Correlation of Prolonged QT Interval and Severity of Cirrhosis of Liver

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Abstract

Objective: To determine correlation between prolonged QT interval and severity of disease in patients of cirrhosis of liver.
Place of Study: Department of Medicine, King Edward Medical University.
Duration of Study: March 2008 to May 2010.
Study Design: Descriptive cross sectional study.
Patients and Methods: One hundred and seventeen patients of cirrhosis were included. Baseline haematological and biochemical parameters were determined. Model for end stage liver disease (MELD) score was determined for all patients to document stage of liver disease. Corrected QT interval was determined from electrocardiography of each patient using QT cirrhosis formula. Correlation between QT interval and MELD score was determined using Pearson correlation and Receiver Operating Characteristic (ROC) curve.
Results: One hundred and seventeen included patients had mean age of 53.58 (± 12.11) while male to female ratio was 1.78/1 (75 / 42). Mean MELD score was 17.08 (± 6.54) in study patients varying between 6 and 37 while mean corrected QT interval was 0.44 seconds (± 0.06). Pearson correlation revealed no significant relation between severity of liver disease as determined with MELD score and prolonged QT interval (p value 0.18) Area under curve with ROC curve for correlation between prolonged QT interval and severity of liver disease was 0.42.
Conclusion: Prolonged QT interval is not an indicator of severity of disease in cirrhosis of liver.
Key Words: Cirrhosis, MELD score, QT interval.

Introduction

Chronic liver disease is amongst leading health problems. It is considered to be a major cause of mortality and morbidity. Almost 30,000 patients per year are reported to develop cirrhosis in United States.[1] In Pakistan, it is the common cause of mortality and morbidity and constitutes a major bulk of hospital admissions.[2]

Several scoring systems have been developed to predict the prognosis and patient survival. One of these is Model for End – Stage Liver Disease (MELD) score for staging cirrhosis. The score uses results of serum bilirubin, serum creatinine and international normalized ratio (INR) in a log transformed equation.[3] It is found to be a better predictor of patient's survival than Child Turcotte Pugh (CTP) score.[4]

The electrocardiographic QT interval reflects ventricular repolarisation. Its prolongation provides substrate for ventricular arrhythmias. QT interval prolongation is one of the electrophysiological indicators of cirrhotic cardiomyopathy.[5,6] It is hypothesized that this abnormality occurs due to cardiotoxins reaching the heart due to portosystemic shunting.[7] QT interval is affected by heart rate, so the disease specific formula was used for QT correction. This is known as QT cirrhosis formula.[8] Few studies have shown prolonged QT interval to be associated with severity of liver

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disease. Study by Mimidis et al showed that prolonged QT interval occurs in cirrhotic patients independent of etiology of the disease. It is also correlated with CTP class B and C.[9] The evidence is far from conclusive and needs further good quality studies.

Our aim was to study the presence of prolonged QT interval using $QT_{cirrhosis}$ formula in patients of cirrhosis and correlate with disease severity, specified by MELD score.

Patients and Methods

This descriptive type of cross sectional study was carried out at Department of Medicine, King Edward Medical University. One hundred and seventeen consecutive cirrhotic patients were enrolled. Sample size was calculated keeping confidence interval at 95% by using Raosoft® software. Diagnosis of cirrhosis was based on combination of physical findings when present i.e. palmar erythema, spider nevi, gynaecomastia, splenomegaly or ascites, impaired liver function tests i.e. deranged clotting profile and low serum albumin and irregular liver surface, detected on ultrasound. Patients having any other cause of prolonged QT interval including diabetes mellitus, electrolyte imbalance like hyperkalemia and anti arrhythmic drugs were excluded. Patients having valvular heart disease and ischemic heart disease were also excluded.

All patients had their baseline clinical evaluation done. Laboratory investigations including complete blood count, prothrombin time with international normalized ratio (INR), liver function tests, serum creatinine, blood urea, serum sodium, potassium, calcium and phosphate levels were checked. Anti HCV and HBsAg status of all patients were checked to determine whether the etiology was viral or otherwise. Ultrasound imaging for hepatobiliary system was carried out.

A twelve lead ECG was carried out in all patients and QT interval was calculated manually. QT interval was calculated from start of Q wave till the end of T wave. All values were corrected by using disease specific formula (QT cirrhosis) i.e. $QTc = QT \times RR^{-1/3.02}$. Prolonged QT interval was defined as value greater than 440 ms (0.44 sec).

