

# Will the Real Risk Factors Stand Up: A Surprise From Bogalusa

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Kelley RE, Dasmahapatra P, Wang J, et al. Prevalence of atherosclerotic plaque in young and middle-aged asymptomatic individuals: the Bogalusa Heart Study. *South Med J*. 2011;104:803-808.

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## Background to the Interview

The Bogalusa Heart Study begun in 1972 as an epidemiology study of cardiovascular risk factors in children and adolescents living in Bogalusa, Louisiana, a biracial (African American/white) rural community located 70 miles north of New Orleans. The Study eventually evolved into long-term observations in young adults.<sup>[1,2]</sup> Originally funded as a Specialized Center of Research-Arteriosclerosis (SCOR-A) by the National Heart, Lung, and Blood Institute (NHLBI), it was part of a project to conduct research on atherosclerosis, coronary artery disease, hypertension, diabetes mellitus, and complications of cardiovascular-renal disease as the major causes of deaths in the United States. The Bogalusa Heart Study has produced many reports demonstrating that the major etiologies of adult heart disease begin in childhood. Early autopsy studies showed atherosclerotic lesions in the aorta and coronary vessels, and changes in the kidney vasculature related strongly to clinical cardiovascular risk factors, clearly indicating that atherosclerosis and hypertension begin in early life. These findings have been extended by noninvasive imaging studies of the heart and carotid and femoral arteries.

In the latest report from the Bogalusa Heart Study, the prevalence of carotid and femoral artery atherosclerotic plaque was determined in asymptomatic African American and white men and women aged 29-51 years and the potential relations with cardiovascular risk factors was examined.<sup>[3]</sup> Data were analyzed from a sample of 851 subjects without a history of cardiovascular/cerebrovascular events (57% women, 70% white) who were part of the initial cohort of approximately of 16,000 children aged 4-17 years enrolled in the study from 1973 onward. They were followed from childhood through adulthood and assessed for carotid and femoral artery plaque formation defined by intima-media thickness (IMT) measured by B-mode ultrasonography.

Plaque prevalence was found to be highest in white men (14%), compared with white women (8%) and African American men and women (9%). This was consistent with findings in autopsy studies of both the Bogalusa Heart<sup>[4]</sup> and the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) studies.<sup>[5]</sup>

Analyses adjusted for age, race, and gender showed that current smoking (OR 2.3,  $P = .0005$ ) was the strongest independent predictor for plaque formation, followed by hypertension (OR 2.2,  $P = .002$ ), diabetes (OR 2.1,  $P = .02$ ), age (OR 1.1,  $P = .02$ ), and white race (OR 1.7,  $P = .05$ ). Neither obesity nor dyslipidemia were independently associated with plaque in this study. Levels of triglycerides, but not low-density lipoprotein cholesterol (LDL-C) or high-density lipoprotein cholesterol (HDL-C) were significantly higher in subjects with plaques. As the researchers noted, the associations of risk factors such as smoking and diabetes with atherosclerosis are well known, but dyslipidemia is also recognized as having a strong correlation with plaque formation. They suggested that in this study, "Interventions such as diet alteration and statin therapy may have a positive impact on these potential contributors to plaque formation."

The author of an invited commentary, Dana E. King, MD, MS (Medical University of South Carolina, Charleston) suggested that the findings of this study, "while not a surprise to vascular researchers, may

challenge the prevailing beliefs of some clinicians. The conclusion that obesity and LDL-cholesterol do not make a significant contribution to the development of carotid atherosclerosis may arouse some skepticism."<sup>[6]</sup> However, Dr. King noted that "recent research indeed supports the idea that LDL-cholesterol may play a lesser role in the development of atherosclerosis than was once believed," pointing out that statins, which reduce LDL-C, only reduce the risk of atherosclerosis by 30%. "These results suggest that the other 70% of the risk is unexplained and due to other non-LDL factors," Dr. King said. "We do not completely understand," he admitted, but "Great research often challenges conventional wisdom. The current study demonstrates that we still have much to learn about the common nemesis, atherosclerosis." Dr. King concluded.

Dr. Berenson spoke about the study's findings with Linda Brookes and recalled the achievements of the Bogalusa Heart Study, which is now in its last stages.

**Medscape: This latest analysis from the Bogalusa Heart Study appeared to conclude that obesity and low-density lipoprotein cholesterol (LDL-C) do not contribute significantly to the development of carotid or femoral atherosclerosis, as Dr. King pointed out in his commentary. Given that LDL-C has been shown to be strongly correlated with carotid plaque formation, how do you explain this?**

**Dr. Berenson:** I do not think that we said that. If we had looked at atherosclerosis by autopsy, certainly LDL-C would be strongly associated with the atherosclerotic lesions, as we showed in previous analyses.<sup>[7-9]</sup> The plaques represent a sort of segmental atheroma, but do not represent the overall atherosclerosis as seen in the vascular tree. The idea of a segmental lesion may be appropriate for looking at risk, but I am not sure that it represents the total picture of significant risk factors that relate to the disease. We know from autopsy studies that LDL-C certainly plays a major role in relating to general atherosclerosis, certainly in the aorta and the coronary vessels. We also need to look at the effects of blood pressure and the carbohydrate-insulin story of the metabolic syndrome.

