

# Correlation between Branched Chain Amino Acids to Tyrosine Ratio and Child Pugh Score in Liver Cirrhosis Patients

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## ABSTRACT

**Background:** The determination of branched chain amino acids (BCAA) to tyrosine ratio (BTR) was available in making differentiation of chronic hepatitis from liver cirrhosis, because there was a strong association between BTR and staging (fibrosis) scores. Branched chain amino acids to tyrosine ratio have a correlation with Fischer ratio and the examination is easier because it can be done by enzymatic assay.

**Materials and Methods:** To evaluate the correlation between BTR and Child-Pugh score, we examined the amino gram of 52 liver cirrhosis patients consisted of 26 Child-Pugh A, 19 Child-Pugh B, and 7 Child-Pugh C. The examination of amino gram was done by High Pressure Liquid Chromatograph (HPLC) analyzer. Branched chain amino acids to tyrosine ratio were compared to Child-Pugh score, albumin, ammonia level, number connection test to Fischer ratio.

**Results:** Significant differences in BTR among Child-Pugh A, B, C were observed (Child-Pugh A  $7.75 \pm 1.2$ ; Child Pugh B  $6.0 \pm 1.23$  and Child Pugh C  $4.38 \pm 3.14$  ( $p = 0.000$ )). Branched chain amino acids to tyrosine ratio had a weak correlation with albumin ( $r = 0.292$ ;  $p = 0.036$ ), ammonia level ( $r = 0.376$ ;  $p = 0.006$ ) and strong correlation with Fischer ratio ( $r = 0.818$ ;  $p = 0.000$ ). There was no significant correlation between BTR and number connection test.

**Conclusion:** These results showed that the determination of the molar ratio of branched chain amino acids to tyrosine well reflected the severity of liver cirrhosis and it can be used as a substitute of Fischer ratio.

**Keywords:** Branched chain amino acids, tyrosine, liver cirrhosis

## INTRODUCTION

Metabolic disorders in patients with chronic liver disease are commonly accompanied by significant changes in amino acid level in blood. The ratio of branched chain amino acid (BCAA) and aromatic amino acid (AAA) known also as Fischer ratio will decrease in accordance with severity of liver disease. This ratio has already been decreased in chronic hepatitis and will be lower in liver cirrhosis.<sup>1,2</sup>

Fischer ratio is not a widely routine examination because amino acid measurement takes much longer time and expensive. For the last few years, it had been found that ratio of BCAA and branched chain amino acids to tyrosine ratio (BTR) had strong correlation with Fischer ratio. The procedure may be conducted more rapidly by

examining ratio of BCAA and tyrosine, without measuring phenylalanine. This is possible because the analysis is conducted by enzymatic method which takes only few minutes to obtain the results.<sup>3,4</sup>

Several studies reported that BTR can be a good indicator to evaluate disease severity in liver and had replaced BRCA-AAA ratio in making diagnosis and management of liver disease.<sup>4,5,6</sup> Study of BTR at different level of severity of liver cirrhosis had never been conducted. This study aims to evaluate BTR at different level of severity of liver cirrhosis according to Child-Pugh criteria.

### SUBJECT AND METHODS

Subjects were patients with liver cirrhosis who had been hospitalized in Cipto Mangunkusumo Hospital, Jakarta. Diagnosis of liver cirrhosis was made based on physical examination, serologic marker of viral hepatitis B and or C, abdominal ultrasound with or without liver biopsy. Patients aged between 20 and 70 years old and were capable to do number connection test (NCT). Patients with hepatic encephalopathy grade III, IV or evidence of hepatoma or receiving albumin treatment were excluded from this study.

Ammonia level in the serum was examined using Du Pont ACA apparatus discrete clinical analyzer with wave length of 340 nm and temperature of 37°C. Amino acid level was examined by Shimatzu Du Pont High Pressure Liquid Chromatograph (HPLC) analyzer at temperature of 55°C.

Data was analyzed with program SPSS. Correlation of BTR with Child-Pugh criteria, RF, albumin, ammonia and NCT was calculated using Pearson's correlation test based on significance level  $p < 0.05$ .

### RESULT

Of 52 patients who fulfilled inclusion criteria, there were 26 patients with Child-Pugh A, 19 patients with Child-Pugh B and 7 patients with Child-Pugh C. Table 1 describes the characteristic of study subjects.

Table 1. Subject Characteristics

	Child-Pugh A	Child-Pugh B	Child-Pugh C
Number of patients	26	19	7
Albumin level (g/dL)	4.2731	3.3579	2.3857
Ammonia level (mmol/L)	48.6154	54.2105	126.7143
NCT (second)	69.1540	90.6316	81.4286

Mean value of BTR was  $6.52 \pm 0.85$ , and it tended to be lower in more severe liver cirrhosis. Mean of BTR in Child-Pugh A was  $7.75 \pm 1.2$ , Child-Pugh B  $6.0 \pm 1.23$  and Child-Pugh C was  $4.38 \pm 3.14$ , and result of statistical calculation found correlation  $r = 0.4914$  ( $p = 0.000$ ).

