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Publication Date

2017-03-01

DOI

10.1016/j.atherosclerosis.2016.11.021

Peer reviewed

HHS Public Access

Author manuscript

Atherosclerosis. Author manuscript; available in PMC 2018 March 01.

Published in final edited form as:

Atherosclerosis. 2017 March ; 258: 89–96. doi:10.1016/j.atherosclerosis.2016.11.021.

Race/ethnic and sex disparities in the non-alcoholic fatty liver disease-abdominal aortic calcification association: The Multi-Ethnic Study of Atherosclerosis

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Abstract

Background and aims—This study investigated the associations of non-alcoholic fatty liver disease (NAFLD) and abdominal aortic calcification (AAC) volume and density, and whether these relationships vary by race/ethnicity and/or sex, information that are limited in current literature.

Methods—We studied 1,004 adults from the Multi-Ethnic Study of Atherosclerosis to assess the relationship between NAFLD (liver-to-spleen ratio <1) and the following measures of AAC: presence (volume score >0, using Poisson regression); change in volume score (increasing *vs.* no change, using Poisson regression); and morphology (volume and density score, where volume score >0, using linear regression); and interaction by race/ethnicity and sex.

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Conflict of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

Author contributions

RAR, MAA and MHC were involved in concept development. RAR conducted all analyses. RAR, MAA, NIF, RL, CAM, MB, JBS, RSB, PO and MHC contributed to the development of the manuscript and the editing process.

Results—Among Blacks, those with NAFLD had greater prevalence for AAC compared to Whites regardless of sex (Prevalence Ratio [PR]=1.41, CI=1.15–1.74, *p*-interaction=0.02). Concurrent interaction by race/ethnicity and sex was found comparing Chinese and Blacks to Whites (*p*-interaction=0.017 and 0.042, respectively) in the association between NAFLD and the prevalence of increasing AAC. Among women, this relationship was inverse among Chinese (PR=0.59, CI=0.28–1.27), and positive among Whites (PR=1.34, CI=1.02–1.76). This finding was reversed evaluating the men counterpart. Black men also had a positive association (PR=1.86, CI=1.29–2.70), which differed from the inverse relationship among White men, and was greater compared to Black women (PR=1.45, CI=1.09–1.94). NAFLD was unrelated to AAC morphology.

Conclusions—NAFLD was related to the presence of AAC, however, limited to Blacks. Significant concurrent interaction by race/ethnicity (Chinese and Blacks *vs.* Whites) and sex was found in the relationship between NAFLD and increasing AAC. These findings suggest disparities in the pathophysiologic pathways in which atherosclerosis develops.

Keywords

Non-alcoholic fatty liver disease (NAFLD); Abdominal aortic calcification (AAC); MESA; Sex; Race/ethnicity

INTRODUCTION

In the United States, non-alcoholic fatty liver disease (NAFLD) is the most prevalent hepatic disease, ranging from 20–30% in population-based cohorts [1–3]. The presence of NAFLD is linked to a greater risk for impaired endothelial function [4], increased carotid intimal-medial thickness [5], increased arterial stiffness [6], and greater cardiovascular events independent of traditional risk factors [7], which largely explain the lower overall survival of individuals with NAFLD (compared to the general population) [8]. Several studies have evaluated the link between NAFLD and calcified coronary plaques [9–12]; however, little is known of the association between NAFLD and abdominal aortic calcification (AAC), which has been shown to be highly prevalent and a better predictor of cardiovascular disease mortality and total mortality than coronary artery calcification (CAC) [9, 12–14]. Furthermore, the relationship of NAFLD to temporal changes in AAC volume and to AAC morphology (comparing volume and density) has yet to be studied.

Little information also exists on the race/ethnic and sex differences in the relationship between NAFLD and AAC. Despite the greater prevalence of cardiovascular disease risk factors such as obesity and adverse metabolic outcomes, Blacks have been shown with similar or lower risk for subclinical atherosclerosis as Whites [15–17]. Blacks also have the lowest reported prevalence of NAFLD [1, 18–20], possibly due to lower visceral adiposity [21], compared to other ethnic groups, and a genetic protection against NAFLD [22]. At an older age where comorbid conditions are more likely (e.g. diabetes), the stage in which NAFLD is present among Blacks may be indicative of greater risk for AAC. Among individuals over 50 years of age, the prevalence of NAFLD among women can exceed that of men [23], which may be due to the redistribution of fat-promoting visceral adiposity during postmenopausal years [24]. Given their greater risk for unfavorable cardiovascular outcomes in the presence of adverse metabolic health [25–28], older women with NAFLD

seem also likely to have greater risk for subclinical atherosclerosis, including AAC, compared to men.

Most studies of NAFLD have been in younger or single-race populations which could limit our understanding of the relationship between NAFLD and AAC in older adults [9, 12] and of potential differences related to race/ethnicity and sex. We therefore evaluated the association between NAFLD and characteristics of AAC including: 1) the presence *vs.* absence of AAC; 2) change in AAC over an average of 5 years; and 3) AAC morphology (volume *vs.* density); and whether these relationships differ by race/ethnicity and sex in an older, multi-racial/ethnic population.

MATERIALS AND METHODS

Study participants

This study uses data from the Multi-Ethnic Study of Atherosclerosis (MESA). Briefly, MESA is a multi-center prospective cohort study of adults aged 45–84 years recruited from 6 US communities: Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; Northern Manhattan and the Bronx, New York; and St. Paul, Minnesota. Study participants were self-identified as White, Chinese, Black or Hispanic and free of known clinical cardiovascular disease at baseline.

