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ASSOCIATION BETWEEN STONE FRUIT INTAKE AND MARKERS OF CARDIOVASCULAR DISEASE RISK AMONG UNITED STATES ADULTS: NHANES 2017-2018

A Thesis

Presented to

The Faculty of the Department of Nutrition, Food Sciences and Packaging

San José State University

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

by

Lasya S. Shah

May 2022

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The Designated Thesis Committee Approves the Thesis Titled

ASSOCIATION BETWEEN STONE FRUIT INTAKE AND MARKERS OF CARDIOVASCULAR DISEASE RISK AMONG UNITED STATES ADULTS: NHANES 2017-2018

by

Lasya S. Shah

APPROVED FOR THE DEPARTMENT OF NUTRITION, FOOD SCIENCE AND PACKAGING

SAN JOSÉ STATE UNIVERSITY

May 2022

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ABSTRACT

ASSOCIATION BETWEEN STONE FRUIT INTAKE AND MARKERS OF CARDIOVASCULAR DISEASE RISK AMONG UNITED STATES ADULTS: NHANES 2017-2018

by Lasya S. Shah

Cardiovascular Disease (CVD) is the most common cause of mortality in the world affecting people from all backgrounds. There is abundant evidence supporting diet affecting the risk for CVD. The consumption of fruits and vegetables is inversely related to CVD risk factors, likely due to their content of phenolic compounds. Although stone fruits contain high quantities of phenolic compounds, it remains unclear if their intake is associated with CVD risk. In this study, data from the National Health and Nutrition Examination Survey 2017-2018 were used to estimate the consumption level of stone fruits and whether it was associated with CVD biomarkers: high sensitivity C-reactive protein, triglycerides, high-density lipoprotein, and low-density lipoprotein across 3 levels of consumption (0, <1, >1 serving/day). Other variables assessed included education, poverty index, alcohol consumption, sedentary activity, smoking, and diet. Data were analyzed using the IBM SPSS Complex Samples software to account for weighting. A total of 2,110 subjects were included in the analysis. No associations between stone fruits consumption level and the CVD biomarkers were observed (all $p>0.05$). However, some secondary variables were associated: education ($p<0.001$), poverty index ($p=0.013$), alcohol consumption ($p=0.004$), sedentary activity ($p<0.001$), smoking ($p=0.001$), and fiber intake ($p=0.002$). More research on a larger sample using individual stone fruits and accounting for confounding factors are needed to determine if there is an association between their consumption and CVD risk.

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LIST OF ABBREVIATIONS

BMI—Body Mass Index
BP—Blood Pressure
CHD—Congenital Heart Disease
CT—Computerized Tomography
CVD—Cardiovascular Disease
FNDDS–Food and Nutrient Database for Dietary Studies
FW—Fresh Weight
HDL—High Density Lipoprotein
hs-CRP—High Sensitivity C-Reactive protein
LDL—Low Density Lipoprotein
MEC—Mobile Examination Center
MI—Myocardial Infarction
MRI—Magnetic Resonance Imaging
NCHS—National Center for Health Care Statistics
NHANES—National Health and Nutrition Examination Survey
TG—Triglycerides

Literature Review

Introduction

Cardiovascular disease (CVD) is the leading cause of death in the world (Dhingra & Vasan, 2017; Guttmacher & Collins, 2002). There are many types of CVD including heart attack, heart disease, stroke, heart failure, and arrhythmias (World Heart Federation, 2021). One person will die every 36 seconds from CVD in the United States and 1 in 4 deaths will be from heart disease (Centers for Disease Control and Prevention [CDC], 2021d). It is a condition where both the heart and the vasculature are affected and are no longer functioning properly (Zhao et al., 2017).

Cardiovascular disease can be caused and exacerbated by many factors including poor diet, lifestyle choices, lack of physical activity, high levels of cholesterol, and high blood pressure (National Cancer Institute [NCI], 2011). The onset of CVD is caused by risk factors which then can combine and contribute to the development of subclinical diseases of CVD (Vasan, 2006). There are specific populations that have a higher chance of developing CVD (Kris-Etherton et al., 2020). It affects those who have a lower socioeconomic status or are non-Hispanic black, as well as those who have a limited education, though there is more complexity to this (Kris-Etherton et al., 2020; Kelli et al., 2019).

Epidemiological studies have shown that risk factors such as poor diet, lack of exercise, excessive smoking and alcohol consumption is associated with the development of heart disease and can contribute to 80% of the population's risk of getting a form of CVD (Sala-Vila et al., 2015). However, there are many ways to help prevent CVD risk factors from developing further. Lifestyle changes are one of the most common ways to help with cardiovascular disease prevention and within this category, nutrition plays a significant role (Sala-Vila et al., 2015).

Previous observational studies have shown that there is a positive association between the consumption of fruits and vegetables and the chances of CVD risk factors (Sala-Vila et al., 2015; Vasan, 2006). Epidemiological studies have shown that there is an inverse association between the consumption of fruits and vegetables and a multitude of inflammatory diseases including CVD (Kelley et al., 2018). Diets containing high quantities of antioxidants have been theorized to be protective against reactive oxygen species which could help protect against CVD (Alissa & Ferns, 2017).

Stone fruits have been found to contain a high quantity of phytonutrients and are well known to be rich in bioactive compounds (Meena et al., 2021). Common stone fruits include peaches, plums, cherries, apricots, and mangoes (Meena et al., 2021). There are links to cherries having beneficial outcomes on lowering blood pressure (BP), modulating blood glucose, enhancing cognitive function, protecting against oxidative stress, and reducing inflammation (Alba C et al., 2019). Studies have shown that olive oil has high cardioprotective effects (Ros, 2012). This is an assumption based on their high antioxidant content (Ros, 2012). There have also been studies on dates that state that they have a beneficial effect and that they are protective against toxicants that can produce free radicals (Al-Dashti et al., 2021). They are also able to modulate markers like triglycerides, cholesterol and indicators of oxidative stress and inflammation (Al-Dashti et al., 2021).

Overall, there are a few things that indicate that the consumption of stone fruits will have a beneficial impact on CVD risk biomarkers. These things include antioxidants and phenolic compounds, how fruits can help lower inflammation, prevent against oxidative stress, help modulate blood glucose and lower BP. This review will explore what is currently known about stone fruit consumption and if there is any potential association with CVD risk biomarkers.

Cardiovascular Disease

Cardiovascular disease is a general term used to describe the diseases that affect the heart and the blood vessels in the body and the way that it affects the heart and vasculature will vary depending on what specific issue is occurring (heart attack, stroke, heart failure) (Mayo Clinic Staff, 2021). It is the number one cause of death worldwide (Dhingra & Vasan, 2017; Guttmacher & Collins, 2002; Lucas et al., 2011). The presence of this disease can be exacerbated by smoking, lack of exercise, obesity, poor diet, high blood pressure and high cholesterol (Cleveland Clinic, 2021). There are multiple ways that these diseases can be diagnosed, and this can include blood work, an electrocardiogram, a cardiac CT (computerized tomography) or MRI (magnetic resonance imaging) (Cleveland Clinic, 2021). Pharmacology is the standard for treatment for CVD, but this is not an option that works for every individual (Zhao et al., 2017) for reasons such as not being able to afford it, or not having the medication that is needed readily available (Wirtz et al., 2016).

Individuals with coronary heart disease have decreased blood flow to the heart and over a period of time, this can lead to a heart attack (CDC, 2021c). Heart attacks also known as myocardial infarction (MI), occur when the blood flow to the heart has been stopped due to a blood clot (Nabel, 2003). This happens when there is a buildup of fat and cholesterol in the veins which then causes narrowing of the vessel (Blaak & de Vos, 2022). When there is buildup in the vessels, it is possible for pieces of the buildup to break off and get lodged in the vessel which then causes a clot which blocks the blood from reaching the heart (Blaak & de Vos, 2022). Heart failure is when the heart is not working as efficiently as it should and is not meeting the body's needs (American Heart Association, 2017a). A stroke is when the supply of blood to the brain has been reduced (National Health for Chronic Disease Prevention and Health Promotion, & Division for Heart Disease and Stroke Prevention [NCCDPHP & DHDSP], 2021).

Having high blood pressure and high blood cholesterol levels can put an individual at risk of having cardiovascular disease (CDC, 2021d). High blood pressure is a medical condition where the blood flowing through the arteries is at high pressure (CDC, 2019). This is a risk factor for heart disease and if left untreated, it can cause irreversible damage to the heart and some of the other major organs in the body (CDC, 2019). It is commonly known as a silent killer due to it not having any symptoms (CDC, 2019). The only way to know whether an individual has high blood pressure is to measure it (CDC, 2019).

Another risk factor that can lead to cardiovascular disease is high blood cholesterol levels (CDC, 2019). Cholesterol is a wax-like substance that is made up of two types of cholesterol. There is low-density lipoprotein cholesterol (LDL) and there is high-density lipoprotein cholesterol (HDL) (CDC, 2019). Consuming too much cholesterol can cause plaque buildup in the arteries and this can eventually lead to a decrease in blood flow to major organs in the body (CDC, 2019). What will happen is that as the plaque forms and builds up on the inside of the arteries, the opening will narrow, and it will be more difficult for the blood to flow through (CDC, 2021d). The plaques could also rupture, and this could cause a blood clot to form on the ruptured plaque which can then block the blood flow (CDC, 2021d).

