

# Correlation Between Liver Cirrhosis and Risk of Cardiac Arrhythmias

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*There are few studies analyzing the correlation between liver cirrhosis and cardiac arrhythmias. Still, factors triggering cardiac arrhythmias occur in many instances in liver cirrhosis. We studied a cohort with patients diagnosed with liver cirrhosis hospitalized to Cardiology Department, to the County Hospital of Craiova, between January 2017 and January 2018. We wanted to study the frequency of cardiac arrhythmias at the patients diagnosed with liver cirrhosis and also to evaluate several associated factors. The frequency of cardiac arrhythmias in the presence of risk factors was analysed using  $\chi^2$  test and statistical models. We analyzed multiple variable including demographics and clinical and biochemical characteristics, frequency of type of arrhythmias and evaluation of the associated factors like diabetes mellitus, hypertension, hypercholesterolemia, hypertriglyceridemia, hyper/hypokalemia and hyper/hyponatremia. From our group, after exclusion criteria, we have a total of 34 patients with alcoholic liver cirrhosis, 37 patients with chronic HCV infection and 36 patients with HBV infection. From 34 patients with alcoholic liver cirrhosis, 23 patients presented atrial fibrillation (67.65%), from 37 patients with chronic HCV infection 21 were diagnosed with atrial fibrillation (56.76%) and from the patients with HBV infection 19 patients were known with atrial fibrillation (52.78%). We have encounter atrial flutter at 2 patients (5.56%) with chronic HBV infection. Atrial extrasystole was found at 7 patients with chronic HBV infection (19.44%), 4 patients with chronic HCV infection (10.81%) and 1 patients with alcoholic liver cirrhosis (2.94%). Ventricular extrasystole was found at 12 patients with chronic HBV infection (33.33%), 3 patients with chronic HCV infection (8.11%) and 5 patients with alcoholic liver cirrhosis (14.71%). We have also correlate the arrhythmias with different biochemical variables from our cohort. In our study there were many association between hepatic cirrhosis and cardiac abnormalities, which is concordant to reports from literature. Compared to population without liver cirrhosis, the prevalence of arrhythmias was increased in our cohort.*

*Key words: liver cirrhosis, arrhythmias, rhythm disorders*

Liver cirrhosis is a public health burden worldwide with a large variety of clinical manifestations and complications, some of those can be life-threatening [1]. The term of cirrhosis can be described by histological point of view like a diffuse liver process. These structural changes represent the results of fibrosis which has a prolonged evolution over months and years and which are converting the normal hepatic architecture into abnormal nodules [2].

Liver cirrhosis has been associated with a couple of cardiovascular complications including hemodynamic changes, hypertension and myocardial dysfunctions. All of these symptoms can develop a serious cirrhotic cardiomyopathy. The patients diagnosed with liver cirrhosis could have various arrhythmias with both systolic and diastolic dysfunctions; they can also present

chronotropic alteration and electromechanical changes [3].

In cirrhosis the cardiac dysfunction remains frequently ignored. Liver cirrhosis is correlated with a group of cardiovascular abnormalities, which include hyperdynamic circulation, portal hypertension, hepatopulmonary syndrome and abnormal features in different vascular territories like renal and cerebral vasculature [4].

Peripheral vasodilatation secondary to a reduce cardiac after load could avert any clinical sign of cardiac dysfunction, but there are many studies which demonstrate that the ventricular systolic function could give a defective response under a physiological or pharmacological stress [5].

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Cirrhosis is related to an increased cardiac output and heart rate, also to a reduced systemic vascular resistance and blood pressure. An important role is given to an impaired autonomic activity and splanchnic arterial vasodilatation[6].

Cirrhotic cardiomyopathy is a pathological condition conceded in cirrhosis [7]. This condition is characterized by a blunted contractile response to stress and an altered diastolic relaxation with electrophysiological abnormalities, like prolongation of the QT interval [8,9]. These changes were before considered to be related to alcoholic liver cirrhosis, but latter studies demonstrate that these cardiac abnormalities are noticed in patients with nonalcoholic cirrhosis [7].

## Experimental part

### Material and methods

The study, was carried on 126 patients admitted to the County Hospital of Craiova, Cardiology Department, between January 2017 and January 2018. The main criteria in our study was the certain of liver cirrhosis, which was based on the clinical history and examination, biochemical and serologic findings, including ultrasonography and Fibroscan. We considered patients with viral etiology, with B and C virus and with alcoholic liver cirrhosis. The exclusion criteria were patients with known primary cardiac pathology like: congenital long QT syndrome, ischemic heart disease, congenital heart disease.

