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QT Interval Prolongation and QRS Voltage Reduction in Patients with Liver Cirrhosis

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article; **G** – other

Abstract

Background. Liver cirrhosis is associated with functional abnormalities of the cardiovascular system with co-existing electrocardiographic (ECG) abnormalities.
Objectives. The aim was to analyze ECG changes in patients with cirrhosis, to evaluate whether alcoholic etiology of cirrhosis and ascites has an impact on ECG changes.
Material and Methods. The study involved 81 patients with previously untreated alcoholic cirrhosis (64 patients with ascites, classes B and C according to the Child-Pugh classification; and 17 without ascites, categorized as class A); 41 patients with previously untreated cirrhosis due to chronic hepatitis C (HCV – 30 patients with ascites, classes B and C; and 11 without ascites, class A); 42 with alcoholic steatohepatitis and 46 with alcoholic steatosis. The control group consisted of 32 healthy volunteers. Twelve-lead ECG recordings were performed and selected parameters were measured.
Results. Significantly longer QT and QTc intervals and lower QRS voltage were found in patients with alcoholic and HCV cirrhosis compared to the controls. Significantly lower QRS voltage was found in subjects with ascites than in those without ascites. Removal of ascites significantly increased QRS voltage.
Conclusions. In cirrhosis, irrespective of etiology, ECG changes involved prolonged QT and QTc intervals and reduced QRS voltage. Prolonged QT and QTc intervals were not related to the severity of cirrhosis or to the presence of ascites. However, low QRS voltage was associated with the presence of ascites. Removal of ascites reverses low QRS voltage (**Adv Clin Exp Med 2015, 24, 4, 615–622**).

Key words: ascites, liver cirrhosis, electrocardiography, QT interval, QRS voltage.

Liver cirrhosis is associated with numerous functional abnormalities of the myocardium and cardiovascular system, which are among the elements of the circulatory dysfunction syndrome and lead to cirrhotic cardiomyopathy. Cirrhotic cardiomyopathy develops in about half of all cirrhotic patients and markedly affects the long-term morbidity and mortality of those patients [1–3]. Cirrhotic cardiomyopathy results from multifactorial organic myocardial changes and is defined as systolic and diastolic cardiac dysfunction with co-existing electrocardiographic (ECG) abnormalities or abnormal serologic markers (brain natriuretic peptide [BNP], troponin 1, adrenomedullin) in patients with cirrhosis in the absence of cardiac diseases [1, 2, 4]. Patients with decompensated cirrhosis have been demonstrated to have elevated levels of the N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and left ventricle (LV) diastolic dysfunction [5]. Cirrhotic cardiomyopathy is characterized by blunted contractile responsiveness to stress and/or altered diastolic relaxation with electrophysiological abnormalities in the absence of any other known cardiac

disease, in patients with liver cirrhosis [6]. The pathogenetic mechanisms of cirrhotic cardiomyopathy include abnormalities in the beta-adrenergic signaling pathway, altered cardiomyocyte membrane fluidity, increased myocardial fibrosis, cardiomyocyte hypertrophy, and ion channel defects [1, 7]. The major vascular pathology observed in the systemic circulation in patients with cirrhosis and portal hypertension is nitric oxide-mediated relaxation in visceral arterioles, leading to a decrease in effective blood volume in the vascular bed and stimulation of hormonal vasopressive and sodium-retentive mechanisms. Compensatory in nature, these mechanisms counteract reductions in arterial pressure and organ perfusion. Compared to other vascular regions, visceral arterioles are characterized by low reactivity to vasoconstrictors. Decreased vascular resistance in the visceral circulation enhances portal hypertension, leading to cardiovascular disorders manifested in increased cardiac output, decreased peripheral resistance and hypotension – elements of the aforementioned circulatory dysfunction syndrome in cirrhosis. Thus, cirrhosis induces the development of hyperkinetic circulation, likely to be characterized by tachycardia and increased myocardial ejection fraction [8]. Additionally, ascites, which commonly coexists with cirrhosis, increases intra-abdominal pressure, leading to hemodynamic abnormalities of the myocardium and impairing renal function; moreover, it affects intra-thoracic pressure and can alter the anatomical position of the heart, and therefore its electrical axis [9, 10].