**Medscape: So how would you interpret the finding that dyslipidemia was not an independent risk factor for plaque formation in this study? In particular, LDL-C, which was shown in the Northern Manhattan Study to have the strongest relation with carotid plaque,<sup>[10]</sup> showed no correlation here.**

**Dr. Berenson:** Of the cardiovascular risk factors we studied, blood pressure was significantly different between those with plaques and those with none. Median waist circumference was greater in subjects with plaques, but not quite significantly different from those without plaques. Median LDL-C was 131.2 mg/dL vs 123.9 mg/dL, respectively, which was not significantly different, and high-density lipoprotein (HDL-C) was 45.6 mg/dL vs 47.1 mg/dL, also not significantly different. Levels of triglycerides, glucose, and rate of smoking were all significantly greater in the group with plaques. When the model was adjusted for age, race, sex, hypertension, diabetes, dyslipidemia, obesity, and smoking, smoking was the most highly significant factor, followed by hypertension, diabetes, age, and white race. That does not mean that the others are not important, just that they are part of those variables blocked out by the others that were adjusted for.

(only partly cited)

## References

1. The Bogalusa Heart Study. 20th Anniversary Symposium. Am J Med Sci. 1995;310(suppl 1):S1-S138. [Abstract](#)
2. Berenson GS; Bogalusa Heart Study Investigators. Bogalusa Heart Study: a long-term community study of a rural biracial (Black/White) population. Am J Med Sci. 2001;322:293-300. [Abstract](#)
3. Kelley RE, Dasmahapatra P, Wang J, et al. Prevalence of atherosclerotic plaque in young and middle-aged asymptomatic individuals: the Bogalusa Heart Study. South Med J. 2011;104:803-808. [Abstract](#)
4. Berenson GS, Wattigney WA, Tracy RE, et al. Atherosclerosis of the aorta and coronary arteries

- and cardiovascular risk factors in persons aged 6 to 30 years and studied at necropsy. The Bogalusa Heart Study. *Am J Cardiol.* 1992;70:851-858. [Abstract](#)
5. Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Natural history of aortic and coronary atherosclerotic lesions in youth. Findings from the PDAY study. *Arterioscler Thromb.* 1993;13:1291-1298. [Abstract](#)
  6. King DE. Atherosclerosis -- challenging the assumptions. *South Med J.* 2011;104:809-810. [Abstract](#)
  7. Berenson GS, Wattigney WA, Tracy RE. Atherosclerosis of aorta and coronary arteries and cardiovascular risk factors in persons aged 6-30 years studied at necropsy: The Bogalusa Heart Study. *Am J Cardiol.* 1992;70:851-858. [Abstract](#)
  8. Tracy RE, Newman WP 3rd, Wattigney WA, et al. Histologic features of atherosclerosis and hypertension from autopsies of young individuals in a defined geographic population: the Bogalusa Heart Study. *Atherosclerosis.* 1995;116:163-179. [Abstract](#)
  9. Berenson GS, Srinivasan SR; Bogalusa Heart Study Group. Cardiovascular risk factors in youth with implications for aging: the Bogalusa Heart Study. *Neurobiol Aging.* 2005;26:303-307. [Abstract](#)
  10. Gardener H, Della Morte D, Elkind MS, et al. Lipids and carotid plaque in the Northern Manhattan Study (NOMAS). *BMC Cardiovasc Disord.* 2009;9:55-62. [Abstract](#)
  11. Castelli WP. The new pathophysiology of coronary artery disease. *Am J Cardiol.* 1998;82(10 suppl 2):60-65.
  12. Lauer RM, Connor WE, Leaverton PE, et al. Coronary heart disease risk factors in school children: the Muscatine study. *J Pediatr.* 1975;86:697-706. [Abstract](#)
  13. Berenson GS, Chen W, Dasmahapatra P, et al. Stimulus response of blood pressure in black and white young individuals helps explain racial divergence in adult cardiovascular disease: the Bogalusa Heart Study. *J Am Soc Hypertens.* 2011;5:230-238. [Abstract](#)
  14. Urbina EM, Bao W, Pickoff AS, Berenson GS. Ethnic (black-white) contrasts in heart rate variability during cardiovascular reactivity testing in male adolescents with high and low blood pressure: the Bogalusa Heart Study. *Am J Hypertens.* 1998;11:196-202. [Abstract](#)
  15. Berenson GS, Voors AW, Webber LS, et al. Racial differences of parameters associated with blood pressure levels in children -- the Bogalusa heart study. *Metabolism.* 1979;28:1218-1228. [Abstract](#)
  16. Berenson GS, Webber LS, Srinivasan SR. Pathogenesis of hypertension in black and white children. *Clin Cardiol.* 1989;12(12 suppl 4):IV3-IV8.
  17. Berenson GS, ed. *Evolution of Cardio-Metabolic Risk from Birth to Middle Age: The Bogalusa Heart Study.* Dordrecht, The Netherlands: Springer Science+Business Media BV; 2011.
  18. The Cardiovascular Risk in Young Finns Study. <http://vanha.med.utu.fi/cardio/youngfinnsstudy/> Accessed February 2, 2012.
  19. Childhood Determinants of Adult Health (CDAH) Study. <http://www.menzies.utas.edu.au/information.php?Doo=ViewData&type=Project&ID=52> Accessed February 2, 2012.
  20. Juonala M, Magnussen CG, Berenson GS, et al. Childhood adiposity, adult adiposity, and cardiovascular risk factors. *N Engl J Med.* 2011;365:1876-1885. [Abstract](#)
  21. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents; National Heart, Lung, and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. *Pediatrics.* 2011;128(suppl 5):S213-S256. [Abstract](#)