Published in final edited form as:

J Am Geriatr Soc. 2011 September ; 59(9): 1763–1764. doi:10.1111/j.1532-5415.2011.03583.x.

AGE-RELATED CHANGES IN MEAN CORPUSCULAR VOLUME IN ADULT WHITES AND AFRICAN AMERICANS

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To the Editor

African Americans tend to have lower mean corpuscular volume (MCV) values than whites,^{1,2} but there is little information on whether age-related changes in MCV are different according to race. Using data collected in the Baltimore Longitudinal Study on Aging, the hypothesis that age-related changes in MCV are different in whites and African Americans and that potential confounders such as hemoglobin, serum folate, serum vitamin B12, serum ferritin, serum iron, erythrocyte sedimentation rate (ESR), and white blood cell count did not explain such difference was tested. Racial groups were examined separately because differences in environmental factors (e.g., socioeconomic status and nutrition) and genetics might explain hematologic differences between African Americans and whites.² Thus, separate analyses would provide a more-accurate estimate of the age-related changes within each racial group.

This study included a sample of 1,780 (755 women and 1,025 men) Baltimore Longitudinal Study of Aging (BLSA) participants. Participants did not have a history of stroke. At initial testing, participants ranged in age from 50 to 97 (mean 62.3 ± 10.8). The average number of years of education was 16.2 ± 2.7 (range 8–20). The sample consisted of 1,470 whites and 310 African Americans. Participants were tested annually or biannually. On average, the current sample of participants had 3.8 ± 3.6 follow-up visits over an average of 6.4 ± 5.4 years. The visits of participants who met criteria for mild cognitive impairment (MCI) or dementia were excluded from the analyses after onset of cognitive impairment. Visits at which hemoglobin concentrations were suggestive of iron-deficiency anemia (< 12 g/dL in women and < 13 g/dL in men)³ were excluded from the analyses.

Blood samples were collected at each BLSA visit. A Coulter counter was used to measure MCV levels in each participant's blood sample. The analyses were adjusted for blood parameters (hemoglobin, albumin, vitamin B12, ESR, ferritin, folate, iron, and white blood cell count) that are associated with different types of anemia.

Author Contributions: Alyssa Gamaldo analyzed data and wrote the letter. Luigi Ferrucci contributed vital new reagents and assisted in writing the letter. Joseph Rifkind contributed new reagents and assisted in writing the letter. Alan Zonderman assisted in data analyses and writing the letter.

Sponsor's Role: The sponsors did not participate in the design or data analysis of any aspect of the study or in manuscript preparation.

Conflict of Interest: There were no relevant financial interests in this manuscript.

Mixed-effects models,⁴ also known as multilevel models were conducted, using SAS (version 9.1.3, SAS Institute, Inc., Cary, NC) to examine the effect of age or change over time in MCV after adjusting for demographics and other covariates separately for whites and African Americans.

A robust, significant, linear, age-related increase in MCV was observed in whites even after controlling for additional blood indices (Table 1), but in African Americans, there was only a slight, nonsignificant trend toward increasing MCV with age.

To determine whether the racial groups were significantly different on MCV trajectories, subsequent analyses including the entire sample were conducted by including an age-by-race interaction term. A significant age-by-race interaction was observed ($\beta = -0.06$ (standard error (SE) = 0.02), $P < .01$), but it became nonsignificant when additional blood confounders were included in the model $\beta = 0.002$ (SE = 0.04), $P > .05$). MCV values for whites over time continued to be greater than those of African Americans, although the changes in MCV over time did not appear to be changing at a different rate.

Previous literature has suggested that, during early adulthood, MCV increases gradually, and levels off around middle adulthood,⁵ to rise again in old age,^{6,7} but no previous study has explored trajectories of MCV changes using a large population. Changes in MCV across the human lifespan, particularly in late adulthood, might be associated with differences in red blood cell (RBC) survival. Younger RBCs tend to have larger volumes, as measured by MCV, soon after they are released into circulation as reticulocytes, and their volume tends to decline.^{6,8} The life span of RBCs is shorter in older adults, and the production of RBCs increases in compensation.^{8,9} A higher percentage of young cells are found in the circulation, leading to higher MCV.

MCV levels appear to increase over time and do not appear to be explained by anemia. Changes in MCV may be a reflection of the normal aging process, but more research is needed to explore whether specific mechanisms associated with aging, such as oxidative stress,¹⁰ may further explain changes in MCV. Although whites typically have greater MCV values than African Americans over time, there appears to be no racial difference in the rate of change in MCV. Further research is needed to understand the specific mechanisms that influence racial differences in MCV.

ACKNOWLEDGMENTS

The Intramural Research Program of the National Institutes of Health, National Institute on Aging supported this research.

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Table 1

Predictors of Mean Corpuscular Volume for Whites and African Americans

Predictor	β (Standard Error)			
	Whites		African Americans	
	Model 1 [*]	Model 2 [†]	Model 1 [*]	Model 2 [†]
Age (linear)	2.00 ^{***} (0.01)	0.11 ^{**} (0.15)	0.04 (0.02)	0.11 (0.04)
Sex	2.48 ^{***} (0.28)	-0.84 (0.37)	1.36 (0.56)	-0.11 (0.86)

* Unadjusted model with age and sex as predictors.

† Adjusted model with the inclusion of the blood confounders (hemoglobin, albumin, vitamin B12, erythrocyte sedimentation rate, ferritin, folate, iron, and white blood cell count).

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 $P < .01$

 $P < .001$.