The primary aim of MESA was to examine the prevalence, correlates and progression of subclinical cardiovascular disease [29]. MESA consisted of five examinations: from 2000 to 2002, from 2002 to 2004, from 2004 to 2005, from 2005 to 2007, and from 2010 to 2011. The study was approved by the Institutional Review Boards at each institution and written informed consent was obtained from participants. Additional details regarding MESA's design and objectives have been published [29].

A random sample of MESA participants (n=2,202) were recruited during the follow-up visits between August 2002 and September 2005 to be included in the MESA Abdominal Aortic Calcium Study. Of those who agreed to participate (n=2,172), 1,968 met the eligibility criteria including age and race/ethnicity subsampling from MESA, postmenopausal status (for women), and no recent diagnostic abdominal computed tomography (CT). Of these, there were 1,926 participants (970 men, 956 women) with available abdominal CT scans.

The derivation of the cohort included in the present analysis is shown in Fig. 1. Of the 6,814 adults at baseline, there were 5,516 participants with no liver, spleen or AAC data, an additional 191 with a history of heavy alcohol consumption, hepatitis C, or use of oral corticosteroid or class-3 anti-arrhythmic medication, and an additional 103 thereafter with missing covariates or an outlying liver-spleen (LS) ratio, leaving a primary study cohort of 1,004 participants. In the analyses evaluating change in AAC volume, 678 participants with missing AAC data at exam 4 were excluded, leaving a total subsample of 326 participants to evaluate the association between NAFLD and change in AAC volume over an average follow-up of 5 years.

NAFLD assessment

MESA participants underwent duplicate consecutive non-contrast cardiac CT scans at baseline that included the upper abdomen. Four areas of the liver and two areas of the spleen were measured for attenuation coefficients in Hounsfield units (HU). This included a minimum, maximum and mean HU for a 2 cm round or ellipse regions of interest (ROI) in the right and left lobes of the liver, as well as in the spleen. A 1 cm measure was obtained if there was insufficient tissue for a 2 cm measure. Less than 1cm tissue was deemed insufficient to measure and these scans were not read. An average of the four ROI produced the final HU value for each liver and spleen. In these assessments, our study population included individuals with both liver and spleen data. Further details have been published [30].

Classification for NAFLD required the exclusion of participants with excessive alcohol consumption [31, 32]. Thus, participants in the current study were limited to those who consumed <8 drinks per week for women and <15 drinks per week for men based on CDC guidelines [33]. Participants with a history of hepatitis C and use of oral corticosteroid or class-3 anti-arrhythmic medication were also excluded, as these drugs are known to have hepatoxicity.

Using the HU for each ROI, NAFLD was defined using an LS ratio of <1 [30]. An LS ratio of <1 corresponds to an area under the receiver operating cure (AUC) of 0.991 based on hepatic steatosis >30% (i.e. moderate to severe steatosis) [34–38]. The prevalence of NAFLD captured by LS ratio in MESA has been shown to be greater than by liver attenuation (17.2 *vs.* 6.3%), possibly due to inclusion of more mild cases of steatosis [30]. In addition to providing internal control for the image quality of the scan by the spleen, the use of LS ratio allowed for greater power to evaluate interaction by race/ethnicity and sex.

AAC assessment

Details of the MESA abdominal CT scanning during exams 2 or 3 for baseline and exam 4 for follow-up, quality assurance procedures and plaque calculations have been published [39, 40]. Briefly, a single CT scan was performed using a scan collimation of 3 mm reconstruction, with a slice thickness of 6 mm, using 6 mm slices (5 mm for sites with multidetector scanners) with 35cm field of view, and normal kernel. Abdominal aorta calcium was scored in an 8cm segment of the aorta, superior to the aorto-iliac bifurcation. A centralized MESA location was used to perform the CT readings. Using a standard phantom to control for scanner differences, scans were brightness adjusted.

The presence of calcified plaque was defined as a plaque of >1 mm^2 with a density of at least 130 HU, and quantified using the Agatston scoring method [41]. If the maximum density value of a discrete plaque was between 130 to 199 HU, the plaque area was multiplied by a density factor of 1, those with 200 to 299 HU by a factor of 2, those with 300 to 399 HU by a factor of 3, and those with 400 HU or greater by a factor of 4. The discrete plaque area was multiplied by the highest density measured in HU anywhere in this discrete plaque area. The minimum number of contiguous pixels to be defined as a discrete plaque was 3. The product for each discrete plaque was summed for all slices to provide the

Agatston score (an area score up-weighted for increased plaque density). The AAC volume score was calculated by multiplying plaque area by CT slice thickness. Density score was calculated by dividing the Agatston score by the area score. The presence of plaque was defined as having a volume score>0.

Covariates

Individual-level covariates including socio-demographics (age, race/ethnicity, sex, highest education attained [less than high school, high school graduate/GED, some college, college degree], study site), health behavior (alcohol consumption per week, smoking status, total intentional exercise), comorbidities (the presence of diabetes and/or hypertension), medication use (anti-hypertensive drugs, lipid-lowering drugs), c-reactive protein (CRP), lipids (high-density lipoprotein [HDL], total cholesterol, triglyceride) and adiposity measures (waist circumference, body mass index [BMI], visceral fat) were assessed using protocols previously described [29, 42, 43].

Statistical analysis

Population characteristics stratified by NAFLD were evaluated using Student's t-test for continuous variables and chi-square tests for categorical variables. Wilcoxon Rank-Sum tests were used to compare medians for AAC volume. Formal tests for interaction were also conducted. For race/ethnicity, dummy variables were created for each group with the exception of Whites who served as the referent cohort. The variable sex and each dummy variable for race/ethnicity were multiplied separately to NAFLD to create first-order multiplicative interaction terms. Each dummy variable for race/ethnicity was also simultaneously multiplied to both sex and NAFLD to create second-order multiplicative interaction terms.

