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Original article

Metabolic syndrome and its association with left ventricular dysfunction in patients with left bundle branch block

Mojgan Gharipour[1], Mohammad Hashemi Jazi[2], Peyman Nilforoush[3], Azadeh Batvandi[3], Robabeh Mohammadi[3], Roya Najafi[3]

[1] Molecular epidemiology, Metabolic Syndrome Department, Isfahan Cardiovascular Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran; [2] Cardiac Rehabilitation Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran; [3] Sina Heart Center. Isfahan, Iran

Summary. *Background:* The present study and for the first time hypothesizes that the patients with left bundle branch block (LBBB) suffer considerably from metabolic syndrome (MetS) and this metabolic phenomenon can be associated with cardiac dysfunction status such as ventricular dilation and reduced left ventricular ejection fraction (LVEF) in these patients. *Methods:* A retrospective study was conducted on 220 consecutive patients with diagnosed LBBB. MetS status was diagnosed using the Adult Treatment Panel III of the National Cholesterol Education Program criteria. Systolic function state was assessed using two-dimensional echocardiography. *Results:* The overall prevalence of MetS among studied LBBB patients was 16.8%. Regarding left ventricular functional status in the two groups, the mean LVEF in the groups with and without MetS was 37.03 ± 9.09% and 43.43 ± 15.62% with a significant difference (p = 0.017). However, left ventricular dilation was similarly detected in both groups with and without MetS (21.6% versus 30.6%, p = 0.273). Multivariable linear regression model showed subjects with MetS had lower LVEF in the presence of confounders (Beta = 6.915, p = 0.039). *Conclusion:* A notable number of LBBB patients suffered from MetS and this metabolic phenomenon is significantly associated with lowering left ventricular function in LBBB patients. (www.actabiomedica.it)

Key words: metabolic syndrome, left ventricular dysfunction, left bundle branch block

Introduction

Abnormal changes in electrocardiographic pattern have been commonly shown following some common metabolic abnormalities such as diabetes mellitus or lipid disorders (1). For instance, glucose intolerance and high fasting serum glucose levels or insulin tolerance have been shown to be associated with prolongation of the heart-rate-corrected QT and also RR intervals in both diabetic and non-diabetic patients (2-4). Left bundle branch block (LBBB) is a common cardiac conductive abnormality particularly in heart failure patients that is accompanied with septal wall motion abnormality leading deterioration of left ventricular function. This abnormality in those with metabolic disturbances such as diabetic patients indicates advanced cardiovascular involvement manifesting with more severe left ventricular systolic dysfunction (5). It has been also found that hypertension and diabetes mellitus are independently associated with right bundle branch block (RBBB) (6). In a study by Garcia et al. a high prevalence of bifascicular block (37.5%) was revealed in diabetic patients (7). Vice versa, it has been found that subjects who develop LBBB are at higher risk for developing diabetes mellitus than those of the control group (8). These evidences emphasize a

strong link between the metabolic abnormalities and LBBB. Some probable mechanisms for this association include some metabolic disarrangements, such as hyperkalaemia as well as autonomic neuropathy (9). Metabolic syndrome(MetS) is a cluster of some metabolic disturbances such as obesity, hypertension, glucose intolerance as well as lipid profile abnormalities. Based on the pointed evidences, we for the first time hypothesize that LBBB patients suffer considerably from MetS and this metabolic phenomenon can be associated with cardiac dysfunction status such as ventricular dilation and reduced left ventricular ejection fraction (LVEF) in these patients.

Methods

A retrospective study was conducted on 220 consecutive patients with diagnosed LBBB on their electrocardiograms diagnosed according to the definition criteria of the New York Heart Association as "QRS interval ≥120 ms, notched, wide and predominant R waves in leads I, a VL, V5, and V6, notched and broad S waves in V1and V2 with absent or small R waves, notching or a plateau in the mid – QRS wave, ventricular activation time >50 ms at the onset of the QRS interval, M-shaped QRS variants with occasionally wide R waves in V5 and V6, no initial Q wave over the left precordium and absence of preexcitation" (10). A cardiologist blinded to the study design performed the diagnosis of LBBB. The study met the requirements for a waiver of informed consent from the institutional review board at Isfahan University of Medical Sciences. Data were collected by reviewing hospital recorded files including demographic characteristics anthropometric parameters, risk profile (current smoking, hypertension, diabetes mellitus, hyperlipidemia, and renal failure, previous myocardial infarction, congestive heart failure, or angina pectoris, previous coronary interventions), and functional status according to The Canadian Cardiovascular Society (CCS) grading of angina pectoris. Along with clinical factors and for determining cases with metabolic syndrome, a fasting plasma lipid profile (including total cholesterol, low-density lipoprotein [LDL] cholesterol, HDL cholesterol, and triglyceride levels) and blood pressure were also assessed in the resting state. Metabolic syndrome was diagnosed using the modified Adult Treatment Panel III of the National Cholesterol Education Program (11) criteria: three of five among body mass index (BMI) greater than 30 kg/m^2, elevated triglycerides (≥150 mg/dL or drug treatment), reduced high-density lipoprotein cholesterol (≤40 mg/dL in men, ≤50 mg/dL in women or drug treatment), elevated arterial blood pressure (≥130 mm Hg systolic, ≥85 mm Hg diastolic or drug treatment), and elevated fasting glucose (≥100 mg/dL or drug treatment). LVEF as well as ventricular diameters for determining left ventricular dilation was assessed by two-dimensional echocardiography. The study endpoint was first to determine prevalence rate of metabolic syndrome in LBBB patients and also assess relationship between the presence of metabolic syndrome and left ventricular state assessed by considering low LVEF and LV dilation.

