

Particularities of Coronary Artery Disease in Hypertensive Patients with Left Bundle Branch Block

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ABSTRACT

Objective: We mean to investigate whether the presence of hypertension could be associated with a more severe atherosclerotic coronary artery disease in patients with left bundle branch block.

Material and methods: To assess the current incidence and meaning of hypertension associated with atherosclerotic coronary artery disease we performed a cross-sectional analysis that included 402 patients with left bundle branch block, admitted between January 2011 and June 2013 in the Cardiovascular Diseases Institute Iasi, Romania. Of these, 194 were hypertensive, especially grade 1 and 2; 272 patients had new or presumably new left bundle branch block on their presenting electrocardiograms. The median follow up was 7 days (hospitalization period).

Results: The results of our study show that hypertensive patients were more likely to have a prior history of cardiovascular events, including myocardial infarction, angina pectoris, diabetes and obesity, with statistically significant differences. On the other hand, the normotensive patients had higher rates of current and previous smoking and congestive heart failure. Conventional coronary angiography was performed in 130 (67.01%) hypertensive patients and demonstrated that almost half (41.76%) of them have coronary artery disease, one in five patients being diagnosed with acute coronary syndromes. The majority of hypertensive patients evaluated by coronary angiography had either one or two coronary lesions (28.86%); in contrast, from 110 normotensive patients evaluated by coronary angiography, 78.36% had no vessel disease ($p = 0.001$). When coronary artery disease was present it was frequently localized on the left descendent artery in both groups, but with statistically significant differences (16.82% in normotensives vs. 32.47% in hypertensives, $p = 0.001$). With regards to systolic left ventricular function, normotensive patients were more likely to have a decreased ejection fraction (EF) $<50\%$ ($p < 0.001$), almost half of them having an EF $<30\%$.

Conclusions: We have found that hypertensive patients with left bundle branch block and a clinical context suggestive of acute coronary syndrome have an elevated risk of coronary artery disease, especially one and two coronary lesions. The association of hypertension with left bundle branch block is a high probability criterion for the diagnosis of coronary artery disease, even in asymptomatic patients.

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INTRODUCTION

Hypertension is a major risk factor for cardiovascular morbidity and mortality. The presence of hypertension more than doubles the risk for coronary heart disease, including acute myocardial infarction and sudden death and more than triples the risk of congestive heart failure as well as strokes (1). Romania is currently a high cardiovascular risk country where unfortunately cardiovascular disease (CVD) prevention still represents a major challenge for the whole population, politicians, and public health workers (2-4) and identification of persons at high risk of developing CVD, but who are currently asymptomatic is one of the main objectives of prevention. Coronary artery disease (CAD) may limit myocardial perfusion and therefore oxygen supply. In hypertension, myocardial oxygen demand is increased for two reasons; first, because of the increased output impedance to left ventricular (LV) ejection, and second, because hypertension can cause LV hypertrophy. This combination of decreased oxygen supply and/or increased oxygen demand is particularly pernicious and explains why hypertensive patients are more likely than normotensive people to develop angina, to have a myocardial infarction (MI) or other major coronary event, and to be at higher risk of death following MI (5). Left bundle branch block (LBBB) is also associated with an increased risk of developing overt cardiovascular disease and may be considered as a predictor of severity of coronary artery disease (5). By screening patients with risk of heart attack according to their resting electrocardiogram, it would be possible to prevent a significant number of acute cardiac events and, as a result, to decrease the morbidity and mortality (6,7). We mean to investigate whether the presence of hypertension could be associated with a more severe atherosclerotic coronary artery disease in patients with LBBB. □

MATERIAL AND METHODS

With a view to assessing the current incidence and meaning of the hypertension associated with extent of coronary artery disease, clinical risk factors, echocardiographic findings in left bundle branch block patients, we performed a cross-sectional analysis in the Cardiology Department of Georgescu Institute

of Cardiovascular Diseases, Iasi. The study included 402 patients with left bundle branch block on their presenting electrocardiogram, admitted between January 2011 and June 2013. The median follow up was 7 days (hospitalization period). Patients were excluded if they were younger than 30 years, did not have an electrocardiogram obtained or declined authorization for the use of their medical records for research.