NAFLD and AAC (presence/absence)

Univariate and multivariable Poisson regression with robust error variance was utilized to evaluate the association between NAFLD (presence/absence) and AAC (presence/absence). The presence of AAC was defined as having an AAC volume score>0.

NAFLD and change in AAC volume

Change in AAC volume was calculated by subtracting the AAC volume at exam 1 from exam 4. Any change >0 was considered as increasing in AAC volume. Individuals with decreasing AAC volume (change <0) were categorized with individuals with no change in AAC volume as there was only a small number of participants with decreasing AAC volume (n=13). Poisson regression with robust error variance was also used for these analyses.

NAFLD and AAC morphology (volume *vs.* density score)

To determine whether NAFLD is associated with AAC morphology, we assessed the association between NAFLD and AAC volume, as well as between NAFLD and AAC density, separately, using linear regression. AAC volume was log-transformed. Only participants with the presence of AAC were included in these latter analyses.

A series of adjustment models were utilized to assess explanatory factors. Model 1 accounted for socio-demographic and health behaviors. Model 2 additionally accounted for comorbidities, medication use, CRP and lipids. Model 3 was fully-adjusted and included Model 2 adjustments along with adiposity measures. For the assessment of NAFLD against AAC volume, AAC density was included in all models. For the assessment of NAFLD and AAC density, AAC volume was included in all models.

A *p*-value of <0.05 was considered significant for main effects and interaction. All analyses were completed using STATA (StataCorp. 2012. Stata Statistical Software: Release 12. College Station, TX).

RESULTS

The overall prevalence of NAFLD was 17.1% (n=172), which was similar for both women and men. Comparing all race/ethnic groups, the prevalence of NAFLD was highest among Hispanics (40.1%) and lowest among Blacks (11.1%) and Chinese (11.6%). The prevalence of AAC was 71.1% (n=714) and also comparable between sex. The prevalence of AAC was 77.9% (Whites), 76.0% (Chinese), 62.8% (Blacks) and 65.6% (Hispanics). Of the 326 participants with follow-up AAC data, 70.3% demonstrated an increase in AAC volume, comparable between sex. The prevalence of increasing AAC volume according to NAFLD status was 11.1% (Whites), 17.7% (Chinese), 12.5% (Blacks) and 28.3% (Hispanics).

Compared to MESA participants excluded from the study with non-missing data on socio-demographics, health behavior, comorbidity, medication use, CRP, lipids and adiposity measures, individuals in the current study were more likely to be Hispanic and less likely to be Black. They also have slightly lower levels of CRP (3.4±4.7 mg/dL *vs.* 3.9±6.1 mg/dL) (Supplemental Table 1).

Baseline characteristics

The population characteristics are provided in Table 1, overall and stratified by race/ethnicity. Among Whites and Hispanics, those with *vs.* without NAFLD had greater waist circumference, BMI, level of CRP, triglyceride level and visceral adiposity, had lower HDL level and were more likely to have diabetes. Among Chinese, those with NAFLD had greater waist circumference, level of cholesterol and visceral adiposity compared to those without NAFLD. Among Blacks, NAFLD was associated with greater prevalence of hypertension and AAC.

NAFLD and AAC (presence/absence)

Table 2 provides a summary of results evaluating the association between NAFLD (presence/absence) and AAC (presence/absence). In the overall population, and after accounting for socio-demographics and health behavior, NAFLD was positively and significantly associated with AAC (Prevalence Ratio [PR]=1.12, CI=1.03–1.22). After additional adjustment for comorbidities, medication use, CRP and lipids, the relationship was no longer significant (PR=1.07, CI=0.98–1.17). Additional adjustment for adiposity measures negligibly changed the result.

Among Blacks, NAFLD was associated with 41% significantly greater prevalence of AAC, fully-adjusted (CI= 1.15–1.74). The presence of NAFLD was not significantly associated with the presence of AAC among the White, Chinese and Hispanic cohorts. A formal test for interaction found significance when comparing Blacks to Whites (p=0.009) but not when comparing Chinese or Hispanics to Whites.

Among women, NAFLD was associated with 13% greater prevalence of AAC taking into account socio-demographics, health behavior, comorbidities, medication use, CRP, lipids and adiposity (CI=1.00–1.27). Among men, the presence of NAFLD was not significantly related to the presence of AAC. The interaction by sex p-value was 0.202.

In an assessment of concurrent interaction by race/ethnicity and sex (Supplemental Table 2), the greatest estimate was found among both Black women (PR=1.47, CI=1.17–1.85) and Black men (PR=1.30, CI=0.89–1.92) in fully-adjusted models compared to other race/ethnicity, though significance was only found among women. Differences in reaching significance for Black men may be due to smaller sample size compared to Black women (n=138 *vs.* 88). The interaction p-value comparing Blacks to Whites was 0.007; however, when sex was additionally considered, the p-value was 0.553.

