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Cardiovascular Disease Among Alaska Native Peoples

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Abstract

Although Alaska Native peoples were thought to be protected from cardiovascular disease (CVD), data now show that this is not the case, despite traditional lifestyles and high omega-3 fatty acid intake. In this article, the current understanding of CVD and its risk factors among Alaska Native peoples, particularly among the Yupik and Inupiat populations, will be discussed, using data from three major studies funded by the National Institutes of Health: Genetics of Coronary Artery Disease among Alaska Natives (GOCADAN), Center for Native Health Research (CANHR), and Education and Research Towards Health (EARTH). Data from these epidemiologic studies have focused concern on CVD and its risk factors among Alaska Native peoples. This review will summarize the findings of these three principal studies and will suggest future directions for research and clinical practice.

Keywords

Cardiovascular disease; Epidemiology; Coronary heart disease; Stroke; Alaska natives; Eskimos; Review

Introduction

Data from major epidemiologic studies have focused concern on CVD and its risk factors among Alaska Native peoples. Alaska is composed of diverse groups of Alaska Native people that are often subdivided within geographic regions, and villages are within these regions. Inupiat (Inupiaq) inhabit the northern and northwestern coastal regions; Yupik live in the southwestern regions (Central Yupik) and on St Lawrence Island (Siberian Yupik), which is in the Bering Strait between the coasts of Alaska and Siberia. Athabaskan Indians reside in the interior of the state, and the coastal Indians (Tlingit, Haida, and Tsimshian) inhabit southeastern coastal Alaska. Aleuts include residents of the Aleutian Islands, the Pribilof Islands, the western tip of the Alaska Peninsula, the Kodiak area, and the coastal regions of south-central Alaska. In the 2010 Census, about 15% of Alaska's state population

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(104,871 people) self-identified as American Indian or Alaska Native.[2] Of these, approximately 95% (99,561 people) also self-identified as being from one of the following Alaska Native groups: Inupiat, Yupik Alaskan Athabaskan, Tlingit, Haida, Tsimshian, or Aleut.[3]

Early Danish researchers found low rates of cardiovascular disease (CVD) among Eskimos in Greenland, which they attributed to high intake of marine oils.[4, 5] This belief was extrapolated to Alaska Native peoples for many years. However, in 2003, a comprehensive review of CVD and its risk factors among Alaska Native people, suggested trends toward increasing occurrence of atherosclerotic disease.[6] The authors reviewed not only published work, but death certificates, non-archival presentations, and reports from the Alaska Native Tribal Health Consortium, the Alaska Division of Public Health, and the Alaska Area Indian Health Service.[6] The CVD increase was thought to be related to the high prevalence of cigarette smoking, ongoing lifestyle changes that favored physical inactivity, and consumption of non-marine fatty acids, leading to an increase in obesity and diabetes.[6]

The 9 years subsequent to the 2003 review have been marked by larger and more rigorous epidemiologic studies, continued population surveillance data, and improved registries. The current review focuses on these more recent epidemiologic studies of CVD and its risk factors among Alaska Native peoples and suggests future directions for research and clinical practice.

Epidemiologic studies

The Alaska Siberia Project (ASP) was among the earliest epidemiologic studies of CVD in Alaska Native people to use thorough and validated methods to assess prevalent CVD and its risk factors.[7] This cross-sectional 1994 survey, which recruited >50% of residents, ≥ age 25 years, from four villages [one Inupiat (n=109), one Central Yupik (n=106), and two Siberian Yupik (n=239); total n=459] in the Bering Straits Region of northwestern Alaska, was modeled after the Strong Heart Study (SHS),[8] which was being conducted among American Indians in the continental United States.

