LEFT BUNDLE BRANCH BLOCK SIGNIFICANCE IN CARDIOVASCULAR PATHOLOGY

PhD THESIS ABSTRACT

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Referrences

Annexes

The PhD research has:

157 pages: 39 pages – Current state of knowledge, 100 pages - Personal contributions;

- 98 figures;
- 11 tables;
- 316 references;
- annex;
- 1 ISI article as first author, 4 BDI articles as first author and another BDI article as corresponding author.

This summary selectively presents the iconography and the bibliography from the PhD thesis, keeping the same numbering and the content from the PhD in full.

Keywords: left bundle branch block; acute myocardial infarction; percutaneous coronary angioplasty; left ventricular dysfunction; arrhythmias; clinical study.
CHAPTER VI
MOTIVATION AND STUDY OBJECTIVES

VI.1 Study motivation

Left bundle branch block is a frequent pathology in our clinical practice, whose implications are becoming increasingly studied (1-4). The presence of left bundle branch block (LBBB) on a 12-lead electrocardiogram, whether new or established, poses multiple important questions to the healthcare provider. Realistically, LBBB should be considered a “cardiac clinical entity,” rather than just an electrocardiographic finding. Its presence has far reaching consequences in acute clinical care, such as in the setting of acute myocardial infarction (AMI), and in chronic conditions, such as heart failure (HF), where it can be helpful in guiding the management of stable coronary artery disease cardiac and resynchronization therapy (CRT) (5-11). LBBB provides prognostic information (5), but it also poses challenges in therapeutic management (3,6).

Cardiovascular pathology, represented particularly by the coronary artery disease, has become a pandemic disease of this century, with an increased incidence and prevalence in all the countries, whether poor or developing (12,13).

Worldwide, coronary heart disease is currently the most common cause of death (14,15). Over 7 million people die each year from coronary disease, representing approximately 12.8% of all causes of death (16). Even if the use of modern methods of reperfusion caused a long-term decreased in mortality secondary to acute coronary syndromes, the high mortality rate justifies the need for continued efforts to improve the quality of life of these patients. It is estimated that every sixth man and the seventh woman in Europe will die of a heart attack (17,18).

Romania is currently on the ascending trend in the incidence of coronary artery disease, which is revealed in the latest data from the study SEPHAR II (19).

By acute and chronic complications, the high rate of morbidity and mortality, the coronary artery disease has become an important socio-economic problem, the costs imposed by this pathology worldwide being extremely high. In this context, to limit the adverse consequences of this disease, it is required a complex approach in the management of these patients, including aggressive strategies for prevention and early diagnosis (20).

Even if the left bundle branch block is traditionally regarded as the equivalent of an acute myocardial infarction with ST segment elevation, it can be a marker of an ischemic or non-ischemic disease progression, affecting not only the cardiac conduction system but also the myocardium. Left bundle-branch block may be associated with a poor prognosis compared to normal intraventricular conduction, as it may be the first manifestation of a diffuse myocardial injury (21). The most common cause still appears to be the ischemic heart disease, found in 70% of patients with left bundle-branch block. (21).

In this clinical and epidemiological context, I consider justified to conduct a study to see the particular aspects of coronary artery disease in patients with bundle-branch block left, through a comprehensive approach, examining this pathology both in terms of risk factors, clinical, laboratory and invasive data, all interpreted in a holistic approach.

VI.2 Study objectives

VI.2.1 General objective:

- identification of clinical and prognostic implications of left bundle-branch block both global and in specific categories of patients (diabetes, hypertension or myocardial infarction).
VI.2.2 Specific objectives:
1. to evaluate the clinical, therapeutic and prognostic significance of new left bundle-branch block occurred in patients with acute myocardial infarction, both during the hospitalization and on long-term;
2. to verify the hypothesis that new left bundle-branch block may be the first manifestation of coronary artery disease in diabetic patients;
3. to quantify the impact of left bundle-branch block on ventricular systolic function and arrhythmic risk in patients with acute myocardial infarction;
4. assessment of coronary artery lesions depending on the presence and severity of hypertension;
5. to study the impact of QRS complex duration on systolic ventricular function, risk of arrhythmias and coronary lesions in patients with left bundle-branch block;
6. to detect some particular aspects of ischemic heart disease according to the chronicity of left bundle-branch block and associated comorbidities;
7. to detect the differences in the management and in hospital particularities of patients with new left bundle-branch block compared to patients with pre-existent left bundle-branch block;
8. identifying the most frequent causes of left bundle-branch block;
9. to identify the best way to minimally invasive detect the severity of coronary artery disease in patients with left bundle-branch block.

CHAPTER VII

MATERIAL AND METHODS

VII.1 Inclusion criteria
With a view to assessing our objectives, we prospectively studied the anamnestic, clinical, paraclinical, electrocardiographic, echocardiographic and angiographic data of 477 LBBB patients admitted from January 2011 to December 2013 in Georgescu Institute of Cardiovascular Diseases.

Our data include basic demographic information, characteristics of chest pain and associated symptoms, cardiac history and risk factors (age, sex, smoking, alcohol consumption, body mass index, lipid profile, dynamics of myocardial cytolisis enzymes), medications, treatment, disposition, ECG, echocardiography, cardiac markers and angiographic data.