NAFLD and change in AAC volume

The results evaluating NAFLD and change in AAC volume is shown in Table 3. Included in these analyses were 326 participants. Overall, those with NAFLD (*vs.* no NAFLD) had 11% greater prevalence for increasing AAC volume, fully-adjusted, compared to those without NAFLD, though not significant (CI=0.91–1.34). Blacks were the only race/ethnic group in whom NAFLD was associated with increasing AAC volume. Specifically, those with NAFLD had 51% greater prevalence of increasing AAC volume compared to those without NAFLD in a fully-adjusted model. The interaction p-values were 0.965 (Chinese *vs.* Whites), 0.018 (Blacks *vs.* Whites), and 0.187 (Hispanics *vs.* Whites). When interaction by sex was evaluated, this relationship was only seen in women. Women with NAFLD had 31% (CI= 1.11–1.54) significantly greater prevalence for increasing AAC volume compared to women without NAFLD after adjustment for socio-demographics and health behaviors. Additional adjustment for comorbidities, medication use, CRP and lipids, as well as adiposity measures negligibly changed the estimates. A formal test for interaction by sex produced a p-value of 0.019. Exclusion of individuals with decreasing AAC volume in the analyses produced similar results (data not shown.).

Table 4 provides the estimates when evaluating concurrent interaction by race/ethnicity and sex. Among women, the presence *vs.* absence of NAFLD was significantly associated with increasing AAC among Whites (PR=1.34, CI=1.02–1.76), Blacks (PR=1.45, CI=1.09–1.94) and Hispanics (PR=1.57, CI=1.21–2.02), fully-adjusted; however, among Asian women, an inverse, though non-significant estimate resulted (PR=0.59, CI=0.28–1.27). Among men, the presence *vs.* absence of NAFLD was significantly associated with increasing AAC only among Blacks (PR=1.86, CI=1.29–2.70, fully-adjusted). Though non-significant, men of other race/ethnicity had the opposite direction of association than their women counterpart, fully-adjusted. The p-value for concurrent interaction by race/ethnicity and sex was significant when comparing Chinese or Blacks to Whites (0.017 and 0.042, respectively).

NAFLD and AAC morphology (volume vs. density score)

The estimates investigating the relationship between NAFLD and AAC volume and density, separately, are provided in the Supplemental Table 3. Overall, NAFLD was not significantly associated with AAC volume in a fully-adjusted model. Similarly, there was no significant difference in AAC density by NAFLD status. Formal tests for interaction by race/ethnicity produced a p-value for volume of 0.662 (Chinese *vs.* Whites), 0.307 (Blacks *vs.* Whites) and 0.072 (Hispanics *vs.* Whites); and a p-value for density of 0.282 (Chinese *vs.* Whites), 0.334 (Blacks *vs.* Whites) and 0.422 (Hispanics *vs.* Whites). Interaction by sex for either volume or density in these analyses was non-significant. Concurrent interaction by race/ethnicity and sex was not found significant for either morphology.

DISCUSSION

Our findings suggested differences by race/ethnicity and sex in the NAFLD-AAC association. Only interaction by race/ethnicity was found significant in the association between NAFLD and AAC whereby Blacks had a greater prevalence compared to Whites regardless of sex. In the association between NAFLD and the prevalence of increasing AAC, concurrent interaction by race/ethnicity and sex was found. NAFLD was associated with greater prevalence for increasing AAC among White women versus decreasing AAC among Chinese women, a trend that was reversed when comparing the men counterpart. Only the relationship for White women was found significant. Additionally, both Black men and Black women had a significantly greater prevalence of increasing AAC in the presence *vs.* absence of NAFLD, although Black men had a greater magnitude of association. No significant relationship was found between NAFLD and AAC volume or density.

Blacks generally have lower visceral adiposity compared to other race/ethnic groups [21], which has been suggested as a reason for their lower prevalence of NAFLD. With age, however, the level of visceral adiposity increases [44]; thus, the previous protection of a lower level of visceral adiposity among Blacks would gradually dissipate and henceforth increase risk for NAFLD. The stage at which NAFLD is present among Blacks may signify a state of health vulnerability and serve as a proxy for an increased risk for calcific atherosclerosis, including AAC. Given Blacks generally have worse health profile than Whites with regards to heart disease risk factors (e.g. obesity, diabetes) [15], the presence of NAFLD may also trigger a faster progression to cardiovascular disease as denoted by the greater prevalence of AAC among Whites *vs.* Blacks in the presence of NAFLD in the current study. Further investigation of the mechanism through which the association between NAFLD and AAC differs by race/ethnicity, particularly between Blacks and Whites, are warranted.

Visceral adiposity is typically greater in men compared to women at a given BMI [45], at least until the set of menopause when this sex difference diminishes [24]. This disproportionate exposure overtime suggests that men may have greater susceptibility to the adverse effects of visceral adiposity (e.g. a faster development of NAFLD and/or cardiovascular disease markers including AAC). If NAFLD serves as a proxy for health vulnerability or motivate rapid progression to heart disease through AAC progression among Blacks, this sex difference in visceral fat exposure overtime may explain the significantly

greater positive association between the presence *vs.* absence of NAFLD and the prevalence of increasing AAC among Black men compared to Black women. Although our adjustment for visceral adiposity did not significantly affect the results, changes in visceral adiposity overtime may be more relevant than a point estimate.

The differences found between Chinese and Whites in the association between the presence *vs.* absence in NAFLD and the prevalence of increasing AAC in which opposite trends are suggested when simultaneously considering sex may imply that a unique mechanism exists not only for each race/ethnicity, but also for each sex. Further investigation is needed using a larger sample size of Chinese participants to better assess these disparate findings.

The 17.1% prevalence of NAFLD in the primary study cohort has also been documented in the Framingham Heart Study and the National Health and Nutrition Examination [46, 47]. The 71.1% prevalence of AAC was higher than reported by other studies on NAFLD and subclinical atherosclerosis [9, 12], but consistent with studies in similar aged populations [14], which implies that our findings may be more comparable to studies of same aged populations.

