Introduction and Objectives: Connective Tissue Growth Factor (CTFG) is a multifunctional protein, plays a crucial role as a mediator in fibrogenic pathways involved in the development of liver disease. Objective: To establish the correlation between the cut-off point of serum CTGF values by ELISA and the degree of liver fibrosis determined by transitional elastography in patients with cholestasis diagnosed with primary biliary cholangitis (PBC).

Materials and Methods: Prolective, descriptive and analytical study, which included patients with cholestasis, with cirrhosis due to hepatitis C and a control group. Serum CTGF levels were quantified in blood. The degree of fibrosis was determined by transitional elastography. The AUROC was calculated and the cut-off point was obtained with the Youden index to obtain sensitivity and specificity, between CT vs HCV-F4, CT vs CBP-F0, CT vs CBP-F4 and HCV-F4 vs CBP-F4.

Results: 51 patients with PBC, 15 HCV and 18 controls were included, Age 48±15 years, 75% female.The AUROC for HCV-F4 vs TC was .856 (.718-.994, CI95%) p<.001, cutoff 592.9, S=66.7%, E=94.4% for TC vs PBC-F0 was AUROC=.974 (.929-1.0,CI95%) p<.001, cutoff=596.18, S=93.3%, E=94. 4%, for TC vs PBC-F4 was AUROC=.997 (.989-1.0, CI95%), p<.001, S=100, E=94.4%, for HCV-F4 vs PBC-F0 was AUROC=.857 (.769-.956, CI95%), p<. 001, cut-off=1284.7, S=69.4%, E=93.3% and for HCV-F4 vs PBC-F4 was AUROC= .738 (.557-.918,IC95%), p=.026, cutoff=1288.6, S=53.3%, E= 93.3%.

Conclusions: There is a direct relationship between serum levels of GFRT of patients with cholestasis and specific cut-off points of discrimination for the different groups.

Conflict of interest: None

https://doi.org/10.1016/j.aohep.2025.101988

#22

EVALUATION OF RESPONSE TO SECOND LINE THERAPY IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS AND INADEQUATE RESPONSE TO UDCA: A PILOT STUDY OF LIVER BIOPSIES FOLLOW UP

Alejandra Villamil[1], Daniela de la Viña[1], Eduardo Mullen[1], Ignacio Lucero[1], Juan Carlos Bandi[1]

[1] *Hospital Italiano de Buenos Aires, Argentina.*

Introduction and Objectives: Response to second line therapy is improvement of cholestatic parameters and prevention of fibrosis or liver events. AIM: to evaluate response at Month 12 and identify epidemiological, clinical and histological findings related to response.

Patients and Methods: 50 patients initiating OCA (n=12), PPAR agonists (n=29) or combination of both (n=9) completed 12 months treatment and had baseline and M12 biopsy. Duct loss was evaluated with cytokeratin 7 and 19 and Scheuer staging applied. Biliary interface activity and bile duct damage recorded. Elastography was done at baseline and at 12 months. Statistical analysis using parametric t tests and 1-way ANOVA was performed.

Results: Mean age 53.6±10.6y and 84 % female. Mean ALP 388.8± 166.6, ALT 71.3±40.6 and BT 0.9±0.4. 10 patients were cirrhotic. Response to second line therapy was 30 % with POISE criteria (n=15) and 14 % for ALP normalization (n=7). Male sex (p.04), moderate/severe ductopenia (p.01), elevated ALT (82 vs 46, p.003), bilirubin (1.07 vs 0.7, p.02) and cirrhosis (p.02) correlated with no response. Moderate/severe portal inflammation with interface hepatitis and lobular spilling was observed in 28 samples, irrespective of age and correlated with fibrosis. No patient with severe inflammation achieved response (n=5), and only 21% with moderate inflammation (n=5). On FU biopsies, response related with improvement of inflammation in 11 patients. Mild ductopenia did not affect response. No LFT predicted cirrhosis or portal inflammation. Cirrhosis at month 12 correlated with liver events in 5 patients resulting in 1 liver related death and 3 transplants. Elastography correlated with cirrhosis and liver events (10.4 vs 22.9, p<0.001) but not with inflammation or ductopenia.

Conclusions: Non response (70 %) related to male sex, cirrhosis, transaminases, moderate/severe inflammation and ductopenia. Cirrhosis and elastography correlated with liver events. Adverse histological findings suggest early second line intervention.

