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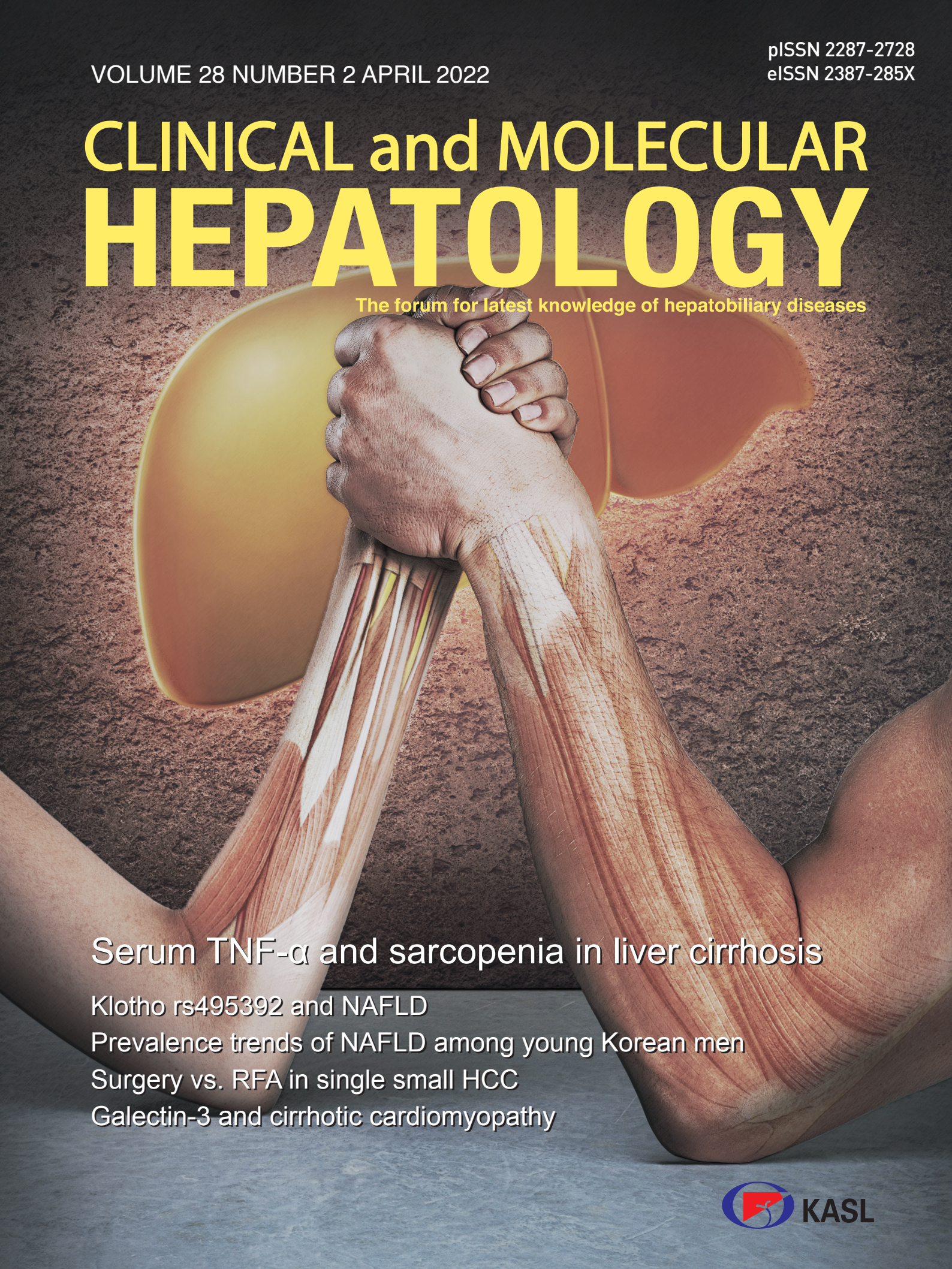

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Editorial

Dyslipidemia in chronic hepatitis B patients on tenofovir alafenamide: Facts and puzzles