Our findings differed from previous studies, particularly when evaluating sub-cohorts. Although our results were consistent with the null association found by vanWagner et al. between NAFLD (defined as liver attenuation ≤40 HU) and AAC (Agatston score >0) in the overall population using the Coronary Artery Risk Development in Young Adults (CARDIA) Study, they did not find any differences by sex or race (Blacks *vs.* Whites) [9]. Additionally, measures of adiposity had a significant role in the study by vanWagner et al. that was not present in our study [9]. Only 9.6% of the CARDIA cohort had NAFLD compared to 17.1% seen in the current study, which may be a product of the difference in the classification of NAFLD. As previously mentioned, the use of LS ratio may likely include milder forms of NAFLD, which, if associated with AAC, may dilute the relationship when classified as no NAFLD. Liu et al. also did not find an association between liver attenuation and AAC (Agatston score >0) among African-Americans in the Jackson Heart Study after accounting for age, sex, smoking and alcohol status, diabetes, systolic blood pressure, total cholesterol and HDL-C and treatments for hypertension, diabetes and dyslipidemia [12]. Interaction by sex was not considered in this study. Differences in how liver fat was assessed as previously mentioned may also likely explain differences in results.

The strengths of this study include evaluation of NAFLD and AAC in a large multi-racial/ethnic, older population. We also investigated multiple potential factors, including visceral adiposity, as a means to help explain the relationship between NAFLD and AAC. Limitations in this study include the inability to infer causality; however, the direction of association is likely from NAFLD to subclinical atherosclerosis based on biological plausibility. We also excluded participants with missing spleen data who were healthier based on parameters such as waist circumference, BMI, hypertension, HDL, triglycerides and AAC, which may have inflated the magnitude of association observed in this study. However, the use of LS ratio over liver attenuation may have included milder forms of NAFLD which may weaken the association with AAC, thus, promoting conservative estimates. Further, the use of CT scans is a relatively insensitive measure of fatty liver

compared to magnetic resonance spectroscope which may have likely underestimated the prevalence of NAFLD [48, 49]. We also were not able to evaluate time from menopause initiation or use of hormone replacement therapy as this may influence the degree to which estrogen may have been protective against AAC for women. Lastly, the impact of NAFLD on change in AAC in our findings may differ between developing AAC (i.e. baseline AAC=0, follow-up AAC>0) and progressing AAC (i.e. baseline AAC>0) as this has been shown in the NAFLD-change in CAC association [50]. This was not considered due to sample size limitations.

Our findings suggest race/ethnic and sex differences in the pathophysiologic pathways in which atherosclerosis develops. Further investigation of the contribution of race/ethnicity and sex on the NAFLD-AAC relationship, particularly in longitudinal assessments using larger sample size, is warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank the other investigators, the staff, and the participants of the MESA study for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org.

Financial support

This work was supported by a training grant through the National Heart, Lung and Blood Institute (NHLBI, No: T32 HL079891). MESA was supported by contracts HHSN268201500003I, N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168 and N01-HC-95169 from NHLBI and by grants UL1-TR-000040, UL1-TR-001079 and UL1-TR-025005 from the National Center for Research Resources. Additionally, the MESA Abdominal Body Composition, Inflammation and Cardiovascular Ancillary Study was funded through a grant from the National Institutes of Health (No: RO1 HL088451); the MESA Abdominal Aortic Calcium Study was funded through a grant from the NHLBI HL72403; and the MESA Non-Alcoholic Fatty Liver Disease Study was supported by NHLBI (R01 HL071739 and contracts N01-HC-95159 through N01-HC-95165 and N01 HC 95169).

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Highlights

- Limited information is known of the race/ethnic and sex disparities in the association between non-alcoholic fatty liver disease (NAFLD) and abdominal aortic calcification (AAC).
- NAFLD was significantly associated with the presence of AAC, however, limited to Blacks.
- NAFLD was also related to increasing AAC among Blacks regardless of sex.
- The findings suggest disparities in the pathophysiologic pathways in which atherosclerosis develops.