VII.2 Exclusion criteria
Patients were excluded if they were younger than 18 or declined authorization for the use of their medical records for research. Vulnerable patients, such as comatose patients or pregnant women were not included in our study. All patients were informed about the study and if they decided to participate, they signed an informed consent.

VII.3 Studied groups
Clinical and paraclinical exams were carried out in Georgescu Institute of Cardiovascular Diseases, Iași. According to the chronicity of left bundle branch block, patients were divided in two groups: left bundle branch block not otherwise known to be old (new or presumably new LBBB) (n = 319) or LBBB known to be old (n = 158). LBBB chronicity 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.

To identify the significance of left bundle-branch block in patients with different pathologies, we analyzed more subgroups of patients.

**Left bundle branch block in diabetic patients**
We analyzed a number of 273 patients with new left bundle branch block, of which:
- 131 diabetic patients;
- 142 non-diabetic patients.

**Left bundle branch block in hypertensive patients**
We included a number of 402 patients, which were divided according to their tensional status:
- 208 normotensive patients;
- 194 hypertensive patients.

**Prolongue QRS duration and the risk of coronary artery disease**
QRS duration was determined on the ECG at presentation. Depending on the QRS complex duration, 323 patients with left bundle-branch block who met the inclusion and exclusion criteria mentioned above were divided into two groups:
- 159 patients with a QRS complex duration between 120-140 ms;
- 164 patients with a QRS complex duration ≥140 ms.

**New left bundle branch block in patients with acute myocardial infarction**
In a substudy of our research we aimed to evaluate the significance of left bundle branch block in patients with acute myocardial infarction and unicoronarian lesions. We evaluated the patients with acute myocardial infarction with or without left bundle-branch block, hospitalized in our clinic for three years. After a mean of 16.51 ± 2.41 months from the onset of acute coronary event, we evaluated these patients in order to study the implications of left bundle-branch block on long-term prognosis of patients.

A sum-total of 82 patients were included in the study, divided as follows:
- 42 patients with acute myocardial infarction and new left bundle branch block;
- 40 patients with acute myocardial infarction without left bundle branch block. These patients were randomly chosen from the total of 387 patients with acute myocardial infarction and one coronary lesion, hospitalized from January 2011 to December 2013 in our clinic.

Patients were informed about the study and their written, informed consent was obtained. The trial protocol was approved by the Medical Ethics Committee of the University of Medicine and Pharmacy "Grigore T.Popa" Iasi and was conducted according to the modified Declaration of Helsinki (Somerset West Amendment, 1996).

**CHAPTER VIII**

**RESULTS**

**VIII.1 Global clinical and prognostic implications of new left bundle branch block**
A sum-total of 477 patients with left bundle branch block was admitted between January 2011 and December 2013 in Georgescu Institute of Cardiovascular Diseases, aged between 21 and 81 years, the median age was 66 ± 11 years. Only 319 patients had new or presumably new LBBB on their electrocardiograms and 158 had a chronic left bundle branch block.
Baseline characteristics

Statistically significant differences in terms of baseline characteristics were found in prior congestive heart failure, myocardial infarction, angina pectoris and prior revascularization, common in patients with chronic LBBB (Table 8.1).

Table 8.1. Baseline characteristics of patients with left bundle branch block

<table>
<thead>
<tr>
<th>Variable</th>
<th>New LBBB (n=319)</th>
<th>Chronic LBBB (n=158)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypertension</td>
<td>162 (50.78%)</td>
<td>73 (46.20%)</td>
<td>0.328</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>68 (21.31%)</td>
<td>34 (21.51%)</td>
<td>0.960</td>
</tr>
<tr>
<td>Current/previous smoker</td>
<td>148 (46.39%)</td>
<td>61 (38.60%)</td>
<td>0.175</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>144 (45.14%)</td>
<td>108 (68.35%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>13 (4.07%)</td>
<td>17 (10.76%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>14 (4.38%)</td>
<td>16 (10.12%)</td>
<td>0.010</td>
</tr>
<tr>
<td>Myocardial revascularization</td>
<td>19 (5.95%)</td>
<td>24 (15.19%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Admission symptoms

Chest pain was the most frequent symptom at presentation. The other symptoms, in order of frequency, were dyspnoea, palpitations and syncope, with statistically significant differences, except dispnoea, which was more common in patients with chronic left bundle-branch block (fig.8.18).

Fig.8.18. Admission symptoms in patients with left bundle branch block

Markers of myocardial injury

If the CKMB value was assessed in all patients included in the study, we can not say the same about the values of troponin I, which were evaluated at about one third of patients with new left bundle-branch block (36.37%) and in less than a quarter of patients with chronic left bundle-branch block (21.52%), with statistically significant differences between the two groups of patients (fig.8.21).