Conflict of interest: None

https://doi.org/10.1016/j.aohep.2025.101989

#24

CORE MUTATIONS IN THE HBEAG-NEGATIVE STAGE ARE KEY DETERMINANTS OF HEPATITIS B VIRUS REPLICATION

Selene Leuzzi[1], Cecilia Garcia[1], Diego Flichman[1], Maria Mercedes Elizalde[1]

[1] *Universidad de Buenos Aires, Argentina.*

Introduction and Objectives: The natural history of chronic HBV infection is characterized by distinct stages resulting from virus-host interactions. In this context, a late and pivotal event is HBeAg seroconversion, marked by the abrogation of HBeAg expression, a significant reduction in viral load, and the accumulation of mutations throughout the genome. While HBeAg abrogation is associated with mutations in the BCP and preCore regions, these mutations do not, per se, account for the observed reduction in viral load. Our aim was to unravel, at the molecular level, the drivers involved in the HBV replication rate.

Materials and Methods: Full-lenght HBV genome obtained from plasma samples of one HBeAg-positive patient and three HBeAg-negative patients was extracted, amplified and cloned. The replicative capacity and HBsAg antigen expresion of these clones and the chimeras obtained through core gene exchanges was evaluated in vitro.

Results: The incorporation of the wild-type (WT) core protein into HBeAg-negative genomes restored all viral replication intermediates (cccDNA, pgRNA, rcDNA, and capsid-associated DNA) to levels comparable to those of the WT virus and vice versa (Figure 1). Furthermore, a regulatory role of mutations in the core protein was observed in the modulation of HBsAg expression and secretion (Figure 2).

Conclusions: HBV viral load is a critical factor in the progression of chronic hepatitis B and its associated adverse outcomes. Mutations identified subsequent to HBeAg seroconversion are frequently found within the core region, and these mutations demonstrate a strong association with both HBV-DNA replication capacity and HBsAg expression levels.

Conflict of interest: None

Figure 1

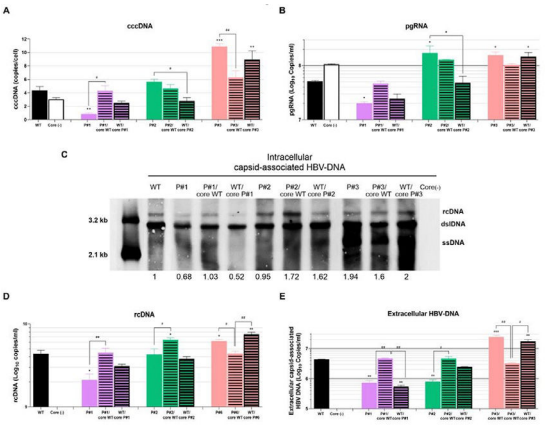

Figure 1: Replicative capacity of the chimeric HBV constructs. Huh-7 cells were transfected with linear full-length HBV genomes from WT, core-deficient (Core (-)), HBeAg-negative clones (P#1, P#2, P#3), and their respective chimeras (P#1/core WT, WT/core P#1, P#2/core WT, WT/core P#2, P#3/core WT, and WT/core P#3). Cells and supernatants were collected 3 days post-transfection. (A) Total DNA was extracted, treated with T5 exonuclease to remove nonsupercoiled dsDNA, and cccDNA levels were assessed by qPCR. Results were normalized to mitochondrial DNA. (B) Total RNA was extracted, and pgRNA levels were analyzed by RT-qPCR. (C) Intracellular capsid-associated HBV DNA was extracted, and replicative intermediates were assessed by Southern blot. The relative amount of ssDNA in relation to WT is shown below the image. (D) Total HBV DNA was quantified by qPCR and rcDNA levels were calculated by subtracting cccDNA from total HBV DNA. (E) Extracellular capsid-associated HBV DNA was quantified by qPCR. Shown values represent the mean ± standard deviation of three independent experiments. *: significant difference compared to WT; #: significant differences among chimeric constructs. Three symbols: p < 0.0001; two symbols: p < 0.005 and one symbol: p < 0.05. cccDNA: covalently closed circular DNA; rcDNA: HBV relaxed circular DNA; dslDNA: HBV double-stranded linear DNA; ssDNA: HBV single-stranded DNA; pgRNA: pregenomic RNA