The subsequent and larger NHLBI-funded Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN) study included methods identical to SHS/ASP, as well as measures of subclinical atherosclerosis, additional biomarkers, and longitudinal surveillance to investigate the genetic and nongenetic determinants of CVD and its risk factors in a population-based study of 1,214 predominantly Inupiat participants from the Norton Sound region on the Northwest coast of Alaska. Participants completed interviewer-administered surveys of demographic and medical history and underwent physical examinations, including the collection of blood, urine, anthropometric measurements, and carotid ultrasound examinations during baseline (2000–2004) and follow-up (2006–2010) examinations.[9]

In 2001, the National Cancer Institute funded three centers to test the feasibility of establishing a cohort of American Indians and Alaska Native people to examine the effects of lifestyle and clinical risk factors on the development of chronic diseases.[10] The study became known as the Education and Research Towards Health (EARTH) study. One of the three centers was in Alaska. The Alaska EARTH study recruited Alaska Native people to participate from several regions in Alaska, providing a diverse representation of people in the Yukon-Kuskokwim (YK) Delta, southeastern Alaska, and Anchorage areas. Of these, more than 1000 were Yupik, predominantly from the YK Delta. Data were collected on diet, physical activity, lifestyle and cultural practices, and medical and family history. Limited physical measurements included height, weight, waist and hip circumferences, oscillometric blood pressure, and point-of-care lipid and glucose measurements.[10]

Also in 2001, the National Center Research Resources established the Center for Alaska Native Health Research (CANHR), which focused on risk factors as well as protective factors for obesity and chronic diseases, including CVD.[11, 12] Between 2003 and 2006, CANHR obtained biological, genetic, nutritional, and psychosocial data from examinations of nearly 1000 Alaska Native people, >age 14 years, from ten communities in the YK Delta.[11, 12]

Cardiovascular Disease

Subclinical atherosclerosis, coronary heart disease, and stroke data obtained from the three systematic epidemiologic studies described above plus reliable registry or mortality data where applicable will be discussed in this article. High rates of rheumatic heart disease and infective endocarditis have been described among Alaska Native people but will not be covered in this review.[6, 13] Furthermore, data on heart failure are limited and will not be discussed.[14]

Subclinical Atherosclerosis

Subclinical atherosclerosis, detected by carotid artery ultrasound and assessed as either intima-media thickness (IMT) or plaque burden, correlates with CVD risk factors and with both prevalent and incident CVD in large population-based studies, and improves CVD prediction in asymptomatic individuals at intermediate cardiovascular risk.[15–1920] In the SHS of American Indians, plaque score was a better predictor of CVD events than IMT in individuals without preexisting CVD, regardless of diabetes and hypertension status.[21]

GOCADAN is the only study among Alaska Native people that includes measures of subclinical atherosclerosis. Among GOCADAN participants, the age-adjusted prevalence of carotid atherosclerosis exceeded that of U.S. black and white population-based samples.[22] Over 90% of GOCADAN participants (n=1,131) had plaque score assessments, and plaque (in one or more of the eight carotid segments studied) was found in 34% (n=384) of participants.[23] Because over two-thirds of GOCADAN participants reported being current or former smokers, the high rate of smoking likely contributes to the CVD rate, as use of tobacco is independently associated with plaque in participants >45 years of age.[23] Similarly, carotid plaque was associated with higher LDL cholesterol (LDL-C), smaller LDL particles and smaller very low-density lipoprotein (VLDL) particles, and a smaller VLDL particle size.[24] IMT was significantly associated with higher LDL-C and total LDL particle concentration, independently of other traditional cardiovascular risk factors, including current smoking status.[24] However, neither IMT nor plaque score was associated with HDL cholesterol (HDL-C) or with HDL subfraction concentrations.[24] Contrary to expectations, there was no (protective) association of omega-3 fatty acid consumption with plaque prevalence, although there was a negative association with IMT.[25] A positive association between plaque and intake of saturated fats was observed.[25]

Coronary Heart Disease

Until recently, the only population-based data on cardiovascular events were derived from self-report or administrative databases. In contrast, GOCADAN included electrocardiograms and standardized review and adjudication of all cardiovascular events and deaths.[14] Among the 500 GOCADAN participants > age 45, definite coronary heart disease (CHD), defined by either an acute myocardial infarction or a coronary revascularization procedure, was found in 4% (n=20).[14] CHD prevalence was higher in men compared with women (prevalence ratio of 2.47 [1.00–6.09]); however, definite myocardial infarction prevalence was low in both sexes, with less than ten participants meeting criteria.[14]

