

Optimization Of The Assessment Of The Functional State Of The Liver In Patients With Cirrhosis Of Various Etiologies Using The ¹³C-Metacetin Respiratory Test

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Abstract: Summary. *¹³C-metacetin breath test is a non-invasive, non-radioactive, sensitive and specific method for determining the functional activity of hepatocytes, liver cell failure and stages of fibrosis.*

Objective: *study the possibility of assessing the functional state of the liver with cirrhosis of various etiologies with the help of index DOB₂₀.*

Materials and methods. *The study included 90 patients (30 patients with liver cirrhosis of alcoholic etiology and 30 patients with liver cirrhosis of viral etiology and 30 healthy volunteers (control group). All patients with cirrhosis were divided into three equal groups of 10 people, depending on their indicators on the Child-Pugh scale. All patients underwent standard clinical, laboratory and instrumental examination and ¹³C-metacetin breath test: both the standard method and the modified method.*

Results. *The revealed direct strong correlation between the indices of the ¹³C-metacetin test at 20 minutes and 120 minutes allows the use of the DOB₂₀ indicator to determine the mass of functioning hepatocytes. Using the DOB₂₀ indicator instead of the “cumulative dose” indicator allows you to significantly speed up the study and reduces its cost. Indicators of the ¹³C-metacetin test at 20 minutes allow us to evaluate the functional state of hepatocytes and also closely correlate with the classes of liver cirrhosis on the Child-Pugh scale.*

Conclusions:

1. The DOB₂₀ indicator allows to determine the pool of functioning hepatocytes with the same accuracy as the cumulative dose indicator.
2. The DOB₂₀ values of the ¹³C-metacetin breath test closely correlate with the results of the assessment of the liver according to the Child-Pugh scale.
3. The etiology of liver cirrhosis does not affect the results of the ¹³C-metacetin breath test

¹³C-metacetin breath test (¹³C-MDT) is a non-invasive, non-radioactive, simple method for determining the functional activity of hepatocytes, liver cell failure and stages of fibrosis [1-3, 6-8]. A feature of ¹³C-MDT is its ability to assess the mass of functioning hepatocytes in diseases

of the liver of various etiologies, determine the prognosis of the course of the disease, and help in choosing therapeutic tactics, including the aim of assessing indications for liver transplantation [4, 5, 9, 10]. ^{13}C -MDT has high sensitivity (up to 92.6%) [1, 3, 5] and specificity (up to 84.1%) [2, 5]. The indicator of the total concentration of $^{13}\text{CO}_2$ at 120 minutes or the "cumulative dose", which is normally 31.0 (25.9-38.7) %, is traditionally estimated [6, 8].

Objective: To study the possibility of assessing the functional state of the liver with cirrhosis of various etiologies with the help of index DOB_{20}

Objective:

1. To determine the value of the indicator "cumulative dose" for various classes of liver cirrhosis
2. To determine the values of the DOB_{20} indicator for various classes of liver cirrhosis
3. To determine the correlation between the indicators DOB_{20} and the "cumulative dose".

Materials and methods. The study included 30 patients with liver cirrhosis of alcoholic etiology (of which 15 men, 15 women, average age 50.16 ± 3.97 years) and 30 patients with liver cirrhosis of viral etiology (of which 16 men, 14 women, average age 51.46 ± 4.62 years). The control group consisted of healthy volunteers ($n = 30$), identical in gender and age ($p > 0.1$). All patients with cirrhosis (both alcoholic ($n = 30$) and viral etiology ($n = 30$)) were divided into three equal groups of 10 people, depending on their indicators on the Child-Pugh scale. All patients underwent standard clinical, laboratory and instrumental examination in order to make a nosological diagnosis and establish the degree of activity of the inflammatory process. To assess the mass of functioning hepatocytes, we used the ^{13}C -metacetin breath test: both the standard method (when using the total concentration of $^{13}\text{CO}_2$ as the endpoint at the 120th minute) and the modified method (using the DOB_{20} as the endpoint, an indicator that reflects the content of $^{13}\text{CO}_2$ in the exhaled air at 20 minutes above the basal level). Breathing samples were analyzed on an Iris Wagner infrared spectroscope (Germany). Conclusions about the presence or absence of impaired liver function were made by comparing the curve of the total concentration of $^{13}\text{CO}_2$ to the outcome of 120 minutes of the study (with the standard method) or 20 minutes of the study (with the modified method) with the curves obtained during the examination of healthy volunteers that reflect the upper and lower boundaries of the norm. The obtained exhaled air samples were processed using a special computer program that takes into account such individual characteristics of the patient as his gender, age, height and weight.

