# Arrhythmia Risk in Patients with Chronic Hepatic Disease

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Cardiac affectation is one of the leading causes of death in the world. Rhythmic disorders such as ventricular extrasystoles, atrial extrasysoles, atrial fibrillation, atrial flutter represent a major risk factor with a gloomy progression and prognosis. Our goal was to analyze the existing arrhythmia risk in patients with chronic hepatic disease. Being known the alteration of the somatic status of the patient with liver cirrhosis or other chronic liver disease in the presence of comorbid cardiac symptoms, we consider vital to prevent arrhythmia risk in hepatic pathology.

Keywords: arrhytmia risk, chronic hepatic disease, cardiac affectation

Cardiac affectation is one of the leading causes of death in the world. Rhythmic disorders such as ventricular extrasystoles, atrial extrasysoles, atrial fibrillation, atrial flutter represent a major risk factor with a gloomy progression and prognosis [1-7].

Numerous cardiac diseases associated with hepatic pathology cause additional comorbidities [8-13]. Thus, early identification of risk factors and immediate therapeutic initiation influence the progression and prognosis of the disease.

Čhronic hepatic disease, regardless of its etiology and even its stage, causes changes in the structure and functions of the heart, usually with latent, infra-clinical progression recognized clinically with difficulty[14-17].

It is vital that in the evolution of hepatic disease, regardless of the etiological factor, to follow the clinical and paraclinical parameters, having a role in early diagnosis and suppression of possible complications [3,13].

Arrhythmia risk from chronic hepatic disease is often underestimated[1-3,13]. For this, starting from data from the literature, we started studying arrhythmic risk in patients with chronic liver disease.

Thus, we have attempted to establish multiple clinical and paraclinical correlations to highlight the importance of the frequency and severity of arrhythmias and the risk of sudden cardiac death in patients with chronic hepatic disease.

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#### **Experimental part**

#### Material and method

In our study, 126 patients were diagnosed based on the clinical and paraclinical examination with chronic hepatic disease and 120 patients without chronic hepatic disease, representing the control group.

The study was conducted over a period of 14 months, from 1.10.2016 to 1.01.2018.

We evaluated patients both from cardiology and hepatology point of view, through anamnesis, clinical examination, abdominal ultrasound, echocardiography, electrocardiogram and laboratory investigations.

We analyzed heart rhythm disorders in patients with chronic hepatic disease, depending on the etiology. The incidence of atrial fibrillation, atrial flutter, atrial and ventricular extrasystoles, bradycardia or tachycardia were monitored. Electrocardiography was performed using the General Electric Mac 2000 machine.

Criteria for inclusion in the study:

-Hospitalized patients with clear diagnosis of chronic liver disease (clinically and paraclinically certified)

-Hospitalized patients with a clear diagnosis of alcoholic liver cirrhosis

-The etiology of chronic liver disease confirmed by viral marker investigations for chronic liver disease with viral etiology

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-Age between 20-88 years

-Patients who are not being treated with drugs that may affect the QT interval

Exclusion Criteria:

-Patients with secondary cirrhosis: cardiac cirrhosis, Budd-Chiari syndrome

-Patients who are being treated with antiarrhythmics

-Atrial or ventricular septal defects

-Chronic pulmonary diseases

## **Results and discussion**

The relationship between chronic hepatic disease and atrial fibrillation. Of the 126 patients surveyed in our study 74 of them presented atrial fibrillation. Of these 21 were previously diagnosed with chronic hepatitis B virus infection, 19 with chronic hepatitis C virus infections, 23 patients had a diagnosis of alcoholic cirrhosis and 11 metabolic toxic hepatitis.

Analyzing the etiological spectrum of the underlying hepatic disease, we can see that of the 73 patients diagnosed with chronic viral hepatic disease, 40 patients had atrial fibrillation. The percentage of patients with hepatic disease of ethanol etiology and atrial fibrillation exceeds 50%, in other words 23 out of 34 patients had atrial fibrillation rhythm disorders. For metabolic toxic hepatitis, 11 out of 19 patients were diagnosed with atrial fibrillation.

More than half of patients with chronic hepatitis of viral etiology had atrial fibrillation (55, 26% of patients with chronic hepatitis B virus and 54.29% of patients with chronic hepatitis C virus). These data are consistent with those described in previous studies in the literature, studies that clearly highlight the incidence of patients with hepatic disease and their arrhythmic risk [1]

The percentage of patients with alcoholic cirrhosis and atrial fibrillation was over 67.65%. This high incidence of atrial fibrillation observed in patients in our study diagnosed with alcoholic cirrhosis is directly correlated with the literature [2,3]. Both, in the studies preceding our research and in the present case the devastating impact of alcohol consumed over a long period of time and its implication in the occurrence of rhythm disorders in a diseased organism have been proved [1-3].