The implicated ECG abnormalities in cirrhotic patients include chronotropic incompetence, electromechanical uncoupling and QT interval prolongation [11, 12]. The QT interval measures the length of ventricular systole. A prolonged QT interval is associated with an increased risk of severe ventricular arrhythmias and sudden cardiac death.

Reports in the literature regarding the effects of cirrhosis on the ECG curve are scarce. Those available focused only on the QT interval and did not assess other ECG elements.

The aim of the present study was (1) to analyze ECG changes in patients with liver cirrhosis in the absence of cardiovascular and respiratory diseases, (2) to evaluate whether alcoholic etiology of liver damage has an impact on ECG changes, (3) to determine whether ascites in cirrhosis affects the possible ECG changes and whether the removal of ascites reverses them.

Material and Methods

Patients

The study involved 64 patients with previously untreated decompensated alcoholic cirrhosis and ascites (48 male and 16 female patients, aged 34–64 years, mean 46 ± 12.7 years), including 28 class B and 36 class C individuals according to the Child-Pugh classification; and 17 patients with previously untreated alcoholic cirrhosis without ascites, categorized as class A according to the above classification (10 male and 7 female patients, mean age 42 ± 12.5); 41 patients with previously untreated hepatitis C (HCV) liver cirrhosis (22 males and 19 females, aged 36–72 years); 42 with alcoholic steatohepatitis (26 males and 16 females, aged 36–69 years) and 46 with alcoholic liver steatosis (31 males and 15 females, aged 34–66 years). The group with HCV cirrhosis included 30 patients with ascites (12 class B and 18 class C subjects according to the Child-Pugh classification) and 11 patients without ascites (class A). The control group consisted of 32 healthy volunteers, including 26 men and 6 women, aged 24–62 years, mean age 42 ± 10.1 years.

Cirrhosis was diagnosed based on the generally accepted criteria: history, physical examinations, laboratory tests, imaging examinations (i.e. panendoscopy), abdominal ultrasound, Doppler ultrasound and computerized tomography. The group with decompensated cirrhosis and ascites included patients with the presence of marked ascites, palpable on physical examination and USG-confirmed, or those who required paracentesis on admission. Alcoholic etiology was determined on the basis of history or information provided by the patients' families. Patients with concomitant infections with hepatitis B virus (HBV), hepatitis C virus (HCV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), autoimmune factors and toxic cirrhosis were excluded from this group. Each patient in this group underwent panendoscopy, which revealed the presence of esophageal varices in 52 patients (stage I: 11, II: 18 and III: 23) and gastric fundal varices in 11 patients.

The etiology of HCV infection in patients with HCV cirrhosis was established based on the presence of serum anti-HCV antibodies or HCV-RNA. In 8 cases the diagnosis was confirmed by liver biopsy. Other causes of cirrhosis in this group (HBV, CMV, EBV infections, autoimmune factors, alcoholic and toxic factors) were excluded. Panendoscopy showed the presence of stage I esophageal varices in 9 patients, stage II in 3 and stage III in 13; and gastric fundal varices in 13 patients.

Alcoholic steatohepatitis and alcoholic steatosis were diagnosed on the basis of liver biopsies.

In the group with alcoholic steatohepatitis, stage I esophageal varices was diagnosed in 2 patients during panendoscopy. In the group with alcoholic steatosis the same diagnosis was established in one patient.

The exclusion criteria were relevant cardiac arrhythmias (atrial fibrillation and flutter, ventricular arrhythmia), electrolyte abnormalities, drugs that might affect the ECG curve, diagnosed cardiac diseases (ischemic heart disease, valve defects, congenital cardiovascular pathologies), arterial hypertension, pulmonary diseases and diabetes mellitus. Prior to inclusion, each patient underwent echocardiography to exclude the presence of fluid in the pericardial sac.

