ALCOHOL CONSUMPTION AND SUBCLINICAL ATHEROSCLEROSIS AMONG SOUTH ASIANS: FINDINGS FROM THE MEDIATORS OF ATHEROSCLEROSIS IN SOUTH ASIANS LIVING IN AMERICA

BY

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LIST OF ABBREVIATIONS

AHA	American Heart Association
BMI	Body mass index
CAC	Coronary artery calcium
cIMT	Carotid intima-media thickness
CVD	Cardiovascular disease
CVH	Cardiovascular health
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
LS7	Life's simple 7
MASALA	Mediators of Atherosclerosis in South Asians Living in America
MESA	Multi-Ethnic Study of Atherosclerosis
METS	Metabolic equivalents

ABSTRACT

In this thesis, we will evaluate the association between alcohol consumption and subclinical atherosclerosis using surrogate markers including coronary artery calcium and carotid intima-media thickness in a unique cohort of South Asian population. South Asians have a higher cardiovascular disease (CVD) risk and higher proportionate mortality from cardiovascular disease compared with most other race/ethnic groups in the United States. Most epidemiological studies have shown an inverse association between alcohol and CVD. Although the cardioprotective association of light or moderate drinking are noted to be highly variable among the different races and ethnicities.

We hypothesized that light to moderate alcohol consumption compared with lifetime abstinence is associated with the decreased prevalence of CAC while moderate to high alcohol consumption is associated with higher CIMT among asymptomatic South Asians aged 40-84 years in the U.S. The first chapter of this thesis will be a literature review and will discuss the underlying mechanism of beneficial and harmful effect on alcohol consumption on CVD. The second chapter will be a manuscript of the association of alcohol consumption and subclinical atherosclerosis in South Asians. The third chapter is comprised of the ancillary studies and discussion of the association of alcohol consumption and ideal cardiovascular health assessed by the American Heart Association's Life's Simple 7 (LS7) health metrics among the South Asian population.

CHAPTER ONE: BACKGROUND

Introduction

Cardiovascular disease (CVD) accounts for more deaths than any other disease in the United States. About 610,000 people die of heart disease in the United States every year, accounting for 1 in every 3 deaths.[1] According to the American Heart Association (AHA), by 2030 43.9% of the US population is projected to have some form of CVD. AHA also estimated that between 2012 and 2030, total direct medical costs of CVD are projected to increase from $396 billion to $918 billion.[1] Due to population-level changes in risk factors and, more recently, improvements in health care, the mortality rate from CVD including heart disease, stroke, peripheral vascular disease, hypertension, and heart failure have decreased globally since 1990 mainly in developed countries.[2] Age-adjusted all CVD mortality rates declined from 2000 to 2014 for all CVD although a deflection point was observed in these trends in 2011, with a substantial slowing in decline from 2011 to 2014.[3]

Cardiovascular Disease (CVD) and Alcohol Consumption

Much of the evidence regarding alcohol consumption and its beneficial effects on the cardiovascular system derives from observational data. Epidemiological studies have been integral to this discussion, with multiple cohorts with cross-cultural and

geographical comparisons reaching similar conclusions.[4] As alcohol intake can lead to various adverse conditions that affect day-to-day life, international institutions and government have defined a unit called a "standard drink."[5,6] According to the 2015–2020 Dietary Guidelines for Americans, one standard drink is described as any beverage containing 14 g (0.6 fl oz) of pure alcohol. The following are reference beverages that are one alcoholic drink-equivalent: 12 fluid ounces of regular beer (5% alcohol), 5 fluid ounces of wine (12% alcohol), or 1.5 fluid ounces of 80 proof distilled spirits (40% alcohol).[7] Moderate alcohol consumption is defined as up to 1 drink per day for women and up to 2 drinks per day for men while binge drinking is a pattern of drinking that brings blood alcohol concentration (BAC) levels to 0.08 g/dL. This typically occurs after 4 drinks for women and 5 drinks for men—in about 2 hours.[6]

The relationship between alcohol consumption and CVD has always been intricate. Alcohol has both protective and detrimental effects on CVD.[8] Most studies to date have shown a J-shaped association of alcohol consumption where light to moderate drinkers have lower CVD risk than non-drinkers and heavy drinkers. A systemic review and meta-analysis in 2011 that included 84 studies showed that compared to non-drinkers, alcohol drinkers had 0.75 times risk for cardiovascular disease mortality and 0.71 times risk for incident coronary heart disease.[9] A recent 2017 meta-analysis of 45 cohort studies indicated significantly lower CVD risks for low- and medium-volume drinkers compared with abstainers.[10]

Although the evidence of a lower risk of CVD among light to moderate drinkers is substantial and consistent, controversy remains about the underlying mechanism by which alcohol consumption affects CVD. The dominant cause of many CVD is

atherosclerosis. Atherosclerosis, a systemic disease process in which fatty deposits, inflammation, cells, and scar tissue build up within the walls of arteries, is the underlying cause of the majority of clinical cardiovascular events.[1] There are biological and nonbiological factors associated with developing CVD including high cholesterol, tobacco smoking, obesity, genetic factors, diabetes, hypertension, physical inactivity, and psychosocial stressors.[1] To understand the relationship between alcohol consumption and CVD, we can examine its association with subclinical atherosclerosis.

Alcohol Consumption and Subclinical Atherosclerosis

Subclinical Atherosclerosis is a disease state where clinical manifestations of atherosclerosis are not present, and it is considered an independent risk factor for CVD. By examining the association between alcohol consumption and subclinical atherosclerosis measured by surrogate markers including coronary artery calcium score (CAC) and carotid intima-media thickness (cIMT), we can understand the relationship between alcohol consumption and CVD.

CAC score is obtained by electron-beam or multidetector computed tomography, which measure the calcium content in the coronary arteries. Scoring systems and thresholds for an elevated CAC score vary across studies, but the baseline comparison is often a CAC score of 0.[11] CAC scoring was not initially accepted as a screening tool for asymptomatic patients within the cardiovascular community. However, the 2010 American College of Cardiology/American Heart Association (ACC/AHA) guidelines on screening for coronary artery disease indicated that measurement of CAC is reasonable

(level of evidence B) for cardiovascular risk assessment in asymptomatic adults at Framingham intermediate risk (10 to 20 percent 10-year risk).[12] cIMT is a noninvasive measurement of the artery wall thickness, inclusive of atherosclerotic plaque, obtained using ultrasound imaging. cIMT assessed by ultrasonography of carotid arteries is a safe, non-expensive, feasible and accurate method for detecting subclinical atherosclerosis. cIMT values at or above the 75th percentile of a reference population indicate increased cardiovascular risk.[13]

Alcohol Consumption and Coronary Artery Calcium(CAC)

The studies examining the relationship between alcohol consumption and CAC have shown inconsistent results. Tofferi et al[14] used a cohort of 731 consecutive, consenting, active-duty US Army personnel (39 to 45 years of age) without known CVD. The result of this cross-sectional study found no relationship between the CAC score and the alcohol intake. It was one of the first studies focusing on the relation between alcohol consumption and CAC in a group at low risk for cardiovascular disease and with early atherosclerosis. The main limitations of this study were the relatively low prevalence of CAC and alcohol consumption and the inability to separate former drinkers from abstainers. Using CAC and atherosclerotic plaque in the aorta as surrogate markers of subclinical atherosclerosis, Ellison et al[15] investigated this relationship using data from a prospective cohort study including 3166 white and African American subjects with mean age around 55 years. The study result showed no evidence for a significant association between total alcohol intake and CAC, although there was a tendency for the increased

prevalence of CAC in the highest category of alcohol intake. Analyses of aortic calcification showed similar nonsignificant associations. There were several limitations to the study. The first weaknesses of the study included the fact that alcohol consumption was self-reported; further, there were very few heavy drinkers, and they did not have data on whether current nondrinkers were lifetime abstainers or ex-drinkers. The first large study to evaluate the association of alcohol with CAC in 4 racial-ethnic groups and to evaluate the progression of calcification, was done by McClelland et al.[16] The researchers studied the association between alcohol consumption and CAC prevalence, incidence and progression in The Multi-Ethnic Study of Atherosclerosis (MESA) which is a prospective community-based cohort study including 6814 participants aged 45–84 y who identified themselves as white, African American, Hispanic, or Chinese. The subjects were categorized as never drinkers, former drinkers, and current drinkers. Both current and former drinkers were asked about a number of years of drinking and the usual number of drinks consumed per week. The result showed that overall alcohol consumption was not associated with the prevalence of any CAC > 0 at baseline regardless of alcohol type. There was a trend for binge drinking to be associated with a slightly increased rate of prevalent CAC. Although light-to-moderate alcohol consumption was associated with lower coronary heart disease risk. The strengths of this study include its large sample size, prospective design, the inclusion of 4 racial-ethnic groups, and community-based nature.

In contrast to these studies, Vliegenthart et al[17] found a U-shaped association between alcohol consumption and CAC performing a cross-sectional analysis using data from the population-based Rotterdam Coronary Calcification Study. Data on alcohol

consumption were available for 1795 individuals without coronary heart disease. Compared with nondrinkers, the odds ratio of extensive coronary calcification was 0.60 for those who consumed 1 drink or less daily; 0.51 for those who consumed 1 to 2 drinks daily; and 0.90 (95% CI, 0.62-1.29) for those who consumed more than 2 drinks. The major limitation was that the data were not available on whether current nondrinkers were lifetime abstainers or former drinkers. By using prospective study design, Yang et al[18] tried to determine if alcohol intake was associated with reduced coronary risk in a high-risk asymptomatic population and whether this effect was independent of coronary risk factors and coronary calcium. In 1,196 asymptomatic subjects with coronary risk factors, investigator assessed alcohol consumption history, performed risk factor measurements, and quantified coronary calcium with electron beam computed tomography. These subjects were then followed for a mean of 41 months, and coronary events (myocardial infarction or coronary death) were noted. The study result showed that subjects with moderate alcohol consumption had a relative risk of 0.3 for developing coronary events. EBCT calcium scores in moderate drinkers were no different from calcium scores in abstainers. Subjects with coronary calcium were 3.1 times more likely to suffer a coronary event than those without calcium. The definition of moderate alcohol consumption was different at that time. Also, the study lacked detail data on alcohol consumption. Interestingly, Pletcher et al[19] found a dose-response relation between alcohol and CAC. The investigators used data from a longitudinal study of risk factors for coronary artery disease in a cohort of Black and White women and men (n = 5,115) aged 18–30 years who were healthy at the time of enrollment in 1985–1986. The study showed that the prevalence of coronary calcification was 8% for participants who consumed 0

drinks/week, 9% for 1–6 drinks/week, 13% for 7–13 drinks/week, and 19% for ≥14 drinks/week ($p < 0.001$ for trend). Odds ratios for having a CAC score in a higher category were 1.2 (95 percent CI:0.9, 1.7) for 1–6 drinks/week, 1.6 (95 percent CI: 1.1, 2.5) for 7–13 drinks/week, and 2.1 (95 percent CI: 1.4, 3.4) for ≥14 drinks/week (in comparison with 0 drinks/week) ($p < 0.001$ for trend). Stratification showed that this dose-response relation was most clearly in Black men. Study limitations included uncertainty about the degree to which findings in this young-to-middle-aged population would apply to older men and women and the suboptimal sample size for subgroup and interaction analysis. Also, this study lacked detailed data on drinking frequency, a potentially crucial factor in characterizing alcohol intake which could have led to potential differential misclassification bias. More recently Yun et al[20] conducted a cross-sectional study to examine whether alcohol flushing could be used as an instrumental variable (IV) and to investigate the effect of alcohol consumption on coronary calcification using alcohol flushing status as an IV. The study included a relatively young population of 24681 Koreans, with a mean age of around 40 years. The result showed that higher levels of alcohol consumption were associated with an increased risk of coronary calcification, especially among men. Doubled alcohol consumption was associated with a 10.9% increase in the likelihood of an elevated CAC score among men in the IV analysis adjusted for confounding variables, compared with a 3.9% increase in the multivariable analysis. Although, the alcohol flushing questions used in this study has not been validated by a genetic study.

In summary, the results of the studies to date examining the association between alcohol consumption and CAC have revealed no association, a U-shaped association, and a dose-response relationship.

Alcohol and Carotid Intima-Media Thickness (cIMT)

As stated previously, cIMT is another non-invasive measure that can be used as a surrogate marker of subclinical atherosclerosis. To address the relationship between alcohol consumption and carotid atherosclerosis in older adults, Mukamal et al[21] used data from the Cardiovascular Health Study (CHS) including 5888 adults aged 65 years and older. The result of this cross-sectional study found that relative to older adults who abstain from alcohol, consumption of 1 to 6 drinks per week had an inverse association with carotid atherosclerosis whereas consumption of 14 or more drinks had a positive association. The CHS participants represent a relatively healthy group of older adults, so the results are only generalized to older adults in similar health. Also, the investigators did not have detailed information on drinking patterns in this study. Kim et al[22] tried to find relationships between alcohol consumption and subclinical atherosclerosis in 5539 Korean subjects (2121 men and 3418 women) who were participants in the Multi-Rural Communities cohort (MRcohort) study. In contrast to previous studies, investigators used carotid artery intima-media wall thickness (CCA-IMT) and brachial-ankle pulse wave velocity (baPWV) as a measure of subclinical atherosclerosis. Carotid IMT quantitatively measures arterial morphology as affected by intimal lesions and medial hypertrophy; PWV reflects arterial stiffening as a result of structural and functional changes of the

vascular tree. Thus, the combination of these measures has been proposed to predict the clinically relevant burden of atherosclerosis. The result showed that the baPWV was positively correlated with alcohol consumption in men. On the other hand, CCA-IMT decreased with alcohol consumption in men. There was no clear relation between alcohol consumption and baPWV/CCA-IMT in women. The limitations of this study included limited generalizability of the finding given study subjects were only Korean who were strictly confined to rural areas. And again, as alcohol consumption was calculated based on self-reported data and hence there could be misclassification bias. Zyriax at al[23] conducted a cross-sectional study with the aim of investigating the relationship between alcohol intake and c-IMT in a selectively healthy population of the Stress Atherosclerosis and ECG Study (STRATEGY study). In this cross-sectional study, laboratory values, anthropometric data, nutrition habits, and physical activity were assessed in 106 men and 107 women, evenly distributed between 30 and 70 years. Carotid IMT was determined by B-mode ultrasonography according to the standardized protocol of the Study of Health in Pomerania. The results revealed a significant positive correlation between daily alcohol consumption and IMT in men, whereas in women the positive correlation was not significant. The type of beverage consumed did not affect this finding. Because of the sample size, the study may have been underpowered to detect an association between mean daily alcohol intake and IMT in women.

In summary, the studies to date examining the association between alcohol consumption and cIMT have found a positive correlation between alcohol consumption and cIMT, and this relationship seems to be different for men and women.

