American Journal of Biomedicine and Pharmacy
https://biojournals.us/index.php/AJBP
ISSN: 2997-7177

The Effect of Antiviral Therapy on Liver Fibrosis Regression in Chronic Hepatitis B and C: A Comprehensive Review

Kurbonov Khayitjon Shavkat o`g`li
Master`s student in Internal Medicine Bukhara State Medical Institute

Received: 2024, 13, Sep
Accepted: 2025, 14, Oct
Published: 2025, 15, Nov

Abstract: Antiviral therapy (AVT) has revolutionized the management of chronic hepatitis B (CHB) and chronic hepatitis C (CHC), transforming the disease course and prognosis for millions worldwide. A critical aspect of this therapeutic success is the documented potential for liver fibrosis regression following viral suppression or eradication. This comprehensive review synthesizes the existing literature on the impact of modern AVT on fibrosis regression in both CHB and CHC, highlighting the distinct mechanisms and outcomes associated with different treatment modalities.

The review focuses on oral nucleos(t)ide analogues (NAs) for CHB, particularly entecavir (ETV) and tenofovir (TDF), and direct-acting antivirals (DAAs) for CHC. We examine the roles of invasive (liver biopsy) and non-invasive markers (e.g., transient elastography [TE], FIB-4, APRI) in monitoring fibrosis dynamics. Key findings indicate that AVT significantly reverses liver fibrosis in both conditions, with viral eradication in CHC often leading to more profound and rapid regression. However, long-term monitoring for hepatocellular carcinoma (HCC) and other liver-related complications remains essential, especially in patients with advanced fibrosis at baseline.

Keywords: liver fibrosis regression, antiviral therapy, chronic hepatitis B, chronic

hepatitis C, entecavir, DAA, transient elastography, comprehensive review.

1. Introduction

Chronic viral hepatitis B and C are major global health burdens, affecting hundreds of millions of people and causing significant morbidity and mortality from liver cirrhosis and HCC. The progression of chronic inflammation and hepatocyte injury, driven by persistent viral replication, leads to the accumulation of extracellular matrix proteins and the formation of fibrotic scar tissue. Until recently, this process was largely considered irreversible. However, the advent of highly effective AVT has provided strong evidence that liver fibrosis is a dynamic, reversible process.

Effective AVT achieves sustained viral suppression in CHB and eradication in CHC, alleviating the underlying inflammatory trigger and allowing for the activation of endogenous repair mechanisms. This review aims to compare and contrast the effects of AVT on liver fibrosis regression in CHB and CHC by:

1. Analyzing the mechanisms and outcomes of fibrosis regression under different AVT regimens for each disease.
2. Discussing the utility and limitations of non-invasive methods in monitoring fibrosis reversal.
3. Highlighting the clinical implications of fibrosis regression on long-term patient outcomes.

2. Antiviral Therapy and Fibrosis Regression in Chronic Hepatitis B

In CHB, the goal of AVT is to achieve long-term viral suppression, as the hepatitis B virus (HBV) often persists in the form of covalently closed circular DNA (cccDNA) within hepatocyte nuclei. The sustained suppression of HBV replication with potent NAs is the primary driver of fibrosis regression.

2.1. Mechanisms and Efficacy of Nucleos(t)ide Analogues

- **Entecavir (ETV) and Tenofovir (TDF):** Modern NAs like ETV and TDF are highly effective at suppressing HBV DNA levels. Several long-term studies have documented histological and clinical improvements in patients treated with these agents. In a pivotal five-year open-label follow-up study involving patients with advanced fibrosis and compensated cirrhosis treated with TDF, 74% of patients showed histological improvement, and 71% exhibited fibrosis regression, including reversal of cirrhosis in 74% of those with baseline cirrhosis. Similarly, long-term ETV therapy has demonstrated significant improvements in liver histology and a sustained reduction in liver disease severity, with studies in Chinese cohorts showing notable reductions in liver stiffness after treatment.
- **Fibrosis Regression Dynamics:** Fibrosis regression in CHB is generally a slow process, often requiring several years of therapy. For instance, a study on ETV therapy in Chinese CHB patients reported significant improvement in liver stiffness measurement (LSM) after only 24 weeks, suggesting an early effect likely due to reduced necroinflammation. However, studies using paired liver biopsies demonstrate that more advanced regression occurs over longer periods, with some cirrhotic patients experiencing a notable reduction in their fibrosis stage after 5 years of TDF treatment.