All the patients gave their informed written consent to be involved in the study. The study was approved by Local Bioethical Committee (No. KE-0254/131/2013).

Laboratory Tests

The following laboratory tests were performed in all the patients: complete blood cell count (CBC), coagulation profile (prothrombin time, kaolin-cephalin time, international normalized ratio [INR]), levels of bilirubin, albumin, creatinine, urea, glycemia, electrolytes (sodium, potassium, calcium), lipidogram (total cholesterol, triglycerides-TG, LDL-cholesterol, HDL-cholesterol), alanine aminotransferase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma gluthamylo transpeptydase (GGTP), C-reactive protein (CRP) and body mass index (BMI)

ECG

A 12-lead ECG recording by AsCard (Aspel S.A., Poland) was performed on each patient with a paper speed of 25 mm/s. Likewise, heart rate was determined (HR/min) and considered as accelerated when it exceeded 100 bpm. The following indices were also measured: mean PQ, QT and QTc intervals, QRS duration and QRS voltage. The PQ interval was measured from the beginning of the P wave to the beginning of the Q wave; the QT interval was measured from the beginning of the Q wave to the beginning of the T wave. OTc was determined according to the Bazett formula: $QTc = QT/\sqrt{RR}$, where RR represents the R-R distance. The PQ, QT, QTc intervals and duration of QRS complexes were measured in milliseconds (msec). The intervals were measured manually in 3 successive cycles in each lead and presented as an arithmetic mean of the 12 leads.

Prolonged PQ and QTc intervals were defined as those over 200 ms and 440 ms, respectively. No range of abnormal values was defined for the QT interval due to its RR-dependence, and the QT interval was individually determined for each patient.

The duration of QRS complexes was measured from the start of the Q wave to the end of the S wave. The QRS voltage (defined in millimetres – 1 mm corresponding to 0.1 mV) was measured as the amplitude of R and S deviations from the isoelectric line. The QRS voltage was determined individually in the limb and precordial leads. The QRS voltage measurements were performed manually in three successive cycles in each lead and presented as an arrhythmic mean obtained from the limb leads (I, II, II, aVR, aVL, aVF) and precordial leads (V1–V6). An amplitude $\leq$ 5 mm and $\leq$ 10 mm in the limb and precordial leads, respectively, was considered low voltage.

In patients with ascites from the groups with alcoholic and HCV cirrhosis, the ECGs were repeated after the removal of the ascites. Ascites was removed by paracenthesis and follow-up diuretic therapy, or by diuretics only, using furosemide and spironolactone. The absence of ascites after treatment was confirmed by USG examination.

Statistical Analysis

All the examined parameters are presented as mean values ± standard deviation. Because of non-normal distribution (as shown by the Shapiro-Wilk test) or heterogeneity of variance (as shown by Levene's test), non-parametric tests (the Mann-Whitney test and Kruskal-Wallis test) were used to compare demographic profiles, the results of the analyzed laboratory tests and the analyzed ECG elements between the examined groups. Student's *t*-test was used to compare the analyzed ECG elements between patients with ascites and patients after ascites removal. Statistical significance between the differences was assumed when $p < 0.05$. All the calculations were done using STATISTICA PL software.

Results

The laboratory findings showed statistically significant differences in platelet count (PTC), mean corpuscular volume (MCV), INR, bilirubin and albumin levels, ALT, ASP and GGTP between each of the examined groups and the controls (Table 1). The remaining laboratory parameters measured did not show statistically significant differences between any of the groups of examined patients and the controls.

