

Exploring Armenian Ethnicity as an Independent Risk Factor for Cardiovascular Disease: Findings from a Prospective Cohort of Patients in a County Hospital

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Abstract

Objectives: While several studies have examined the risk of cardiovascular disease (CVD) in larger racial and ethnic groups within the United States, limited information is available on smaller sub-populations, such as Armenians, with high rates of CVD in their home country. This study examined the association between Armenian ethnicity and a positive exercise treadmill test (ETT).

Design: Prospective cohort study of patients at a 377-bed county hospital in Los Angeles, California from 2008–2011.

Setting: All patients were interviewed at the time of ETT to assess their cardiovascular risk factors at the cardiac laboratory of the hospital.

Participants: 5,006 patients between 18–89 years of age, of whom 12.6% were of Armenian ethnicity and 54.4% were female.

Main Outcome Measure: ETT results as a proxy for CVD risk.

Results: After adjusting for cardiovascular risk factors, Armenian ethnicity was significantly associated with higher odds of positive ETT (OR = 1.40, $p = 0.01$). Known coronary artery disease CAD (OR = 2.28, $p < 0.01$), hyperlipidemia (OR = 1.37, $p < 0.01$), and hypertension (OR = 1.24, $p = 0.05$) were significantly associated with higher odds of a positive ETT. In subgroup analyses, hyperlipidemia was the only significant predictor of positive ETT (OR = 1.92, $p = 0.02$) among Armenians, while patient history of CAD (OR = 2.49, $p < 0.01$), hyperlipidemia (OR = 1.29, $p = 0.03$), and age (OR = 1.04, $p < 0.01$) were significant predictors among non-Armenians. Armenian ethnicity remained associated with higher odds of positive ETT (OR = 1.40, $p < 0.01$) when patients with CAD were excluded.

Conclusion: Armenian ethnicity may be an independent risk factor for CVD, influenced by the uniformity of the genetic pool and cultural and dietary exposures.

Keywords

race, ethnicity, exercise treadmill test, cardiovascular disease, coronary artery disease

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Introduction

The burden of cardiovascular disease (CVD) is disproportionately greater among certain racial/ethnic and socioeconomic subgroups of the United States (US) population.¹ Health disparities that contribute to poor health outcomes result from a number of complex factors such as income, education, genetic and physiological factors, access to care, and cultural

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behaviors.^{2–6} While several studies have examined the risk of CVD among larger racial and ethnic groups such as Hispanics and African Americans, limited information is available on smaller subgroups of the US population, such as Armenians.^{7–9} Because ethnic subgroups tend to concentrate geographically, identifying such risk factors could have an overall impact on community health outcomes and care delivery.^{10–12}

According to the World Health Organization (WHO), coronary heart disease deaths claimed 19,980 lives in Armenia, accounting for 54% of total deaths and placing Armenia 8th globally in percent deaths from coronary heart disease.¹³ Armenians in the US are exposed to different risk factors than Armenians living in Armenia, but share cultural, behavioral, and genetic predispositions. Thus, we sought to test the hypothesis that Armenians would be more likely to have positive exercise treadmill tests (ETTs) than non-Armenians at a hospital in Los Angeles, CA that serves a large Armenian community.

Methods

Patient population and data collection

Prospectively collected data on all adult patients who received an ETT from 2008–2011 at the Olive View-UCLA Medical Center (OVMC; Sylmar, CA) were used for this study. Patients were interviewed at the time of their ETT to determine CV risk factors such as sex, age, hypertension, hyperlipidemia, diabetes mellitus, coronary artery disease (CAD), tobacco use, and family history of CAD. The analysis was repeated excluding 155 patients who had established CAD to better assess risk of probable CAD based on ETT results. The data collected on CV risk factors are qualitative, and patient reported. ETT results were interpreted by cardiologists as normal or abnormal based on the presence of ischemic electrocardiogram changes and/or the presence of exertional chest pain. More specifically, Bruce Protocol was used to interpret the ETTs, chest pain and ST segment depressions of at least 1 mm (down-sloping or horizontal) were also considered positive. Patients were defined as Armenian or non-Armenian based on the etymology of Armenian surnames, which has previously been shown to be a reliable marker of Armenian descent.^{14–16} Specifically, patients with surnames ending with “-ian” and “-yan” were selected and reviewed by a native speaker. Given the possibility of some overlap with Iranian surnames ending in “-ian”, if the first name was not clearly recognized as an Armenian first name, the name was not classified as Armenian. This classification was reviewed by a native Farsi and Armenian speaker. For patients with multiple ETT visits, only the first ETT visit was

included in the study as it was deemed to have the highest utility as an estimator of CVD risk. The study was approved by the Institutional Review Board of the Olive View-UCLA Education and Research Institute.