For statistical data processing, the Excel - 2019 application package, the data analysis package, and the Statistica 10 program were used. A variance analysis was performed of the difference in the average values of the cumulative dose indicator between the samples of patients with cirrhosis of the liver in accordance with the Child-Pugh scale and healthy individuals. We also performed a variance analysis of the difference in the average values of the DOB_{20} indicator between two samples - patients with cirrhosis of the liver and healthy individuals.

Results and its discussion.

When studying the values of the indicator "cumulative dose" in patients with cirrhosis of the liver of class A, B and C according to Child-Pugh and correlation with similar data from the control group, it was found that the level of this indicator in patients with cirrhosis of the liver of class A was 12.81 ± 0.63 , while normally the average cumulative dose was 28.16 ± 1.55 ($p < 0.01$). The average cumulative dose in patients with class C liver cirrhosis was significantly lower than normal and significantly differed from the average values measured in the control group ($p < 0.005$). The most pronounced deviations from the control group were observed in the child-Pugh class C cirrhosis group. Determination of the significance of differences between samples of healthy individuals and patients with liver cirrhosis of alcoholic and viral etiology of class C by the method of analysis of variance allowed us to conclude that there is a high degree of significance of differences between them ($p < 0.001$) (Figure 1).

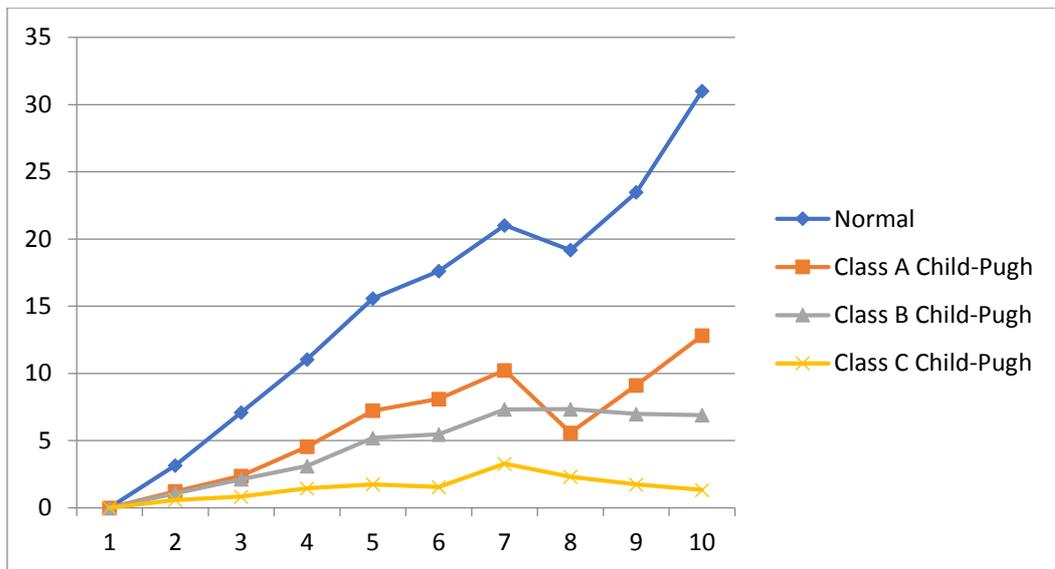


Fig. 1. The dynamics of the indicator "cumulative dose" in patients with cirrhosis of the liver of class A, B and C according to Child-Pugh.