MELD Score was calculated to determine severity of liver disease according to the formula
3.8 [log serum bilirubin (mg/dl) + 11.2 [log INR]+9.6 [log serum creatinine (mg/dl)] +6.4

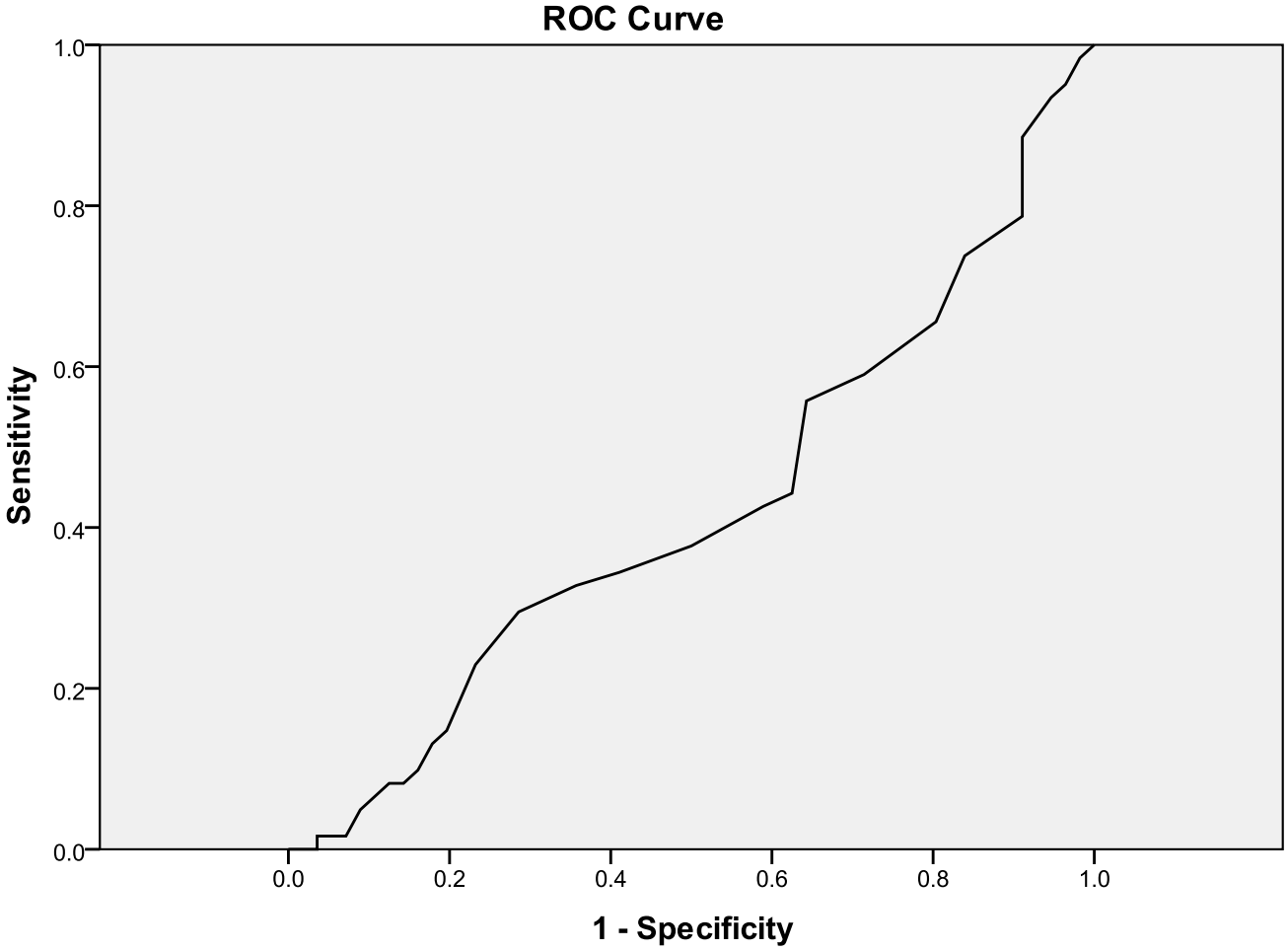
Statistical Analysis

Results were analyzed using PASW® version 18.0. Quantitative variables were described as mean ± standard deviation (SD) while qualitative variables were mentioned as percentage. To correlate the $QT_{cirrhosis}$ and MELD score, Pearson's correlation test was applied. Prolonged QT interval and MELD score were correlated using Reciever Operator Characteristic (ROC) curve. P value less than 0.05 was considered significant.

Table 1: Comparison of patients with normal and high corrected QT interval.