In all the patients the ECG recordings revealed regular sinus cardiac rhythm with a frequency of

Table 1. Comparison of demographic profiles and selected laboratory results in the examined patients and the controls. Age and results of laboratory tests are presented as mean ± SD. An asterisk indicates a statistically significant difference ($p < 0.05$)

Parameter	Alcoholic cirrhosis (n = 81)	HCV cirrhosis (n = 41)	ASH (n = 42)	ALS (n = 46)	Controls (n = 32)
Gender f/m (n)	23/58	19/22	16/26	15/31	6/26
Age (years)	44.54 ± 12.7*	37.23 ± 11.40	41.57 ± 9.22	38.34 ± 12.76	42.0 ± 10.1
PTC (× 103/μL)	164.08 ± 89.14*	145.80 ± 79.23*	201.45 ± 92.30	221.25 ± 98.94	248 ± 56.93
MCV (fL)	96.3 ± 12.74*	88.45 ± 18.54	93.0231.06*	89.83 ± 12.95	82.36 ± 15.31
INR	1.62 ± 0.65*	1.24 ± 0.45	1.03 ± 0.48	0.96 ± 0.28	0.88 ± 0.12
Bilirubin (mg/dL)	3.30 ± 1.74*	5.94 ± 3.25*	2.95 ± 1.56*	1.06 ± 0.87	0.83 ± 0.10
Albumin (g/dL)	3.03 ± 0.76*	3.93 ± 1.34	3.97 ± 1.45	3.98 0.98	4.21 ± 0.58
ALT (U/L)	49.33 ± 28.92*	51.23 ± 90*	63.23 ± 37.96*	42.29 ± 36*	26.84 ± 6.99
AST (U/L)	68.58 ± 36.31*	45.03 ± 12.34	78.29 ± 23.56*	56.47 ± 27.34*	23.84 ± 5.23
GGTP (U/L)	141.36 ± 77.90*	95.04 ± 56.23*	132.47 ± 45.84*	100.32 ± 21.90*	30.5 ± 12.69

* statistically significant differences vs. controls, $p < 0.05$, ALS – alcoholic liver steatosis, ALT – alanine aminotransferase, ASH – alcoholic steatohepatitis, AST – aspartate transaminase, CRP – C-reactive protein, GGTP – gamma gluthamylo-transpeptydase, MCV – mean corpuscular volume, n – number of patients, PTC – platelet count, SD – standard deviation.

65–125 bpm. Five patients with alcoholic cirrhosis, 5 with HCV cirrhosis and two with alcoholic steatohepatitis had accelerated heart rates, over 100 bpm; all of them had ascites and belonged to classes B and C according to the Child-Pugh classification. Eight patients with decompensated alcoholic cirrhosis demonstrated left His bundle branch block. The results of the remaining ECG parameters are presented in Table 2. Significantly longer QT and QTc intervals as well as lower QRS voltage in limb and precordial leads were found in patients with alcoholic and HCV cirrhosis as compared to the controls. An extremely low voltage of the QRS complexes in limb leads below 5 mm (0.5 mV) and in precordial leads below 10 mm (1 mV) was observed in 18 and in 26 patients, respectively, with alcoholic cirrhosis, and in 10 and 13 patients, respectively, in the group with HCV cirrhosis. All of these patients belonged to the decompensated cirrhosis group with the presence of ascites (class

Table 2. Comparison of ECG indices between the examined groups and the controls. ECG parameters are presented as mean ± SD. An asterisk indicates a statistically significant difference ($p < 0.05$)

Examined groups	HR/min	PQ (ms)	QT (ms)	QTc (ms)	QRS duration (ms)	QRS voltage in limb leads (mm)	QRS voltage in precordial leads (mm)
Alcoholic cirrhosis n = 81	85.12 ± 17.98	169.41 ± 40.54	376.47 ± 36.90*	443.30 ± 7.30*	87.65 ± 24.88	5.81 ± 2.04*	9.71 ± 2.72*
HCV cirrhosis n = 41	76.11 ± 9.41	175.70 ± 40.77	379.70 ± 42.16*	455.68 ± 49.95*	89.70 ± 17.23	5.32 ± 1.56*	9.06 ± 2.98*
ASH n = 42	74.93 ± 6.54	171.83 ± 49.98	345.00 ± 18.34	392.42 ± 32.39	87.50 ± 18.15	7.00 ± 1.11	11.5 ± 1.79
ALS n = 46	70.59 ± 16.47	181.46 ± 25.15	351.80 ± 34.72	393.77 ± 33.97	89.62 ± 14.78	6.92 ± 1.15	11.38 ± 1.80
Controls n = 32	77.09 ± 7.29	162.73 ± 29.70	350.00 ± 20.98	393.61 ± 22.56	80.00 ± 14.83	7.44 ± 1.01	12.22 ± 1.48

