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The effects of multiple coronary artery disease risk factors on subclinical atherosclerosis in a rural population in the United States

Hadii M. Mamudu [a,*], Timir K. Paul [b], Liang Wang [c], Sreenivas P. Veeranki [d], Hemang B. Panchal [e], Arsham Alamian [c], Kamrie Sarnosky [c], Matthew Budoff [f]

[a] Department of Health Services Management and Policy, College of Public Health, East Tennessee State University, P.O. Box 70264, Johnson City, TN, United States
[b] Division of Cardiology, James. H. Quillen College of Medicine, East Tennessee State University, 329 N State of Franklin Rd, Johnson City, TN 37604, United States
[c] Department of Biostatistics and Epidemiology, College of Public Health, East Tennessee State University, United States
[d] Department of Preventive Medicine and Community Health, University of Texas Medical Branch, Galveston, TX, United States
[e] Department of Internal Medicine, James H. Quillen College of Medicine, East Tennessee State University, Johnson City, TN 37604, United States
[f] Los Angeles Biomedical Research Institute, 1124 W Carson Street, Torrance, CA 90502, United States

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ABSTRACT

Introduction. The risk factors for cardiovascular disease (CVD) are associated with coronary atherosclerosis and having multiple risk factors potentiates atherosclerosis. This study examined the prevalence of multiple biological and lifestyle/behavioral risk factors and their association with coronary artery calcium (CAC), a marker for subclinical coronary atherosclerosis.

Methods. This is a cross-sectional study of 1607 community-dwelling asymptomatic individuals from central Appalachia who participated in CAC screening between January 2011 and December 2012. Data on demographics (sex and age) and 7 traditional risk factors for coronary artery disease (CAD) were collected and categorized into 5 groups (0–1, 2, 3, 4, and ≥5). Prevalence of these risk factors and CAC scores (0, 1–99, 100–399, ≥400) were assessed, and the impact of the number of risk factors on CAC scores were delineated using multiple logistic regression.

Results. Over 98% of participants had ≥1 risk factor. While obesity, diabetes, hypertension, and family history of CAD significantly increased the odds of having CAC, CAC scores significantly increased with number of risk factors. After adjusting for demographic factors, having 3, 4, and ≥5 risk factors was significantly associated with increased odds of having higher CAC scores when compared to zero CAC score by more than one and half times [OR = 1.65, CI (1.20–2.25)], two times [OR = 2.32, CI (1.67–3.23)] and three times [OR = 3.45, CI (2.42–4.92)], respectively.

Conclusion. The high prevalence of multiple risk factors in the study population suggests the need for aggressive multiple risk factors interventions for primary prevention of CAD, which could address CVD health disparities.

1. Introduction

Cardiovascular diseases (CVD) remain the leading cause of morbidity and mortality in the United States (US), accounting for 1 in 3 deaths and contributing to over $300 billion in direct and indirect annual healthcare costs. These costs are expected to reach over $900 billion by 2030 (Mozaffarian et al., 2015). The American Heart Association (AHA) has identified 7 ideal metrics (4 health behaviors — absence of smoking/tobacco use, physical activity, healthy diet, and maintaining normal weight; 3 biological factors/conditions — controlling hypertension, hypercholesterolemia, and fasting blood glucose) to improve and control CVD risk factors to address this public health burden (Mozaffarian et al., 2015). Research suggests that 80–90% of patients with coronary artery disease (CAD) have at least 1 of the 4 modifiable risk factors (diabetes, hypertension, hypercholesterolemia, and smoking) (Canto et al., 2011; Khot et al., 2003; Greenland et al., 2003) and multiple risk factors are associated with increased risk for CAD, compared to a single risk factor (Berrigan et al., 2003; Yusuf et al., 2004). As such, there is a critical need for investigation into how the co-existence of these risk factors in individuals affects the risk for CAD.

Atherosclerosis is the underlying cause of many CVD that takes several years to manifest into clinical events such as acute myocardial infarction or sudden cardiac death (Toth, 2008) and multiple risk factors potentiate atherosclerosis (Berenson et al., 1998; Urbina et al., 2005;

* Corresponding author.
E-mail addresses: mamudu@etsu.edu (H.M. Mamudu), pault@etsu.edu (T.K. Paul), WANGL2@etsu.edu (L. Wang), spveeran@utmb.edu (S.P. Veeranki), hemangbpanchal@gmail.com (H.B. Panchal), ALAMIAN@etsu.edu (A. Alamian), sarnosky@goldmail.etsu.edu (K. Sarnosky), mbudoff@labiomed.org (M. Budoff).

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Paul et al., 2005). Because risk assessment tools based on traditional CVD risk factors often underestimate risks in patients with subclinical coronary disease, (Toth, 2008; Budoff, 2003) clinical guidelines have indicated the potential use of markers of subclinical atherosclerosis such as coronary artery calcium (CAC) to overcome the shortcomings of risk prediction by such global risk assessment tools (Mozaffarian et al., 2015). Previous studies have established that the presence of calcification in coronary arteries is a quantifiable marker for coronary atherosclerosis and shows increased risk of CAD (Agatston et al., 1990; Chu et al., 2009). The detection of CAC is valuable in diagnosing CAD and has prognostic value for future coronary events among symptomatic and asymptomatic patients (Janne d'Othee et al., 2008; Stein et al., 2008; Ardehali et al., 2007) as Framingham risk assessment scores predict only 60–65% of hard cardiac events, including acute myocardial infarction (Budoff, 2003). Although studies using different populations have found a strong relationship between CAC and traditional risk-factors for CAD such as demographics (e.g., age), biological (e.g., hypertension) and lifestyle/behavioral (e.g., smoking) (Pletcher et al., 2004; Taylor et al., 2006; Goel et al., 1992), little data is available on the relationship between the co-existence (a composite) of these risk factors and CAC. The paucity of this research on subclinical atherosclerosis is even more in rural areas of the US, including Appalachia (Mensah et al., 2005; Melvin et al., 2013).