Statistical analysis: Results were reported as mean ± standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student's *t*-test or Mann-Whitney U test for the continuous variables and the chi-square test (or Fisher's exact test if required) for the categorical variables. Predictors exhibiting a statistically significant relation with study endpoints in univariate analyses (with a p-value >0.1) were taken for a multivariable linear regression analysis to investigate their independence as predictors. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA).

Results

The average age of the participants was 66.06 ± 10.15 years (ranged 40 to 97 years) and 43.2% were male. The overall prevalence of MetS among studied LBBB patients was 16.8%. Comparing patients with MetS and those without this phenomenon (table 1) showed higher prevalence of hypertension, hyperlipidemia, and diabetes mellitus in former group; but

the two groups were matched for gender, age, current smoking, and heart failure NYHA classification. Regarding left ventricular functional status in the two groups, the mean LVEF in the groups with and without METS was 37.03 ± 9.09% and 43.43 ± 15.62% with a significant difference (p = 0.017). However, left ventricular dilation was similarly detected in both groups with and without MetS (21.6% versus 30.6%, p = 0.273). Multivariable linear regression model (table 2) showed lower LVEF in MetS status with the presence of confounders (Beta = 6.915, p = 0.039).

Discussion

It has been recently showed that the patients with MetS experience higher both left and right ventricular dysfunction than those with this syndrome. Among different components of MetS, hyperglycemia has strongest association for development of ventricular dysfunction (12,13). It has been also shown that hyperlipidemia as a major component of MetS is significantly associated with low LVEF as well as with the changes in LV systolic diameters. In this regard, the decrease in serum lipid profile occurs in parallel with improvement of LVEF (14). It has been also suggested that following a variety of dietary patterns predispose to different components of MetS may be associated with the increase in left ventricular mass and also decrease in stroke volume leading lowering LVEF (15). All these evidences on association between the components of METS including hyperglycemia and serum lipids can confirm our hypothesis in triggering role of MetS in lowering LVEF. This association can be more highlighted in LBBB patients because of more common abnormalities in septal wall glucose metabolism in these patients (16). Besides of relationship between different components of MetS and reducing left ventricular dysfunction, this syndrome can increase the risk for left ventricular dysfunction by a complex mechanism that probably involves arterial hypertension and diabetic cardiomiopathy (17-20). For instance, insulin resistance even independent of hyperglycemia, predisposes to heart failure, and in patients without overt heart failure is associated with echocardiographic signs of left ventricular dysfunction. In these patients, MetS may be associated with increased left ventricle mass and left ventricular hypertrophy (21,22).

More important than hyperglycemia and lipid disturbances as the main component of MetS, the role of hypertension to lower left ventricular dysfunction has been also addressed. HTN can worsen the loading conditions of the failing ventricle, and thus small increases in afterload can produce large decreases in stroke volume. Furthermore, higher blood pressures continue to worsen ventricular structure and performance. Increases in systolic blood pressure slow myocardial relaxation, and hypertrophy increases passive chamber stiffness (23).

Also, as previously noted, in ventricular dyssynchrony that is a fundamental feature in LBBB, a significant decrease in symmetrical ventricular contraction is well identified resulting in increased ventricular

Table 1. Baseline characteristics and clinical data of study subjects

Characteristics	Group with MetS (N = 37)	Group without MetS (N = 183)	p-value
Male gender	13 (35.1)	82 (44.8)	0.279
Age (year)	67.57 ± 10.63	65.75 ± 10.05	0.323
Hyperlipidemia	30 (81.1)	110 (60.1)	<0.001
Diabetes mellitus	24 (64.9)	27 (14.8)	<0.001
Hypertension	36 (97.3)	55 (30.1)	<0.001
Current smoking	16 (17.8)	24 (18.5)	0.895
NYHA score			0.269
I	16 (43.2)	80 (43.7)	
II	13 (35.1)	56 (30.6)	
III	5 (13.5)	42 (23.0)	
IV	3 (8.1)	5 (2.7)	

Table 2. Multivariate linear regression model to determine association between MetS status and LVEF with the presence of confounders

Variable	Beta	Standard Error	P-value
MetS	6.915	3.324	0.039
Male gender	8.286	1.928	<0.001
Age	-0.107	0.095	0.261
Hyperlipidemia	0.224	0.085	0.124
Diabetes mellitus	5.666	2.581	0.029
Hypertension	4.150	2.305	0.073
Current smoking	0.546	0.124	0.256
NYHA score	-2.777	1.069	0.010

volumes, decreased ejection fraction and a decrease in overall ventricular function and efficiency (24). This deleterious effect of LBBB on LVEF concurrently with pointed effects of METS and its components led to deterioration of left ventricular function that is in line with our viewpoints.

In summary, a notable number of LBBB patients suffered from MetS and this metabolic phenomenon is significantly associated with lowering left ventricular function in LBBB patients. Both deleterious effects of ventricular dysfunction in LBBB state and adverse effects of MetS and its related components can simultaneously deteriorate left ventricular function.

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Correspondance:
Mojgan Gharipour,
Isfahan Cardiovascular Research Center,
Isfahan Cardiovascular Research Institute
(WHO Collaborating Center),
Isfahan University of Medical Sciences, Isfahan, Iran
PO Box: 81465-1148, Isfahan, Iran
Tel. +98 311 3377888-9
E-mail: gharipour@crc.mui.ac.ir