Correlation between the Severity of Liver Cirrhosis (Child-Pugh Score) and QTc Interval Prolongation

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ABSTRACT

Background: *Liver cirrhosis causes changes in cardiovascular system. Electrographic (ECG) abnormality commonly found in cirrhosis patients is QT interval prolongation. It is part of cirrhotic cardiomyopathy. QTc interval prolongation is correlated to the incidence of life-threatening arrhythmias. The objective of this study was to recognize the correlation between the severity of liver cirrhosis and QTc interval prolongation in patients with liver cirrhosis at Sardjito General Hospital, Jogjakarta.*

Method: *The design of this study was cross-sectional. The subjects were hospitalized patients with liver cirrhosis at the Department of Internal Medicine, Sardjito Hospital, Jogjakarta between January 2011 and March 2012. ECG was performed in all patients and QTc interval was measured. The severity of liver cirrhosis was determined by Child-Pugh score. Spearman correlation analysis was used to determine the correlation between variables of QTc interval prolongation and Child-Pugh score.*

Results: *A total of 73 patients were enrolled, including 51 (69.9%) male and 22 (31.1%) female patients with mean age of 54.05 ± 12.55 years (range 20-80). Liver cirrhosis was caused by hepatitis B virus in 36 (49.3%) patients, hepatitis C virus in 20 (27.4%) patients and other causes in 19 (26%) patients. The Child-Pugh score for liver cirrhosis was found as follows: child A in 10 (13.6%) patients, child B in 27 (36.9%) patients and child C in 36 (49.3%) patients. The correlation between the severity of liver cirrhosis and QTc interval prolongation was weak (r = 0.255; p = 0.029).*

Conclusion: *Severity of liver cirrhosis has a weak positive correlation with QTc interval prolongation.*

Keywords: *liver cirrhosis, QTc interval, Child-Pugh score*

ABSTRAK

Latar belakang: *Sirosis hati menyebabkan perubahan sistem kardiovaskuler. Abnormalitas elektrokardiograf yang sering ditemukan pada pasien sirosis adalah pemanjangan internal QT. Hal tersebut merupakan bagian dari kardiomiopati sirosis. Pemanjangan interval QTc terkait dengan kejadian aritmia yang mengancam jiwa. Tujuan penelitian ini untuk mengetahui hubungan antara derajat keparahan sirosis hati dengan pemanjangan interval QTc pada pasien sirosis hati di Rumah Sakit Sardjito, Yogyakarta.*

Metode: *Desain penelitian adalah studi potong lintang pada pasien sirosis hati yang menjalani rawat inap di Bagian Penyakit Dalam Rumah Sakit Sardjito, Yogyakarta dari bulan Januari 2011 sampai dengan Maret 2012. Dilakukan EKG dan pengukuran interval QTc pada pasien sirosis. Derajat keparahan sirosis hati ditentukan dengan Child-Pugh score. Analisis korelasi Spearman digunakan untuk mengetahui hubungan variabel pemanjangan interval QTc dan Child-Pugh score.*

Hasil: *Terdapat 73 pasien yang masuk dalam penelitian, laki-laki 51 (69,9%), perempuan 22 (31,1%), rerata usia 54.05 ± 12.55 tahun, umur antara 20 sampai dengan 83 tahun. Sirosis hati disebabkan oleh virus hepatitis B 36 (49,3%) pasien, virus hepatitis C 20 (27,4%) pasien dan lainnya 19 (26%) pasien. Sirosis hati child A*

pada 10 (13,6%) pasien, child B 27 (36,9%) pasien dan child C 36 (49,3%) pasien. Hubungan antara derajat keparahan sirosis dengan pemanjangan interval QTc adalah lemah (r = 0,255; p = 0,029).

Simpulan: *Derajat keparahan sirosis hati berkorelasi lemah dengan pemajangan interval QTc.*

Kata kunci*: sirosis hati, interval QTc, Child-Pugh score*

INTRODUCTION

Liver cirrhosis cause changes in cardiovascular and circulation system. The changes vary from subclinical symptoms to hyperdynamic (hyperkinetic syndrome), which may lead to cardiac decompensation. Long QT interval is one of the most common electrocardiographic abnormality in patient with liver cirrhosis[1] and part of cirrhotic cardiomyopathy.[2,3] QT interval prolongation is correlated to life-threatening arrhythmias.[1]

Clinical manifestation of cirrhosis cardiomyopathy can be recognized by using the following categories: 1) systolic dysfunction; 2) diastolic dysfunction; 3) electrophysiological changes; 4) structural and histological abnormalities; 5) serum biochemical changes.[1] The objective of this study was to recognize the correlation between the severity of liver cirrhosis and QTc interval prolongation in patients with liver cirrhosis at Sardjito Hospital, Jogjakarta.