The consumption of fruits and vegetables have been shown to have some protective effects against certain diseases, CVD being one of them (Ferretti et al., 2010). The reason for this has been hypothesized to be that the components of fruits and vegetables (i.e., vitamins, fiber, and phytonutrients) are allowing for those protective effects (Ferretti et al., 2010). Epidemiological studies have shown that there is a positive correlation between the increased consumption of fruits and vegetables and the decrease in heart disease mortality (Al-Farsi & Lee, 2008; Gallaher & Gallaher, 2009). Other studies have shown that the consumption of fruits high in phenolic acids is more health protective due to their increased antioxidant content (Abidi et al., 2011). The consumption of fruits and vegetables has been linked to better outcomes with stroke due to the low levels of sodium and high levels of potassium which can help lower blood pressure (Sala-Vila et al., 2015). Fiber-rich diets have also been linked to better CVD risk outcomes, specifically for coronary heart disease (CHD) (Satija & Hu, 2012).

What Causes CVD?

Cardiovascular disease can be caused by a multitude of varied factors (Forouhi & Sattar, 2006). Diet and lifestyle both play a role in the development of CVD and physical activity, or lack thereof can cause the development of diabetes in combination with other risk factors (Forouhi & Sattar, 2006). Smoking and alcohol intake are also factors to look at when talking about CVD (Forouhi & Sattar, 2006).

How to Prevent CVD

There are so many things that could cause someone to develop CVD (Mohammadnezhad et al., 2016). Diet, smoking status, alcohol consumption and physical inactivity are examples of modifiable risk factors, and some not modifiable risk factors include age, gender, and ethnicity (Mohammadnezhad et al., 2016). However, there are some ways to help diminish the risks of developing CVD and this includes things like consuming food low in salt, cholesterol, trans fat, saturated fat, high in fruits and vegetables can help decrease LDL levels and increase HDL levels (Forman & Bulwer, 2006). In addition to this, limiting smoking and decreasing alcohol can help decrease the chance of getting CVD (Forman & Bulwer, 2006).

Prevalence of Cardiovascular Disease

The prevalence of CVD is high, and it is still a main cause of morbidity and mortality in western society (Harchaoui et al., 2009). They are the most common cause of death worldwide and in the United States alone, there are about 805,000 heart attacks every year (CDC, 2021d). Heart disease kills about 1 in 5 women (CDC, 2020b) and 1 in 4 men (CDC, 2021a). In Europe, it is responsible for 48% of deaths each year (Chong et al., 2010).

Who is affected?

Having multiple medical conditions like being overweight or obese, and diabetes mellitus can cause the risk for CVD to increase (CDC, 2021d).

Postmenopausal women are also at risk of CVD (Hong et al., 2021). This is caused by the decrease in their estrogen levels which then causes alterations in their lipid metabolism, vascular function, and blood pressure (Hong et al., 2021). In addition to those factors, it can also increase oxidative dress and the production of pro-inflammatory molecules. (Hong et al., 2021)

In addition to having medical conditions and being postmenopausal, there are certain groups that are more susceptible to developing cardiovascular diseases (Kris-Etherton et al., 2020). CVD affects non-Hispanic Black people more than other groups as well as those who have a lower socioeconomic status (Kris-Etherton et al., 2020). Having more than one socioeconomic factor or environmental burden can also increase an individual's chances of developing CVD (Kris-Etherton et al., 2020).

Demographics

Heart diseases are the leading cause of death for white women as well as African American women in the United States (CDC, 2020b). This is also true for those who have American Indian or Alaskan native backgrounds (CDC, 2020b). For those who are Hispanic, or Asian or Pacific islander heart disease is the second leading cause of death after cancer (CDC, 2020b).

The values for men vary compared to women. Heart disease is the leading cause of death in most of the racial and ethnic groups in the United States for men (CDC, 2021a). Once again this includes African Americans, Native Americans, Alaska natives, Hispanics, and white people (CDC, 2021a). Again, for men heart disease is second to cancer for those who have an Asian American background or a Pacific islander background (CDC, 2021a).

Biomarkers

There are many biomarkers and risk factors that can contribute to the development of cardiovascular diseases (Dhingra & Vasan, 2017). Cardiovascular disease biomarkers are grouped based on the disease specificity (Dhingra & Vasan, 2017). For example, Troponin-T is a biomarker indicating atherosclerotic coronary disease (Dhingra & Vasan, 2017).

Biomarkers can also be classified by the pathologic process that they are representing such as inflammation, oxidative stress, and metabolic stress (Dhingra & Vasan, 2017). A list of some of the biomarkers are shown in Table 1. These biomarkers are high sensitivity C-reactive protein (hs-CRP), low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides (TG).

Table 1.
Description and Use of Cardiovascular Disease Blood Biomarkers

Biomarker	Description	Use	Reference
High Sensitivity C-Reactive Protein	A marker of inflammation that can help predict the occurrence of cardiovascular diseases. Its use is becoming common practice.	Can be used as a predictor of future cardiovascular morbidity and mortality among individuals with known cardiovascular disease. Also, can help predict the occurrence of heart attack, stroke, peripheral arterial disease, and sudden cardiac death in healthy individuals with no history of cardiovascular disease.	(Bassuk et al., 2004; Rifai & Ridker, 2001; Windgassen et al., 2011)
Low-Density Lipoprotein	Carries cholesterol to the areas of the body that need it.	High levels can indicate that an individual is more likely to have heart disease, heart attacks, stroke, coronary artery disease and peripheral artery disease.	(CDC, 2020a; Hoffman, 2022)
High-Density Lipoprotein	Transports cholesterol to the liver where it can be flushed from the body.	High levels improve the risk of heart disease, however low levels can increase the risk of heart disease, especially when coupled with high low-density lipoprotein and high triglycerides.	(CDC, 2020a; Hoffman, 2020)
Triglyceride	TGs are fat that are used to help store unused calories in the body.	High uncontrolled levels can indicate that an individual is at a higher risk for coronary heart disease and stroke. Very high levels can lead to other issues like acute pancreatitis.	(CDC, 2021b; National Heart, Lung, and Blood Institute, n.d.)

C-reactive protein is a marker for inflammation and has been used as a screening tool to predict the presence of cardiovascular disease (Bassuk et al., 2004). Total cholesterol and LDL cholesterol are well recognized risk factors for CVD (Gallaher & Gallaher, 2009). The national cholesterol education program, also known as NCEP, recommends that target levels of LDL cholesterol and HDL cholesterol can be used to determine potential cardiovascular risk factors (Fernandez & Webb, 2008).

The biomarkers that are of interest in this study are hs-CRP, LDL, HDL, and TG. High sensitivity-C reactive protein is classified as an inflammation biomarker (Dhingra & Vasan, 2017). LDL and HDL are both classified as metabolic biomarkers (Dhingra & Vasan, 2017).

Table 2.
Cardiovascular Disease Biomarkers of Interest and Their Ranges

Biomarkers					**References**
High Sensitivity C-Reactive Protein	Low risk: <1 mg/L	Average risk: 1–3 mg/L	High risk: >3 mg/L		(Pfützner & Forst, 2006; Begum, 2021)
Low-Density Lipoprotein	Optimal: <100 mg/dL	Near optimal: 100–129 mg/dL	Borderline high: 130–159 mg/dL	High: 160–189 mg/dL	(Miller, 2020)
High-Density Lipoprotein	Desirable: 60 mg/dL or more	At risk: <40 mg/dL			(Miller, 2020)
Triglyceride	Normal: <150 mg/dL	Borderline-High: 150–199 mg/dL	High: 200–499 mg/dL	Very High: 500 mg/dL	(Miller, 2020)

High sensitivity C-reactive protein is a marker of inflammation (Bassuk et al., 2004). It is secreted by hepatocytes and monocytes in the body in response to inflammatory conditions including CVD (Castro et al., 2018). It is an acute phase protein that is produced in the liver and binds to phosphorylcholine (Seo, 2012). When there is increased inflammation in the body, then the Hs-CRP levels will also increase and the level in which it rises is based on the increase in the plasma concentration of interleukin-6 (Seo, 2012).

The hs-CRP test is different from the general CRP test because the general test measures for what diseases may be causing inflammation and the hs-CRP test focuses on heart disease and stroke risk (Healthwise Staff, 2020).

High values of hs-CRP are an issue because it is an indicator of inflammation and the higher it is the higher the chance that there is inflammation in the body (Begum, 2021). High sensitivity-C reactive protein can predict future CVD risk in many populations such as healthy individuals, individuals presenting with acute coronary syndrome, those with stable angina or those who are stable post heart attack (Bassuk et al., 2004).

High-density lipoprotein is the cholesterol that has been historically known as “good cholesterol” (Olsson, 2009). It carries cholesterol to the liver where the body can flush it out (CDC, 2020a; Hoffman, 2020). HDL cholesterol has an inverse association with CVD as it protects against it through mechanisms like reversing cholesterol transport, antioxidant mechanisms and anti-inflammatory mechanisms (Cooney et al., 2009). High HDL levels improve the risk of heart disease, however low levels of HDL can increase the risk of heart disease (CDC, 2020a; Hoffman, 2020).