Multiple variable were evaluated including demographics and clinical and biochemical characteristics, frequency of arrhythmias and evaluation of the associated factors: diabetes mellitus, hypertension, hypercholesterolemia, hypertriglyceridemia, hyper/hypokalemia, hyper/hyponatremia.

## Results and discussions

We analyzed our cohort of 126 patients with liver cirrhosis, female/men=41/85.

**Table 1**

DISTRIBUTION OF THE PATIENTS ACCORDING TO GENDER

Gender	Total
Women	43
Men	83
Total	126

**Table 2**

DISTRIBUTION OF THE PATIENTS ACCORDING TO ENVIRONMENTAL AREA

MEDIU	Total
RURAL	53
URBAN	73
Grand Total	126

**Table 3**

DISTRIBUTION OF THE PATIENTS BY AGE

Group of age	Total
<60 years old	29
60-69 years old	52
>70 years old	45
Total	126

The distribution of the patients by environmental are reveal a number of 49 patients from rural areas and 77 patients from urban areas.

We classified our patients in 3 groups of age. We had 29 patients under 60 years old, 52 patients with age between 60 and 69 years old and 45 patients with age above 70 years.

From our group, after exclusion criteria, we have a total of 34 patients with alcoholic liver cirrhosis, 37 patients with chronic HCV infection and 36 patients with HBV infection.

From 34 patients with alcoholic liver cirrhosis, 23 patients presented atrial fibrillation(67.65%), from 37 patients with

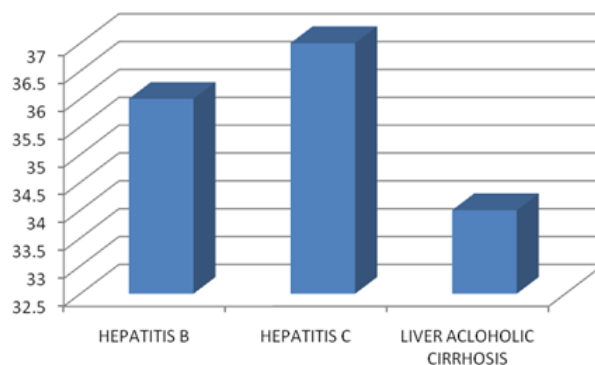


Fig. 1. distribution of hepatic diseases

chronic HCV infection 21 were diagnosed with atrial fibrillation(56.76%) and from the patients with HBV infection 19 patients were known with atrial fibrillation(52.78%) (tables 4,5).

We have encounter atrial flutter at 2 patients (5.56%) with chronic HBV infection. None of the patients with chronic HCV infection or alcoholic liver cirrhosis presented with atrial flutter (tables 6,7).

From the patients diagnosed with atrial tachycardia we found 3 patients with chronic HBV infection (8.33%), at 4 patients with chronic HCV infection(10.81%) and at 2 patients with alcoholic liver cirrhosis(5.88%) (tables 8,9).

Bradycardia was met at 4 patients with chronic HBV infection(11.11%), 3 patients with alcoholic liver cirrhosis(8.82%) and 3 patients with HCV(8.11%) (tables 10,11).

Atrial extrasystole was found at 7 patients with chronic HBV infection (19.44%), 4 patients with chronic HCV infection (10.81%) and 1 patients with alcoholic liver cirrhosis (2.94%) (tables 12,13).

Ventricular extrasystole was found at 12 patients with chronic HBV infection (33.33%), 3 patients with chronic HCV infection (8.11%) and 5 patients with alcoholic liver cirrhosis (14.71%) (tables 14,15).

We also try to correlate the arrhythmias with different biochemical variables from our cohort.

So, 22 patients of our patients with atrial fibrillation had hyperkalemia (StdDev 0.71) and 3 hypokalemia, from the patients with bradycardia 3 of them presented hyperkalemia(StdDev 0.71) and one patient with atrial tachycardia presented hyperkalemia (StdDev 0.58) (tables 16-18).

One of the patient with atrial fibrillation presented hypernatremia and 31 presented hyponatremia (table 19).

Two patients with bradycardia presented hypernatremia and 3 patients presented hyponatremia. Also from the patients with atrial tachycardia two of them presented hyponatremia.

Hypercholesterolemia was found at nine patients with atrial fibrillation (StdDev 48.41), at 5 patients with bradycardia(StdDev 62.92) and at 2 patients with atrial tachycardia (StdDev 54.67) (tables 20-23).