Mechanisms for Beneficial and Harmful Action of Alcohol

As we can see, the results of studies on the association between alcohol use and subclinical CVD are conflicting, and the explanation for these conflicting results is unclear. **Figure-1** depicts the potential mechanism of action by which moderate alcohol consumption lowers the risk of CVD. Moderate alcohol acts upon the liver and can, therefore, serve to directly increase the hepatic production and secretion of apolipoproteins and lipoprotein particles, increase triglyceride concentrations, and decrease the removal of circulating high-density lipoprotein cholesterol.[24] Systemic inflammation is a known aggravating factor in the pathogenesis of CVD and studies have shown that moderate alcohol intake is associated with lower levels of inflammatory markers such as IL-6, TNF-α, and CRP.[25-27] This anti-inflammatory effect associated with moderate alcohol consumption may mediate the observed reduction of atherosclerotic burden. It has also been noted that moderate alcohol use reduces fibrinogen levels, clotting factors, and platelet aggregation, which affects the CVD hallmark hypercoagulability. However, the precise mechanisms governing these reductions are not known.[24] Alcohol also reduces hyperglycemia through the inhibition of hepatic gluconeogenesis, with a resulting reduction in plasma glucose levels. Reduced plasma glucose levels serve to decrease the incidence of hyperglycemia and hyperinsulinemia, which are both CVD hallmarks.[28]

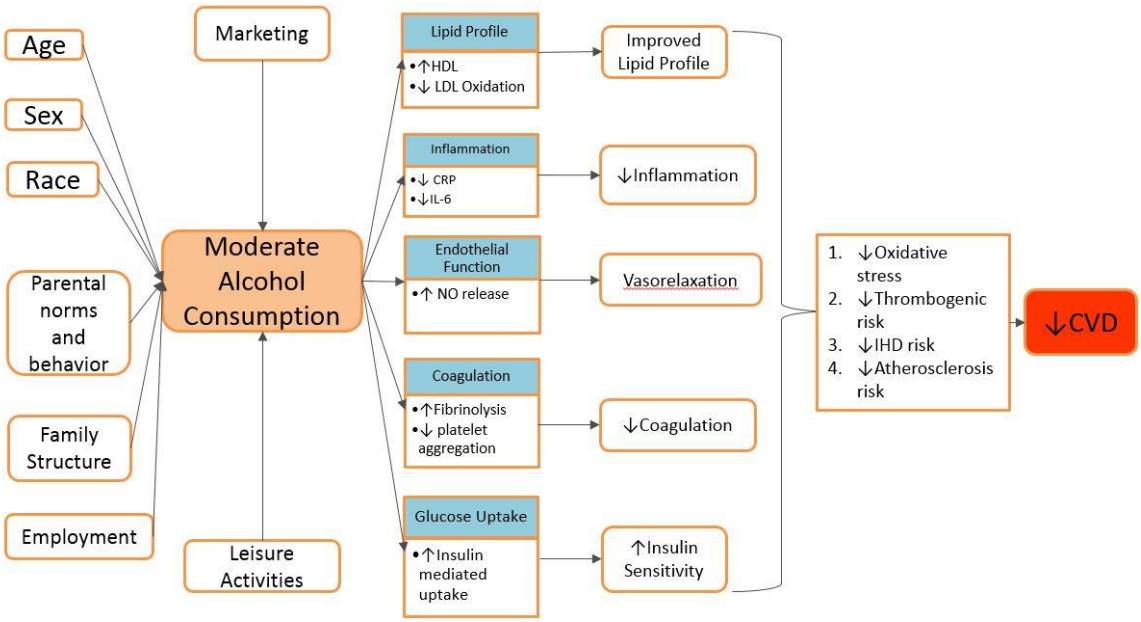

Figure-1. Moderate alcohol consumption and CVD (HDL, High-density lipoprotein; LDL, Low-density lipoprotein; CRP, C-Reactive protein; IL, Interleukin; NO, Nitric oxide)

In contrast to moderate consumption, heavy alcohol consumption which is usually defined as >2 drinks daily for men and >1 per day for women, increases the risk of CVD as shown in **Figure-2**. Heavy alcohol intake has been shown to increases blood pressure in a dose-dependent fashion. [29] A positive association between alcohol intake and serum triglycerides have been found and raised levels of triglycerides have shown to increase the risk of CVD.[8] Alcohol is the second most energy-dense macronutrient consumed and also has an appetite enhancing the effect, which could lead to an increased energy-intake, thereby causing weight gain.[8]

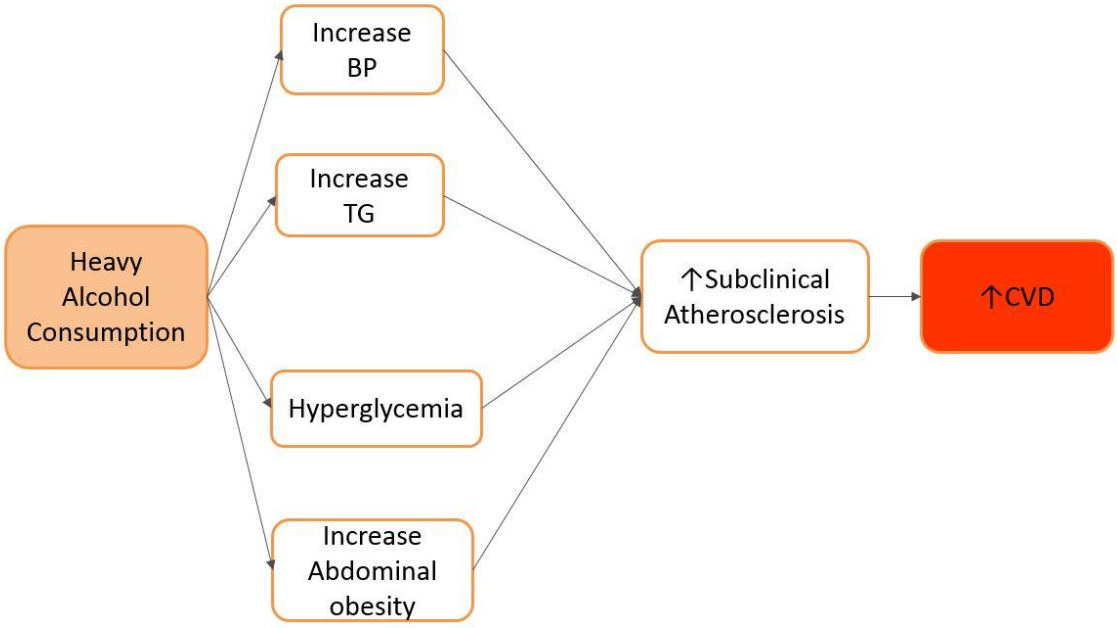

Figure-2. Heavy alcohol consumption and CVD (BP, Blood Pressure; TG, Triglyceride)

South Asians and Subclinical Atherosclerosis

Individuals who identify as South Asians are from a diverse set of communities and cultures with family origins from 7 countries that are most commonly listed as part of South Asia: Bangladesh, Bhutan, India, the Maldives, Nepal, Pakistan, and Sri Lanka. South Asians have a tradition of being dispersed around the world as a result of a number of factors, including colonialism, political instability, persecution, and economic opportunity.[30] By 2010, according to the US Census, there were >3.4 million South Asians living in the United States.[31] Most South Asians in the United States are of Asian Indian origin (≈80%), with rapidly growing Bhutanese and Nepali populations.[31] An estimated 226 000, or 6%, of South Asians in the United States are ≥65 years of age.[30]

Geographically, the top states that had the largest numbers of South Asians were California, New York, New Jersey, Texas, and Illinois, with most of the South Asians residing in urban metropolitan areas in these states.[32] South Asians constitute a relatively young population compared with other minority groups in the United States (in 2012, the mean age of South Asians was 36 years compared to a mean age of 40.2 years in NHWs) and continue to show a slightly greater proportion of females than males (53% versus 47% in 2008–2012).[33]

The medical literature has demonstrated a higher CVD risk in South Asians residing in the United States and Canada compared with other race/ethnicities.[34-36] Although people living in South Asian countries share genetic and cultural risk factors with South Asians living abroad, South Asians residing in the United States can differ in socioeconomic status, education, health care behaviors, attitudes, and health insurance, which can affect their risk and the treatment and outcomes of CVD. Among other cohorts of 4 ethnicities (Non-Hispanic Whites, Asians, Hispanics, and blacks), Asian Indians were investigated for CAC burden compared with the other racial/ethnic groups.[37] Asian Indians, who represented ≈10% of the cohort, had an increased mean calcium score, and the Asian Indian race was a significant independent predictor of CAC severity, even when controlling for traditional CVD risk factors. Among those >60 years of age, the prevalence of high CAC burden (scores >100) in Asian Indians is greater than in all other ethnic groups. More recently, a study from a community-based cohort of South Asians in the United States comparing the prevalence and distribution of CAC to four racial/ethnic groups showed that South Asian men have similarly high CAC burden as White men, but

higher CAC than other racial/ethnic groups. The high burden of CAC in South Asians may partly explain higher rates of cardiovascular disease in South Asians.

Alcohol Consumption and South Asians

It is difficult to stereotype degree and pattern of alcohol use among a group as broad as South Asians given the diversity of language, cultural and religious practices. Moreover, differences between generations and increased alcohol consumption from acculturation further complicate the picture.[38] For younger South Asians, being raised in a strict environment can often lead to increased drinking once young adults enter college or become independent from their parents. Also, many South Asians do not feel comfortable speaking openly about topics like stress and mental health disorders with their family members and peers. Unfortunately, this may lead some South Asians to turn to alcohol as a source of comfort. As described previously, alcohol affects many components of metabolic syndrome which may, in turn, lead to increased CVD. Although, it is not known if this relationship is different in South Asians compared to other ethnicities.

In summary, studies examining the association between alcohol consumption and subclinical atherosclerosis have yielded conflicting results. Moreover, no previous study has examined the association between alcohol consumption and subclinical atherosclerosis in the South Asian population. The studies examining the association of alcohol consumption and subclinical atherosclerosis in South Asians living in the United States, are critical for understanding the potential mechanism involved in the relationship

between alcohol consumption and CVD in this understudied population. From a population perspective, it is imperative that the health needs of this racial/ethnic minority group are critically examined to ensure culturally appropriate medical and health services, to address a variety of serious health conditions they face, to create informed policy decisions, and to improve current and future clinical research in this racial/ethnic minority group.

We, therefore, propose to conduct a secondary data analysis examining the effect of alcohol consumption on subclinical atherosclerosis in South Asians Living in America (MASALA) population. The MASALA study is a community based longitudinal cohort study designed to understand the risk factors and etiology of CVD among South Asians living in the United States aged 40-79 years who were free of CVD at baseline.[39] Baseline clinic visits were conducted from 2010 to 2013. The proposed study can contribute to the literature in several meaningful ways. We have an understudied cohort of the South Asian population. We have detailed data on aspects of consumption (such as binge drinking, beverage preference, and former drinking) that were not available (at least simultaneously) in previous studies. We also have baseline data including CAC score and cIMT which can be utilized as simultaneous surrogate markers of CVD, which has not been studied before.

Specific Aims

South Asians have the highest death rate from heart disease compared to other ethnic group.[40-42] South Asians (people from Bangladesh, Bhutan, India, the Maldives, Nepal, Pakistan, and Sri Lanka) make up one-quarter of the world's population[43] and are one of the fastest-growing ethnic groups in the United States.[31] South Asians are more likely to develop coronary heart disease (CHD) at a younger age, often before the age of 40 years in men.[35] In an analysis of >10 million national death records of the United States, South Asian men and women had higher mortality from ischemic heart disease compared to other diseases.[44] The proportionate mortality burden from ischemic disease, as reflected by the proportional mortality rates, was highest in Asian Indian men (1.43) and women (1.12), compared with non-Hispanic white (NHW) men (1.08) and women (0.92).[44] This high proportional mortality is not explained by widely known risk factors such as high blood pressure, diabetes or smoking.[39] Ethnicity is known to account in part for inter-individual variability in the prevalence and incidence of cardiovascular disease (CVD).[45]

The effects of drinking alcohol within recommended limits on risks of CVD is perhaps one of the most important questions yet to be answered in the fields of alcohol, nutrition, or prevention. Alcohol has both protective and detrimental effects on cardiovascular disease.[8] Epidemiological studies have consistently found that alcohol intake within recommended limits is associated with lower risk of CVD.[10,24,46] One potential mechanism is the effect of alcohol consumption on atherogenesis.[47] The relationship between alcohol, and subclinical atherosclerosis could provide clues about

the mechanisms underlying the relationship between alcohol and CVD.[48] To understand this relationship, we can examine its association with subclinical atherosclerosis measured by surrogate markers including coronary artery calcium (CAC) and carotid intima-media thickness(cIMT). A focused area of interest is to understand better the impact of alcohol on non-communicable chronic diseases, and the factors that may interact with alcohol to modify risk in an understudied population and our study will address this area of interest. Our Specific aims are:

Aim 1: To examine the association between alcohol consumption and the presence and degree of prevalent CAC (CAC>0) among asymptomatic South Asians age 40-84 living in the U.S

Aim 2: To examine the association between alcohol consumption and cIMT score among asymptomatic South Asians age 40-84 living in the U.S.

These aims will allow for the testing of the following primary hypotheses:

Hypothesis #1: Light to moderate alcohol consumption compared with lifetime abstinence is associated with the decreased presence of prevalent CAC among asymptomatic South Asians age 40-84 living in the U.S

Hypothesis #2: Moderate to high alcohol consumption compared with lifetime abstinence is associated with higher cIMT among asymptomatic South Asians age 40-84 living in the U.S.

To achieve these aims, we will describe the pattern of alcohol consumption (current, former, never); and the quantity of alcohol consumed in 906 MASALA participants. We will perform a cross-sectional analysis examining the association of alcohol consumption and CAC and cIMT.

The proposed analysis focuses on the association of alcohol consumption and CVD surrogate markers in the South Asian population which is an understudied population. The study will help to fill gaps in our understanding of the antecedents of CVD in South Asians. The study will be a novel approach to expand our knowledge about the relationship of alcohol consumption and CVD in South Asians living in the U.S. The results of the study will have an impact on understanding the benefits or risks that alcohol poses on cardiovascular health of South Asians living in the US.

References

1. Benjamin. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association (vol 135, pg e146, 2017). *Circulation.* 2017;136(10):E196-E196.
2. Ford ES, Ajani UA, Croft JB, et al. Explaining the decrease in US deaths from coronary disease, 1980-2000. *New England Journal of Medicine.* 2007;356(23):2388-2398.
3. Sidney S, Quesenberry CP, Jaffe MG, et al. Recent Trends in Cardiovascular Mortality in the United States and Public Health Goals. *Jama Cardiology.* 2016;1(5):594-599.
4. Haseeb S, Alexander B, Baranchuk A. Wine and Cardiovascular Health A Comprehensive Review. *Circulation.* 2017;136(15):1434-1448.
5. Rehm J, Mathers C, Popova S, Thavorncharoensap M, Teerawattananon Y, Patra J. Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. *Lancet.* 2009;373(9682):2223-2233.
6. Kalinowski A, Humphreys K. Governmental standard drink definitions and low-risk alcohol consumption guidelines in 37 countries. *Addiction.* 2016;111(7):1293-1298.
7. Helfand BK, Mukamal KJ, Mittleman MA. Trends in alcohol use among women with and without myocardial infarction in the United States: 1997-2008. *J Stud Alcohol Drugs.* 2011;72(6):885-891.
8. Gronbaek M. The positive and negative health effects of alcohol- and the public health implications. *Journal of Internal Medicine.* 2009;265(4):407-420.
9. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. *Bmj-British Medical Journal.* 2011;342.
10. Zhao J, Stockwell T, Roemer A, Naimi T, Chikritzhs T. Alcohol Consumption and Mortality From Coronary Heart Disease: An Updated Meta-Analysis of Cohort Studies. *Journal of Studies on Alcohol and Drugs.* 2017;78(3):375-386.
11. Helfand M, Buckley DI, Freeman M, et al. Emerging risk factors for coronary heart disease: a summary of systematic reviews conducted for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2009;151(7):496-507.
12. Greenland P, Alpert JS, Beller GA, et al. 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology.* 2010;56(25):E50-E103.
13. Touboul PJ, Grobbee DE, den Ruijter H. Assessment of subclinical atherosclerosis by carotid intima media thickness: technical issues. *European Journal of Preventive Cardiology.* 2012;19:18-24.

