DESIGN AND QUANTITATIVE ANALYSIS OF A PULSE WAVE VELOCITY BLOOD-PRESSURE MEASUREMENT SUBSYSTEM WITH MULTIPLE – SUBJECT CONTROLLED EXPERIMENTS

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DESIGN AND QUANTITATIVE ANALYSIS OF A PULSE WAVE VELOCITY BLOOD-PRESSURE MEASUREMENT SUBSYSTEM WITH MULTIPLE – SUBJECT CONTROLLED EXPERIMENTS

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I dedicate this thesis to the loving memory of my mother

Hatice Erkurşun

You have successfully made me the woman who I am becoming
You will always be remembered

ABSTRACT

The main purpose of this study is to perform the pulse wave velocity (PWV) measurements with a new noninvasive optoelectronic continuous-time wearable sensor design and analyze the quantitative relation between the reference blood pressure (BP) measurement. PWV was measured at baseline 32 normotensive volunteers, including 15 females and 17 males aged between 23 and 41 years old. The day before the measurements, the volunteers were not allowed to drink alcohol, stay up late or use any medicine that would affect BP. Repeated BP measurements were performed with an average follow-up system at certain times of the day. Equivalent constituents were established after questioning age, height, weight, physical activity levels in daily life, genetic predisposition for blood pressure and diabetic from all volunteers participating in the measurements. Systolic BP (SBP), diastolic BP (DBP), heart rate (HR), pulse pressure (PP), mean arterial pressure (MAP), a distance between brachial to radial artery (D), pulse transit time between brachial to radial artery (brPTT) and PWV measurements were taken. Following the experimental results, a linear correlation was found between SBP and PWV when the two groups separated by certain components were examined. Measurements taken with the new non-invasive low-power continuous-time sensor design show that the PWV may in the near future be used as a screening tool to identify continuous SBP values in clinical practice. The new non-invasive design suggests that SBP is the main correlation factor in the relationship with PWV compared to any other BP parameters.

ÖZET

Bu çalışmanın temel amacı, nabız dalga hızı (NDH) ölçümlerini yeni bir noninvaziv optoelektronik sensör tasarımı yaklaşımı ile yapmak ve referans kan basıncı (KB) ölçümü arasındaki niceliksel ilişkiyi analiz etmektir. NDH, 23 ve 41 yaşları arasındaki 15 kadın ve 17 erkek dahil olmak üzere 32 normotansif gönüllünün katılımı ile ölçülmüştür. Ölçümlerden önceki gün, gönüllülerin alkol almasına, geç saatte uyanmasına ve KB'yi etkileyecek herhangi bir ilaç kullanmasına izin verilmemiştir. Tekrarlanan KB ölçümleri günün belirli saatlerinde, ortalama bir takip sistemi ile yapılmıştır. Eşdeğer bileşenler olarak yaş, boy, kilo, günlük yaşamdaki fiziksel aktivite düzeyleri, tansiyon ve diyabet için genetik yatkınlık bilgileri katılan tüm gönüllülerden sorgulandıktan sonra oluşturulmuştur. Sistolik KB (SKB), diyastolik KB (DKB), kalp atım hızı (KAH), nabız basıncı (NB), ortalama arter basıncı (OAB), brakiyalden radyal arter (D) arasındaki mesafe, brakiyalden radyal arter arasındaki nabız geçiş süresi (brNGS) ve NDH ölçümleri alınmıştır. Deney sonuçlarının ardından, gruplar belirli bileşenlerine göre ayrıldığında SKB ve NBH arasında lineer bir korelasyon saptanmıştır. Yeni invaziv olmayan düşük güçlü sürekli-zaman sensör tasarımı ile yapılan ölçümler, NBH'ın yakın gelecekte klinik uygulamada sürekli SKB değerlerini tanımlamak için bir tarama aracı olarak kullanılabileceğini göstermektedir. Yeni invaziv olmayan tasarım, SKB'nin çeşitli KB parametreleri arasında NBH ile en güçlü korelasyona sahip olduğunu göstermektedir.

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CHAPTER I

INTRODUCTION

1.1 *Motivation*

Cardiovascular diseases (CVDs) are lead to a huge number of lives according to World Health Organization. 17.7 million People died in 2017 due to CVDs, which are thought to be about 31% of all world deaths [1]. CVDs manifested primarily as heart attacks and strokes. It is triggered mainly tobacco use, unhealthy diet, physical inactivity and harmful use of alcohol in the form of heart attacks and strokes. These are emerging as people with increased blood pressure, high blood sugar, overweight and obesity can't manage the disease as much as needed. All these indications can be easily measured in primary care facilities. Determining the highest risk factors of CVDs and receiving appropriate treatment while continuously monitoring the symptoms may prevent early deaths [2].

When the incidences of CVDs worldwide and mortality rates are assessed, people have been led to seek new solutions based on more accurate diagnoses, which will allow early detection of pathological processes and assessment of multiple parameters. The early diagnosis depends on multiple parameters of the pathological conditions, and it is the most important actions to help prevent the deaths of the patients.

Arterial stiffness is a key factor in cardiovascular (CV) physiology. Arterial stiffness reflects the viscoelastic property of the vessel wall. Elasticity decreases as arterial stiffness increases. All factors that cause atherosclerosis increase arterial

stiffness. Pulse wave velocity (PWV) is one of the indicators of arterial stiffness. Measurement of pulse wave velocity can be pointed out as one of the easiest approaches to evaluate arterial stiffness. PWV is an acknowledged method which directly measures arterial stiffness and has proven its prescient incentive in numerous epidemiological examinations in different geological areas and population [3, 4, 5]. It has become as important as the calculation of risk with cardiovascular risk calculation systems. Hence, it is considered as the main tool for this research in an effort to implement a low-cost continuous blood pressure (BP) monitoring device.

1.2 *Scope of this Thesis*

There are many studies carried out early on to detect cardiovascular diseases. Measurement of arterial stiffness studies have gained importance in recent years. Pulse wave velocity is one of the most important parameters used in determining arterial stiffness. In this study, we aimed that design and quantitative analysis of a continuous Optoelectronic PVW Blood Pressure (BP) sensor with multiple-subject controlled experiments. The result of these measurements will be discussed in the related chapters.

CHAPTER II

BACKGROUND

For many years, blood pressure measurement techniques are based on methods developed in the nineteenth century. Blood pressure can be measured by the use of a brachial pressure cuff and auscultation of the brachial artery, in order to detect the appearance and disappearance of Korotkoff sounds.Cuff occlusion techniques were originally developed by Italian doctor Riva-Rocci in 1896 and Korotkoff, Russian surgeon, described the sounds after nine years later in 1905 by placing a stethoscope over the brachial artery at the cubical fossa [6].

Blood pressure is the most important measurement parameter in daily clinic. There is a positive relationship between cardiovascular disease and blood pressure level and it is approved by several studies. The use of an automatic device by clinics, hospitals and individuals to measure the blood pressure on a daily basis has been increased in the last decade. Moreover, remote devices are also being used to measure blood pressure over a programmed period during day and night hours. Blood pressure is highly dependent on several factors such as postural, room temperature and pain & discomfort or stress and these factors cause blood pressure to vary [7]. Other than these direct factors, indirect factors like suitability of the cuff size, the deflation rate of the cuff, the deflation of the sleeve and the measurement period's accuracy, or the automatic blood pressure monitor may affect the blood pressure.

2.1 *Blood Pressure Measurement Techniques*

Although William Harvey (1578 – 1657) was the first person to develop the concept of the circulation of blood [8], Stephen Hales (1677 – 1761) was the first person to discover of blood pressure. The accurate study of blood pressure started with mercury manometer designed by physician-physicists, Jean Poiseuille (1797 – 1869) in 1828. Following the development of the non-invasive techniques, with the sphymomanometer method of indirectly measuring blood pressure (Vierordt, 1855), significant progress has been ruined in techniques for measuring blood pressure and pulse contour. The methods for measuring BP that we still use in daily routine practice today were developed with the invention of Riva-Rocci cuff sphygmomanometer in 1896 and the description by Korotkoff sounds [6, 9].

2.1.1. Invasive Techniques

Invasive measurement of blood pressure is accepted as the "gold standard" in the medical literature and it reaches the most accurate measurement result when compared to other methods [10]. It is anticipated that the method must be used in the intensive care medicine, anesthesiology and research purposes in daily clinical methods which are totally dependent on the person applying setup. Generally, a catheter is introduced into the brachial or radial artery and is connected to a pressure transducer positioned at the heart level via a fluid filled manometer tube. Invasive monitoring provides information about beat-to-beat BP variability and allows identification of transient pressure changes. Invasive blood pressure measurement is not preferred in everyday routine measurements, although it is safer and less stressful than known. Since it is accepted as the gold standard, it leads the

new technologies that come after itself and is used during the verification of new techniques[11].

2.1.2. Sphygmomanometer

The blood pressure changes in between maximum (systolic) and minimum (diastolic) pressures, during each heart beat. The maximum (systolic) pressure is the pressure reached during the systole as a result of the increase in volume in the blood. The minimum (diastolic) pressure is the pressure resulting from the precapillary arteriolar resistance (peripheral resistance), which regulates tissue perfusion. Blood pressure measuring instrument are called “sphgmomanometry”.

Sphygmomanometers consist of a pneumatic tire made of rubber for air pumping, a check valve on the neck of the pillar, a sleeve which can be of various sizes, air-conducting rubber tubes and a manometer. The measurement is based on the principle that the air pressure in the sleeve is compared to the blood pressure in the artery. Blood pressure is measured by evaluating the low and medium frequency sounds (Korotkoff voices) generated by the turbulence generated by the blood passing through the artery trapped between the high pressure inflated sleeve and the bone. It is considered to be more insecure results and reproducible when compared with the direct blood pressure measurement method due to people and equipment dependency. Despite all the inaccuracies, it is the most used method in today's medical literature.