The statistical analysis we performed revealed a 1.23fold greater risk of atrial fibrillation in patients with alcoholic cirrhosis than in patients with chronic hepatic disease of viral etiology. We also analyzed the risk of atrial fibrillation in patients with alcoholic cirrhosis versus patients with chronic hepatitis of metabolic toxic etiology. In this case, although the value of the Student t test was p = 0.4962, the relative risk is 1.1684 times the occurrence of atrial fibrillation in patients with alcoholic cirrhosis. The total prevalence of atrial fibrillation in subjects with chronic hepatic disease included in our study was 58.73%.

The incidence of atrial flutter in patients in our research was only 3.17%. In other words, only 4 patients out of a total of 126 experienced atrial flutter.

For chronic viral hepatitis C and alcoholic cirrhosis there was no patient with atrial flutter.

Table	1
Table	1

THE RISK OF ATRIAL FIBRILLATION IN PATIENTS WITH ALCOHOLIC CIRRHOSIS VERSUS CHRONIC HEPATITIS OF VIRAL FTIOLOGY

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Relative risk	1.2346
95% CI	0.9035 to 1.6869
z statistic	1.323
Significance level	P = 0.1858

Table 2

THE RISK OF ATRIAL FIBRILLATION IN PATIENTS WITH ALCOHOLIC CIRRHOSIS VERSUS CHRONIC METABOLIC TOXIC

HEPAITIS	
Relative risk	1.1684
95% CI	0.7462 to 1.8296
z statistic	0.68
Significance level	P = 0.4962

The highest proportion of patients with atrial flutter (10.53%) was present in subjects diagnosed with metabolic toxic hepatitis.

Table 3
THE RISK OF ATRIAL FLUTTER AT PATIENTS WITH CHRONIC
HEPATIC DISEASE

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Relative risk	0.4229
95% CI	0.0209 to 8.5759
z statistic	0.561
Significance level	P = 0.5751

Atrial extrasystoles were analyzed in close correlation with the hepatic etiology, regardless of whether we have reported at the disease individually or to the etiologic group. Out of the 38 patients diagnosed with chronic viral hepatitis B, only 7 subjects representing 18.42% had atrial extrasystoles. The prevalence was even lower in patients with chronic viral hepatitis C (11.43%). Only 2 out of 19 patients diagnosed with metabolic toxic hepatitis presented atrial extrasystoles. The lowest prevalence of atrial extrasystoles was recorded in patients with alcoholic cirrhosis.

With a percentage of 15.07% the viral etiology of hepatic disease seems to be most correlated with the risk of installing atrial extrasistols.

The relative risk of atrial extrasystoles in patients with chronic viral hepatitis is 5.1233 times higher than those affected by alcoholic cirrhosis and 1.4315 times higher than those with metabolic toxic hepatitis. The exact Fisher test had Positive value of P = 0.027551.



 Table 4

 THE RISK OF ATRIAL EXTRASYSTOLES IN PATIENTS WITH CHRONIC

 HEPATIC DISEASE OF VIRAL ETIOLOGY VERSUS ALCOHOLIC

 CIRRHOSIS

Relative risk	5.1233
95% CI	0.889 to 38.0954
z statistic	1.596
Significance level	P = 0.1105
Significance level	P = 0.027551
Testul exact Fisher	

 Table 5

 THE RISK OF ATRIAL EXTRASYSTOLES IN PATIENTS

 WITH CHRONIC HEPATIC DISEASE OF VIRAL ETIOLOGY

 VERSUS METABOLIC TOXIC HEPATITIS

Relative risk	1.4315
95% CI	0.3462 to 5.9199
z statistic	0.495
Significance level	P = 0.6204

As can be seen in the graph below, ventricular extrasystoles had the highest incidence in hepatic viral pathology, not less than 20.55% of subjects had this type of rhythm disorder. On second and third place were patients diagnosed with alcoholic cirrhosis (14.71%) and those with metabolic toxic hepatitis (10.53%).

Statistical analysis confirms correlations between ventricular extrasystoles and hepatic disease of viral etiology, describing a relative risk of 1.9521 times greater in hepatic viral pathology than in toxic hepatitis pathology. The Student t test was P = 0.3443.

