A study of cardiac dysfunction in cirrhotics


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Abstract

**Background:** The heart and liver are organs that are closely related in both health and disease. Due to the limited number of human studies, the management of cirrhotic cardiomyopathy remains largely empirical.

**Material and methods:** 30 Patients included in the study were recruited from the Department of Medical Gastroenterology, Narayana Medical College Hospital, Nellore. Consecutive patients diagnosed to have cirrhosis of nonalcoholic etiology formed the study group. The parameters that were assessed in echocardiography are E/A ratio, end diastolic volume (EDV), end systolic volume (ESV), ejection fraction. QTc interval more than 440 msec and E/A ratio less than 1 were considered diagnostic of cirrhotic cardiomyopathy in this study.

**Results:** In 9 cases, cirrhosis was due to hepatic B viral infection, 4 due to hepatitis C and in 17 patients it was cryptogenic. Of the 30 cases included in the study, 7 cases (23.3%) had Class A CTP. 16 cases (53.3%) had Class B CTP, 7 cases had Class C CTP. Of the 30 patients included in this study, 21 patients had end diastolic volume above 90. 2 patients had end systolic volume above 38. 29 patients had ejection fraction above 60%. Out of the 30 cases, 23 showed features of cirrhotic cardiomyopathy. 7 patients had CTP Class A. 16 patients had CTP Class B. 7 patients had CTP Class C. 12 patients with cirrhotic cardiomyopathy had CTP Class B. 7 patients with cirrhotic cardiomyopathy had CTP Class C. 3 patients with CTP Class A and 4 patients with CTP Class B did not have cirrhotic cardiomyopathy. The QTc was prolonged in 16 (53.3%) of patients in this study. 29 cases had ejection fraction above 60. Of the 23 cases that had cirrhotic cardiomyopathy 21 cases had ascites. 27 of the 30 cases had varices. 70.0% of the cases had end diastolic volume above 90. 76.2% of the cases with EDV above 90 had E/A ratio below 1.

**Conclusion:** Cirrhotic patients with non alcoholic etiology do have evidence of cirrhotic cardiomyopathy. The presence of cirrhotic cardiomyopathy was independent of the etiology. Some degree of diastolic dysfunction is seen in most of the cirrhotics. Prolongation of QTc interval...
correlates with severity of cirrhosis. Ventricular end diastolic volume, end systolic volume and ejection fraction do not correlate with severity of cirrhosis.

**Key words**

Child Turcotte Pugh, Cirrhotic cardiomyopathy, Ejection fraction, 2 dimensional echocardiography.

**Introduction**

The heart and liver are organs that are closely related in both health and disease [1]. Elevated resting cardiac output in cirrhosis, which is out of proportion to the oxygen consumption, has been first described about 60 years ago [2]. Later, various observations have indicated the presence of a latent cardiac dysfunction, which includes a combination of reduced cardiac contractility with systolic and diastolic dysfunction and electrophysiological abnormalities. These abnormalities were initially thought to be a manifestation of latent alcoholic cardiomyopathy. But in the mid-1980s, studies in nonalcoholic patients and in experimental animal models showed a similar pattern of blunted cardiac contractile responsiveness. This syndrome is termed cirrhotic cardiomyopathy [3].

Cirrhotic cardiomyopathy is defined as a chronic cardiac dysfunction in patients with cirrhosis, characterized by blunted contractile responsiveness to stress, and/or altered diastolic relaxation with electrophysiological abnormalities, in the absence of known cardiac disease [4]. The term cirrhotic cardiomyopathy was coined by Lee about two and a half decades ago [5]. The prevalence of cirrhotic cardiomyopathy remains unknown at present.

Features include structural, histological, electrophysiological, systolic and diastolic dysfunction. Multiple factors are considered as responsible, including impaired beta-adrenergic receptor signal transduction, abnormal membrane biophysical characteristics, and increased activity of cardio depressant systems mediated by cGMP [6].