Study location

OVMC is a 377-bed Los Angeles County hospital, which serves a population of 1,584,000 adults. Approximately 80% of patients treated in the OVMC emergency department list Spanish as their primary language. OVMC is located in a unique geographic area, serving as one of the main safety net hospital for the largest community of Armenians in the United States.¹⁷

Statistics

Demographic characteristics were described using frequencies and proportions for categorical variables and means and standard deviations for continuous variables. The bivariate association between Armenian ethnicity and a positive ETT was assessed using the Chi-square test. A multivariate logistic regression was used to examine the association between ETT and Armenian ethnicity after adjusting for patient reported CV risk factors including age, sex, hypertension, hyperlipidemia, diabetes mellitus, CAD, tobacco use, and family history of CAD.

Stratified analyses were conducted to assess predictors of positive ETT separately among the subgroup of Armenian patients and the subgroup of non-Armenian patients.

A significance level of $\alpha = 0.05$ was used for all statistical tests. All analyses were performed using STATAv13 (College Station, TX).

Results

Of 5,006 patients who received an ETT between 2008–2011 at OVMC, 629 (12.6%) were categorized as Armenian based on their last names. Baseline characteristics are reported in Table 1. The majority of patients were female (N=2,721; 54.4%) and the mean (\pm standard deviation) age was 53.0 (\pm 9.29) years. Hypertension (54.8%), hyperlipidemia (39.8%), and family history of CAD (27.0%) were the three most common risk factors encountered in the population. Notably, the majority of the patients (96.1%) did not have established CAD diagnosis at the time of the ETT. Compared to non-Armenian patients, Armenian patients were more likely to be smokers (37% vs 20%, $p < 0.01$) and male (55% vs 44%, $p < 0.01$), but were less likely to have diabetes (16% vs 25%, $p < 0.01$).

Table 1. Baseline demographic and clinical characteristics of the study population.

	All (N = 5,006)	Armenian (N = 629)	Non-Armenian (N = 4,377)	P-value ^a
Demographic variables				
Male - no. (%)	2,285 (45.65)	343 (54.53)	1,942 (44.37)	<0.01
Mean age - yrs (\pm SD)	53.03 (\pm 9.29)	52.70 (\pm 7.91)	53.08 (\pm 9.47)	0.35
Clinical variables				
Hypertension - no. (%)	2,744 (54.81)	330 (52.46)	2,414 (55.15)	0.21
Hyperlipidemia - no. (%)	1,993 (39.81)	273 (43.40)	1,720 (39.30)	0.05
Diabetes mellitus - no. (%)	1,177 (23.51)	100 (15.90)	1,077 (24.60)	<0.01
Coronary artery disease (%)	155 (3.10)	19 (3.02)	136 (3.11)	0.91
Tobacco use - no. (%)	1,118 (22.33)	233 (37.04)	885 (20.22)	<0.01
Family history of CAD- no. (%)	1,352 (27.01)	183 (29.10)	1,169 (26.71)	0.21

^aP-value comparing the Armenian vs. non-Armenian cohorts calculated using a Chi-square for categorical variables and t test continuous variables.

Table 2. Tabulation of positive ETT test results.

	All (N = 5,006)	Armenian (N = 629)	Non-Armenian (N = 4,377)	P-value ^a
Positive ETT - no. (%)	493 (9.85)	79 (12.56)	414 (9.46)	0.02

Abbreviations: ETT, exercise treadmill test.

^aP-value comparing the Armenian vs. non-Armenian cohorts calculated using the chi-square test.

