Bangladesh Journal of Medicine (BJM)
ISSN : 1023 - 1986
eISSN : 2408 - 8366

ORIGINAL ARTICLE

ACCURACY OF TRANSIENT ELASTOGRAPHY IN IDENTIFYING FIBROSIS AMONG PATIENTS WITH CHRONIC HEPATITIS B: A CROSS-SECTIONAL OBSERVATIONAL STUDY

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Abstract:

Background: *Hepatitis B virus (HBV) infection is a significant global public health problem, affecting millions of people worldwide. Liver biopsy is the gold standard for assessing fibrosis but is invasive and carries post-procedural risks. Noninvasive tests to evaluate liver fibrosis are needed, and transient elastography is one such method. This cross-sectional observational study aimed to assess the accuracy of transient elastography in identifying fibrosis among patients with chronic hepatitis B.* ***Methods:*** *The study was conducted at the Department of Medicine and Hepatology, Sir Salimullah Medical College Mitford Hospital, Dhaka. The study subjects were patients diagnosed with chronic hepatitis B infection, both outpatient and inpatient cases. Data were collected from 25 patients using convenient and purposive sampling techniques. Demographic data, clinical examination, and relevant investigations were recorded in a structured case report form. Data were processed, registered, edited, computerized, and analyzed.* ***Results:*** *The study included 25 patients with a mean age of 26.8±6.5 years, predominantly male (80%). All patients were HBsAg positive, 12.0% were HBeAg positive, and 56.0% were antiHBe positive. The mean HBV DNA PCR was 1516293.4±7475976.3 IU/ml. The mean ALT level was 45.4±13.8 U/L. The mean liver stiffness measurement (LSM) was 7.5±2.3 kPa, with 64.0% of patients showing fibrosis stage F0-F1. The mean periportal +/- bridging necrosis was 2.92±1.58, intralobular degeneration and focal were 1.16±0.55, portal inflammation was 2.52±0.87, histological activity index was 6.6±2.2, and fibrosis score was 1.44±1.04. Positive correlations were observed between LSM and histological activity index (r=0.239; p=0.251) and between LSM and fibrosis score (r=0.107; p=0.612).Conclusion: Our study demonstrates that transient elastography provides a non-invasive, easy, and cost-effective method for identifying fibrosis in chronic hepatitis B patients, serving as a potential alternative to liver biopsy.*

Key words: *Transient Elastography Liver Fibrosis, Chronic Hepatitis B*

Received: 05.07.2023 *Accepted: 16.08.2023*
DOI: https://doi.org/10.3329/bjm.v34i3.68423

Citation: *Rony RS, Hossain A, Islam MD, Karim MF, Rahman A, Jui SS. Accuracy of Transient Elastography in Identifying Fibrosis among Patients with Chronic Hepatitis B: A Cross-Sectional Observational Study. Bangladesh J Medicine 2023; 34: 199-205.*

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Introduction:

Viral hepatitis, including Hepatitis B virus (HBV) infection, is a significant global public health concern affecting millions of people worldwide.[1] In Bangladesh, HBV is of intermediate prevalence, with an estimated 5.4% prevalence in the general population.[2] HBV infection can lead to chronic disease, and its complications, such as cirrhosis and hepatocellular carcinoma, are of grave concern. The progression of liver fibrosis is a key factor in determining the severity of HBV-related liver disease.[3]

Liver fibrosis results from the accumulation of extracellular matrix proteins and activation of hepatic stellate cells. The host immune response plays a crucial role in the natural history of HBV infection, with chronic infection leading to liver injury primarily caused by the host's immune cells.4 Additionally, viral genomic factors, such as genotype D of HBV, have been associated with more severe diseases and increased hepatocellular carcinoma risk, especially in young patients.[4,5]

Liver biopsy is the gold standard for evaluating liver fibrosis, but its invasiveness and post-procedural risks make noninvasive alternatives highly desirable.[6] Transient elastography, also known as FibroScan, is a promising noninvasive test that assesses liver fibrosis by measuring liver stiffness.[7,8] It uses shear waves to determine tissue stiffness, providing immediate, operator-independent results.

