

**“LUCIAN BLAGA” UNIVERSITY OF SIBIU  
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**CARDIOVASCULAR DYSFUNCTION IN LIVER  
CIRRHOSIS**

**Ph.D. THESIS SUMMARY**

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# CONTENTS

LIST OF ABBREVIATIONS .....	5
INTRODUCTION.....	6

## I. GENERAL PART

### CHAPTER 1- *Liver cirrhosis - definition, etiology, pathogenesis, pathophysiology*

<b>1.1. DEFINITION.....</b>	<b>10</b>
<b>1.2. ETHIOLOGY.....</b>	<b>10</b>
1.2.1. Alcohol .....	13
1.2.2. Hepatic viruses .....	13
1.2.3. Hepatotoxic substances .....	14
1.2.4. Nutritional factors.....	14
1.2.5. Cardiac cirrhosis .....	15
1.2.6. Hereditary causes of cirrhosis .....	15
1.2.7. Biliary obstruction .....	15
<b>1.3. PATHOGENESIS .....</b>	<b>16</b>
1.3.1. Classification of cirrhosis .....	18
1.3.2. Pathological anatomy.....	20
<b>1.4. PATHOPHYSIOLOGY.....</b>	<b>21</b>
1.4.1. Carbohydrate metabolism.....	22
1.4.2. Metabolism of amino acids and ammonia.....	22
1.4.3. Protein synthesis and degradation .....	23
1.4.4. Hormonal metabolism.....	23
1.4.5. Lipid metabolism .....	24
1.4.6. Acid-base balance disorders .....	24
1.4.7. Antitoxic function deficit.....	24
1.4.8. Drug intoxication .....	24
1.4.9. Endotoxemia and endogenous bacteremia .....	24
1.4.10. Bilirubin metabolism .....	25
1.4.11. Portal hypertension syndrome .....	25
1.4.12. Ascites in liver cirrhosis .....	26
1.4.13. Hepatoportal encephalopathy .....	26

## CHAPTER 2 - *Cardiovascular dysfunction in liver cirrhosis: theoretical considerations*

<b>2.1. INTRODUCTION</b> .....	27
<b>2.2. CIRRHOTIC CARDIOMYOPATHY</b> .....	29
2.2.1. Definition .....	29
2.2.2. Epidemiology.....	29
2.2.3. Etiopathogenesis .....	30
2.2.3.1. <i>Role of changes in cardiomyocyte membrane</i> .....	30
2.2.3.2. <i>Role of ventricular <math>\beta</math>-adrenoceptors</i> .....	31
2.2.3.3. <i>Role of ventricular muscarinic receptors</i> .....	32
2.2.3.4. <i>Role of ventricular <math>K^+</math> channels</i> .....	32
2.2.3.5. <i>Role of extracellular <math>Ca^{2+}</math> channels and sarcoplasmic reticulum</i> ..	33
2.2.3.6. <i>Role of ionic regulation of <math>Na^+/Ca^{2+}</math> exchange</i> .....	34
2.2.3.7. <i>Role of carbon monoxide</i> .....	35
2.2.3.8. <i>Role of cannabinoids and their receptors</i> .....	35
2.2.3.9. <i>Role of nitric oxide</i> .....	37
2.2.3.10. <i>Role of apoptosis in impaired myocardial function in cirrhosis</i> ...	38
2.2.4. Pathophysiology.....	39
2.2.4.1. <i>Vascular dysfunction</i> .....	39
2.2.4.2. <i>Systolic dysfunction</i> .....	40
2.2.4.3. <i>Diastolic dysfunction</i> .....	43
2.2.4.4. <i>Electrophysiological abnormalities</i> .....	45
2.2.5. Positive diagnosis .....	46
2.2.5.1. <i>ECG in cirrhotic cardiomyopathy</i> .....	48
2.2.5.2. <i>Echocardiography in cirrhotic cardiomyopathy</i> .....	49
2.2.5.3. <i>The natriuretic peptides</i> .....	52
2.2.5.3.1. <i>B (BNP) natriuretic peptide</i> .....	53
2.2.5.3.2. <i>N-terminal fragment of the BNP</i> .....	54
2.2.5.3.3. <i>BNP and NT-pro-BNP in cirrhotic cardiomyopathy</i> .....	54
2.2.5.3.4. <i>Diagnosis and prognostic value of natriuretic peptides</i> .....	54
2.2.6. Potential lines of therapeutic approach.....	55