METHOD

The design of this study was cross-sectional. The enrolled subjects were hospitalized patients with liver cirrhosis at the Department of Internal Medicine, Sardjito Hospital, Jogjakarta between January 2011 and March 2012. The inclusion criteria were patients who had confirmed diagnosis of liver cirrhosis as written in their medical record and those who aged more than 18 years; while the exclusion criteria were patients who were taking anti-arrhythmia drugs, patients with valvular heart disease, ischemic heart disease, and chronic kidney disease.

The baseline characteristic of patients in our study were demographic status, comorbidities, the results of complete blood count, prothrombin time and international normalized ratio (INR), as well as blood glucose level, uric acid serum level, the results of liver function test, kidney function test, electrolyte test, HBsAg and total anti hepatitis virus C (anti-HCV) screening.

A standard 12-lead electrocardiogram recording was performed in all patients and QT interval was measured manually. The interval was assessed from the beginning of Q wave to the end of T wave. All values were corrected by Bazett formula, as follows:

$$QTc = QT / \text{square root of the R-R interval}$$

QTc interval prolongation was defined as an interval of more than 0.44 seconds.[4]

The severity of liver cirrhosis was determined using the Child-Pugh score, which employs five variables, i.e. two clinical variables (ascites and encephalopathy, which was measured by the West Haven Criteria), and three laboratory variables (bilirubin, albumin, INR). Each variable was scored 1 to 3, with 3 indicating most severe derangement. The total score was between 5 and 15. A total score of 5-6 was categorized as child A cirrhosis; while 7-9 as child B and 10-15 as child C. Higher Child-Pugh score indicates that the disease is more severe.[5]

Quantitative variable data was presented as mean ± standard deviation and qualitative variable was represented in percentage. The correlation between the severity of liver cirrhosis and QTc interval prolongation was analysed by Pearson correlation when the data was normally distributed and by Spearman correlation if it was not normal. Statistical analysis was considered significant when $p < 0.05$.

RESULTS

Seventy three patients were included in this study, including 51 (69.9%) male patients. The mean age was 54 ± 12.25 years, with the youngest subject of 20 years old and the oldest was 83 years old. In majority of patients, 54 (74%) cirrhosis cases were caused by viral infection and 19 (26%) patients had non-viral infection. Among the group with viral infection, 36 (49.3%) patients had positive HBsAg and 20 (37%) patients had positive total anti-HCV. QTc interval prolongation was found in 27 (37%) patients (Table 1).

Patients with prolonged QTc interval were older than those with normal QTc (58.22 ± 7.67 years vs. 51.61 ± 14.20 years). Diabetes mellitus as comorbidity was found in 14 patients; however, there was no difference between two groups. There was also no difference between both groups regarding the blood glucose level, creatinine clearance, uric acid, and

Table 1. Baseline characteristics and differences between patients with normal and prolonged QTc interval group

	All (n = 73)	Normal QTc (n = 46)	Prolonged QTc (n = 27)	p
Age (years) (mean ± SD) ‡	54.05 ± 12.55	51.61 ± 14.20	58.22 ± 7.67	0.012 *
Male (n %) +	51 (69.9)	32 (69)	19 (75)	0.942
Female (n %)	22 (31.1)	14 (31)	8 (25)	
Viral etiology (n %) +	54 (73.9)	35 (76)	19 (75)	0.591
Diabetes mellitus (n %) +	14 (19.2)	8 (17.3)	6 (22)	0.613
Child-Pugh score (mean ± SD) ‡	8.71 ± 1.93	8.30 ± 1.74	9.41 ± 2.08	0.017 *
Child A (n %) +	10 (13.6)	7 (15.2)	3 (11.1)	
Child B (n %)	27 (36.9)	21 (45.7)	6 (22.2)	
Child C (n %)	36 (49.3)	18 (39.1)	18 (66.7)	0.023 *
Hemoglobin (mean ± SD) ‡	8.94 ± 2.35	8.38 ± 2.48	9.89 ± 1.80	0.004 *
Blood glucose (mean ± SD) ‡	143.09 ± 72.06	141.21 ± 56.49	146.04 ± 92.55	0.796
Creatinine clearance (mean ± SD) ‡	76.73 ± 54.71	83.91 ± 63.42	64.51 ± 32.90	0.145
Uric acid (mean ± SD) ‡	5.79 ± 3.09	5.58 ± 3.06	6.16 ± 3.18	0.490
Potassium (mean ± SD) ‡	4.23 ± 0.89	4.16 ± 0.91	4.35 ± 0.87	0.375

+ Analysis was performed using Mann–Whitney U test; ‡ analysis was performed using Mann-Whitney; *statistically significant; SD: standard deviation.

potassium level. Mean hemoglobin level in all patient was 8.94 ± 2.35 mg/dL. The patients with prolonged QTc interval had higher hemoglobin level than those with normal QTc interval (9.89 ± 1.80 mg/dL vs. 8.38 ± 2.48 mg/dL).