14. Tofferi JK, Taylor AJ, Feuerstein IM, O'Malley PG. Alcohol intake is not associated with subclinical coronary atherosclerosis. *American Heart Journal.* 2004;148(5):803-809.
15. Ellison RC, Zhang YQ, Hopkins PN, Knox S, Djousse L, Carr JJ. Is alcohol consumption associated with calcified atherosclerotic plaque in the coronary arteries and aorta? *American Heart Journal.* 2006;152(1):177-182.
16. McClelland RL, Bild DE, Burke GL, Mukamal KJ, Lima JA, Kronmal RA. Alcohol and coronary artery calcium prevalence, incidence, and progression: results from the Multi-Ethnic Study of Atherosclerosis (MESA). *American Journal of Clinical Nutrition.* 2008;88(6):1593-1601.
17. Vliegenthart R, Oei HHS, van den Elzen APM, et al. Alcohol consumption and coronary calcification in a general population. *Archives of Internal Medicine.* 2004;164(21):2355-2360.
18. Yang T, Doherty TM, Wang ND, Detrano RC. Alcohol consumption, coronary calcium, and coronary heart disease events. *American Journal of Cardiology.* 1999;84(7):802-806.
19. Pletcher MJ, Varosy P, Kiefe CI, Lewis CE, Sidney S, Hulley SB. Alcohol consumption, binge drinking, and early coronary calcification: Findings from the coronary artery risk development in young adults (CARDIA) study. *American Journal of Epidemiology.* 2005;161(5):423-433.
20. Yun KE, Chang Y, Yun SC, et al. Alcohol and coronary artery calcification: an investigation using alcohol flushing as an instrumental variable. *International Journal of Epidemiology.* 2017;46(3):950-962.
21. Mukamal KJ, Kronmal RA, Mittleman MA, et al. Alcohol consumption and carotid atherosclerosis in older adults - The cardiovascular health study. *Arteriosclerosis Thrombosis and Vascular Biology.* 2003;23(12):2252-2259.
22. Kim MK, Shin J, Kweon SS, et al. Harmful and beneficial relationships between alcohol consumption and subclinical atherosclerosis. *Nutrition Metabolism and Cardiovascular Diseases.* 2014;24(7):767-776.
23. Zyriax BC, Lau K, Klahn T, Boeing H, Volzke H, Windler E. Association between alcohol consumption and carotid intima-media thickness in a healthy population: data of the STRATEGY study (Stress, Atherosclerosis and ECG Study). *European Journal of Clinical Nutrition.* 2010;64(10):1199-1206.
24. Rimm EB, Williams P, Fosher K, Criqui M, Stampfer MJ. Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors. *British Medical Journal.* 1999;319(7224):1523-1528D.
25. Libby P. Inflammation in atherosclerosis. *Nature.* 2002;420(6917):868-874.
26. Becker AE, de Boer OJ, van der Wal AC. The role of inflammation and infection in coronary artery disease. *Annual Review of Medicine.* 2001;52:289-297.
27. Wood D, Joint European Soc Task F. Established and emerging cardiovascular risk factors. *American Heart Journal.* 2001;141(2):S49-S57.
28. Siler SQ, Neese RA, Christiansen MP, Hellerstein MK. The inhibition of gluconeogenesis following alcohol in humans. *American Journal of Physiology-Endocrinology and Metabolism.* 1998;275(5):E897-E907.
29. Puddey IB, Beilin LJ. Alcohol is bad for blood pressure. *Clinical and Experimental Pharmacology and Physiology.* 2006;33(9):847-852.

30. Volgman AS, Palaniappan LS, Aggarwal NT, et al. Atherosclerotic Cardiovascular Disease in South Asians in the United States: Epidemiology, Risk Factors, and Treatments: A Scientific Statement From the American Heart Association. *Circulation.* 2018.
31. SAALT (South Asians Learning Together). A demographic snapshot of South Asians in the United States. 2015. http://saalt.org/wp-content/uploads/2016/01/Demographic-Snapshot-updated_Dec-2015.pdf. In.
32. M P. Asian American maps. Pew Research Center's Social & Demographic Trends Project. 2012; 2017. http://www.pewsocialtrends.org/asianamericans-maps/#indian, 2018.
33. Ramakrishnan K AF. Demographics: Center for American Progress: part of the "State of Asian Americans and Pacific Islanders Series." 2014. 2014. https://cdn.americanprogress.org/wp-content/uploads/2014/04/AAPIDemographics.pdf.
34. Hajra A, Li Y, Siu S, et al. Risk of coronary disease in the South Asian American population. *J Am Coll Cardiol.* 2013;62(7):644-645.
35. Enas EA, Garg A, Davidson MA, Nair VM, Huet BA, Yusuf S. Coronary heart disease and its risk factors in first-generation immigrant Asian Indians to the United States of America. *Indian Heart J.* 1996;48(4):343-353.
36. Gupta M, Brister S. Is South Asian ethnicity an independent cardiovascular risk factor? *Can J Cardiol.* 2006;22(3):193-197.
37. Hatwalkar A, Agrawal N, Reiss DS, Budoff MJ. Comparison of prevalence and severity of coronary calcium determined by electron beam tomography among various ethnic groups. *American Journal of Cardiology.* 2003;91(10):1225-1227.
38. Orford J, Johnson M, Purser B. Drinking in second generation black and Asian communities in the English Midlands. *Addict Res Theory.* 2004;12(1):11-30.
39. Kanaya AM, Kandula N, Herrington D, et al. Mediators of Atherosclerosis in South Asians Living in America (MASALA) Study: Objectives, Methods, and Cohort Description. *Clinical Cardiology.* 2013;36(12):713-720.
40. Tuomilehto J, Ram P, Eseroma R, Taylor R, Zimmet P. CARDIOVASCULAR-DISEASES AND DIABETES-MELLITUS IN FIJI - ANALYSIS OF MORTALITY, MORBIDITY AND RISK-FACTORS. *Bulletin of the World Health Organization.* 1984;62(1):133-143.
41. McKeigue PM, Miller GJ, Marmot MG. CORONARY HEART-DISEASE IN SOUTH ASIANS OVERSEAS - A REVIEW. *Journal of Clinical Epidemiology.* 1989;42(7):597-609.
42. Harding S. Mortality of migrants from the Indian subcontinent to England and Wales: Effect of duration of residence. *Epidemiology.* 2003;14(3):287-292.
43. Central Intelligence Agency. The World Fact Book. 2017. https://www.cia.gov/library/publications/the-world-factbook/geos/in.html. In.
44. Jose PO, Frank ATH, Kapphahn KI, et al. Cardiovascular Disease Mortality in Asian Americans. *Journal of the American College of Cardiology.* 2014;64(23):2486-2494.
45. Budoff MJ, Young R, Lopez VA, et al. Progression of Coronary Calcium and Incident Coronary Heart Disease Events MESA (Multi-Ethnic Study of

Atherosclerosis). *Journal of the American College of Cardiology.* 2013;61(12):1231-1239.
46. O'Keefe JH, Bybee KA, Lavie CJ. Alcohol and cardiovascular health - The razor-sharp double-edged sword. *Journal of the American College of Cardiology.* 2007;50(11):1009-1014.
47. Gaziano JM, Gaziano TA, Glynn RJ, et al. Light-to-moderate alcohol consumption and mortality in the physicians' health study enrollment cohort. *Journal of the American College of Cardiology.* 2000;35(1):96-105.
48. Rehm JT, Bondy SJ, Sempos CT, Vuong CV. Alcohol consumption and coronary heart disease morbidity and mortality. *American Journal of Epidemiology.* 1997;146(6):495-501.

CHAPTER TWO: MANUSCRIPT

Alcohol Consumption and Subclinical Atherosclerosis among South Asians: Findings from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study

Short Title: Alcohol and subclinical atherosclerosis

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Key Words: 1. South Asian 2. Alcohol 3. Subclinical atherosclerosis

Abstract

Background: South Asians are the second fastest growing ethnic group in the United States, and they have a high risk for cardiovascular disease (CVD). Moderate alcohol consumption has been associated with lower CVD risk in some race/ethnic groups, but the association of alcohol consumption and atherosclerosis in South Asians has not been investigated.

Methods: We used data from 906 South Asian participants who participated in the Mediators of Atherosclerosis in South Asians Living in America (MASALA) cohort (2010-2012). Alcohol consumption was ascertained via questionnaire, coronary artery calcium (CAC) was measured with computed tomography, and common carotid artery intima-media thickness (cIMT) was measured using B-mode ultrasonography. We used multivariable regression models to examine cross-sectional associations of alcohol consumption with the presence and amount of CAC and with cIMT.

Results: Compared with never drinkers, participants consuming 4-7 drinks/week had a 64% decreased odds of any CAC after adjusting for potential confounders and mediators. Participants consuming 4-7 drinks/week had significantly lower odds of CAC score between 1-300 [OR (95% CI): 0.34 (0.16-0.73)] compared with never drinkers**.** A similar inverse association was seen for the odds of CAC>300 [OR (95% CI): 0.25 (0.07-0.98)]**.** Alcohol consumption of >7 drinks/week was associated with 0.095 mm increase in common-cIMT compared to no alcohol intake.

Conclusion: There was an inverse association between the amount of alcohol intake and CAC among South Asians while a positive association was found between alcohol consumption and common-cIMT. Long-term follow-up of the MASALA cohort will examine prospective associations of alcohol intake with the progression of subclinical atherosclerosis, incident CVD events, and mortality.

Introduction

South Asians – individuals with ancestry from Bangladesh, Bhutan, India, the Maldives, Nepal, Pakistan, and Sri Lanka - are one of the fastest-growing ethnic groups in the United States[1] and make up one-quarter of the world's population.[2] South Asians are more likely to develop coronary heart disease (CHD) at a younger age[3] and have higher mortality from ischemic heart disease compared to other populations[4] that is not explained by widely known risk factors. Ethnicity is known to account in part for inter-individual variability in the prevalence and incidence of cardiovascular disease (CVD).[5]

An important question yet to be answered definitively is whether alcohol influences the risk of cardiovascular disease (CVD). Alcohol has both protective and detrimental effects on CVD.[6] Epidemiological studies have consistently found that alcohol intake within recommended limits is associated with lower risk of CVD.[7-10] One potential mechanism is the effect of alcohol consumption on atherogenesis.[11] The relationship between alcohol and subclinical atherosclerosis could provide clues about the mechanisms underlying the relationship between alcohol and CVD.[12] To understand this relationship; we can examine its association with subclinical atherosclerosis measured by surrogate markers including coronary artery calcium (CAC) and carotid intima-media thickness (cIMT). However, the studies examining the relationship between alcohol consumption and subclinical atherosclerosis have shown inconsistent results, either no association[13-16], a dose-response relation[17,18] or a U-shaped relationship.[19] Similarly, the studies examining the association of alcohol consumption and cIMT have yielded conflicting results.[20-22]

Among all the ethnicities and nations that have been studied previously, the cardioprotective effect of light to moderate drinking has not been consistently replicated.[23-25] The INTERHEART study that included 27,000 subjects from 52 different countries showed that moderate (but not high levels of) alcohol use was associated with a reduced risk of MI. Although moderate or low alcohol consumption was protective in most countries, such an effect was not seen in South Asia[26]. Our study may provide insights into the understanding of the association between alcohol intake and subclinical atherosclerosis in South Asians. We examined cross-sectional association between alcohol consumption and subclinical atherosclerosis using data from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study, a community-based sample of asymptomatic South Asians in the United States. We hypothesized that light to moderate alcohol consumption is associated with decreased prevalence of CAC and lower CIMT among asymptomatic South Asians aged 40-84 years in the U.S

Methods

Study population

A detailed description of the MASALA study design and methodology have been previously published.[27] MASALA is a prospective community-based cohort study of South Asians to examine the etiology and prognostic significance of subclinical atherosclerosis. This project is similar in measures and methods to a large ongoing Multi-Ethnic Study of Atherosclerosis (MESA).[28] The sampling frames were created by clinical

site and included all 9 counties of the San Francisco Bay Area for the UCSF field site, and the 7 census tracts closest to the NWU medical center and secondary suburban locations around Chicago where census data revealed high proportions of South Asian residents. Between October 2010 and March 2013, 906 South Asians with a mean age of 55 ± 9 years were enrolled. All participants signed informed consent forms before undergoing study procedures. The study protocol was approved by the institutional review boards of the University of California, San Francisco, and Northwestern University.

Assessment of alcohol consumption

Based on the personal history questionnaire, alcohol consumption was assessed. The participants were asked, "Have you ever consumed alcoholic beverages?" If yes, they were then asked, "Do you presently drink alcoholic beverages?" Based on the answers given to these 2 questions, the participants were categorized into never, former, and current drinkers. Both current and former drinkers were asked, "For how many years did you drink alcoholic beverages?" They were also asked about the usual number of drinks consumed per week (before stopping drinking in the case of former drinkers). Current drinkers were asked about the number of drinks consumed during the past 24 hours, and the largest number of drinks consumed in 1 day in the past month. If the participant consumed ≥5 drinks on one occasion in the past month, it was defined as binge drinking.[27]

Measurement of coronary artery calcium

Non-contrast cardiac CT scans were performed using cardiac gated computed tomography scanners (UCSF: Phillips 16D scanner or a Toshiba MSD Aquilion 64; and NWU: Siemens Sensation Cardiac 64 Scanner). A four-sample calibration phantom was placed under the thorax for attenuation correction. All scans were interpreted at the CT reading center at Harbor-UCLA using the Rephot Imaging Software. Coronary Artery Calcium (CAC) Agatston scores were reported for each of the four major coronary arteries, and the summed score was used.

Measurement of carotid artery intima-media thickness

High-resolution B-mode ultrasonography was conducted for measurement of right and left internal and common carotid artery intima-media thickness (cIMT). The vascular technician located the bifurcation of the carotid artery distinguished the internal from an external carotid artery, and identified the maximal wall thickening in the near or far wall, in the carotid bulb or internal carotid artery. Each of these images was collected in a specified order and recorded. The digitized data were batched and mailed on magneto-optical disks to the Reading Center at Wake Forest University for wall-thickness measurements. For quality control, a single reader completed 25 repeat CIMT measures. The intra-class correlation coefficient for the internal carotid IMT was 0.96 and 0.78 for the common carotid IMT.

Measurement of covariates

Other covariates include demographic characteristics and potential confounders and mediators of alcohol-subclinical atherosclerosis association. Information on participant's demographic data, income, tobacco use, family history, medical history, and medication use was obtained using standard questionnaires and structured interview conducted by trained bilingual study staff. Education was categorized as having >=bachelor's degree or <bachelor's degree. Physical activity was assessed using the Typical Week's Physical Activity Questionnaire[29]. Resting blood pressure was measured three times in the seated position, using an automated blood pressure monitor (V100 Vital sign monitor, GE Medical Systems, Fairfield, CT) and the average of the last two readings was used for analysis. Participant height was measured using a stadiometer, and weight was measured using a standard balance beam scale or digital weighing scale. Waist circumference was measured using a flexible tape measure tape at the site of maximum circumference midway between the lower ribs and the anterior superior iliac spine. Fasting plasma glucose was measured by the glucose oxidase method; total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol and creatinine were measured by enzymatic methods (Quest, San Jose, CA) and low-density lipoprotein (LDL) cholesterol was calculated. Fasting serum samples were batched for insulin measured by the sandwich immunoassay method (Roche Elecsys 2010, Roche Diagnostics, Indianapolis, IN). Diabetes mellitus was defined as fasting glucose ≥126 mg/dL, or a post-challenge glucose ≥200 mg/dl, or by use of a glucose-lowering medication. Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic

blood pressure ≥90 mmHg or medication use for hypertension. Use of an HMG-coA reductase inhibitor, fibrate, or niacin was categorized as cholesterol medication use.

Statistical Analysis

Baseline characteristics of the total population were compared across alcohol consumption categories (never drinker, former drinker, 1-3 drinks/week, 4–7 drinks/week, and >7 drinks/week). Continuous variables were summarized using the mean (standard deviation) or median (interquartile range) depending on the normality of the data. Categorical variables were summarized using frequency (percentages). Analysis of variance (ANOVA) was used to compare the continuous variables while the chi-squared test was used to compare categorical variables. CAC scores were analyzed as a dichotomous outcome for the presence of any CAC (CAC>0), and as a categorical outcome for the degree of prevalent CAC (CAC = 0, 1–300, and >300). We used multivariable logistic regression models to compute odds ratios and 95% confidence intervals (CI) for the cross-sectional association between each alcohol consumption categories (never drinker (reference), former drinker, 1-3 drinks/week, 4–7 drinks/week, and >7 drinks/week) with the presence of any CAC, while multinomial logistic regression models were used to examine the association between alcohol consumption and degree of prevalent CAC (CAC = 0, 1–300, and >300). Linear regression models were used to examine the associations between categories of alcohol consumption and common CIMT modeled on a continuous scale. Model 1 was adjusted for age, sex and education level. Model 2 was adjusted for model 1 plus smoking (never, former, current, and pack-years),

BMI, self-reported physical activity and family history of heart attack, systolic and diastolic blood pressures, HDL-C, LDL-C, use of cholesterol medications, diabetes, and C-reactive protein.

