Study Protocol and Statistical Analysis Plan

Official Title: Effects of Coffee Versus Hibiscus Tea Consumption During Prolonged Sitting on Blood Pressure and Heart Rate

Document date: 08/23/2025

- **STUDY SYNOPSIS/PROTOCOL SUMMARY (Background, objectives, and methods.**

Modern lifestyles have undergone radical changes due to technological, economic, and social transformations, leading to increased sedentary behavior, particularly prolonged sitting, which has been associated with a higher risk of cardiovascular diseases, obesity, and mortality—the leading cause of death worldwide. Dietary habits are also crucial in the prevention or development of cardiovascular diseases, and among the most common are the consumption of coffee and hibiscus tea. This study aims to examine and compare the effects of consuming coffee versus hibiscus tea during prolonged sitting on blood pressure, heart rate, and heart rate variability. Data will be collected using the International Physical Activity Questionnaire, measurements of height and weight (seca), body composition (Tanita device), a blood pressure variability measurement device, and a Polar device to assess heart rate and its variability. A randomized crossover design will be implemented with 30 participants (15 females and 15 males) recruited through advertisements distributed via King Saud University email and social media. During Visit 1, participants will provide informed consent, undergo initial screening in the Exercise Physiology Laboratory to assess eligibility (age, education, physical activity, smoking status, and medical conditions), and be randomly assigned to consume either coffee or hibiscus tea. After consumption, they will sit continuously for 3 hours, with blood pressure and heart rate variability measured at baseline, immediately after drinking, and after 1, 2, and 3 hours of sitting. In Visit 2, participants will consume the alternative drink and undergo the same sitting protocol, with an additional reaction time test included. Sitting for three continuous hours is considered a globally standardized method in prolonged sitting research. Data analysis will be performed using the Statistical Package for the Social Sciences (SPSS), including descriptive statistics (mean, standard deviation, median, and percentages) for independent variables such as age, BMI, and resting blood pressure, and multiple linear regression models to compare the effects of coffee and hibiscus tea on blood pressure, heart rate, heart rate variability, and reaction time during prolonged sitting.

- **RESEARCH SIGNIFICANCE (Please describe briefly how this study will contribute to existing knowledge in the field).**

This study is significant because it highlights the impact of consuming coffee compared to hibiscus tea on blood pressure and heart rate in women during prolonged sitting periods. Coffee contains caffeine, which may elevate blood pressure and heart rate, whereas hibiscus tea has been shown in previous studies to exert a calming effect on these vital signs. Therefore, this study will provide evidence-based recommendations regarding the consumption of these common beverages during prolonged sitting, potentially contributing to the improvement of cardiovascular health in women. In addition, the findings may help raise awareness about the importance of choosing appropriate beverages to support heart health, particularly in lifestyles characterized by prolonged sitting.

- **DETAILED RESEARCH PROPOSAL (delete the text in Red once details are provided)**

Research Objectives:

This study aims to examine and understand the effects of consuming coffee compared to hibiscus tea during prolonged sitting on blood pressure, heart rate, and heart rate variability in healthy women. It is assumed that coffee consumption will have a statistically significant inverse effect compared to hibiscus tea during prolonged sitting on these variables.

Literature Review:

Physical Inactivity (Prolonged Sitting)

Saudi Arabia has undergone immense social and economic development and urbanization over recent decades (1). This progress has significantly shifted lifestyle patterns. According to a previous study, physical inactivity—defined as any waking behavior with an energy expenditure of less than 1.5 metabolic equivalents, such as sitting, reclining, or lying down (2,3)—was found to affect 69.4% of the Saudi population (4). This inactivity raises multiple risk factors that contribute to the rising prevalence of cardiovascular diseases and early mortality (5). Another study suggested that physical inactivity accounts for 9% of premature deaths worldwide (1) and is the fourth leading risk factor for mortality globally (6). Furthermore, global rates of insufficient physical activity show that women are 5% less active than men, a trend that has remained unchanged since 2000, with increasing inactivity rates observed in both genders after the age of 60 (7).

A study on young women found that inactivity negatively impacts their quality of life, particularly through autonomic heart rate regulation during rest and physiological responses to stress (8). Another study indicated a strong correlation between the high prevalence of physical inactivity (49.3%) and elevated blood pressure (60%) in adults (9). Concerns about sedentary behavior, including screen time and occupational sitting, are also on the rise (10). According to research, adults in sedentary occupations report an average inactivity time of ≥9 hours daily, accounting for 55%–70% of waking hours (10).