* – statistically significant differences vs. controls, $p < 0.05$; HR – heart rate, n – number of patients, ALS – alcoholic liver steatosis, ASH – alcoholic steatohepatitis, SD – standard deviation.

Table 3. Comparison of ECG elements in the examined patients according to the Child-Pugh classification (classes A, B or C). ECG parameters are presented as mean ± SD

Examined patients	HR/min	PQ (ms)	QT (ms)	QTc (ms)	QRS duration (ms)	QRS voltage in limb leads (mm)	QRS voltage in precordial leads (mm)
class A n = 28	76.0 ± 10.72	181.43 ± 56.13	367.46 ± 37.54	438.41 ± 35.07	89.70 ± 31.78	7.18 ± 1.41	11.88 ± 0.93
class B n = 40	86.43 ± 18.22	193.00 ± 50.66	361.86 ± 28.28	434.36 ± 39.73	88.42 ± 19.80	4.89 ± 2.11	8.11 ± 2.28
class C n = 54	81.10 ± 18.13	155.00 ± 25.50	389.00 ± 47.01	476.01 ± 39.86	88.46 ± 15.73	4.86 ± 1.35	8.33 ± 1.53
p-value	ns.	ns.	ns.	ns.	ns.	ns. (B vs. C); p = 0.00003 (A vs. B)*; p = 0.0001 (A vs. C) *	ns. (B vs. C); p = 0.0000 (A vs. B)* p = 0.0005 (A vs. C)*

* – statistically significant differences, $p < 0.05$, ns. – not statistically significant, HR – heart rate, n – number of patients, SD – standard deviation.

C and B according to the Child-Pugh classification). No statistically significant differences in the remaining ECG parameters were noted between either of these groups and the control group. The measured ECG parameters did not show any statistically significant differences between the alcoholic liver cirrhosis group and the HCV liver cirrhosis group. The groups with alcoholic steatohepatitis and with alcoholic steatosis did not show statistically significant differences in the measured ECG parameters in comparison to the controls.

A comparison of class A patients (without ascites) and class B and C patients (with ascites) according to the Child-Pugh classification showed statistically significant differences only in QRS voltage, which was lower in class B and C patients than in class A patients (Table 3). There were no statistically significant differences between classes B and C (with ascites). The remaining ECG elements were not significantly different in class A compared to class B and class C patients, nor in class B compared to class C patients.

Ascites was removed in the examined patients within eight to 62 days (mean 15.6 days). In 4 subjects removal of ascites failed (in three with alcoholic cirrhosis: 2 class B and 1 class C; and in 1 patient with HCV cirrhosis, class C according to the Child-Pugh classification). One patient died of hepatic encephalopathy. Thus, the further analysis included 100 patients. A comparison of the measured ECG elements in patients with ascites (classes B and C according to the Child-Pugh classification) and after the ascites removal is presented in Table 4. After the removal of ascites, a statistically significant increase in QRS voltage in the limb and precordial leads was observed. This voltage did not show statistically significant differences in comparison to the group of patients with cirrhosis but without ascites (class A according to the Child-Pugh classification). In the remaining evaluated ECG parameters, the removal of ascites did not result in statistically significant differences between the groups.