Hypertriglyceridemia was found at 15 patients with atrial fibrillation(StdDev 52.86), at 5 patients with bradycardia(StdDev 76.60) and at 2 patients with atrial tachycardia (StdDev 45.62) (tables 24-29).

From the patients with atrial fibrillation we found 26 with diabetes mellitus and 46 with hypertension. Also, from the patients with bradycardia we found 2 patients with diabetes mellitus and 9 patients with hypertension. From the patients with tachycardia, 3 of them had diabetes mellitus and 11 had hypertension (tables 30-33).

Liver cirrhosis is detected all over the world and is responsible for a huge morbidity and mortality all over the

HEPATITIS	FIBRILATION	NO FIBRILATION	Total
NON HEPATITIS	11	8	19
HEPATITIS B	19	17	36
HEPATITIS C	21	16	37
ALCOHOLIC LIVER CIRRHOSIS	23	11	34
<b>Total</b>	<b>74</b>	<b>52</b>	<b>126</b>

**Tables 4, 5**  
CORRELATIONS BETWEEN HEPATIC DIAGNOSIS AND ATRIAL FIBRILLATION

HEPATITIS	FIBRILATION	NO FIBRILATION	Total
	57.89%	42.11%	100.00%
HEPATITIS B	52.78%	47.22%	100.00%
HEPATITIS C	56.76%	43.24%	100.00%
LIVER ALCOHOLIC CIRRHOSIS	67.65%	32.35%	100.00%
<b>Total</b>	<b>58.73%</b>	<b>41.27%</b>	<b>100.00%</b>

**Tables 6, 7**  
CORRELATION BETWEEN HEPATIC DISORDERS AND ATRIAL FLUTTER

	ATRIAL FLUTTER	NO ATRIAL FLUTTER	Total
<b>HEPATITIS</b>			
NO HEPATITIS	2	17	19
HEPATITIS B	2	34	36
HEPATITIS C	0	37	37
ALCOHOLIC LIVER CIRRHOSIS	0	34	34
<b>Grand Total</b>	<b>4</b>	<b>122</b>	<b>126</b>

	ATRIAL FLUTTER	NO ATRIAL FLUTTER
<b>HEPATITIS</b>		
NO HEPATITIS	10.53%	89.47%
HEPATITIS B	5.56%	94.44%
HEPATITIS C	0.00%	100.00%
ALCOHOLIC LIVER CIRRHOSIS	0.00%	100.00%
<b>Total</b>	<b>3.17%</b>	<b>96.83%</b>

	ATRIAL TACHYCARDIA	NO ATRIAL TACHYCARDIA	Total
<b>HEPATITIS</b>			
NO HEPATITIS		4	15
HEPATITIS B		3	33
HEPATITIS C		4	33
ALCOHOLIC LIVER CIRRHOSIS		2	32
<b>Grand Total</b>	<b>13</b>	<b>113</b>	<b>126</b>

	ATRIAL TACHYCARDIA	NO ATRIAL TACHYCARDIA
<b>HEPATITIS</b>		
NO HEPATITIS	21.05%	78.95%
HEPATITIS B	8.33%	91.67%
HEPATITIS C	10.81%	89.19%
ALCOHOLIC LIVER CIRRHOSIS	5.88%	94.12%
<b>Grand Total</b>	<b>10.32%</b>	<b>89.68%</b>

**Tables 8,9**  
CORRELATION BETWEEN HEPATIC DIAGNOSIS AND ATRIAL TACHYCARDIA

globe. It is characterized by a hyperdynamic circulation, which is related to a high cardiac output, reduced systemic vascular resistance and a global arterial vasodilatation. In many studies, liver cirrhosis was associated with an abnormal cardiac feature [10,11].

Cirrhotic cardiomyopathy is characterized by abnormal heart structure and function at patients with liver cirrhosis.

The leading etiological factors in Romania are the viral etiology: Hepatitis B and C, followed by alcohol and NALD [12]. Other significant causes include autoimmune hepatic diseases, toxins, drugs, hepatic venous outflow tract

obstruction, heart failure, metabolic and genetic abnormalities.

In our study there were many association between hepatic cirrhosis and cardiac abnormalities, which is concordant to reports from literature [13, 14].

In patients with liver cirrhosis the prevalence of arrhythmic events increase with the progression of the liver disease and there are occurring independent of cirrhosis aetiology [15,16]. Despite of this, Baik et al described that sudden cardiac death is uncommon in cirrhosis. As a consequence the significance of QT prolongation in liver cirrhosis still need to be explored [17,18].