Of the 51 patients with new left bundle branch block and elevated troponin I, 35 had a final diagnosis of acute myocardial infarction. In contrast, only a quarter of patients with chronic left bundle-branch block who had elevated troponin I values at admission, were finally diagnosed with acute myocardial infarction.
Patients with left bundle branch block who had elevated markers of myocardial injury

**Left ventricular systolic function**

Depending on the left ventricular systolic function, patients were divided in three groups: EF < 30 %; EF 30-50 %; EF > 50 %.

In general, patients with new left bundle branch block had no impaired left ventricular systolic function or whether it was present it was not significant, so that 39.18% of them had an EF > 50% and 31.97% had an EF between 30 and 50% (fig. 8.22).

**Angiographic data**

If the coronary angiography was performed in 80.56% of patients with new left bundle branch block, in patients with chronic left bundle branch block it was performed only in 18.35% of patients (fig. 8.25).

Also, 13 patients with new left bundle branch block and only one patient with chronic left bundle branch block were evaluated by computed tomography angiography which revealed significant coronary lesions in 5 cases and in the only patient in the second group, confirmed by coronary angiography.
Patients with left bundle branch block who had coronary angiography

Almost half of patients with new left bundle branch block had significant coronary lesions, most frequently being one- or two coronary lesions (15.67% and 12.22%), frequently localized on the left descendent artery (32.91%) (fig.8.27).

Most of the percutaneous coronary interventions were performed on the left descendent artery in patients with both new or presumably new LBBB, also in those with chronic LBBB, and the differences between these two groups were statistically significant (12.22 % vs. 3.16%, p = 0.004).

**Left bundle branch block and cardiac arrhythmias**

Almost a third of patients with chronic left bundle-branch block had atrial fibrillation, with statistically significant differences between the two groups (31.64% vs. 15.05%, p <0.001). Also, patients with chronic left bundle-branch block had a reserved prognosis due to the higher risk of ventricular tachycardia (15.18% vs. 14.10% in patients with new left bundle branch block, p = 0.43) (fig.8.32).
Our study is among the few studies that have evaluated the association of AV block in patients with left bundle branch block, the risk of these conduction disorder being double in patients with chronic left bundle-branch block (fig.8.33).

**Fig. 8.33.** Presence of conduction disorders in patients with left bundle branch block.

**Left bundle branch block contribution in establishing the final diagnostic**

Our results show that almost two-thirds of patients with chest pain and new left bundle branch block were diagnosed with ischemic heart disease (63.32% vs 30.37%, p < 0.001).

About one in four patients with new left bundle branch block were diagnosed with acute coronary syndrome (41 patients with acute myocardial infarction with ST-segment elevation, 9 patients with acute myocardial infarction without ST segment elevation and 28 patients with unstable angina) (fig.8.36).
Fig. 8.36 Final diagnostic in patients with left bundle branch block

VIII.2 Significance of new left bundle branch block in diabetic patients

Baseline characteristics

Almost all the patients had type 2 diabetes mellitus and only 3 patients had type 1 diabetes mellitus. Baseline characteristics are listed in Table 8.II.

Table 8.II. Characteristics of patients with new left bundle branch block according to diabetes status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetics (n=131)</th>
<th>Non-diabetics (n=142)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.86 ± 10.39</td>
<td>66.86 ± 11.88</td>
<td>0.198</td>
</tr>
<tr>
<td>Men</td>
<td>85 (64.88%)</td>
<td>84 (59.15%)</td>
<td></td>
</tr>
<tr>
<td>Previously diagnosed or treated hypertension</td>
<td>76 (58.01%)</td>
<td>55 (38.73%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Current/ previous smoker</td>
<td>60 (45.80%)</td>
<td>63 (44.36%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Previous congestive heart failure</td>
<td>63 (48.09%)</td>
<td>52 (36.61%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>8 (6.10%)</td>
<td>3 (2.11%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Previous angina pectoris</td>
<td>4 (3.05%)</td>
<td>4 (2.81%)</td>
<td>0.021</td>
</tr>
<tr>
<td>Previous percutaneous coronary intervention</td>
<td>9 (6.87%)</td>
<td>4 (2.81%)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Left ventricular systolic function

Patients with diabetes were more likely to have a decreased ejection fraction (EF) < 50% (81 patients (61.83%) vs. 79 (55.63%), p <0.001), almost half of them having an ejection fraction less than 30% (fig.8.38).
Left ventricular diastolic function

It is well known that left ventricular diastolic dysfunction is an early complication in type 2 diabetes mellitus and it has been suggested to be the first stage in the development of diabetic cardiomyopathy. Since coronary blood flow predominantly occurs during diastole, an impairment in left ventricular diastolic function may also play an important role in coronary artery disease impairment in diabetics as well as prediabetics. In line with these suggestions, we found that there was an association between left ventricular diastolic function and coronary artery disease in both diabetics and non-diabetics (fig.8.40).

Left bundle branch block and cardiac arrhythmias in diabetic patients

We found a more frequently association between diabetes and the risk of ventricular tachycardia (23 vs. 18 patients, p = 0.001) and in-hospital mortality (7 vs. 3 patients, p = 0.001) in patients with left bundle branch block (fig.8.41).
Coronary lesions

Conventional coronary angiography was performed in 117 (89.31%) patients with diabetes and in 102 (71.83%) non-diabetic patients. The majority of diabetic patients with new or presumably new left bundle branch block had either one, two or three vessel coronary lesions (48.09%) unlike those without diabetes, 72.53% of them having no vessel disease (fig. 8.43).