Overt heart failure is not generally a feature of cirrhotic cardiomyopathy, because the associated marked vasodilatation accompanying the hyperdynamic circulation significantly reduces ventricular afterload. However, major stresses on the cardiovascular system such as liver transplantation, infections and insertion of transjugular intrahepatic portosystemic shunts (TIPS) can unmask the presence of cirrhotic cardiomyopathy and thereby convert latent to overt heart failure. Cirrhotic cardiomyopathy may also contribute to the pathogenesis of hepatorenal syndrome and circulatory failure in liver cirrhosis [7, 8].

Diastolic dysfunction is present in the vast majority of patients with cirrhotic cardiomyopathy and simple echocardiographic indices such as the E/A ratio may detect diastolic dysfunction even at rest. This may therefore represent the best available screening test to diagnose cardiac dysfunction [9]. Due to the limited number of human studies; the management of cirrhotic cardiomyopathy remains largely empirical. Treatment of this condition is mainly supportive. Orthotopic liver transplantation appears to improve or normalize the condition, generally after a period of several months [10, 11].

**Materials and methods**

Patients included in the study were recruited from the Department of Medical Gastroenterology, Narayana Medical College.
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Hospital, Nellore. The study period was from January 2012 to January 2014.

Inclusion criteria
Consecutive patients diagnosed to have cirrhosis of nonalcoholic etiology formed the study group.

Exclusion criteria
Patients with the following features were excluded from the study – Patients who were alcoholics; Patients with severe ascites; Patients who had coronary artery disease; Patients who had risk factors for cardiomyopathy other than cirrhosis; Patients with history of recent bleed; Patients with severe anemia; Patients who were hypertensive; Patients who were diabetics; Investigations done include complete blood count, liver function test; Ultrasound scan of the abdomen, viral markers, ascitic fluid analysis, electrocardiography, and echocardiography. The parameters that were assessed in echocardiography are E/A ratio, end diastolic volume (EDV), end systolic volume (ESV), ejection fraction.

QTc interval more than 440 msec and E/A ratio less than 1 were considered diagnostic of cirrhotic cardiomyopathy in this study. End diastolic volume of 90, end systolic value of 38 and ejection fraction of 60% were considered mean of the normal values while doing statistical analysis.

The data were analyzed using SSPS software version 20.0. For categorical variables, frequencies, percentages were calculated and to test the association between the groups chi square test was used. P value of < 0.05 was found to be significant.

Results
The total number of cases included in this study was 30. Of these, there were 16 males and 14 females. Of the 30 cases included in this study 4 patients were below 40 years of age, 3 cases were between 40 and 50 years of age and 23 cases were above 50 years of age.

In 9 cases, cirrhosis was due to hepatic B viral infection, 4 due to hepatitis C and in 17 patients it is cryptogenic.

Clinical findings
Child Turcotte Pugh Class: Of the 30 cases included in the study, 7 cases (23.3%) had Class A CTP. 16 cases (53.3%) had Class B CTP, 7 cases had Class C CTP. Of the 30 cases included in the study, 23 cases had ascites (76.7%), and 27 cases had varices (90.0%).

Conduction disturbances
Out of the 30 cases who were included in the study, 16 patients had QTc interval of more than 440 msec. Of these 16 patients 7 were males and 9 were female patients.

Left ventricular dysfunction
Out of the 30 cases, the ratio of early diastolic and late diastolic filling velocity (E/A ratio) was less than 1 in 21 cases. Of these 21 cases, 10 were males and 11 were females. Out of the 30 cases included in this study 23 patients had features cirrhotic cardiomyopathy. These cases had a prolonged QTc interval of more than 440 msec or an E/A ratio of less than 1. Of these 23 cases, 11 were males and 12 were females.

Cirrhotic cardiomyopathy
Of the 30 patients included in this study, 21 patients had end diastolic volume above 90. 2 patients had end systolic volume above 38. 29 patients had ejection fraction above 60%.