## II. SPECIAL PART

### CHAPTER 3 - *Personal research on cardiovascular dysfunction in liver cirrhosis*

<b>3.1. INTRODUCTION</b> .....	56
<b>3.2. PURPOSE OF THE THESIS</b> .....	57
<b>3.3. PATIENTS AD METHOD</b> .....	57
<b>3.4. STRUCTURE OF THE GROUP OF PATIENTS</b> .....	58
<b>3.5. STUDY 1 – Correlation between stage of cirrhosis, its complications and NT-pro-BNP values</b> .....	64
3.5.1. Purpose.....	64
3.5.2. Material and method .....	64
3.5.3. Results.....	65
• <i>Correlation between stage and etiology of cirrhosis</i> .....	65
• <i>Correlation between stage of cirrhosis and NT-pro-BNP</i> .....	69
• <i>Cirrhosis-related complications and diseases</i> .....	72
• <i>Correlation between the length of registration of cirrhosis and NT-pro-BNP values</i> .....	76
• <i>Correlation between chronic renal failure (IRC) and NT-pro-BNP</i> .....	77
• <i>Correlation between diabetes mellitus (DZ) and NT-pro-BNP</i> .....	78
3.5.4. Discussions .....	81
• <i>Variability of NT-pro-BNP, selection of reference values, results</i> .....	81
• <i>Complications of cirrhosis</i> .....	84
3.5.5. Conclusions.....	85
<b>3.6. STUDY 2- Analysis of the degree of heart failure detected by clinical examination, ECG, echocardiography and its relation with NT-pro-BNP values</b> .....	86
3.6.1. Purpose.....	86
3.6.2. Material and method .....	86
3.6.3. Results.....	87
• <i>Correlation between NT-pro-BNP and left atrium (AS)</i> .....	95
• <i>Correlation between NT-pro-BNP and Mitral Regurgitation</i> .....	97
• <i>Correlation between NT-pro-BNP and Tricuspid Valve Outflow</i> .....	98
• <i>Correlation between NT-pro-BNP and Pulmonary Valve Outflow</i> ...	100
• <i>Correlation between NT-pro-BNP and Aortic Outflow</i> .....	101
• <i>Correlation between NT-pro-BNP and QT interval</i> .....	105
3.6.4. Discussions .....	108
3.6.5. Conclusions.....	111
<b>3.7. STUDY 3- Correlation between the values of NT-pro-BNP and TIPS insertion</b> .....	112
3.7.1. Premise.....	112

3.7.2. Purpose.....	112
3.7.3. Material and method .....	112
3.7.4. Results.....	112
3.7.5. Discussions .....	115
3.7.6. Conclusions.....	117
<b>3.8. STUDY 4 – Correlation between NT-pro-BNP values and QT- medication</b> .....	118
3.8.1. Purpose.....	118
3.8.2. Material and method .....	118
3.8.3. Results.....	118
• <i>Correlation between NT-pro-BNP values and diuretic therapy</i> .....	118
• <i>Correlation between QT-interval and the treatment with Propranolol</i> .... .....	122
3.8.4. Discussions .....	126
3.8.5. Conclusions .....	127
<b>3.9. RESULTS AND CONCLUSIONS</b> .....	128
3.9.1. Results.....	128
3.9.2. Conclusions.....	132
<b>3.10. LIMITATIONS OF THE STUDY</b> .....	133
<b>3.11. ORIGINALITY OF THE THESIS</b> .....	133
 <b>REFERENCES</b> .....	134

## INTRODUCTION

The word "cirrhosis" derives from Greek "khirros", meaning orange-yellow, the name of the disease being thus determined by the pale brown color of the liver, and not by its increased consistency. Laënc, who developed the understanding of cirrhosis, states in his treaty that he was impressed by the color of the liver. Over time, the term of cirrhosis has been identified with the liver sclerosis, almost forgetting the color significance.

Vascularization of the liver comes from the portal vein and the hepatic artery, the portal vein providing 75% of the total hepatic flow. These two vessels provide a double movement: nutritional (hepatic artery) and functional (portal vein). Suprahepatic veins drain into the inferior vena cava, near its entry into the right atrium. The liver is interposed between the abdominal blood drained by the portal vein and inferior vena cava and the heart.