Therefore, we consider that the presence of left bundle branch block in diabetic patients may be the first manifestation of a coronary artery disease.

Localization of the coronary lesions

When coronary artery disease was present it was frequently localized on the left descendent artery in both groups, but with statistically significant differences (40.45% vs. 22.53%, p<0.001) (fig.8.44).
Fig. 8.44. Localization of the coronary lesions in diabetic patients with left bundle branch block which were evaluated by coronary angiography. Abbreviations: LAD, left descendent artery; LCX, left circumflex artery; RCA, right coronary artery.

Left bundle branch block contribution in establishing the final diagnostic in diabetic patients

Of the diabetic patients, 21 (16.03%) had final diagnostic of acute myocardial infarction with ST segment elevation, 14 (10.68%) had other acute coronary syndrome, 63 (48.09%) had stable angina and 17 (12.97%) had cardiac diagnoses other than coronary artery disease. Only 16 diabetic patients were finally diagnosed with non cardiac chest pain compared with non-diabetic patients, about a third of them having non cardiac chest pain (30.30%), with statistically significant differences between these two groups (p 0.001) (fig.8.46).

Fig. 8.46. Final diagnostic in patients with left bundle branch block according to diabetes status
VIII.3 Significance of left bundle branch block in hypertensive patients

Baseline characteristics

**Table 8.III.** Characteristics of patients with left bundle branch block according to hypertensive status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normotensive patients (n=208)</th>
<th>Hypertensive patients (n=194)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>128 (61.53 %)</td>
<td>119 (61.34 %)</td>
<td>0.823</td>
</tr>
<tr>
<td>Obesity</td>
<td>144 (76.47 %)</td>
<td>164 (85.53 %)</td>
<td>0.009</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>32 (15.38 %)</td>
<td>55 (28.35 %)</td>
<td>0.001</td>
</tr>
<tr>
<td>Current/previous smoker</td>
<td>94 (45.19 %)</td>
<td>79 (40.72 %)</td>
<td>0.268</td>
</tr>
<tr>
<td>Previous congestive heart failure</td>
<td>110 (52.88 %)</td>
<td>87 (44.84 %)</td>
<td>0.214</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>10 (4.8%)</td>
<td>15 (7.73 %)</td>
<td>0.292</td>
</tr>
<tr>
<td>Previous angina pectoris</td>
<td>7 (3.36 %)</td>
<td>14 (7.21 %)</td>
<td>0.157</td>
</tr>
<tr>
<td>Previous percutaneous coronary intervention</td>
<td>10 (4.80 %)</td>
<td>22 (11.34 %)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

**Left ventricular systolic function**

Normotensive patients were more likely to have a decreased ejection fraction (EF) < 50%, almost half of them having an EF less than 30% (fig.8.49).

![Fig.8.49. Left ventricular ejection fraction in hypertensive patients with left bundle branch block](image)

**Coronary lesions in hypertensive patients with left bundle branch block**

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 (fig.8.50).

**Left bundle branch block contribution in establishing the final diagnostic in hypertensive patients**

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%) or cardiac diagnoses other than coronary artery disease (22.11%)) (fig.8.53).
Fig. 8.50. Coronary lesions in hypertensive patients with left bundle branch block which were evaluated by coronary angiography (1 – one coronary artery disease; 2 – two coronary artery disease; 3 – three coronary artery disease)

Fig. 8.53. Final diagnostic in patients with left bundle branch block according to hipertensive status

VIII.4 Prolonged QRS duration – poor outcome for coronary artery disease in left bundle branch block patients

Between January 2011 and June 2013, 402 patients with left bundle branch block were admitted in Georgescu Institute of Cardiovascular Diseases. Only 323 of them were included in the study after exclusion of patients with a permanent pacemaker or automated implantable cardiac defibrillator, patients with myocardial infarction and those with valvular heart disease.
Baseline characteristics

Patients with QRS duration ≥ 140 ms were older, predominantly males and with new or presumably new left bundle branch block. They were more likely to have a prior history of diabetes mellitus and cardiovascular events, including hypertension, congestive heart failure, angina and percutaneous coronary intervention (fig. 8.55).

![Fig.8.55. Characteristics of patients with left bundle branch block according to QRS complex duration. AP: angina pectoris; HTA: arterial hypertension; DM: diabetes mellitus; HF: congestive heart failure.](image)

Left ventricular systolic function

Patients with QRS duration ≥ 140 ms were more likely to have a decreased ejection fraction, 111 patients vs. 81 patients, p= 0.001, more than half of them having an ejection fraction less than 30% (fig.8.56).