Our data included basic demographic information, characteristics of chest pain and associated symptoms, cardiac history and risk factors, diabetes and cardiac markers, treatment, electrocardiographic (ECG), echocardiographic and angiographic data. All subjects were reviewed for hypertension, diabetes mellitus, hyperlipidemia, smoking, ischemic heart disease, cardiomyopathy and valvular heart disease. The electrocardiograms were classified according to the standardized guidelines, including LBBB not known to be old (new or presumably new LBBB) or LBBB known to be old. The chronicity of the LBBB was determined by comparison with the most recent ECG available. If no prior ECG was available for comparison, patients were classified as having a presumably new LBBB.

Acute coronary syndromes were defined in accordance with the European Society of Cardiology (8) and American College of Cardiology (9) guidelines. To estimate the presence and extent of CAD, the coronary angiograms of all patients were analyzed. Patients with no angiographic disease or irregularities in any of the epicardial coronary arteries were considered to have normal coronary arteries on angiography. CAD was defined as at least one vessel with greater than 70% stenosis or documented acute myocardial infarction (which presumed underlying coronary disease). Revascularization was defined as a percutaneous coronary intervention (PCI) with or without stent placement or coronary artery bypass grafting.

Patients were divided into two groups according to their hypertensive status: hypertensive and normotensive patients. This arrangement was made in order to be able to analyze the impact of hypertension on mortality, baseline data, echocardiographic and angiographic findings in LBBB patients.

Continuous variables are given as mean $\pm$ standard deviation, and categorical variables as numbers and percentages. Quantitative vari-

ables were tested for normality of distribution by means of Kolmogorov-Smirnov test and were described by median and percentiles or by mean and standard deviation, whenever the case. The frequencies of nominal variables were compared with a chi-square test. Differences in the means and medians or between groups were analyzed using t-test or Mann-Whitney test when appropriate. Comparisons were made among hypertensive and normotensive patients. A p value of <0.05 was considered statistically significant. SPSS 17.0 (SPSS inc., Chicago, IL, USA) statistical software package was used for all calculations.

The study was approved by the Committee on the Conduct on Human Research of University of Medicine and Pharmacy, Iași. □

RESULTS

A sum-total of 402 patients with left bundle branch block was admitted between January 2011 and June 2013 in Georgescu Institute of Cardiovascular Diseases. Only 208 (51.74%) of these patients were normotensive. In general, the patient population presented frequent comorbidities and were older (227 patients had ≥ 65 years, the median age in hypertensive patients was 70.5 years and in those normotensive 65.5 years).

The results of our study show that hypertensive patients were more likely to have a prior history of diabetes mellitus, obesity and cardiovascular events, including myocardial infarction, angina and percutaneous coronary intervention. Normotensive patients were more likely to have a history of congestive heart failure and tobacco use. However, statistically significant differences in terms of baseline characteristics were found in prior diabetes mellitus, obesity and prior revascularization, common in hypertensive patients. The clinical characteristics of the patients are summarized in Table 1.

Although the chest pain was the most frequent symptom at presentation, there were statistically significant differences between the two groups, more than four of five hypertensive patients being evaluated for chest pain (81.95% vs. 72.11%, $p = 0.047$). The other symptoms, in order of frequency were palpitations and syncope, twice the percentage of normotensive patients having a history of syncope (16.34% vs. 8.24%, $p = 0.011$). Most of the hypertensive patients had a history of grade 2 of hyper-

tension (28.11%), only 7.21% of them having grade 3 of hypertension.

We also studied the echocardiographic characteristics of normotensive patients compared with those of the hypertensive patients. Normotensive patients were more likely to have a decreased ejection fraction (EF) $<50\%$ (142 patients (68.26%) vs. 110 (56.70%), $p < 0.001$). Almost half of the patients with a decreased ejection fraction had an EF less than 30%.