The Appalachian region involves 420 counties across 13 states and consists of mostly rural, hard-to-reach, disadvantaged, and underserved populations in isolated and mountainous areas of the US. The region is characterized by high economic distress. Poor health, and health disparities (Mensah et al., 2005; Melvin et al., 2013), which implies that achieving the US public health goal of reducing health disparities in diseases such as CVD requires addressing health issues confronted by people in the region. In this regard, the study aimed to: 1) assess the prevalence of multiple CAD risk factors, and 2) determine the association between the number of risk factors and subclinical atherosclerosis (i.e., CAC) in a predominantly rural population. It is hypothesized that a majority of the participants in the CAC screening will have ≥1 CAD risk factor and that the number of risk factors will be associated with positive and higher CAC scores. Profiling patients for subclinical atherosclerosis through the presence of risk factors could lead to early identification of higher risk individuals for early intervention and prevention of CAD events. Thus, this study on multiple CAD risk factors in an asymptomatic rural hard-to-reach population would provide insight on how to develop preventive strategies for the control of CAD. Ultimately, this study will contribute to efforts addressing CAD-related morbidity and mortality and CVD health disparities (Mensah et al., 2005; Ezzati et al., 2002) as articulated in the US Centers of Disease Prevention and Control (CDC)'s *Healthy People 2020* and AHA's Impact Goals (Lloyd-Jones et al., 2010).

2. Methods

2.1. Study population

The detailed description of this population and recruitment procedures was published in an earlier study (Mamudu et al., 2015). Briefly, the study participants consisted of asymptomatic individuals without prior history of CVD or taking medications to control CVD risk factors from the central Appalachian region of northeast Tennessee, western North Carolina, southeast Kentucky, and southwest Virginia. This region is characterized by the highest economic distress, poor healthcare services, high educational and health disparities, and geographic isolation in the U.S. (Griffith et al., 2011). The participants, both self- and physician-referred, were assessed for eligibility using standard protocol and had CAC screening using computed tomography (CT) at the largest tertiary heart institute in the region between January 2011 and December 2012 to determine their status of coronary artery and risks for CAD. Before undergoing a CT scan, each participant completed a baseline questionnaire, which collected information on demographics, health conditions, current health behaviors, and family history of CAD. A total of 1701 individuals participated in the screening and nonwhites were excluded from the study because of the small sample size ($n = 8$; 0.47%). However, participants with missing data for CAC score ($n = 19$; 1.11%) and risk factors ($n = 67$; 3.94%) were excluded. The final study sample was 1607. There was no significant difference in demographic characteristics (sex, age) in the excluded sample and analytic sample that seems representative of the central Appalachian region. This study was approved by the Institutional Review Boards of the authors' university and the collaborating hospital system.

2.2. Variables and measurements

2.2.1. Dependent variable: coronary artery calcium score

The dependent variable was CAC score, which was ascertained using CT, a diagnostic tool for identification of CAC. All CT scans were performed using a 64-slice multi-detector CT scanner based on a standard procedure and protocol for identifying and assessing CAC. After the procedure, the person was given his/her CAC score based on the Agatston method (Agatston et al., 1990), which quantifies the volume of calcification (calculated as the product of the area of calcification per coronary tomographic segment and a factor rated 1 through 4 depending on the maximal x-ray density in that segment) and categorizes CAC based on the severity of risk for CAD as 0 (zero), 1–99, 100–399, and ≥400. The study utilized this standard Agatston scale for the bivariate and multivariate analyses.

2.2.2. Independent variables

Previous studies have examined clustering of biological risk factors (or medical conditions) (Berenson et al., 1998; Raitakari et al., 1994; Twisk et al., 2001) and lifestyle-behavior-related health risk factors (Berrigan et al., 2003; Raitakari et al., 1994; Fine et al., 2004; Pronk et al., 2004). Based on this literature, the study included 9 self-reported CAD risk factors as independent variables: 2 demographic factors (age, sex), 4 biological factors (obesity, diabetes, hypercholesterolemia, and hypertension), 2 lifestyle/behavioral factors (smoking status and sedentary lifestyle), and family history of CAD. The demographic factors were obtained by asking participants in the screening to self-identify their sex (male or female) and provide their age and date of birth to determine their age at the time of the screening. The biological factors were ascertained by asking participants whether they had been informed by their physicians or health professionals that they have any of the conditions (diabetes, hypercholesterolemia, and hypertension; yes/no) and/or are taking medication for such conditions. Body mass index (BMI; kg/m^2), used to determine whether the participant was obese (yes, if BMI ≥ 30 kg/m^2), was calculated based on self-reported height and weight. Smoking status was determined by asking a participant to indicate whether she/he is current, former, or never smoker. The participants were asked to report whether or not they consider themselves as having a sedentary lifestyle (yes/no). For family history of CAD, a participant was asked whether she/he knows or is aware of anyone in her/his family (immediate and extended) with any coronary artery disease (e.g., heart attack, stent, angioplasty, and bypass surgery; yes/no). While sex, smoking status, and other risk factor variables were measured on a nominal scale (yes/no), age (in years) was measured an interval (mean ± SD) and ordinal scales.

2.3. Statistical analysis

Descriptive statistics, including frequencies and percentages were summarized for sample characteristics according to the prevalence of the number of CAD risk factors in the study (0 to 7) and the demographic and CAD risk factors. Bivariate analyses between CAC scores