Table 4. Comparison of ECG elements between patients with ascites (classes B and C according to the Child-Pugh classification) and patients after ascites removal. ECG parameters are presented as mean ± SD

Examined patients	HR/min	PQ (ms)	QT (ms)	QTc (ms)	QRS duration (ms)	QRS voltage in limb leads (mm)	QRS voltage in precordial leads (mm)
Patients with ascites	84.45 ± 18.42	167.87 ± 56.83	378.59 ± 37.61	441.71 ± 35.73	88.72 ± 35.24	4.88 ± 1.65	8.53 ± 2.39
Patients after ascites removal	82.43 ± 17.74	190.00 ± 54.60	367.8 3 ± 45.80	434.36 ± 39.73	88.92 ± 21.80	7.05 ± 1.16	11.44 ± 2.13
p-value	ns.	ns.	ns.	ns.	ns.	p = 0.0000*	p = 0.0013*

* – statistically significant differences, ns. – not statistically significant, HR – heart rate, SD – standard deviation.

Discussion

To date, the only ECG changes analyzed and described in patients with cirrhosis of various etiologies was a prolongation of QT and QTc intervals. However, studies devoted to this issue are scarce and their results inconclusive.

According to some reports in the literature, prolonged QT and QTc intervals are correlated with the stage of cirrhosis, and also are observed in patients who undergo living donor liver transplantation. The highest values of QT and QTc intervals were observed in class C (Child-Pugh) [4, 13–16]. Mozos et al. confirmed these observations in a study involving 38 patients with cirrhosis; additionally they demonstrated a correlation with alcoholic cirrhosis etiology and the level serum uric acid [17]. Another study carried out on a Greek population revealed a correlation between the QT interval and the severity of cirrhosis, but not between the QT interval and cirrhosis etiology [18]. Genovesi et al. demonstrated a significant correlation between the stage of cirrhosis according to the Child-Pugh classification, the hepatic venous pressure gradient (HVPG) and QT interval prolongation, which was more common in patients with alcoholic than viral cirrhosis [13]. QT interval prolongation independently predicts bleeding-induced mortality in patients with cirrhosis [19].

Some other authors have suggested that a prolonged QT interval was likely to be associated with hepatic dysfunction and not with the action of vasoactive peptides (endothelin, calcitonin gene-related peptide) [20].

In contrast, some studies found no correlation between a prolonged QT interval and the severity of cirrhosis [21]. A Danish study did not demonstrate any correlation between a prolonged QT interval and the severity of portal hypertension in patients with cirrhosis; the QTc intervals were comparable in patients with mild (HVPG < 12 mm Hg) and severe (HVPG ≥ 12 mm Hg) portal hypertension, [22]. Similar results were presented by Zambruni et al. [23].

In their retrospective study, Bal and Thuluvath reported that a prolonged QTc interval was common in patients with cirrhosis, but did not influence the mortality rate [24]. According to their findings, the prolonged QTc returned to normal values in about half of the patients after liver transplantation, suggesting that liver disease may not be the only factor involved in the pathogenesis of prolonged QTc.

The present study, as opposed to other reports available in the literature, evaluated many ECG elements and not only QT intervals. The study focused on ECG assessment in patients with HCV cirrhosis and different stages of alcoholic liver disease. It seems that the study group was quite homogenous; there were no factors that could affect ECG recordings; moreover, the biochemical results (significantly different from those in the controls) did not show any abnormalities that could influence ECG recordings, particularly a QT interval or QRS voltage. According to the findings, liver cirrhosis (both alcoholic and HCV) significantly prolonged the QT and QTc intervals and reduced QRS voltage. It was not, however, found that the stage of cirrhosis (classes B and C according to the Child-Pugh classification) affected the prolongation of the QT and QTc intervals. In contrast, it was clearly shown that class B and C patients had significantly decreased QRS voltage as compared to class A patients. Thus, considering that fact and classes B and C included patients with ascites, it should be assumed that a reduction in QRS voltage was enhanced by ascites. Additionally, removal of ascites increased QRS voltage in both limb leads and precordial leads. This voltage was similar to the QRS voltage in patients with cirrhosis but without ascites. It is likely that ascites that induces an increase in intra-abdominal pressure impairs myocardial kinetics. The only study on this issue available in the literature demonstrated reduced QRS voltage in patients with ascites of various etiologies [11]. The study in question was conducted in a small and non-homogenous group of patients (20 with neoplastic ascites or in the course of alcoholic cirrhosis and 10 controls). Low QRS voltage in the limb leads was observed in more than half of the patients, and in the precordial leads in 4 patients. Paracentesis, performed in only 6 patients, normalized QRS voltage in the precordial leads without affecting the limb leads [11].