This position makes the liver to be affected by abnormal hemodynamic pressure on either of these two levels (portal vein and inferior vena cava). The best known of these anomalies is the portal hypertension syndrome.

The drainage of suprahepatic veins near the right atrium also favors repercussions of pressure increase in the right atrium on hepatic circulation. High right atrial pressure increases in the inferior cava, which will cause congestion in suprahepatic veins and intrahepatic stasis.

Cardiac cirrhosis is an exceptional form of liver cirrhosis; it occurs at a low frequency (0,4% of cases) in congestive heart failure, predominantly in old cardiac insufficiencies, with repeated episodes of decompensation of the tricuspid insufficiency, constrictive pericarditis or pulmonary stenosis.

Hemodynamic factors responsible for the production of cirrhosis are: decreased cardiac output, increased right atrial pressure, where we can add reduced sinusoidal circulation and superimposed infections (bacterial endocarditis, respiratory infection).

On the other hand, there are hepatic changes in heart failure and heart rate changes in liver cirrhosis. The liver and heart are directly interconnected to veins, as we explained above, the primary impairment of one of them causes a secondary damage to the other. If the liver disease in heart failure is well known, the words "cardiac cirrhosis" or "cardiac liver" being rooted, not the same thing happens with compromised cardiac cirrhosis, the new clinical entity called "cirrhotic cardiomyopathy" not being so well-known.

Moreover, liver cirrhosis is not only a disease of the body; changes made as a result of damage of various functions of the liver have echoes in the entire

body. The lungs are affected with hepatopulmonary syndrome, kidney with hepatorenal syndrome, brains with hepatic encephalopathy, etc.

"Cirrhotic cardiomyopathy" is a recently recognized entity consisting in systolic incompetence in conditions of stress, diastolic dysfunction due to changes in diastolic relaxation and electrophysiological changes in the absence of any known cardiac disease.

Clinically, systolic incompetence is most obvious when patients are subjected to stress, whether physical or pharmacological, or when peripheral arterial vasodilation requires an increased cardiac output, as in the case of bacterial infections.

It is known that patients with cirrhosis are very likely to develop bacterial infections; spontaneous bacterial peritonitis is the most frequent infection in advanced cirrhosis. Patients with cirrhosis may also become at some point during therapy, candidates for liver transplantation or for an insertion of a transjugular intrahepatic portosystemic shunt (TIPS), both interventions being stressful to the heart and may unmask a cirrhotic cardiomyopathy.

Moreover, it was observed that up to 56% of transplanted patients experienced hypoxemia and pulmonary edema in the postoperative period. Also the mortality associated with cardiac causes reaches 7% in the immediate and medium-term post-transplantation period.

Given this situation, the ability to discover the individuals who will present cardiovascular events during and after liver transplantation is of great importance in the selection of patients.

Cirrhotic cardiomyopathy can be diagnosed using a combination of ECG, two-dimensional echocardiography and serum markers as natriuretic peptide B. Due to concomitant pulmonary complications, increased reliability and ability to provide a cardio-pulmonary overall image, a chest x-ray can be added as first intention.

## **SPECIAL PART**

### **Personal research on cardiovascular dysfunction in liver cirrhosis**

#### **PURPOSE OF THE THESIS**

The purpose of this paper is to evaluate NT-pro-BNP as a cardiac biomarker, demonstrating the relationship between its increased level and the degree of heart failure in patients with liver cirrhosis.

#### **PATIENTS AND METHOD**

The study group consisted of patients hospitalized in Liver Transplantation Clinic in Homburg, Germany, where for 3 months, from February to April 2011, we selected and monitored patients and have established the patient monitoring records necessary for the study.

The inclusion criteria for participation in the study were represented by: patients with clearly established diagnosis of liver cirrhosis (clinical and paraclinical) and the symptoms attributed to this disease.

Patients with secondary cirrhosis were not included: cardiac cirrhosis, Budd-Chiari syndrome, etc.

The group consisted of 54 patients hospitalized for monitoring liver cirrhosis previously diagnosed by clinical, paraclinical and laboratory tests. Most patients (45) were on the liver transplantation waiting list of the clinic.

