

USING THE VENDYS PERIPHERAL VASCULAR FUNCTION TEST AND BLOOD  
GLUCOMETER TO DETERMINE THE EFFECTS OF DIABETES MELLITUS  
ON VASCULAR ENDOTHELIAL FUNCTION

By

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## Abstract

It has been long established through scientific research that diabetes has a negative impact on the circulatory system and is one of the leading causes of cardiovascular disease. Endothelial dysfunction is seen frequently in those diagnosed with diabetes, and it is associated with atherosclerosis and other cardiovascular risk factors. The activity of the endothelium that is involved in both macro- and microvascular diseases extends far beyond the control of vascular reactivity. It is also involved in the release of vasodilating mediators. Although glycemic control delays the onset of diabetic vascular complications, this strategy may not always be successful in all patients. Endothelial cells form a single layer of cells that line the blood vessels of the body and regulate exchanges between the bloodstream and surrounding tissues. This single layer of cells is known as the endothelium. However, dysfunction can occur in the endothelium for a multitude of reasons, including but not limited to inflammation, tobacco use, hypertension, hyperglycemia, and more. Increased glucose variability leads to endothelial dysfunction and accelerated atherosclerosis through increased oxidative stress (Schofield et al., 2019). The purpose of this study is to determine whether those diagnosed with diabetes mellitus, as evidenced by HbA1C levels, differ from those not diagnosed with diabetes mellitus when comparing the measurement of vascular reactivity.

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## **Using the VENDYS Peripheral Vascular Function Test and Blood Glucometer to Determine the Effects of Diabetes Mellitus on Cardiovascular Endothelial Function**

According to a 2022 report by the Center for Disease Control, 37.3 million people, or 11.3% of the U.S. population, have diabetes. The impact of diabetes on the circulatory system has been widely accepted and long established (Schofield et al., 2019). However, less is known about the underlying mechanisms for this relationship. The growing body of evidence (Schofield et al., 2019) shows endothelial dysfunction is seen frequently in those diagnosed with diabetes and is associated with atherosclerosis and other cardiovascular risk factors. The activity of the endothelium that is involved in both macro- and microvascular diseases extends far beyond the control of vascular reactivity. It is also involved in the release of vasodilating mediators. Although glycemic control delays the onset of diabetic vascular complications, this strategy may not always be successful in all patients.

Endothelial cells form a single layer of cells that line the blood vessels of the body and regulate exchanges between the bloodstream and surrounding tissues. This single layer of cells is known as the endothelium. However, dysfunction can occur in the endothelium for a multitude of reasons, including but not limited to inflammation, tobacco use, hypertension, hyperglycemia, and more. Increased glucose variability leads to endothelial dysfunction and accelerated atherosclerosis through increased oxidative stress (Schofield et al., 2019). Atherosclerosis is one of the leading factors related to cardiovascular disease. Therefore, uncontrolled blood glucose can negatively affect the endothelium, leading to an increased risk of cardiovascular disease in those diagnosed with diabetes.

The evidence supporting the relationships between endothelial dysfunction and diabetes is lacking objective comparison to those not diagnosed with diabetes. The purpose of this

proposed study is to describe vascular reactivity and endothelial function in a sample of young adults diagnosed with diabetes mellitus in comparison to those without diabetes, utilizing VENDYS II device to assess vascular reactivity.

### **Clinical Question**

In those diagnosed with diabetes mellitus, as evidenced by HbA1C levels, does the VENDY™ (VENDYS-II, 2014) measurement of vascular reactivity, and endothelial dysfunction differ from those not diagnosed with diabetes? Is there a relationship between HbA1C and vascular reactivity/ endothelial function?

### **Theoretical Framework and Conceptual Definitions**

This study focuses on the differences in the endothelium between those diagnosed with diabetes and those not diagnosed with diabetes. The non-DM group in the study consists of the 6 participants who report no history of diabetes, whereas the DM group consists of the 6 participants who report being diagnosed with type 1 diabetes. Because the endothelium has such an impact on the body's circulatory system, this research will further analyze the differences in the vascular endothelium between diabetics and non-diabetics.