All the patients with a coronary artery disease probability (new or presumably new left bundle branch block and clinical context of acute coronary syndrome) were evaluated through conventional coronary angiography or computed tomography angiography. Conventional coronary angiography was performed in 130 (67.01%) hypertensive patients and demonstrated that almost half of them (41.76%) had either one, two or three vessel coronary lesions. In contrast, from 110 normotensive patients evaluated by coronary angiography, 35.45% had significant coronary lesions. When coronary artery disease was present it was frequently localized on the left descending artery in both groups, but with statistically significant differences (32.47% in hypertensives vs. 16.82% in normotensives, $p = 0.001$). Most of the percutaneous coronary interventions were also performed on the left descending artery in hypertensive and normotensive patients, and the differences were also statistically significant between these two groups (13.91% vs. 4.80%, $p = 0.021$) (Table 2). Only two hypertensive and six normotensive patients were evaluated using computed tomography angiography

Variable	Normotensive patients (n=208)	Hypertensive patients (n=194)	p Value
Men	128 (61.53%)	119 (61.34%)	0.823
Diabetes mellitus	32 (15.38%)	55 (28.35%)	0.001
Obesity	144 (76.47%)	164 (85.53%)	0.009
Current/ previous smoker	94 (45.19%)	79 (40.72%)	0.268
Previous congestive heart failure	110 (52.88%)	87 (44.84%)	0.214
Previous myocardial infarction	10 (4.8%)	15 (7.73%)	0.292
Previous angina pectoris	7 (3.36%)	14 (7.21%)	0.157
Previous percutaneous coronary intervention	10 (4.80%)	22 (11.34%)	0.003
Chest pain	150 (72.11%)	159 (81.95%)	0.047
Palpitations	38 (18.26%)	28 (14.43%)	0.305
Syncope	34 (16.34%)	16 (8.24%)	0.011

TABLE 1. Clinical characteristics of left bundle branch block patients.

Variable	Normotensive patients (n=208)	Hypertensive patients (n=194)	p Value
Number of diseased vessels on angiography			
• 1 coronary artery disease	16 (7.69%)	30 (15.46%)	0.001
• 2 coronary artery disease	13 (6.25%)	26 (13.40%)	0.001
• 3 coronary artery disease	16 (7.69%)	25 (12.88%)	0.001
LAD disease	35 (16.82%)	63 (32.47%)	0.001
RCA disease	25 (12.01%)	36 (18.55%)	0.120
LCX disease	19 (9.13%)	32 (16.49%)	0.011
Overall PCI use	13 (6.25%)	29 (14.94%)	0.001
PCI on LAD	10 (4.80%)	27 (13.91%)	0.021
PCI on RCA	3 (1.44%)	14 (7.21%)	0.057
PCI on LCX	3 (1.44%)	13 (6.70%)	0.010

TABLE 2. Procedural characteristics of left bundle branch block patients.

Abbreviations: LAD, left descendend artery; LCX, left circumflex artery; RCA, right coronary artery; PCI, percutaneous coronary intervention.

which revealed no significant coronary artery lesions.

With regards to the treatment strategies, hypertensive patients were more likely to receive angiotensin converting enzyme-inhibitors (85.05% vs. 54.32% in normotensive patients), beta-blockers (76.80% vs. 54.32%), diuretics (64.43% vs. 50.48%) and calcium channel blockers (21.65% vs. 8.1%).