2.1.3. Non-invasive Continuous Techniques

Invasive BP measurement is widely used in high-risk surgical procedure and intensive care applications. This method should be operated with a trained operator.

Operator error can cause significantly wrong readings. Because of this reason, BP is commonly measured through non-invasive techniques which are less sensitive to the person conducting the measurement. In non-invasive methods, occlusive devices are used to measure blood pressure. The most commonly used closure is a rubber bag that can be filled with air, called a cuff. It is made in various sizes according to the age of the patient. There are different kind of methods for non-invasive techniques such as; palpatory, oscillometric, auscultatory, ultrasonic, flush methods. Besides, new methods are as well being developed [12, 13].

2.2 *Blood Pressure Measurement Clinical Relationship*

2.2.1 Hypertension

Hypertension (HT) is the high pressure that the blood in the vein makes to the vessel wall. In the long term, the effect of blood on the vein walls causes damage on the inner surface of the vein. Due to hypertension, the veins feeding the organs may become clogged, enlarged or torn. Hypertension may cause organ failure by impairing blood flow to organs.

The definition of hypertension can be expressed as systolic blood pressure (SBP) is being equal to or more than 140 mmHg and diastolic blood pressure (DBP) of 90 mmHg or more, or using an antihypertensive drug [14]. Hypertension is classified as primary (essential) HT and secondary HT according to etiology.

Primer Hypertension: 90-95% of hypertensive patients are in this group and there is no specific reason to raise blood pressure. Although there is no direct reason to increase blood pressure, some conditions such as sedentary life, smoking, emotional

stress, obesity and alcohol are thought to cause primary HT.

Secondary Hypertension: It is defined as the elevation of blood pressure due to an underlying disease such as endocrinological diseases, kidney diseases and pregnancy, and constitutes about 5% of all hypertensive cases and the majority of these cases develop due to chronic renal parenchymal disease. All other causes play a role of 1-3% in HT etiology.

Hypertension is classified according to its severity and divided into stages. Classification of the European Hypertension Community / European Cardiology Society (ESH / ESC) according to severity of HT in the 2013 guideline is presented in Table 1 - Definition and Classification of Office Blood Pressure Level (mmHg)* [15].

Table 1 - Definition and Classification of Office Blood Pressure Level (mmHg)*

Category	Systolic Blood Pressure		Diastolic Blood Pressure
Optimal	**<120**	**and**	**<80**
Normal	120–129	and/or	80–84
High Normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

*The blood pressure (BP) category is defined by the highest level of BP, whether systolic or diastolic. Isolated systolic hypertension should be graded 1, 2, or 3 according to systolic BP values in the ranges indicated.
**Adapted from [15].

2.2.2 Systolic Blood Pressure

Instead of being a constant, the pressure applied by the flow of blood is a dynamic variable and the state of heart is constantly reflected.

The event called systole is commanly identify as the heart bleeding into the veins. The increase in the pressure inside the artery is caused by the ejection of blood into the veins. Hence, systolic blood pressure can be defined as the peak level of blood pressure reached during active heart contraction.

2.2.3 Diastolic Blood Pressure

Similar to the systolic blood pressure, the diastolic blood pressure can be expressed as the pressure when the heart does not actively pump blood into the arteries. In other words, pressure which the artery applies to the arteries between the heartbeats.

Once the heart has contracted, in order to get prepared for the next contraction, the cardiac ventricles relax for a period of time. Hence, diastole blood pressure is the blood pressure during this period of ventricular relaxation.

2.2.4 Heart Rate

The heart rate (HR) or pulse rate is determined by how many times the heart beats in minutes. The normal heart rate depends on each individual person. Knowing heart rate individually is necessary in the name of cardiovascular diseases pre-diagnosis and heart health indicator. Depending on age and gender, changes in the speed and pattern of the pulse can be seen. The most suitable places where the heart rate can be measured are wrists, inside of elbow, side of neck and top of the foot.

At rest position, heart rate is expected to be between 60-100 beats per minute for healthy individuals. Besides, it is not a sign of disease that heart rate is lower in physically active and athletic people because heart muscles are developed, so it is not necessary to work hard to maintain constant rhythm.

Among many other variables that affect heart rate, factors like air temperature, body position, emotions, body size and drug use can be listed as leading ones [16].

2.2.5 Pulse Pressure

The numerical difference between systolic and diastolic blood pressures is called pulse pressure. Pulse pressure (PP) was obtained by the formula ***PP=SBP-DBP.*** The most important cause of the high pulse rate is the aortic stiffness, which is the largest artery in the body. Hardness may cause less elastic (atherosclerosis) due to high blood pressure or fatty deposits that damage arterial walls. The larger your pulse rate, the tougher and more damaged the ship is thought to be. Pulse pressure is a clinical parameter with an arterial stiffness indicator.

2.2.6 Mean Arterial Pressure

As blood being pumped into the aorta from left ventricle and the arteries are being dissipated, pressure is generated. Mean arterial pressure (MAP) is determined by cardiac output (CO), systemic vascular resistance (SVR) and central venous pressure (CVP) depend on the relationship between flow, pressure and resistance.

However, in practice, MAP is determined by measuring arterial pressure directly or indirectly, not by definition of CO and SVR. Over time, aortic pressure gives an average pressure value lower than the arithmetic average of shape, systolic and diastolic

pressures. At normal resting heart rates, MAP was obtained by ***MAP=DBP+PP/3*** [17].

MAP measurement is not needed in normal clinical practice, only systolic and diastolic pressures are being measured. MAP measurement is only being used when the SVR has to be calculated.

2.3 Arterial Stiffness

In biophysics, the theory of elasticity is based on the force applied to a body and deals with form changes. [18,19]. The force that falls on the unit field is called 'stress-pressure'. The rate of distortion from the square to the original is called 'strain-overload'. The curve of the pressure-load relationship is called the elastic coefficient-modulus.

In the biology of arterial vessels, mechanical stress is represented as pressure, and strain is represented as a change in diameter. Since the relationship between them is not linear, the slope of the curve at the given pressure reflects elasticity or vice versa. Both elasticity and stiffness are qualitative terms. The quantitative provisions are harmonization (compliance) and flexibility (distensibilty). Compliance is the rate of volume change seen as a result of a pressure change applied to a stretchable tube or artery. Whether hard or elastic, a large artery has a greater volume compliance than a small artery due to increased pressure. This change may be misleading in the comparison of changes in arterial compliance. Flexibility is the change in the pitch or volume that corresponds to the partial changes. Flexibility is useful in comparing arteries of different sizes.

2.3.1 Arterial Stiffness Parameters

Pulse wave velocity, arterial strain (distensibility), arterial compliance (compliance) and elastic coefficient (modulus) are indicators of arterial stiffness. [20].

Pulse wave velocity; is the velocity of the blood flow spreading across the arterial segment [Distance / Time difference (m / sec)].

Arterial distensibility; is the change in the relative change according to the pressure increase [(Diameter difference / Pressure difference) x Diameter].

Arterial compliance; is the absolute change over the pressure increase (Diameter difference / Pressure difference).

Elastic coefficient (modulus); is the pressure required to increase the basal diameter by 100% [(Pressure difference x Volume) / (Volume difference x Wall thickness)].

2.3.2 Arterial Stiffness Principles

The emergence and recording of the arterial pulse wave is based on the 1800's. While physicists like Young (1808), Poiseuille (1840), Moens (1878) and Korteweg develop the hydraulic and elastic theory; Physiologists and clinicians such as Marey (1860), Mahomed (1872) and Mackenzie (1902) have developed a variety of devices called 'sphygmograph' and are widely acknowledged for their contributions to the analysis of pressure waves. It was subsequently noticed that the arteries were in different structures, that they had nonlinear viscoelastic properties and that they had strong adaptive mechanisms and that the mechanical behavior of large arteries was

visible. It would be wrong to argue about the entire arterial tree according to the characteristic of an arterial segment. As a result of all these developments, models related to arterial stiffness and pressure wave were developed. [21].

2.3.3 Arterial Stiffness Measurement Techniques

Arterial stiffness analysis involves two different methods. The first is the analysis of the arterial stiffness while the other is the reflected wave analysis. Determination of arterial stiffness is related with regional stiffness, local stiffness and systemic stiffness (analysis of waveform shapes). Local stiffness includes measurements of aorta, carotid-femoral, carotid-radial, and femoral - tibial pulse wave velocities while local stiffness includes pulse wave velocity measurements of the main carotid artery, main femoral artery, brachial artery, radial artery and all superficial arteries. The greatest advantage of regional and local stiffness measurements is that it directly measures wall stiffness. Systemic arterial stiffness is obtained only from circulatory models.

In evaluating regional stiffness, the main artery is aorta. There are two reasons for this. First; the thoracic and abdominal aorta have the greatest share in the arterial buffering function, and the second is that the aortic pulse wave velocity is an independent predictor of outcomes in various populations. All other arteries can also be used to assess regional stiffness. The method used is pulse wave velocity measurement. This is the simplest, non-invasive and healthy measurement. Carotid-femoral pulse wave velocity measurement is the **golden standard** for arterial stiffness [21].