The VENDYS™ device, which is a non-invasive measurement tool, is used during the research to measure vascular function through reactive hyperemia assessments (Ahmadi et al., 2008). The VENDYS™ vascular function test occludes the participants right arm using a blood pressure cuff, taking note of the participant's blood pressure, as well as being used to study the participant's vascular response to reactive hyperemia. The participant's left arm is used as the control arm where researchers will use a push-button lancet to prick a participant's finger, then use the glucometer to measure one's random blood sugar and converting the measurement to A1C.

### Determination of Evidence Base for Clinical Question

A literature review was conducted using the Joanna Briggs Institute database, CINAHL, and PubMed. Keywords used included “endothelial dysfunction”, “diabetes mellitus”, “atherosclerosis”, “HbA1C”, “endothelium”, and “cardiovascular disease”. The strength of the articles was determined by the Johns Hopkins Nursing Evidence-Based Practice Research Evidence Appraisal tool (Dearholt & Dang, 2012). This process awards different levels of strength dependent on type of study, sample size, and variables. Level I connotes strong research while Level III is given to the weakest studies. See table.

Article (author/date)	Evidence Type	Level	Quality
Ahmadi, N., et al. (2008)	Quasi-Experimental	I	High
Brooks, B., et al (1999)	Experimental	I	High
Calver, A., et al. (1992)	Experimental	I	High
Centers for Disease Control. (2022)	Nonexperimental	II	Good
Funk, S. D., Yurdagul, A., & Wayne Orr, A. (2012)	Nonexperimental	I	High
Ladeia, A. M., et al. (2014)	Nonexperimental	II	Good
Matsuda, E., & Brennan, P. (2014)	Systematic Review	III	Good



Retnakaran, R., & Zinman, B. (2008)	Nonexperimental	II	Good
Schächinger, V., et al. (2000)	Experimental	I	High

### Literature Review

Vriese et al. (2009) explains endothelium-derived relaxing factors (EDRF) are nitric oxide (NO), prostacyclin, and an endothelium-derived hyperpolarizing factor (EDHF). Endothelial dysfunction has been reported due to impaired release of EDRFs and an enhanced release of endothelium-derived constricting factors. Several studies included in this article have demonstrated a downhill slope in the release of EDRFs with a significant increase in the endothelium-derived constricting factors (Vriese et al., 2009). The results of these studies indicate a rise in vasoconstriction in those diagnosed with diabetes mellitus, leading to an increased likelihood of diabetics developing atherosclerosis and other cardiovascular diseases (Calver et al., 1992). Most of the studies included demonstrate an impaired vasodilation of the endothelium in diabetics.

Endothelial dysfunction alters the typical function and mechanics of the vascular system, aggravates blood pressure control, and accelerates the development of atherosclerosis. The endothelium is a dynamic organ that responds to environmental stimuli and activates vasoactive substances including vasoconstrictors and vasodilators. Schiffrin (2002) illustrates that subjects with mild coronary artery disease demonstrated a relationship between endothelial dysfunction and atherosclerosis. Diabetes mellitus, specifically, contributes to oxidative stress, which in turn impairs endothelial vasomotor function. The secretion of nitric oxide is decreased, therefore leading to a lack of vasodilation in response to hemodynamic stress. Studies conducted within

Schiffrin (2002) show the relationship between endothelial dysfunction and cardiovascular disease.

In Type I diabetes mellitus, the acceleration of atherosclerosis is likely a result from the effects of inflammation, dyslipidemia, hypertension, and neuropathy. Additionally, hyperglycemia appeared to have a more profound effect on the cardiovascular risk in those with Type I diabetes mellitus versus those with Type II diabetes mellitus (Schofield et al., 2019). From studies conducted, it is clear the patients with high HbA1C concentrations are at higher risk for cardiovascular disease than those with lower HbA1C concentrations. Schofield (2019) explains that along with hyperglycemia, hypertension is also a typically unaddressed risk factor for major diabetic complications. A hyperglycemic setting results from a lack of insulin management in diabetics. In this state, vascular endothelial cells are at particular risk of developing intracellular hyperglycemia due to the reuptake of glucose. This intracellular hyperglycemia causes an oxidative stress that leads to DNA damage. A lack of insulin management in Type I diabetics can lead to endothelial changes including vasoconstriction, inflammatory gene expression, and enhanced tissue factors promoting coagulation and hyperlipidemia soon (Retnakaran et al., 2008).