Additionally, we examined the interaction of alcohol consumption with sex, and age using the likelihood ratio χ^2 test, by including interaction terms in model 2. A two-sided p-value of <0.05 was considered statistically significant. All statistical analyses were performed using with SAS version 9.4 (SAS Institute Inc., Cary, North Carolina).

Results

Baseline Characteristics

Sociodemographic characteristics by alcohol consumption categories are shown in Table 1. The average age of the 906 MASALA participants was 55.3 (±9.4) years, and 46% of participants were women. Among these, 304 (34.6%) were never drinkers, 303 (33.4%) were former drinkers, and 299 (33%) were current drinkers. Of the current drinkers, 182 (60.9%) reported consuming 1-3 drinks/week, 75 (25.1%) reported consuming 4-7 drinks/week, and 42 (18%) reported consuming >7 drinks/week. Participants consuming >7 drinks/week were more likely to be older, male and current smokers. Higher categories of drinks per week were associated with higher blood pressure and waist circumference. In univariate analysis, higher alcohol consumption was associated with a higher cIMT score. The prevalence of any CAC was 37%, 43.2%,

44.4%, 43.8% and 63.4% in never drinkers, former drinkers, those who consume alcohol 1-3 drinks/week, 4–7 drinks/week, and >7 drinks/week, respectively.

Alcohol consumption and presence of CAC

Table 2 displays the association between levels of alcohol consumption and any prevalent CAC using multivariable logistic regression. In the model adjusted for sociodemographic factors, alcohol consumption of 4-7 drinks/week was associated with decreased odds of any CAC presence (odds ratio [OR] (95% CI):0.53 (0.28-1.00), P = 0.05). Compared with never drinkers, participants consuming 4-7 drinks/week had a 64% lower odds of any CAC after adjusting for potential confounders and mediators (OR (95% CI): 0.36 (0.18-0.72), P < 0.01). The interaction between alcohol consumption and sex or age was not statistically significant. After adjustment for all mediators and confounders, there was no association between binge drinking in the past month and any CAC presence.

Figure 1 and 2 shows the association between alcohol consumption and the burden of CAC. For the categorical model, participants consuming 4-7 drinks/week had significantly lower odds of CAC = 1-300 compared with never drinkers (OR (95% CI): 0.34 (0.16-0.73), P = 0.005) (Figure 1). A similar inverse association was observed for the odds of CAC>300 (OR (95% CI): 0.25 (0.07-0.98), P = 0.04) (Figure 2).

Alcohol consumption and common cIMT

Table 3 shows the multivariable model result for the association between alcohol consumption categories and common cIMT. Alcohol consumption of >7 drinks/week was associated with a 0.95 mm increase in common cIMT compared to no alcohol intake in a fully adjusted model. (β (95% CI): 0.095 (0.023-0.167), P = 0.009). Using multiple linear regression analysis, we also calculated the least mean square and standard error (SE) of association of alcohol consumption categories and cIMT (Table 4). There was an incremental increase in mean cIMT across alcohol consumption categories with the higher score in >7 drinks/week followed by 4-7 drinks/week followed by 1-3 drinks/week followed by former drinker and then never drinker (trend P-value of 0.01 for Model 1 and 0.09 for Model 2).

Discussion

Main Findings

Several important insights were obtained in this study about alcohol consumption and subclinical atherosclerosis among middle-aged US South Asian adults free of CVD at baseline. We found an inverse association of light alcohol consumption of 4-7 drinks/week with presence and amount of CAC. In contrast, moderate to high alcohol consumption of >7 drinks/week was associated with higher cIMT. Moreover, there was a graded association with the number of drinks/week and common cIMT, with higher

alcohol consumption associated with the higher cIMT. Our study was designed to further the understanding of the relationship between alcohol consumption and subclinical atherosclerosis. To our knowledge, this is the first study assessing the association of alcohol consumption and measures of subclinical atherosclerosis in South Asians in the U.S.

Comparison with previous studies

The studies examining the relationship between alcohol consumption and CAC have shown inconsistent results. Tofferi et al[14] used a cohort of 731 consecutive, consenting, active-duty US Army personnel (39 to 45 years of age) without known CVD. This cross-sectional study found no relationship between the CAC score and the alcohol intake. It was one of the first studies focusing on the relation between alcohol consumption and CAC in a group at low risk for cardiovascular disease and with early atherosclerosis. Using CAC and atherosclerotic plaque in the aorta as surrogate markers of subclinical atherosclerosis, Ellison et al[15] investigated this relationship using data from a prospective cohort study including 3166 white and African American subjects with mean age around 55 years. They found no evidence of an association between total alcohol intake and CAC, although there was a tendency for the increased prevalence of CAC in the highest category of alcohol intake. Analyses of aortic calcification showed similar nonsignificant associations. Yang et al[16] tried to determine if alcohol intake was associated with reduced coronary risk in a high-risk asymptomatic population and whether this effect was independent of coronary risk factors and coronary calcium. The

study showed no relation between alcohol use and CAC. The definition of moderate alcohol consumption was different at that time. Also, the study lacked detail data on alcohol consumption. The first large study to evaluate the association of alcohol with CAC in 4 racial-ethnic groups and to evaluate the progression of calcification, was done by McClelland et al.[13] The researchers studied the association between alcohol consumption and CAC prevalence, incidence and progression in The Multi-Ethnic Study of Atherosclerosis (MESA) which is a prospective community-based cohort study including 6814 participants aged 45–84 y who identified themselves as white, African American, Hispanic, or Chinese. They showed that overall alcohol consumption was not associated with the prevalence of any CAC > 0 at baseline regardless of alcohol type.

In contrast to these studies, Vliegenthart et al[19] found a U-shaped association between alcohol consumption and CAC performing a cross-sectional analysis using data from the population-based Rotterdam Coronary Calcification Study. By using prospective study design. Interestingly, Pletcher et al[17] found a dose-response relation between alcohol and CAC. Our study did have some evidence of J-shaped association of alcohol with the presence and degree of CAC.

Carotid IMT is another non-invasive measure that can be used as a surrogate marker of subclinical atherosclerosis. To address the relationship between alcohol consumption and carotid atherosclerosis in older adults, Mukamal et al[20] used data from the Cardiovascular Health Study (CHS) including 5888 adults aged 65 years and older. The result of this cross-sectional study found that relative to older adults who abstain from alcohol, consumption of 1 to 6 drinks per week had an inverse association with carotid atherosclerosis whereas consumption of 14 or more drinks had a positive

association. The CHS participants represent a relatively healthy group of older adults, so the results can only be generalized to older adults in similar health. Kim at al[21] tried to find relationships between alcohol consumption and subclinical atherosclerosis in 5539 Korean subjects (2121 men and 3418 women) who were participants in the Multi-Rural Communities cohort (MRcohort) study. The result showed that carotid artery intima-media wall thickness (CCA-IMT) was lower with alcohol consumption in men only. Zyriax at al[22] conducted a cross-sectional study with the aim of investigating the relationship between alcohol intake and c-IMT in a selectively healthy population of the Stress Atherosclerosis and ECG Study (STRATEGY study). The results revealed a significant positive correlation between daily alcohol consumption and IMT in men, whereas in women the positive correlation was not significant. Our study found a positive association between alcohol consumption and cIMT. In our study, we could not do a stratified analysis by gender given a small sample size of women in 4-7 drinks/week and >7 drinks/week categories.

Potential mechanisms

An explanation for these conflicting results is unclear. Moderate alcohol acts upon the liver and can, therefore, serve to directly increase the hepatic production and secretion of apolipoproteins and lipoprotein particles, increase triglyceride concentrations, and decrease the removal of circulating high-density lipoprotein cholesterol.[8] We did not find any association between alcohol consumption categories and HDL or LDL in MASALA participants (Table 1). Systemic inflammation is a known

aggravating factor in the pathogenesis of CVD and studies have shown that moderate alcohol intake is associated with lower levels of inflammatory markers such as IL-6, TNF-α, and CRP.[30-32] This anti-inflammatory effect may mediate the observed reduction of atherosclerotic burden. Alcohol also reduces hyperglycemia through the inhibition of hepatic gluconeogenesis, with a resulting reduction in plasma glucose levels.[33]

In contrast, moderate to heavy alcohol intake has been shown to increases blood pressure in a dose-dependent fashion.[34-36] Our study confirmed this finding showing that both SBP and DBP increased with higher levels of alcohol consumption. Alcohol is the second most energy-dense macronutrient consumed and also has an appetite enhancing the effect, which could lead to an increased energy-intake, thereby causing weight gain.[6] We found that the level of alcohol consumption was positively associated with waist circumference in MASALA participants. These findings, if causal, could partly explain the dose-response relationship of alcohol consumption and cIMT in MASALA cohort.

Implications

Due to the diversity of language, cultural and religious practices, it is difficult to stereotype degree and pattern of alcohol use among a group as diverse as South Asians. Moreover, differences between generations and increased alcohol consumption due to acculturation further complicate the picture.[37] The recommended limit of alcohol consumption vary substantially across different national guidelines.[38] Despite multiple studies revealing the benefits of moderate alcohol consumption to lower CVD risk, a recent study analyzing data from nearly 600,000 people concluded that in current

drinkers of alcohol in high-income countries, the threshold for lowest risk of all-cause mortality was about 100 g/week (<7 drinks/week).[39] Even though our study showed the inverse association of consuming 4-7 drinks/week with respect to CAC, we also observed that >7 drinks/week of alcohol consumption was related to greater cIMT. Thus, it would be difficult to make any recommendations regarding a safe threshold in South Asian population.

Strengths and limitations

The major strength of our study is the understudied and unique population of South Asian. Also, we were able to adjust for many potential confounders and mediators including lifestyle variables and CVD risk factors. There are certain limitations that need to be taken into consideration in the interpretation of our study. First, alcohol consumption was based on questionnaire responses, and participants may have underreported heavy or any consumption. These would most likely attenuate the association due to misclassification. Second, our study design was cross-sectional, and therefore, a causal relationship between alcohol and subclinical atherosclerosis cannot be established. Third, there were very few participants with heavy alcohol consumption defined as >14 drinks/week, which limited our ability to explore alcohol associations among this subset. Finally, we adjusted for several confounders, but residual confounding remains a possibility.

Conclusion

In conclusion, we found different associations of alcohol consumption with surrogate markers of subclinical atherosclerosis. We observed an inverse association of alcohol consumption and presence and burden of CAC while alcohol seems to have an unfavorable association with cIMT. Future research can examine the association between alcohol consumption and incidence and progression of CAC as well as incident coronary heart disease in MASALA cohort.

Tables and Figures

Table 1. Baseline Characteristics of MASALA Participants

	Alcohol consumption (number of drinks/week)					
Characteristics Mean± SD or N (%)	**Never** N=304	**Former** N=303	**1-3** N=182	**4-7** N=75	**>7** N=42	***P* value**
Male	93 (31)	173 (57)	116 (64)	63 (84)	41 (98)	**<0.001**
Age (years)	55.9 ± 9.4	54.6 ± 9.1	54.4 ± 9.6	56.1 ± 8.3	59 ± 11.5	**0.021**
Systolic Blood Pressure (mm Hg)	124.6 ± 16.5	123.4 ± 14.1	124.2 ± 16	128 ± 17.3	131.1 ± 14.5	**0.014**
Diastolic Blood Pressure (mm Hg)	71.7 ± 9.6	73.3 ± 9.9	74.4 ± 9.3	76.3 ± 9.4	78.4 ± 10.1	**<0.001**
LDL Cholesterol (mg/dl)	111.7 ± 32.3	112.7 ± 32.4	108.2 ± 29.8	108.1 ± 33.6	116.5 ± 31.7	0.374
HDL Cholesterol (mg/dl)	50.9 ± 12.9	48.5 ± 12.9	50.5 ± 14	50.8 ± 15.3	51.7 ± 13.6	0.168
BMI (kg/m2)	25.9 ± 4	26 ± 4	26.2 ± 4.5	25.8 ± 4	25.6 ± 3.8	0.879
Physical activity (METs per week) *	929 (689-1230)	951 (744-1191)	974 (805-1187)	899 (739-1172	933 (746-1148)	0.776
Waist Circumference (cm)	91.3 ± 10.4	93 ± 10.2	93.4 ± 10.2	94.4 ± 10.7	96.3 ± 9.6	**0.009**
Family Income ≥ $75,000 per year	121 (40)	68 (23)	152 (84)	63 (84)	32 (75)	**0.001**
Education < Bachelor's Degree	37 (12)	36 (12)	21 (12)	7 (9)	9 (21)	**<0.001**
Diabetes Mellitus †	77 (26)	80 (27)	40 (22)	24 (32)	8 (19)	0.47
Smoker Status						**<0.001**
Never	290 (95)	265 (88)	135 (74)	45 (60)	16 (38)	
Former	11 (4)	28 (9)	42 (23)	25 (33)	18 (43)	
Current	3 (1)	10 (3)	5 (3)	5 (7)	8 (19)	
Lipid-Lowering Medication use	93 (31)	80 (26)	58 (32)	28 (37)	13 (31)	0.39
Family history of heart attack (%)	120 (40)	157 (52)	82 (45)	36 (48)	17 (40)	**0.04**

C-Reactive Protein (CRP) (ug/ml) *	1.37 (0.7-3.2)	1.3 (0.6-2.9)	1.03 (0.7-2.5)	0.96 (0.5-2.3)	0.96 (0.5-2.6)	0.376
Common Carotid IMT (mm)	0.84 (0.73-0.95)	0.84 (0.72-0.95)	0.84 (0.72-1.00)	0.89 (0.77-1.06)	0.93 (0.82-1.17)	**<0.001**
CAC Presence(CAC>0)	112 (37)	130 (43)	80 (44)	32 (44)	26 (63)	**0.021**

* median (interquartile range) shown for skewed variables
†diabetes defined by fasting plasma glucose ≥126 mg/dl, or a post-challenge glucose ≥200 mg/dl, or by use of a glucose-lowering medication
LDL, low- density cholesterol; HDL, high-density cholesterol; BMI, body mass index; MET, metabolic equivalent; IMT, intima-media thickness; CAC, coronary artery calcium

Table 2. Adjusted Odds Ratio and 95% CI of association between alcohol consumption and CAC presence (CAC>0)

Alcohol Consumption	**Model 1**		**Model 2**	
	Odds Ratio (95% CI)	***p-value***	***Odds Ratio (95% CI)***	***p-value***
		<0.01		**<0.01**
Never Drinker	*reference*		*reference*	
Former Drinker	1.03(0.68, 1.56)	0.89	0.97(0.63, 1.51)	0.90
1-3 drinks/week	1.01 (0.62, 1.63)	0.98	0.85(0.50, 1.43)	0.54
4-7 drinks/week	0.53 (0.28, 1.00)	0.05	0.36 (0.18, 0.72)	**0.007**
>7 drinks/week	0.92 (0.40, 2.16)	0.85	0.66 (0.27, 1.63)	0.37

Model 1 adjusted for age, sex, education and income
Model 2 adjusted for Model 1 plus smoking (never, former, current, and pack-years), BMI, self-reported physical activity, family history of heart attack, systolic and diastolic blood pressures, HDL-C, LDL-C, use of cholesterol medications, diabetes, and C-reactive protein.
CAC, coronary artery calcium; BMI, body mass; HDL, high-density cholesterol; LDL, low-density cholesterol

Table 3. Adjusted Beta-coefficient and 95% CI of association between alcohol consumption Categories and common cIMT

Alcohol Consumption	Model 1		Model 2	
	Beta-Coefficient (95% CI)	***p-value***	***Beta-Coefficient (95% CI)***	***p-value***
		<0.001		**<0.001**
Never Drinker	*reference*		*reference*	
Former Drinker	0.016 (-0.018, 0.050)	0.37	0.010 (-0.024, 0.045)	0.56
1-3 drinks/week	0.039 (-0.00, 0.079)	0.06	0.031 (-0.009, 0.072)	0.13
4-7 drinks/week	0.049 (-0.006, 0.103)	0.08	0.039 (-0.017, 0.094)	0.17
>7 drinks/week	0.114 (0.045, 0.183)	**0.001**	0.095 (0.023, 0.167)	**0.009**

Model 1 adjusted for age, sex, education, and income
Model 2 adjusted for Model 1 plus smoking (never, former, current, and pack-years), BMI, self-reported physical activity, family history of heart attack, systolic and diastolic blood pressures, HDL-C, LDL-C, use of cholesterol medications, diabetes, and C-reactive protein.
cIMT, carotid intima-media thickness; BMI, body mass; HDL, high-density cholesterol; LDL, low-density cholesterol

Table 4. Least Mean Square and SE of common cIMT across alcohol categories.