Prior to GOCADAN, the ASP had begun to re-address the hypothesis that diets rich in omega-3 fatty acid were associated with less CHD. In the ASP, 450 Alaska Native people were screened for CHD using a standardized protocol, and only 6% of the cohort <age 55 years, and 26% of those > age 55 years, had CHD, and no associations were observed between omega-3 fatty acid consumption or plasma concentrations and prevalent CHD.[26]

Recently, an examination of national mortality rates using the NCI's Surveillance Epidemiology and End Results (SEER) program, found that heart disease (as defined by International Classification of Diseases [ICD-10] codes) was the second leading cause of death among Alaska Native people, after cancer.[27] The heart disease mortality rates for Alaska Native people were lower than those for U.S. Whites (270.6 vs. 304.6, 169.5 vs. 197.1, and 210.4 vs. 243.6 per 100,000; for men, women, and overall, respectively), although these differences only reached significance ($p<0.05$) for Alaska Native women.[27] Heart disease mortality for Alaska Native people declined 25% between 1979 and 2003, compared with a 39% decline for U.S. Whites; most of the decline was observed between 1999–2003.[27] Some of this decline may be due to improved survival and treatment of CHD among the general population.[28]

Stroke

Stroke, or cerebrovascular disease, is the fourth leading cause of death in the U.S., with Indian Health Service data suggesting higher than expected stroke rates among Alaska Native people, similar to observations among other Inuit populations.[29–32]

Stroke prevalence, based on adjudicated events at the GOCADAN baseline exam, was 6% in men and about 2% in women > age 45 years, similar to the prevalence of CHD and higher than expected for the average age.[14] This is consistent with recent SEER mortality data which found that cerebrovascular disease was the fifth leading cause of death between 1999–2003, with a 30% higher rate of death due to cerebrovascular disease for Alaska Native people compared with U.S. whites (77.9 vs. 56.6 and 65.2 vs. 54.1 per 100,000, for men and women, respectively), although this difference was only significant in men.[27] Alaska death certificate data suggest no significant decline in stroke mortality among Alaska Native people between 1984 and 2003.[33] Stroke mortality, compared with U.S. Whites, was highest in Alaska Native women of all age groups and in Alaska Native men < age 45 years.[33] Unfortunately, data are not available stratified by Alaska Native groups.

Cardiovascular Disease Risk Factors

Hypertension

Hypertension is an independent risk factor for CVD.[34, 35] Standardized blood pressures, by auscultation with a mercury sphygmomanometer, were measured in GOCADAN, where hypertension was defined as systolic blood pressure (SBP) ≥140 mm Hg, diastolic blood pressure (DBP) ≥90 mm Hg, or currently taking anti-hypertensive medication.[9] Approximately 20% of the 1108 GOCADAN participants with available data had hypertension at baseline, with age-standardized prevalence being higher in men (29%) than in women (25%).[36] Hypertension prevalence increased with participant age; prevalence data from the GOCADAN baseline exam in Alaska Native people were similar to that of U.S. Whites but lower than that of American Indians.[36]

Additionally, the GOCADAN described sex-specific associations of nutritional factors with prevalent hypertension and SBP.[37] After covariate adjustment, men not taking antihypertensive medication had significantly higher average SBP with increasing quartiles of dietary trans fatty acid (p for linear trend=0.01) and sodium intakes (p for linear trend=0.02). In women not taking antihypertensive medication, average SBP decreased with increasing quartiles of omega-3 fatty acid intake, even after adjustment (p for linear trend <0.01).[37]

In EARTH, oscillometric BP was measured in a standardized manner. In an EARTH study examining risk factors for chronic disease, hypertension was defined as SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg and overall was found to be less prevalent than the other studies, occurring in only 13% (n=195) of men and 11% (n=255) of women.[38] However, this rate may be an underestimation because it included all participants, even those with self-reported hypertension. Furthermore, the EARTH study did not assess use of hypertension medication, which may have influenced BP values. As expected, hypertension prevalence increased with participant age, although with an apparent sex disparity in this EARTH study, in which hypertension was found in 29% (n=81) of women and only 22% of men (n=30) aged ≥ 60 years.[38]