Endothelial cell dysfunction is regarded as an early step in atherosclerotic plaque formation primarily due to its effects on endothelial cell activation. The endothelial layer has the power to prevent thrombosis and leukocyte adhesion, as well as a significant factor in diagnosing cardiovascular disease in those diagnosed with diabetes mellitus. Funk et al. (2012) illustrated the significance of Protein Kinase C (PKC), metabolic pathway flux, and the formation of atherosclerosis due in part to endothelial dysfunction found in those with diabetes mellitus. Funk

et al. (2012) aimed to study how different parts of the endothelium contribute to the formation of atherosclerosis and cardiovascular disease risks.

## **Methods**

### **Design**

This study was a pilot feasibility study and was a quasi-experimental design. Through the quasi-experimental design, the research conducted was aiming to discover the effects diabetes has on the vascular endothelial function.

### **Setting**

The research will take place at the TCU Harris College Research Lab. This research design also consists of interrupted times-series designs. This means that during the time of the study, participants will be evaluated individually at different times. This gives researchers the opportunity to document and analyze the findings, while still conducting research on participants.

### **Sample**

Participants will be recruited for this study through word of mouth, recruiting from clubs on TCU's campus, and interactions both within and out of TCU's student body. The participants recruited (n=12), both male and female, with ages ranging from 18 years old to 30 years old. There will be 6 participants who are diagnosed with type 1 diabetes, and 6 participants who do not have a history of diabetes. Before testing on human subjects, researchers complete biomedical CITI certification to work on human subjects prior to conducting research. Human subjects who participate in the study will also receive a \$20 gift card for their time dedicated to further research.

### **Consent Procedures**

Once participants arrive at the research lab in the TCU Anne Richardson Bass building, they will review and sign the TCU IRB approved consent form, as well as a questionnaire for demographics and health history. TCU's IRB approved consent form confirms the participants confidentiality, rights, and HIPAA protocol as a subject in this study.

### **Data Collection**

The questionnaire provided asks participants about their demographics and health history including questions regarding exercise routines, medications taken at home, height, weight, A1C, etc. An A1C test result reflects your average blood sugar level for the past two to three months. Specifically, the A1C test measures what percentage of hemoglobin proteins in your blood are coated with sugar (glycated). The higher your A1C level is, the poorer your blood sugar control and the higher your risk of diabetes complications (Mayo Clinic, 2022). There will also be a flier provided to participants explaining the research lab and the tools used for research.

In this study, researchers will be using statistical operations to analyze the data collected: primarily descriptive and correlational statistics. Following the data collection, a comparison of means between the two groups will be conducted using a standard t-test.

Data observed from participants will be secured throughout the research. Participants will be assigned anonymous numbers (ex: 001 – A), and the personal identity of the numbers assigned will only be known by Dr. Cheek and the researchers observing data in the lab. Results from the research done will be secured on TCU's secured computer which is always locked away in the research lab. The research lab is also not accessible to the public.

Measurements from the research conducted will be observed using multiple tools: the VENDYS™ machine, demographic questionnaire, and a glucometer. The VENDYS™ vascular function test occludes the participants right arm using a blood pressure cuff, taking note of the

participant's heart rate and blood pressure, as well as being used to study the participant's reactive hyperemia. The participant's left arm is used as the control arm, where researchers will use a push-button lancet to prick a participant's finger, then use the glucometer to measure spot glucose. The blood sample will also be analyzed for HbA1C. The VENDYS™ tool allows researchers to observe the vascular reactivity index along with the supplemental measurements listed above.

## **Results**

### **Demographics**

The participants were all female: six subjects without type 1 diabetes mellitus, the control group, and six subjects diagnosed with type 1 diabetes mellitus using insulin therapy, as the experimental group. Age, height, weight, and body mass index (BMI) for the females with and without type 1 diabetes mellitus were not significant (see Figure 1).

### **Hemoglobin A1C**

The experimental group was found to have higher hemoglobin A1C levels than the control group. The blood glucose results from the glucometer were converted into A1C levels and then compared between the control and experimental groups. The average HbA1C result in the control group was 5.26%, compared to the average HbA1C result in the experimental group which was 6.92%. Based on these calculations, the difference in hemoglobin A1C for a female with T1DM and without T1DM was not statistically significant (see Figure 3).