Low density lipoprotein is a fat that circulates in the bloodstream (Pirahanchi et al., 2021). Its purpose is to move cholesterol around the body to where it is needed (Pirahanchi et al., 2021). Low-density lipoprotein is the cholesterol that causes plaque buildup in the arteries (Hoffman, 2022). Increased levels of LDL are associated with an increased risk of developing CVD (Pirahanchi et al., 2021).

There are multiple ways that LDL cholesterol can be calculated. In NHANES laboratory values, there were three ways that LDL was listed: Friedewald’s, Martin-Hopkins, and NIH eq^2. The Martin Hopkins equation was created even though Friedewald's has been used historically because there are some inaccuracies to it, so it was developed to account for the discrepancies in the Friedwalds' calculation (Ferraro et al., 2019).

Triglycerides are another form of lipid that is present in the blood and these lipid cells are calories that the body does not need immediately that have been stored away (Mayo Clinic Staff, 2020). If an individual consistently consumes more calories than needed, then their TG level may be higher and this is important because an increased value of TG can cause issues such as thickening of the artery walls which then lead to more severe issues such as heart disease, stroke, and heart attacks (Mayo Clinic Staff, 2020). Elevated levels of triglycerides and plasma LDL have been associated with increased levels of coronary heart disease, especially when it is coupled with low HDL levels (Alsaif et al., 2007).

High dietary cholesterol has been known to increase total cholesterol, triglycerides, and lipoprotein levels (Alsaif et al., 2007). These high lipid levels increase the risk of developing atherosclerosis (Alsaif et al., 2007). Excessive quantities of dietary cholesterol are linked to increased susceptibility of myocardial ischemia and can irritate ischemic heart disease (Alsaif et al., 2007).

Risk Factors

There are both modifiable and non-modifiable risk factors for cardiovascular disease (Mohammadnezhad et al., 2016). Non-modifiable risk factors are those that an individual has no control over such as age and gender and modifiable risk factors are those that an individual has more control over like diet and physical activity (Mohammadnezhad et al., 2016). Smoking, alcohol consumption, blood lipids, socioeconomic status and blood pressure are other risk factors that are modifiable (Mohammadnezhad et al., 2016). There has been consistent evidence from epidemiological studies stating these risk factors (smoking, alcohol, poor diet, lack of physical activity) contributes to about 80% of the population attributable risk for CVD (Sala-Vila et al., 2015).

Alcohol. Excessive alcohol consumption has been linked to an increased incidence of cardiovascular disease (Costanzo et al., 2010). The recommended dietary allowance for alcohol is 1 to 2 drinks per day for men and for women, it is about one drink per day. These values have been associated with lower risk of things like stroke, coronary artery disease, type 2 diabetes, and heart failure (O'Keefe et al., 2018). On the opposite side of this, more than four drinks per day can lead to CVD (O'Keefe et al., 2018). Studies have shown that consuming more than five standard drinks in a single period can increase BP (Piano, 2017).

Studies say that the excessive consumption of alcohol can be shown in a "j-shaped" curve in that the increase in alcohol can be connected to increased mortality (Costanzo et al., 2010). In a study conducted by Kiechl et al. (1998), the consumption of alcohol was depicted as harmful if consumed in copious quantities and also if not consumed at all. It was seen that consumption of small amounts of alcohol consumed on a regular basis could have some protective effects against cardiovascular disease (Kiechl et al., 1998).

Blood Pressure. Blood pressure is known as a silent killer because Those who have high blood pressure may not know that they have high blood pressure and the only way to know is to measure their blood pressure (American Heart Association, 2017b). There is no way to know just by looking at an individual (American Heart Association, 2017b). Blood pressure readings are shown in Table 3.

Table 3.
Blood Pressure Reading

Blood Pressure Reading	Systolic	&/or	Diastolic
Normal	<120 mm Hg	and	<80
Elevated	120–129	and	<80
High (Stage 1)	130–139	or	80–90
High (Stage 2)	140+	or	90+
Hypertensive Crisis	80+	and/or	120+

Adapted from (American Heart Association, n.d.)

Physical Activity. Physical activity or lack thereof is another risk factor that can increase the chances of an individual developing CVD (Buttar et al., 2005). Taking part in regular physical activity reduces the possibility of developing hypertension, diabetes and helps maintain weight loss, however, by not taking part in regular physical activity can increase the chances of developing CVD (New York State Department of Health, 1999). Inadequate exercise can also cause the development of other heart disease risk factors like high blood pressure, high cholesterol, and obesity (CDC, 2022).

Diet. Poor diet can exacerbate CVD risk (Wang, 2004). Consuming a diet high in sodium, saturated fats, and other highly processed foods can increase the risk of developing cardiovascular disease risk, especially when an individual ages (Wang, 2004). Some studies say that habits developed in childhood will follow an individual into adulthood (Wang, 2004). Consuming a diet high in nutritious foods like fruits, vegetables, and low in fats is important for the prevention of cardiovascular disease risks (Wang, 2004).

Fruits and vegetables are known to be part of a well-balanced diet (Bazzano et al., 2002) The recommendation for fruits and vegetables is >5 servings per day (Sala-Vila et al., 2015).

In fact, past studies have shown that nutrients like antioxidants, folic acid, and potassium are related to lower cardiovascular disease risk (Bazzano et al., 2002). These nutrients are available in fruits and vegetables (Bazzano et al., 2002). These foods are also high in fiber (Sala-Vila et al., 2015). And fiber has been shown to help reduce LDL levels as well as lower blood pressure (Satija and Hu 2012). Bioactive compounds found in food are the more appealing option to treat chronic diseases (Lucas et al., 2011). Some epidemiological studies have shown that there are positive associations with increased fruit and vegetable intake and decreased heart disease mortality (Al-Farsi & Lee, 2008). Other studies have determined that the intake of fruits and vegetables has an inverse association with CVD risk factors (Zhao et al., 2017).

Smoking. Smoking has an impact on developing CVD as it is the leading cause of death for smokers (Erhardt, 2009). Cardiovascular disease risks related to smoking are higher among the younger population (Erhardt, 2009). The risk of a heart attack is higher in those who are over the age of sixty is higher in smokers than in non-smokers (Erhardt, 2009). Also, the dose is important as it increases the relative risk of having something like ischemic heart disease, where the dose is important to its development (Erhardt, 2009).

Not smoking would be the best option so that an individual will not develop CVD due to this risk factor, however, if an individual already smokes, smoking cessation can, over time, help reduce the levels of risk to pre-smoking levels if given the opportunity (Campbell et al., 2008).

Stone Fruit and CVD. As mentioned before, diet plays a key role in the development of CVD as well as can help prevent CVD from developing (Alissa & Ferns, 2017). Recent studies have been looking at fruits and vegetables as a way to help deal with cardiovascular risks (Zhao et al., 2017). Fruit and vegetable consumption have been shown to have an inverse association with certain cardiovascular risk factors (Zhao et al., 2017).

Phenolic Compounds

Phenolic compounds are phytochemicals that are found in most plants including fruits and vegetables (Kan et al., 2014). They play a sensory role in the taste of fruits and vegetables as they contribute to the astringency and bitterness in crops (Kan et al., 2014). They also have been seen to play a role in defense against pathogens and against stresses and injuries (Lara et al., 2020). Studies are showing that the consumption of phenolic rich fruits and vegetables are lowering the risk of cardiovascular diseases like stroke and heart attack (Gonçalves et al., 2018, Lara et al., 2020).

Anthocyanins are a form of phenolic compounds that impacts the color of fruits and vegetables (Kan et al., 2014). Anthocyanins also show anti-inflammatory properties and have been proposed to prevent CVD (Lara et al., 2020). Flavonoids are the most commonly consumed of the phenolic compounds and play a role defending against chronic diseases (Lara et al., 2020).

Phenolics have been thought to have antioxidant properties as well anti-carcinogenic, anti-microbial, anti-allergenic, anti-mutagenic, and anti-inflammatory properties (Kan et al., 2014). They are secondary metabolites that provide health protective effects even though they are not nutrients (De la Rosa et al., 2019). They can help protect against CVD through their antioxidant activity (De la Rosa et al., 2019). Some common groups of phenolic compounds include flavan-3-ols, flavanols, flavanones and hydroxycinnamic acids (Redondo et al., 2017).

Epidemiological studies have shown an inverse association between increased fruit and vegetables intake and the incidence of non-transmissible diseases like CVD (De la Rosa et al., 2019). It is suggested that the antioxidant phytochemicals that are present scavenge the reactive oxygen species which helps remove their harmful effects (De la Rosa et al., 2019).

Some polyphenols that are found in stone fruits include epicatechin (found in flat peach), catechin (cherry and nectarine),neochlorogenic acid (flat peach, peach and plum) and chlorogenic acid (apricot) (Redondo et al., 2017). The amounts of these compounds will vary between stone fruits, and this can be due to the maturity of the stone fruit (Fatima et al., 2018). For example, the total phenolic composition of apricots can range from 50.00-563.00 mg GAE. A study done by Blando & Oomah (2019), mentions that sweet cherries can have about 171.4 mg of anthocyanins, but tart cherries have about 54.5 mg of anthocyanin. Another study conducted by Kim et al. (2005) found that sweet cherries had a total phenolic content of 92.1 to 146.8 mg GAE and tart cherries had a total phenolic content of 146.1 to 312.4 mg GAE (Kim et al., 2005).