2.4 Pulse Wave Velocity

Arterial stiffness is a key factor in cardiovascular physiology. Pulse wave velocity measurement (PWV), a technique used to assess the severity of the arterial system is a simple, non-invasive method [22]. The PWV is defined as the velocity of the arterial pulse wave that is generated by the aortic filling of the blood of the heart and advancing towards the arterial system. It can be measured invasively and non-invasively in human and can be reproducible [23]. PWV has a highly correlation with CVDs [3, 24, 25].

2.4.1 Regional Pulse Wave Velocity

Regional PWV assessment is based on two different arteries. The most commonly used arteries are the radial artery, carotid artery, brachial artery or femoral artery in which the pulse rate is clearly taken. When evaluating the regional PWV measurement, it gives an average value because a path is used on the long segment of arteries with different mechanical properties. The distance between the used arteries is measured approximately. The devices in the market are evaluating PWV using regional assessment [26].

2.4.2 Local Pulse Wave Velocity

Local PWV assessment is based on two different arteries, but unlike regional PWV assessment, it is performed in a short arterial segment. The distance between the measuring points is determined to be as short as possible and far from rough approaches. Local PWV is responsible for the early detection of local stiffness of the arterial wall. In new studies, researchers focus on local PWV assessment and new technological measuring devices are developed by local PWV measurement method.

[26].

2.5 Pulse Wave Velocity Measurement

PWV is assessed by measuring distance and pulse transit time between two sites in the arterial system with sensitive sensors placed on the skin and taking their pulse arrival time difference. (Figure 1)

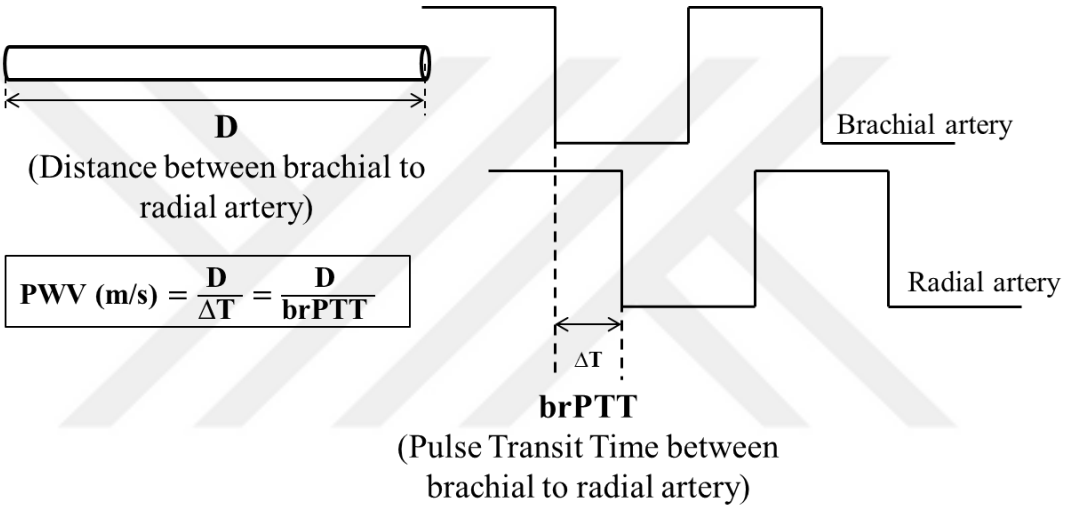

Figure 1- Measurement of brachial to radial pulse wave velocity.

The idea of applying PWV as CVDs determinant parameters depends on the Moens-Korteweg condition, which frames a PWV of a long straight versatile tube [27]. PWV can be calculated using parameters such as Young's modulus of the arterial wall E, wal thickness h, vessel radius r and blood density ρ associated with the vessel using the Moens and Korteweg formula. ($PWV^2 = Eh/2r\rho$) [10]. On the other hand, Moens-Korteweg condition contains a few suspicions that are not substantial for human vessels. The Moens-Korteweg condition applies only when the arterial wall is loaded with non-adhesive fluid, a thin, smooth, non-mechanical, and at the same time, geometrically inhomogeneous. Besides, blood does not move, time and space stream at

different paces. Hence, CVDs assessments by estimating PWV depending on the Moens-Korteweg equation are unquestionably not right. The PWV estimated by human vessels is an aftereffect of numerous covering factors that associate with each other, and the Moens-Korteweg condition is not proper to apply. With a specific end goal to make estimations of PWV more reliable CVD determination, it is important to comprehend the wave propagation in the vessels [27].

2.5.1 Measurement of Pulse Transit Time

Pulsed Transit Time (PTT) is the pulse needed to propagate the pulse pressure waveform over a length of the arterial tree. The pulse pressure waveform is caused by the ejection of blood from the left ventricle and the blood moves at a much greater rate than the forward motion of the blood itself [28, 29].

2.5.2 Measurement of Distance

The distance between the carotid artery and the femoral artery is seen as the most preferred distance in PWV measurement in current studies [10]. Besides, it is also possible to take measurements from different arteries such as carotid to radial arteries or brachial to radial arteries. Distance between brachial to radial artery and most preferred measurement positions are represented in Figure 2.

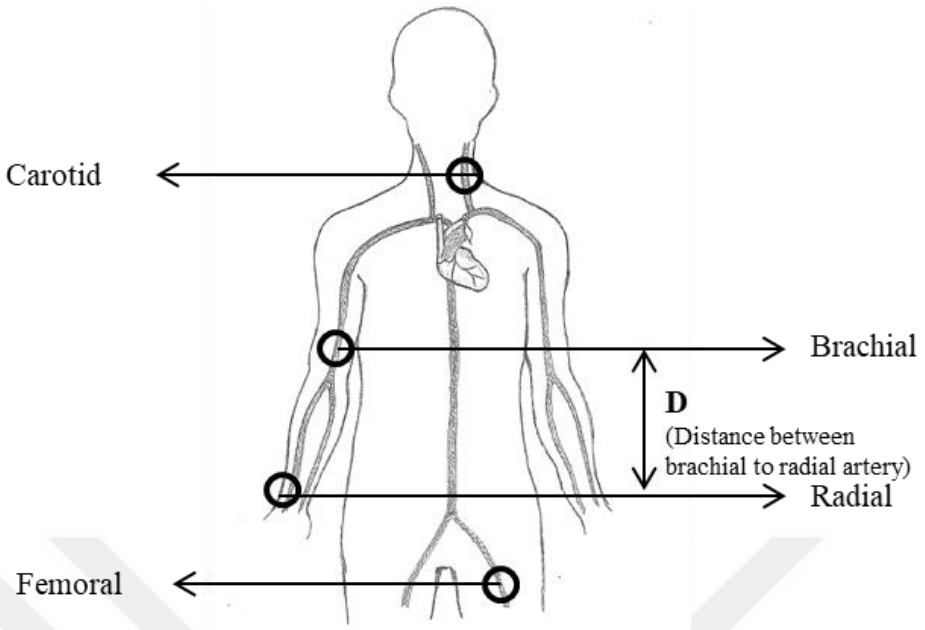

Figure 2 - Measurement points of pulse wave velocity.

2.6 Pulse Wave Velocity Measurement Devices

The summary table for commercial and non-commercial devices according to methods and measurement types is given in Table 2.

Table 2 - Devices and Methods for PWV Assessment

Methods	Measurements	Devices
Non-invasive	Regional PWV	PulsePen
		Complior
		SphygmoCor
		Ultrasound
	Local PWV	Magnetic resonance image
		Ultrasound
Invasive	Local PWV	Angiography

*Adapted from [30].

2.6.1 PulsePen

PulsePen is a non-invasive device consisting of a tonometer and an electrocardiogram (ECG) unit. It evaluates the PWV as a regional and is lightweight and easily portable when evaluated in terms of size. Having wireless communication without the need for extra wiring for computer transmission makes it even easier to use. The PWV measurement is based on a rule-based principle - golden standard and the measurement is taken between carotid and femoral arteries. [31].

2.6.2 Complior

Complior is a non-invasive and regional PWV assessment device that was created using two piezoelectric pressure mechanotransducers. It was designed based on the golden standard for accuracy of the measurements. Unlike the devices on the market, measurements can be taken between other arteries such as carotid–brachial or femoral–dorsalis pedis. [32].

2.6.3 SphygmoCor

SphygmoCor is a non-invasive device that performs PWV measurement in two separate stages. Performs a regional PWV assessment and analyzes the pulse wave velocity of the carotid - femoral arteries. In the first stage, carotid pulse wave and ECG are recorded. In the second stage, the femoral pulse wave and the ECG are recorded and PWV evaluation is performed based on the delay between first and second records. [32].

2.6.4 Ultrasound

Ultrasound PWV assessment can be non-invasive, both regional and local

measurements. The regional assessment can estimate the PWV value by estimating the time difference between the two nearest vessels. The local assessments can be evaluated as the ratio between change in the flow and change in cross-sectional area during the heart cycle. [33].

2.6.5 Magnetic Resonance Imaging

As a non-invasive and local technique, without the use of any physical assumptions, MRI allows direct imaging of the aorta. The most significant advantage of MRI technique over other similar methods is the measurement of the path length of arteries in an exact and straightforward way. PWV assessments are depend on blood flow velocity and accurate distance measurement. The system is used in hospital and it is operator-dependent.

2.6.6 Angiography

Angiography is a medical imaging technique of particular interest to the arteries, veins and heart chambers used to visualize the blood vessels and the organs of the body. This is usually done by injecting a radio-opaque contrast material into the blood vessel and using X-ray based techniques. It is an invasive method and makes a local assessment. Although it is a technology that is more expensive than all other devices in the market, it can reach the exact results.