This study aims to assess the accuracy of transient elastography in identifying fibrosis among patients with chronic hepatitis B(9).By comparing its effectiveness against liver biopsy, we can determine if transient elastography could be a reliable alternative for identifying liver fibrosis in these patients, reducing the need for invasive procedures and improving patient care.

Methods:

Study Design, Population, and Settings:

This cross-sectional observational study was conducted at the Department of Medicine and Hepatology, Sir Salimullah Medical College & Mitford Hospital, Dhaka, Bangladesh, from August 2019 to February 2020. The study included 25 patients with chronic hepatitis B infection who met the inclusion and exclusion criteria. Written approval was obtained from all participating patients. Inclusion criteria comprised age ≥18 years, compensated liver disease with chronic hepatitis B infection, chronic hepatitis B-infected individuals not meeting treatment criteria, transient elastography value ≥7 kPa with other normal parameters, and coarse liver on ultrasound with other normal parameters. Patients with co-infection with hepatitis C or human immunodeficiency virus, history of anti-viral drug use for more than six months or current treatment, hepatic encephalopathy, prolonged prothrombin time (>4 seconds), platelet count < 80,000/cumm, ascites, severe anemia, advanced chronic obstructive pulmonary disease (COPD), heart failure, or chronic kidney disease were excluded from the study.

Data Collection and Laboratory Procedures:Data were collected through face-to-face interviews using a semi-structured questionnaire to obtain socio-demographic information and clinical presentations. Physical examinations were performed, and reports of ultrasound, blood tests, and transient elastography were recorded during hospital admission. Liver biopsy and relevant laboratory test results were also recorded.

Data Management and Analysis:

Data on socio-demographic and clinical variables were collected using a pre-designed questionnaire, ensuring clarity and accuracy in respondents' answers. Data were checked, verified for consistency, and edited for final analysis. Statistical analysis was performed using the Statistical Program for Social Science (SPSS), version 25, IBM Corp., Chicago, USA, 2017. P values of 0.05 or higher were considered significant, and p values below 0.01 were considered highly significant.

Results :

Table I

Demographic characteristics of the study patients (n=25)

Demographic characteristics	Number of patients	Percentage
Age (years)		
≤20	4	16.0
21-25	10	40.0
26-30	6	24.0
31-35	2	8.0
36-40	2	8.0
>40	1	4.0
Mean±SD	26.8	±6.5
Range (min-max)	16.0	-41.0
Sex		
Male	20	80.0
Female	5	20.0

Table I shows that 10(40.0%) patients belonged to age 21-25 years. The mean age was found 26.8±6.5 years with range from 16 to 41 years. Majority (80.0%) patients were male and 5(20.0%) were female. Male female ratio was 4:1.

Table II

Distribution of the study patients according to HBV serology(n=25)

HBV serology	Number of patients	Percentage
HBsAg		
Positive	25	100.0
Negative	0	0.0
HBeAg		
Positive	3	12.0
Negative	22	88.0
AntiHBe		
Positive	14	56.0
Negative	11	44.0
HBV DNA PCR (IU/ml)	1516293.4	±7475976.3
Range (min-max)	200.0	-37400000.0

Table II shows that all (100.0%) patients were found in HBsAg positive, 3(12.0%) in HBeAgpositive and 14(56.0%) in antiHBe positive. Mean HBV DNA PCR was found 1516293.4±7475976.3 IU/ml with range from 200 to 37400000IU/ml.

Table III

Distribution of the study patients according to ALT (n=25)

ALT (U/L)	Number of patients	Percentage
≤40 9	36.0	
>40 16	64.0	
Mean±SD	45.4	±13.8
Range (min-max)	19.0	-64.0

Table III shows that 16(64.0%) patients were found ALT level >40 U/L. The mean ALT was found 45.4±13.8 U/L with range from 19 to 64 U/L.

Table IV

Distribution of the study patients according to fibroscan of liver (n=25)

Fibroscan of liver	Number of patients	Percentage
LSM (kPa)		
≤10	22	88.0
>10	3	12.0
Mean±SD	7.5	±2.3
Range (min-max)	5.1	-14.2
Fibrosis stage		
F0 -F1	16	64.0
F2	3	12.0
F2 -F3	4	16.0
F3 - F4	2	8.0

Table-IV shows that mean LSM was found 7.5±2.3 kPa with range from 5.1 to 14.2 kPa.Majority (64.0%) patients was found fibrosis stage F0-F1.