Alcohol categories	Model 1		Model 2	
	Mean ± SE	***Trend p-value***	***Mean ± SE***	***Trend p-value***
Never Drinker	0.86±0.013	**0.01**	0.86±0.013	0.09
Former Drinker	0.87±0.012		0.87±0.012	
1-3 drinks/week	0.89±0.015		0.89±0.015	
4-7 drinks/week	0.90±0.024		0.90±0.024	
>7 drinks/week	0.97±0.032		0.97±0.032	

Least mean square and standard error calculated from multiple linear regression analysis
Model 1 adjusted for age, sex, race, and education
Model 2 adjusted for Model 1 plus smoking (never, former, current, and pack-years), BMI, self-reported physical activity, family history of heart attack, systolic and diastolic blood pressures, HDL-C, LDL-C, use of cholesterol medications, diabetes, and C-reactive protein.
SE, standard error; cIMT, carotid intima-media thickness; BMI, body mass; HDL, high-density cholesterol; LDL, low- density cholesterol

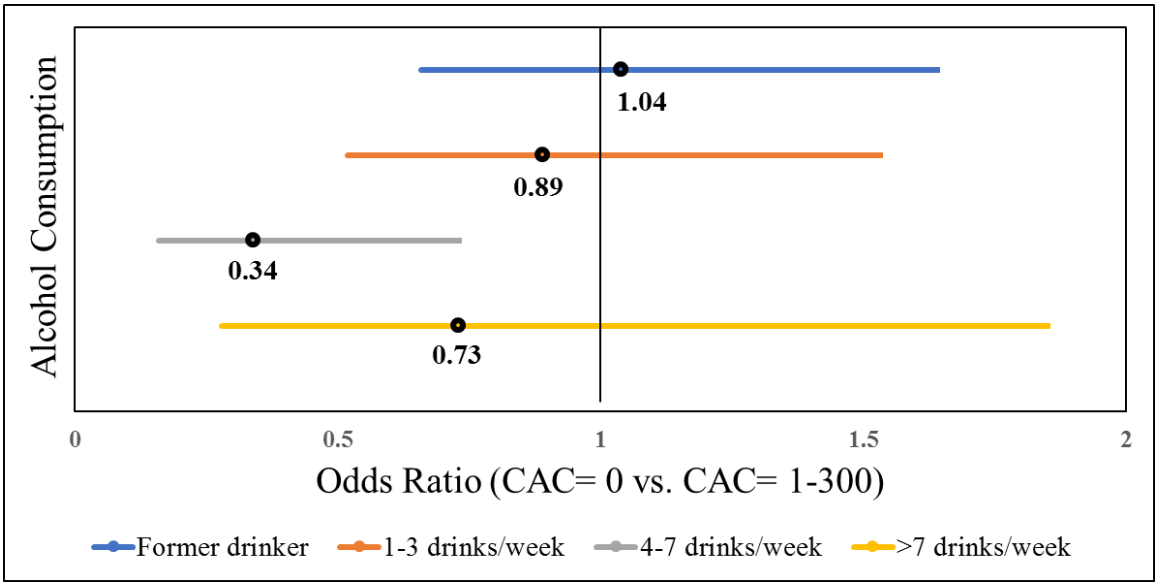

Figure 1. Adjusted Odds Ratio and 95% CI of association between alcohol consumption and degree of CAC (CAC = 1-300)
Reference group = Never drinker

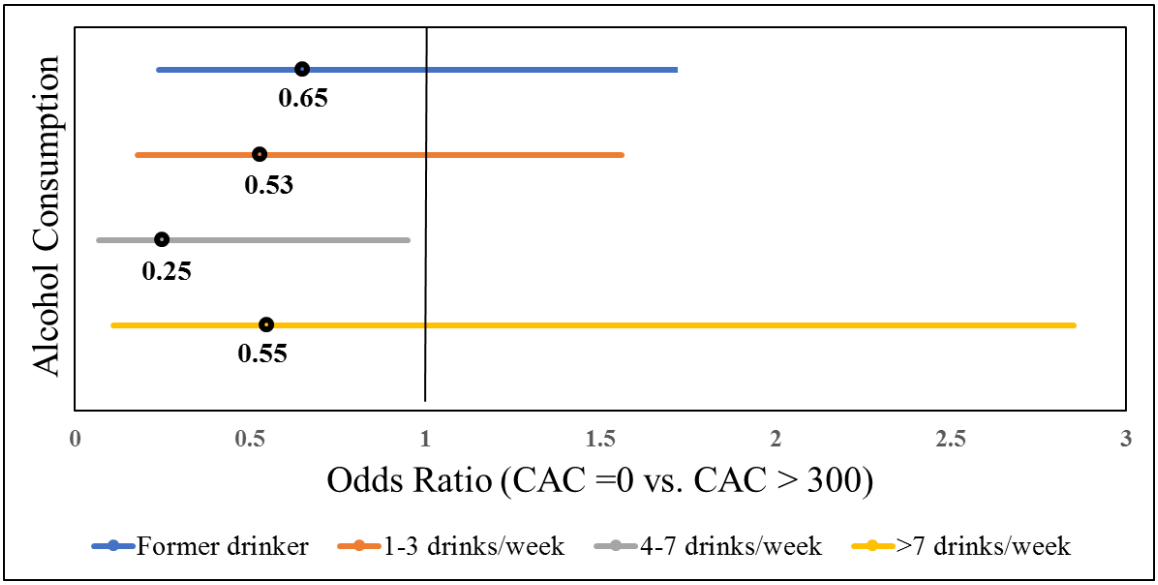

Figure 2. Adjusted Odds Ratio and 95% CI of association between alcohol consumption and degree of CAC (CAC > 300)
Reference group = Never drinker

References

1. SAALT (South Asians Learning Together). A demographic snapshot of South Asians in the United States. 2015. http://saalt.org/wp-content/uploads/2016/01/Demographic-Snapshot-updated_Dec-2015.pdf. In.
2. Central Intelligence Agency. The World Fact Book. 2017. https://www.cia.gov/library/publications/the-world-factbook/geos/in.html. In.
3. Enas EA, Garg A, Davidson MA, Nair VM, Huet BA, Yusuf S. Coronary heart disease and its risk factors in first-generation immigrant Asian Indians to the United States of America. *Indian Heart J.* 1996;48(4):343-353.
4. Jose PO, Frank ATH, Kapphahn KI, et al. Cardiovascular Disease Mortality in Asian Americans. *Journal of the American College of Cardiology.* 2014;64(23):2486-2494.
5. Budoff MJ, Young R, Lopez VA, et al. Progression of Coronary Calcium and Incident Coronary Heart Disease Events MESA (Multi-Ethnic Study of Atherosclerosis). *Journal of the American College of Cardiology.* 2013;61(12):1231-1239.
6. Gronbaek M. The positive and negative health effects of alcohol- and the public health implications. *Journal of Internal Medicine.* 2009;265(4):407-420.
7. O'Keefe JH, Bybee KA, Lavie CJ. Alcohol and cardiovascular health - The razor-sharp double-edged sword. *Journal of the American College of Cardiology.* 2007;50(11):1009-1014.
8. Rimm EB, Williams P, Fosher K, Criqui M, Stampfer MJ. Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors. *British Medical Journal.* 1999;319(7224):1523-1528D.
9. Zhao J, Stockwell T, Roemer A, Naimi T, Chikritzhs T. Alcohol Consumption and Mortality From Coronary Heart Disease: An Updated Meta-Analysis of Cohort Studies. *Journal of Studies on Alcohol and Drugs.* 2017;78(3):375-386.
10. Chevli PA, Ahmad MI, Jogu HR, et al. Electrocardiographic subclinical myocardial injury and alcohol consumption: a cross-sectional analysis of data from the Third National Health and Nutrition Examination Survey. *Am J Cardiovasc Dis.* 2018;8(5):58-65.
11. Gaziano JM, Gaziano TA, Glynn RJ, et al. Light-to-moderate alcohol consumption and mortality in the physicians' health study enrollment cohort. *Journal of the American College of Cardiology.* 2000;35(1):96-105.
12. Rehm JT, Bondy SJ, Sempos CT, Vuong CV. Alcohol consumption and coronary heart disease morbidity and mortality. *American Journal of Epidemiology.* 1997;146(6):495-501.
13. McClelland RL, Bild DE, Burke GL, Mukamal KJ, Lima JA, Kronmal RA. Alcohol and coronary artery calcium prevalence, incidence, and progression: results from the Multi-Ethnic Study of Atherosclerosis (MESA). *American Journal of Clinical Nutrition.* 2008;88(6):1593-1601.

14. Tofferi JK, Taylor AJ, Feuerstein IM, O'Malley PG. Alcohol intake is not associated with subclinical coronary atherosclerosis. *American Heart Journal.* 2004;148(5):803-809.
15. Ellison RC, Zhang YQ, Hopkins PN, Knox S, Djousse L, Carr JJ. Is alcohol consumption associated with calcified atherosclerotic plaque in the coronary arteries and aorta? *American Heart Journal.* 2006;152(1):177-182.
16. Yang T, Doherty TM, Wang ND, Detrano RC. Alcohol consumption, coronary calcium, and coronary heart disease events. *American Journal of Cardiology.* 1999;84(7):802-806.
17. Pletcher MJ, Varosy P, Kiefe CI, Lewis CE, Sidney S, Hulley SB. Alcohol consumption, binge drinking, and early coronary calcification: Findings from the coronary artery risk development in young adults (CARDIA) study. *American Journal of Epidemiology.* 2005;161(5):423-433.
18. Yun KE, Chang Y, Yun SC, et al. Alcohol and coronary artery calcification: an investigation using alcohol flushing as an instrumental variable. *International Journal of Epidemiology.* 2017;46(3):950-962.
19. Vliegenthart R, Oei HHS, van den Elzen APM, et al. Alcohol consumption and coronary calcification in a general population. *Archives of Internal Medicine.* 2004;164(21):2355-2360.
20. Mukamal KJ, Kronmal RA, Mittleman MA, et al. Alcohol consumption and carotid atherosclerosis in older adults - The cardiovascular health study. *Arteriosclerosis Thrombosis and Vascular Biology.* 2003;23(12):2252-2259.
21. Kim MK, Shin J, Kweon SS, et al. Harmful and beneficial relationships between alcohol consumption and subclinical atherosclerosis. *Nutrition Metabolism and Cardiovascular Diseases.* 2014;24(7):767-776.
22. Zyriax BC, Lau K, Klahn T, Boeing H, Volzke H, Windler E. Association between alcohol consumption and carotid intima-media thickness in a healthy population: data of the STRATEGY study (Stress, Atherosclerosis and ECG Study). *European Journal of Clinical Nutrition.* 2010;64(10):1199-1206.
23. Schooling CM, Wenjie S, Ho SY, et al. Moderate Alcohol Use and Mortality from Ischaemic Heart Disease: A Prospective Study in Older Chinese People. *PLoS One.* 2008;3(6).
24. Halanych JH, Safford MM, Kertesz SG, et al. Alcohol Consumption in Young Adults and Incident Hypertension: 20-Year Follow-up From the Coronary Artery Risk Development in Young Adults Study. *American Journal of Epidemiology.* 2010;171(5):532-539.
25. Nunez-Cordoba JM, Martinez-Gonzalez MA, Bes-Rastrollo M, Toledo E, Beunza JJ, Alonso A. Alcohol Consumption and the Incidence of Hypertension in a Mediterranean Cohort: the SUN Study. *Revista Espanola De Cardiologia.* 2009;62(6):633-641.
26. Leong DP, Smyth A, Teo KK, et al. Patterns of Alcohol Consumption and Myocardial Infarction Risk Observations From 52 Countries in the INTERHEART Case-Control Study. *Circulation.* 2014;130(5):390-398.
27. Kanaya AM, Kandula N, Herrington D, et al. Mediators of Atherosclerosis in South Asians Living in America (MASALA) Study: Objectives, Methods, and Cohort Description. *Clinical Cardiology.* 2013;36(12):713-720.

28. Bild DE, Bluemke DA, Burke GL, et al. Multi-ethnic study of atherosclerosis: Objectives and design. *American Journal of Epidemiology.* 2002;156(9):871-881.
29. Ainsworth BE, Irwin ML, Addy CL, Whitt MC, Stolarczyk LM. Moderate physical activity patterns of minority women: the Cross-Cultural Activity Participation Study. *J Womens Health Gend Based Med.* 1999;8(6):805-813.
30. Libby P. Inflammation in atherosclerosis. *Nature.* 2002;420(6917):868-874.
31. Becker AE, de Boer OJ, van der Wal AC. The role of inflammation and infection in coronary artery disease. *Annual Review of Medicine.* 2001;52:289-297.
32. Wood D, Joint European Soc Task F. Established and emerging cardiovascular risk factors. *American Heart Journal.* 2001;141(2):S49-S57.
33. Siler SQ, Neese RA, Christiansen MP, Hellerstein MK. The inhibition of gluconeogenesis following alcohol in humans. *American Journal of Physiology-Endocrinology and Metabolism.* 1998;275(5):E897-E907.
34. Puddey IB, Beilin LJ. Alcohol is bad for blood pressure. *Clinical and Experimental Pharmacology and Physiology.* 2006;33(9):847-852.
35. Santana NMT, Mill JG, Velasquez-Melendez G, et al. Consumption of alcohol and blood pressure: Results of the ELSA-Brasil study. *PLoS One.* 2018;13(1).
36. Aladin A, Chevli P, Ahmad MI, Rasool S, Herrington D. Alcohol Consumption and Risk of Hypertension. *Journal of the American College of Cardiology.* 2019;73(9):12-12.
37. Orford J, Johnson M, Purser B. Drinking in second generation black and Asian communities in the English Midlands. *Addict Res Theory.* 2004;12(1):11-30.
38. Kalinowski A, Humphreys K. Governmental standard drink definitions and low-risk alcohol consumption guidelines in 37 countries. *Addiction.* 2016;111(7):1293-1298.
39. Wood AM, Kaptoge S, Butterworth AS, et al. Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies. *Lancet.* 2018;391(10129):1513-1523.

CHAPTER THREE: ANCILLIARY ANALYSIS

Association of Alcohol Consumption and Ideal Cardiovascular Health among the South Asian Population: The Mediators of Atherosclerosis in South Asians Living in America (MASALA) study

Short Title: Alcohol and Ideal Cardiovascular Health

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Abstract

Background: Alcohol consumption above the recommended limit has shown to be associated with increased cardiovascular disease (CVD) although its association in South Asian is unclear. Less is known whether alcohol consumption is associated with cardiovascular health (CVH), assessed by the American Heart Association's Life's Simple 7 (LS7) health metrics in South Asian ancestry.

Methods: This analysis included 701 participants without CVD from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) cohort (2015-2018). Alcohol consumption was ascertained via questionnaire and participants were divided into never, former and current drinkers. Current drinkers were further categorized into1-3 drinks/week, 4–7 drinks/week, and >7 drinks/week. Binge drinking was defined as the consumption of 5 or more drinks on 1 occasion in the past month. Each LS7 component was given a point score of 0, 1, or 2. The total score was categorized into 0 to 6, 7 to 10, and 11 to 14 to represent poor, intermediate, and ideal CVH respectively. Multivariable logistic regression was used to examine the association between alcohol consumption and CVH.