A total of 493 (9.85%) patients had positive ETTs (Table 2), 272 had positive ischemic ECG changes, and the rest were symptomatic or were unable to continue due to chest pain, shortness of breath, or other exercise limiting factors. A significantly higher proportion of Armenians had positive ETTs compared to non-Armenian (12.6% vs. 9.5%; $p=0.02$). After adjustment for confounders, patients of Armenian ethnicity continued to have higher odds of positive ETT compared to non-Armenians (OR = 1.40, $p=0.01$). Age (OR = 1.04, $p<0.01$), hypertension (OR = 1.24, $p=0.05$), hyperlipidemia (OR = 1.37, $p=0.01$), and patient history of CAD (OR = 2.28, $p<0.01$) were also significantly associated with having a positive ETT (Table 3). However, gender, diabetes, tobacco use, and family history of CAD were not significantly associated with ETT result.

In stratified analyses conducted to assess predictors of positive ETT separately in subgroups defined by ethnicity (Table 4), hyperlipidemia was found to be the only statistically significant risk factor for a positive ETT (OR = 1.92, $p=0.02$) among Armenian patients. Among non-Armenian patients, patient history of CAD had the strongest relationship with positive ETT (OR = 2.49, $p<0.01$). Hyperlipidemia (OR = 1.29, $p=0.03$) and age (OR = 1.04, $p<0.01$) were also significant predictors of positive ETT in this subgroup.

In order to better assess the risk of probable CAD based on ETT results, the analyses was repeated in the cohort excluding patients with already established

CAD diagnosis ($n=155$) and the results were similar to the full study sample; Armenian ethnicity remained associated with higher odds of positive ETT compared to non-Armenian ethnicity (OR = 1.41, $p=0.01$). In this cohort, age (OR = 1.03, $p<0.01$) and hyperlipidemia (OR = 1.37, $p<0.01$) remained significantly associated with having a positive ETT while hypertension (OR = 1.23, 0.07) became marginally non-significant (Table 5).

Lastly, to further study the relationship between smoking and ETTs, given that 37% of Armenians in this cohort are smokers compared to 20.2% of non-Armenians, we performed a sensitivity analysis using the original multivariate logistic regression model amongst non-smokers, and Armenian ethnicity remained a significant predictor of positive ETTs (OR 1.43, $p=0.04$). Furthermore, to test the hypothesis that people with poor diets may also be more prone to smoking, we created an interaction term between smoking and hyperlipidemia, and found that Armenian ethnicity (OR 1.41, $p=0.01$) and hyperlipidemia (OR 1.51, $p<0.01$) both still remain significant predictors of positive ETTs.

Discussion

Our data suggest that Armenians living in Los Angeles have a higher prevalence of CVD, as estimated by positive ETTs, than non-Armenians, and that this association persists after adjusting for traditional CV risk factors. In fact, after excluding patients with known

Table 3. Multivariate logistic regression examining the association between positive ETT and Armenian ethnicity, adjusting for patient-reported cardiovascular risk factors (N = 5,006).

	OR (95% CI)	P-value
Armenian ethnicity (ref: all other ethnicities)	1.40 (1.07, 1.83)	0.01
Male sex	1.18 (0.97, 1.44)	0.10
Age ^a	1.04 (1.02, 1.05)	<0.01
Hypertension	1.24 (1.00, 1.55)	0.05
Hyperlipidemia	1.37 (1.11, 1.70)	<0.01
Diabetes mellitus	1.13 (0.91, 1.41)	0.27
Coronary artery disease	2.28 (1.54, 3.39)	<0.01
Tobacco use	0.99 (0.78, 1.26)	0.96
Family history of CAD	0.98 (0.79, 1.23)	0.89

Abbreviations: CAD, coronary artery disease; CI, confidence interval; OR, odds ratio.

^aOR estimated for a 1-unit increase in age.

Table 4. Stratified multivariate logistic regression examining the association between positive ETT and patient-reported cardiovascular risk factors separately in the subgroup of Armenian patients (N = 629) and non-Armenian patients (N = 4,377).