In CAHNR, BP measurement methods were similar to those in EARTH, although hypertension prevalence was not reported. Abnormally elevated values were defined as SBP ≥ 130 mm Hg and/or DBP ≥ 85 mm Hg. Of the 710 CANHR participants, 23% had an abnormal SBP reading and 10% had an abnormal DBP reading.[39] When stratified by sex, men had a higher prevalence of abnormal SBP (26% vs 20%) compared with women, who had a somewhat higher prevalence of abnormal DBP (11% vs 9%) compared with men.[39]

Lipids

In GOCADAN, fasting lipid profiles were obtained from participants via venipuncture and were analyzed in a central laboratory with standardized assays.[9] Of 1026 participants, 48% had high total cholesterol (≥ 200 mg/dL), 32% had high LDL-C (≥ 130 mg/dL), 26% had high triglycerides (≥ 150 mg/dL), and 11% had low HDL-C (≤ 40 mg/dL).[40] Among GOCADAN participants ≥ ages 45 years (n=499), 34% (n=71) of men and 40% (n=115) of women had hyperlipidemia, defined as LDL-C > 160 mg/dL, non-HDL-C >190 mg/dL, Apo-B>120 mg/dL, or taking lipid lowering medications.[14]

In the CAHNR study, fasting lipid panels also were obtained via venipuncture and analyzed in a central laboratory.[39] Compared with the U.S. general population, mean total cholesterol was higher among CANHR participants (220 vs 203 mg/dL).[39] Fewer than 10% of the participants had elevated triglycerides (≥ 150 mg/dL) and 13% had low HDL (≤ 40 mg/dL for men and ≤50 mg/dL for women).[39]

In the EARTH study, fasting lipid measures were determined from finger-stick whole blood specimens obtained from point-of-care testing.[10] Of the 3822 participants with fasting lipid data, 40% had high total cholesterol (≥ 200 mg/dL), 26% had high LDL-C (≥ 130 mg/dL), 28% had high triglycerides (≥ 150 mg/dL), and 19% had low HDL-C (≤ 40 mg/dL).[38] More lipid abnormalities were found among men compared with women and among those who were older.[38]

Obesity

Age-adjusted prevalence of obesity in the United States during 2007–2008 was 33.8% overall, 32.2% among men, and 35.5% among women.[41] Earlier, the ASP study of Inupiat and Yupik participants from four villages in the Bering Straits Region of northwestern Alaska had found that 33% of the women were obese, body mass index (BMI) ≥ 30 kg/m^2, compared with 16% of the men.[42]

More recently, the GOCADAN study found that almost a third, or 30% of the 1026 participants were obese and another 31% were overweight (BMI 25–29 kg/m^2).[40] Similar to the gender differences found in the ASP, 37% (n=602) of the women in the GOCADAN study were obese, compared with 20% (n=456) of the men.[37] Likewise, in CANHR, nearly a third or 32% of the 753 participants were obese and another 33% were overweight.[12]

In the EARTH study, the prevalence of obesity, also defined as BMI ≥ 30 kg/m^2, was even higher at 51%. These data were from 3822 Alaska Native people, representing many Alaska Native groups.[38] More women (60%) than men (38%) met the criteria for obesity.[38] Taken together, the data suggest that obesity rates for Inupiat and Yupik are lower than among other Alaska Native people and, for men, are lower than those of U.S. whites.

Diabetes/Metabolic Syndrome

In the GOCADAN study, among the 1189 who underwent standardized oral glucose tolerance testing, overall diabetes prevalence was low, (5.0%, 2.2%, and 3.8%, respectively, in women, men, and overall.[43] Diabetes prevalence was similarly low, 3.3% overall among 753 adult participants in the CANHR study, where diabetes was defined by self-report, use of hypoglycemic medication, or based on American Diabetes Association fasting glucose criteria.[12] However, diabetes prevalence was slightly higher (5.4% overall) in the EARTH study, with no significant differences found between the sexes.[38] In contrast, the prevalence of diabetes had been more than twice as high among the Siberian Yupik (9.6%) as among the Central Yupik (2.8%) and Inupiat participants (3.7%) in the earlier ASP, in which overall diabetes prevalence in women was about double that in men (8.8 vs 4.2%).[7] Despite a possible variability among Alaska Native groups, all of these rates appear exceedingly low compared with American Indian groups in the continental United States, where prevalence is reaching epidemic proportions, and are likewise low compared with U.S. Whites[44]