The relative risk of ventricular extrasystoles is 1.3973 times higher in patients with hepatic disease of viral etiology compared to those diagnosed with alcoholic cirrhosis. The Student t test was P=0.4793.



 
 Table 6

 THE RISK OF VENTRICULAR EXTRASYSTOLES IN PATIENTS WITH CHRONIC HEPATIC DISEASE OF VIRAL ETIOLOGY VERSUS METABOLIC TOXIC HEPATITIS

Relative risk	1.9521
95% CI	0.488 to 7.809
z statistic	0.946
Significance level	P = 0.3443

 
 Table 7

 THE RISK OF VENTRICULAR EXTRASYSTOLES IN PATIENTS WITH CHRONIC HEPATIC DISEASE OF VIRAL ETIOLOGY VERSUS ALCOHOLIC CIRRHOSIS

пасополю симповы	
Relative risk	1.3973
95% CI	0.5531 to 3.5298
z statistic	0.707
Significance level	P = 0.4793

We considered it useful to analyze these changes in heart rate and in relation to the wider etiological palette. In the case of viral etiology, the prevalence of synus bradycardia and atrial tachycardia had identical value of 9.59%.

Patients with synus bradycardia were more numerous than those with atrial tachycardia in case of alcoholic cirrhosis (8.82% versus 5.88%). The situation changes when we discuss about metabolic toxic etiology. In this case the proportion of subjects with atrial tachycardia

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(21.05%) is superior to those with synus bradycardia (15.79%).

However, it is interesting that the ratio of synus bradycardia / atrial tachycardia to the entire etiological spectrum of our research is perfectly balanced. The incidence of bradycardia and tachycardia in our study was 10.32%.

The statistical analysis we performed revealed a 2.13fold higher risk of synus bradycardia in patients with metabolic toxic hepatitis than in patients with alcoholic cirrhosis, despide the fact that Student t test was P =0.3151. We also analyzed the risk of synus bradycardia in patients with metabolic toxic hepatitis versus patients with chronic hepatitis of viral etiology. In this case, although the value of the Student t test was p = 0.3125, the relative risk is 1.88 times the occurrence of synus bradycardia in patients with metabolic toxic hepatitis.

Regarding atrial tachycardia we can state that there is a 5,0667-fold higher risk in patients with metabolic toxic hepatitis than patients with alcoholic cirrhosis. Although the value of the Student t test is 0.1267, the risk of atrial tachycardia is 2, 35 times higher in patients with metabolic toxic hepatitis compared to those diagnosed with hepatic disease of viral etiology.

Data from the literature suggests a higher arrhythmic risk in patients with comorbid hepatic disease compared to the non-hepatic injury population, so it is fundamental to have a complex multidisciplinary approach to patients with chronic liver disease [3,13].



 Table 8

 THE RISK OF BRADYCARDIA IN PATIENTS WITH CHRONIC

 METABOLIC TOXIC HEPATITIS VERSUS ALCOHOLIC CIRRHOSIS

Relative risk	2.1333
95% CI	0.4865 to 9.3542
z statistic	1.005
Significance level	P = 0.3151

Table 9THE RISK OF BRADYCARDIA IN PATIENTS WITH CHRONICMETABOLIC TOXIC HEPATITIS VERSUS CHRONIC HEPATICDISEASE OF VIRAL ETIOLOGY

Relative risk	1.8857
95% CI	0.5507 to 6.457
z statistic	1.01
Significance level	P = 0.3125

## Table 10

THE RISK OF SYNUS TAHYCARDIA IN PATIENTS WITH CHRONIC METABOLIC TOXIC HEPATITIS VERSUS ALCOHOLIC CIRRHOSIS

Relative risk	5.0667
95% CI	1.0346 to 24.8136
z statistic	2.002
Significance level	P = 0.0453

#### Table 11

THE RISK OF SYNUS TAHYCARDIA IN PATIENTS WITH CHRONIC METABOLIC TOXIC HEPATITIS VERSUS CHRONIC HEPATIC DISEASE OF VIRAL ETIOLOGY

Relative risk	2.3571
95% CI	0.7843 to 7.0841
z statistic	1.527
Significance level	P = 0.1267

## Conclusions

Early detection of cardiac arrhythmias is of great importance in the evolution of the patient with chronic hepatic disease. The diversity of etiology and varied clinical picture compels us to investigate all aspects of the arrhythmogenic substrate and the triggering and aggravating factors of chronic hepatic disease. At the same time, our study draws attention to the importance of following rhythm disturbances in order to improve prognosis and specific therapeutic behaviors.

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Manuscript received: 5.03.2018