November 2013.The research protocol was approved by the Manipal university Institutional ethics committee. The metabolic syndrome was defined as following:

Central obesity (defined as waist circumference of greater than or equal to 90 cm in men and 80 cm in women)

Plus any two out of three of the following

i. TG Levels > 150 mg/dl or specific treatment for this lipid abnormality
ii. HDL < 40 mg/dl in males or < 50 mg/dl in females
iii. Systolic BP greater than or equal to 130 mm Hg and diastolic BP greater than or equal to 85 mm Hg or previously diagnosed hypertension

Patients with established diabetes mellitus or on treatment for same as well as impaired fasting glucose were excluded from the study as were patients with any myocardial disease other than diastolic dysfunction.

A total of 100 patients of non-diabetic MS were selected. Eligible patients were enrolled into the study after taking informed consent at visit 1. A detailed history and physical examination was done which included anthropometry, blood pressure measurement, signs and symptoms of diastolic heart failure.

Echocardiogram was performed by Tissue Doppler Imaging and the parameters were noted. Chi square test was used for determination of statistical significance

Results

Out of hundred patients 30 were females and 70 were males. The minimum age was 21 years and maximum of 60 years with a mean of 43.23+/-8.75.Weight ranged between 58 kgs to 117 kgs with a mean of 78.65+/-12. 17 patients had a normal BMI (b/w 18-24.99kg/m2),49 patients were overweight (BMI b/w 25-29.99 kg/m2) and 33 patients were obese(BMI >30 kg/m2)

42 out of hundred patients had a past history of hypertension, out of the rest 15 patients were normotensive at the time of examination and the remaining 43 had never been diagnosed with hypertension but had systolic and/or diastolic blood pressures elevated as per the IDF criterion.

Out of hundred patients, 27 had past history of dyslipidemia, and 73 were newly diagnosed with at the time of study. Out of the 27 pateints, 19 had poor lipid control with both components, i.e,triglycerides and HDL in abnormal range. 3 patients had abnormal HDL values (as per IDF) and 4 had elevated triglycerides.2 patients had normal HDL and triglyceride levels. Among the newly diagnosed, 52 had both components of lipid profile abnormality,18 patients had only elevated triglyceride and 3 had isolated HDL abnormality. 53 of the patients had impaired fasting glucose but did not meet the IDF criterion for Diabetes mellitus. The most prevalent metabolic abnormality was dyslipidemia, present in 100% of patients.

Out of 100 patients screened 34 had diastolic dysfunction. Out of 34, 27 had grade 1 diastolic dysfunction and 7 had grade 2 diastolic dysfunction

Table 1: Co-relation of diastolic dysfunction with individual components of metabolic syndrome compared by Chi-Square test:

Components of metabolic syndrome	p-value	Significance
Systolic blood pressure	0.267	n.s
Diastolic blood pressure	0.404	n.s
Fasting plasma glucose	0.155	n.s
Triglycerides	0.465	n.s
HDL	0.807	n.s
Past h/o hypertension	<0.001	Vhs
Past h/o dyslipidemia	<0.001	Vhs

Diastolic dysfunction was significantly correlated only with past h/o hypertension and dyslipidemia. There was no correlation found between the other components of metabolic syndrome and diastolic dysfunction.

Table 2:Freqency of impaired parameters in patients with diastolic dysfunction:

Parameters of diastolic dysfunction	Percentage with impaired value
E/A	100%
MITRAL DT	17%
IVRT	0%
E/E'	61.76%
E'	41.17%

The most frequently found impaired parameter in the 34 patients who had metabolic syndrome was E/A,whichwas found impaired in 100% of the patients.61.76%(21 out of 34) patients had an abnormal E/E' ratio ,while 41.17% (14 out of 34) had abnormal E' values. MITRAL DT was impaired in 17% (6 out of 34) of the patients. There was no impairment of IVRT in any of the patients.