![Fig.8.56. Left ventricular systolic fraction (EF < 50%) according to QRS complex duration.](image)

Left ventricular diastolic function

Patients with left bundle branch block and a QRS complex ≥ 140 ms had a more frequent left ventricular diastolic dysfunction, with a restrictive mitral profile, without significant differences between the two groups (p = 0.425).
Left bundle branch block and cardiac arrhythmias in patients with prolonged QRS duration ≥ 140 ms

We found a more frequent association between a prolonged QRS duration ≥ 140 ms and the risk of ventricular tachycardia, but without statistically significant differences between the two groups (fig.8.58).

![Fig.8.58. Cardiac arrhythmias in patients with left bundle branch block, according to the QRS complex duration.](image)

Coronary lesions in patients with left bundle branch block and a prolonged QRS duration

Conventional coronary angiography was performed in 49 (29.87%) patients with QRS ≥ 140 ms and 5 (3.04%) patients were evaluated using computed tomography angiography (CTA). Most of them had no vessel disease (67.29%) and when this was the case, it was frequently localized on the left descendent artery (24.39%). The majority of patients with QRS duration ≥ 140 ms had two or three-vessel coronary lesions (12.19% vs. 5.66%) (fig.8.59).

![Fig.8.59. Coronary lesions in patients with left bundle branch block and a prolonged QRS duration which were evaluated by coronary angiography (1 – one coronary artery disease; 2 – two coronary artery disease; 3 – three coronary artery disease)](image)
Left bundle branch block contribution in establishing the final diagnostic in patients with a prolonged QRS complex

Of the patients with QRS duration ≥ 140 ms, 104 (63.41%) had final diagnosis of stable angina, the remaining 60 patients (36.59%) being diagnosed with a non-coronary pathology (fig.8.61).

**Fig.8.61.** Final diagnostic of patients with left bundle branch block according to the QRS complex duration.

VIII.5 Significance of left bundle branch block in patients with acute myocardial infarction

**Age**

Patients with acute myocardial infarction and new left bundle branch block, had a higher mean age at onset of the acute coronary event compared with patients in the control group, with a statistically significant differences between the two groups (67 ± 9.31 vs. 58 ± 10.39 years, p=0.007).

**Sex**

Compared to other studies, we observed a higher number of male patients with acute myocardial infarction without left bundle branch block (p=0.005) (fig.8.64).

**Fig.8.64.** The gender distribution of patients included in study
Baseline characteristics of patients with acute myocardial infarction and new left bundle branch block patients

Patients with left bundle branch block had a more frequent history of myocardial infarction, percutaneous coronary revascularization, hypertension, diabetes mellitus, heart failure, obesity and dyslipidemia. In contrast, patients without left bundle branch block had a more frequent history of current or previous smoker (fig.8.65).

![Graph showing baseline characteristics of patients](image)

**Fig.8.65.** Baseline characteristics of patients with acute myocardial infarction and new left bundle branch block patients (AP: angina pectoris; HTA: arterial hypertension; DM: diabetes mellitus; HF: congestive heart failure)

**Smoker status**

In our study we observed that more than half of patients without left bundle branch block were smokers or former smokers (57.14%), compared with a rate of 35.71% for those with left bundle branch block, but without statistically significant differences between the two groups of patients (p = 0.076) (fig.8.67).

![Pie charts showing smoker status](image)

**Fig.8.67.** Smoker patients with acute myocardial infarction and new left bundle branch block (A) vs. without left bundle branch block (B)

**Lipid profile**

Half of the patients in the control group had a normal cholesterol value compared with a low percentage of 19.04% in patients with left bundle branch block, with statistically significant differences between the two groups (p = 0.003) (fig.8.69).
Lipid profile of patients with acute myocardial infarction and new left bundle branch block

**Left ventricular systolic function**

Patients with left bundle branch block had a normal left ventricular systolic function (fig. 8.70). In contrast, patients from the control group had a moderate left ventricular systolic dysfunction, 64.28% had an ejection fraction of 30-50%.

**Angiographic data**

Although there were no statistically significant differences in terms of the interval from the onset of symptoms to coronary angiography (p = 0.290), we observed that most patients (64.28%) in the control group had a late presentation, to over 10 hours of the onset of symptoms (fig 8.72).

When coronary artery disease was present it was frequently localized on the left descendent artery in both groups, but without statistically significant differences (54.77% vs. 69.12% in control group, p = 0.131).

**Cardiac arrhythmias in patients with acute myocardial infarction and new left bundle branch block patients**

Nearly a third of patients with left bundle branch block had extrasystolic ventricular arrhythmias (33.33% vs. 4.76%, p = 0.001) and five patients developed postprocedural atrial fibrillation (11.9% vs. 2.38%, p = 0.05).
Medication given within 24 hours of admission

Assessing the medication given within 24 hours of hospitalization, we observed that patients with left bundle branch block more frequently received beta-blocker treatment, antiarrhythmic, diuretics and ACE inhibitors (fig.8.77).

VIII.6 Long term prognosis induced by new left bundle branch block in patients with acute myocardial infarction

The mean follow-up

We prospectively studied all the patient included in this study after a mean follow-up of 16.51 ± 2.41 months, assessing the symptoms, biological and echocardiographic characteristics of these patients (fig.8.78).