Table V

Distribution of the study patients according to histological activity index (n=25)

Histological activity index (HAI)	Mean	±SD
Periportal +/- bridging necrosis	2.92	±1.58
Range (min-max)	1.0	-5.0
Intralobular degeneration and focal necrosis	1.16	±0.55
Range (min-max)	1.0	-3.0
Portal inflammation	2.52	±0.87
Range (min-max)	1.0	-3.0
Histological activity index	6.6	±2.2
Range (min-max)	3.0	-11.0

Table V shows that mean periportal +/- bridging necrosis was found 2.92±1.58 with range from 1.0 to 5.0. The mean intralobular degeneration and focal was found 1.16±0.55 with range from 1.0 to 3.0. The mean portal inflammation was found 2.52±0.87 with range from 1.0 to 3.0. The mean histological activity index was found 6.6±2.2 with range from 3.0 to 11.0.

Table VI

istribution of the study patients according to fibrosis score (n=25)

	Mean	±SD
Fibrosis score	1.44	±1.04
Range (min-max)	0.0	-3.0

Table VI shows that mean fibrosis score was found 1.44±1.04 with range from 0.0 to3.0.

Table VII

Distribution of the study patients according to knodell score (n=25)

	Mean	±SD
Knodell score	8.04	±3.13
Range (min-max)	3.0	-14.0

Table VII shows that mean knodell score was found 8.04±3.13 with range from 3.0 to 14.0.

Correlation between LSM and periportal necrosis

Spearman's rank correlation, ρ(rho) = 0.207 (p=0.320)

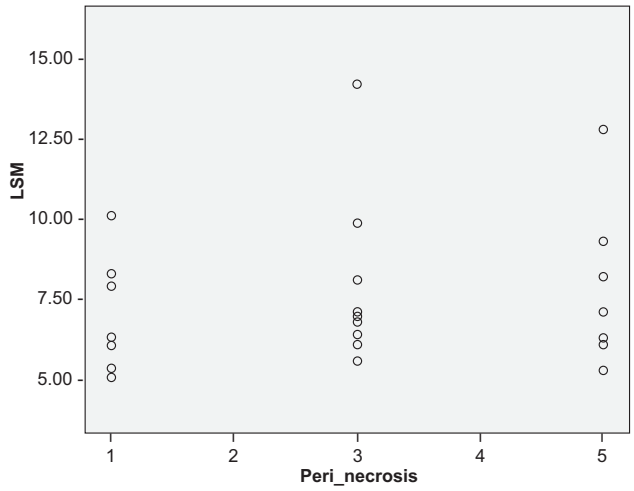

Fig.-1: *Correlation between LSM and periportal necrosis*

This figure 1 shows Correlation between LSM and periportal necrosis.

According to Spearman's rank correlation, it is ñ (rho) = 0.207 (p=0.320)

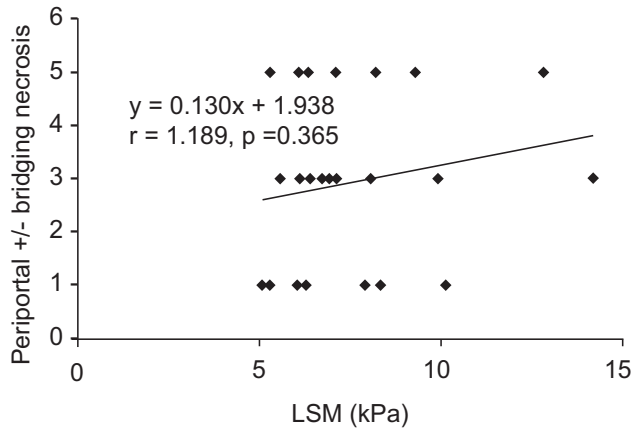

Fig.-2: *Scatter diagram showing positive correlation (r=0.189; p=0.365) between LSM and periportal +/- bridging necrosis*

