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Nonalcoholic Fatty Liver Disease in Human Immunodeficiency Virus : The (Not So) New Kid on the Block? Reply

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2020-07-01

Yki-Järvinen , H , Lallukka-Bruck , S & Sutinen , J 2020 , ' Nonalcoholic Fatty Liver Disease
in Human Immunodeficiency Virus : The (Not So) New Kid on the Block? Reply ' , Clinical
Infectious Diseases , vol. 71 , no. 1 , pp. 245-245 . <https://doi.org/10.1093/cid/ciz930>

<http://hdl.handle.net/10138/332689>

<https://doi.org/10.1093/cid/ciz930>

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Reply to Krahn and Sebastiani

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Dear Editor,

We thank Drs Krahn and Sebastiani for their valuable thoughts regarding the rate of progression of non-alcoholic fatty liver disease (NAFLD) to advanced fibrosis in HIV-infected patients. The authors wonder whether progression of NAFLD is as rare as we suggest. As described above, in our study, liver fat content remained unchanged when measured by state-of-the-art proton magnetic resonance spectroscopy (^1H -MRS) during 16 years of follow-up in 41 HIV-positive (HIV+) subjects and 28 healthy control subjects [1]. Liver fibrosis was estimated by measuring liver stiffness using state-of-the-art magnetic resonance elastography (MRE) as well as the less accurate technique of transient elastography (TE) at the time of follow-up but not at baseline [2]. There were no significant differences in liver stiffness measured by TE between the HIV+ and healthy subjects at follow-up and no differences in stiffness measured by MRE between HIV+ patients with lipodystrophy compared to those without lipodystrophy. However, as pointed out by Krahn and Sebastiani, including the individual patient who died of liver cirrhosis, 4/42 (9.52%) of the HIV+ patients had clinically significant fibrosis at follow-up. A maximum incidence rate of significant fibrosis can be calculated by assuming that no patient had advanced fibrosis at baseline. This rate would be approximately 0.6 cases of advanced fibrosis/100 person years. The question is how does this maximum rate compare to other studies in HIV+ subjects and to non-HIV subjects? The studies in HIV+ subjects are listed in the above Table 1. None of the studies included healthy control subjects and it is thus difficult to judge the clinical significance of the reported incidences. Furthermore, the studies did not address the incidence of advanced fibrosis since the cut-off for fibrosis using TE was 7.1 kPa in the Canadian [3] and 7.2 kPa in the Spanish [4] studies. The recently recommended cut-off for advanced fibrosis is 9.7 kPa [5] i.e. even higher than was considered appropriate at the time of our study (8.7 kPa). In one of the studies, no imaging

studies were performed [3]. Regarding progression of fibrosis in non-HIV subjects, longitudinal data have been surprisingly sparse and based on very few subjects. In a meta-analysis of paired biopsy studies, 5 of 81 patients (6.2%) with initial non-alcoholic fatty liver progressed to bridging fibrosis over 9.3 years (incidence approximately 0.7 cases/100 person years) [6]. Taken together all currently available studies including our own have weaknesses, which make it difficult to conclude as to whether HIV+ patients are at higher risk of liver fibrosis than HIV-negative subjects. However, it is clear that features of the insulin resistance, such as increased liver fat content, waist circumference, and waist-to-hip ratio, which are particularly prevalent in HIV+ patients with lipodystrophy or obesity, predict NAFLD-fibrosis similarly in HIV+ and HIV-negative subjects [1]. This implies that it is as essential to pay attention to risk factors of advanced liver fibrosis and type 2 diabetes in HIV+ subjects as it is in obese subjects and those with the metabolic/insulin resistance syndrome.

All authors have no potential conflicts to disclose.

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