The distribution of End Diastolic Volume in study population observed as follows. Below 90 groups, 9 (30%) cases; above 90 group, 21(70%) cases were observed.
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The distribution of End Systolic Volume in study population observed as follows. Below 38 group, 28(93.3%) cases and Above 38 group, 2(6.7%) cases observed.

The distribution of ejection Fraction in study population was as follows. Below 60 group, 1 (3.3%) cases, Above 60 group, 29 (96.67%) cases observed.

Out of the 30 cases, 23 showed features of cirrhotic cardiomyopathy. 7 patients had CTP Class A. 16 patients had CTP Class B. 7 patients had CTP Class C as per Table - 1. Association between Cirrhotic Cardiomyopathy and CTP class patients with cirrhotic cardiomyopathy had CTP Class A. 12 patients with cirrhotic cardiomyopathy had CTP Class B. 7 patients with cirrhotic cardiomyopathy had CTP Class C. 3 patients with CTP Class A and 4 patients with CTP Class B did not have cirrhotic cardiomyopathy. The ‘p’ value of this association between Child Turcotte Pugh score and cirrhotic cardiomyopathy was 0.161 and it was not significant. This implied that cirrhotic cardiomyopathy was not influenced by the CTP class. (Table - 1)

Out of the 30 cases, 23 showed features of cirrhotic cardiomyopathy. 7 patients had CTP Class A. 16 patients had CTP Class B. 7 patients had CTP Class C. 4 patients with cirrhotic cardiomyopathy had CTP Class A. 12 patients with cirrhotic cardiomyopathy had CTP Class B. 7 patients with cirrhotic cardiomyopathy had CTP Class C. 3 patients with CTP Class A and 4 patients with CTP Class B did not have cirrhotic cardiomyopathy. The ‘p’ value of this association between Child Turcotte Pugh score and cirrhotic cardiomyopathy was 0.161 and it was not significant. This implied that cirrhotic cardiomyopathy is not influenced by the CTP class.

The QTc interval was more than 440 msec 16 patients of which 9 were females and 7 were males. It was below 440 msec in 14 patients of which 5 were females and 9 were males. These associations have a ‘p’ value of 0.543 which is not significant. This implies that sex differences among cirrhotic patients with QTc prolongation is not a significant finding.

The QTc was prolonged in 16 (53.3%) of patients in this study. It was prolonged in 9 patients with CTP class B, 7 patients with CTP class C. No patients in CTP class A had prolongation of QTc. The p value of this association was 0.001 and it was significant. This implied that prolongation of QTc was significantly associated with CTP class of cirrhosis. The QTc was prolonged in 16 (53.3%) of patients in this study. It was prolonged in 9 patients with CTP class B, 7 patients with CTP class C. No patients in CTP class A had prolongation of QTc. The p value of this association was 0.001 and it was significant. This implied that prolongation of QTc was significantly associated with CTP class of cirrhosis (Table - 2).

21 patients had end diastolic volume above 90. 9 patients had EDV below 90. 18 patients with cirrhotic cardiomyopathy had EDV above 90. 14 patients with diastolic dysfunction had EDV below 90. 3 patients with EDV above 90 did not have cirrhotic cardiomyopathy. The ‘p’ value of this association between EDV and cirrhotic cardiomyopathy was 0.073 and it was not significant. This implies that abnormality of EDV was not a significant feature of cirrhotic cardiomyopathy.

2 cases had end systolic volume above 38. 28 cases had ESV below 38. 2 cases with cirrhotic cardiomyopathy had ESV above 38. 21 cases with cirrhotic cardiomyopathy had ESV below 38. The ‘p’ value of this association between ESV and cirrhotic cardiomyopathy was 0.419 and it
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was not significant. This implied that abnormality of ESV is not a significant feature of cirrhotic cardiomyopathy.