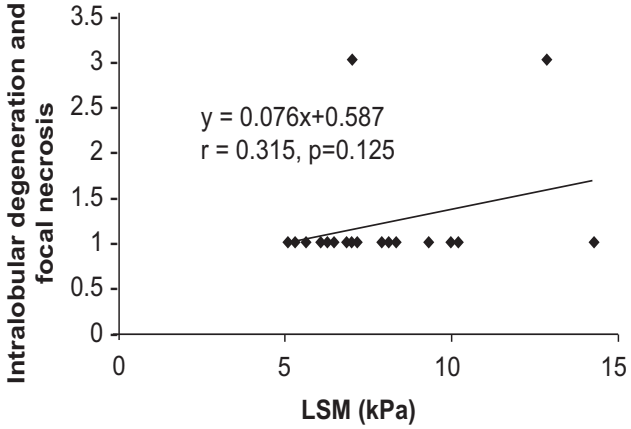

Fig.-3: *Scatter diagram showing positive correlation (r=0.315; p=0.125) between LSM and intralobular degeneration and focal necrosis.*

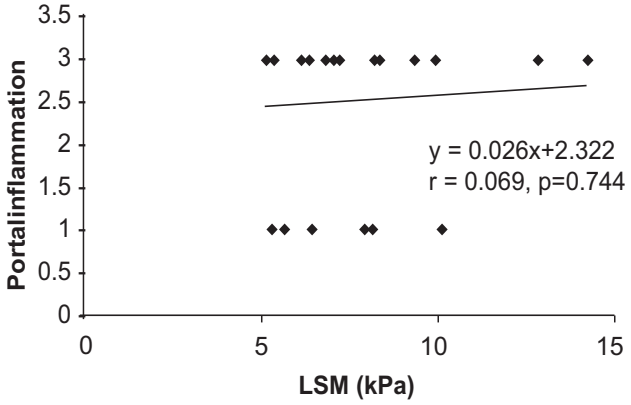

Fig.-4: *Scatter diagram showing positive correlation (r=0.069; p=0.744) between LSM and portal inflammation.*

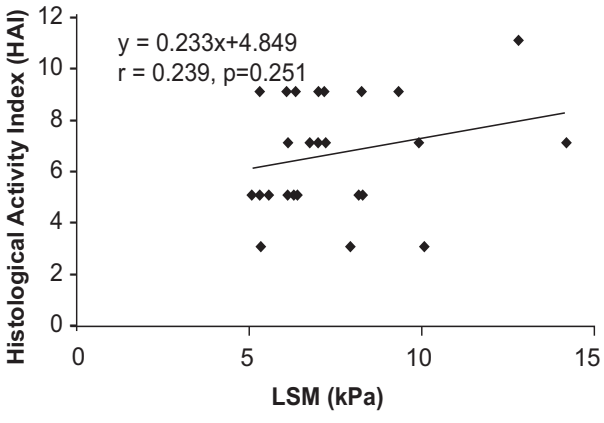

Fig.-5: *Scatter diagram showing positive correlation (r=0.239; p=0.251) between LSM and histological activity index.*

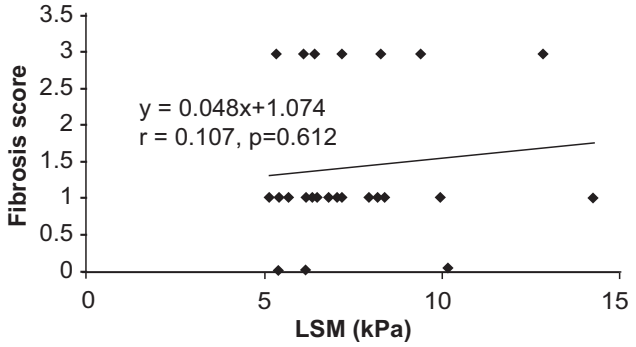

Fig.-6: *Scatter diagram showing positive correlation (r=0.107; p=0.612) between LSM and fibrosis score.*