Patients were evaluated in terms of hepatology and cardiology by clinical examination, abdominal ultrasound, echocardiography, chest X-ray, electrocardiogram and laboratory tests as bilirubin, liver transaminases, coagulation factors, albumin, creatinine. In addition, NT-pro-BNP was determined in all patients on the day of admission to the clinic.

We drafted a patient monitoring record in each patient, it includes the initials of the surname and first name, age, gender, significant physiological and pathological personal history, diagnosis, outcomes of laboratory tests and investigations and the treatment followed.

To achieve the purpose of the paper, we studied the relationship between stage of cirrhosis, its complications and NT-pro-BNP values; we analyzed the heart disease by clinical examination, ECG, echocardiography and relationship with NT-pro-BNP; we studied the correlation between the values of NT-pro-BNP and cardiac specific impairment; the correlation between NT-pro-BNP values and transjugular intrahepatic portosystemic shunt insertion; the



correlation between NT-pro-BNP values , QT interval and drug treatment followed by patients.

Statistical analysis:

The data we have obtained from each patient were collected in a nominal table and inserted into a database that allows statistical analysis based on the parameters in the study: gender, age, registration date with the diagnosis of liver cirrhosis, etiology of cirrhosis, stage of cirrhosis, NT-pro-BNP values, cirrhosis-related complications and diseases, signs of cardiac disease, QT interval duration, valve outflows.

We used the "Epi Info" programme for creating and managing the database, programme developed by the World Health Organization to study the disease epidemiology and perfected over time, from its creation in Atlanta, Georgia - USA, in order to meet the finest medical research needs.

Given the alternative qualitative characteristics (presence or absence of symptoms, complications or changes), we used the "Chi-squared" statistical significance test to demonstrate the presence or absence of significant differences between:

- patients who have undergone a specific treatment, compared with those who did not receive this treatment. We thus examined the relationship between TIPS insertion and NT-pro-BNP values, the relationship between chronic treatment with diuretics and NT-pro-BNP values, as well as the relationship between Propranolol treatment and the length of the QT interval.
- NT-pro-BNP values and the signs of heart failure, QT-interval length and the presence or absence of valvular outflows
- correlation between cirrhosis stage and NT-pro-BNP values and the correlation between associated complications/diseases and etiology of cirrhosis.

The results we presented in tables that allow a detailed analysis of the phenomenon, and graphics that suggestively highlight this phenomenon.

## **STRUCTURE OF THE GROUP OF PATIENTS**

The study group was constituted mostly of men aged 50-59 years.

Studying the structure of the group according to the etiology of cirrhosis and gender, we found that the group was constituted mostly of patients with ethanol cirrhosis (24), where the majority were men (17).

The most common was the cirrhosis of viral etiology (HCV), while autoimmune and drug cirrhosis was registered a year ago.

## **STUDY 1 – Correlation between stage of cirrhosis, its complications and NT-pro-BNP values**

### **Material and method**

We studied the patient monitoring records of the 54 patients and we extracted data about age, gender, diagnosis and the value of NT-pro-BNP.

NT-pro-BNP was determined by Electrochemiluminescent Immunoassay (ECLIA), using a COBAS system (proBNP<sub>II</sub>\_cobas\_2011-06, V6 pdf BNP\_CalSet\_2007-10\_V2pdf).

NT-pro-BNP values obtained in human subjects that we studied were laid out on a great range from 15 to 2342 pg/ml. Values less than 250 pg/ml were considered negative and values greater than or equal to 250 pg/ml were considered positive, in order to study the relationship between NT-pro-BNP and heart failure from liver cirrhosis on the basis of positive values.

Data obtained were collected and processed statistically.

Child-Pugh-Turcotte score was used for cirrhosis stage. This score is used to estimate the prognosis of a chronic liver disease associated with hepatic impairment (liver cirrhosis). It involves five altered parameters in liver diseases whose severity is graded from 1 to 3 (3 being the most severe).

### **Results and conclusions**

- The majority of positive values of NT-pro-BNP were found in the 50-59 year age group in stage B.
- Most complications were found in the 50-59 year age group because there were most human subjects, but the percentage reference of complications in a number of human subjects in an age group has shown us that there are no statistically significant differences between age groups, except for liver cancer.
- We have noticed a positive correlation between NT-pro-BNP and IRC (chronic renal failure) and a negative correlation between NT-pro-BNP and the patients without IRC, although the Chi-square test did not confirm a statistically significant correlation.
- We did not notice a positive correlation between the presence of diabetes mellitus and NT-pro-BNP or a negative correlation between the absence of diabetes mellitus and NT-pro-BNP.