Smoker status

If in the onset of coronary event almost half (46.42%) of patients included in the study were smokers, at the control visit 82.15% of patients were no longer smokers.
Fig. 8.7. The mean follow-up of patients with acute myocardial infarction and new left bundle branch block

**Obesity**

We observed a significant reduction of the body mass index in both study groups, but without statistically significant differences between patients with and without left bundle branch block (p = 0.782).

**Lipid profile**

We also observed a significant reduction in lipid profile values in the control evaluation as compared to the initial values. However, only 20 patients with left bundle branch block and 15 patients in the control group reached the target LDLc, respectively ≤ 70 mg/dl or more than 50% reduction from baseline (fig. 8.82).

Fig. 8.82. Lipid profile in patients with acute myocardial infarction and left bundle branch block: initial vs. control

**Left ventricular systolic function in patients with myocardial infarction and left bundle branch block - control**

In assessing control, we noticed an increase number of patients with severe systolic dysfunction, especially those with left bundle-branch block. Thus, almost a double number of
patients with left bundle branch block had an ejection fraction below 30%, despite an early revascularization in these patients compared with those in the control group, the differences being statistically significant, \( p = 0.001 \) (fig.8.83).

![Fig.8.83. Left ventricular systolic function in patients with myocardial infarction and left bundle branch block: initial vs. control assessment](image)

In contrast, in patients with acute myocardial infarction without left bundle branch block, we observed a significant improvement of left ventricular systolic function (9 vs. 24 patients in control assessment having an ejection fraction > 50%).

Studying the link between QRS complex duration from the initial hospitalization and ejection fraction from control assessment, we noticed that a prolonged QRS duration in the initial hospitalization was associated with an important systolic dysfunction in control assessment (Table 8.VII).

<table>
<thead>
<tr>
<th></th>
<th>EF</th>
<th>QRS duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF</td>
<td></td>
<td>-0.522</td>
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<tr>
<td>Sig. (2-tailed)</td>
<td>1</td>
<td>0.000</td>
</tr>
<tr>
<td>N</td>
<td>84</td>
<td>84</td>
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<tr>
<td>QRS duration</td>
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<td>N</td>
<td>84</td>
<td>84</td>
</tr>
</tbody>
</table>

**Correlation between QRS duration, left ventricular systolic function, the interval from the onset of symptoms to coronary angiography and the risk of ventricular arrhythmias**

Using another model of multivariate regression, we did not observe a statistically significant association between QRS duration, the initial ejection fraction, the interval from the onset of symptoms to coronary angiography and the risk of ventricular tachycardia.

**Long term arrhythmic risk in patients with acute myocardial infarction and left bundle branch block**

We observed a higher risk of ventricular premature beats in patients with left bundle branch block (18 vs. 5, \( p = 0.003 \)), both on the initial hospitalization and control assessment, with statistically significant differences compared with patients without left bundle branch block (fig.8.85).
Fig. 8.85. Long term arrhythmic risk in patients with acute myocardial infarction and left bundle branch block

**QRS complex duration – negative long term predictor of ventricular systolic dysfunction**

We also observed that the presence of left bundle branch block ($F = 3.64; p < 0.005$; partial $\eta^2 = 0.33$) and the duration of the QRS complex ($F = 4.17; p < 0.005$; partial $\eta^2 = 0.36$) is statistically significantly correlated with the value of left ventricular ejection fraction (Table 8.X).

**Table 8.X.** Multivariate analysis for evidence of a possible association between various risk factors and left ventricular systolic function

<table>
<thead>
<tr>
<th>Source</th>
<th>Dependent Variable</th>
<th>Type III Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>$F$</th>
<th>Sig</th>
<th>Partial $\eta^2$</th>
<th>Noncent. Parameter</th>
<th>Observed Power</th>
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</thead>
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<tr>
<td>Intercept</td>
<td>BRS</td>
<td>11,242</td>
<td>1</td>
<td>11,242</td>
<td>58.57</td>
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<td>.445</td>
<td>58.575</td>
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</tr>
<tr>
<td></td>
<td>DURATAQRS</td>
<td>488952,572</td>
<td>1</td>
<td>488952,572</td>
<td>2717,205</td>
<td>.000</td>
<td>.974</td>
<td>2717,205</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>TIMP</td>
<td>8860,944</td>
<td>1</td>
<td>8860,944</td>
<td>1437,093</td>
<td>.000</td>
<td>.952</td>
<td>1437,093</td>
<td>1.000</td>
</tr>
<tr>
<td>FE%2</td>
<td>BRS</td>
<td>6,869</td>
<td>10</td>
<td>.699</td>
<td>3.642</td>
<td>.001</td>
<td>.333</td>
<td>36,417</td>
<td>.990</td>
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<tr>
<td></td>
<td>DURATAQRS</td>
<td>7505,630</td>
<td>10</td>
<td>750,563</td>
<td>4.171</td>
<td>.000</td>
<td>.364</td>
<td>41,710</td>
<td>.996</td>
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<tr>
<td></td>
<td>TIMP</td>
<td>34,879</td>
<td>10</td>
<td>3,488</td>
<td>566</td>
<td>.837</td>
<td>.072</td>
<td>5,657</td>
<td>.289</td>
</tr>
</tbody>
</table>

- a. R Squared = .333 (Adjusted R Squared = .241)
- b. Computed using alpha = .05
- c. R Squared = .364 (Adjusted R Squared = .276)
- d. R Squared = .072 (Adjusted R Squared = .055)

Comparing the distribution of patients according to QRS duration, we noted that patients with a prolonged QRS duration have a severe systolic dysfunction on long term (fig.8.86).