Correlation between LSM and Knodel score

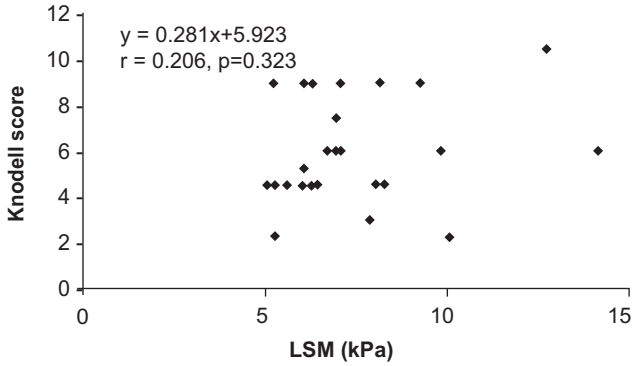

Fig.-7: *Scatter diagram showing positive correlation (r=0.206; p=0.323) between LSM and knodell score.*

Discussion:

In this study observed that 10(40.0%) patients belonged to age 21-25 years. The mean age was found 26.8±6.5 years with range from 18 to 41 years. Majority (80.0%) patients were male and 5(20.0%) were female. Male female ratio was 4:1. Li et al. reported that the mean age was found 36±10 years and 66.4% were male. Xu et al. reported the mean age was 33.5±10.4 years. Male sex was predominant in both patients with CHB with and without NAFLD (84.0% and 78.6%, respectively. Paul et al. also observed these patients were 176 males and 64 females, of mean age 32.6±11.6 years (range 15-75 years). Mansour et al. observed 62 females (68.9%) and 28 males (31.1 %), aging 18–72 years (mean age 45.53 ± 11.5 years).

In this study showed that all (100.0%) patients were found in HBsAg positive, 3(12.0%) in HBeAg positive and 14(56.0%) in antiHBe positive. Mean HBV DNA PCR was found 1516293.4±7475976.3 IU/ml with range from 200 to 37400000 IU/ml. Han et al. reported that the one-way ANOVA of the correlations between serological indexes and liver hardness in the 36 patients showed statistically significant ($P < 0.05$) differences in HA, type III procollagen (PCIII), LN, and type IV collagen (CIV) levels among patients with different liver hardness. The early screening of hepatitis B and timely administration of antiviral therapy are important measures to reduce the risk of liver failure and death.[7] Li et al. observed HBeAg positive cases were found 92(79.3%) and median HBV DNA was found 7.5 log10 copies/mL.[10]

In this study itis observed that 16(64.0%) patients were found ALT level >35 U/L. The mean ALT was found 45.4±13.8 U/L with range from 19 to 64 U/L.Han et al. In addition, patients with HBV DNA levels of >2,000 IU/mL regardless of ALT level should receive antiviral therapy. When the ALT level is <2 ULN, the pathological changes of the liver are taken into account to determine whether antiviral treatment is required.[8,9] Parikh et al.reported the AAR, has been widely utilized as a predictor of cirrhosis in different aetiologies of liver disease.[11] In a study published by Williams et al.[12] among 100 patients with HBV, the mean AST/ALT ratio was 0.59 in those without and 1.02 in those with cirrhosis respectively. However, Eminler and colleagues[12] found that the AAR performed inferiorly to other blood-based non-invasive algorithms in estimating the fibrosis stage in 237 HBV patients. Xu et al. reported that the median ALT was 84.0 U/L. Li et al. observed among the 116 enrolled patients, 37 (31.9%) had normal ALT levels, 52 (44.8%) had mildly elevated ALT levels (1–2 upper limit of normal [ULN]) and 27 (23.3%) had significantly elevated ALT levels (>2 ULN).

In current study showed that mean LSM was found 7.5±2.3 kPa with range from 5.1 to 14.2 kPa. The majority (64.0%) patients were found fibrosis stage F0-F1.Han et al. reported among 36 patients, 15 patients were at F1–F2 stage, 17 patients were at F2–F3 stage, and 4 patients were at F3 or above stage(13). Parikh et al. also observed the stiffer the liver, the higher is the velocity, indicated by a numeric value between 4.0 to 75 kPa. The cut-off values for significant fibrosis (e"F2) ranged from 5.8 to 8.8 kPa, for fibrosis ≥F3 from 7.0 to 13.5 kPa, and for cirrhosis (F4) from 9.0 to 16.9 kPa (97-103)(11). Qi et al. observed that the presence of an IQR/M > 30% and liver stiffness median ≥7.1 kPa lead to a lower accuracy determined by the area under receiver operating curve (AUROC) and these cases were considered "poorly reliable".[14] Zhang et al. reported liver stiffness measured with TE ranged from 3.2 to 38.5 kPa (IQR, 5.1-9.5 kPa)(12). Xu et al. reported that the mean LSM was 11.0±5.5 kPa.[9]