29 cases had ejection fraction above 60. 1 patient had EF below 60. 22 patients with CC had EF above 60. 1 patient with CC had EF below 60. 7 patients with EF above 60 did not have CC. The 'p' value of this association between EF and CC was 0.575 and it was not significant. This implied that abnormality of EF was not a significant feature of cirrhotic cardiomyopathy. 29 cases had ejection fraction above 60. 1 patient had EF below 60. 20 patients with diastolic dysfunction had EF above 60. 1 case with diastolic dysfunction had EF below 60. 9 patients with EF above 60 did not have diastolic dysfunction. The 'p' value of this association between EF and diastolic dysfunction is 0.506 and it is not significant. This implied that abnormality of EF is not a significant feature of cirrhotic cardiomyopathy.

23 of the 30 cases had ascites. Of the 23 cases that had cirrhotic cardiomyopathy 21 cases had ascites. 21 cases that had ascites showed features of cirrhotic cardiomyopathy. 2 cases without ascites also showed features of cirrhotic cardiomyopathy. 5 of the 7 cases without cirrhotic cardiomyopathy did not have ascites. The 'p' value of the association of ascites and cirrhotic cardiomyopathy was 0.0001 and it was significant. This implied presence of ascites was a significant finding in cases that had cirrhotic cardiomyopathy. (Table - 3)

6.7% of the cases had end systolic volume above 38. 100.0% of the cases with ESV above 38 had E/A ratio below 1. 67.9% of the cases with ESV below 38 also had E/A ratio below 1. These findings indicate that end systolic volume is not significant indicator of cardiac dysfunction ('p' = 0.338). (Table - 4)

70.0% of the cases had end diastolic volume above 90. 76.2% of the cases with EDV above 90 had E/A ratio below 1. 55.6% of cases with EDV below 90 also had E/A ratio below 1. 76.2% of the cases with E/A ratio below 1 had EDV above 90. 23.8% of the cases with E/A ratio below 1 had EDV below 90. These findings indicate that end diastolic volume is not significant indicator of diastolic dysfunction ('p' = 0.258). (Table - 5)

Discussion

Cirrhotic cardiomyopathy denotes an impaired contractile responsiveness to stress, altered diastolic relaxation, and presence of electrophysiological abnormalities. It is independent of etiology of cirrhosis, may be diagnosed at rest in some patients but demasked by physical or pharmacological stress [11]. Cardiac failure is an important cause of mortality after liver transplantation, but improved liver function has also been shown to reverse the cardiac abnormalities [12]. The frequency and the etiology of CC are still under investigation [13]. Study by Wong, et al., has shown that 56.3% patients had diastolic dysfunction [14]. In the study by Karagiannakis, et al., diastolic dysfunction was observed in 37.77% of Patients. In the study done by Piyush Somani, et al., the prevalence of cirrhotic cardiomyopathy was 25.86%. Ruiz-del-Árbol, et al., found a prevalence of 46% of cardiac dysfunction in cirrhotics. In the study done by Salari, et al., diastolic dysfunction was seen in 51% of cirrhotics [14]. In our study, cirrhotic cardiomyopathy is present in 76.7% of patients. These differences could be because of different methods used to investigate cardiac dysfunction in different studies.

In the study done by Salari, et al., cirrhosis was due to HBV infection in 9%, HCV in 22%, cryptoenic in 62% of patients, other causes being primary sclerosing cholangitis, Budd chiari syndrome. In our study, HBV was seen in 30%,
HCV in 13.3%, cryptogenic cirrhosis in 56.7%. Absence of patients with other etiologies of cirrhosis could be because of exclusion criteria of this study like severe anemia, gross ascites, recent gastrointestinal bleeding etc. Torregrosa, et al., found that the cardiac changes were independent of the etiology of cirrhosis [15]. In our study also, cardiac changes seen were independent of the etiology of cirrhosis. In the study done by Salari, et al., cirrhotic cardiomyopathy was more frequent in female patients, 67.6%, compared to male cirrhotics. In the present study, 85.7% of female cirrhotics had features of cirrhotic cardiomyopathy. This female predilection may be due to the differences of sex hormones in each gender. In our study, 50% of patients younger than 40 years of age had cardiac dysfunction whereas 80.7% of patients older than 40 years of age had cardiac dysfunction. Salari, et al., found that older individuals had a higher prevalence of diastolic dysfunction.