2.7 Advantages & Disadvantages of Methods to Pulse Wave Velocity Measurement

The PWV assessment methods are grouped under three headings in the today's literature. These are called imaging, non-imaging and optical methods. These three methods have advantages and disadvantages in themselves. Table 3 provides a summary version of the advantages and disadvantages of the PWV measurement methods. PWV measurement is still an up-to-date issue in today's studies because disadvantageous method has not been found yet.

2.7.1 Imaging Method

The PWV measurement results are the most accurate because the path length is measured directly within the imaging methods. Besides all this, it is one of the biggest disadvantages of being an expensive technology and not being used in everyday clinical applications. It is not suitable for home use and the system is operator dependent. Ultrasound and Magnetic Resonance Image are suitable examples for the imaging method.

2.7.2 Non-imaging Method

The non-imaging method is distinguished by the fact that it is cheaper than the imaging method. The non-imaging method, which was started to be used for daily clinical applications, was widely used and experiments were conducted on large populations to confirm the results. [26]. On the positive side as well as on the results, it was seen that the measurement results did not provide sufficient information in obese and very light-skinned & dark-skinned people. The distance estimation is based on an

approximation of the path length and for these reasons, it is one of the disadvantages of the distance measurement and the inadequacy method of the specific population.

2.7.3 Optical Method

Optical method studies have emerged in order to take advantage of the disadvantages of using the output of imaging and non-imaging methods. The greatest advantage of optical method is that it is a non-invasive measurement method and that the effects of different wave lengths in the human body have been studied in the literature for a long time, so the invisible range allows signal perception in obese people and people with different color tones and helps to obtain valid results. It is a cheaper technology than other methods, but it is a newer technology because the use of optical methods in PWV evaluation does not depend much on the old versions. In the thesis study, PWV assessment was done by optical method when contributing to the literature and evaluating the advantages & disadvantages.

Table 3 - Advantages and Disadvantages of Methods to PWV Assessment

Methods	Advantages	Disadvantages
Imaging	Direct measurement of the path length	Expensive technology
Non-Imaging	More affordable (less expensive) and validated technology	Error associated with distance estimation, distortion in the acquisition signal, problems to access the signal in obese people, only allow a regional assessment.
Optical	Low cost technology, measurement without contact, capability to acquire the signal in obese people	Early stage validation

*Adapted from [26].

CHAPTER III

EXPERIMENTS

3.1 Sensor Design

In order to measure the pulse travel time, non-invasive high sensitivity low-power wearable pulse sensor front-ends were designed first. The overall sensor system block diagram is to be integrated into a patch form with the final system components depicted in Figure 3. An optoelectronic front-end utilizing a 650-nm red LED direct light into the area, whereas the photodiode pick back the light reflected from the tissue. A three stage amplifier-filter chain along with a final stage comparator feeds the heart pulse signal to Bluetooth-Low-Energy processor for processing. Once the 60 second measurement cycle is completed, BLE puts all the active circuits into sleep and goes into an IDLE mode for about 10mins to save power.

Power is to be supplied by 8mAh LiR1220 2mm thick small size 3.7V rechargeable battery which is charged through wireless charger after a predicted operation time of a day.

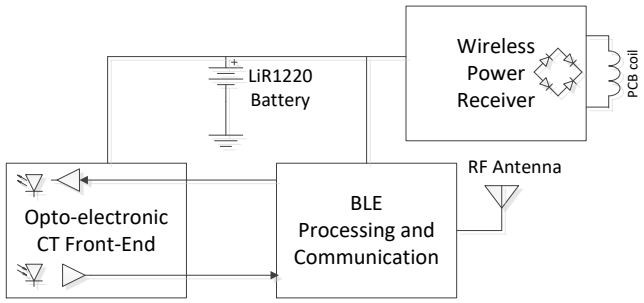

Figure 3 - Wearable water-resistant optoelectronic sensor system diagram.

In order to perform the in vivo experiments, first, the sensor front-end has been implemented and characterized by capturing the heart rate pulse waveforms from two identical sensors on brachial and radial artery track. The circuit diagram of the sensor front-end design is shown in Figure 4. In order not to be impacted by the placement or patient muscle and skin characteristics, the front-end employs 3 high-gain stages. Heavy filtering and AC coupling was implemented not to saturate the chain with noise or DC offset. The final stage is a high gain comparator to convert the final waveform into a full-swing pulse for the BLE controller processing. Initial experimental test prototypes of these sensor front-ends are also shown in Figure 5. Each of the sensors consume around 5mA from 3.7V including the 7-MHz GBW low-noise amplifiers.

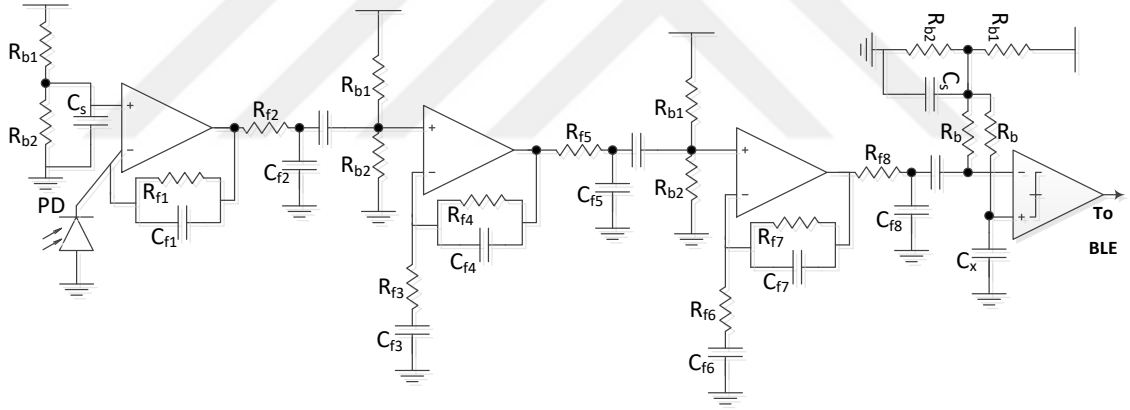

Figure 4 - Optoelectronic sensor front-end gain and filtering circuits

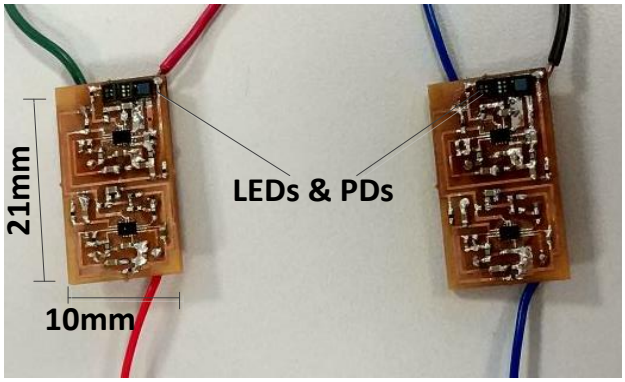

Figure 5 - Initial pulse sensor prototypes that were employed in the experiments

3.2 Measurement Position and Setup

Pulse wave velocity requires the pulse transit time and distance between two anatomical sites to be known. For this study, pulse transit time measurements were made by taking at the difference between the synchronous waveforms of the system designed with the new noninvasive approach. Distance was measured using a tape measure, along a straight line between brachial artery and radial artery. Measurements to points on the arm were made with above the elbow and wrist straight, and the shoulder was allowed to remain at 90° without extension or movement.

Mixed domain oscilloscope (Tektronix MDO3012) was used for the analysis of the synchronous waveforms of the system and the measurement of the PTT value. Two different power supplies were used to power the system and minimize the noise between the circuits.

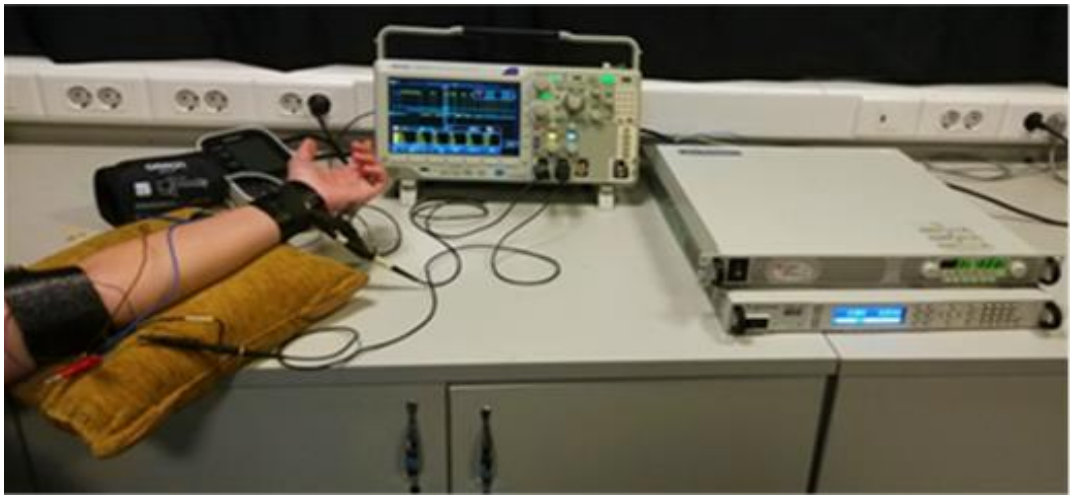

Figure 6 - Measurement position and setup

3.3 Subject Characteristics

A total of 32 normotensive volunteers, including 15 females and 17 males aged between 23 and 41 years old, participated in this study. Volunteers were questioned about their age, height, weight, physical activity levels in daily life, genetic predisposition for blood pressure and diabetic in order to be used in measurement evaluations. All of them are healthy individuals without any known cardiovascular diseases. Table 4 shows the characteristics of the volunteers.