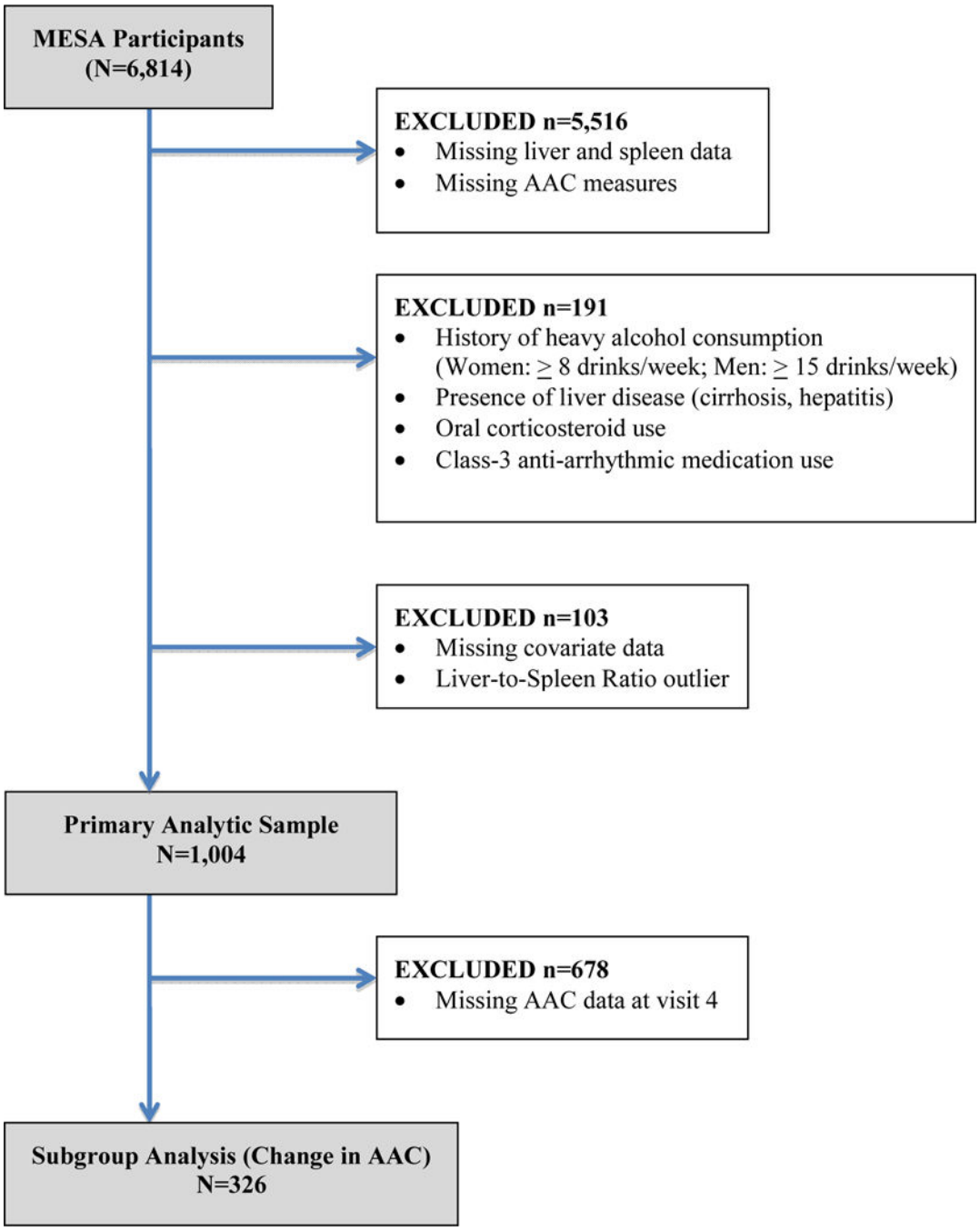

FIGURE 1.
Sample Selection Chart

Table 1

Clinical and demographic characteristics by non-alcoholic fatty liver disease (NAFLD)[a] status by race/ethnicity.

Characteristics	Race/ethnicity											
	White (n=394)			Chinese (n=125)			Black (n=226)			Hispanic (n=259)		
	NAFLD=0 (n=330, 83.8%)	NAFLD=1 (n=64, 16.2%)	*p*	NAFLD=0 (n=105, 84.0%)	NAFLD=1 (n=20, 16.0%)	*p*	NAFLD=0 (n=207, 91.6%)	NAFLD=1 (n=19, 8.4%)	*p*	NAFLD=0 (n=190, 73.4%)	NAFLD=1 (n=69, 26.6%)	*p*
Age in years (mean, SD)	63.6 (10.1)	61.5 (8.3)	0.114	64.2 (10.2)	65.2 (11.3)	0.706	63.5 (9.7)	62.9 (9.7)	0.798	61.1 (10.1)	60.3 (9.1)	0.532
Sex in %			0.848			0.280			0.492			0.551
Women	48.2 (n=159)	46.9 (n=30)		58.1 (n=61)	45.0 (n=9)		60.4 (n=125)	68.4 (=13)		55.3 (n=105)	59.4 (n=41)	
Men	51.8 (n=171)	53.1 (n=34)		41.9 (n=44)	55.0 (n=11)		39.6 (n=82)	31.6 (n=6)		44.7 (n=85)	40.6 (n=28)	
Education in %			0.129			0.746			0.309			0.948
Less than high school	3.0 (n=10)	1.6 (n=1)		24.8 (n=26)	25.0 (n=5)		12.6 (n=26)	5.3 (n=1)		45.3 (n=86)	47.8 (n=33)	
High school graduate/GED	15.5 (n=51)	21.9 (n=14)		20.0 (n=21)	20.0 (n=4)		18.4 (n=38)	5.3 (n=1)		17.4 (n=33)	18.8 (n=13)	
Some college	24.9 (n=82)	34.4 (n=22)		14 (13.3)	5.0 (n=1)		30.4 (n=63)	36.8 (n=7)		21.1 (n=40)	18.8 (n=13)	
College degree	56.7 (n=187)	42.2 (n=27)		41.9 (n=44)	50.0 (n=10)		38.7 (n=80)	52.6 (n=10)		16.3 (n=31)	14.5 (n=10)	
Health behavior (mean, SD)												
#Alcohol consumption/week	2.7 (3.3)	3.3 (4.4)	0.209	0.5 (2.0)	0.5 (1.4)	0.944	1.8 (2.9)	1.9 (3.2)	0.869	1.8 (3.1)	1.5 (2.6)	0.428
Exercise in MET-min/week	1842 (2353)	1700 (3037)	0.673	1510 (1990)	1009 (996)	0.274	1607 (2441)	2097 (2699)	0.407	1594 (2422)	1093 (2232)	0.114
Anthropometric measures (mean, SD)												
Waist circumference in cm	97.2 (13.0)	107.8 (12.2)	<0.001*	87.4 (9.5)	92.1 (8.5)	0.044*	99.2 (14.0)	105.2 (15.1)	0.077	97.8 (11.4)	103.6 (12.0)	<0.001*
BMI in kg/m^2	27.3 (4.4)	31.0 (4.6)	<0.001*	24.4 (3.1)	25.6 (2.9)	0.116	29.2 (5.3)	30.9 (5.3)	0.173	28.1 (4.3)	31.2 (4.7)	<0.001*
Comorbidities												
Diabetes in %	4.9 (n=16)	15.6 (n=10)	0.001*	11.4 (n=12)	20.0 (n=4)	0.293	16.4 (n=34)	15.8 (n=3)	0.943	10.5 (n=20)	27.5 (n=19)	0.001*
Hypertension in %	40.0 (n=132)	51.6 (n=33)	0.086	47.6 (n=50)	35.0 (n=7)	0.299	59.4 (n=123)	73.7 (n=14)	0.223	43.2 (n=82)	43.5 (n=30)	0.963
Systolic blood pressure in mmHg	123.8 (n=330)	131.2 (n=64)	0.006*	127.9 (n=105)	125.5 (n=20)	0.644	133.7 (n=207)	135.3 (n=19)	0.761	126.1 (n=190)	131.5 (n=69)	0.088
Diastolic blood pressure in mmHg	70.6 (n=330)	73.3 (n=64)	0.041*	72.0 (n=105)	72.7 (n=20)	0.750	74.9 (n=207)	73.4 (n=19)	0.564	71.6 (n=190)	73.5 (n=69)	0.168
Medication in %												
Anti-hypertensive drugs	34.9 (n=115)	46.9 (n=30)	0.068	35.2 (n=37)	15.0 (n=3)	0.075	46.9 (n=97)	73.7 (n=14)	0.025*	33.2 (n=63)	30.4 (n=21)	0.679
Lipid-lowering drugs	20.0 (n=66)	21.9 (n=14)	0.733	17.1 (n=18)	25.0 (n=5)	0.406	11.1 (n=23)	15.8 (n=3)	0.541	14.2 (n=27)	18.8 (n=13)	0.362
Blood markers (mean, SD)												