Therefore, the presence of left bundle branch block and especially a prolonged QRS duration, is significantly associated with a severe left ventricular systolic dysfunction on long-term, in our case, after a mean follow-up of 17 months.
CHAPTER IX
DISCUSSIONS

Our results show that, in a suggestive clinical context, the presence of new left bundle branch block indicates a high probability of coronary artery disease, so these patients should be angiographically evaluated. Almost half of patients with angina and new left bundle branch block from our study were diagnosed with coronary lesions. In our study we managed to prove that the presence of new left bundle branch block, in a clinical context of acute myocardial infarction has important prognostic implications on long term, especially in terms of left ventricular systolic dysfunction, which is more severe in these patients.

Also, our study is among the few studies that have shown that the presence of new left bundle branch block in diabetic patients is associated and may be the first manifestation of coronary artery disease, almost half of diabetic patients being diagnosed with coronary lesions, unlike patients without diabetes that in over two thirds of cases had no coronary disease.

Hypertensive patients with left bundle branch block from our study had a more frequent history of diabetes, myocardial infarction and angina as compared with normotensive patients. In the same time, coronary lesions, especially one or two coronary lesions, were more common in hypertensive patients.

Our results show that patients with left bundle branch block and a prolonged QRS duration, have a more reserved prognosis due to left ventricular systolic dysfunction, the severity of coronary lesions and arrhythmic risk.

Another objective of our study was to quantify the impact of left bundle branch block on ventricular systolic function and arrhythmic risk. We observed a more frequent association (almost in two thirds of patients) between the anterior myocardial infarction and left bundle branch block. Also, patients with acute myocardial infarction and new left bundle branch block had a higher risk of atrial fibrillation and premature ventricular beats as compared with patients without left bundle branch block. After a median follow-up of 17 months, patients with new left bundle branch block had a worsening left ventricular systolic function, with a significant correlation between the initial QRS duration and the value of ejection fraction. Basically, patients with prolonged QRS duration had a severe systolic dysfunction on long term.
Also, we observed statistically significant differences between patients with new and persistent left bundle branch block, in terms of angiographic exploration. If only one fifth of patients with persistent left bundle branch block were angiographically evaluated, in patients with new left bundle branch block, coronary angiography was performed in more than 80% of patients.

Assessing the long term prognosis of patients with acute myocardial infarction and new left bundle branch block, we noticed that despite an earlier myocardial revascularization of these patients, there is a progressive reduction of the left ventricular systolic function after a median follow-up of 17 months, with a statistically significant correlation between the initial QRS duration and the value of ejection fraction in the control evaluation.

In our study we observed that left bundle branch block was more frequent in patients with anterior myocardial infarction.

We also noticed a direct correlation between the initial QRS duration and the value of left ventricular ejection fraction in assessing control, practically a greater QRS duration at the onset of myocardial infarction is associated with a severe left ventricular systolic dysfunction in the assessing control. Instead, we found no correlation between the QRS duration, the value of ejection fraction from initial hospitalization and the risk of long term ventricular arrhythmias in patients with acute myocardial infarction and new left bundle branch block. In the same time, a prolonged QRS duration in patients with left bundle branch block is associated with a reserved prognosis due to severe left ventricle systolic dysfunction, the severe coronary lesions and the increased risk of arrhythmia.

Patients with acute myocardial infarction and left bundle branch block represent a relatively small group but with an increased risk of malignant ventricular arrhythmias. These patients should therefore benefit from a promptly and appropriately treatment in order to improve long term outcome. Also, considering the fact that one in two patients with acute myocardial infarction and new left bundle branch block die in the first year after the acute coronary event, we believe that these patients are candidates for automatic implantable defibrillators, with or without cardiac resynchronization therapy.

In conclusion, in the absence of a single criterion that clearly distinguish patients with acute myocardial infarction in the presence of left bundle branch block, all patients with new left bundle branch block and high clinical suspicion of acute myocardial infarction should benefit of urgent reperfusion therapy, preferable percutaneous coronary intervention, if is timely available.

**CHAPTER X**

**CONCLUSIONS**

1. Conventional coronary angiography was performed in more than two thirds of patients with new or presumably new left bundle branch block, which revealed significant coronary lesions in nearly half of them, especially one or two coronary lesions, localized on the left descendent artery.

2. Compared with patients with new left bundle branch block, coronary angiography was performed only in one-fifth of patients with chronic left bundle branch block, over two thirds of them having insignificant coronary lesions. Patients who still had coronary disease, most commonly presented three coronary lesions.

3. Patients with new left bundle branch block were more likely to have a prior history of hypertension, dyslipidemia and tobacco use. Patients with chronic left bundle branch block were more likely to have a history of congestive heart failure, myocardial infarction, angina
and percutaneous coronary intervention, with statistically significant differences between the two groups.