3.4 Data analysis

Microsoft Excel (v10.0, Microsoft Corp.) and MedCalc (v16.0, MedCalc Software) were used for data analysis and scattered plots. Data are generally presented in terms of mean ± standard deviation when describing the study population. The analysis is based on the examination identity plot (a scatter plot of the PWV vs BMI/SBP/DBP/HR/PP/MAP with regression line).

Table 4 – Main Characteristics of the Volunteers

Parameter	Group 1	Group 2	Total
N	15	17	32
Age*	30.13 ± 4.16	31.88 ± 3.18	31.06 ± 3.77
Gender (M/F)	F	M	-
Height* (m)	1.65 ± 0.05	1.79 ± 0.08	1.72 ± 0.1
Body Mass* (kg)	61.07 ± 10.34	81.47 ± 10.76	71.91 ± 14.67
BMI* (kg/m²)	22.48 ± 3.24	25.36 ± 2.76	24.01 ± 3.32
Hypertension (N, %)	0 (0%)	0 (0%)	0 (0%)
Diabetes (N, %)	0 (0%)	0 (0%)	0 (0%)
Treated Hypertension (N, %)	8 (53%)	6 (35%)	14 (44%)
Treated Diabetes (N, %)	5 (33%)	5 (29%)	10 (31%)
Current Smoker (N, %)	9 (60%)	9 (53%)	18 (56%)
Physical Inactivity (N, %);			
Low	7 (47%)	6 (35%)	13 (41%)
Middle	7 (47%)	7 (41%)	14 (44%)
High	1 (7%)	4 (12%)	5 (9%)
Obesity N	1 (0%)	2 (12%)	3 (6%)

*Data are mean ± S.D.
BMI indicates body mass index. Treated hypertension and treated diabetes;
Cardiovascular disease in first degree relative aged 75 years or less.

CHAPTER IV

ASSESSMENT OF PULSE WAVE VELOCITY MEASUREMENT

4.1 Introduction

A total of 32 normotensive volunteers, including 15 females and 17 males aged between 23 and 41 years old, participated in this study. Volunteers were questioned about their age, height, weight, physical activity levels in daily life, genetic predisposition for blood pressure and diabetic in order to be used in measurement evaluations. All of them are healthy individuals without any known cardiovascular diseases. In this chapter, we will examine how the values of SBP, DBP, HR, PP, MAP change according the PWV by creating two groups separated by certain components.

4.2 Methodology

Ambient conditions during the measurement significantly affect the blood pressure. Measurements were taken in dark room conditions, in a quiet and controlled temperature range (24±2°C), after participants were at rest for at least 5 minutes in order to reach the physiological baseline conditions of the participants as well as to prevent ambient noise in the used system. Participants were seated on a backboard and the arm to be measured was left naked. The day before the measurements, the volunteers were not allowed to drink alcohol, stay up late or use any medicine that would affect blood pressure. During the measurement, the measuring arm was supported in order not to

move and also to reduce impact of the external factors that may affect the measurement accuracy. Participants were also asked not to speak during the measurements.

SBP-DBP-HR values were recorded using Omron M7 Intelli IT Electronic Sphygmomanometers as well to generate reference measurements within minutes from PWV recording time. During the measurement with the sphygmomanometers, the sleeve was wrapped around the arm at the level of the heart and placed on the both left and right brachial artery.

Pulse pressure (PP) was obtained by the formula **PP=SBP-DBP** and mean arterial pressure (MAP) was obtained by **MAP=DBP+PP/3**.

PWV was calculated determining the transit time of the pulse between brachial and radial arteries at the sensor location and the distance between arteries were recorded in this study. During PTT measurements, the sensor circuits were placed on the brachial artery and radial artery and covered with black tape not to leak interference from the ambient light. The straight-line distance between measurement points was used as a path length.

The measurements were taken at least two times during the interval of two minutes and three times during the day and the average of the results was taken. If the difference between the two values was greater than 5 mmHg, the measurements were repeated and their results were averaged out. The measurements were repeated at regular intervals and recorded at both left and right brachial artery. The numbers of the measurements were identical at each period.

4.3 Results

4.3.1 Assessment of Pulse Wave Velocity Measurement Related with Gender

Men are generally at greater risk than women, given the possibility of cardiovascular disease. Recent studies using a 24-h remote blood pressure monitoring technique have shown that blood pressure in men is higher than in similar-age women. [34]. All blood pressure measurements of these normotensive individuals were taken at certain intervals of the day, in both left and right arms. The average measurement results are shown in Table 5 for both genders. In bivariate analysis (Table 6 for group 1 _females and Table 7 for group 2_males), BMI, SBP, DBP, HR, PP and MAP were positively correlated with PWV. The relations of PWV to BMI, SBP, DBP, HR, PP and MAP were displayed in Figures 7–18, respectively. SBP, ($r=0.99$, $P<0.001$) for females and ($r=0.99$, $P<0.001$) for males remained significantly correlated with PWV according to our measurements.

According to BMI analysis for both two groups, BMI Group I ($r=0.46$, $P= 0,085$) and BMI Group II ($r=0.52$, $P=0.032$) highly correlated with PWV but they do not give us enough information about CVDs. Figure 7 and Figure 8 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI with regression line and correlation coefficient for both two genders.

Table 5 - Measurement Results Related with Gender

Parameter	Group 1	Group 2
N	15	17
Age	30.13 ± 4.16	31.88 ± 3.18
Gender (M/F)	F	M
Height (m)	1.65 ± 0.05	1.79 ± 0.08
Body Mass (kg)	61.07 ± 10.34	81.47 ± 10.76
BMI (kg/m^2)	22.48 ± 3.24	25.36 ± 2.76
SBP (mmHg)	110.12 ± 8.15	114.59 ± 9.65
DBP(mmHg)	75.3 ± 5.07	72.84 ± 7
Pulse(bpm)	82.06 ± 5.57	71.55 ± 7.76
Pulse Pressure (PP)	34.82 ± 5.14	41.75 ± 7.25
Mean Arterial Pressure (MAP)	86.91 ± 5.78	86.76 ± 7.22
Pulse Transit Time PTT(ms)	48.13 ± 3.9	49 ± 5.11
Brachial to radial distance-D (m)	0.26 ± 0.01	0.3 ± 0.02
Pulse Wave Velocity (PWV) (m/s)	5.52 ± 0.43	6.19 ± 0.57

*Data are mean ± S.D.
SBP indicates systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

Table 6 - Correlation coefficient between pulse wave velocity and blood pressure parameters for Females

Parameter	r	P
BMI (kg/m²)	0.46	0.085
SBP (mmHg)	0.99	<0.001
DBP(mmHg)	0.77	0.001
HR (bpm)	0.12	0.662
PP (mmHg)	0.81	<0.001
MAP (mmHg)	0.92	<0.001

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

Table 7 - Correlation coefficient between pulse wave velocity and blood pressure parameters for Males

Parameter	r	P
BMI (kg/m²)	0.52	0.032
SBP (mmHg)	0.99	<0.001
DBP(mmHg)	0.72	0.001
HR (bpm)	0.11	0.685
PP (mmHg)	0.61	0.009
MAP (mmHg)	0.91	<0.001

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

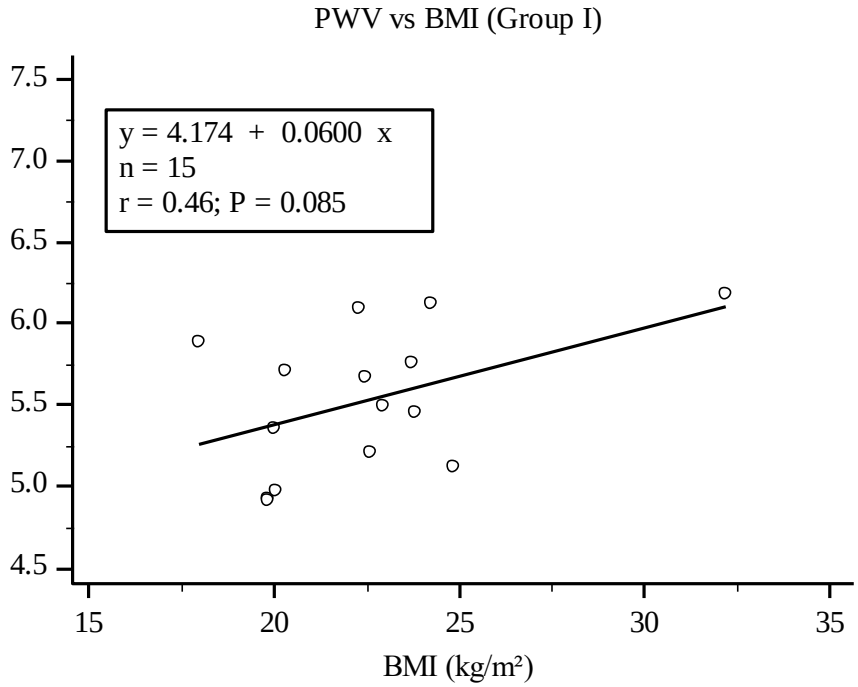

Figure 7 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Females with regression line