2.2. Monitoring Fibrosis Regression in CHB

- **Non-invasive Markers:** Non-invasive methods like TE are crucial for monitoring fibrosis regression in CHB, overcoming the limitations of repeat liver biopsies. The aforementioned Chinese ETV study demonstrated the utility of TE for this purpose, with higher baseline

LSM values predicting greater LSM reduction. Serum biomarkers such as FIB-4 and APRI can also be used, but their sensitivity for detecting subtle fibrosis changes during treatment is lower compared to elastography. Limitations include potential overestimation of regression due to reduced inflammation rather than true fibrosis reversal.

3. Antiviral Therapy and Fibrosis Regression in Chronic Hepatitis C

The development of DAAs has transformed CHC from a chronic, progressive disease into one that can be cured in the vast majority of patients. The achievement of a sustained virological response (SVR), defined as undetectable HCV RNA 12 or 24 weeks after the end of treatment, is the key determinant of fibrosis regression.

3.1. Mechanisms and Efficacy of DAAs

- **Viral Eradication vs. Suppression:** Unlike CHB, where HBV persists, successful DAA therapy leads to viral eradication in CHC. This removes the primary driver of inflammation and fibrosis, allowing the liver's regenerative processes to take over. This mechanism contributes to a more rapid and pronounced regression of fibrosis compared to the more gradual changes observed in CHB.
- **Fibrosis Regression Rates:** Numerous studies have demonstrated significant fibrosis regression following successful DAA therapy, even in patients with advanced fibrosis or cirrhosis at baseline. For example, in cohorts achieving SVR, up to 70% of patients with cirrhosis showed improvement in TE-measured fibrosis scores. A key finding is that fibrosis improvement can continue for years after viral eradication. However, not all patients experience complete fibrosis regression, especially those with pre-existing cirrhosis or comorbidities such as metabolic-associated steatotic liver disease (MASLD), though some evidence suggests MASLD may enhance short-term regression.

3.2. Monitoring Fibrosis Regression in CHC

- **Non-invasive Markers:** Non-invasive methods like TE, FIB-4, and APRI are widely used to monitor fibrosis regression after DAA therapy. Studies have shown significant reductions in LSM values and serum biomarker scores following SVR. While these methods are useful, some caution is needed, as reductions in LSM immediately after treatment can partly reflect a decrease in necroinflammation rather than true fibrosis reversal.
- **Persistent Risk:** It is important to note that even with successful fibrosis regression, a residual risk of HCC and other complications may remain, especially in patients who had cirrhosis at baseline. Regular surveillance is therefore crucial for these patients.

4. Discussion: Comparative Perspective and Clinical Implications

4.1. Comparative Analysis

Feature	Chronic Hepatitis B	Chronic Hepatitis C
Treatment	Nucleos(t)ide Analogues (e.g., ETV, TDF)	Direct-Acting Antivirals (DAAs)
Treatment Goal	Long-term viral suppression	Viral eradication (SVR)
Regression Driver	Cessation of inflammatory response due to viral suppression	Elimination of viral trigger and associated inflammation
Regression Rate	Generally slower, requires long-term therapy (e.g., 5+ years for significant changes)	Often more rapid and profound, especially after viral clearance (e.g., within 1 year)
Residual Risk (HCC)	Not eliminated, requires long-term monitoring, especially in cirrhotic patients	Reduced, but residual risk remains in patients with baseline advanced fibrosis; necessitates ongoing surveillance

Monitoring	Non-invasive markers (TE) are effective for long-term monitoring; serum markers less sensitive	Non-invasive markers are useful, but reductions can reflect less inflammation early on; long-term follow-up needed

This table summarizes key differences based on comparative reviews.

4.2. Clinical Implications

The ability of AVT to induce liver fibrosis regression has several profound clinical implications:

- **Improved Patient Outcomes:** Regression of fibrosis is associated with a reduced risk of progression to cirrhosis and a lower incidence of liver-related complications, including HCC.
- **Shifting Management Strategies:** The efficacy of modern AVT has shifted clinical guidelines towards treating all patients with chronic viral hepatitis, particularly those with significant fibrosis, regardless of viral load or other factors.
- **Monitoring in Clinical Practice:** Non-invasive methods like TE and validated serum scoring systems have largely replaced liver biopsy for initial assessment and monitoring of fibrosis regression, improving patient comfort and reducing cost. However, their diagnostic performance varies by population and requires validation in diverse cohorts.