Stone Fruits/Drupes

Stone fruits, also commonly known as drupes, include many fruits such as sweet and sour cherries, peaches, and nectarine, as well as multiple species of plums (Famiani et al., 2020). Apricots, olives, and mangos are more examples of stone fruits (Fatima et al., 2018). The term stone fruit comes from the endocarp or the pit of the fruit which is hard. The other parts of stone fruits include the epicarp or skin, and the mesocarp or flesh of the fruit (Famiani et al., 2020). The term drupe includes all the fruit from the *prunus* genus as well as some palm fruits (Fruit Identification Outline, n.d.).

The term stone fruit comes from the stonelike pit (Young, 2019). There are also two separate ways that the pit is embedded in the fruit—clingstone and freestone (Young, 2019). Clingstone fruit has pits that are more attached to the fruit and are more difficult to remove and freestone fruits are those whose pits are more easily removed and in some cases can fall out of the fruit when the fruit has been cut (Young, 2019). Peaches are referred to as clingstone or freestone (Young, 2019).

There are many fruits that are classified as drupes. However, they are not all of the same genus. Some of the genera are *prunus* (Peaches, plums, cherries, etc.), *cocos* (Coconut), *Mangifera* (Mango) and *phoenix* (dates) (Al-Farsi & Lee, 2008; Etienne et al., 2002; Gallaher & Gallaher, 2009; Kelley et al., 2018; Parlakpinar et al., 2009; Rodriguez-Rodriguez, 2015; Shah et al., 2010).

Stone fruits are abundant in sugars, vitamins, minerals, antioxidants, organic acids, dietary fiber, and other beneficial compounds (Wills et al., 1983). The levels of all of these compounds vary between fruit types (Wills et al., 1983).

Apricots

Apricots are also known as *Prunus armeniaca* (Fatima et al., 2018). They are small and are reddish in color. They can be consumed in a variety of ways including raw, dried, and frozen as well as in products like jams and jellies and other mixed food products. They are high in carbohydrates, vitamins, minerals, and dietary fibers as well as phytochemicals, phenolic compounds, and carotenoids (Fatima et al., 2018).

The total phenolic composition of apricots ranges from 50.00-563.00 mg GAE (gallic acid equivalents), and this is determined based on one hundred grams of fresh apricots (Fatima et al., 2018). The concentration of the apricots will depend on the maturity of the apricot (Fatima et al., 2018). The flavonoid composition consists of flavanols, and anthocyanins. They can also range in apricots from 1 to 12 mg per one hundred grams of fresh weight (Fatima et al., 2018).

Apricots have been linked to helping CVD as they are high in antioxidants, as well as phenolic compounds (Fatima et al., 2018). These compounds help inhibit the oxidation of LDL. The dietary fiber present in the apricots also helps the levels of LDL in the body by binding to the cholesterol/bile salts (Fatima et al., 2018). In a study conducted by (Parlakpinar et al., 2009) it was found that the consumption of apricots decreased the size of an infarct in rats compared to those in the control group. In that same study, evaluations using light and electron microscopes determined that there were some similar benefits on ischemia reperfusion in the rats that were fed apricots (Parlakpinar et al., 2009).

Cherries

Cherries are a commonly produced crop in several countries (Chockchaisawasdee et al., 2016). Sour Cherries are known as *Prunus cerasus,* and sweet cherries are known as *Prunus avium* (Kelley et al., 2018). They are the two main cherries that are produced in the United States which are Bing for sweet cherries and Montmorency for tart cherries (Kelley et al., 2018). The cherry fruits are small, about 2 cm in diameter and round and the color of cherry skin ranges from yellow to red to almost black (The Editors of Encyclopedia Britannica, 2021).

Cherries are found in many forms such as fresh, canned, frozen, dried, juiced and processed (Kelley et al., 2018). Some processed cherries include things like cherry pie filling and commercial cherry desserts (U.S. Department of Agriculture, n.d.).

Cherries are high in compounds like polyphenols and antioxidants, and bioactive compounds (Kelley et al., 2018)). Tart cherries are said to have more phenolic compounds and sweet cherries have more anthocyanins (Blando & Oomah, 2019; Kelley et al., 2018). In a study conducted by Blando & Oomah (2019), it was found that sweet cherries have about 171.4 mg of anthocyanins while tart cherries have about 54.5 mg. The level of flavanols in sweet cherries was 2.64 mg where there was no value for tart cherries. For flavanols, there was 15.07 mg in sweet cherries and no value for tart cherries. Lastly, the level of phenol in sweet cherries was 174.9 mg GAE, and 254.1 mg GAE in tart cherries (Blando & Oomah, 2019).

Phenolic-rich fruits and vegetables have been shown to lower the risk of cardiovascular diseases like heart attacks, heart failure, stroke, and arterial hypertension (Gonçalves et al., 2018). Some animal and human studies have shown that the consumption of cherries may reduce some inflammatory diseases including CVD (Kelley et al., 2018). In a study conducted by Chai et al. (2019) tart cherry juice was consumed, and it was found that it helped reduce the systolic blood pressure and LDL cholesterol. This was theorized to be due to the anti-oxidative and anti-inflammatory properties, but more studies need to be done to confirm this (Chai et al., 2019).

Coconuts

Coconuts are classified as drupes. They are also known as *Cocos nucifera* (DebMandal & Mandal, 2011). Some common coconut products include fresh coconut, dried/flaked coconut, coconut milk, coconut cream, coconut water and coconut oil (U.S. Department of Agriculture, n.d.).

Coconut oil is a common way that coconut is used, and it is made of medium chain fatty acids or MCFAs. There are long chain fatty acids in coconut oil as well (Neelakantan et al., 2020). Virgin coconut oil is another coconut oil; however, it is rich in polyunsaturated fatty acids which are beneficial to cardiovascular health (Ma & Lee, 2016). Studies have shown that diets that have elevated levels of saturated fatty acids could lead to increased LDL levels and that could increase the risk of CVD (Neelakantan et al., 2020).

While some studies have shown that coconut oil consumption has increased the levels of HDL in the body, the levels of LDL and TG also increased (Santos et al., 2019). There is still a need for more research on the effect that coconut oil has on HDL (Santos et al., 2019).

Dates

Dates, though considered a stone fruit, are not of the *prunus* genus. They are scientifically known as *Phoenix dactylifera* (Al-Dashti et al., 2021). Dates are a seasonal fruit and there are over two thousand diverse types of dates. They are oblong but there are certain varieties which are round. (Al-Farsi & Lee, 2008).

Dates are about 70% carbs, but they also contain a large amount of dietary fiber and are a reliable source of iron, potassium, and calcium (Al-Farsi & Lee, 2008). They also contain antioxidants which help with the prevention of cardiovascular disease as well as other diseases, cancers, and ailments (Al-Farsi & Lee, 2008).

In the study conducted by (Alsaif et al., 2007) hypercholesterolemic hamsters given a diet supplemented with dates had lower plasma total cholesterol, lower TGs, and lower LDL cholesterol levels. They also had higher HDL cholesterol levels. This data suggests that the consumption of dates could have a beneficial effect in controlling the development of atherosclerosis in humans (Alsaif et al., 2007).

Lychee

Lychee (*Litchi chinensis sonn.*) is also known as litchi or litchee and is a subtropical fruit that originated from China but spread to some tropical and subtropical countries like India, Madagascar, Vietnam, Australia, and Thailand (Sinha et al., 2012). Lychees are grown on trees and the fruit is grown in bunches. When ripe, the exterior is usually hard and bumpy in texture and the color can range from bright red to pale green. Fresh lychee is the most valued, however, because it can desiccate over long distances canning or making lychee juice are some other options for consumption (Sinha et al., 2012).

Lychee has been said to have cardio-protective effects, antioxidants, and anti-inflammatory properties. This has been concluded according to folk medicine and pharmacological studies (Queiroz et al., 2018).

Mango

Mangos (*Mangifera indica L)* are an immensely popular fruit (Shah et al., 2010). They are tropical fruit and have been used in Ayurvedic and indigenous medical use indigenous medical systems for over four thousand years (Shah et al., 2010).

Mangos contain bioactive compounds such as carotenoids, vitamin C and phenolic compounds (Maldonado-Celis et al., 2019). They have also been shown to have anti-inflammatory properties (Lucas et al., 2011). Their total phenolic composition ranges from 0.1 - 33.75 mg per 100 G FW based on the type of mango being looked at (Maldonado-Celis et al., 2019). Mangos have been shown to have both antioxidant and anti-inflammatory properties (Lucas et al., 2011; Meena et al., 2021). Prior to the study conducted by Lucas et al. (2011) there were no studies comparing the consumption of mango and its effect on cardiovascular disease risk factors. (Lucas et al., 2011).

Olives

Olive oil is a common component of the Mediterranean diet (Marcelino et al., 2019). Olive oil is made by pressing ripe olives and the first press of these olives will result in what is called virgin olive oil and virgin olive oil has a blend of beneficial compounds (Ros, 2012).