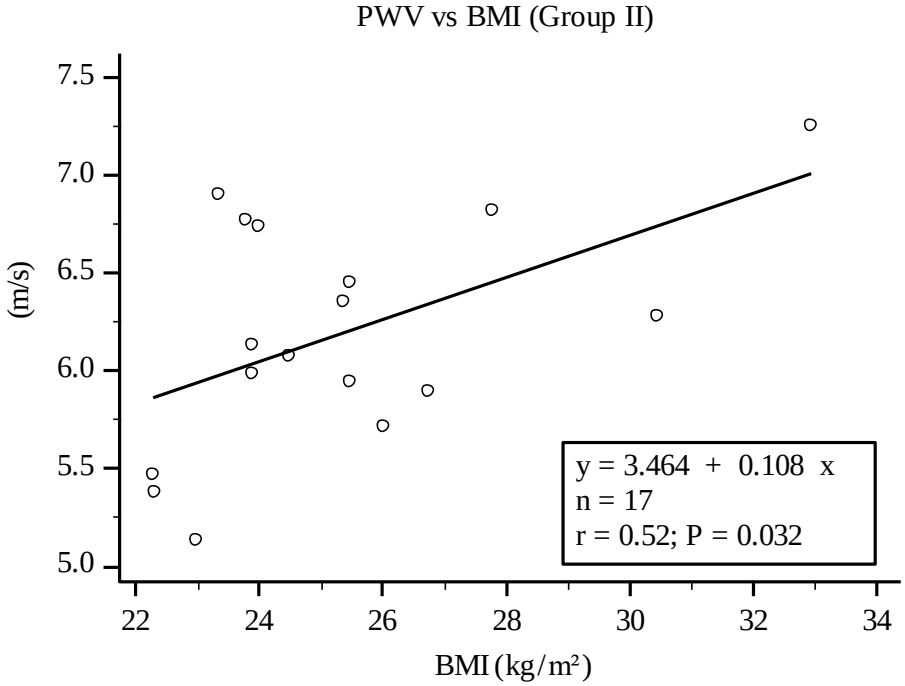

Figure 8 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Males with regression line.

According to SBP analysis for both two groups, SBP Group I ($r=0.99$, $P<0.001$) and BMI Group II ($r=0.99$, $P<0.001$) highly correlated with PWV and SBP provides sufficient information in the PWV measurements. SBP plays a leading role in the diagnosis of CVDs and shows that PWV results can be used in daily clinical measurements because of its direct association with PWV. Figure 9 and Figure 10 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP with regression line and correlation coefficient for both two genders.

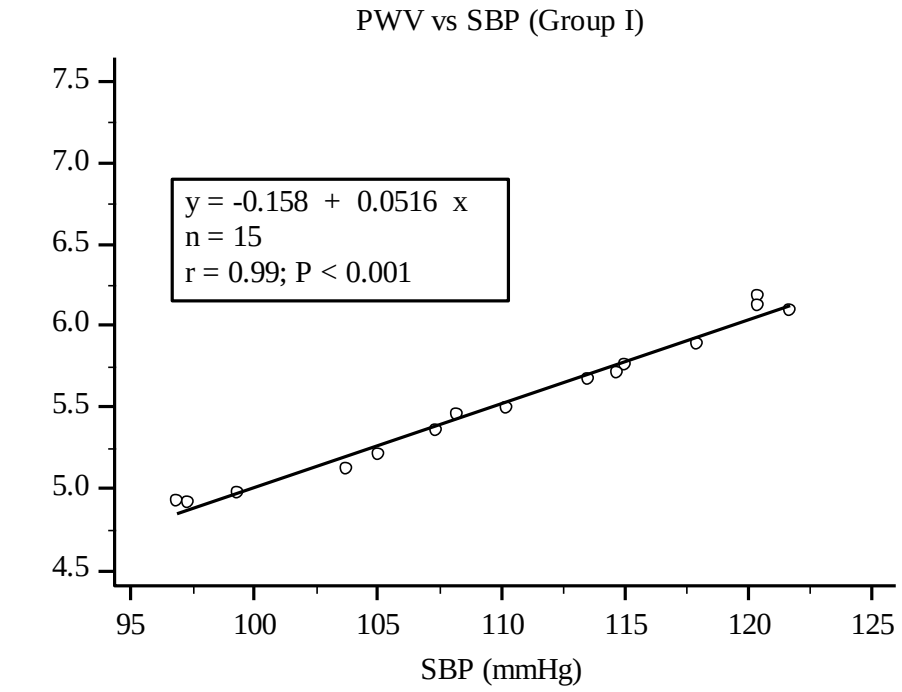

Figure 9 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Females with regression line.

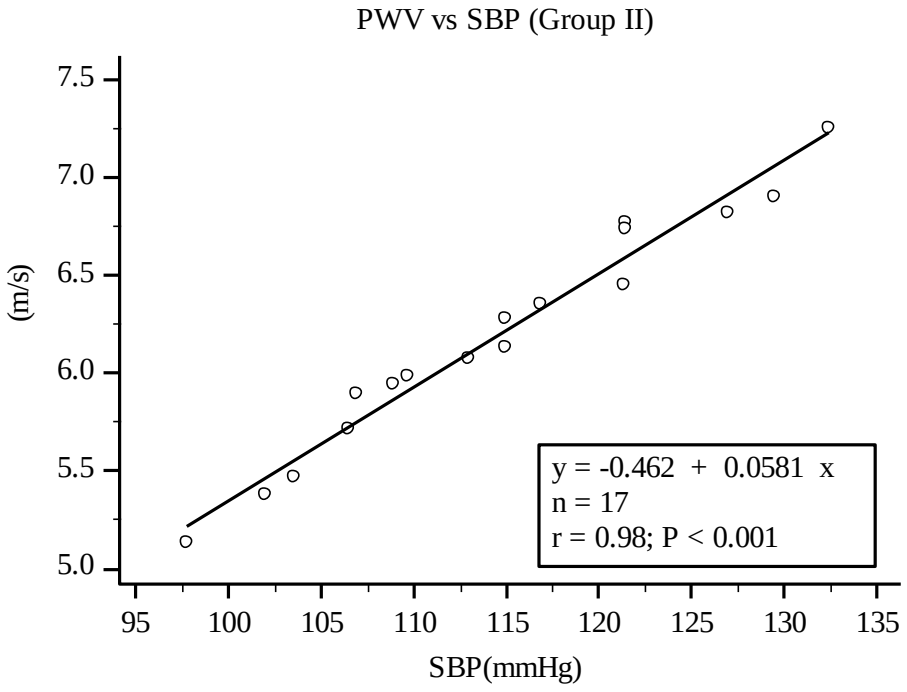

Figure 10 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Males with regression line.

According to DBP analysis for both two groups, DBP Group I (r=0.77, P=0.001) and DBP Group II (r=0.72, P=0.001) highly correlated with PWV but they do not give us enough information about CVDs. Figure 11and Figure 12 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP with regression line and correlation coefficient for both two genders.

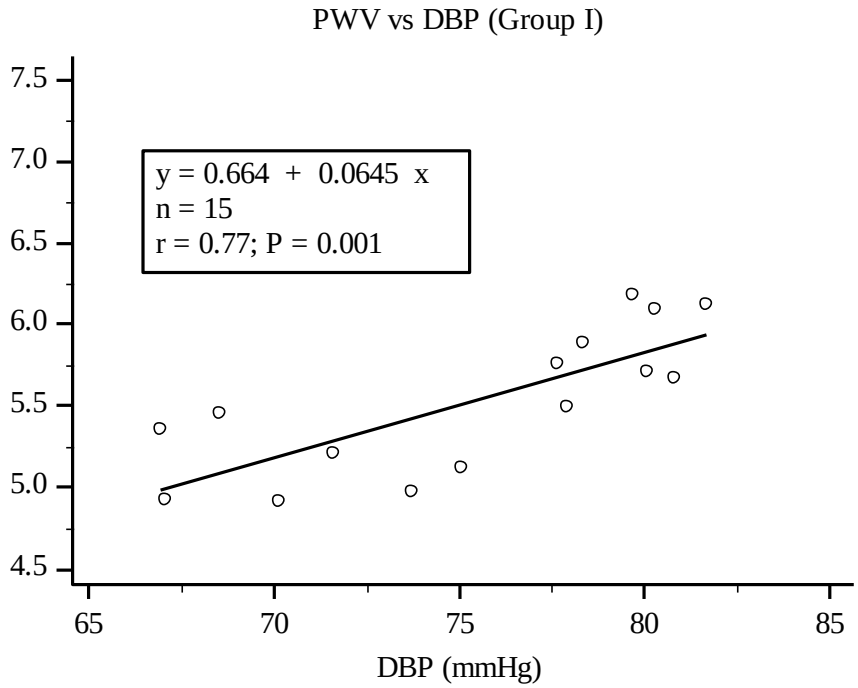

Figure 11 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Females with regression line.

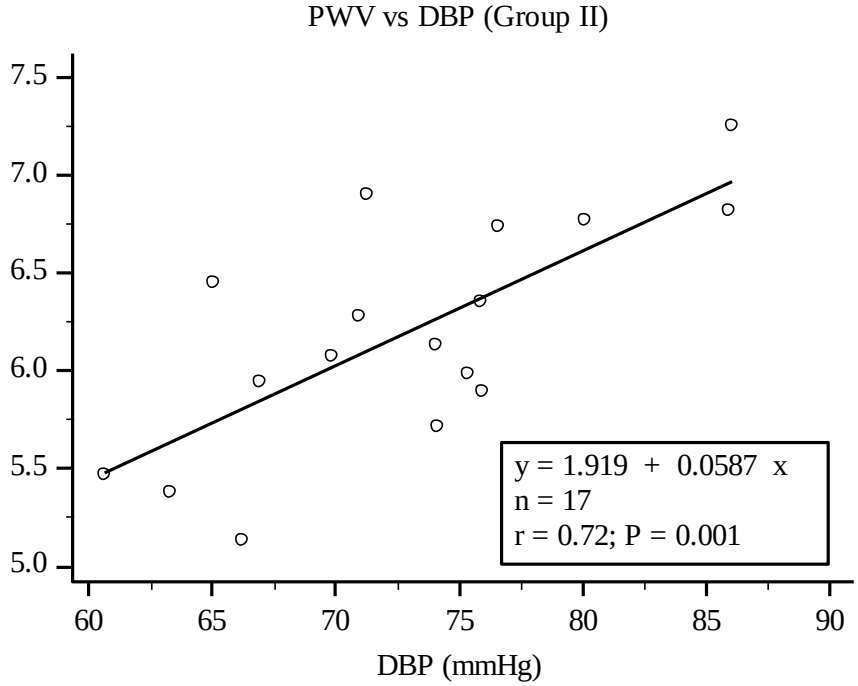

Figure 12 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Males with regression line.