Metabolic syndrome is diagnosed, according to ATP III criteria, if three or more of the following criteria are met: an abnormal waist circumference; elevated triglycerides; low HDL-C; arterial hypertension (SBP ≥ 130 mmHg, DBP ≥ 85 mmHg); or impaired fasting glucose (≥100 mg/dL).[45] The U.S. prevalence of metabolic syndrome from 1999–2006 was found to be 34% overall, 35% among women and 33% among men.[46]

In contrast, prevalence of metabolic syndrome in the CANHR study was low, 15% (9% among men and 20% among women).[39] Correspondingly, the overall prevalence of metabolic syndrome in the GOCADAN study also was low, 14% overall (11% men, 17% women).[47] Additionally, GOCADAN participants with metabolic syndrome had an associated spectrum of VLDL, LDL, and HDL distribution and size abnormalities, independent of age, BMI, systolic BP, smoking, and lipid concentrations.[48] Insulin resistance may be a major determinant of these lipoprotein subfraction abnormalities.[48]

Concern has been voiced for nearly 2 decades that increases in diabetes and CVD among Alaska Native people may be related to lifestyle changes, including decreased physical activity (e.g., as dog sledding is supplanted by use of snow mobiles) and by changes from traditional to non-traditional diets, which are higher in calories, saturated fat, and sugar.[49–51] Indeed, consumption of a traditional diet was related to a better profile of cardiovascular risk factors in GOCADAN.[52] Similarly, in CANHR, diets emphasizing traditional Alaska Native foods were associated with a fatty acid profile promoting greater cardiovascular health than diets emphasizing Western foods.[53]

A population-based Alaska Native Diabetes Registry, including all people with diabetes who receive care through the Alaska Tribal Health System, was established in the 1980s.[54] Registry data show a dramatic increase in the prevalence of diabetes across all native groups from about 17 per 1000 persons to 47 per 1000 persons between 1985 and 2006.[54] Broken down by groups, diabetes prevalence increased from 9.6 to 34.3/1000, 24.2 to 52.4/1000, and 30.2–89.8/1000 for Inupiat and Yupik, Tlingit/Haida/Tsmishian/Athabascan, and Aleut, respectively. Thus, rates appear to be increasing in all groups, although they remain lower among the Inupiat and Yupik.[54]

Given the dramatic and ongoing increases in prevalence of impaired fasting glucose, or prediabetes, among Alaska Native People in multiple studies, increased urgency is called for in the design and implementation of culturally appropriate community-based interventions to improve diet, increase physical activity, and prevent diabetes.[7, 38, 43, 49, 50]

Tobacco Use—Tobacco is not part of the traditional culture of the Alaska Native people, but was introduced with European contact.[55] However, tobacco use among Alaska Native people, both cigarette smoking and in smokeless or chewed form, is now high compared with the general U.S. population.[56, 57]

In EARTH, about a third of participants (35%, n=1207) reported current cigarette use and a quarter (27%, n=933) reported former smoking.[57] Similarly, 17% (n=678) reported current smokeless tobacco use and the same percentage (17%, n=677) reported former use of smokeless tobacco.[57] Even higher rates were found in the GOCADAN study, where 60% (n=721) of participants reported current cigarette use and an additional 21% (n=253) reported former smoking.[23] The overwhelming majority of current or former smokers reported smoking initiation by age 18 years, demonstrating the need for aggressive early tobacco prevention.[57]

Overall tobacco use in CANHR (>75%, n=853) was similar to that observed in the GOCADAN and EARTH populations.[58] Cultural differences in this cohort, however, appear to favor smokeless tobacco, as 47% reported exclusive use of smokeless tobacco compared with 28% who regularly smoked cigarettes.[58] Similarly, the CANHR study found differences in tobacco preference, with younger participants and men favoring cigarette smoking, while older participants and women favored smokeless tobacco.[58]

Because the high smoking rate is likely a major determinant of vascular disease, it is imperative that communities, clinicians, and researchers work together to design and implement culturally appropriate community-based interventions to discourage young people from using tobacco and to create effective smoking cessation programs to lower the smoking rates. Additionally, there was no data on secondhand smoke.