There have been studies conducted to show that consuming virgin olive oil has beneficial effects on blood lipids, blood pressure, inflammation, and thrombosis which are all cardiovascular biomarkers (Ros, 2012). Olive oil is primarily made up of monounsaturated fatty acids with oleic acid being the primary one (Marcelino et al., 2019). Because of these beneficial compounds and the antioxidant potential found in virgin olive oil, it is assumed that that is what makes the Mediterranean diet cardioprotective (Ros, 2012). Compounds found in olive oil have been seen to have anti-inflammatory properties which help reduce oxidative stress and improve lipid profiles by increasing HDL levels and decreasing LDL and TG levels (Marcelino et al., 2019).

Peaches

Peaches (*Prunus persica*) are drupes which are consumed fresh. Some are processed into juices, peach halves, jams, jellies, and peach baked goods (Zheng et al., 2021). Peaches are commonly consumed summer fruit that has been increasing in interest due to their nutritional makeup. Peaches are high in vitamins, minerals, fiber, and antioxidants (Abidi et al., 2011). It was also found that at various levels of ripening the quantities of organic acids changed (Wang et al., 1993).

In a study conducted by Kono et al. (2013), peach pulp was studied to see if there was any potential to help protect against cardiovascular diseases. At the time that this study took place, there were no reports indicating that peach pulp was effective against a vascular disease (Kono et al., 2013). The study concluded that the solution of the peach and ethyl acetate mixture may have clinical potential for preventing cardiovascular disease like atherosclerosis and hypertension (Kono et al., 2013).

Plums and Prunes

Plums and prunes (dried plums) are also part of the genus *Prunus* and are known as *Prunus domestica* or *Prunus salicina* (Meena et al., 2021).

Plums have high antioxidant levels with the peel having 20% more total antioxidant compared to the flesh of the fruit (Meena et al., 2021). The level of total phenolics in plums will range from cultivar to cultivar with a range of 38.45 - 841.50 mg GAE per one hundred grams fresh weight (Meena et al., 2021). The levels of anthocyanins and carotenoids will also range across cultivars. Carotenoid levels can range from 0.9 - 1.9 mg per one hundred grams fresh weight (Meena et al., 2021).

There have been some human studies in which the consumption of dried plums has helped reduce total and low-density lipoprotein cholesterol (Hong et al., 2021). They have also helped decrease systemic inflammatory biomarkers and reduce lipid peroxidation (Hong et al., 2021). Previous studies have shown that there is a positive effect of dried plum consumption on CVD risk factors, however, there is not enough data about how much dried plum would really be effective on multiple CVD risk factors (Hong et al., 2021).

The National Health and Nutrition Examination Survey

The National Health and Nutrition Examination Survey (NHANES) is a survey that is used to gather information about the health and nutrition status of the US population. NHANES originally began in the 1960s, however, in 1999 the survey started to be conducted more frequently. They look at a sample of about five thousand individuals across the country, per year. This number is representative of the national population. (NHANES, 2020)

The NHANES survey covers the noninstitutionalized population in the United States. Over time, there have been certain subgroups in the population that have been over-sampled to represent the United States population more reliably. The groups that were over-sampled in the 2017–2018 survey included Hispanic people, non-Hispanic Black people, non-Hispanic Asian people, non-Hispanic white and other people who were near or below the 185% of the department of health and human services poverty guidelines, and non-Hispanic whites and others who were 80 years or older. (National Center for Health Statistics, 2017-2018)

NHANES started in 1960 as the National Health Examination Survey (NHES, 2015). After the initial three rotations, each of which focused on their own issue, a new emphasis was put on the program and in 1970 (NHES, 2015). More emphasis was put on the survey and more in-depth data were collected about health and nutrition. This included the interview, the medical examination, and all the clinical measurements (NHES, 2015).

The survey combines physical examinations with interviews to collect the data (NHANES, 2020). The physical examination looks at medical, dental, and physiological data as well as laboratory data which is taken by trained medical professionals (NHANES, 2020). The interview includes questions about individuals' demographics, their socioeconomic status, dietary habits, and general health-related questions. (NHANES, 2020).

NHANES data has been used to gather information about major diseases and risk factors of those diseases in the population, but it has also been used to create national standards like height, weight, and blood pressure (NHANES, 2020). NHANES data has also been used in scientific journals as well as policies, health programs, food regulations, increasing public awareness and even children's growth charts. (NHANES, 2020)

There are some strengths and limitations to using NHANES data. Some strengths of this data are that the data has already been collected and done so in a meticulous fashion (NHANES, 2020). The data are also representative of the population (NHANES 2020). The data are collected in 2-year increments, and it collects data from different races and ethnicities, socioeconomic status, gender, and age (NHANES, 2020). They also increase/decrease the weight of a specific demographic to make it more representative of the population (NHANES, 2020).

Some of the limitations are that since the data are already collected, there is no way to go back and gather more data on the same population. Another limitation is that dietary recalls are not always correct. They can be biased, and they only collect a two-day recall. This was one weekday and one weekend, and this is not representative of the individuals' normal dietary habits. There is also the issue of missing data which can be due to many reasons.

Also, the data are based on the interviewer/researcher's interpretation of what the individual said. If this is the case, then there can be some incorrect information (NHANES, 2020).

Conclusion

Cardiovascular disease is the number one cause of mortality in the world (Dhingra & Vasan, 2017; Guttmacher & Collins, 2002; Lucas et al., 2011). There are many diseases within the CVD category (World Heart Federation, 2021). Smoking, insufficient physical activity, poor diet, obesity, and high blood pressure and cholesterol are all factors that can cause the disease to be exacerbated (NCI, 2011). Currently, pharmacology is the standard for treatment, but this is not an option that works for every individual (Zhao et al., 2017). Ways to help improve these risk factors include more physical activity (New York State Department of Health, 1999), consuming a diet low in fat and cholesterol (Al-Farsi & Lee, 2008), limiting alcohol intake (Kiechl et al., 1998) and smoking cessation (Campbell et al., 2008). The consumption of fruits and vegetables has been shown to have an inverse association with CVD risk factors (Zhao et al., 2017).

Diet plays an important role in the development of CVD as well as can help prevent CVD from developing (Alissa & Ferns, 2017). Studies have been looking at fruits and vegetables to help deal with cardiovascular risks as a few have shown an inverse association between diet and the risk factors (Zhao et al., 2017). Stone fruits are rich in many beneficial compounds including sugars, vitamins, minerals, antioxidants, organic acids, and dietary fiber (Wills et al., 1983). Polyphenols are also present in stone fruits and can be beneficial (Kelley et al., 2018)). Phenolic-rich fruits have been shown to help lower the risk of cardiovascular diseases like heart attacks, heart failure, stroke, and arterial hypertension

(Gonçalves et al., 2018). Some stone fruits have had more research conducted on them than others. For example, olives and olive oil have been studied extensively and have been shown to have positive effects on blood lipids, blood pressure and inflammation (Ros, 2012).

However, studies showing the association between stone fruit consumption and the biomarkers of CVD in humans is limited. For example, apricots have had research done on rats, but it is limited in humans (Parlakpinar et al., 2009). There are some studies on humans for cherries, however, there needs to be further research done before anything definitive can be said (Chai et al., 2019).

There is also a lack of research on certain forms of stone fruits, for example, when looking at coconut, there is more evidence about coconut oil, but there was little to no information about the meat of the coconut itself (Ma & Lee, 2016). There is also a need for more research on coconut oil's effect on HDL and LDL levels (Santos et al., 2019).

There was also limited information on lychee fruit and mango in relation to CVD. Lychee has been said to have cardio-protective effects; however, this was based on folk medicine and still requires more research (Queiroz et al., 2018). Mango has limited studies relating it to CVD and until 2011, there were no studies comparing it to any CVD risk factors (Lucas et al., 2011).

For peaches, there is also limited data on its association with CVD (Kono et al., 2013). While the study did indicate there is potential for helping prevent CVD, there still is a need for more research (Kono et al., 2013). For plums and prunes, there have been studies to measure their consumption and some CVD factors, however, there is not enough data to definitively determine how much dried plum would have an effect on more than one CVD risk factor (Hong et al., 2021).

There have also not been any studies to look at stone fruits in aggregate. Some studies have looked at other fruits such as berries, apples, and hawthorn (Zhao et al., 2017). However, for stone fruits, there is no study directly assessing the association between them and CVD.

While some stone fruits have more data regarding their consumption and potential beneficial effects on CVD risk factors, there is a need for more research to be done across the board.

Associations between stone fruit intake and markers of cardiovascular disease risk among United States adults: NHANES 2017–2018

Abstract

Background: Cardiovascular disease (CVD) is the most common cause of mortality in the world. Fruit and vegetable intake have been known to help improve CVD risk biomarkers. Objective: To determine if there was an association between the consumption of stone fruits and CVD risk factors.

Methods: Using the National Health and Nutrition Examination Survey 2017–2018 (NHANES) database, we evaluated high sensitivity C-reactive protein (Hs-CRP), triglycerides (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) across 3 levels of stone fruit consumption (0, <1, >1 serving). Secondary variables were also assessed, including education, poverty index, alcohol consumption, sedentary activity, smoking, and diet. Data were analyzed using the IBM SPSS Complex Samples software to account for weighting. Wald Chi square and Wald F-Tests were used to compare groups and a p-value of ≤0.05 was considered statistically significant.