Figure 2

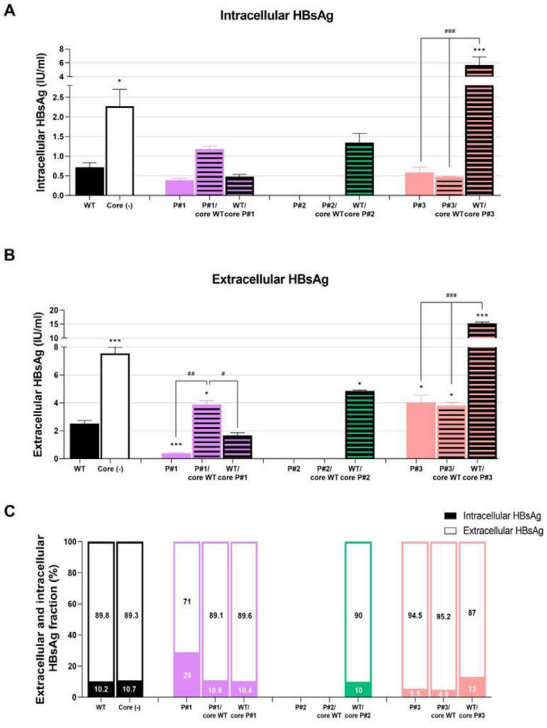

Figure 2: Intracellular and secreted HBsAg levels in chimeric HBV constructs. Huh-7 cells were transfected with linear full-length HBV genomes from WT, core-deficient (Core (-)), HBeAg-negative clones (P#1, P#2, P#3), and their respective chimeras (P#1/core WT, WT/core P#1, P#2/core WT, WT/core P#2, P#3/core WT, and WT/core P#3). Cells and supernatants were collected 3 days post-transfection. (A) Intracellular and (B) extracellular HBsAg levels were quantified using electrochemiluminescence immunoassay (ECLIA). (C) Extracellular/intracellular HBsAg ratio. Values shown represent the mean ± standard deviation of three independent experiments. *: significant difference compared to WT; #: significant differences among chimeric constructs. Three symbols: p < 0.0001; two symbols: p < 0.005 and one symbol: p < 0.05.

https://doi.org/10.1016/j.aohep.2025.101990

#26

METABOLIC ASSOCIATED STEATOTIC LIVER DISEASE-RELATED SIGNIFICANT AND ADVANCED FIBROSIS' PREVALENCE IN BRAZIL AND THE ASSOCIATED ACCURACY OF FIB-4 AND VIBRATION-CONTROLLED ELASTOGRAPHY - A NATIONAL REGISTER

Cristiane Alves Villela-Nogueira[1], Cristiane Valle Tovo[2], Nathalie Carvalho Leite[3], Mário Reis Álvares-da-Silva[4], Claudia Alexandra Ivantes[5], Claudia Alves Couto[6], Giovanni Faria Silva[7], Edson Roberto Parise[8], Ana Carolina Cardoso[3], Natalia Ballassiano Wajsbrot[3], Luis Fernando Ferreira[2], Muriel Manica[2], Gabriela Perdomo Coral[2], Matheus Michalczuk[4], Rafael Biesek Novaes[9], Brian Vinícius Batista Pinheiro[9], Rosangela Réa[9], Luciana Costa Faria[6], Fernando Gomes Romeiro[7], Leila Priscilla Pinheiro da Silva[7], Roberto Carvalho Filho[8], Marcelo Chagas[10], Mariana Sharp[10], Luiza Soares Dantas[10], José Tadeu Stefano[11], Isabel Veloso Pereira[11], Patricia Momoyo Zitelli[11], Mário Guimarães Pessoa[11], Carlos Terra[10], Claudia P.M.S. Oliveira[12]

[1] *Faculdade de Medicina. Serviço de Hepatologia. Universidade Federal do Rio de Janeiro, Brasil.*
[2] *Universidade Federal de Ciências da Saúde de Porto Alegre, Brasil.*
[3] *Serviço de Hepatologia. Hospital Universitário Clementino Fraga Filho. Universidade Federal do Rio de Janeiro, Brasil.*
[4] *Faculdade de Medicina. Universidade Federal do Rio Grande do Sul, Brasil.*
[5] *Faculdade de Medicina. Universidade Federal do Paraná, Brasil.*
[6] *Faculdade de Medicina. Universidade Federal de Minas Gerais, Brasil.*
[7] *Faculdade de Medicina de Botucatu. UNESP, Brasil.*
[8] *Universidade Federal de São Paulo, Brasil.*
[9] *Departamento de Clínica Médica. Universidade Federal do Paraná, Brasil.*
[10] *Serviço de Gastroenterologia. Universidade do Estado do Rio de Janeiro, Brasil.*
[11] *Hospital das Clínicas da Faculdade de Medicina. Universidade de São Paulo, Brasil.*
[12] *Departamento de Gastroenterologia. Universidade de São Paulo, Brasil.*

Introduction and Objectives: Recent data regarding the prevalence of significant and advanced MASLD-related fibrosis in Brazil is unknown. We aimed to evaluate the prevalence of significant (SF, F≥2) and advanced (AF, F≥F3) fibrosis according to its different geographic regions, and the accuracy of FIB-4 and liver elastography by VCTE (Fibroscan, Echosens, Fr) for the diagnosis of SF and AF respectively.

Patients and Methods: This was a sectional study in ten Brazilian University Centers (Southeast, n=6; Northeast, n=1; South, n=3). Demographic, clinic, laboratory, liver stiffness measurement by VCTE (Fibroscan®, Echosens, Fr), and liver biopsy (LB) results were registered. The AUROCs for FIB-4 and VCTE regarding SF and AF were plotted with LB as a reference.

Results: 2905 patients were included (53% women, 64% white, 51 ± 14 yrs, 44% T2DM) According to LB (n=2122), most form the South