When comparing the average DOB_{20} values of the group of patients with cirrhosis of the liver of class A according to Child-Pugh (10.81 ± 0.53) and the average DOB_{20} values of the control group (20.84 ± 1.11), significant statistical differences were obtained ($p < 0,01$). In the group of patients with class C liver cirrhosis, there was a more pronounced tendency to a decrease in DOB_{20} (5.74 ± 0.25) compared with the control ((20.84 ± 1.11)) ($p < 0.005$). The most pronounced pathological changes in DOB_{20} values were noted by us in the group of patients with class C cirrhosis where the DOB_{20} value was 3.07 ± 0.15 ($p < 0.001$), which indicated a sharp decrease in the mass of functioning hepatocytes. The data obtained indicate that already at the 20th minute of the study, the DOB_{20} indicator allows a high degree of reliability to determine the decrease in the mass of functioning hepatocytes (Figure 2).

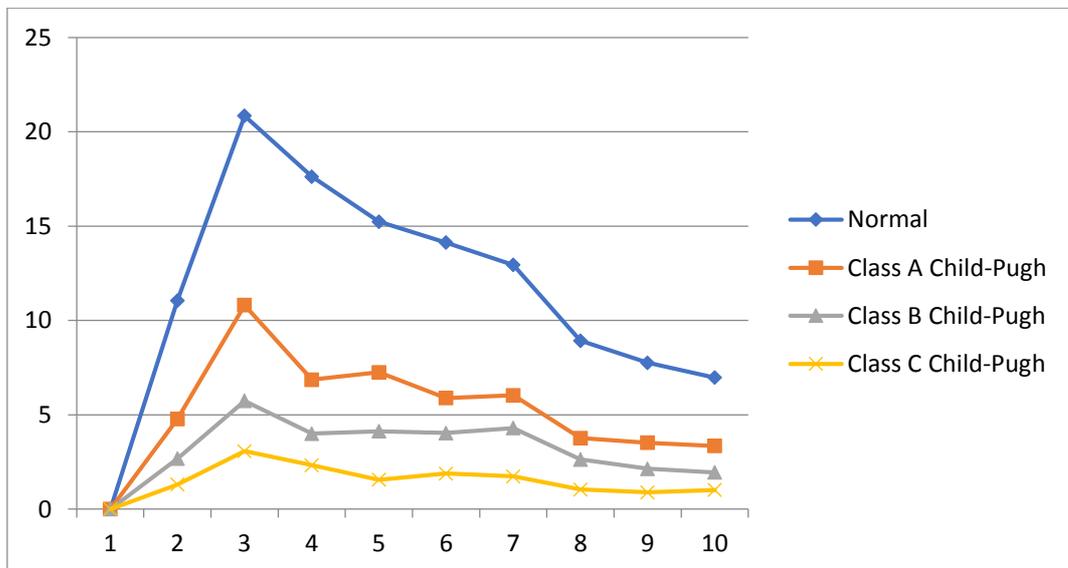
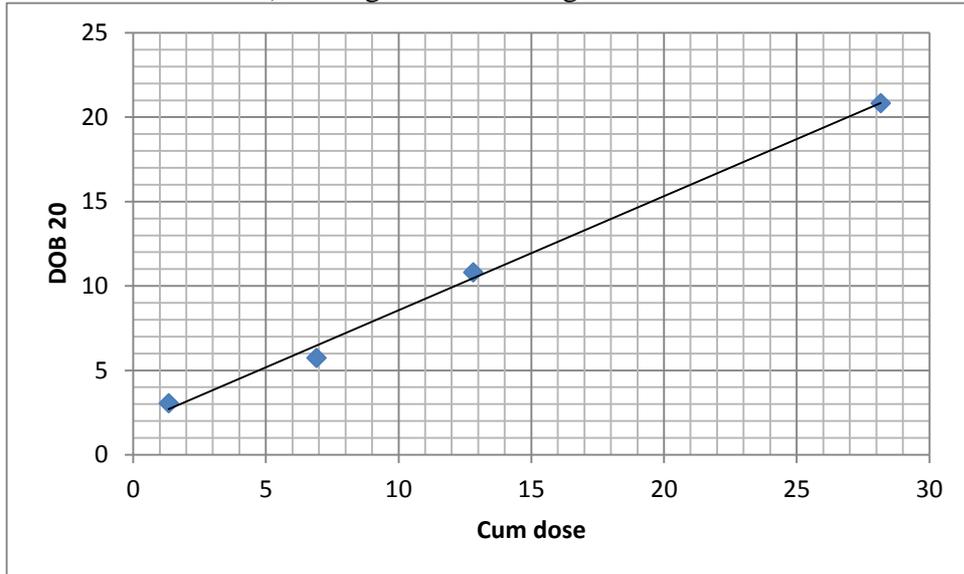