### **Vital Signs**

The systolic, diastolic, and mean blood pressure were taken at the beginning of every individual's procedure to formulate baseline data. The systolic blood pressure, diastolic blood

pressure, and mean blood pressure were similar amongst both groups of females. The difference was not significant (see Figure 2).

### **Vascular Reactivity Index (VRI)**

Vascular reactivity is the responsiveness of a blood vessel tone and diameter to a specific stimulus. The vascular reactivity index (VRI) is used to show the endothelial function health since the endothelial cells play critical roles in the vascular beds. The VRI scores range from 0.0 to 3.5 with a goal range of a “good” VRI being greater than 2.0. In this study, the trends observed by the data noted the non-DM group had higher VRI scores and lower HbA1C levels when compared to the DM group, but this difference was not statistically significant (see Figure 3).

### **Discussion**

While further research analyzing endothelial dysfunction in those diagnosed with diabetes compared to those who are not diagnosed should be conducted, the articles included have identified the connection between endothelial dysfunction and diabetes clearly (Funk, et al., 2012). The proposed study aims to provide more understanding regarding the impact of a history of diabetes mellitus type I, HbA1C levels, and spot blood glucose on vascular reactivity, thus providing indispensable information about endothelial function and associated risk factors for cardiovascular disease. The trends observed by the preliminary data note the non-DM group had higher VRI scores compared to the DM group. However, through this data, when the experimental group has controlled HbA1C levels, the divide in the VRI scores between the two groups is not statistically significant.

### **Limitations**

The small sample size and homogenous subject group may limit these results to a certain population of young females. The subjects somewhat varied in age, BMI, and ethnicity leading to differing results in vascular reactivity. Vascular reactivity may have been influenced by the participant's medication regimen and diet the day of utilizing the VENDYS-II system. The inability to directly measure the hemoglobin A1C of the control group forced the authors to rely on the average score for nondiabetic individuals to conclude results.

### **Nursing Implications**

Nursing care for individuals with type 1 diabetes extends beyond glycemic control to encompass the intricate management of vascular complications, particularly concerning the endothelium. Endothelial dysfunction significantly predisposes patients to a heightened risk of cardiovascular diseases such as atherosclerosis and hypertension. Diligent monitoring of blood glucose levels, implementing evidence-based interventions to optimize metabolic control, and fostering patient education on lifestyle modifications is pivotal in mitigating endothelial dysfunction. It was proven that intensive glycemic therapy, aiming to achieve glycemia as close to the nondiabetic range as safely as possible, reduced all the microvascular and cardiovascular complications that diabetes causes (Nathan, D. et al, 2014). This comprehensive approach emphasizes the critical role of glycemic management in safeguarding endothelial health and promoting cardiovascular well-being in individuals with type 1 diabetes. By prioritizing glycemic control through personalized treatment regimens and lifestyle modifications, healthcare teams can significantly contribute to the preservation of endothelial function and enhance the overall quality of life in patients who are diagnosed with type 1 diabetes.