4. Chest pain was the most common symptom at presentation. Over two thirds of patients with new left bundle branch block and half of patients with chronic left bundle branch block had chest pain, with statistically significant differences.

5. Patients with new left bundle branch block most commonly had a normal left ventricular systolic function, and over two thirds of patients with chronic left bundle branch block had left ventricular systolic dysfunction.

6. In about two thirds of patients, new left bundle branch block occurred in a clinical context of acute myocardial infarction, was a complication of anterior myocardial infarction. They were followed by inferior and lateral myocardial infarctions, which occurred in an equal number of patients with new left bundle branch block.

7. Patients with chronic left bundle branch block were more likely to have ventricular and supraventricular arrhythmias and also atrioventricular conduction disorders, as compared with new left bundle branch block patients, the differences between the two groups being statistically significant.

8. Patients with new left bundle branch block were more likely to receive the proper medication for an acute coronary syndrome, with statistically significant differences in terms of beta-blockers, antiplatelet treatment and statins.

9. Almost two thirds of patients with new left bundle branch block presented with chest pain were diagnosed with ischemic coronary artery disease, one in four patients being diagnosed with acute coronary syndrome.

10. About 90% of diabetic patients with new left bundle branch block were angiographically evaluated, almost half of them being diagnosed with significant coronary lesions, unlike non-diabetic patients that in two third of cases had no coronary artery disease.

11. A small number of patients with left bundle branch block from our study were evaluated by computer tomography angiography, a third of them were diagnosed with significant coronary lesions, later confirmed angiographically.

12. Patients with left bundle branch block and a prolonged QRS duration had a more reserved prognostic compared to patients with a QRS duration less than 140 ms, both due to left ventricular systolic dysfunction, the severity of coronary lesions and arrhythmic risk.

13. The risk of supraventricular and ventricular arrhythmias, especially atrial fibrillation and extrasystolic ventricular beats is higher in patients with acute myocardial infarction and new left bundle branch block than in patients without left bundle branch block.

14. After a median follow-up of 17 months, evaluation of patients with acute myocardial infarction, one coronary lesion, with and without left bundle branch block, showed a significant reduction of modifiable cardiovascular risk factors (smoking, hypertension, obesity, dyslipidemia) in both groups of patients, especially in those with left bundle branch block.

15. Despite an earlier myocardial revascularization of patients with myocardial infarction and left bundle branch block, we observed a progressive reduction of the left ventricular systolic function after a median follow-up of 17 months, with a statistically significant correlation between the initial QRS duration and the value of ejection fraction in the control evaluation.

16. Analyzing the correlation between QRS duration, initial left ventricular ejection fraction, time from onset of symptoms to revascularization and the long term risk of ventricular tachycardia, we didn’t observed a statistically significant associations.

17. The presence of LBBB and especially the QRS duration is significantly correlated with the severity of left ventricular systolic dysfunction, so that patients with a prolonged QRS duration have a severe left ventricular dysfunction on long term.
CHAPTER XI
ORIGINALITY AND PERSPECTIVES OF THE PhD RESEARCH

In our study we demonstrated that almost two thirds of patients with new left bundle branch block and chest pain had coronary artery disease, one in four patients being diagnosed with an acute coronary syndrome. By demonstrating this high prevalence of coronary artery disease in patients with new left bundle branch block, we consider that it is necessary to evaluate by coronary angiography all patients with high risk of acute coronary occlusion and caution in therapeutic approach of those with an unclear clinical context. This would reduce delays in optimal therapeutic treatment of patients with acute myocardial infarction and coronary disease.

By demonstrating the reserved prognostic of patients with left bundle branch block and a prolonged QRS duration, because of left ventricular systolic dysfunction and risk of arrhythmias, we have emphasized the necessity for careful evaluation of these patients, both in terms of cardiovascular background and in terms of echocardiography, even in asymptomatic patients.

Another novelty of our study is the fact that patients with acute myocardial infarction and new left bundle branch block had a progressive worsening of left ventricular ejection fraction in the control evaluation, despite an early myocardial revascularization. This element of originality supports the need for closer monitoring of patients with myocardial infarction and left bundle branch block in order to initiate timely appropriate treatment of heart failure. The correlations between the presence of left bundle branch block in patients with acute myocardial infarction and increased risk of arrhythmia, is an additional argument for automatic implantable defibrillators, with or without cardiac resynchronization therapy in these patients.

Because this doctoral research was limited to a certain time, we intend to continue monitoring the evolution of the patients included in this study, up to 10 years to evaluate the effect of left bundle branch block on the evolution of these patients.

By creating a monitoring program for patients with left bundle branch block, initially by CT examination that could evidence the presence of coronary lesions, and after that frequent medical controls, could identify earlier and prevent acute coronary events. In this regard, we proposed a program of collaboration with internal doctors and cardiologists from other hospitals, in order to further evaluation of these patients.
Selective references


List of papers published by the author from the study results and theme

1. ISI JOURNALS


2. INTERNATIONAL DATABASE INDEXED JOURNALS