Studies in various countries have found a positive correlation between prolonged sitting duration and increased systolic blood pressure (b = 0.42 mmHg/h, 95% CI 0.18–0.60), diastolic blood pressure (b = 0.24 mmHg/h, 95% CI 0.06–0.42), and mean arterial pressure (b = 0.66 mmHg/h, 95% CI 0.36–0.90) (11). In older women, extended sitting periods have been linked to heightened risks of cardiovascular disease and coronary heart disease (12). Sedentary behavior has been classified as continuous or intermittent, with studies suggesting that each type may influence cardiometabolic risk biomarkers and early mortality differently (13). Despite these substantial lifestyle changes, research on the effects of prolonged sitting among Saudi women remains limited (14).

Cardiovascular Diseases

Cardiovascular diseases (CVDs) represent a major and growing global issue (15). They encompass a range of disorders affecting the heart and blood vessels, including coronary heart disease, hypertension, peripheral artery disease, valvular heart disease, heart failure, heart attacks, and strokes (16). It is estimated that there are approximately 5,601–6,600 cases of CVDs per 100,000 individuals in Saudi Arabia, with over a third of adult Saudis at risk, as reported by the Saudi Health Council (17).

Risk factors for CVD are categorized into modifiable and non-modifiable factors. Non-modifiable factors include age (18), gender—where decreased estrogen levels in women increase risk (19)—family history, and ethnicity, whose causes are still not fully understood (20). Modifiable risk factors such as systolic and diastolic blood pressure are closely linked to CVD (21). Global public health issues such as smoking, obesity, and diabetes also negatively impact cardiovascular health due to the multiple pathophysiological changes they trigger. Physical inactivity is another major risk factor (20).

Heart rate is a critical indicator of cardiovascular and cerebrovascular mortality (22), with a resting heart rate below 60 beats per minute considered desirable for cardiovascular health and prevention (23). Heart rate variability (HRV) analysis is a reliable, non-invasive method for evaluating autonomic nervous system activity and assisting in diagnostics (24). Combining heart rate and HRV values can enhance understanding of autonomic activity in both health and disease (25). The autonomic nervous system (ANS) plays a crucial role in cardiovascular health

by balancing sympathetic and parasympathetic functions and regulating blood pressure and heart rate (26).

Effects of Prolonged Sitting on Blood Pressure

Blood pressure is a dynamic phenomenon influenced by numerous factors (27), and hypertension is a common, modifiable disease that significantly impacts global health by contributing to morbidity and mortality (28). Blood pressure is generated by two forces: systolic pressure, which occurs when blood is pumped from the heart into the arteries, and diastolic pressure, which occurs when the heart rests between beats (29).

Systolic blood pressure, which drives blood against arterial walls during heartbeats, is particularly significant for individuals over 50, as arteries stiffen with age, increasing the risk of cardiovascular disease (29). Diastolic blood pressure measures the pressure on arterial walls while the heart muscle rests between beats (29).

High blood pressure is a critical risk factor for cardiovascular and chronic kidney diseases. It is defined as a systolic reading of 140 mmHg or higher or a diastolic reading of 90 mmHg or higher (30). Studies have shown that elevated systolic and diastolic pressures independently increase the risk of adverse cardiovascular events, regardless of the hypertension definition used (140/90 mmHg or 130/80 mmHg) (31). The global prevalence of hypertension was estimated at 1.13 billion in 2015 (20%–24% of men and women worldwide) (32), while in Saudi Arabia it was 10.0% among women aged 15 and above (33). Lower blood pressure has been associated with reduced risk of cardiovascular diseases, including stroke (34).

Accurate blood pressure measurement is essential, as it can be influenced by factors such as breathing, emotions, exercise, meals, tobacco, alcohol, temperature, bladder fullness, and pain, as well as age, gender, and medication (27). Most blood pressure devices work by occluding an extremity artery (arm, wrist, finger, or leg) with an inflatable cuff, measuring oscillometric changes or Korotkoff sounds. Other non-occlusive techniques, such as pulse waveform analysis, are less common in clinical practice (27).

Studies on healthy young adults have shown that uninterrupted sitting for 120–180 minutes significantly reduces lower limb vascular function, though no significant reductions were observed at 30 and 60 minutes. However, a downward trend in vascular function with prolonged sitting was noted (35). Prolonged sitting has also been shown to significantly impair lower limb vascular function, with evidence suggesting that interrupting sitting, especially with aerobic or simple resistance activities, may prevent vascular dysfunction (36).

Moderate levels of physical activity, such as brisk walking for three hours per week, significantly lower blood pressure, reducing risks of cardiovascular disease and stroke (37). Another study found that breaking prolonged sitting with light- to moderate-intensity activity intervals lowers both systolic and diastolic blood pressure (38).