According to HR analysis for both two groups, HR Group I (r=0.12, P=0.662) and HR Group II (r=0.11, P=0.685) correlated with PWV but they do not give us any information about CVDs. When we analysed the measurement results, the parameter with the least correlation between the BP parameters and the PWV is the heart rate. Figure 13 and Figure 14 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR with regression line and correlation coefficient for both two genders.

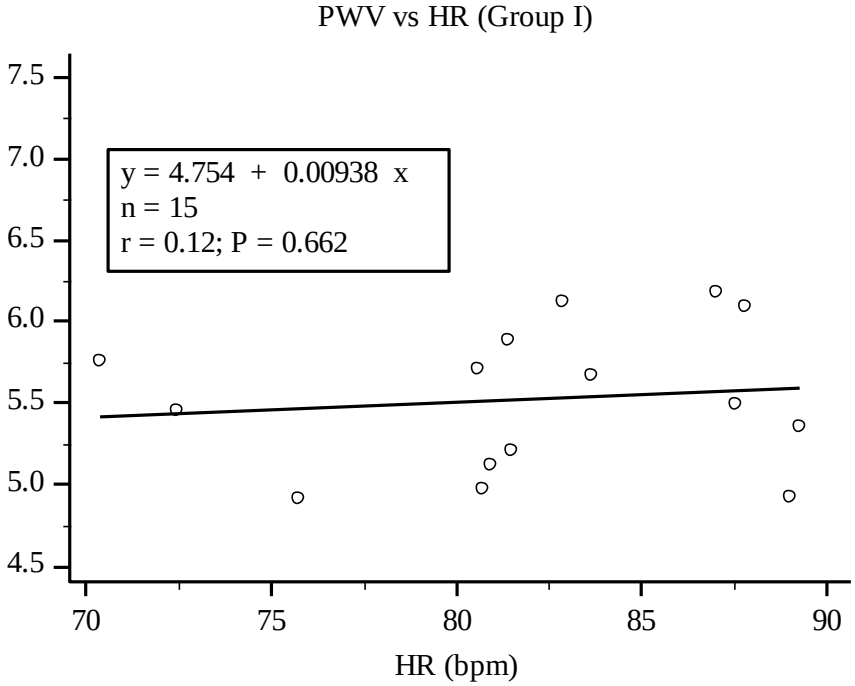

Figure 13 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Females with regression line.

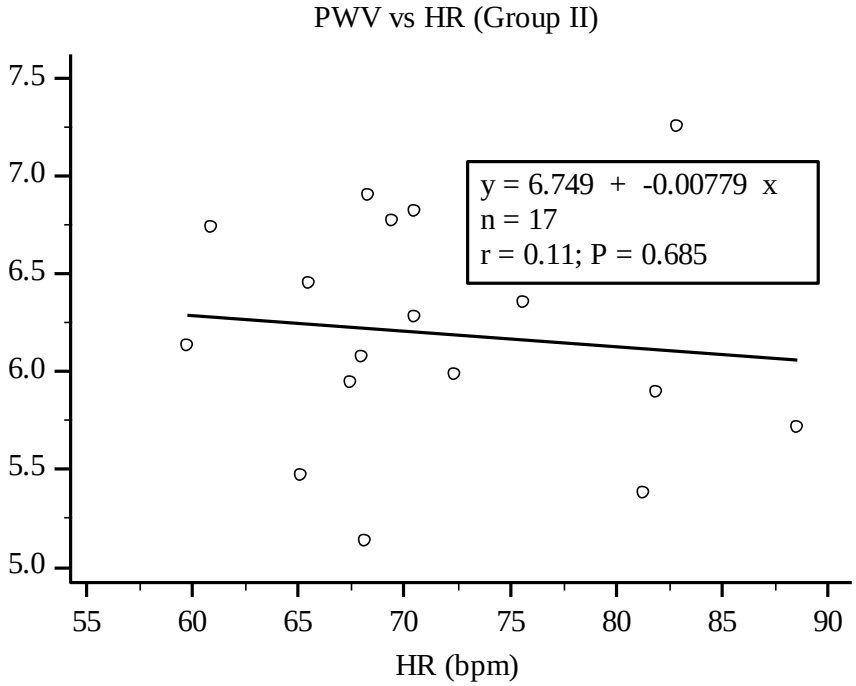

Figure 14 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Males with regression line.

According to PP analysis for both two groups, PP Group I (r=0.81, P<0.001) and PP Group II (r=0.61, P=0.009) highly correlated with PWV but they do not give us enough information about CVDs. Figure 15and Figure 16 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP with regression line and correlation coefficient for both two genders. When we analysed the graph, females groups PP has strongest relationship with PWV than males group PP.

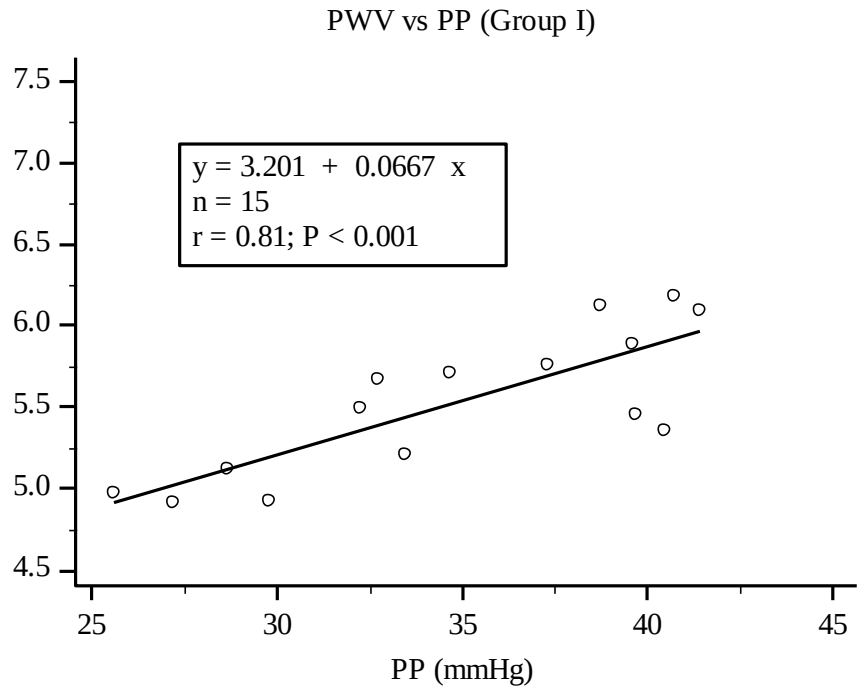

Figure 15 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Females with regression line.

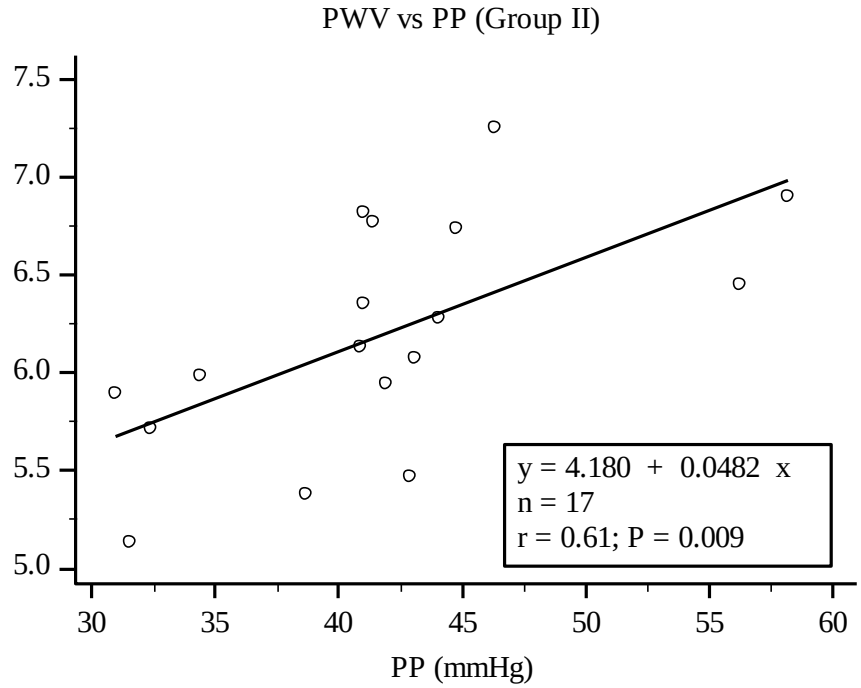

Figure 16 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Males with regression line.

