To the Editor:
We thank Drs. Toyoda and Kumada for raising the additional point that HCV amino acid substitutions have also been demonstrated to influence steatosis in the setting of HCV infection. In their study of 122 patients, 85 of whom had a beneficial IL28B genotype, Toyoda and Kumada found a trend for steatosis to be associated with IL28B polymorphism, as only 22% of the patients with beneficial genotype have steatosis compared to 40% of patients with the less beneficial genotype. Thus, their r, though not significant, is in line with our study, where we likewise found a 25% and 27% higher rate of steatosis in patients with the less beneficial IL28B ("non-C/C" for rs12979860 or "non-T/T" for rs8999017) genotype in two different cohorts of 145 and 180 patients, respectively. Similar to our and Toyoda and Kumada’s results, Cai et al. found an association between the beneficial IL28B genotype and lower steatosis frequency [1]. However, a three center study by Trépo et al. failed to find a relevant association between IL28B genotype and steatosis, according to their statement [2]. This latter paper, however, did not show the data, and therefore it cannot be assessed whether the association was absent or only not significant. Toyoda and Kumada’s study showed a similar trend for steatosis with IL28B, whereby IL28B is associated with different mutations in the core region, the HCV core mutation clearly shows a higher association with steatosis. In our article, we indicate that response to treatment in relation to steatosis seems unlikely to be explained by IL28B alone, and though not specifically mentioned, IL28B is likely not solely responsible for the association with steatosis. We had a small cohort of 54 non-genotype 1 patients of whom 19 were genotype 3 and 35 were genotype 2. Despite the fact that steatosis tended to be higher in “non-C/C” patients (4/20 [20%] vs. 7/15 [46%] in genotype 2 patients and 4/8 [50%] vs. 7/11 [63%] in genotype 3 patients; Table 1) this was not significant. However, the trend was similar across genotypes. Furthermore, we have data on genotype 1a and 1b in 60 and 75 patients from the fibrosis study, respectively. In concordance with the overall results, steatosis was less frequently present in C/C genotype patients with both HCV genotype 1a and 1b (Table 1).

A possible explanation lies in the virus itself as the authors correctly point out with a focus on HCV’s core protein. Unfortunately, we do not have the core antigen sequence of our patients. A previous work by Jhaeveri et al. suggested a role for amino acids 182 and 186 of the core protein, linking steatosis in vitro to steatosis [3], but certainly amino acid 70 seems to be especially relevant in genotype 1b infection. There is also some evidence indicating that not all differences can be explained by viral core sequence variation [4].

References

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