Effects of Prolonged Sitting on Heart Rate and HRV

The human heart is complex and adaptable, enabling the cardiovascular system to respond to sudden physical and psychological challenges (39). Heart rate (HR) is the number of heartbeats per minute (40), and heart rate variability (HRV) is the variation in intervals between successive heartbeats (41). HRV represents the neurocardiac function generated by interactions between the heart, brain, and the dynamic autonomic nervous system, helping individuals adapt to environmental and psychological stressors. HRV reflects autonomic balance regulation, blood pressure (BP), and various other functions (39).

Regarding the acute effect of prolonged sitting (≥4 hours) on heart rate or HRV, studies have shown that neither is significantly affected. However, prolonged, intermittent sitting may cause a minor, non-significant increase in heart rate (42)

Coffee

Coffee is one of the most popular and widely consumed beverages worldwide due to its stimulating effects on the central nervous system, as well as its flavor and aroma (43). Roasted coffee contains a complex mix of over 1,000 bioactive compounds, some with therapeutic properties such as antioxidant, anti-inflammatory, antifibrotic, or anticancer effects (44). Coffee's key bioactive components include phenolic compounds (such as chlorogenic acids and derivatives), methylxanthines (caffeine, theophylline, theobromine), diterpenes (cafestol and kahweol), nicotinic acid (vitamin B3) and its precursor trigonelline, magnesium, and potassium (44).

Polyphenols and caffeine are particularly valued for their health benefits. Light and medium roasting preserve polyphenols and enhance coffee's antioxidant properties, while intense roasting reduces caffeine content (45). Cold brew coffee also extracts certain compounds differently from hot coffee, making it less potent in some effects (46).

Over the past few decades, coffee consumption has gained popularity in the Middle East, including Saudi Arabia. In a study involving 930 healthy female students from different departments at King Saud University, 88% were found to consume coffee regularly (47). Regular coffee and caffeine intake often lead to increases in blood pressure, with more pronounced effects in hypertensive individuals (48). However, moderate coffee intake (3–4 cups per day) is associated with preventive benefits against various chronic diseases, including type 2 diabetes and liver diseases (43). One study demonstrated that moderate coffee consumption (3–4 cups per day) might contribute to the prevention of chronic diseases (49).

Higher coffee consumption has also been associated with lower mortality rates, possibly due to decreased resting heart rate in addition to the positive effects of coffee on atherosclerosis (50). Another study reported that regular coffee consumption led to an increase in blood pressure, a decrease in heart rate, and an increase in plasma catecholamines; however, decaffeinated coffee caused a smaller increase in diastolic blood pressure without changes in other variables. This suggests that the cardiovascular effects of coffee consumption are primarily attributed to its caffeine content (51).

Recommendations suggest moderate and safe coffee intake of 3–4 cups per day, providing 300–400 mg of caffeine (52,49). However, the effects of coffee during prolonged sitting on blood pressure, heart rate, and HRV, particularly over several hours of sitting, remain unknown.

Hibiscus (Hibiscus sabdariffa)

There is growing interest in natural antioxidants from plant sources, particularly bioactive compounds such as polyphenols and flavonoids (53). Anthocyanins, a subgroup of flavonoids, predominantly appear in plants as glycosides, such as anthocyanidin (53). Hibiscus belongs to the Malvaceae family and is described as an annual herbaceous plant that can grow up to 2.5 meters, characterized by smooth cylindrical red stems, red veins, and long green leaves (53). It is rich in phytochemicals and has potential therapeutic uses in preventing chronic diseases associated with oxidative stress (53).

Hibiscus is widely used in traditional medicine due to its accessibility, low cost, and bioactive components (55). It is rich in polyphenols, anthocyanins, sugars, and organic acids, which contribute to its therapeutic potential (54). In recent years, there has been a global focus on plant research to explore the extensive applications of medicinal plants (54,56).

Regarding its effects on blood pressure and heart rate, hibiscus has been used in various countries as an antihypertensive agent (57). A study concluded that regular consumption of hibiscus can reduce the risk of cardiovascular disease (58). This benefit is attributed to its flavonoid and anthocyanin content, which effectively lower both systolic and diastolic blood pressure in individuals with hypertension (59). Additionally, polyphenols in hibiscus play a

regulatory role in metabolic health and blood pressure maintenance, with beneficial actions against inflammation and cardiovascular disease (60).

Furthermore, hibiscus possesses hypoglycemic, hypolipidemic, kidney-protective, antioxidant, and anti-inflammatory properties (61). However, excessive consumption of hibiscus may increase total antioxidant capacity, potentially leading to an inflammatory condition associated with elevated blood pressure (62). The recommended dosage is three servings per day (240 ml containing 1.25 g of hibiscus per serving) to reduce blood pressure in adults with mild or prehypertension (63).