In the study done by Alexander J et al., in the nonalcoholic cirrhotics, 3.3% belonged to CTP class A, 70% to CTP class B, 26.67% to CTP class C [16]. In our study also patients mostly had cirrhosis of intermediate severity as nearly 54% of them belonged to CTP class B. CTP class A patients may be underrepresented since most of them are asymptomatic and do not seek medical consultation. CTP class C patients mostly had exclusion criteria of the study. In our study, cirrhotic cardiomyopathy was seen in 57.1% of CTP class A cirrhosis, 75% of CTP class B, 100% of CTP class C, but it was statistically not significant (p value: 0.161). Bernardi, et al. in their study found that the frequency of cardiac dysfunction was dependent on the severity of cirrhosis as assessed by Child Turcotte Pugh score [17]. Similar observation was made by Salari, et al. in their study on diastolic dysfunction in cirrhotics [18]. But in our study no such correlation was found. This could be because of low proportion of patients belonging to CTP class A and CTP class C in our study.

Prolonged Q-T interval predicts severe arrhythmias and sudden death, and has been shown to occur in cirrhotic patients who are candidates for liver transplantation [7]. In our study, QTc was prolonged in 53.3% of patients. Bernardi, et al. found that QTc interval was significantly prolonged in cirrhotic patients when compared with healthy individuals [7]. Ytting, et al. showed that QTc was prolonged in 49% of cirrhotics [19]. In the study by Zambruni, et al., QTc was prolonged in 33% of cirrhotics. Zamirian et al. showed that QTc is prolonged in 43.2% of cirrhotics [20]. Kosar, et al. showed that QTc was prolonged in 32% of cirrhotics [21].

In our study, QTc was prolonged in 56.2% of CTP class B cirrhotics, 100% in CTP class C cirrhotics which was statistically significant. Bali J S, et al., found that 40% of cirrhotics had a prolonged QTc interval and that Child-Pugh scores were independent predictors of prolonged QTc interval [22]. Zamirian, et al. showed that QTc was prolonged in 33% of cirrhotics and that QTc correlated with CTP score [20].

The splanchnic vasodilation, high-output state and hyperaldosteronism seen in cirrhosis contribute to myocardial stiffening, which manifests as a decreased E/A ratio on 2-D echo. Recently, Holt, et al., have shown that diastolic dysfunction defined by an E/A ratio < 1 on 2D echo is an independent predictor of liver transplantation or death in patients with cirrhosis [23]. In their study, 27.8% of patients had an E/A ratio of < 1. In our study, E/A ratio was < 1 in 70% of patients.

In our study, 70.0% of the cases had end diastolic volume above 90, but there was no correlation with E/A ratio. These findings indicate that end diastolic volume is not a
significant indicator of diastolic dysfunction (’p’ = 0.258). Alexander J, et al. in their study done in Asian population with cirrhosis have found that end diastolic volume is not statistically significant in them [16]. Laffi, et al., in their study have found that left ventricular end diastolic volume is increased in cirrhotic patients [24]. In our study 6.7% of the cases had end systolic volume above 38, but there was no correlation with E/A ratio. These findings indicate that end systolic volume is not significant indicator of cardiac dysfunction (’p’ = 0.338). Alexander J, et al. had found that end systolic volume is not statistically significant in Asian cirrhotics [16]. Laffi, et al. in their study have found that left ventricular end systolic volume is increased in cirrhotic patients [24]. In our study, EF did not correlate with diastolic dysfunction. Alexander J, et al. had found that ejection fraction is not statistically significant in Asian population with cirrhosis [16]. Because the cardiac reserve function is borderline in patients with cirrhosis, cardiovascular status should be carefully monitored, especially when patients undergo stresses such as liver transplantation or portosystemic shunting procedures.