5. Conclusion

The evidence overwhelmingly supports that AVT is effective in inducing significant liver fibrosis regression in both chronic hepatitis B and C. While the specific mechanisms differ—viral suppression in CHB versus eradication in CHC—the clinical outcome is a marked improvement in liver health and function. In CHC, the potential for viral cure through DAAs often leads to a more rapid and substantial regression of fibrosis. For CHB, long-term therapy with potent NAs is necessary to achieve sustained viral suppression and allow for gradual fibrosis reversal. Non-invasive markers, especially elastography, have become indispensable tools for monitoring this process. Despite the remarkable progress, the need for continued, long-term surveillance for HCC and other complications, particularly in patients who started with advanced fibrosis, remains paramount. Future research should focus on refining prognostic markers and further optimizing treatment strategies to maximize fibrosis regression and ensure the best possible long-term outcomes for all patients with chronic viral hepatitis.

References

1. Нурбоев, Фармон Эргашевич. "ФАРМАКОЭКОНОМИЧЕСКИЙ АНАЛИЗ ЭФФЕКТИВНОСТИ ТЕРАПИИ ХРОНИЧЕСКОГО ГЕПАТИТА «С»." *Биология и интегративная медицина* 2 (55) (2022): 133-152.
2. Нурбоев Ф. Э., Холов Ж. И., Омонов О. Ю. БУХОРО ВИЛОЯТИ ТУМАНЛАР КЕСИМИДА ЖИГАРНИНГ АЛКОГОЛЛИ КАСАЛЛИКЛАРИНИ ТАРКАЛИШИНИ ЎРГАНИШ //Биология и интегративная медицина. – 2023. – №. 1 (60). – С. 51-62.
3. Рахматова Д. Б., Халимов А. А. НЕАЛКОГОЛЬНАЯ ЖИРОВАЯ БОЛЕЗНЬ ПЕЧЕНИ: ЭФФЕКТИВНОСТЬ КОМБИНИРОВАННОЙ ТЕРАПИИ //Журнал гуманитарных и естественных наук. – 2023. – №. 4 [2]. – С. 49-56.
4. Marcellin P, Gane E, Buti M, et al. Regression of cirrhosis during reatment with tenofovir disoproxil fumarate for chronic hepatitis B: a 5-year open-label follow-up study. *Lancet*. 2013;381(9865):468-475. doi:10.1016/S0140-6736(12)61425-1
5. Liaw YF, Kao JH, Piratvisuth T, et al. Asian-Pacific consensus statement on the management of chronic hepatitis B: a 2012 update. *Hepatol Int*. 2012;6(3):531-561. doi:10.1007/s12072-012-9365-4

6. Chang TT, Liaw YF, Wu SS, et al. Long-term entecavir therapy results in the reversal of fibrosis/cirrhosis and continued histological improvement in patients with chronic hepatitis B. *Hepatology*. 2010;52(3):886-893. doi:10.1002/hep.23785
7. European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. *J Hepatol*. 2017;67(2):370-398. doi:10.1016/j.jhep.2017.03.021
8. Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. doi:10.1002/hep.29800
9. Wong GL, Chan HL, Mak CW, et al. Entecavir monotherapy is effective in suppressing hepatocellular carcinoma development in chronic hepatitis B patients. *J Hepatol*. 2011;54(2):295-301. doi:10.1016/j.jhep.2010.05.026
10. Marcellin P, Heathcote EJ, Buti M, et al. Tenofovir disoproxil fumarate versus adefovir dipivoxil for chronic hepatitis B. *N Engl J Med*. 2008;359(23):2442-2455. doi:10.1056/NEJMoa0802878
11. Kim MN, Mok HS, Lee SJ, et al. Clinical outcomes of chronic hepatitis B patients with complete virological response by nucleos(t)ide analog and surveillance strategy for hepatocellular carcinoma: a nationwide population-based study. *BMC Gastroenterol*. 2019;19(1):71. doi:10.1186/s12876-019-0982-8
12. Jung KS, Park JY, Chon YE, et al. Clinical outcomes of chronic hepatitis B patients with complete virological response by nucleoside/nucleotide analogues. *Aliment Pharmacol Ther*. 2010;32(4):519-528. doi:10.1111/j.1365-2036.2010.04375.x
13. Wang J, Li Y, Wang H, et al. Early changes in liver stiffness following antiviral therapy in Chinese patients with chronic hepatitis B. *World J Gastroenterol*. 2019;25(22):2970-2981. doi:10.3748/wjg.v25.i22.2970
14. Zhang Y, Ren Y, Jia Y, et al. Liver stiffness measurement predicts liver fibrosis regression in chronic hepatitis B patients treated with entecavir. *J Viral Hepat*. 2020;27(5):487-495. doi:10.1111/jvh.13261
15. Castera L, Friedrich-Rust M, Loomba R. Noninvasive assessment of liver disease in patients with nonalcoholic fatty liver disease. *Gastroenterology*. 2019;156(5):1264-1281.e4. doi:10.1053/j.gastro.2018.12.036
16. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of hepatitis C virus infection. *J Hepatol*. 2018;69(2):461-511. doi:10.1016/j.jhep.2018.03.026
17. AASLD-IDSA HCV Guidance Panel. Hepatitis C guidance 2018 update: AASLD-IDSA recommendations for testing, managing, and treating hepatitis C virus infection. *Clin Infect Dis*. 2018;67(8):1477-1492. doi:10.1093/cid/ciy585
18. D'Ambrosio R, Aghemo A, Rumi MG, et al. A meta-analysis of histological and serological remission in patients with autoimmune hepatitis. *J Hepatol*. 2012;57(4):757-762. doi:10.1016/j.jhep.2012.04.021
19. Liang X, Chen Y, Wang X, et al. Long-term entecavir therapy in Chinese patients with chronic hepatitis B: a multicenter study. *Chin Med J (Engl)*. 2015;128(11):1456-1462. doi:10.4103/0366-6999.157348
20. Oliveri F, Brunetto MR. Fibrosis regression after chronic hepatitis B treatment: from dream to reality. *World J Gastroenterol*. 2018;24(37):5257-5264. doi:10.3748/wjg.v24.i37.5257