Results: In MASALA cohort (N=701, mean age=59 y, 43% female), participants consuming >7 drinks/week had the lowest mean CVH score. In multivariable logistic regression models, compared with never drinkers, participants consuming >7 drinks/week were less likely to have intermediate CVH [0.33 (0.11, 0.96)] and ideal CVH [0.21 (0.11, 0.86)]. Binge drinking was associated with significantly decreased odds of ideal CVH compared to never drinkers.

Conclusion: There was evidence of the inverse association of moderate to heavy alcohol consumption and ideal CVH in South Asian population. These findings suggest that the recommended limit for alcohol consumption to maintain ideal CVH could be lower among South Asians.

Introduction

Health behaviors play a significant role in maintaining and modifying disease processes. While some health behaviors may lead to improvement of health, such as exercise for hypertension[1], others can lead to deterioration of health[2]. Furthermore, other health behaviors can be more complex with both beneficial and harmful effects, such as alcohol consumption. Alcohol, when consumed in moderation, has shown to be associated with reduced risk of cardiovascular disease (CVD) and mortality while excess consumption is associated with increased risk[3]. For example, one study with more than 5000 participants with baseline vascular disease or diabetes revealed a U-shaped relationship between alcohol consumption and all-cause mortality, vascular mortality, and amputation. It also showed that 1-2 alcoholic drinks per day were associated with reduced all-cause mortality, vascular death, the risk of congestive heart disease, and stroke[4]. While a recent study analyzing data from nearly 600,000 people showed that more than 1 drink per day was associated with increased all-cause mortality[5].

In 2010, the American Heart Association (AHA) declared its strategic impact goal which stated: "By 2020, to improve the cardiovascular health of all Americans by 20% while reducing deaths from cardiovascular diseases and stroke by 20%." To help achieve this goal, the concept of "ideal cardiovascular health" was created and defined by 7 metrics (healthy diet, physical activity, body mass index, smoking, blood pressure, blood glucose, and total cholesterol) called Life's Simple 7[6]. Very few studies have examined the association of alcohol consumption and cardiovascular health (CVH) using Life's Simple 7 (LS7) health metrics[7,8].

South Asian is one of the rapidly growing ethnicities in the United States, and they are at high risk of CVD which is not explained by traditional risk factors[9]. The Mediators of Atherosclerosis in South Asians Living in America (MASALA) study can contribute in a unique way to the literature on the association of alcohol consumption and other health behaviors that can influence cardiac risk. The objective of this cross-sectional study from MASALA cohort was to examine the association between alcohol use and ideal cardiovascular health using AHA's LS7 metrics among asymptomatic South Asians age 45-89 living in the U.S. We postulated that increased alcohol consumption would be inversely associated with ideal CVH.

Methods

Study population

A detailed description of the MASALA study design and methodology have been reported previously[9]. The MASALA study is a prospective community-based cohort study of South Asian men and women from 2 clinical sites (San Francisco Bay Area at the University of California, San Francisco and the greater Chicago area at Northwestern University). Between October 2010 and March 2013, 906 South Asians were enrolled. All surviving cohort participants were invited for the second clinical examination during September 2015 through March 2018, and 749 (83%) participants completed this examination[10]. We excluded 48 participants with missing data for one or more components of the CVH score from this analysis resulting in a sample of 701

participants. The study protocol was approved by the institutional review boards of the University of California, San Francisco, and Northwestern University.

Assessment of alcohol consumption

Based on the personal history questionnaire, alcohol consumption was assessed. The participants were asked, "Have you ever consumed alcoholic beverages?" If yes, they were then asked, "Do you presently drink alcoholic beverages?" Based on the answers given to these 2 questions, the participants were categorized into never, former, and current drinkers. Both current and former drinkers were asked, "For how many years did you drink alcoholic beverages?" They were also asked about the usual number of drinks consumed per week (before stopping drinking in the case of former drinkers). Current drinkers were asked about the number of drinks consumed during the past 24 hours, and the largest number of drinks consumed in 1 day in the past month. Based on the answers, the current drinkers were divided into the categories of 1-3 drinks/week, 4–7 drinks/week, and >7 drinks/week. If the participant consumed ≥5 drinks on one occasion in the past month, it was defined as binge drinking.[9]

Assessment of Life's Simple 7 Metrics

Based on data available for the MASALA cohort, the AHA's LS7 components were defined as follows[11]. Smoking status was self-reported and assessed using a questionnaire[9]. Body mass index (BMI) was calculated from measurements of weight and

height. Participant weight was measured on a standard balance-beam scale or a digital weighing scale, and height was measured using a stadiometer. Weight (in kgs) divided by height (in meters) squared was used to calculate BMI. Total Cholesterol was measured using enzymatic methods. Resting blood pressure was measured three times in the seated position, using an automated blood pressure monitor (V100 Vital sign monitor, GE Medical Systems, Fairfield, CT) and the average of the last two readings was used for analysis. Fasting plasma glucose was measured by the glucose oxidase method. The Study of Health Assessment and Risk in Ethnic food frequency questionnaire (FFQ) developed and validated for South Asians in Canada was used to assess dietary intake. As defined by the AHA, a healthy diet contained adequate quantities of 5 items (fruits and vegetables, fish, whole grains, sodium, and sugar-sweetened beverages). The Typical Week's Activity Survey was used to assess levels of various types of physical activity and exercise, and the Metabolic Equivalents (METs) of each activity was specified by Ainsworth et al[12]. Specifically, we used intentional exercise, including walking for exercise, dance, conditional activities, and sports to calculate time spent in moderate and vigorous activities. Time spent in activities identified as either vigorous (>6 METs) or moderate (3–6 METs) were used in the derivation. The average time per week spent engaged in all activities at either a vigorous or moderate level was computed for each participant and participants were then categorized based on the AHA criteria[6].

Each LS7 component was given a point score of 0, 1, or 2 to represent poor, intermediate, or ideal health, respectively. The individual component scores were summed to derive CVH score which could range from 0-14. The CVH score was classified as poor (0–6), intermediate (7–10), or ideal (11–14) CVH.

Measurement of covariates

Using a structured interview and standard questionnaires, information on age, sex, education, income and acculturation status was obtained. Education was categorized as having >=bachelor's degree or <bachelor's degree. A traditional cultural beliefs scale was used as a marker of acculturation[13]. Scores on this scale were categorized as strong (scores <12), moderate (scores 12–17) or weak (scores >17) traditional beliefs.

Statistical Analysis

Baseline characteristics of the total population were compared across alcohol consumption categories (never drinker, former drinker, 1-3 drinks/week, 4–7 drinks/week, and >7 drinks/week). Continuous variables were summarized using the mean (standard deviation) or median (interquartile range) depending on the normality of the data. Categorical variables were summarized using frequency (percentages). Analysis of variance (ANOVA) was used to compare the continuous variables while the chi-squared test was used to compare categorical variables.

The prevalence of each LS7 metric was reported by alcohol consumption categories. We used multinomial logistic regression models to examine the cross-sectional association between alcohol consumption categories and CVH. Odds ratios (ORs) and 95% CIs were calculated for intermediate CVH score (7-10) and ideal CVH score (11–14) across the categories of alcohol consumption. In both approaches, model 1 was unadjusted, and model 2 was adjusted for age, sex, education, and income. The reference groups were "never" categories for alcohol consumption and binge drinking[14]

and poor score for CVH categories[7]. We also examined the association between alcohol consumption and each LS7 metric. Moreover, we examined whether age, sex, or traditional cultural beliefs, modified the associations between alcohol consumption and CVH. Finally, linear regression models were used to examine the associations between categories of alcohol consumption and CVH score modeled on a continuous scale.

Additionally, we performed subgroup analysis stratified by age (using 54 years as a cut point). A two-sided p-value of <0.05 was considered statistically significant. All statistical analyses were performed using with SAS version 9.4 (SAS Institute Inc., Cary, North Carolina).

Results

Table 1 shows the baseline characteristics of the MASALA participants by alcohol consumption categories. Among 701 participants included in the analysis (aged 59 ± 9 years, 43% women), 198 (28%) were never drinkers, 247 (35%) were former drinkers, and 256 (37%) were current drinkers. Of the current drinkers, 147 (57%) reported consuming 1-3 drinks/week, 68 (27%) reported consuming 4-7 drinks/week, and 41 (16%) reported consuming >7 drinks/week. Also, 11% of current drinkers reported binge drinking in the past month. For the overall cohort, 10% (n=69) had poor CVH, 20% (n=141) had ideal CVH, and the remaining 70% (n=491) had intermediate CVH. Participants with >7 drinks/week and binge drinkers had the lowest proportion of ideal CVH. Of note, only 5% of the female participants consumed >7 drinks/week.

Table 2 shows the distribution of LS7 metrics by alcohol consumption categories. The proportion of participants consuming > 7 drinks/week who met the ideal criteria for smoking, total cholesterol, and blood glucose were significantly lower compared to never drinkers. For the overall cohort, only 4% of the participants met the ideal criteria for diet. Interestingly, the proportion of never drinkers who met the ideal criteria for the physical activity was lower than that for current drinkers who consumed more than 7 drinks/week.

Table 3 displays the association between levels of alcohol consumption and CVH using multivariable logistic regression. In the model adjusted for sociodemographic factors, alcohol consumption of >7 drinks/week was associated with decreased odds of having intermediate (odds ratio [OR] (95% CI):0.33 (0.12-0.96), P = 0.04) and ideal (odds ratio [OR] (95% CI):0.32 (0.09-0.86), P = 0.03) CVH compared to never drinking. Using CVH as a continuous variable, alcohol consumption of >7 drinks/week was associated with 0.87-point decrease in CVH score compared to no alcohol intake in a fully adjusted model. (β (95% CI): -0.87 (-1.52, -0.21), P = 0.009) (Table S3). Table 4 shows the association between binge drinking in the past month and CVH. Compared to never drinkers, participants who reported binge drinking were less likely to have ideal CVH (odds ratio [OR] (95% CI): 0.10 (0.01-0.93), P = 0.04). In age-stratified analysis (Table S1), those who were ≥58 years and consumed >7 drinks/week had 73% decreased odds of having intermediate CVH, and 81% decreased odds of having ideal CVH, compared to nondrinkers. There was no significant association between alcohol consumption and CVH in those who were <58 years. Evaluation of the association by sex was limited by sample size, especially among females. Although, men with alcohol consumption of >7 drinks/week were 77% less likely to have ideal CVH.

We formally tested for interaction of the associations by sex and age, even though results were stratified given a priori interest in the relation of alcohol consumption and CVH among subgroups. For the CVH scores, there was no significant interaction for alcohol consumption with sex or age.

Figure-1 displays the mean CVH score by alcohol consumption categories. Participants consuming >7 drinks/week as well as those with binge drinking had lower mean CVH scores. We also examined the association between alcohol consumption and individual LS7 metrics (Table S2). Regardless of the category of alcohol consumption, participants had lower odds of achieving the ideal criteria for smoking. Participants consuming >7 drinks/week were 71% less likely to meet the ideal criteria for total cholesterol. Also, those who reported 4-7 and >7drinks/week were had lower odds of achieving ideal blood pressure and blood glucose criteria.

Discussion

There are several important findings demonstrated by this investigation from a large community-based population of South Asians in the United States free of CVD. First, participants consuming >7 drinks/week were less likely to achieve intermediate and ideal CVH. Second, we found that participants who reported binge drinking in the past month had lower odds of having ideal CVH compared to never drinkers. Third,

participants who consumed >7 drinks/week were less likely to achieve ideal criteria for total cholesterol, blood pressure, and blood glucose.

Although multiple epidemiological studies have examined the association between alcohol consumption and CVD[15-18], the studies examining the association between alcohol consumption and CVH are very few. A recent study from the Multi-Ethnic Study of Atherosclerosis (MESA) showed that compared to never drinkers, participants consuming >14 drinks/week were less likely to have intermediate and ideal CVH. Similar to our results, binge drinking in the MESA participants was also associated with unfavorable CVH. They also showed that women with 7 to 14 drinks/week were more likely to have ideal CVH compared to non-drinking women, which was not seen in men. Moreover, the findings of an inverse relationship of heavy and binge drinking with ideal CVH was noted to be consistent among different racial/ethnic groups in the MESA. The cardioprotective effect of light or moderate drinking has found to be inconsistent among the different races and ethnicities[19-21]. The INTERHEART study that included 27,000 subjects from 50 different countries showed that regular alcohol intake reduced the risk of MI by 14%; although, this beneficial association was not apparent among the cohort from India[22]. Our study also did not show any association between light drinking and CVH.

Health behaviors are influenced by an individual's "motives, self-regulation, resources, habits, and environmental and social influences[23]." Similarly, health behaviors can often influence other health behaviors. None of the participants met ideal criteria for smoking regardless of the level of alcohol consumption compared to never drinkers. Alcohol consumption has shown to increase smoking behavior[24,25]. Not only has alcohol

shown to reduce smoking resistance in an inverse dose-dependent fashion[26], but it has also shown to be associated with more tobacco use on heavy drinking days[27]. One study showed that tobacco use was more prominent after approximately 3 drinks[28]. Moderate alcohol consumption has been associated with increased high-density lipoprotein (HDL) cholesterol[16]. Although MASALA participants with >7 drinks/week were less likely to have ideal total cholesterol. Our study showed that consumption of 4-7 drinks/week and >7 drinks/week was associated with decreased odds of achieving ideal blood pressure. A recent systematic review and dose-response meta-analysis of the association between alcohol consumption and incident hypertension found that no level of alcohol intake was associated with a lower risk of developing hypertension in either sex[29]. Loss of relaxation due to inflammation and oxidative injury of the endothelium by angiotensin II leading to inhibition of endothelium-dependent nitric oxide production is considered to be the major contributors of the alcohol-induced hypertension[30]. We also found that >7 drinks/week of alcohol consumption had 73% decreased odds of having ideal blood glucose levels. Most alcoholic beverages have very high amounts of sugar. Alcohol-induced increase in blood glucose levels may result from its adverse effect on insulin secretion and insulin resistance[31].

Our study has a public health implication given that alcohol is a modifiable risk factor. Alcohol consumption guidelines vary substantially across different countries[32]. Importantly, the pattern of alcohol consumption could vary among a diverse group of South Asian given their cultural and religious practices. Recent study results support limits for alcohol consumption that are lower than those recommended in most current

guidelines[5]. Our study also suggests that the recommended drinking limit could be lower for South Asian population to maintain ideal CVH.

Strengths and limitations

The strength of our study includes its community-based South Asian population which is an understudied but fast-growing minority with high risk for chronic disease including heart disease. Many key variables in the MASALA study including diet have been collected using culturally appropriate and validated instruments. Study limitations include the cross-sectional analysis of the association between alcohol consumption and CVH, and, therefore, a causal relationship could not be established. The MASALA study has a relatively small cohort size, which is drawn from only 2 geographic centers in the United States which limit the generalizability of the findings. We were unable to make inferences regarding a female who reported >7 drinks/week and who reported binge drinking given small sample sizes in these categories. Alcohol consumption was based on questionnaire responses, and participants may have underreported heavy or any consumption. These would most likely attenuate the association due to misclassification. Lastly, we adjusted for several confounders, but residual confounding remains a possibility.

Conclusion

We observed an inverse association between alcohol consumption and CVH in South Asian population. These results further highlight the importance of healthy behaviors in maintaining ideal CVH. Future research can focus on the impact of these healthy behaviors and examine the association between alcohol consumption and incident coronary heart disease in MASALA cohort.