Characteristics	Race/ethnicity											
	White (n=394)			Chinese (n=125)			Black (n=226)			Hispanic (n=259)		
	NAFLD=0 (n=330, 83.8%)	NAFLD=1 (n=64, 16.2%)	*P*	NAFLD=0 (n=105, 84.0%)	NAFLD=1 (n=20, 16.0%)	*p*	NAFLD=0 (n=207, 91.6%)	NAFLD=1 (n=19, 8.4%)	*p*	NAFLD=0 (n=190, 73.4%)	NAFLD=1 (n=69, 26.6%)	*p*
CRP in mg/L	3.1 (5.0)	5.1 (6.0)	0.006*	1.4 (1.4)	1.3 (1.2)	0.788	4.0 (4.7)	4.5 (6.9)	0.690	3.3 (4.1)	5.5 (5.6)	<0.00
HDL in mg/dL	51.3 (15.0)	44.6 (13.0)	<0.001*	52.8 (14.5)	44.9 (10.3)	0.020*	53.5 (15.6)	49.7 (14.0)	0.301	49.7 (14.2)	44.7 (11.5)	0.010*
Total cholesterol in mg/dL	195.0 (33.8)	195.8 (37.6)	0.872	189.4 (31.2)	192.7 (28.5)	0.666	193.2 (34.0)	184.7 (31.6)	0.300	203.1 (32.0)	201.8 (33.3)	0.778
Triglyceride in mg/dL	137.2 (82.7)	185.1 (124.8)	<0.001*	128.8 (74.7)	186.5 (169.8)	0.015*	99.1 (50.2)	120.2 (82.0)	0.102	143.2 (74.2)	174.2 (73.3)	0.003*
Visceral fat (mean, SD) in cm^2	490 (255)	698 (216)	<0.001*	377.6 (178.6)	472.0 (173.2)	0.032*	382.2 (179.1)	443.7 (177.4)	0.153	488.4 (202.8)	600.0 (199.5)	<0.001*
Abdominal aortic calcification (AAC)												
AAC prevalence in %	77.3 (n=255)	81.3 (n=52)	0.483	76.2 (n=80)	75.0 (n=15)	0.909	60.9 (n=126)	84.2 (n=16)	0.044*	63.7 (n=121)	71.0 (n=49)	0.272
Volume (median, IQR) in mm^3	413 (22, 2143)	692 (34, 2418)	0.277	255 (21, 1154)	527 (33, 1185)	0.684	87 (0, 699)	327 (51, 664)	0.161	104 (0, 1088)	126 (0, 951)	0.789
Density (mean, SD) (n=307 [White]; n=95 [Chinese]; n=142 [Black]; n=170 [Hispanic])	3.0 (0.6)	2.9 (0.7)	0.334	3.2 (0.7)	3.3 (0.5)	0.498	3.0 (0.6)	3.0 (0.5)	0.912	3.0 (0.6)	3.0 (0.7)	0.491

Overall, the prevalence of NAFLD was 37.2% (Whites), 11.6% (Chinese), 11.1% (Blacks) and 40.1% (Hispanics).

[a]NAFLD = liver-to-spleen ratio < 1.

*Significant *p*-value<0.05.

Table 2

Prevalence ratios of the association between non-alcoholic fatty liver disease (presence vs. absence) and the presence of abdominal aortic calcification, overall, by race/ethnicity and by sex.