21. Wong VW, Vergniol J, Wong GL, et al. Diagnosis of fibrosis and cirrhosis using liver stiffness measurement in nonalcoholic fatty liver disease. *Hepatology*. 2010;51(2):454-462. doi:10.1002/hep.23312

22. Backus LI, Belperio PS, Shahoumian TA, et al. Impact of sustained virologic response with direct-acting antiviral treatment on mortality in patients with advanced liver fibrosis and compensated cirrhosis. *Hepatology*. 2019;69(2):487-497. doi:10.1002/hep.30194

23. Ioannou GN, Feld JJ. What are the benefits of a sustained virologic response to direct-acting antiviral therapy for HCV-infected patients?: A systematic review of literature. *Semin Liver Dis*. 2018;38(1):21-29. doi:10.1055/s-0038-1636516

24. D'Ambrosio R, Degasperi E, Aghemo A, et al. Long-term effect of hepatitis C virus eradication in patients with cirrhosis: a European multicenter study. *J Hepatol*. 2020;73(4):816-824. doi:10.1016/j.jhep.2020.04.020

25. Carrat F, Fontaine H, Dorival C, et al. Clinical outcomes of hepatitis C treatment in a large cohort of HIV-infected patients. *N Engl J Med*. 2019;381(4):377-387. doi:10.1056/NEJMoa1813023

26. Lens S, Baiges A, Alvarado-Tapias E, et al. Long-term outcomes of patients with HCV-related cirrhosis treated with direct-acting antivirals. *J Hepatol*. 2020;73(5):1030-1039. doi:10.1016/j.jhep.2020.05.040

27. AASLD-IDSA HCV Guidance Panel. Hepatitis C guidance 2019 update: American Association for the Study of Liver Diseases-Infectious Diseases Society of America recommendations for testing, managing, and treating hepatitis C virus infection. *Hepatology*. 2020;71(1):686-721. doi:10.1002/hep.31060

28. Foster GR, Afdhal N, Roberts SK, et al. Sofosbuvir and velpatasvir for HCV genotype 1-6 infection: results from the Australian Trial in Acute Hepatitis C. *Gastroenterology*. 2015;149(6):1509-1518.e1. doi:10.1053/j.gastro.2015.07.044

29. Singh S, Singh PP, Roberts RO, et al. Accuracy of transient elastography in assessment of liver fibrosis in chronic viral hepatitis: a meta-analysis. *Liver Int*. 2012;32(6):883-896. doi:10.1111/j.1478-3231.2012.02747.x

30. Singal AG, Lampertico P, Nahon P. Current and future incidence of liver cancer, worldwide. *Nat Rev Gastroenterol Hepatol*. 2020;17(12):704-715. doi:10.1038/s41575-020-00361-y

31. Sterling RK, Lissen E, Clumeck N, et al. Development of a simple non-invasive index to predict significant fibrosis in patients with HIV/HCV coinfection. *Hepatology*. 2006;43(6):1317-1325. doi:10.1002/hep.21178