Fatty Acids

Polyunsaturated fatty acid intakes, particularly of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), differed significantly between participants maintaining a more traditional diet, who had higher EPA and DHA intake, compared with those consuming a more Western diet.[53] In a CANHR sub-study of 330 Yupik, high red blood cell EPA and DHA were associated with attenuated dyslipidemia profiles among overweight and obese persons.[59]

In GOCADAN, red blood cell levels of DHA and EPA were negatively associated with heart rate and may explain the relations between omega-3 fatty acid and ventricular arrhythmia and sudden death.[60] The GOCADAN study also found that saturated fatty acids were associated with insulin resistance and glucose intolerance.[61]

Kidney Disease

Thus far, only GOCADAN has measured albuminuria and chronic kidney disease (CKD), both known CVD risk factors, in Alaska Native people.[62, 63] Albuminuria (urine albumin to creatinine ratio ≥ 30 mg/g), was less prevalent among GOCADAN participants compared with the general U.S. population (6% vs 10%).[40] The prevalence of CKD (estimated glomerular filtration rate <60 mL min 1.73 m^2), was likewise low (7%), perhaps because of the lower burden of diabetes thus far.[64] Consistent with the GOCADAN data, the Alaska Native Diabetes Registry reports low rates of end-stage renal disease, again, differing from observations in several American Indian populations.[54]

Inflammation

It is thought that pathogen-triggered (particularly from H.pylori infection) autoimmunity may play a role in early atherosclerosis.[65] In GOCADAN, a high level of and lifelong persistence of multiple antibodies against cytomegalovirus, herpes simplex virus types 1 and 2, H.pylori, and Chlamydia pneumoniae were found among a subset of participants, suggesting high prevalence of chronic infection.[66] Further evidence of chronic infection has been obtained from Indian Health Service records showing high rates of gastric ulcers and H.pylori infections among Alaska Native people.[67] Close living quarters during much of the year may contribute to the chronic infections. Future work is needed to explore the potential relationship that chronic infection and inflammation may have in CVD risk in this population.

Genetics

Both GOCADAN and CANHR have included projects focused on the genetic epidemiology of CVD in the areas of lipids and metabolism,[68, 69] obesity,[70] and fatty acids.[71, 72] While the work in these areas among this unique and understudied population is promising, continued study is needed to understand not only the mechanisms of disease, but significance to the population in terms of risk reduction and outcomes, including CVD and death.

Striking in this review is the lack of adequately powered studies providing systematic assessment of CVD endpoints. Recognition of this void led to the 2009 funding, via the American Recovery and Reinvestment Act, of the Western Alaska Tribal Collaboration for Health (WATCH). WATCH is a unique collaboration between the CANHR, GOCADAN, and EARTH investigators to harmonize data and methods to improve cardiovascular surveillance and facilitate studies relating CVD risk factors and outcomes in Alaska Native people. Together, the three studies comprise a cohort of more than 6000 Alaska Native people, including approximately 3800 Inupiat and Yupik, living mostly in rural and remote villages in western and southwestern Alaska. Availability of a harmonized dataset and procedures for outcome ascertainment and adjudication will allow for better assessment and development of interventions to address the CVD health disparities affecting this unique population.

Summary and Future Directions

More recent epidemiologic studies of CVD and its risk factors among Alaska Native people reveal a higher than anticipated burden of CVD, especially stroke. Continued efforts are needed to decrease the risk factors for incident and progressive CVD, with particular attention to the high tobacco use and LDL-C levels. While obesity and diabetes rates are relatively low, changing lifestyle patterns point to rising rates of diabetes. As lifestyles change, a focus is needed on the prevention of CVD risk factors.

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