Results: A total of 2,110 subjects were included in the analysis. The four CVD biomarkers were not associated with stone fruit consumption level: HDL (p=0.290), hs-CRP (p=0.121), LDL (p=0.754), and TG (p=0.600). However, some secondary variables were: education (p<0.001), poverty index (p=0.013), alcohol consumption (p=0.004), sedentary activity (p<0.001), smoking (p=0.001), and fiber intake (p=0.002).

Conclusion: Although there was no indication that the CVD biomarkers were associated with aggregate stone fruit consumption, future studies should be conducted on a larger sample using individual stone fruits and accounting for confounding factors.

Keywords: Stone Fruit, CVD, NHANES, Hs-CRP, LDL, HDL, TGs

Introduction

Cardiovascular disease (CVD), also known as heart disease, adversely affects the functionality of the heart and vasculature. This disease impacts both men and women, and many ethnic groups (1). It is the number one cause of death in the world (2) and is a major cause of morbidity and mortality in Western societies (3), accounting for 1 in 4 deaths, and 1 in 5 heart attacks (4).

There are multiple biomarkers used to assess CVD risk (2), including blood levels of high-sensitivity C-reactive protein (hs-CRP), low-density lipoprotein (LDL), triglycerides (TGs), and high-density lipoprotein (HDL) (5–8).

High-sensitivity C-reactive protein is a positive acute-phase protein of innate immunity that is commonly used as a marker of acute and chronic inflammation, a feature of CVD (5). It can be used to diagnose, as well as aid in the prevention and treatment of CVDs (9). Elevated circulating LDL is associated with a plaque buildup in the arteries (8). An elevated level of LDL for an extended period is equally impactful on coronary heart disease risk as compared to higher levels for a shorter period (10). Elevated levels of TGs are associated with thickening and increased rigidity of arteries, which can negatively impact their function (7). On the other hand, elevated HDL levels have protective effects against CVD through reversing cholesterol transport, acting as an antioxidant, and inducing anti-inflammatory mechanisms (6).

There are many risk factors for CVD including poor diet, low levels of physical activity, consuming >1 serving of alcohol, smoking, high blood pressure, high cholesterol (11) and obesity (12). High blood pressure is one of the most preventable risk factors that can lead to cardiovascular diseases (13). Consuming alcohol in excess has been linked to an increased incidence of CVD (14). By consuming excessive amounts of alcohol, more than five standard drinks, an individual's blood pressure can increase by 4 to 7 mmHg for systolic BP and by 4 to 6 mmHg for diastolic BP (15). There are some risks that are not modifiable like genetics and age (12). Epidemiological studies have shown that these factors contribute up to 80% of the risk of developing CVD (16).

Additionally, ethnicity, socioeconomic status, and preexisting health conditions can be contributing risk factors for CVD (1). Ethnicities at higher risk include non-Hispanic Black people, South Asians, Mexican Americans, and Caribbean Americans, especially those of lower socioeconomic status (1,17)). Individuals with multiple health conditions including being overweight/obese and having diabetes, or postmenopausal women also are at a higher risk of developing CVD (4,18). In postmenopausal women, a decrease in estrogen levels can adversely affect lipid metabolism, vascular function, and blood pressure (18).

Diet plays a significant role in the development and prevention of CVD (17,19). There is an inverse association between fruit consumption and CVD risk (20,21). For example, consuming the recommended number of fruits (>5 servings/day) has been linked to more positive outcomes within stroke patients as compared to those that consume less (16). Fruit consumption reduces the risk of CVD likely due to their nutrient content (19,22). Fruits have lower levels of sodium and higher levels of potassium compared to other foods, which have been shown to lower blood pressure (16). Fruits are also rich in dietary fiber, which can help lower both LDL cholesterol and blood pressure levels and protect against hypertension (21,23). Additionally, fruits are a source of phenolic compounds (24) which have been shown to play a role defending against pathogens, stresses, and illness (25). Anthocyanins have anti-inflammatory properties and flavonoids defend against chronic diseases ((24); (25).

Drupes, more commonly known as stone fruits, are fruits that have a fleshy exterior and a hard, stonelike pit in the middle (26). Stone fruits contain elevated levels of phytochemicals, which have been shown to decrease the risk of CVD when consumed in the diet (25). Previous studies show that the consumption of fruits rich in phenolic compounds helps lower the risk of heart attacks, heart failure, and stroke (20,27). Common stone fruits include apricots, cherries, plums, peaches, dates, olives, mangos, lychee, and coconut (28). These fruits are abundant in vitamins, minerals, organic acids, antioxidants, and fiber (29). Intake of cherries has improved systolic blood pressure and lowered LDL cholesterol levels in a population of men and women between the ages of 65 and 80 years old (30). Olive oil consumption has been found to have anti-inflammatory properties that help improve lipid profiles by increasing HDL and lowering LDL and TG levels (31).

Currently, the studies evaluating the association between the consumption of stone fruits and biomarkers of CVD in humans is limited. The purpose of this study was to determine the association between stone fruit consumption and primary biomarkers of CVD in the United

States adult population. It was hypothesized that a higher intake of stone fruit is associated with improved biomarkers of CVD risk.

Methods

NHANES sample

This study evaluated data collected by the National Health and Nutrition Examination Survey (NHANES) which is a cross-sectional survey that is conducted by the National Center for Health Statistics (NCHS) every 2 years. Over time, the program has evolved to focus on a variety of health and nutrition-related topics that are important to the United States population (32). There were no identifying factors for the participants as NHAHES gives individuals a number identifier so there was no need for an Institutional Review Board approval for the present study.

Study population

The population data came from the NHANES 2017–2018 cycle and included those that were 18 years or older, completed the interview and physical examination, had two days of dietary intake data (dietary recall), and had a fasted blood sample taken for laboratory measurements of CVD biomarkers (hs-CRP, LDL, HDL, and TG). Subjects were excluded if they reported taking any medications for a heart attack, heart failure, or stroke.

In total, 9,254 individuals completed the NHANES interview. After accounting for the remaining inclusion and exclusion criteria, in this study, there was complete data for 2,110 individuals. When accounting for weighting done by NHANES, this group represented over 226 million individuals in the United States over the age of eighteen who did not take medications for heart attack, heart failure, or stroke.

Dietary data collection

The dietary data were collected through two non-consecutive 24-hour dietary recalls (33). The first 24-hour recall was conducted in person on the day of the initial interview with an interviewer that was fluent in both English and Spanish, and tools like measuring utensils and dishware were used to help participants properly estimate the portion sizes of the items they had consumed (32). The second 24-hour recall was conducted over the phone, and this took place between three to ten days later (33).

Stone fruit intake

The consumption level of stone fruits estimated in this study was based on what was available and recorded in the dietary recalls. This information was available through the Food and Nutrient Database for Dietary Studies (FNDDS) (34). The stone fruits and mixed foods containing the stone fruits were selected from the FNDDS database. For mixed foods, the ingredients were converted to grams to quantify the amount of the particular stone fruit in that mixed food. The ingredients for this were collected through Food Data Central (35).

The consumption level of stone fruits was divided into three groups based on average servings over the two days of recorded intake: 0 servings, >0–1 serving, and >1 serving. The average serving size of stone fruits was based on data reported elsewhere (35–37). This was done using the average serving size of all stone fruits and taking the average of those values.

CVD risk factors

The information related to the risk factors for this research was collected during the examination portion of the NHANES interview (36). Some of the available information includes blood pressure (BP), high blood cholesterol levels, TG, and Hs-CRP. There is also information pertaining to smoking, alcohol, poor diet, and activity levels (36).

High blood cholesterol is when there is an excess amount of cholesterol in the blood (37). There are two types of lipoproteins that carry cholesterol in the blood, LDL, and HDL (37). Low-density lipoprotein will allow for plaque buildup in the blood vessels where HDL is what removes the cholesterol from the vessels and brings it back to the liver (37). However, when these lipoproteins are out of their normal range, they can cause some major health problems. Elevated levels of LDL and low levels of HDL are caused by factors such as genetics and lifestyle factors (37).

Triglycerides are a form of lipid that is present in the blood and these lipid cells store calories that the body does not need immediately (7). Elevated TGs have been associated with increased levels of coronary heart disease, especially when combined with high LDL and low HDL (3).

High values of hs-CRP are bad because it is an indicator of inflammation and the higher it is the more chance that there is inflammation in the body (38).

Statistical analysis

The sample used in this research was collected from the NHANES dataset from 2017 to 2018. NHANES weighs their sample so that it is more representative of the actual population of the United States (39).

The analysis was done on the population described in the Methods. Those who have completed both the interview and physical exam, are 18 years of age and above, do not take prescription medication for heart attack, heart failure, or stroke, those who have two days of dietary data, and those who have CVD biomarkers measured, including the fasting data.

Statistical analysis was done using SPSS version 27 (Armonk, NY). Descriptive analysis was done using complex samples. Considering that NHANES uses a complex multistage probability design, using the more traditional methods of statistical analysis is not possible (32). There was a confidence interval of 95%. The continuous variables' p-values were calculated using a Wald F test, and the categorical variables p-values were calculated using a Wald Chi-squared test. A p≤0.05 was considered statistically significant.