Hypertensive patients with LBBB, had the final diagnostic of coronary artery disease in a significantly higher percentage, both as acute coronary syndrome (22.16%), as well as stable angina (38.14%). More than half of the normotensive patients had another final diagnostic instead of coronary artery disease (non-cardiac chest pain (37.50%)/ cardiac diagnoses other than coronary artery disease (22.11%) (Table 3). $\square$

DISCUSSIONS

Our study is among the few who has demonstrated that hypertensive patients

Final diagnostic	Normotensive patients (n=208)	Hypertensive patients (n=194)	p Value
Acute coronary syndrome	24 (11.53%)	43 (22.16%)	0.001
Stable angina	60 (28.84%)	74 (38.14%)	0.032
Cardiac diagnoses other than coronary artery disease	46 (22.11%)	28 (14.43%)	0.053
Non-cardiac chest pain	78 (37.50%)	49 (25.25%)	0.231

TABLE 3. Final diagnostic of left bundle branch block patients.

with left bundle branch block and a clinical context suggestive of acute coronary syndrome have an elevated risk of coronary artery disease, especially one and two coronary lesions. The overall proportion of hypertensive patients with STEMI corresponds well with previously data from emergency departments, in less selected populations, where the proportion is between 6-29% (10,11). In the emergency department study by Chang et al. (12) the rate of MI did not differ between patients with LBBB and patients with other ECG findings. This raises the question whether LBBB is a sign of acute myocardial infarction or rather a sign of underlying structural heart disease, including coronary heart disease and previous myocardial infarction (13). Furthermore, the frequency of LBBB increases with age (14) and we observed that 81.20% of our patients had between 60-80 years old.

Individuals with LBBB and acute coronary syndromes are more likely to be older, to be female, and to have a history of pre-existing cardiovascular disease, hypertension, and congestive heart failure (15). In our case, hypertensive patients were more likely to have a prior history of diabetes mellitus, obesity and cardiovascular events, including myocardial infarction, angina and percutaneous coronary intervention. On the other hand, normotensive patients were more likely to have a history of congestive heart failure and tobacco use.

Of the 43 hypertensive patients with a final diagnosis of acute coronary syndrome, only 14 (32.55%) had new or presumably new left bundle branch block. This frequency is lower than in studies from 1970s (16), but comparable to recent reports from Chang et al. (12) and Liakopoulos et al. (17). This may reflect temporal changes in the myocardial infarction with increasing age and comorbidities. This issue is discussed at length in a recent review by Nee-land et al. (13).

It has been suggested that acute coronary syndromes might be favoured by an increased flow velocity and shear stress which could contribute to plaque disruption. It is important to emphasise that treatment of hypertension reduces significantly the number of fatal and non-fatal cardiovascular events in patients with CHD (18). In our case, hypertensive patients were more likely to receive angiotensin converting enzyme-inhibitors, beta-blockers, diuretics and calcium channel blockers, with sta-

tistically significant differences between the two groups.

Patients identified as having LBBB and demonstrating acute clinical signs associated with AMI have the highest mortality rates of all the patients presenting AMI. The long-term outcomes of unselected patients with angina pectoris, and BBB on the initial electrocardiogram, are not well established. Over a median follow-up of 7.3 years, patients with angina and bundle branch block were at higher risk for major cardiovascular events (RBBB HR 1.85, 95% CI 1.44–2.38; $p < 0.001$ and LBBB HR 2.04, 95% CI 1.62–2.56; $p < 0.001$) compared to those without BBB. Over a median of 16.6 years and after adjustment for multiple risk factors, an increased risk of mortality was still significant for LBBB (15). The long-term outcomes of LBBB patients have not been our case, but in-hospital mortality for hypertensive patients do not differ from those normotensive with LBBB (1.24% in both groups).

The therapeutic implications of the relations between left bundle branch block and other preventable cardiovascular disease risk factors such as hypertension, highlight the potential public health impact of cardiovascular risk control through controlling multiple risk factors. $\square$

CONCLUSIONS

Based on the results of our study, the association of hypertension with left bundle branch block is a high probability criterion for the diagnosis of coronary artery disease, even in asymptomatic patients. In a clinical context suggestive of acute coronary syndrome, hypertensive patients with left bundle branch block have a high probability of a more severe atherosclerotic coronary artery disease and they should be evaluated through coronary angiography.

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