**Conclusion**

Cirrhotic patients with non alcoholic etiology do have evidence of cirrhotic cardiomyopathy. They have features in the form of diastolic dysfunction and prolonged QTc interval. Diastolic dysfunction is manifested as E/A ratio < 1. The presence of cirrhotic cardiomyopathy was independent of the etiology. Some degree of diastolic dysfunction is seen in most of the cirrhotics. The severity of cirrhosis does not correlate with the presence of diastolic dysfunction. Prolongation of QTc interval correlates with severity of cirrhosis. Ventricular end diastolic volume, end systolic volume and ejection fraction do not correlate with severity of cirrhosis. 2D Echocardiography can be suggested for evaluating cardiac function at any stage of cirrhosis.

**References**

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Source of support: Nil

Conflict of interest: None declared.
### Table 1: Association between Cirrhotic Cardiomyopathy and CTP class.

<table>
<thead>
<tr>
<th>CTP</th>
<th>CC</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>4 (57.1%)</td>
<td>3 (42.9%)</td>
<td>7 (23.3%)</td>
</tr>
<tr>
<td>B</td>
<td>12 (75%)</td>
<td>4 (25%)</td>
<td>16 (53.3%)</td>
</tr>
<tr>
<td>C</td>
<td>7 (100.0%)</td>
<td>0 (0.00%)</td>
<td>7 (23.3%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>23 (76.7%)</td>
<td>7 (23.3%)</td>
<td>30 (100.00%)</td>
</tr>
</tbody>
</table>

### Table 2: Association between QTc group and CTP class.

<table>
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<th>CTP</th>
<th>QTc group</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
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<tr>
<td></td>
<td>Below 440 msec</td>
<td>Above 440 msec</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>7 (100.0%)</td>
<td>0 (0.00%)</td>
<td>7 (23.3%)</td>
</tr>
<tr>
<td>B</td>
<td>7 (43.8%)</td>
<td>9 (56.2%)</td>
<td>16 (53.3%)</td>
</tr>
<tr>
<td>C</td>
<td>0 (0.00%)</td>
<td>7 (100.0%)</td>
<td>7 (23.3%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>14 (46.7%)</td>
<td>16 (53.3%)</td>
<td>30 (100.00%)</td>
</tr>
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### Table 3: Association between cirrhotic cardiomyopathy and ascites.

<table>
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<th>Ascites</th>
<th>CC</th>
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<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>21 (91.3%)</td>
<td>2 (8.7%)</td>
<td>23 (76.7%)</td>
</tr>
<tr>
<td>Absent</td>
<td>2 (28.6%)</td>
<td>5 (71.4%)</td>
<td>7 (23.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>23 (76.7%)</td>
<td>7 (23.3%)</td>
<td>30 (100.00%)</td>
</tr>
</tbody>
</table>

### Table 4: Association between E/A group and End Systolic Volume.

<table>
<thead>
<tr>
<th>ESV group</th>
<th>E/A group</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Below 1</td>
<td>Above 1</td>
<td></td>
</tr>
<tr>
<td>Below 38</td>
<td>19 (67.9%)</td>
<td>9 (32.1%)</td>
<td>28 (93.3%)</td>
</tr>
<tr>
<td>Above 38</td>
<td>2 (100.0%)</td>
<td>0 (0.00%)</td>
<td>2 (6.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>21 (70.0%)</td>
<td>9 (30.0%)</td>
<td>30 (100.00%)</td>
</tr>
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</table>

### Table 5: Association between E/A and End Diastolic Volume.

<table>
<thead>
<tr>
<th>EDV group</th>
<th>E/A group</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Below 1</td>
<td>Above 1</td>
<td></td>
</tr>
<tr>
<td>Below 90</td>
<td>5 (55.6%)</td>
<td>4 (44.4%)</td>
<td>9 (30.0%)</td>
</tr>
<tr>
<td>Above 90</td>
<td>16 (76.2%)</td>
<td>5 (23.8%)</td>
<td>21 (70.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>21 (70.0%)</td>
<td>9 (30.0%)</td>
<td>30 (100.00%)</td>
</tr>
</tbody>
</table>