Discussion

Our study showed a prevalence of 34% DD in non-diabetic patients of MS. This is significantly lower than the prevalence seen in other studies from the Indian subcontinent (1,3,4). All of these studies were done in diabetic MS patients. A study by Dinh et al in 2011 was done on 166 patients, dividing them into 3 groups; Impaired Glucose Tolerance (IGT), Diabetic and Non Diabetic group (NGT). The prevalence of DD was 81% in the IGT group, 96% in the diabetic group and 61% in the NGT group, respectively (P< 0.001). Twelve percent of subjects with NGT, 28% of patients with IGT and 35% of the diabetic group were classified as having a more severe form of LVDD (14).

Given the high prevalence of DD in diabetic patients, with some studies showing a prevalence up to 100% (15), it would be tempting to conclude that Diabetes is the predominant contributor to DD in MS.

The review of literature places the prevalence of DD in hypertensive patients in a variable range. While in the Caucasian population, the incidence appears to be in the range of 40-45% (16), the prevalence in South East Asian and African populations are higher. Independent small sample size studies from India report the prevalence of DD in hypertensives to be between 55-70% (17,18) while a Nigerian population study placed the incidence of DD in hypertensive patients at 82% (19). The E-ECHOES study done in the United Kingdom on hypertensive patients of South East Asian ethnicity put the prevalence at 73%,which was comparable to that seen in the African-Caribbean population (72%).However, the parameters of DD were worse in the South East Asian group translating to worse clinical outcomes.(20)

In our study 42 patients had past history of hypertension, 57% of whom had DD. 43 were newly diagnosed,20 % of whom had DD. Long standing history of hypertension was significantly associated with DD in our study.27 patients had history of dyslipemia,22 of whom had DD(84%). Out of the 73 newly diagnosed patients,12 had DD(17%).Thus while no significant association between dyslipidemia and hypertension with DD in our study, a very strong association is present between past h/o hypertension and dyslipidemia.

The lack of significant association between individual variables of MS and DD is a feature unique to our study;almost all other studies have shown significant association between each component with DD { exception being some studies which showed no association with low HDL levels (8) }. However, after carefully reviewing all literature,we were unable to find whether the patients who were selected in various studies, had long standing history of the 3 central disorders which comprise MS or whether the elevations were stand alone values. We propose that it is not isolated elevations of the components, but long standing disease which is responsible for causing the cardiac effects.

There are conflicting reports regarding gender distribution of DD in MS(21). Our study did not reveal any gender inequality which is similar to several other studies(17,18)

MS is a complex constellation of various diseases which is greater than the sum of its whole. How the components interact with each other and whether one component is more important than others, is a question which has not been answered yet. It would require studies both long term and well defined before we come close to the answer. While the significantly lower prevalence of DD in our study after excluding diabetics, certainly appears to suggest that diabetes is a major contributor to DD in MS, more such studies are required before we can reach a conclusion.

Limitations:

One of the major limitations of our study is the comparatively younger group of patients studied. The average age of our patients was 43years. Since age has a well known association with DD in MS (17,18) it is a possibility that the lower prevalence of DD in our study could be explained by this.

Conclusion

1) The prevalence of diastolic dysfunction was found to be 34% in the patients of non-diabetic/prediabetic metabolic syndrome,which is less than that found in the diabetic metabolic syndrome group.

2) No correlation was found between parameters of diastolic dysfunction and components of metabolic syndrome. There was significant correlation between past history of dyslipidemia and hypertension with diastolic dysfunction indicating that prolonged exposure to metabolic syndrome parameters are responsible for the development of diastolic dysfunction.

Declarations

ETHICS APPROVAL:

Consent for the study was obtained from Manipal Ethics committee prior to starting the study

CONSENT FOR PUBLICATION:

NOT APPLICABLE

AVAILABILITY OF DATA AND MATERIALS:

Data available on request from authors and after obtaining permission from MAHE University

COMPETING INTERESTS:

Authors declare no competing interests either financial or non financial

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K.K collected the material. P.A analysed the data. K.K and P.A wrote the manuscript in collaboration.

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