## **STUDY 2- Analysis of the degree of heart failure detected by clinical examination, ECG, echocardiography and its relation with NT-pro-BNP values**

### **Material and method**

In order to analyze the degree of heart failure, each patient of the group was subjected to a cardiovascular examination which consisted of:

1. Clinical examination of the cardiovascular system, noting positive signs and symptoms, namely those that suggest heart damage.
2. Chest radiography for detecting changes in shape, size and alignment of the heart.
3. ECG to detect electrical changes and their notation, focusing on the QT interval. During the electrocardiogram we mainly monitored the length of the QT interval, knowing that its extension may be part of electrophysiological changes of cirrhotic cardiomyopathy. An adjusted QT interval of 460 ms or more in women, and 450 ms or more in men, is considered a long QT interval, and a QT of 390 ms or less is considered a short interval. The electrocardiography was performed using a computer programme, "SmartSoft-ECG", developed by Dr. Gerhard Schmidt in Neunkirchen, Germany.
4. Echocardiography for marking the presence of cardiac changes specific for heart damage, focusing on left atrial dilation, and mitral, tricuspid, aortic and pulmonary outflows. Vivid E9 ultrasound of General Electric company was used herein.
5. Determination of natriuretic peptide in the serum of patients in order to study the relationship between increased NT-pro-BNP and the degree of heart failure. We used the same Cobas system mentioned in the previous study.

Data were collected and statistically processed using the methods described in the general methodology.

### **Results and conclusions**

Most patients in our study had no cardiovascular symptoms or signs when we started the study, but there were few who had systolic or diastolic murmurs. There were also patients with a diagnosis of tricuspid or mitral insufficiency in their medical history (1 patient with tricuspid and mitral insufficiency diagnosis and 2 patients with a diagnosis of mitral insufficiency), as well as 1 patient with a diagnosis of atypical atrial fibrillation. Given that the number was very small and there was no correlation between symptoms, signs and diagnosis (there are patients with signs and without diagnosis and vice versa) and because we did not

find a relation between their existence and values of NT-pro-BNP, we did not insist on these cases.

The standard chest X-ray in patients in whom changes were detected highlighted: slightly enlarged heart, COPD with emphysema or vascular signs of pulmonary venous pressure.

The echocardiography in all patients studied revealed a normal systolic pump function, normal-sized left ventricle and lack of regional ventricular wall-motion abnormalities, respectively akinesia. The systolic function was also normal in patients with transjugular intrahepatic portosystemic shunt insertion (TIPS), leading thus to the conclusion that we can not confirm a systolic dysfunction in patients studied.

One patient showed echocardiographic grade II diastolic dysfunction (E/A 1,11) and two other patients had signs of early diastolic dysfunction, but all had negative values of NT-pro-BNP. We statistically studied the relationship between the 5 types of signs: clinical, radiological, ECG, ultrasound and laboratory.

Thus, we observed the frequency in the presence of signs (P = present/positive) and the frequency in the absence of signs (N = normal, negative, absent) in the 54 human subjects and we found that 38 patients (70,4%) have echocardiographic changes, 28 patients (51,9%) have ECG changes, 17 patients (31,5%) have the level of NT-pro-BNP over 250 pg/ml. Clinical signs of heart disease were found only in 14 out of the 54 human subjects (25,9%) and radiological signs were found in only 10 out of the 54 human subjects (18,5%).

- It was observed the positive correlation between NT-pro-BNP and increased AS and the negative correlation between NT-pro-BNP and normal AS, although the application of Chi-square test does not confirm a statistically significant correlation.
- It was observed the positive correlation between NT-pro-BNP and the mitral regurgitation and the negative correlation between NT-pro-BNP and patients without mitral outflow, although the application of Chi-square test does not confirm a statistically significant correlation.
- It was observed the positive correlation between NT-pro-BNP and the tricuspid outflow and the negative correlation between NT-pro-BNP and patients without outflow, and the application of Chi-square test confirms a statistically significant correlation.
- We found no statistically significant correlation between NT-pro-BNP values and the pulmonary outflow.
- We found no statistically significant correlation between NT-pro-BNP values and the aortic outflow.
- The positive correlation between NT-pro-BNP and the elongation of the QT interval is statistically significant.