Results

The demographics and other characteristics of the subjects are shown in **Table 4**.

TABLE 4 Characteristics of US adults aged 18 and older from National Health and Nutrition Examination Survey 2017–2018 by stone fruit consumption level

Variable	All	0 servings	>0–1 serving	>1 serving	p-value
Sample Size, n	2110	1765	244	101	
Age, mean years (SE)	46.6 (0.8)	45.6 (0.7)[a]	51.3 (1.4)[b]	51.8 (3.3)[ab]	**0.004**
Men, %	48	48.8	40.6	36.6	0.350
Race Ethnicity %					0.715
Mexican American	9.5	9.8	7.6	9.2	
Other Hispanic	6.6	5.9	7.0	18.0	
Non-Hispanic White	63.1	62.6	71.0	50.6	
Non-Hispanic Black	11.0	12.2	5.7	5.0	
Non-Hispanic Asian	4.9	4.5	5.5	9.3	
Other race including multiracial	5.0	5.1	3.2	8.0	
Education < high school %	11.3	11.7	7.8	12.7	**<0.0001**
Family Monthly Poverty Index %					**0.013**
< 1.50	25.9	26.8	20.7	24.4	
1.50 - 3.49	28.8	29.9	22.2	27.0	
3.50+	29.8	27.7	40.0	39.7	
No Data	15.5	15.6	17.1	8.8	
Alcohol Consumption %					**0.004**
Never	8.8	9.0	5.6	14.1	
Rarely	47.6	48.4	41.6	48.5	
Sometimes	29.3	28.0	37.4	30.6	
Often	14.4	14.6	15.4	6.8	
Avg minutes sedentary activity	352 (9)	349 (8)[a]	397 (14)[b]	293 (17)[c]	**<0.0001**
Current smoker %	16.3	17.9	9.1	6.2	**0.001**

Nutrient intakes					
Cholesterol (mg)	561 (11)	559 (11)	561 (47)	602 (59)	0.760
Dietary Fiber (gm)	31 (1.0)	29(1)[a]	41 (3)[b]	38 (2)[b]	**0.002**
Saturated Fats (gm)	52 (1)	52 (1)	54 (3)	49 (3)	0.643
Sodium (mg)	6354 (81)	6503 (92)	6908 (254)	6071 (485)	0.267
Total Fat (gm)	159 (2)	158 (3)	169 (6)	153 (9)	0.352

All results have taken the complex design of NHANES into account. Results for the continuous variables are reported as mean values (with standard error) and P values calculated Wald F test. Results for categorical variables are reported as percentages and p values are calculated using a Wald Chi-square. N = 2110, weighted n = 226,562,563. [abc]Paired groups are significantly different if the notations do not share the same alphabetic letter.

Overall, the participants' mean age was 46.6 years, which differed when compared across stone fruit consumption level based on the Wald F test (p=0.004). The mean age in the 0 serving group was 5.7 years younger than those in the >0–1 serving group (p=0.001). Age did not differ between any other consumption levels. When comparing the individual consumption groups, it was found that the p value between the 0 serving group and the >0–1 serving group was significant (p = 0.001). Between the 0 serving group and the >1 serving group, there was not a significant difference however, the p value was close at 0.065. There was no significance between the >0–1 serving group and the >1 serving group (p=0.875).

The characteristic of having an education less than a high school diploma was found to be significant (p<0.001). When looking at the p values between the groups, it was found that between the 0 serving group and the >0–1 serving groups was significant (p>0.001). Between the 0 serving group and the >1 serving group, it was found that the p-value was not significant (p=0.729). The >0–1 serving group and the >1 serving group also had p-values that were not significant (p=0.097).

The family monthly poverty index was found to be significant (p=0.013). When looking at the 0 serving group and the >0–1 serving group, the p value indicated that there was an association with the family monthly poverty index (p=0.009). The p-values between the 0 servings group and the >1 serving group as well as the >0–1 serving group and the >1 serving group were not significant ($p=0.153$ and $p=0.633$, respectively).

For alcohol consumption it was found to be significantly associated with stone fruit intake ($p=0.004$). Between the 0 servings group and the >0–1 serving group, the p value was 0.015. Between the 0 servings group and >1 serving group, the p-value was 0.07, which was not significant, but it was close to significance. Lastly, between the >0–1 serving group and the >1 serving group, the p-value was 0.002.

The average number of minutes of sedentary activity was also found to be significant ($p<0.001$). When looking at the p values between the groups, all three of them were found to be significant.

Being a current smoker was found to be significant ($p=0.001$). Between the 0 serving group and the >0–1 serving group, the p value was found to be significant at $p=0.002$. Between the 0 serving and >1 serving group it was found to be not significant ($p=0.129$). Also, between the >0–1 serving group and the >1 serving group, it was not significant ($p=0.0946$).

Of the nutrient intakes measured, the dietary fiber was the only one that had a significant p-value. The 0 serving group and the >0–1 serving group was significant ($p=0.002$) and the 0 serving groups and >1 serving groups were also found to be significant ($p=0.002$). The >0–1 and >1 serving groups were not significantly different.

The average intake of stone fruit and biomarkers of CVD are shown in **Table 5**. The primary biomarkers of CVD did not differ by the amount of stone fruit consumption.

TABLE 5 Average intake of stone fruits and biomarkers of cardiovascular disease in US adults aged 18 and older from the National Health and Nutrition Examination Survey 2017–2018 by stone fruit consumption level

Variable	All	0 servings	>0–1 serving	>1 serving	p-value
Sample Size, n	2110	1765	224	101	
Stone Fruit intake (g), mean (SE)	10 (1)	0 (0)[a]	25 (3)[b]	148 (10)[c]	<0.0001
Blood Glucose (mg/dl) (SE)	109 (1)	109 (1)	109 (2)	114 (4)	0.317
BMI (kg/m^2) (SE)	29.4 (0.3)	29.6 (0.4)	28.4 (0.7)	28.4 (0.6)	0.464
HDL (mg/dl) (SE)	54 (1)	54 (1)	56 (1)	57 (3)	0.290
hs-CRP (mg/dl) (SE)	3.9 (0.2)	4.1 (0.3)	3.0 (0.4)	3.4 (0.6)	0.121
LDL (mg/dl) (SE)	112 (2)	111(1)	115 (6)	116 (9)	0.754
TG (mg/dl) (SE)	187 (2)	186 (2)	192 (7)	194 (8)	0.600
Blood pressure (mm/Hg)					
Systolic (mm/Hg)	123(1)	123 (6)	120(2)	119 (3)	0.167
Diastolic (mm/Hg)	721(1)	73 (1)	70 (1)	69 (1)	0.076

All results have taken the complex design of NHANES into account. Results for the continuous variables are reported as mean values (with standard error) and P values calculated Wald F test. Results for categorical variables are reported as percentages and p values are calculated using a Wald Chi-square. [abc]Paired groups are significantly different if the notations do not share the same alphabetic letter. Abbreviations: BMI = body mass index (n=2086), HDL = high-density lipoprotein (n=2072), hs-CRP = high sensitivity C-Reactive protein (n=2061), LDL (Martin-Hopkins) = low-density lipoprotein Martin Hopkins Eq (n=2051), TG = triglyceride (n=2072).

When looking at the p-value for HDL, it was found not to be significant. Looking at the three consumption groups, it was found that none of the combinations were significant. This was found to be the case for LDL as well as TG.

High sensitivity C-reactive protein was also found to be not significant overall. However, when looking at the 0 serving group and the >0–1 serving group, the p-value was significant (p=0.045). The 0 serving group and >1 serving group and the >0–1 serving group and the >1 serving group were not significant.

The systolic blood pressure was not significant. And when looking at the consumption levels, there was no significant difference between the groups. The diastolic blood pressure was not significant, but it was closer to significance at a value p=0.076. When looking at the p-value between the 0 serving group and the >0–1 serving group and the >0–1 serving group and the >1 serving group, they were not significant. But the 0 serving group and the >1 serving group did have a significant p-value of 0.026.

The blood glucose levels were not significant, however the data showed that those who consumed more stone fruit had a higher BG.

Discussion

The purpose of this study was to determine if there was an association between the consumption level of stone fruit and biomarkers of CVD risk using data collected from the NHANES 2017–2018 cycle. Overall, when comparing hs-CRP, TG, LDL, or HDL across three intake levels of stone fruit (0 servings, >0–1 serving, >1 serving), no differences were detected among these biomarkers of CVD risk.

High sensitivity C-reactive protein is a common marker for atherosclerosis and cardiovascular disease risk, and it has been found to be modestly elevated in a sizable portion of the general population (40). One study found that consuming a higher intake of fruit and vegetables is inversely related to hs-CRP values (41). A study evaluating the association of fruit consumption and CVD factors indicated an inverse association with fruit intake and hs-CRP levels (42).