Tables and Figures

Table 1. Baseline Characteristics of MASALA Participants						
	Alcohol consumption (number of drinks/week)					
Characteristics Mean± SD or N (%)	**Never** N=198	**Former** N=247	**1-3** N=147	**4-7** N=68	**>7** N=41	***P* value[a]**
Male	61 (31)	141 (57)	98 (67)	53 (78)	39 (95)	**<0.001**
Age (years)	60 ± 9.2	59.3 ± 9.1	58.4 ± 9.8	58.9 ± 8.3	60.9 ± 10.5	0.449
Education < Bachelor's degree	39 (20)	20 (8)	8 (5)	6 (9)	2 (5)	**<0.001**
Family Income ≥ $75,000 per year	126 (67)	193 (79)	118 (82)	59 (88)	30 (79)	**0.001**
LS 7 metrics						
Smoker Status						**<0.001**
Never	191 (97)	211 (85)	111 (75)	46 (68)	20 (49)	
Former	5 (2)	31 (13)	32 (22)	18 (26)	16 (39)	
Current	2 (1)	5 (2)	4 (3)	4 (6)	5 (12)	
BMI (kg/m^2)	26.4 ± 4	26.8 ± 4.2	26.4 ± 4.3	26.1 ± 3.3	26.1 ± 3.6	0.575
Total Cholesterol (mg/dl)	189.1 ± 37.5	184.1 ± 42.7	189.2 ± 41.3	181.6 ± 37	187.3 ± 42.1	0.506
Lipid-lowering medications	59 (30)	80 (32)	45 (31)	31 (46)	18 (44)	0.08
Systolic Blood Pressure (mm Hg)	127.3 ± 18.8	127.1 ± 17.7	126.8 ± 17.8	129.6 ± 13	131.1 ± 16	0.563
Diastolic Blood Pressure (mm Hg)	73.6 ± 9.8	74.7 ± 9.8	75.7 ± 8.6	78.7 ± 8.5	77.9 ± 10.1	**<0.001**
Antihypertensive Medications	66 (33)	89 (36)	54 (37)	26 (38)	18 (44)	0.754
Fasting blood glucose (mg/dl)	107.6 ± 24.6	110.1 ± 24.2	104.8 ± 18.3	117.2 ± 26.3	112.8 ± 20.8	**0.004**
Diabetic medications	31 (16)	60 (24)	25 (17)	17 (25)	7 (17)	0.121
Diet Score	2.06 (0.91)	2.12 (0.90)	1.99 (0.90)	1.99 (0.91)	2.0 (0.92)	0.604
Physical activity (MET-min per week)	1295.3 (1299.2)	1544.9 (1537.2)	1621.3 (1235.1)	1911.7 (1632.6)	1805.6 (1677.6)	**0.016**
CVH Score, N (%)						
Poor (0-6)	15 (7.6)	31 (12.6)	8 (5.4)	6 (8.8)	9 (21.9)	
Intermediate (7-10)	138 (69.7)	167 (67.6)	108 (73.5)	51 (75)	27 (65.9)	0.054
Ideal (11-14)	45 (22.7)	49 (19.8)	31 (21.1)	11 (16.2)	5 (12.2)	
Abbreviations: BMI, body mass index; CVH, Cardiovascular health; LS7, Life's Simple 7; MET, metabolic equivalent **[a] P value by ANOVA for continuous variables and chi-square for categorical variables**						

Table 2. Distribution of Life's Simple 7 metrics by alcohol consumption						
	Alcohol consumption (number of drinks/week)					
	Never N=198	**Former** N=247	**1-3** N=147	**4-7** N=68	**>7** N=41	***P* value[a]**
Smoking						
Poor	2 (1%)	5 (2%)	4 (3%)	4 (6%)	5 (12%)	**<0.001**
Intermediate	5 (3%)	31 (13%)	32 (22%)	18 (26%)	16 (39%)	
Ideal	191 (96%)	211 (85%)	111 (75%)	46 (68%)	20 (49%)	
Body Mass Index						
Poor	32 (16%)	43 (18%)	19 (13%)	7 (10%)	6 (15%)	0.736
Intermediate	94 (47%)	112 (45%)	63 (43%)	30 (44%)	19 (46%)	
Ideal	72 (37%)	92 (37%)	65 (44%)	31 (46%)	16 (39%)	
Total Cholesterol						
Poor	13 (6%)	24 (10%)	17 (11%)	3 (5%)	4 (10%)	**0.044**
Intermediate	110 (56%)	135 (54%)	79 (54%)	52 (76%)	25 (61%)	
Ideal	75 (38%)	88 (36%)	51 (35%)	13 (19%)	12 (29%)	
Blood Pressure						
Poor	46 (23%)	62 (25%)	29 (20%)	16 (23%)	11 (27%)	0.764
Intermediate	97 (49%)	119 (48%)	78 (53%)	38 (56%)	23 (56%)	
Ideal	55 (28%)	66 (27%)	40 (27%)	14 (21%)	7 (17%)	
Blood Glucose						
Poor	27 (14%)	43 (17%)	20 (13%)	19 (28%)	7 (17%)	**<0.01**
Intermediate	82 (41%)	108 (44%)	57 (39%)	33 (48%)	28 (68%)	
Ideal	89 (45%)	96 (39%)	70 (48%)	16 (24%)	6 (15%)	
Diet Quality						
Poor	61 (31%)	69 (28%)	49 (33%)	22 (32%)	12 (29%)	0.920
Intermediate	130 (66%)	163 (66%)	91 (62%)	42 (62%)	28 (68%)	
Ideal	7 (3%)	14 (6%)	7 (5%)	4 (6%)	1 (3%)	
Physical Activity						
Poor	28 (14%)	28 (11%)	8 (5%)	2 (3%)	6 (15%)	**0.029**
Intermediate	43 (22%)	41 (17%)	23 (16%)	12 (18%)	5 (12%)	
Ideal	127 (64%)	178 (72%)	116 (79%)	54 (79%)	30 (73%)	
[a] P-value compares differences between never, former, 1–3, 4-7 and >7						

Table 3. Adjusted Multivariable Odds Ratio and 95% CI of association between alcohol consumption and cardiovascular health

Alcohol Consumption	Intermediate vs Poor		Ideal vs Poor	
	Odds Ratio (95% CI)	*p-value*	*Odds Ratio (95% CI)*	*p-value*
Model 1[a]		**<0.001**		**<0.001**
Never Drinker	*reference*		*reference*	
Former Drinker	0.59 (0.30, 1.13)	0.11	0.53 (0.25, 1.10)	0.09
1-3 drinks/week	1.45 (0.60, 3.59)	0.40	1.29 (0.49, 3.42)	0.60
4-7 drinks/week	0.92 (0.34, 2.5)	0.87	0.61 (0.19, 1.94)	0.40
>7 drinks/week	**0.33 (0.13, 0.82)**	**0.02**	**0.19 (0.05, 0.64)**	**0.008**
Model 2[b]				
Never Drinker	*reference*	**<0.001**	*reference*	**<0.001**
Former Drinker	0.54 (0.26, 1.10)	0.09	0.46 (0.20, 1.04)	0.06
1-3 drinks/week	1.19 (0.45, 3.15)	0.73	0.90 (0.31, 2.65)	0.85
4-7 drinks/week	0.72 (0.24, 2.17)	0.56	0.40 (0.11, 1.45)	0.16
>7 drinks/week	**0.33 (0.11, 0.96)**	**0.04**	**0.21 (0.05, 0.86)**	**0.03**

[a]Model 1 unadjusted
[b]Model 2 adjusted for age, sex, education, and income
OR < 1 is interpreted as decreased odds of having an ideal or intermediate cardiovascular health score

Table 4. Adjusted Odds Ratio and 95% CI of association between binge drinking and cardiovascular health

Binge drinking past month	**Intermediate vs Poor**		**Ideal vs Poor**	
	Odds Ratio (95% CI)	***p-value***	***Odds Ratio (95% CI)***	***p-value***
Model 1[a]		**<0.001**		**<0.001**
No (Never) (n= 198)	*reference*		*reference*	
No (current) (n=229)	0.94 (0.46, 1.92)	0.86	0.80 (0.37, 1.78)	0.60
Yes (n=27)	0.60 (0.18, 1.97)	0.40	**0.08 (0.01, 0.81)**	**0.03**
Model 2[b]		**<0.001**		**<0.001**
No (Never) (n= 198)	*reference*		*reference*	
No (current) (n=229)	1.21 (0.51, 2.86)	0.66	0.85 (0.32, 2.26)	0.76
Yes (n=27)	0.75 (0.20, 2.83)	0.66	**0.10 (0.01, 0.93)**	**0.04**

[a]Model 1 unadjusted
[b]Model 2 adjusted for age, sex, education, and income
OR < 1 is interpreted as decreased odds of having an ideal or intermediate cardiovascular health score

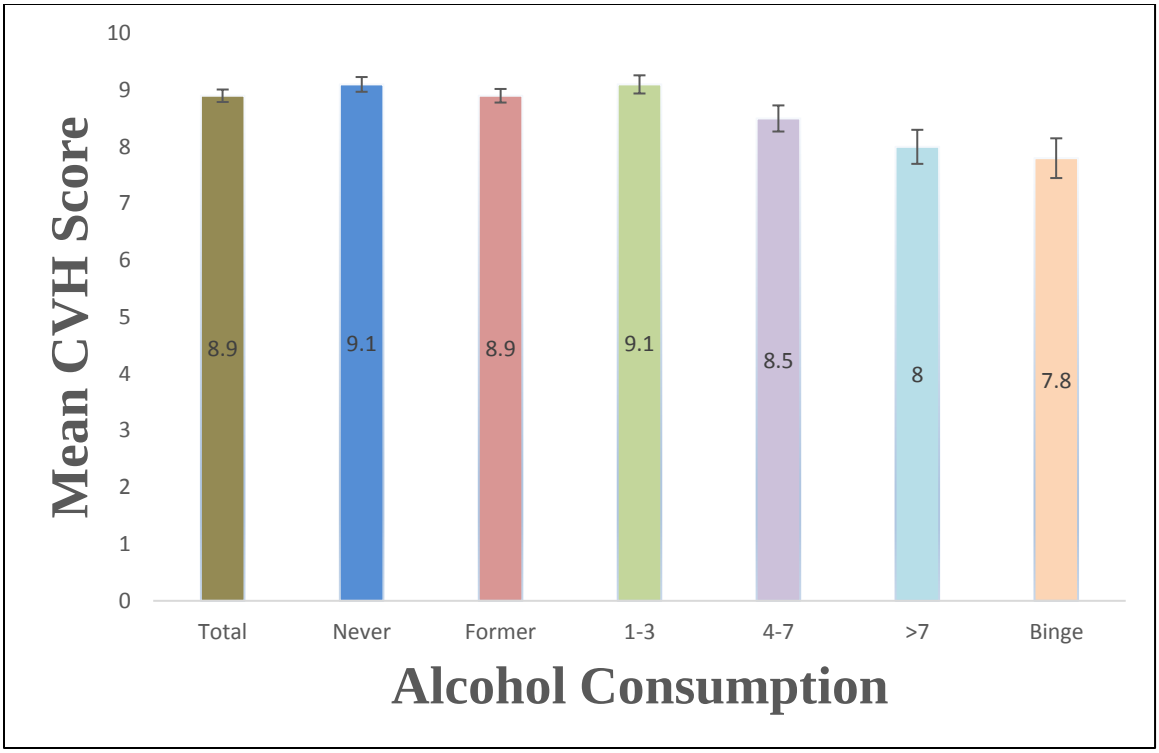

Figure-1 Mean CVH score (and SE) for alcohol consumption

Supplemental Material

Table S1. Adjusted Odds Ratio and 95% CI of association between alcohol consumption and cardiovascular health, by Age

	<58		**≥58**	
Alcohol Consumption	**Intermediate vs Poor**	**Ideal vs Poor**	**Intermediate vs Poor**	**Ideal vs Poor**
	Odds Ratio (95% CI)		***Odds Ratio (95% CI)***	
Model 1[a]				
Never Drinker	*reference*		*reference*	
Former Drinker	0.54 (0.18, 1.65)	0.53 (0.16, 1.74)	0.61 (0.27, 1.38)	0.50 (0.19, 1.32)
1-3 drinks/week	1.75 (0.40, 7.68)	1.25 (0.26, 5.93)	1.18 (0.39, 3.65)	1.24 (0.35, 4.44)
4-7 drinks/week	0.95 (0.17, 5.25)	0.63 (0.10, 4.05)	0.90 (0.26, 3.11)	0.60 (0.13, 2.71)
>7 drinks/week	0.47 (0.08, 2.76)	0.31 (0.04, 2.38)	**0.29 (0.10, 0.86)**	**0.14 (0.02, 0.78)**
Model 2[b]				
Never Drinker	*reference*		*reference*	
Former Drinker	0.44 (0.13, 1.53)	0.37 (0.10, 1.41)	0.58 (0.24, 1.44)	0.53 (0.18, 1.55)
1-3 drinks/week	1.55 (0.31, 7.75)	0.89 (0.11, 4.95)	0.98 (0.29, 3.38)	1.09 (0.26, 4.51)
4-7 drinks/week	0.74 (0.11, 4.88)	0.37 (0.05, 2.91)	0.72 (0.19, 2.78)	0.45 (0.08, 2.55)
>7 drinks/week	0.43 (0.06, 2.99)	0.26 (0.03, 2.44)	**0.27 (0.07, 0.99)**	**0.19 (0.03, 0.95)**

[a]Model 1 unadjusted
[b]Model 2 adjusted for sex, education and income
OR < 1 is interpreted as decreased odds of having an ideal or intermediate cardiovascular health score

Table S2. Adjusted Odds Ratio and 95% CI of association between alcohol consumption and Life's simple 7 metrics

	Smoking	**BMI**	**Total Cholesterol**	**Blood Pressure**
Alcohol Consumption	**Ideal vs. Poor**	**Ideal vs. Poor**	**Ideal vs. Poor**	**Ideal vs. Poor**
	Odds Ratio (95% CI)			
Never Drinker	*reference*	*reference*	*reference*	*reference*
Former Drinker	**0.32 (0.13, 0.76)**	0.91 (0.60, 1.38)	0.61 (0.27, 1.38)	0.82 (0.54, 1.23)
1-3 drinks/week	**0.16 (0.06, 0.39)**	1.12 (0.70, 1.81)	1.18 (0.39, 3.65)	0.71 (0.44, 1.16)
4-7 drinks/week	**0.12 (0.04, 0.31)**	1.21 (0.66, 2.22)	0.90 (0.26, 3.11)	**0.33 (0.16, 0.66)**
>7 drinks/week	**0.06 (0.02, 0.17)**	0.78 (0.36, 1.69)	**0.29 (0.10, 0.86)**	**0.49 (0.22, 0.98)**
	Blood Glucose	**Healthy Diet**	**Physical Activity**	
Alcohol Consumption	**Ideal vs. Poor**	**Ideal vs. Poor**	**Ideal vs. Poor**	
	Odds Ratio (95% CI)			
Never Drinker	*reference*	*reference*	*reference*	
Former Drinker	0.78 (0.51, 1.19)	1.55 (0.60, 4.03)	1.33 (0.86, 2.05)	
1-3 drinks/week	1.09 (0.67, 1.77)	1.28 (0.42, 3.96)	1.67 (0.98, 2.86)	
4-7 drinks/week	**0.34 (0.17, 0.69)**	1.20 (0.28, 5.15)	1.67 (0.82, 3.37)	
>7 drinks/week	**0.27 (0.10, 0.71)**	0.77 (0.08, 6.94)	1.59 (0.67, 3.78)	

Model adjusted for age, sex, education, and income
OR < 1 is interpreted as decreased odds of having an ideal or intermediate cardiovascular health score

Table S3. Adjusted Beta-coefficient and 95% CI of association between alcohol consumption Categories and CVH score

Alcohol Consumption	Model 1		Model 2	
	Beta-Coefficient (95% CI)	***p-value***	***Beta-Coefficient (95% CI)***	***p-value***
Never Drinker	*reference*		*reference*	
Former Drinker	-0.149 (-0.502, 0.205)	0.41	-0.17 (-0.52, 0.18)	0.35
1-3 drinks/week	0.080 (-0.323, 0.484)	0.70	-0.05 (-0.47, 0.36)	0.80
4-7 drinks/week	-0.511 (-1.033, 0.009)	0.06	-0.62 (-1.15, -0.09)	**0.02**
>7 drinks/week	-1.056 (-1.692, -0.419)	**0.001**	-0.87 (-1.52, -0.21)	**0.009**

Abbreviations: CVH, Cardiovascular health
Model 1 Unadjusted
Model 2 adjusted for age, sex, race, and income