### **STUDY 3- Correlation between the values of NT-pro-BNP and TIPS insertion**

#### **Material and method**

Analyzing the patient monitoring records, we found that eight patients in the study group had a history of TIPS insertion. We analyzed these patients in terms of age, gender and NT-pro-BNP values. Data were collected and statistically processed as presented in the general methodology.

#### **Results and conclusions**

- The frequency of NT-pro-BNP positive values was 7% higher among patients with TIPS insertion, than among those without TIPS insertion; although this value does not show a statistically significant difference, showing a trend for increasing values of NT-pro-BNP in patients with TIPS (increases preload).
- Positive NT-pro-BNP is 11% more common in women.
- We have noticed an increasing trend in the number of human subjects with positive NT-pro-BNP in the age group over 60 years among those with TIPS insertion.
- Regarding the human subjects without TIPS insertion, there were no significant differences for the three age groups.

In my study, as I mentioned earlier, one could not confirm a systolic dysfunction in the patients studied, and those 3 patients in the group who presented signs of diastolic dysfunction had negative NT-pro-BNP.

The results obtained in the present study look like this because of the time elapsed between TIPS insertion and the NT-pro-BNP determination (over 1 year), time which probably allowed NT-pro-BNP values to normalize, and also because of the small number of patients with TIPS insertion studied.

### **STUDY 4 – Correlation between the values of NT-pro-BNP and QT-medication**

#### **Material and method**

In the study group we selected patients who were treated with diuretics and those who were treated with Propranolol. We included Spironolactone, Furosemide, Torsemide in the category of "diuretics".

We monitored the values of NT-pro-BNP and the length of the QT interval in these patients. Data were collected and statistically processed by age groups and gender.

## **Results and conclusions**

- We cannot say that the long-term treatment with diuretics may influence in one way the values of NT-pro-BNP.
- There were no statistically significant differences in the analysis by age groups and gender.
- The change of the QT interval occurred more frequently in patients who have not taken Propranolol, which leads us to say that Propranolol protects the normal length of the QT interval primarily by preventing its elongation.
- There was a significantly lower number of cases with normal QT interval in human subjects without Propranolol treatment, unlike those who have followed this treatment in all age groups.

## **RESULTS AND CONCLUSIONS**

### **Results**

1. The study group consisted mainly of men, most of them falling in the age group 50-59 years.

2. Regarding the etiology of liver cirrhosis, it was mostly ethanolic, most patients with this cirrhosis are also men.

3. Regarding the length of registration, the highest value was recorded for patients with cirrhosis of viral etiology (HCV), with autoimmune and drug cirrhosis at the opposite side.

4. Most patients in the study group were classified in Child B stage, the predominant etiology of this stage is also the ethanol stage, followed by HCV. This stage of cirrhosis predominated in all age groups, with a peak in men between 50-59 years old.

5. Most of the positive values of NT-pro-BNP were found in the 50-59 year age group, Child B cirrhosis stage.

6. Most patients in the study group showed complications of cirrhosis like: ascites (70,4%), esophageal varices (79,6%), splenomegaly (70,4%), hepatic encephalopathy (42,6 %) and liver cancer (14,8%). Most complications were found in the 50-59 year age group, because most human subjects were included here, but the percentage reference found no statistically significant differences between age groups, except for liver cancer.

7. Regarding the relationship between the etiology of cirrhosis and ascites appearance, we observed that most cases of ascites were recorded in patients with ethanol cirrhosis. Regarding distribution of complications by age groups, we noted the presence of splenomegaly in all human subjects under 50 years old and the presence of esophageal varices in 93% of human subjects aged over 60 years.

8. The signs of portal hypertension predominated in males in all age groups, most occurring in the 50-59 year age group where most human subjects are included, but the percentage distribution showed no statistically significant differences between the number of signs of portal hypertension.

9. No statistically significant relationship was found between the length of registration and NT-pro-BNP values, which prompted me to say that the date of registration does not match the date of cirrhosis occurrence. A statistically significant correlation was found only between ascites and positive NT-pro-BNP, so we can draw the conclusion that the presence of portal hypertension does not significantly influence the increase of natriuretic peptide in the serum of patients.