	Armenians		Non-Armenians	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Male sex	1.29 (0.76, 2.20)	0.35	1.16 (0.94, 1.44)	0.17
Age ^a	1.03 (0.99, 1.07)	0.10	1.04 (1.02, 1.05)	<0.01
Hypertension	1.55 (0.87, 2.73)	0.14	1.20 (0.94, 1.53)	0.14
Hyperlipidemia	1.92 (1.12, 3.30)	0.02	1.29 (1.02, 1.63)	0.03
Diabetes mellitus	1.25 (0.69, 2.27)	0.47	1.13 (0.89, 1.43)	0.33
Coronary artery disease	1.41 (0.46, 4.28)	0.55	2.49 (1.63, 3.80)	<0.01
Tobacco use	0.99 (0.58, 1.70)	0.96	0.99 (0.76, 1.29)	0.94
Family history of CAD	0.73 (0.41, 1.28)	0.27	1.04 (0.82, 1.32)	0.76

Abbreviations: CAD, coronary artery disease; CI, confidence interval; OR, odds ratio.

^aOR estimated for a 1-unit increase in age.

Table 5. Multivariate logistic regression examining the association between positive ETT and Armenian ethnicity, adjusting for patient-reported cardiovascular risk factors excluding patients with CAD (N = 4,851).

	OR (95% CI)	P-value
Armenian ethnicity (ref: all other ethnicities)	1.40 (1.07, 1.85)	0.01
Male sex	1.20 (0.98, 1.47)	0.08
Age ^a	1.04 (1.02, 1.05)	<0.01
Hypertension	1.23 (0.98, 1.54)	0.07
Hyperlipidemia	1.37 (1.10, 1.70)	<0.01
Diabetes mellitus	1.12 (0.89, 1.41)	0.34
Tobacco use	1.07 (0.83, 1.36)	0.61
Family history of CAD	0.97 (0.77, 1.21)	0.79

Abbreviations: CAD, coronary artery disease; CI, confidence interval; OR, odds ratio.

^aOR estimated for a 1-unit increase in age.

CAD, Armenian ethnicity was the strongest risk factor for a positive ETT.

According to the WHO,¹³ 92% of all deaths in Armenia are due to non-communicable disease and CVD is responsible for 54% of total mortality. A high proportion of people living in Armenia have CV risk factors: 47% of males and 2% of females are

smokers, 43.5% of males and 40.7% of females have hypertension, and 14.3% of males and 31.7% of females are obese. Since a large proportion of Armenians living in the US immigrated from Armenia, it can be expected that American Armenians have similar risk profiles to individuals living in Armenia.¹⁸

Determining that Armenian ethnicity is associated with positive ETT as an estimator of CVD risk is an important finding with implications for clinical practice and the implementation of preventive measures. This information will help in risk-stratifying Armenian patients with regard to CVD and CAD. Such classifications could further help with making patient-centered recommendations for different risk groups.

Stratified analyses were conducted to compare the subgroup of Armenian patients to the subgroup of non-Armenian patients in order to identify differences in risk factors between the two groups. Hyperlipidemia was the only risk factor significantly associated with positive ETT among Armenians. The OR for hyperlipidemia of 1.92 was higher than that seen in non-Armenians, 1.63. While the confidence intervals for the ORs between the two subgroups overlap, the higher magnitude of the OR and the upper confidence limit of 3.30 for Armenian patients suggests that hyperlipidemia may be a more important risk factor in Armenians than non-Armenians. This may be explained by poor dietary choices among Armenian patients that results in heavy consumption of saturated fats, red meat, alcohol, and carbohydrates. However, it may also suggest an underlying genetic predisposition for hyperlipidemia among Armenians that requires further exploration.

The odds ratios for male sex, diabetes, and hypertension have ORs greater than 1, which supports previous findings from other studies that show an association between these variables and CVD. While these ORs are not statistically significant, the magnitude of the ORs and the upper bound of the confidence intervals indicate that the results are compatible with a strong impact on CVD.

Despite the magnitude of the ORs and the upper bound of the confidence interval supporting the expected association between diabetes and a positive ETT, the fact that Armenians had a lower prevalence of diabetes compared to non-Armenians (15.9% vs. 24.6%) and a non-significant OR for the association between diabetes and positive ETT among the subgroup of Armenians may suggest that Armenian ethnicity, in and of itself, is a more important risk factor for possible CVD among Armenians.

Also, given the striking difference in smoking rates for Armenians vs non-Armenians (37% vs 20%), we performed a sensitivity analysis whereby we revisited the original multivariate logistic model and repeated the analysis for non-smokers only, decreasing the number of subjects from 5006 (all) to 3888 (non-smokers), and found that Armenian ethnicity still remains a significant predictor of positive ETTs (OR 1.43, $p=0.04$).