The majority of patients had liver cirrhosis of Child C (36 (49.3%) patients); while child B was found in 27 patients (36.9%) and child A was recognized in 10 patients (13.6%). Patient with normal QTc interval had lower total Child-Pugh score, with mean score of 8.30 ± 1.74 vs. 9.41 ± 2.08; p = 0.023 (Figure 1).

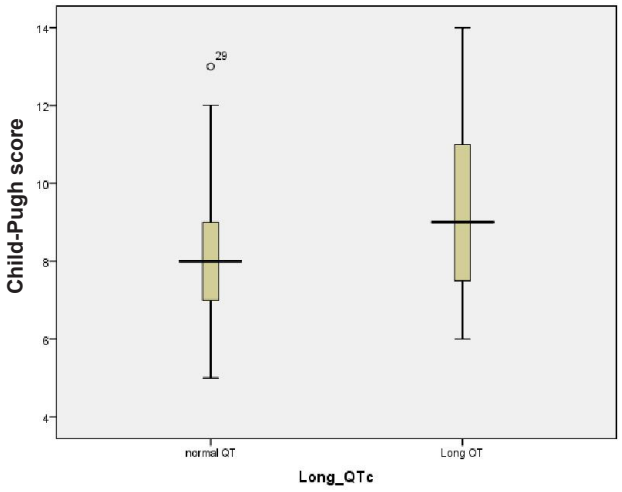

Figure 1. Compared Child-Pugh score between patients with normal QTc and prolonged QTc interval

Spearman correlation between the severity of liver cirrhosis and prolonged QTc interval was expressed as r = 0.225, p = 0.029 (Figure 2). It indicated a positive correlation, however, it was weak.

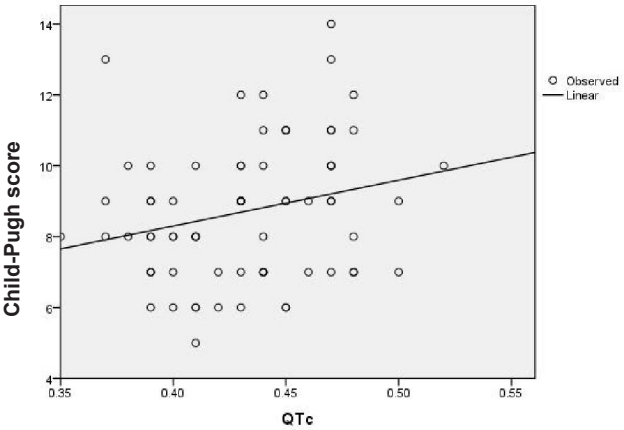

Figure 2. Correlation between Child-Pugh score and QTc interval prolongation

DISCUSSION

Cirrhosis cardiomyopathy is a new clinical entity and rarely diagnosed. It has a lot of features including QTc interval prolongation, increasing heart rate, decreasing myocardial contraction, and diastolic dysfunction.[6] QT interval prolongation is found in about 30-60% cirrhosis patients and correlates with long term morbidity and mortality.[3,7] In this study, prolonged QTc interval was observed in 37% patient with liver cirrhosis, which was caused by viral infection (73.9%). QT interval is influenced by heart rate; thus, it must be corrected (QTc interval).

QT interval prolongation worsen in parallel with the severity of liver cirrhosis, and it is often improved (back to normal) after liver transplantation; however it has no effect on mortality.[8,9] This study showed that there was a positive correlation between the severity of

liver cirrhosis and QTc interval prolongation, but the correlation was weak (r = 0.225; p = 0.029). Bernardi et al observed positive correlation between prolonged QT interval and Child-Turcotte-Pugh class B and C.[10] Mimidis et al also reported a positive correlation between the severity of liver cirrhosis measured by Child-Pugh score and QTc interval prolongation.[11]

There are several mechanisms involved for disorder in electrophysiology and impaired cardiac contractility including decreased β adrenergic receptor function, post receptor dysfunction, defective excitation contraction coupling, and conductance abnormalities. Moreau et al have demonstrated an altered control of vascular tone by K^+ and Ca^{++} channels in various cells in experimental and human cirrhosis.[12] It may result in myocardial excitation disorder. Ward et al have recently shown a decreased K^+ in ventricular myocytes of cirrhotic rats, which would tend to prolong QT interval.[13] A prolonged QT interval has previously been described in patients with liver disease, which may lead to ventricular arrhythmias and sudden cardiac death.[14]

CONCLUSION

Patients with severe liver cirrhosis tend to experience QTc interval prolongation. Severity of liver cirrhosis is weakly correlated with QTc interval prolongation.

SUGGESTION

The limitation in this study is that we did not evaluate echocardiogram to identify heart dysfunction as well as its correlation to the severity of liver cirrhosis and QTc interval prolongation. Another study design is required to assess heart function and to establish the diagnosis of cirrhosis cardiomyopathy.

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