In this study showed that mean periportal +/- bridging necrosis was found 2.92±1.58 with range from 1.0 to 5.0. The mean intralobular degeneration and focal was found 1.16±0.55 with range from 1.0 to 3.0. The mean portal inflammation was found 2.52±0.87 with range from 1.0 to 3.0. The mean histological activity index was found 6.6±2.2 with range from 3.0 to 11.0.Some authors have suggested that TE cut-offs should incorporate ALT levels which fluctuate with inflammation in HBV, and TE may be particularly useful forHbeAg-negative patients with normal LFTs to guide the need for biopsy of treatment.[6,9,12,13]

In this study observed that mean fibrosis score was found 1.44±1.04 with range from 0.0 to 3.0. Han et al. reported hepatic fibrosis refers to the condition when excessive extracellular matrix (ECM) deposition occurs in the liver, and the abnormal hyperplasia of a large number of fibrous tissues occurs in the portal area. This is a reversible pathological condition during the process where various chronic liver diseases develop to cirrhosis.[10–12]

In current study observed that the positive correlation (r=0.239; p=0.251) between LSM and histological activity index. A Han et al. reported that hepatic stiffness was measured to monitor the outcomes of hepatic fibrosis in antiviral therapy, and the result confirmed that long-term viral inhibition was correlated with the outcomes of hepatic fibrosis.[13]. Therefore, monitoring the degree of hepatic fibrosis is useful during antiviral treatment. In China, the Guidelines for the Prevention, Management, and Treatment of Chronic HBV Infection (2015 Edition) also emphasize that FibroScan can be used to monitor hepatic hardness in chronic HBV infection, to improve the success rate and speed of detection.[1]

In present study positive correlation (r=0.107; p=0.612) between LSM and fibrosis score. Han et al. reported serum fibrosis indexes are associated with liver stiffness values ($P < 0.05$). Zhang et al. also observed that the correlation coefficients of TE and US scores with fibrosis stage were 0.69 (95% CI: 0.55, 0.78; P<0.001) and 0.47 (95% CI: 0.30, 0.61; P<0.001), respectively.[15] The correlation coefficients of TE were significantly higher than that of the US scores (P=0.022). However, the degree of hepatic steatosis did not correlate with fibrosis stage (r=0.041, P=0.69), TE scores (r=0.037, P=0.72), or US scores (r=0.091, P=0.38). Li et al. observed FibroScan (r=0.67, P<.001), GPR (r=0.44, P<.001) and APRI (r=0.34, P<.001) demonstrated a correlation with liver histological fibrosis stages.[10]

Conclusion:

Our study highlights the value of transient elastography as a viable, noninvasive, and cost-effective tool for identifying fibrosis. This technique provides a valuable alternative to liver biopsy, offering physicians and patients a more accessible and less intimidating option for monitoring disease progression. As we continue to address the complexities of Chronic Hepatitis B, integrating such noninvasive methods into clinical practice can significantly enhance patient care and outcomes.

Limitations:

Small sample size and this single hospital based study did not reflect exact scenario of the whole community. Patients from all socioeconomic status and all parts of the country did not come to seek medical attention in the study place.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study

Funding:

Funding from Bangabandhu Fellowship under the Ministry of Science and Technology, Bangladesh was received for this study.

Ethical consideration:

The study was conducted after approval from the ethical review committee. The confidentiality and anonymity of the study participants were maintained.

Authors' Contributions:

RSR was responsible for conception and design, obtaining funds, data interpretation, manuscript drafting and manuscript editing, and final approval data acquisition, data interpretation and critical revision for important intellectual content conception and design, obtaining funds, data interpretation, manuscript editing, and final approval. MDI was responsible for data analysis and statistical analysis. AR and MDI were responsible manuscript writing and editing RSR and SSJ were responsible for data collection. All authors have read and approved the final version of the manuscript.

Acknowledgments:

The authors were grateful to the staffs and management of the Department of Hepatology and Medicine in Sir Salimullah Medical College Mitford Hospital, Bangladesh.

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