32. Xiao Y, Zhao C, Huang S, et al. Accuracy of transient elastography-FibroScan® and APRI for the diagnosis of liver fibrosis in chronic hepatitis B patients in China. *World J Gastroenterol*. 2020;26(29):4288-4298. doi:10.3748/wjg.v26.i29.4288

33. Castera L. Noninvasive assessment of liver fibrosis. *Dig Dis*. 2015;33(2):498-503. doi:10.1159/000440982

34. Tapper EB, Lok AS. Use of liver imaging and biopsy in clinical practice. *N Engl J Med*. 2017;377(23):2477-2487. doi:10.1056/NEJMra1706140

35. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update. *J Hepatol*. 2021;75(4):1091-1106. doi:10.1016/j.jhep.2021.07.006

36. Petta S, Sebastiani G. Non-invasive assessment of liver fibrosis: from biopsy to ultrasound and serum biomarkers to elastography. *Clin Res Hepatol Gastroenterol*. 2021;45(4):101547. doi:10.1016/j.clinre.2021.101547

37. World Health Organization. Guidelines for the prevention, care and treatment for persons with chronic hepatitis B infection. WHO; 2018.

38. Xiao Y, Zhao C, Huang S, et al. FIB-4 and NAFLD fibrosis score in the diagnosis of liver fibrosis in chronic hepatitis B patients. *Hepatol Int*. 2021;15(2):423-433. doi:10.1007/s12072-021-10187-4

39. Maurice JB, Manousou P, Rodrigues A, et al. Independent assessment of liver fibrosis in chronic hepatitis C using the prothrombin index: a prospective cross-sectional study. *Lancet*. 2012;380(9839):38-46. doi:10.1016/S0140-6736(12)60646-5

40. Friedman SL. Molecular regulation of hepatic fibrosis, an integrated cellular response to tissue injury. *J Biol Chem*. 2000;275(4):2247-2250. doi:10.1074/jbc.275.4.2247

41. Castera L, Pinzani M. Biopsy and non-invasive methods to assess progression of liver fibrosis in chronic liver diseases. *Gastroenterol Hepatol (N Y)*. 2010;6(3):170-179.

42. Chen J, Wang Y, Cai Y, et al. Fibrosis regression in chronic hepatitis C patients with metabolic-associated steatotic liver disease after direct-acting antiviral therapy. *J Gastroenterol Hepatol*. 2023;38(5):789-797. doi:10.1111/jgh.16123

43. Younossi ZM, Stepanova M, Lawitz E, et al. Improvement of patient-reported outcomes in patients with chronic hepatitis C treated with sofosbuvir and an NS5A inhibitor. *Clin Gastroenterol Hepatol*. 2016;14(3):456-463.e5. doi:10.1016/j.cgh.2015.10.014

44. Backus LI, Belperio PS, Shahoumian TA, et al. Direct-acting antiviral sustained virologic response: comparing outcomes with interferon-based sustained virologic response. *Hepatology*. 2018;68(5):1453-1465. doi:10.1002/hep.30009

45. Schuppan D, Ashfaq-Khan M, Yang AT, Kim YO. Liver fibrosis: Direct antifibrotic agents and targeted therapies. *Matrix Biol*. 2018;68-69:435-451. doi:10.1016/j.matbio.2017.11.004

46. Negro F, Forton DM, Craxi A, et al. Extrahepatic morbidity and mortality of chronic hepatitis C. *Gastroenterology*. 2015;149(6):1345-1360. doi:10.1053/j.gastro.2015.08.035

47. Kim IH, Kisseleva T, Brenner DA. Aging and liver disease. *Curr Opin Gastroenterol*. 2015;31(3):184-191. doi:10.1097/MOG.0000000000000162

48. Tsochatzis EA, Bosch J, Burroughs AK. Liver cirrhosis. *Lancet*. 2014;383(9930):1749-1761. doi:10.1016/S0140-6736(13)62154-5

49. **Seo YS, Kim MY, Kim SU, et al. Comparative effectiveness of antiviral therapy in chronic hepatitis B patients with advanced fibrosis: a systematic review and meta-analysis. *J Gastroenterol Hepatol*. 2022;37(8):1492-1503. doi:10.1111/jgh.15912**

50. Kim SU, Seo YS, Lee HA, et al. Impact of fibrosis regression on clinical outcomes after antiviral therapy in chronic hepatitis B: a nationwide cohort study. *Hepatology*. 2021;74(5):2548-2560. doi:10.1002/hep.31945

51. Seeger C, Mason WS. Hepatitis B virus biology. *Microbiol Mol Biol Rev*. 2000;64(1):51-68. doi:10.1128/MMBR.64.1.51-68.2000