Variable	QT ≥ 0.44 sec (n – 61)	QT < 0.44 sec (n – 56)	P value
Age (years)	53.31 (± 12.3)	51.69 (11.66)	0.10
Bilirubin (mg/dl)	1.31 (0.46)	1.39 (0.52)	0.48
INR	1.76 (0.79)	2.09 (0.94)	0.04
Creatinine (mg/dl)	1.33 (0.84)	1.27 (0.72)	0.67
Albumin (g/dl)	3.30 (0.50)	3.30 (0.70)	0.98
Ascites (no of patients / Total patient)	34/61	35/56	0.45
Variceal bleeding (no of patients / total patients)	44/61	28/56	0.014
PSE (no of patients / total patients)	21/61	21/56	0.72

*PSE – Portosystemic encephalopathy
† p value < 0.05 was considered significant



Graph 1: ROC (Reciever operating characteristic) curve for correlation between QT interval > 0.44 sec and MELD score.

Area Under the Curve

Test Result Variable(s): Meld Score

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.425	.053	.162	.321	.529

Results

One hundred and seventeen patients were included in final analysis. Mean age of patients was 53.58 (± 12.11) while male to female ratio was 1.78/1 (75/42). Ascites was noted in 69 (58.5%) patients, 72 (61%) had history of variceal bleeding, spontanuous bacterial peritonitis was present in 3 (2.5%) patients and 42 (35.6%) were admitted due to portosystemic encephalopahty. Mean MELD score was 17.08 (± 6.54) in study patients varying between 6 and 37 while mean corrected QT interval was 0.44seconds (± 0.06). Minimum QT interval noted was 0.27 seconds while maximum value was 0.76 seconds. Considering QT interval

≥ 0.44 seconds as prolonged, we compared patient with normal QT interval [n – 56 (47.9%)] and those with prolonged QT interval [n – 61 (52.1%)] as shown in table 1.

In our study, QT interval ≥ 440 msec was significantly correlated with variceal bleed (p value 0.014) and increased INR (p value 0.04). Pearson correlation revealed no significant relation between severity of liver disease as determined with MELD score and prolonged QT interval (p value 0.18). We used AUC curve to identify correlation between QT interval > 0.44 sec and severity of cirrhosis as depicted by MELD score but had very low area under curve (AUC) of 0.42 indicating poor predictability of QT interval prolongation for stage of liver disease (Graph 1).

Discussion

Cirrhotic cardiomyopathy is a well known entity and prolonged QT interval is one of the indicators of latent cardiac dysfunction. It occurs in about half the cirrhotic patients, and can have long term effect on morbidity and mortality.[10]

Our study revealed no correlation between presence of prolonged QT interval and severity of liver disease. This could be important in patients who are candidates for liver transplant. In a study, QT interval prolongation was found to be common in cirrhosis. Value returned to normal after liver transplant, but it had no independent effect on mortality.[11] Using Bazett's formula,Kosar etal reported that QT interval prolongation was not a significant indicator of mortality.[12] In our study no such correlation was identified as well. We tested its correlation with severity of liver disease using MELD score as the parameter. On the other hand Bernardi M etal have described significant correlation between prolonged QT interval and CTP score class B and C.[13] Mimidus etal reported significant correlation with disease severity using Child Pugh score.[9] In our study, we used MELD score as marker of severity. Genovesi et al have established significant correlation of increased hepatic venous pressure gradient and prolonged QT interval.[14] MELD score has significant association with increased portal pressure as noted by Wang et al.[14] A study by Cazzaniga etal suggested interrelationship between MELD score and diastolic dysfunction in patients undergoing TIPS.[15] Diastolic dysfunction is manifestation of cirrhotic cardiomyopathy, as is QTc prolongation. Genovesi et al have established significant correlation of increased hepatic venous pressure gradient and prolonged QT interval.[16] These studies provide evidence that cardiac dysfunction in cirrhosis and portal pressure changes can be correlated. In our study, QT interval ≥ 440 msec was significantly correlated with variceal bleed (p value 0.014) and increased INR (p value 0.04). However study did not show significant correlation between prolonged QT interval and severity of liver disease using MELD score. Similar conclusion was drawn by Zambruni et al,[17] where they studied the effect of beta blockade on QT interval. They reported insignificant correlation of QT interval with hepatic venous pressure gradient, which is in contrast to study by Genovesi et al. The reason for insignificant correlation can be that cirrhotic patients have QT interval prolongation due to adrenergic drive affecting the ventricular action potential. Factors affecting portal pressure are not correlated with QT interval.

Our study is limited by absence of echocardiographic study of patients to identify cardiac dysfunction and had it correlated with severity of liver disease and prolonged QT interval. Further work with cardiac functional assessment will further verify the value of QT interval for diagnosing cirrhotic cardiomyopathy.

Conclusion

Prolonged QT interval in patients of cirrhosis has no correlation with severity of liver disease.

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