Fig. 2 Dynamics of the indicator "DOB₂₀" in patients with cirrhosis class A, B and C by Child-Pugh

Correlation analysis was carried out between indicators of ^{13}C -metacetin test ("cumulative dose" and DOB_{20}), during which a strong direct correlation was revealed ($p = 0.97$)



(Figure 3).

Fig. 3 Correlation between indicators ^{13}C -MBT ("cumulative dose" and DOB_{20})

A correlation analysis was also performed between the "cumulative dose" and DOB_{20} for various classes of cirrhosis (A, B, C on the Child-Pugh scale) separately. During the correlation analysis, a direct strong correlation was also found (for Child A, $\rho = 0.79$; Child B, $\rho = 0.96$; Child C, $\rho = 0.82$) (Fig. 4, 5, 6).

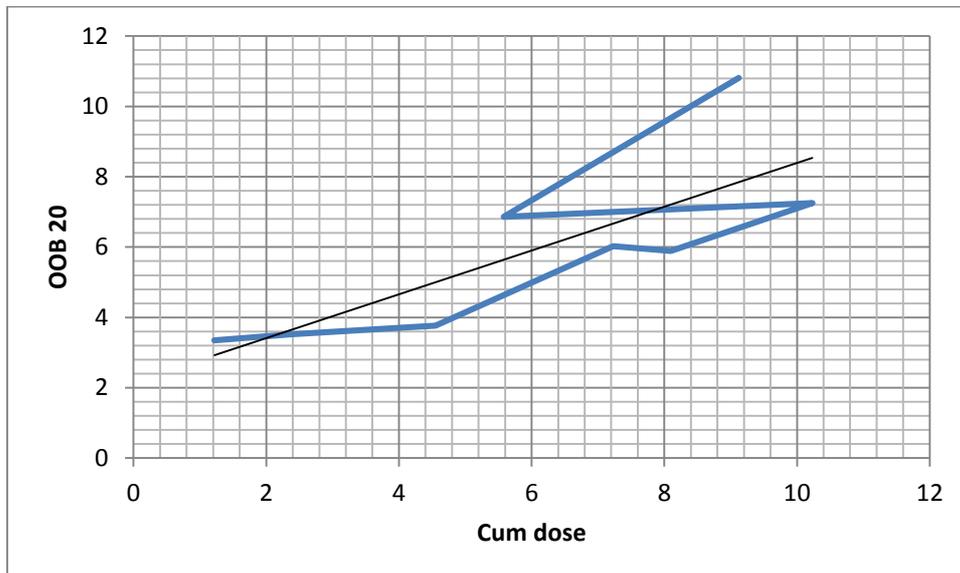


Figure: 4 Correlation between "cumulative dose" and DOB_{20} for patients with Child-Pugh class A cirrhosis