Figures

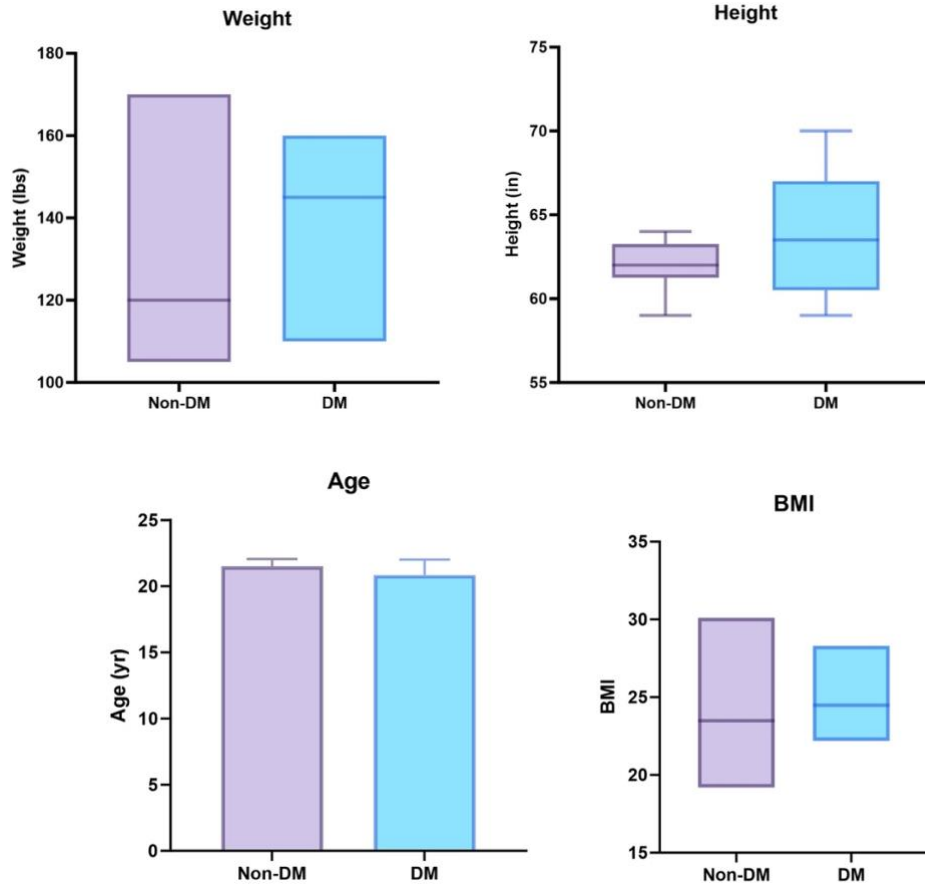
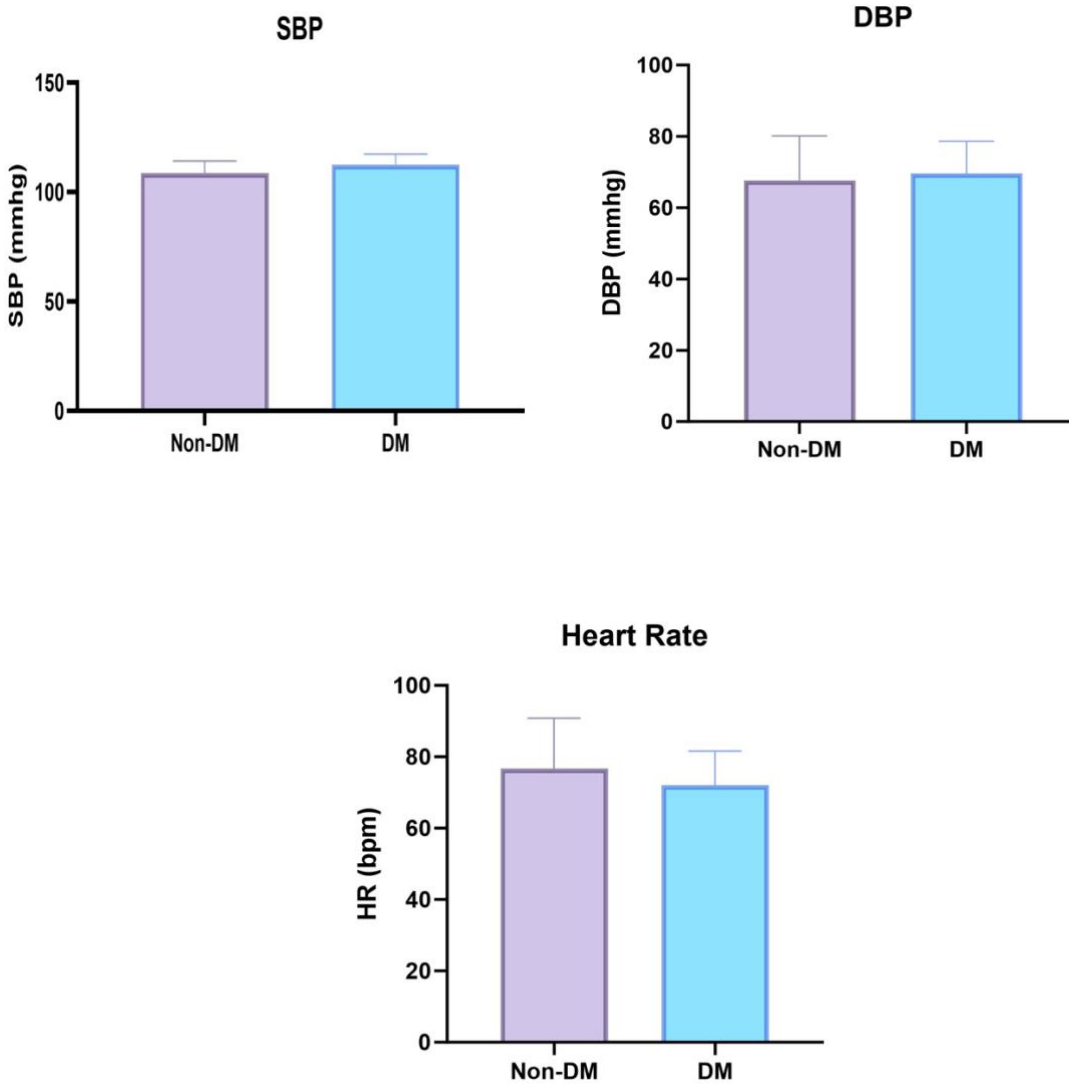
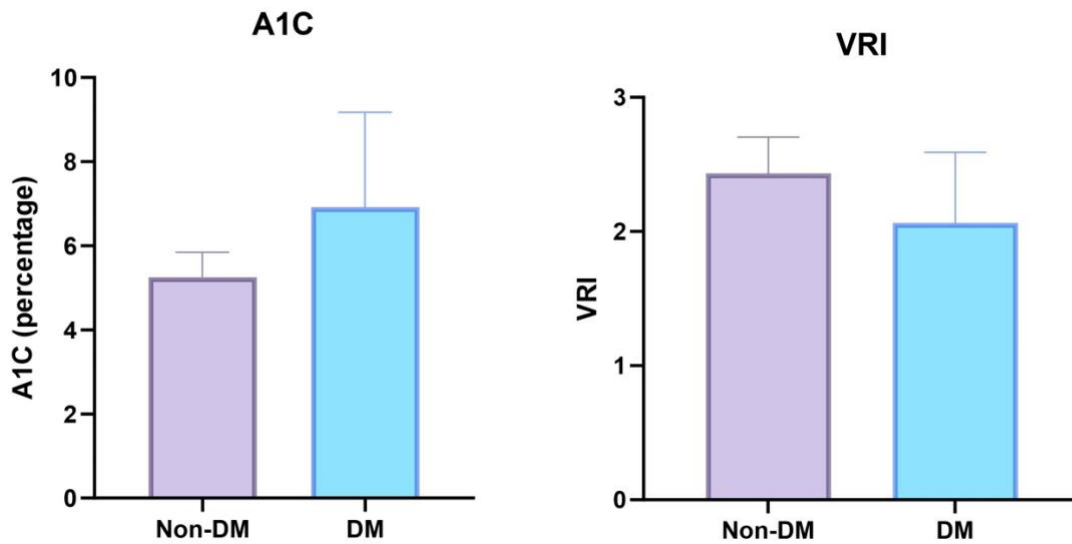


Figure 1-Participants Demographic Data: Height, Weight, & BMI results between non-DM (purple) and DM group (blue).





*Figure 2 - Systolic Blood Pressure, Diastolic Blood Pressure, & Heart Rate results from non-DM group (purple) and DM group (blue). The systolic and diastolic blood pressure between the control and experimental groups were compared. The experimental group had insignificantly higher systolic and diastolic blood pressure compared to the control group. The VENDYS-II system compared the average heart rates (HR) of the diabetic and nondiabetic participants. There was not a significant difference between the heart rates of the nondiabetic and diabetic females.*



*Figure 3 - A1C and VRI results between non-DM group (purple) and DM group (blue). The hemoglobin A1C levels were compared between the nondiabetic and diabetic female participants. The females with diabetes had a higher hemoglobin A1C than the non-diabetic females; it was not statistically significant. The vascular reactivity index (VRI) for the control and experimental group were tested. The control group consisting of the non-diabetics had insignificantly better VRI scores compared to the experimental group.*

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