Further research is needed to explain the findings of this study and determine the role of biological, genetic, or epigenetic differences versus social disparities, cultural and health behaviors, and access to care. Previous research has shown the importance of lifestyle choices (including diet and physical activity), access to care, socioeconomic status (SES), and education as determinants of health. Data on these factors were not available for this analysis, and thus cultural and/or health behaviors, SES, and education level were not adjusted for when assessing the relationship between Armenian ethnicity and positive ETT.

Study limitations

This study has a number of limitations. First, patient-reported ethnicity was not used; rather ethnicity was retrospectively classified based on the etymology of Armenian names, leading to potential misclassification. However, the extent of misclassification is expected to be minimal due to the identifiable name suffixes used in Armenian last names (i.e., last names ending in “-ian”, “-yan”)¹⁵ together with unique Armenian first names which provide a reliable and specific marker of this particular ethnic group.

Second, results from this study may not be widely generalizable, as the select population of patients treated at OVMC may not represent Armenian patients treated in other hospitals, counties, or states across the US. In addition, the majority of patients treated at OVMC are Hispanic and of lower SES. As a comparator group, these patients may have a different CV risk profile than the general population in the United States. It should also be noted that patients were recruited in 2008–2011, despite prospective inclusion at the time of data collection, the period of inclusion can be considered outdated at this time and results may not apply to contemporary patients, due to possible lifestyle changes, improved medical care, and accessibility.

Third, it cannot be assumed that all ETTs included in the study were ordered to evaluate CAD. Thus, the assumption that ETT is a surrogate measure for CAD may not hold across all patients. In addition, due to its suboptimal sensitivity and specificity in diagnosing ischemic heart disease, ETT is a better clinical estimator of general cardiovascular risk rather than a CAD risk estimator.^{19,20} However, the same criteria were used to interpret all ETTs, which can mitigate this limitation by increasing inter-rater reliability. Furthermore, some patients may be more likely than others to acknowledge chest pain during the ETT which could render the test subjectively positive (i.e., based on symptoms) rather than objectively positive (i.e., based on ischemic electrocardiogram changes).

This analysis assumed an equal probability of such subjectivity with regards to symptoms for the average patient.

Fourth, the data on risk factors used for this analysis were patient-reported and thus subject to reporting error. For example, diagnoses of diabetes, hypertension, hyperlipidemia, and family history of CAD were not confirmed for each patient. Information to quantify the degree of tobacco exposure (i.e., pack-year history of smoking) was not available. However, all the ORs except for smoking and family history are greater than 1 suggesting the expected association between ETT result and traditional CV risk factors. This could be explained by the fact that smoking was considered as a binary variable ignoring the clear dose dependent relationship between smoking (i.e. packs per year) with CVD. Furthermore, it is difficult to confirm whether patients actually knew the exact cardiac history of their family members as they reported positive family histories of heart disease.

Lastly, as the study is limited by the information gathered in the database, there could be a significant amount of residual confounding by unidentified risk factors such as SES, diet, physical activity, obesity, and alcohol consumption. There are no data available regarding patient's medications that could influence the outcome of the stress test; however, this bias is partly mitigated in the analysis excluding patients with established CAD diagnosis (Table 5).

Conclusion

Patients of Armenian ethnicity may have a higher likelihood of having a positive ETT than non-Armenian patients, independent of traditional CV risk factors. Further research is needed to understand the role of cultural and/or genetic factors as underlying causes of this association. These findings are especially relevant for hospitals that serve a large population of Armenian patients, as this information will help in risk-stratifying Armenian patients (as is currently done for patients of other ethnicities) with regard to CVD and CAD.

Authors note

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Ethical approval

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Contributorship

Ara Rostomian MD, MBA, MPH: conception and design; collection, analysis, and interpretation of data; drafting of the manuscript and revising it critically for important intellectual content; revision and resubmission; final approval of the manuscript submitted. Jonathan Soverow MD, MPH: conception and design; revision of the manuscript for critically important intellectual content; final approval of the manuscript submitted. Daniel Sanchez MD: conception and design, interpretation of data; revision of the manuscript for critically important intellectual content; final approval of the manuscript submitted.

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