	SINUSAL BRADYCARDIA	NO SINUSAL BRADYCARDIA	Total
<b>HEPATITIS</b>			
NO HEPATITIS	3	16	19
HEPATITIS B	4	32	36
HEPATITIS C	3	34	37
ALCOHOLIC LIVER CIRRHOSIS	3	31	34
<b>Total</b>	<b>13</b>	<b>113</b>	<b>126</b>

**Tables 10,11**  
CORRELATION BETWEEN HEPATIC DISORDERS AND SINUSAL BRADYCARDIA

	SINUSAL BRADYCARDIA	NO SINUSAL BRADYCARDIA	Total
<b>HEPATITIS</b>			
NO HEPATITIS	15.79%	84.21%	100.00%
HEPATITIS B	11.11%	88.89%	100.00%
HEPATITIS C	8.11%	91.89%	100.00%
ALCOHOLIC LIVER CIRRHOSIS	8.82%	91.18%	100.00%
<b>Total</b>	<b>10.32%</b>	<b>89.68%</b>	<b>100.00%</b>

**Tables 12,13**  
CORRELATION BETWEEN HEPATIC DISORDERS AND ATRIAL EXTRASYSTOLE

	ESA	NO ESA	Total
<b>HEPATITIS</b>			
NO HEPATITIS	2	17	19
HEPATITIS B	7	29	36
HEPATITIS C	4	33	37
ALCOHOL LIVER CIRRHOSIS	1	33	34
<b>Total</b>	<b>14</b>	<b>112</b>	<b>126</b>

	ESA	NO ESA	Total
<b>HEPATITA</b>			
NO HEPATITIS	10.53%	89.47%	100.00%
HEPATITIS B	19.44%	80.56%	100.00%
HEPATITIS C	10.81%	89.19%	100.00%
ALCOHOLIC LIVER CIRRHOSIS	2.94%	97.06%	100.00%
<b>Total</b>	<b>11.11%</b>	<b>88.89%</b>	<b>100.00%</b>

**Tables 14,15**  
CORRELATION BETWEEN HEPATIC DISORDERS AND VENTRICULAR EXTRASYSTOLE

	ESV	NO ESV	Total
<b>HEPATITIS</b>			
NO HEPATITIS	2	17	19
HEPATITIS B	12	24	36
HEPATITIS C	3	34	37
ALCOHOLIC LIVER CIRRHOSIS	5	29	34
<b>Total</b>	<b>22</b>	<b>104</b>	<b>126</b>

	ESV	NO ESV	Total
<b>HEPATITIS</b>			
NO HEPATITIS	10.53%	89.47%	100.00%
HEPATITIS B	33.33%	66.67%	100.00%
HEPATITIS C	8.11%	91.89%	100.00%
ALCOHOLIC LIVER CIRRHOSIS	14.71%	85.29%	100.00%
<b>Total</b>	<b>17.46%</b>	<b>82.54%</b>	<b>100.00%</b>

**Tables 16 ,17,18**  
CORRELATIONS BETWEEN ATRIAL FIBRILLATION AND HIPER/ HIPOKALEMIA

ATRIAL FIBRILLATION	HIPERKALEMIA	HIPOKALEMIA	NORMAL	Total
YES	22	3	49	74
NO	6	2	44	52
<b>Total</b>	<b>28</b>	<b>5</b>	<b>93</b>	<b>126</b>

Average of K+	
ATRIAL FIBRILLATION	Total
YES	4.70
NO	4.38
<b>Total</b>	<b>4.566984127</b>

StdDev of K+	
ATRIAL FIBRILLATION	Total
YES	0.71
NO	0.84
<b>Total</b>	<b>0.780140777</b>

ATRIAL FIBRILLATION	HIPERNATREMIA	HIPONATREMIA	NORMAL	Total
YES	1	31	42	74
NO	5	11	36	52
<b>Total</b>	<b>6</b>	<b>42</b>	<b>78</b>	<b>126</b>

**Table 19**  
CORRELATIONS BETWEEN ATRIAL FIBRILLATION AND HIPER/HIPONATREMIA



**Tables 20,21,22**  
CORRELATIONS BETWEEN ATRIAL FIBRILLATION AND CHOLESTEROL LEVEL

ATRIAL FIBRILLATION	Hypercholesterolemia	No-Hypercholesterolemia	Total
YES	9	65	74
NO	19	33	52
<b>Total</b>	<b>28</b>	<b>98</b>	<b>126</b>