Recently, Madias, who described 2 patients with cirrhosis, peripheral edema and low QRS voltage in the limb leads, suggested that decreased QRS voltage in the limb leads was caused by the presence of peripheral edemas, whereas low QRS voltage in the precordial leads occurred in patients with ascites and was strictly correlated with it [25].

The presence of ascites during cirrhosis correlates with peripheral arterial visceral vasodilatation and cardiac hyperkinesis. Patients with cirrhosis show decreased right ventricular volumes, continuous activation of the adrenergic system, hypervolemia and, in some cases, portopulmonary shunts. All the above can lead to QRS voltage changes in ECGs.

The described changes in ECGs in patients with decompensated liver cirrhosis have essential practical importance. However, a prolonged QT interval may be a feature of long QT syndrome (LQTS) and lead to the formation of reentry circuits with

syncope, seizures, torsades de pointes (TdP) or ventricular fibrillation and fatal cardiac arrest. On the other hand, it should be remembered that low QRS voltage, prolonged QT and QTc are not always associated with cardiac pathology. It should be kept in mind that these changes can be observed in patients with ascites and liver cirrhosis without heart disease. QT interval prolongation leading to fatal arrhythmia including TdP may be caused by numerous medications available on the market. Therefore, the possible influence of drugs should be excluded in each case. A modest prolongation of the QT interval has been observed in patients taking the selective serotonin reuptake inhibitors citalopram, sertraline, escitalopram, mirtazapine, amitriptyline and fluoxetine, as well as the opioid methadone [26]. Every 5 patient taking these drugs shows QT prolongation in the ECG record [27]. Electrolyte imbalance (hypokalemia, hypomagnesemia, hypocalcemia), antiarrhythmic drugs, some antimicrobials (erythromycin, biseptol), certain antifungal medicines (ketokonazole), some antihistamines (astemizole, terfenadine) and calcium channel blockers (prenylamine, bepridil) may cause prolongation of the QT interval [28, 29]. Cirrhotic patients with transjugular intrahepatic portosystemic shunts are potentially at increased risk for abnormal QT prolongation when exposed to oral CYP 3A substrates with a prolonging effect (e.g. erythromycin) [30]. Similarly, halogenated volatile anesthetics (halothane, enflurane, isoflurane, desflurane, sevoflurane) are among the drugs that cause QTc interval prolongation, and they should therefore be avoided in anesthetic procedures in LQTS and liver cirrhosis patients, due to the increased risk of perioperative malignant ventricular arrhythmias [31]. Recently, Chung et al. presented a case report on a patient with liver cirrhosis scheduled for emergency cadaveric donor liver transplantation who developed TdP after sevoflurane use during general anesthesia [32]. Di Micoli et al. showed TdP in a patient with decompensated liver cirrhosis during amiodarone infusion because of new-onset atrial fibrillation [33]. Beta-blockers are the drugs of choice for patients with prolonged QT intervals and LQTS. Their protective effect is related to their adrenergic blockade, which diminishes the risk of cardiac arrhythmias. It is also important to correct potassium and magnesium deficiencies.

From a practical point of view, the described ECG changes are important for the treatment of cirrhotic patients. There is a long list of medications that should be avoided or used to a limited extent in this group of patients, due to the risk of fatal arrhythmia.

In conclusion, the authors noticed that in patients with cirrhosis, irrespective of etiology, ECG changes involved prolonged QT and QTc intervals and reduced QRS voltage. Prolonged QT and QTc intervals were not related to the severity of cirrhosis or to the presence of ascites. However, low QRS voltage was associated with the presence of ascites. Removal of ascites reverses low QRS voltage.

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