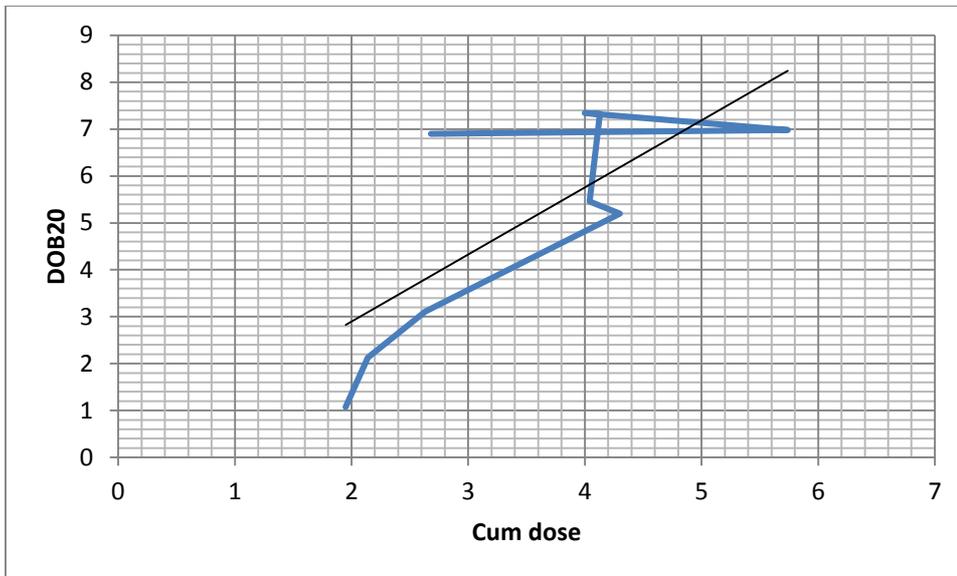


Fig. 5 Correlation between the “cumulative dose” and DOB₂₀ for patients with child-Pugh class B cirrhosis

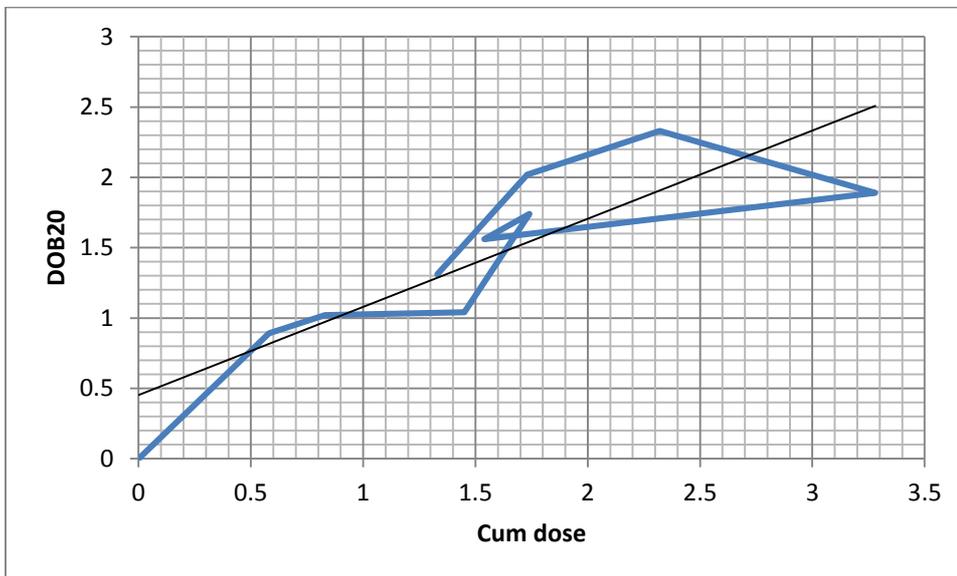


Fig. 6 Correlation between the “cumulative dose” and DOB₂₀ for patients with class C cirrhosis according to Child-Pugh

Thus, the revealed direct strong correlation between the indices of the ¹³C-metacitin test at 20 minutes and 120 minutes allows the use of the DOB₂₀ indicator to determine the mass of functioning hepatocytes. Using the DOB₂₀ indicator instead of the “cumulative dose” indicator allows you to significantly speed up the study and reduces its cost.

Thus, indicators of the ¹³C-metacitin test at 20 minutes allow us to evaluate the functional state of hepatocytes and also closely correlate with the classes of liver cirrhosis on the Child-Pugh scale.

Conclusions:

1. The DOB₂₀ indicator allows to determine the pool of functioning hepatocytes with the same accuracy as the cumulative dose indicator.
2. The DOB₂₀ values of the ¹³C-metacitin respiratory test closely correlate with the results of the assessment of the liver according to the Child-Pugh scale (for Child A, $\rho = 0.79$; Child B, $\rho = 0.74$; Child C, $\rho = 0.81$)
3. The etiology of liver cirrhosis does not affect the results of the ¹³C-metacitin breath test.

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