10. It was noted a positive correlation between NT-pro-BNP and IRC (chronic renal failure) and a negative correlation between NT-pro-BNP and patients without IRC, although the Chi-square test did not confirm a statistically significant correlation.

11. Regarding the relationship diabetes mellitus - NT-pro-BNP, there is no positive correlation between the presence of diabetes mellitus and NT-pro-BNP or a negative correlation between the absence of diabetes mellitus and NT-pro-BNP.

12. There is a statistically significant correlation between the method used to detect heart failure and the presence of signs of heart failure. The frequency of signs of heart failure by 4 methods (clinical examination, radiological examination, ECG, echo and laboratory tests) is higher in case of ultrasound method (38 out of 54 human subjects with ultrasound changes = 70%), followed by ECG (28 out of 54 human subjects with ECG changes = 52 %), and the clinical examination (14 out of 54 human subjects = 26%), with the radiological investigation on the last place, where 10 out of 54 human subjects show signs of heart failure = 18%. We note that clinical examination and radiological investigations were focused on cirrhosis investigation against heart investigation.

The signs of heart failure are more in males because 34 out of the 54 human subjects are male (63%), the frequency of signs of heart failure is

46/20=2,3 signs in a woman, or 61/34=1,8 signs in a man, gender differences being statistically insignificant.

Similarly, the signs of heart failure are more common in the 50-59 year age group because 29 out of the 54 human subjects (54%) are included in this group, the frequency of signs of heart failure is 52/29=1,9 signs in a 50-59 year age group human subject, and 34/14=2,4 signs in a human subject over 60 years old, as well as 21/11=1,9 signs in a human subject below 50 years old, the differences between age groups being statistically insignificant.

13. The correlation between the values of NT-pro-BNP and the presence or absence of signs of heart failure obtained by the 4 methods of heart investigation (clinical, radiological, ECG and echo) is not statistically significant, which is why we checked the correlation between the values of NT-pro-BNP and the presence of signs obtained by each method, avoiding thus any overlap of signs from one method over the other method's signs.

14. The association of NT-pro-BNP with clinical signs (5 out of 14 clinical signs are associated with positive NT-pro-BNP = 36%), NT-pro-BNP - echo association (15 out of 38 echo signs are associated with positive NT-pro-BNP = 39%), as well as NT-pro-BNP - ECG association (8 out of 28 ECG signs are associated with positive NT-pro-BNP = 29%), are not statistically significant, while NT-pro-BNP - Rx association (6 out of 10 Rx signs are associated with positive NT-pro-BNP = 60%) is statistically significant.

53% of female human subjects with positive NT-pro-BNP showed signs of heart failure, while only 27% of male human subjects showed signs of heart failure.

Most signs of heart failure positively associated with NT-pro-BNP are present in the age group over 60 years old (14 out of 29, i.e. 48%), where ultrasound signs are on the first place (5 out of 9, i.e. 55%); and the fewest signs of heart failure positively associated with NT-pro-BNP are present in the age group under 50 years.

15. There is a statistically significant correlation between NT-pro-BNP values and the length of the QT interval. The majority of human subjects with normal NT-pro-BNP have normal or short QT interval (33 out of 37 human subjects, i.e. 89 %), and most human subjects with positive NT-pro-BNP have normal or long QT interval (17 out of 17 human subjects, i.e. 100%, and no case of positive NT-pro-BNP is associated with the short QT interval.

Among human subjects with positive NT-pro-BNP, the QT-interval elongation is more common in women (37%) than in men (11%). The correlation between positive NT-pro-BNP and long QT interval is more common in the age group over 60 years (40% of human subjects with positive NT-pro-BNP are associated with long QT).



16. There is a correlation between positive NT-pro-BNP and the left atrial dilatation and between normal NT-pro-BNP and the normal-sized AS, stronger in women (6 out of 8 women with positive NT-pro-BNP have increased AS, i.e. 75 %) and in the age group over 60 years (4 out of the 5 human subjects with positive NT-pro-BNP have dilated AS = 80%).

