



RESPONSE TO COMMENT ON BRIL ET AL.

Clinical and Histologic Characterization of Nonalcoholic Steatohepatitis in African American Patients. *Diabetes Care* 2018;41:187–192

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We thank Pearlman et al. (1) for their interest in our article, which recommended screening for nonalcoholic steatohepatitis (NASH) in African American patients with nonalcoholic fatty liver disease (NAFLD), as steatohepatitis may occur in these patients as frequently as in Caucasian patients (2).

The authors mention a “recent large systematic review of 34 studies and over 350,000 subjects” where the risk of NASH in African Americans was lower than in Caucasians (relative risk 0.72 [95% CI 0.60–0.87]) (3). However, in a closer look, only 16,083 patients were part of the studies assessing the risk of NASH in patients with NAFLD (10 studies). Moreover, Pearlman et al. (1) missed that from this pool of studies, 8 out of the 10 included fewer African American patients than our study, ranging from 2 to 63 (median 25.5). In the review, the study by Younossi et al. (4) included 211 African American patients, but the authors did not perform liver biopsies and based the diagnosis of NASH on elevated alanine aminotransferase and aspartate aminotransferase levels. Finally, the study by Kallwitz et al. (5) included 92 African American patients and found a prevalence of NASH of 36% among African Americans with NAFLD, supporting the concept that NASH occurs with high frequency in this population. Based on these numbers, our study including 67 African American patients

is one of the largest studies assessing the risk of NASH in this population. Moreover, in none of the above studies were patients of different ethnic groups matched for important clinical characteristics (e.g., BMI, prevalence of diabetes, or hemoglobin A_{1c}) as in our study.

We agree with Pearlman et al. (1) that hepatic fibrosis is the most important predictor of liver-related mortality. In our study, we did not observe any difference in the degree of fibrosis between ethnic groups. This finding is consistent with results from smaller studies and even with the meta-analysis that the authors referenced (3). This reinforces the most important message of our study: that the risk of NASH and advanced fibrosis should not be underestimated in African American patients. As clear proof of this, NASH has become the second cause of cirrhosis in this ethnic group (6).

Pearlman et al. (1) also showed some concern that the separation of ethnic groups based on self-reporting may not reflect the presence of widespread genetic heterogeneity. While we largely agree with their statement, this is a general limitation of all studies comparing ethnic groups and not a limitation of our study in particular. Genome-wide association studies are likely to contribute to overcoming this problem in the near future by identifying specific genetic markers in each ethnic group. Finally, the

authors suggested that groups may not have been matched for PNPLA3 polymorphisms. Although this information was not previously reported, as only 61 patients had this genetic information available (19 African Americans and 42 Caucasians), we found no significant differences between ethnic groups in rs738409 (I148M variant; $P = 0.47$) or rs2281135 ($P = 0.78$).

In summary, our study provides significant evidence to support the notion that NASH also affects African American patients with NAFLD. Changing perceptions in medicine is always a challenge, but we hope that our work will modify the current paradigm that this population “is protected from NASH” and make health care providers aware not to underestimate their risk of liver disease.

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References

1. Pearlman BL, Hinds A, Dakaud A-EZ. Comment on Bril et al. Clinical and histologic characterization of nonalcoholic steatohepatitis in African American patients. *Diabetes Care*

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- 2018;41:187–192 (Letter). *Diabetes Care* 2018;41:e136
2. Bril F, Portillo-Sanchez P, Liu I-C, Kalavalapalli S, Dayton K, Cusi K. Clinical and histologic characterization of nonalcoholic steatohepatitis in African American patients. *Diabetes Care* 2018;41:187–192
 3. Rich NE, Oji S, Mufti AR, et al. Racial and ethnic disparities in nonalcoholic fatty liver disease prevalence, severity, and outcomes in the United States: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2018;16:198–210.e2
 4. Younossi ZM, Stepanova M, Negro F, et al. Nonalcoholic fatty liver disease in lean individuals in the United States. *Medicine (Baltimore)* 2012;91:319–327
 5. Kallwitz ER, Guzman G, TenCate V, et al. The histologic spectrum of liver disease in African-American, non-Hispanic white, and Hispanic obesity surgery patients. *Am J Gastroenterol* 2009;104:64–69
 6. Setiawan VW, Stram DO, Porcel J, Lu SC, Le Marchand L, Nouredin M. Prevalence of chronic liver disease and cirrhosis by underlying cause in understudied ethnic groups: the Multiethnic Cohort. *Hepatology* 2016;64:1969–1977