A study on sun-dried hibiscus leaves found that optimal extraction efficiency in water is achieved after 10 minutes at 100 °C, resulting in the highest antioxidant yield and concentrations of cyanidin-3-sambubioside and delphinidin (53). Despite the growing number of studies, the effects of hibiscus during prolonged sitting on blood pressure, heart rate, and HRV remain unknown.

Research Methodology: Data Collection and Measurement Tools

General information form:

Personal data about the participants will be collected using a general questionnaire, which includes age and medical condition.

Physical activity level questionnaire:

Participants will complete the physical activity questionnaire. The researcher will analyze the responses and select participants who meet the study's inclusion criteria.

Physical measurements:

Height will be measured using an electronic height measuring device (Stadium scale). Weight will be measured using a regular scale (seca), and BMI will be calculated using a bioelectrical resistance device (Bioelectrical Tanita Japan MC-980).

Blood pressure measurement:

Systolic and diastolic blood pressure will be measured using an oscillometric device (USA, Illinois, Omron Healthcare, Omron HEM 7124 CP). Measurements will follow the guidelines of the American Heart Association (AHA) and the American College of Cardiology (ACC).

Heart rate and HRV measurement:

The Polar V800 will be used to measure heart rate and HRV. The device consists of a watch and a Bluetooth heart rate sensor. Data will be collected according to the manufacturer's instructions (88) and analyzed using Kubios HRV Premium software to calculate HRV time-domain metrics. The heart rate sensor will be placed on the participant's chest, below the pectoral muscles. The participant will sit quietly for 10 minutes in a chair while continuous measurements are taken. The clearest five continuous minutes of the 10-minute HRV recording will be analyzed using Kubios HRV Premium software. Time-domain metrics to be extracted include:

- HR (Heart Rate): The number of beats per minute; a direct measure of heart rhythm.
- NN interval: The time interval between successive heartbeats, used to assess heart rhythm patterns and variability.
- SDNN (Standard Deviation of NN Intervals): The standard deviation of the time intervals between successive heartbeats.

HRV measurements will be performed at several time points: before sitting, after beverage consumption, after one hour, after two hours, and after three hours of sitting during both visits.

These variables were selected based on the study duration criterion and the TAKEI physical fitness test.

Study Design:

Randomized crossover experimental design

Study Duration:

Two visits across two weeks

Study Population and Sample Size with Sampling Technique:

Using G*Power software, the required sample size was calculated as 30 participants—15 males and 15 females—with a 10% increase to account for potential data loss or incomplete responses. Participants will be recruited via university email. Interested participants will be contacted, provided with study details, and asked to complete consent forms.

Subject Recruitment Procedures

Study Subject Selection

Inclusion Criteria:

- Age between 18–35 years.
- Normal to elevated blood pressure (less than 130/80 mmHg) and a normal resting heart rate (between 60–100 bpm) to ensure the study targets healthy adults and avoids factors that could influence results.
- Free from any health issues to minimize external influences on study outcomes.
- Not adhering to physical activity guidelines, as the study focuses on physically inactive individuals.

Exclusion Criteria:

- Participants with any allergy to hibiscus or coffee (since both beverages will be consumed).
- Participants taking medications that may affect blood pressure, heart rate, or heart rate variability, such as antihypertensive drugs.

Study Procedures

Visit 1: Screening and Initial Procedures

- Participants will sign the informed consent form.
- Participants will visit the Exercise Physiology Laboratory at King Saud University for initial assessments, including: Age, education level, physical activity level, smoking status, and medical conditions to determine eligibility.
- Participants will be randomly assigned to consume either coffee or hibiscus first.
- They will sit continuously for 3 hours after consuming the drink.

Measurements (blood pressure and heart rate variability) will be taken at five time points: Before drinking (baseline), one hour after drinking, after 1 hour of sitting, after 2 hours of sitting, and after 3 hours of sitting

Visit 2:

Participants will consume the alternate drink (opposite of Visit 1). The same prolonged sitting period (3 hours) and measurements will be conducted. An additional reaction time test will be included. Both beverages will be provided in controlled doses, following moderate and safe consumption recommendations for coffee and hibiscus, during the morning period (7:00–11:00 AM).

Hibiscus: 3 servings/day, with each 240 ml serving containing 1.25 g of hibiscus.

Coffee: 3–4 cups/day, providing 300–400 mg of caffeine.

Data Collection Method / Data Source

Data will be collected using both paper-based forms and direct entry into an electronic system.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) will be used to conduct the following analyses:

- Calculate the mean and standard deviation or number and percentage to describe the levels of independent variables, including age, body mass index, and resting blood pressure.
- Use mixed linear regression models to compare the effect of drinking coffee and hibiscus during prolonged sitting on the dependent variables (blood pressure, heart rate, and heart rate variability).
- Determine statistical significance at $p < 0.05$.

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