17. There is a positive correlation between NT-pro-BNP and the presence of mitral outflow and a negative correlation between NT-pro-BNP and the absence of the mitral outflow. The correlation is 100% for female subjects, all 8 women with positive NT-pro-BNP were registered with mitral outflow at Doppler echocardiogram. The correlation is also 100% in the age group over 60 years; all human subjects with positive NT -pro - BNP have mitral insufficiency.

18. There is a positive correlation between NT-pro-BNP and the presence of tricuspid outflow and a negative correlation between NT-pro-BNP and the absence of tricuspid outflow, statistically significant in both genders (8 out of 9 males with positive BNP have mitral outflow = 89% and 7 out of 8 females with positive NT-pro-BNP have tricuspid outflow = 87%). In the 50-59 year age group, 8 cases out of 10 with positive NT-pro-BNP are associated with tricuspid outflow (80%) and in the age group over 60 years, all 5 cases with positive NT-pro-BNP are associated with tricuspid insufficiency (100%).

19. There is no statistically significant correlation between positive NT-pro-BNP and pulmonary outflow, respectively the aortic outflow, overall or by gender and age groups.

20. Regarding TIPS - NT-pro-BNP relationship, there is no statistically significant difference between the frequency of BNP > 250 pg/ml in patients with TIPS insertion older than 3 years, compared to those without TIPS insertion, overall, by gender and age group.

21. Regarding the relationship between NT-pro-BNP values and long-term treatment with diuretics, we found no statistically significant correlation overall, by gender and age group.

22. There is a statistically significant correlation between the length of the QT interval and long-term treatment (over 3 years) with Propranolol in patients with cardiovascular dysfunction and liver cirrhosis. Thus, 50% of human subjects who were not treated with Propranolol, have normal QT interval, half of them having it short and half long, while among patients receiving long-term treatment with Propranolol, only 23,1% have changed the QT interval, with a

shorter duration (19,2%), so it seems that Propranolol protects the normal size of QT interval, primarily by preventing its elongation.

When analyzing the gender, the difference between patients treated with Propranolol and those who did not receive this treatment, is statistically significant in both men and women, with no differences between genders.

When analyzing the age groups, differences remain the same between the two categories of human subjects, without significant differences between age groups.

## **Conclusions**

- Detection and diagnosis of cardiac dysfunction of patients with liver cirrhosis requires specific methods to highlight the signs of heart failure and their correlation (clinical, ECG, X-ray, echocardiography and laboratory) simultaneously/ in parallel with those used for the analysis of the stage of cirrhosis.
- In the absence of markers indicating the cirrhotic origin of cardiovascular dysfunction, it is very difficult to prove the presence of cause-effect correlation between liver cirrhosis and cardiac dysfunction, given that the incidence of heart failure increases with age in all individuals, including those who do not have liver cirrhosis.
- The increase of natriuretic peptide NT-pro-BNP above 250 pg/ml in the blood of cirrhotic patients may be only a presumptive indicator of a cardiovascular disorder.
- The correlation between increased natriuretic peptide NT-pro-BNP above 250pg/ml in the blood and the presence of signs of heart failure in patients with liver cirrhosis is an indication of a possible correlation between cirrhosis and cardiac dysfunction.
- Elongation of the QT interval is more frequent in cirrhotic patients with the level of natriuretic peptide NT-pro-BNP above 250 pg/ml in the blood.
- Among echocardiographic signs, dilated left atrium, as well as the mitral outflow and/or the tricuspid outflow, are more frequent in cirrhotic patients with the level of natriuretic peptide NT-pro-BNP above 250 pg/ml in the blood.

- The research could be extended by increasing the limit of 250 pg/ml in the blood, where natriuretic peptide NT-pro-BNP was considered positive, but it is possible that too few positive results of NT-pro-BNP be an obstacle in calculating statistical significance of the results.
- The natriuretic peptide NT-pro-BNP in the blood of cirrhotic patients was not influenced by the presence of portacaval shunt (TIPS).
- Long-term diuretic treatment (over 3 years) in patients with liver cirrhosis does not affect the value of natriuretic peptide NT-pro-BNP in the blood.
- Long-term treatment of cardiac dysfunction with Propranolol in patients with liver cirrhosis has a protective role on the modification of the normal length of the QT interval, primarily by preventing the increase of its length.

**Key words:** NT-pro-BNP, cirrhotic cardiomyopathy, liver cirrhosis