Albumin and Child-Pugh criteria was correlated with  $r = 0.671$  ( $p = 0.000$ ). Ratio of BCAA and tyrosine had strong correlation with Fischer ratio.

BTR and albumin apparently demonstrated a weak correlation ( $r = 0.292$ ,  $p = 0.036$ ) and the same result was also seen between ammonia and BTR ( $r = 0.376$ ,  $p = 0.006$ ). It appears that NCT which was widely used as simple tool for evaluation of hepatic encephalopathy had no correlation with BTR.

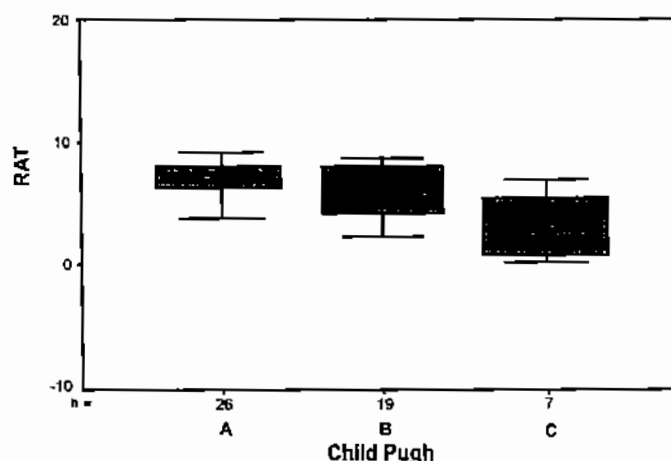


Figure 1. BTR according to Child Pugh Criteria

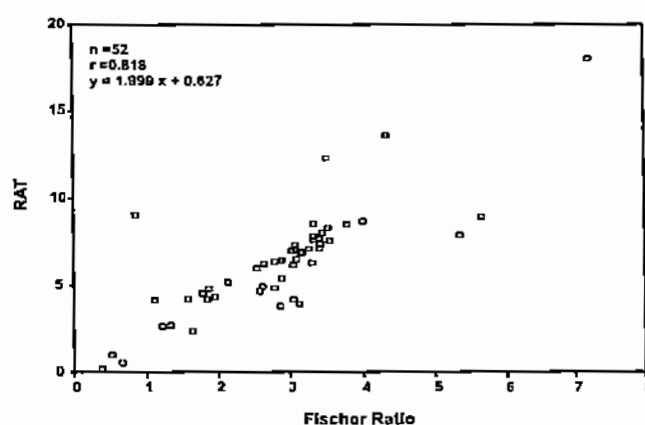


Figure 2. Correlation between BTR and Fischer Ratio

### DISCUSSION

BTR measurement in the previous studies was considered useful in assessment of liver disease severity. BTR value was found different among normal people, patients with acute hepatitis, chronic hepatitis, and liver cirrhosis. This study had demonstrated significant level of BTR according to Child-Pugh criteria. More severe liver cirrhosis had lower BTR. This result was in accordance to study conducted by Tameda et al which found higher level of BTR in decompensate liver cirrhosis compare to non-decompensate ( $4.0 \pm 1.7$  vs.  $2.9 \pm 1.2$ ). This was due by increasing level of aromatic amino acid (AAA) like phenylalanine, tyrosine and thryptophane because they were less degraded in the liver. On the other hand, AARC (valin, leucine, and isoleucine) were decreased due by increasing catabolism in the muscle as consequence of hyperinsulinemia and insulin resistance.<sup>1,6</sup>

Correlation between BTR and Child-Pugh criteria was weak compare to BTR and albumin. Tameda also reported the same result when he compared these two kind examinations to differentiate chronic hepatitis and liver cirrhosis. It indicated that albumin level was more superior than BTR in assessment of liver disease severity in chronic hepatitis as well as cirrhosis according to Child-Pugh criteria A,B, and C.<sup>6</sup>

BTR had strong correlation with Fischer ratio. This result was supported by studies conducted by Abe et al and Nakamura et al. This had proved that examination of BTR level using enzymatic method may be an alternative procedure to Fischer ratio which was more expensive and complicated.<sup>4,5</sup>

BTR had merely weak correlation with albumin and ammonia level and appeared had no correlation with NCT. This result might due to different factors that influence level of albumin, amino acid and ammonia. It found no correlation between BTR and NCT. This result supported Morgan who concluded that ratio of BCAA and AAA had stronger correlation with liver disease severity regardless the presence of hepatic encephalopathy.<sup>7,8</sup>

#### CONCLUSION

1. Ratio of BCAA and tyrosine may be used to replace Fischer ratio
2. Decrease ratio of BCAA and tyrosine is in accordance with severity of liver cirrhosis

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