ATRIAL FIBRILLATION	Total
YES	74.00
NO	52.00
<b>Total</b>	<b>126</b>

ATRIAL FIBRILLATION	Total
YES	147.34
NO	175.77
<b>Total</b>	<b>159.0714286</b>

FLUTTER, TAHI, BRADI	YES	NO	Total
SINUSAL BRADYCARDIA	5	8	13
ATRIAL FLUTTER	0	4	4
ATRIAL TACHYCARDIA	2	11	13
NONE	21	75	96
<b>Total</b>	<b>28</b>	<b>98</b>	<b>126</b>

**Table 23**  
CORRELATIONS BETWEEN SINUSAL BRADYCARDIA, ATRIAL FLUTTER, ATRIAL TACHYCARDIA AND CHOLESTEROL LEVEL

**Tables 24, 25,26**  
CORRELATIONS BETWEEN ATRIAL FIBRILLATION AND TRIGLICERIDES LEVEL

ATRIAL FIBRILLATION	Hypertriglyceridemia	No Hypertriglyceridemia	Total
YES	15	59	74
NO	15	37	52
<b>Total</b>	<b>30</b>	<b>96</b>	<b>126</b>

StdDev of TRYGLYCERIDE	Total
ATRIAL FIBRILLATION	
YES	52.86
NO	53.67
<b>Total</b>	<b>53.740113</b>

Average of TRYGLYCERIDE	Total
ATRIAL FIBRILLATION	
YES	100.38
NO	118.54
<b>Total</b>	<b>107.873016</b>

**Table 27, 28, 29**  
CORRELATIONS BETWEEN SINUSAL BRADYCARDIA, ATRIAL FLUTTER, ATRIAL TACHYCARDIA AND TRYGLICERIDES LEVEL

Diagnosis	HIPERTRYGLYCERIDEMIA	NO HIPERTRYGLYCERIDEMIA	Total
SINUSAL BRADYCARDIA	5	8	13
ATRIAL FLUTTER		4	4
ATRIAL TACHYCARDIA	2	11	13
NONE	23	73	96
<b>Total</b>	<b>30</b>	<b>96</b>	<b>126</b>

Diagnosis	Total
SINUSAL BRADYCARDIA	125.62
ATRIAL FLUTTER	113.75
ATRIALTACHYCARDIA	115.31
NONE	104.22
<b>Total</b>	<b>107.873016</b>

StdDev of TRYGLYCERIDE	Total
Diagnosis	
SINUSAL BRADYCARDIA	76.60
ATRIAL FLUTTER	50.94
ATRIAL TACHYCARDIA	45.62
NONE	51.46
<b>Total</b>	<b>53.740113</b>

Other causes known to induce abnormal cardiac and hepatic feature are oxidative stress, inflammation and insulin resistance [19].

ATRIAL FIBRILATION	DIABETES MELLITUS	NO DIABETES	Total
YES	26	48	74
NO	13	39	52
<b>Total</b>	<b>39</b>	<b>87</b>	<b>126</b>

FLUTTER, TAHI, BRADI	DIABETES MELLITUS	NO DIABETES	Total
SINUSAL BRADYCARDIA	2	11	13
ATRIAL FLUTTER		4	4
ATRIAL TACHYCARDIA	3	10	13
NONE	34	62	96
<b>Total</b>	<b>39</b>	<b>87</b>	<b>126</b>

ATRIAL FIBRILATION	HIPERTENSION	NO HIPERTENSION	Total
YES	46	28	74
NO	45	7	52
<b>Total</b>	<b>91</b>	<b>35</b>	<b>126</b>

FLUTTER, TAHI, BRADI	HIPERTENSION	NO HTA	Total
SINUSAL BRADYCARDIA	9	4	13
ATRIAL FLUTTER	3	1	4
ATRIAL TACHYCARDIA	11	2	13
NONE	68	28	96
<b>Total</b>	<b>91</b>	<b>35</b>	<b>126</b>

**Table 30,31**  
CORRELATIONS BETWEEN ATRIAL FIBRILLATION AND DIABETES MELLITUS

**Table 32,33**  
CORRELATIONS BETWEEN SINUSAL BRADYCARDIA, ATRIAL FLUTTER, ATRIAL TACHYCARDIA AND HIPERTENSION

Arrhythmic events occur frequent at patients with liver cirrhosis [20] and the risk of developing heart failure increases [21].

## Conclusions

The arrhythmias represent a significant factor for the evolution and the prognosis of the patients with hepatic cirrhosis. In order to avoid the complication or to threat both cardiovascular and hepatic disorders, we have to perform a complex and a permanently cardiovascular evaluation of the patients with liver cirrhosis.

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