Although the average value of hs-CRP was lower in the >0–1 serving and >1 serving when compared to the 0 serving group, which is in accordance with the research described above, it was not significant. Another reason that hs-CRP can be elevated includes age (43). As an individual ages, their hs-CRP levels will also increase and this was also seen to be significantly higher in women, and especially high in those who were postmenopausal and on hormone replacement therapy (43). Another cause of increased hs-CRP could be stress due to work which has been associated with increased hs-CRP levels (44). In these cases, the individuals can be consuming stone fruits but due to these other factors such as aging, or stress, the levels of hs-CRP may not decrease as expected.

When comparing the serum TG concentrations across stone fruit consumption levels, they were also found to not differ. This was surprising because this goes against some other studies which state that foods rich in phenolic compounds lead to decreased TG levels in humans (45). Triglycerides have been shown to increase with age and are still predictors of coronary heart disease (46). They are connected to the development of CHD specifically in females and when joined with low levels of HDL, it can be applied to males (47). Triglycerides are obtained from dietary sources and elevated TG levels have been connected to low HDL levels (3).

Some reasons that the TG levels were still high include not consuming a heart healthy diet and continuing to consume a diet high in fats and processed foods (48). While consuming foods like the stone fruits can potentially help decrease the levels of TG, if an individual is continuing to consume a diet high in fats and processed foods, there will be little change.

Serum LDL and HDL were not associated with stone fruit consumption levels in the present study. In one study, it was concluded that the consumption of tart cherry juice did not alter the concentrations of blood lipids in healthy adults (49). However, in those who were obese or overweight who had elevated blood lipids, there was a decrease in the TG/HDL ratio (49). Another study showed that as humans age, their LDL and HDL levels may decrease (50). Like TGs, foods rich in phenolic compounds have been shown to decrease plasma LDL levels and increase plasma HDL levels (45) and stone fruits are abundant sources of phenolic compounds (51).

Reasons that the LDL may be high and the HDL low, is that lifestyle choices like low physical activity, poor diet, smoking and alcohol may be influencing the values (52). Similar to TG, if an individual is consuming a poor diet and following other poor lifestyle choices, the levels of LDLs and HDLs will not change to reflect the benefits of the stone fruit consumption.

There are other factors that can affect CVD risk differing across stone fruit consumption levels. These variables included physical activity, education, and smoking. When analyzed in SPSS v27, all three of these were found to be significant in this population.

Physical activity has been linked to better cardiovascular outcomes, and lack of activity has been shown to increase CVD mortality risk (53). It has been strongly reported that a decrease in TG levels should be observed since exercise requires a large quantity of energy (54).

Education has been found to have an inverse association with CVD (55). One study divided individuals into 4 groups (graduate school, college, high school, and middle/elementary) and in this sample, those who had a lower level of education had a higher risk of heart attack or developing other forms of CVD (56). This study determines that education is just as important as socioeconomic status, income and stress when determining risk for CVD.

Smoking has been determined to be a major factor in the development of CVD and there is also a proportional association between the amount that an individual smokes and their risk (57). Smoking affects the body by damaging the blood vessels and the heart and the smoke can even alter the blood chemistry which also leads to CVD (58). The change in the blood chemistry then can cause the vessels to become covered in plaque which then makes it difficult for the blood to move through the body and leads to atherosclerosis (58).

Strengths and limitations

A strength of this study is that the data collected by NHANES represents the United States population due to its multistage probability sampling strategy. Even though only a subset of the US population participates in each cycle, the information gathered from the participants is weighted to account for the different demographics in the US population of all ages. Another strength of this study was that it was the first to investigate the association between stone fruit consumption and CVD risk biomarkers utilizing NHANES data. This study also looked at stone fruits in aggregate.

A limitation to this study is that by using NHANES data, the data that is available was limited to what had been collected for that cycle. It was not possible to go back and gather more data for the year 2017–2018. This study only used the data from the 2017–2018 NHANES cycle. Also, NHANES uses dietary recalls to measure their diet intake, and this is not indicative of normal intake, it is a snapshot of an individual’s diet. Stone fruits were not assessed individually. This study did not account for confounding factors of CVD.

Implications and future directions

The data used in this study was collected in 2017–2018. Because of this the data were limited to what was collected in that year. One direction for future research could be to use data from multiple NHANES cycles and this could increase the population of individuals that did consume stone fruits. Another direction that this study could go would be to use usual intake (utilizing a food record, or food frequency questionnaire) to better account for an individual's stone fruit consumption. Another direction could be to conduct analyses on the association between individual stone fruits and CVD. Finally, accounting for confounding factors of CVD would be important.

Conclusion

In conclusion, this study's findings indicate that overall, there is no association between the consumption of stone fruits and CVD risk factors. However, other studies have found that there are some associations between different stone fruits and certain CVD risk factors. Further observational studies or even experimental studies are needed to more accurately determine if there is an association between stone fruit consumption and CVD risk factors.

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Summary and Recommendations

Summary

Cardiovascular Disease (CVD) is the most common cause of mortality in the world (Dhingra & Vasan, 2017; Guttmacher & Collins, 2002; Rodríguez-Monforte et al., 2015). There are many types of CVD, and sixty-two million people are estimated to have CVD (Guttmacher & Collins, 2002). In 2012, it was responsible for 17.5 million deaths (Zhao et al., 2017).

The current standard for treating CVD is the use of pharmacology, however, this may not always be the best option for all the patients who have this condition (Zhao et al., 2017). Availability and affordability are important factors in why someone may not be able to take medication to treat their CVD (Wirtz et al., 2016). Diet can be an alternative for the prevention and treatment of CVD, especially by increasing fruit and vegetable intake (Chong et al., 2010).

Diet has been shown to play a significant role in the development of CVD (Alissa & Ferns, 2017). Epidemiological studies have determined that consuming fruits and vegetables is inversely related to CVD risk (Zhao et al., 2017). Phenolic rich foods (including fruits) have been linked to lower CVD risk (Gonçalves et al., 2018). Some studies have shown that consuming fruits high in phenolic compounds have lowered the risk of strokes and heart attacks (Gonçalves et al., 2018, Lara et al., 2020). There are studies that have shown that the consumption of fruits is protective against CVD risk, including grape, pomegranate, apple, hawthorn, avocado, and blueberry (Zhao et al., 2017). Cherries are also known to have protective effects and reduce inflammatory diseases (Kelley et al., 2018). Finally, peaches may have clinical potential to help prevent atherosclerosis and hypertension (Kono et al., 2013).

The biomarkers observed in this study were hs-CRP, HDL, LDL, and TG. High sensitivity C-Reactive protein is a marker of inflammation that when increase, indicates that there in inflammation in the body (Bassuk et al., 2004, Seo, 2012). High density lipoprotein carries cholesterol to the liver and low levels of this can lead to an increased risk of heart disease (CDC, 2020a). Low density lipoprotein moves the cholesterol in the body to where it needs to go however, high levels of LDL in the body has been associated with an increased risk of developing CVD (Pirahanchi et al., 2021). Triglycerides are a form of fat in the body in which excess calories that the body in not currently in need of are stored (Mayo Clinic Staff, 2020). Elevated TG levels can cause issues such as thickening the artery which then can lead to more severe issues like heart disease, heart attack and stroke (Mayo Clinic Staff, 2020). Elevated TGs, high LDL levels and low HDL levels have been linked to coronary heart disease (Alsaif et al., 2007).

This present study determined whether there was an association between the consumption level of stone fruits and biomarkers of CVD risk. Overall, there was little to no association between the varying levels of stone fruit consumption 90 servings, >0–1 serving, and >1 serving) and the biomarkers of CVD. This outcome may be due to a lack of power using only one NHANES cycle and the limited stone fruit data available in the dataset because of the use of 24-hour dietary recalls rather than a food frequency questionnaire to estimate usual intakes.

Recommendations

From much of the literature available, there appears to be new interest in the consumption of certain fruits and CVD risk factors (Chong et al., 2010; Hartley et al., 2013; Zhao et al., 2017; Zheng et al., 2017). Consuming fruit juices has also become a popular topic for getting some of the benefits of fruits (Zheng et al., 2017). There are studies that evaluate the benefits of fruits and fruit juices specifically and their effects on CVD risk (Zheng et al., 2017). Few studies have assessed the benefits of cherry consumption, which have improved risk factors like systolic BP and LDL cholesterol, reducing the risk for developing CVD (Chai et al., 2019). However, there are a lack of studies that focus on the consumption of stone fruits and their effects on CVD risk.

A recommendation for future research to fill this gap is to perform experimental studies where individuals with CVD are provided stone fruit through diet to determine if it reduces biomarkers of CVD risk. Additional research could evaluate the consumption of individual stone fruit juices, dried fruits, or mixed foods.

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APPENDIX A

List of fruits evaluated when identifying stone fruits in FNDDS

Apricots	Grape	**Peaches**
Banana	Guava	Persimmon
Blackberry	Honeydew Melon	Pineapple
Blueberry	Huckleberry	**Plums**
Boysenberry	Kiwi	Pomegranate
Cantaloupe	Kumquat	Prunes
Casaba Melon	Lemon	Raisin
Cherry	Lime	Raspberry
Clementine	**Lychee**	Rhubarb
Coconut	**Mango**	Soursop
Cranberry	**Nectarine**	Starfruit
Currants	**Olives**	Strawberry
Dates	Orange	Tamarind
Fig	Papaya	Tangerine
Fruit cocktail	Passionfruit	Watermelon