	Model 1[a]	Model 2[b]	Model 3[c,d]
All (n=1,004)	1.12 (1.03 - 1.22)*	1.07 (0.98 - 1.17)	1.07 (0.98 - 1.17)
By race/ethnicity			
White (n=394)	1.10 (0.97 - 1.25)	1.02 (0.90 - 1.17)	1.02 (0.90 - 1.17)
Chinese (n=125)	0.91 (0.74 - 1.13)	0.90 (0.72 - 1.13)	0.90 (0.72 - 1.13)
Black (n=226)	1.45 (1.17 - 1.79)*	1.41 (1.15 - 1.73)*	1.41 (1.15 - 1.74)*
Hispanic (n=259)	1.13 (0.95 - 1.34)	1.08 (0.92 - 1.28)	1.08 (0.91 - 1.28)
By sex			
Women (n=543)	1.20 (1.07 - 1.35)*	1.13 (1.00 - 1.27)*	1.13 (1.00 - 1.27)*
Men (n=461)	1.03 (0.91 - 1.18)	1.00 (0.88 - 1.15)	1.00 (0.87 - 1.15)

[a] Model 1=adjusted for age, sex, race/ethnicity, education, study site, alcohol consumption/week, smoking status, exercise.

[b] Model 2=adjusted for Model 1+diabetes, hypertension, antihypertensive medication use, lipid-lowering drug use, c-reactive protein, HDL, cholesterol, triglyceride.

[c] Model 3=adjusted for Model 2+waist circumference, BMI, visceral fat.

[d] Interaction *p*-value: Chinese *vs.* Whites = 0.347, Blacks *vs.* Whites = 0.009, Hispanics *vs.* Whites=0.601, sex = 0.202.

* Significant *p*-value<0.05.

Table 3

Prevalence ratios of the association between non-alcoholic fatty liver disease (presence *vs.* absence) and change in abdominal aortic calcification (increasing *vs.* no change), overall, by race/ethnicity and by sex.

	Model 1[a]	Model 2[b]	Model 3[c,d]
All (n=326)	1.12 (0.94 - 1.33)	1.07 (0.89 - 1.29)	1.11 (0.91 - 1.34)
By race/ethnicity			
White (n=81)	0.86 (0.55 - 1.32)	0.81 (0.53 - 1.25)	0.86 (0.55 - 1.33)
Chinese (n=47)	0.90 (0.62 - 1.31)	0.84 (0.55 - 1.28)	0.85 (0.56 - 1.30)
Black (n=110)	1.53 (1.22 - 1.93)*	1.45 (1.14 - 1.84)*	1.51 (1.17 - 1.95)*
Hispanic (n=88)	1.18 (0.89 - 1.58)	1.17 (0.88 - 1.57)	1.20 (0.89 - 1.61)
By sex			
Women (n=181)	1.31 (1.11 - 1.54)*	1.29 (1.07 - 1.54)*	1.36 (1.11 - 1.65)*
Men (n=145)	0.83 (0.55 - 1.23)	0.78 (0.52 - 1.18)	0.79 (0.52 - 1.19)

[a] Model 1=adjusted for age, race/ethnicity, education, study site, alcohol consumption/week, smoking status, exercise.

[b] Model 2=adjusted for Model 1+diabetes, hypertension, antihypertensive medication use, lipid-lowering drug use, c-reactive protein, HDL, cholesterol, triglyceride.

[c] Model 3=adjusted for Model 2+waist circumference, BMI, visceral fat.

[d] Interaction *p*-value: Chinese *vs.* Whites = 0.965, Blacks *vs.* Whites = 0.018, Hispanics *vs.* Whites = 0.187, sex = 0.019.

* Significant *p*-value<0.05.

Table 4

Prevalence ratios of the association between non-alcoholic fatty liver disease (presence *vs.* absence) and change in abdominal aortic calcification (increasing *vs.* no change), by sex and race/ethnicity.

	Model 1[a]	Model 2[b]	Model 3[c,d]
Women (N=181)			
White (n=34)	1.32 (1.07 - 1.64) *	1.22 (0.95 - 1.58)	1.34 (1.02 - 1.76) *
Chinese (n=25)	0.62 (0.27 - 1.41)	0.58 (0.27 - 1.25)	0.59 (0.28 - 1.27)
Black (n=67)	1.45 (1.14 - 1.85) *	1.36 (1.06 - 1.76) *	1.45 (1.09 - 1.94) *
Hispanic (n=55)	1.48 (1.15 - 1.89) *	1.50 (1.17 - 1.92) *	1.57 (1.21 - 2.02) *
Men (N=145)			
White (n=47)	0.28 (0.05 - 1.57)	0.27 (0.05 - 1.52)	0.28 (0.05 - 1.54)
Chinese (n=22)	1.21 (0.94 - 1.57)	1.21 (0.86 - 1.69)	1.21 (0.85 - 1.71)
Black (n=43)	2.03 (1.61 - 2.57) *	1.83 (1.28 - 2.60) *	1.86 (1.29 - 2.70) *
Hispanic (n=33)	0.74 (0.36 - 1.53)	0.71 (0.35 - 1.44)	0.71 (0.35 - 1.45)

[a] Model 1=adjusted for age, sex, race/ethnicity, education, study site, alcohol consumption/week, smoking status, exercise.

[b] Model 2=adjusted for Model 1+diabetes, hypertension, antihypertensive medication use, lipid-lowering drug use, c-reactive protein, HDL, cholesterol, triglyceride.

[c] Model 3=adjusted for Model 2+waist circumference, BMI, visceral fat.

[d] Interaction *p*-value: sex=0.073; Chinese *vs.* Whites=0.042; Blacks *vs.* Whites=0.625; Hispanics vs. Whites=0.351; sex and race/ethnicity (Chinese vs. Whites)=0.017; sex and race/ethnicity (Blacks *vs.* Whites)=0.042; sex and race/ethnicity (Hispanics vs. Whites)=0.411.

* Significant *p*-value<0.05.