Hung-Yao Lin[1] and Tai-Chung Tseng[1,2,3]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Taiwan University Hospital, Taipei; [2]Hepatitis Research Center, National Taiwan University Hospital, Taipei; [3]Department of Medical Research, National Taiwan University Hospital, Taipei, Taiwan

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Most chronic hepatitis B (CHB) patients need to stay in indefinite nucleos(t)ide analogue (NA) treatment to reduce hepatitis B virus (HBV)-related complications as HBV could only be contained but not cured by NA.[1] Tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide (TAF) are two potent NAs and TAF is favored over TDF due to less renal and bone toxicities.[2] However, deterioration of lipid profile has been shown after switching from TDF- to TAF-containing antiretroviral regimens in human immunodeficiency virus (HIV) infected patients in both clinical trials and real-world data.[3,4] Since dyslipidemia is associated with cardiovascular disease and metabolic/non-alcoholic associated fatty liver disease, and the latter could increase hepatocellular carcinoma risks, it should be clarified whether TAF therapy alone deteriorates lipid profile in CHB patients.

In this study, Jeong et al.[5] applied propensity score-matching to compare the changes of lipid profile among CHB patients receiving TAF or TDF, inactive CHB, and non-HBV infected control groups in a follow-up period of 48 weeks. The results showed a significant decrease of serum total cholesterol (TC) level in the TDF group when compared with TAF (156.7±27.7 vs. 176.3±32.9, $P<0.001$) and non-HBV infected (156.2±28.3 vs. 175.0±29.5, $P<0.001$) group. In contrast, comparable lipid profiles were identified among TAF group, inactive CHB, and non-HBV infected control groups. The authors concluded that TAF is a lipid-neutral agent as the alterations of lipid profile were comparable between TAF and control groups. In contrast, TDF is potentially associated with lipid-lowering effect.

Jeong et al.[5] further postulated that the higher circulating tenofovir concentration in TDF users than that in TAF users might explain the results. Their theory was supported by another paper from Canada in which lower lipids were observed in TDF group when compared with the entecavir group in CHB patients.[6] However, the underlying mechanism remains unclear.

Although this study shows that TAF may be lipid-neutral in CHB patients without dyslipidemia, several issues need to be addressed. First, the effect of TAF on CHB patients with dyslipidemia remains unknown as they were excluded in this study. In a retro-

Abbreviations:

CHB, chronic hepatitis B; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HIV, human immunodeficiency virus; NA, nucleos(t)ide analogue; TAF, tenofovir alafenamide; TC, total cholesterol; TDF, tenofovir disoproxil fumarate

Editor: Chang Wook Kim, The Catholic University of Korea College of Medicine, Korea

Corresponding author : Tai-Chung Tseng
Department of Medical Research, National Taiwan University Hospital, 1 Chang-Te St., Taipei 10002, Taiwan
Tel: +886-2-23123456 ext. 66144, Fax: +886-2-23825962
E-mail: tctsenghbv@gmail.com
https://orcid.org/0000-0003-0420-8311

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spective, observational, multicenter study targeting HIV patients, no significant increment of TC level was found in TAF group if the patient had underlying hyperlipidemia.[7] More studies are needed to address the issue. Nevertheless, physicians should keep a close eye on patients with lipid levels near the upper limit of normal when switching from TDF to TAF. Second, even if switching from TDF to TAF causes more patients developing dyslipidemia, there are multiple potent lipid-lowering agents available. The benefit of lipid-lowering effect of TDF should not outweigh the risks of well-documented bone and kidney adverse events.

In summary, this well-designed study indicates that TAF itself could be a lipid-neutral rather than a lipid-increasing agent. Physicians should monitor the lipid profile more closely in their patients when switching their TDF with TAF. Future studies with longer follow-up periods and broader patient inclusion criteria to explore cardiovascular outcomes, together with the findings of this research, may impact the way CHB patients are managed.

Authors' contribution

Conception: TC Tseng; Drafting of the manuscript: HY Lin; Critical review of the manuscript: HY Lin and TC Tseng

Conflicts of Interest

Hung-Yao Lin declares no conflict of interest. Tai-Chung Tseng has served on speaker's bureaus for Fujirebio, Bristol-Myers Squibb, and Gilead Sciences and received grant support from Gilead Sciences.

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