References

1. Pescatello LS, MacDonald HV, Lamberti L, Johnson BT. Exercise for Hypertension: A Prescription Update Integrating Existing Recommendations with Emerging Research. *Curr Hypertens Rep.* 2015;17(11):87.
2. Kelly MP, Barker M. Why is changing health-related behavior so difficult? *Public Health.* 2016;136:109-116.
3. Polsky S, Akturk HK. Alcohol Consumption, Diabetes Risk, and Cardiovascular Disease Within Diabetes. *Curr Diabetes Rep.* 2017;17(12).
4. Beulens JWJ, Algra A, Soedamah-Muthu SS, et al. Alcohol consumption and risk of recurrent cardiovascular events and mortality in patients with clinically manifest vascular disease and diabetes mellitus: The Second Manifestations of ARTerial (SMART) disease study. *Atherosclerosis.* 2010;212(1):281-286.
5. Wood AM, Kaptoge S, Butterworth AS, et al. Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies. *Lancet.* 2018;391(10129):1513-1523.
6. Lloyd-Jones DM, Hong Y, Labarthe D, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. *Circulation.* 2010;121(4):586-613.
7. Ogunmoroti O, Osibogun O, McClelland RL, Burke GL, Nasir K, Michos ED. Alcohol and ideal cardiovascular health: The Multi-Ethnic Study of Atherosclerosis. *Clin Cardiol.* 2019;42(1):151-158.
8. Piano MR, Burke L, Kang M, Phillips SA. Effects of Repeated Binge Drinking on Blood Pressure Levels and Other Cardiovascular Health Metrics in Young Adults: National Health and Nutrition Examination Survey, 2011-2014. *Journal of the American Heart Association.* 2018;7(13).
9. Kanaya AM, Kandula N, Herrington D, et al. Mediators of Atherosclerosis in South Asians Living in America (MASALA) Study: Objectives, Methods, and Cohort Description. *Clinical Cardiology.* 2013;36(12):713-720.
10. Kanaya AM, Vittinghoff E, Lin F, et al. Incidence and Progression of Coronary Artery Calcium in South Asians Compared With 4 Race/Ethnic Groups. *Journal of the American Heart Association.* 2019;8(2).
11. Jin YC, Kanaya AM, Kandula NR, Talegawkar SA. The AHA Life's Simple 7 Metric is Inversely Associated with Subclinical Atherosclerosis Among South Asians: Findings From the Mediators of Atherosclerosis in South Asians Living in America Study. *Circulation.* 2016;133.
12. Ainsworth BE, Irwin ML, Addy CL, Whitt MC, Stolarczyk LM. Moderate physical activity patterns of minority women: the Cross-Cultural Activity Participation Study. *J Womens Health Gend Based Med.* 1999;8(6):805-813.
13. Mukherjea A, Underwood KC, Stewart AL, Ivey SL, Kanaya AM. Asian Indian views on diet and health in the United States: importance of understanding cultural and social factors to address disparities. *Fam Community Health.* 2013;36(4):311-323.
14. McClelland RL, Bild DE, Burke GL, Mukamal KJ, Lima JA, Kronmal RA. Alcohol and coronary artery calcium prevalence, incidence, and progression: results from the Multi-Ethnic Study of Atherosclerosis (MESA). *American Journal of Clinical Nutrition.* 2008;88(6):1593-1601.

15. O'Keefe JH, Bybee KA, Lavie CJ. Alcohol and cardiovascular health - The razor-sharp double-edged sword. *Journal of the American College of Cardiology.* 2007;50(11):1009-1014.
16. Rimm EB, Williams P, Fosher K, Criqui M, Stampfer MJ. Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors. *British Medical Journal.* 1999;319(7224):1523-1528D.
17. Zhao J, Stockwell T, Roemer A, Naimi T, Chikritzhs T. Alcohol Consumption and Mortality From Coronary Heart Disease: An Updated Meta-Analysis of Cohort Studies. *Journal of Studies on Alcohol and Drugs.* 2017;78(3):375-386.
18. O'Keefe EL, DiNicolantonio JJ, O'Keefe JH, Lavie CJ. Alcohol and CV Health: Jekyll and Hyde J-Curves. *Prog Cardiovasc Dis.* 2018;61(1):68-75.
19. Schooling CM, Wenjie S, Ho SY, et al. Moderate Alcohol Use and Mortality from Ischaemic Heart Disease: A Prospective Study in Older Chinese People. *PLoS One.* 2008;3(6).
20. Halanych JH, Safford MM, Kertesz SG, et al. Alcohol Consumption in Young Adults and Incident Hypertension: 20-Year Follow-up From the Coronary Artery Risk Development in Young Adults Study. *American Journal of Epidemiology.* 2010;171(5):532-539.
21. Nunez-Cordoba JM, Martinez-Gonzalez MA, Bes-Rastrollo M, Toledo E, Beunza JJ, Alonso A. Alcohol Consumption and the Incidence of Hypertension in a Mediterranean Cohort: the SUN Study. *Revista Espanola De Cardiologia.* 2009;62(6):633-641.
22. Yusuf S, Hawken S, Ounpuu S. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study (vol 364, pg 937m 2004). *Lancet.* 2004;364(9450):2020-2020.
23. Kwasnicka D, Dombrowski SU, White M, Sniehotta F. Theoretical explanations for maintenance of behaviour change: a systematic review of behaviour theories. *Health Psychol Rev.* 2016;10(3):277-296.
24. McKee SA, Krishnan-Sarin S, Shi J, Mase T, O'Malley SS. Modeling the effect of alcohol on smoking lapse behavior. *Psychopharmacology (Berl).* 2006;189(2):201-210.
25. King A, McNamara P, Conrad M, Cao D. Alcohol-induced increases in smoking behavior for nicotinized and denicotinized cigarettes in men and women. *Psychopharmacology (Berl).* 2009;207(1):107-117.
26. Kahler CW, Metrik J, Spillane NS, et al. Acute effects of low and high dose alcohol on smoking lapse behavior in a laboratory analogue task. *Psychopharmacology (Berl).* 2014;231(24):4649-4657.
27. Jackson KM, Rohsenow DJ, Piasecki TM, Howland J, Richardson AE. Role of Tobacco Smoking in Hangover Symptoms Among University Students. *Journal of Studies on Alcohol and Drugs.* 2013;74(1):41-49.
28. Harrison ELR, Mckee SA. Young adult non-daily smokers: Patterns of alcohol and cigarette use. *Addict Behav.* 2008;33(5):668-674.
29. Roerecke M, Tobe SW, Kaczorowski J, et al. Sex-Specific Associations Between Alcohol Consumption and Incidence of Hypertension: A Systematic Review and Meta-Analysis of Cohort Studies. *Journal of the American Heart Association.* 2018;7(13).
30. Husain K, Ansari RA, Ferder L. Alcohol-induced hypertension: Mechanism and prevention. *World J Cardiol.* 2014;6(5):245-252.
31. Emanuele NV, Swade TF, Emanuele MA. Consequences of alcohol use in diabetics. *Alcohol Health Res W.* 1998;22(3):211-219.
32. Kalinowski A, Humphreys K. Governmental standard drink definitions and low-risk alcohol consumption guidelines in 37 countries. *Addiction.* 2016;111(7):1293-1298.

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2011 – Present	American Medical Association
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2011 – Present	American Heart Association
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2016 – Present	Preceptor, Physician Assistant students
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2017 – Present	Member, Hospitalist Scheduling Committee
2017 – Present	Member, Lead (Admin) of Day Committee
2017 – Present	Member, HM Research Committee
2018 – Present	Member, HM Education Committee

HONORS AND AWARDS

2014	Most Academically Oriented Resident of the Year
2017	Nominee, Harrison Award for resident education
2019	Winner of the best oral presentation and the best overall abstract 2019 Perioperative Medicine Summit (SPAQI)

BIBLIOGRAPHY

ORAL PRESENTATIONS

Corrected QT and JT dispersion in EKG of alcoholics. Jersey City Medical Center Resident Research Day, June 2012

Prediction of anxiety in relative s of ICU patients. Jersey City Medical Center Resident Research Day, June 2012

Strongyloidiasis and diffuse alveolar hemorrhage in patient with systemic lupus erythematosus. Jersey City Medical Center Resident Research Day, June 2013

Acute Chest Syndrome: Role of exchange transfusion. Jersey City Medical Center Resident Research Day, June 2013

DRESS syndrome: The great masquerader. Jersey City Medical Center Resident Research Day, June 2014

Squamous cell carcinoma of de novo kidney allograft: An extremely rare tumor.Jersey City Medical Center Resident Research Day, June 2014

POSTER PRESENTATIONS

Corrected QT and JT dispersion in EKG of alcoholics. Jersey City Medical Center Resident Research Day 2012

Incidence of GI Bleed in Setting of Acute Myocardial Infarction: A Single Center Expereince. Jersey City Medical Center Resident Research Day 2012

Mortality in Severe Sepsis: Is it gender biased? Jersey City Medical Center Resident Research Day 2012

Prediction of anxiety in relative s of ICU patients. 2012 Annual Graduate Medical Education Research Day: Mount Sinai School of Medicine, Jersey City Medical Center Resident Research Day 2012

A rare cause of acute coronary syndrome: spontaneous coronary dissection. ACP 2012 National Abstract Competition

Aortic dissection after chemotherapy with Docetaxel and Cyclophosphamide for breast cancer: A case report. Jersey City Medical Center Resident Research Day 2013

Acute Chest Syndrome: Role of exchange transfusion. Jersey City Medical Center Resident Research Day 2013

Endobronchial-covered stent insertion in the management of massive hemoptysis caused by lung cancer. CHEST Annual Meeting 2013; Chicago, IL, Jersey City Medical Center Resident Research Day 2013

Vanishing lung syndrome in a patient with HIV infection and heavy marijuana use

CHEST Annual Meeting 2013; Chicago, IL, Jersey City Medical Center Resident Research Day 2013

Strongyloidiasis and diffuse alveolar hemorrhage in patient with systemic lupus erythematosus. ACP 2013 New Jersey local chapter, CHEST Annual Meeting 2013; Chicago, IL, Jersey City Medical Center resident research day 2013

Improper Use of Antinuclear Antibody (ANA) Test Can Result in Misdiagnosis, Increased Patient Anxiety, and Wasted Health Care Resources. American College of Rheumatology Annual Meeting 2014; Boston, MA

Squamous cell carcinoma of de novo kidney allograft: An extremely rare tumor Society of Hospital Medicine Annual Meeting 2015; National Harbor, MD, 2016 ACP North Carolina Chapter Annual Meeting, Greensboro, NC

Dramatic response to Infliximab in refractory neurosarcoidosis complicated by cryptococcal meningitis. Society of Hospital Medicine Annual Meeting 2015; National Harbor, MD, 2016 ACP North Carolina Chapter Annual Meeting, Greensboro, NC

Hyperammonemia: It's not always liver. Society of Hospital Medicine Annual Meeting 2015; National Harbor, MD

Collapsing FSGS caused by acute Epstein- Barr virus infection: a case report. Society of Hospital Medicine Annual Meeting 2015; National Harbor, MD

Beta Blocker Use in Asymptomatic Patients with Sepsis and Elevated Troponin is Associated with Lower Risk of Mortality. AHA-Basic Cardiovascular Sciences Scientific Sessions; 2017 July 13; Portland, OR

Impact of Multidisciplinary Team Based Patient Care in a Geographically Positioned Hospital Medicine Unit at a Large Academic Medical Center. Annual Research Symposium, Department of Internal Medicine, Wake Forest University School of Medicine, May 2018

Alcohol Consumption and Subclinical Atherosclerosis Among South Asians: Findings From the Mediators of Atherosclerosis in South Asians Living in America (MASALA) Study. American Heart Association, Scientific Sessions 2018, Chicago, IL

Impact of Subclinical Hypoglycemia on Mortality: Findings From the Third National Health and Nutrition Examination Survey. American Heart

Association, Epi/lifestyle Scientific Sessions 2019, Houston, TX

Alcohol Consumption And Risk Of Hypertension. American College of Cardiology 68th Annual scientific session & Expo, 2019, New Orleans, LA

PUBLICATIONS

Aziz F, **Chevli P** "Hyperthyroid Induced Cardiomyopathy in an adult: A case report" The Internet Journal of Cardiology. 2012 Volume 10 Number 2

Brown RE, Surapaneni S, **Chevli P** "Survival with Complete Neurological Recovery after Prolonged Resuscitation" The Internet Journal of Cardiology. 2013 Volume 11 Number 1

Gonzalez-Ibarra F, **Chevli P**, Schachter L, Kaur M, Eivaz-Mohammadi S, Tashtoush B, Matta J, Syed AK, Marian V "Strongyloidiasis and diffuse alveolar hemorrhage in a patient with systemic lupus erythematosus" Case Reports in Medicine. 2014; 2014:278390 PMID: 25024706

Chevli P, Kelash F, Gadhvi P, Grandhi S, Syed A "Spontaneous coronary artery dissection causing acute coronary syndrome in a young patient without risk factors" J Community Hosp Intern Med Perspect. 2014 Sep 29; 4(4) PMID: 25317268

Zeeshan H , Zeeshan A, Polsani S, **Chevli P**, Luqman-Arafath TK, Andleeb S, Kumar P, Menon S, Sunkara P, Bose A. Severe rhabdomyolysis in a sickle cell trait patient associated with consumption of an energy drink. Open J Clin Med Case Rep. 2017; 1346
Ahmad MI, **Chevli PA**, Li Y, Soliman EZ. Vitamin D deficiency and electrocardiographic subclinical myocardial injury: Results from National Health and Nutrition Examination Survey-III. Clin Cardiol. 2018;41(11):1468-1473.

Chevli PA, Ahmad MI, Jogu HR, et al. Electrocardiographic subclinical myocardial injury and alcohol consumption: a cross-sectional analysis of data from the Third National Health and Nutrition Examination Survey. Am J Cardiovasc Dis. 2018;8(5):58-65

Ahmad MI, **Chevli PA**, Li Y, Soliman EZ. Vitamin D deficiency and electrocardiographic subclinical myocardial injury: Results from National Health and Nutrition Examination Survey-III. Clin Cardiol. 2018;41(11):1468-1473.

Anees MA, Ahmad MI, **Chevli PA**, Li Y, Soliman EZ. Association of vitamin D deficiency with electrocardiographic markers of left atrial abnormalities. Ann Noninvasive Electrocardiol. 2019:e12626

Ahmad MI, **Chevli PA**, Barot H, Soliman EZ. Interrelationships Between American Heart Association's Life's Simple 7, ECG Silent Myocardial Infarction, and Cardiovascular Mortality. Journal of the American Heart Association. 2019 Mar 19;8(6):e011648.

MANUSCRIPTS REVIEWED

Association of Homocysteinaemia with Hyperglycaemia, Dyslipidaemia, Hypertension and Obesity. Shirley et al. CVJSA-D-13-00062

Management of Ischemic Heart Disease in Sub-Saharan Africa: The Experience of the Shisong Cardiac Centre. Cabral et al. CVJSA-D-12-00072R1

Ross procedure in a child with Aspergillus endocarditis and bicuspid aortic valve. Kanakis et al. CVJSAD-13-00059

A Penetrating Nail-prick Injury of the Lateral Plantar Artery Leading to Pseudoaneurysm Formation and Rupture a Case Report. Sisli et al. CVJSA-D-13-00078

IN PROGRESS

Type II MI Study: IRB approved study:
Type II MI study is a retrospective, single center study with the goal to examine the relationship of various predictors of adverse outcomes in type II MI. The study is investigating the role of EKG, Echocardiography, stress testing and medication use in type II MI patients that presented with sepsis to the hospital. We identified several key findings and have submitted abstracts related to these findings to national cardiology meetings. The primary outcomes studied are coronary heart disease, heart failure, stroke, myocardial infraction, and mortality.

The role of statin in reducing mortality of hospitalized patients with Type 2 MI
It’s a retrospective study looking at mortality of patients who were found to have Type 2 MI and were discharged on statin.

Alcohol Consumption and Subclinical Atherosclerosis among South

Asians: Findings from the Mediators of Atherosclerosis in South Asians Living in America (Masala) Study
It is a cross-sectional analysis examining the association of alcohol consumption and subclinical atherosclerosis in a healthy South Asian population

COMMUNITY ACTIVITIES AND SERVICE

2003	Polio Immunization Camp, Surat, India
2006	Health Camps after floods in Surat, India