According to MAP analysis for both two groups, MAP Group I ($r=0.92$, $P<0.001$) and MAP Group II ($r=0.91$, $P<0.001$) highly correlated with PWV and MAP also provides sufficient information in the PWV measurements. When assessed according to gender, it was found that the MAP value was used in PWV assessments in addition to the SBP value. However, when examining the other sections, it may not be possible to obtain clear results in daily clinical practice because it does not provide sufficient information in some areas. We can not say that MAP should be used in PWV assessments considering the studies done in the thesis. Figure 17and Figure 18 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP with regression line and correlation coefficient for both two genders.

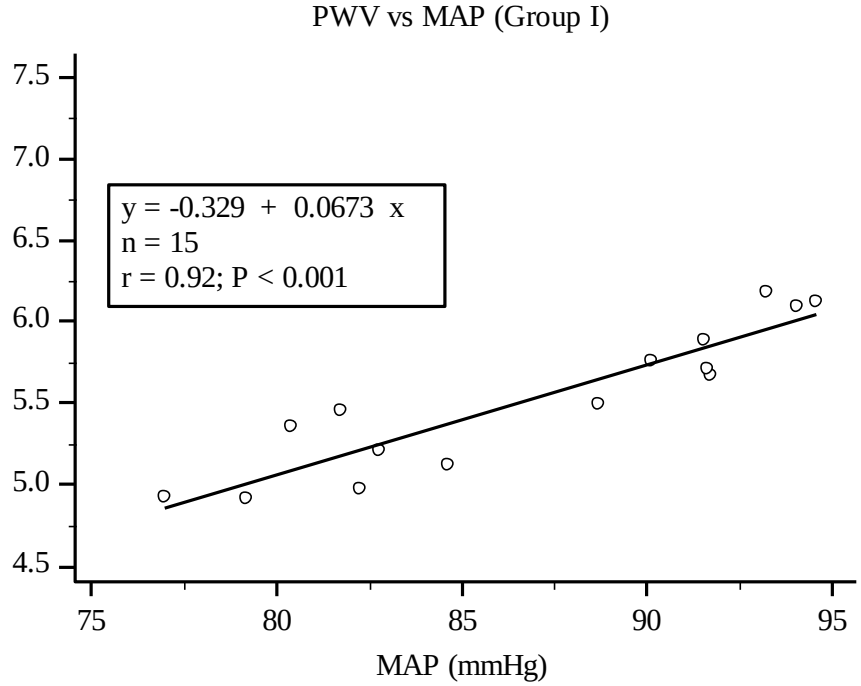

Figure 17 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Females with regression line.

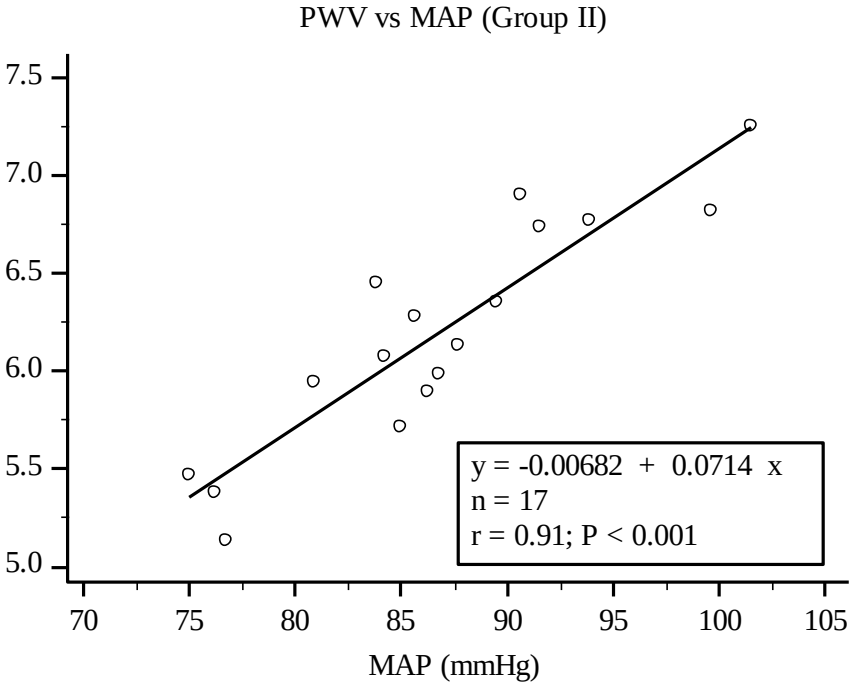

Figure 18- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Males with regression line.

4.3.2 Assessment of Pulse Wave Velocity Measurement Related with Age

When considering the possibility of age-related cardiovascular disease, older people seem to be at greater risk. In this thesis, we will show graphically how the PWV value varies with age. All blood pressure measurements of these normotensive individuals were taken at the right and left corners, at certain intervals of the day. The average measurement results are shown in Table 8 for both age groups. It has been seen that the results obtained are very close to each other since there is no significant age difference among the subjects. The selection of a wider age group for the monitoring of changes depending on age should take place among future studies of the project. In bivariate analysis (Table 9 for group 1 _ Age $\leq$ 30 and Table 10 for group 2_ Age > 30), BMI, SBP, DBP, HR, PP and MAP showed positive correlation with PWV. The relationships of PWV with BMI, SBP, DBP, HR, PP and MAP are shown in Figures 19-30, respectively. SBP, ($r=0.92$, $P<0.001$) for Age $\leq$ 30 and ($r=0.96$, $P<0.001$) for Age > 30 remained significantly correlated with PWV according to our measurements.

According to BMI analysis for both two groups, BMI Group I ($r=0.61$, $P=0,009$) and BMI Group II ($r=0.63$, $P=0.011$) highly correlated with PWV but they do not give us enough information about CVDs. Figure 19 and Figure 20 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI with regression line and correlation coefficient for both two age-related groups.

Table 8 - Measurement Results Related with Age

PARAMETER	GROUP 1	GROUP 2
N (female)	17 (10)	15 (5)
Age	28.29 ± 1.74	34.2 ± 2.9
Height (m)	1.7 ± 0.09	1.74 ± 0.1
Body Mass (kg)	67.35 ± 13.5	77.07 ± 14.23
BMI (kg/m^2)	22.94 ± 2.54	25.23 ± 3.67
SBP (mmHg)	113.16 ± 8.53	111.74 ± 9.95
DBP(mmHg)	75.33 ± 5.29	72.48 ± 6.96
Pulse(bpm)	77.93 ± 7.23	74.83 ± 9.68
Pulse Pressure (PP)	37.84 ± 7.12	39.26 ± 7.28
Mean Arterial Pressure (MAP)	87.94 ± 5.63	85.57 ± 7.31
Pulse Transit Time PTT(ms)	47.87 ± 4.01	49.41 ± 5.07
Brachial to radial distance-D (m)	0.28 ± 0.02	0.29 ± 0.02
Pulse Wave Velocity (PWV) (m/s)	5.85 ± 0.54	5.91 ± 0.68

*Data are mean ± S.D.
BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity

Table 9 - - Correlation coefficient between pulse wave velocity and blood pressure parameters for Age ≤ 30.

Parameter	r	P
BMI (kg/m²)	0.61	0.009
SBP (mmHg)	0.92	<0.001
DBP(mmHg)	0.38	0.130
HR (bpm)	0.44	0.078
PP (mmHg)	0.81	<0.001
MAP (mmHg)	0.70	0.002

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

Table 10 - - Correlation coefficient between pulse wave velocity and blood pressure parameters for Age > 30.

Parameter	r	P
BMI (kg/m²)	0.63	0.011
SBP (mmHg)	0.96	<0.001
DBP(mmHg)	0.62	0.014
HR (bpm)	0.30	0.281
PP (mmHg)	0.72	0.003
MAP (mmHg)	0.83	<0.001

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

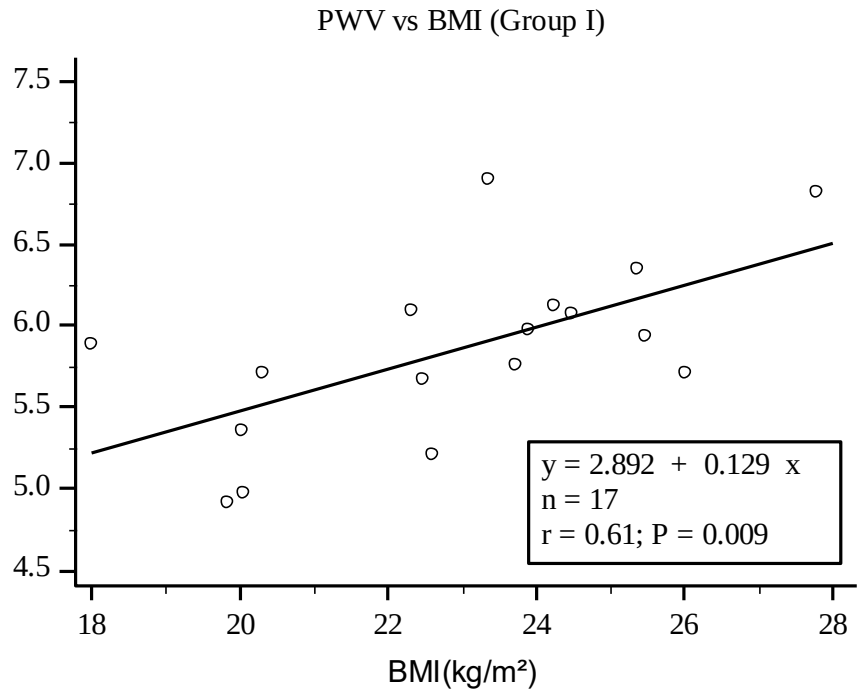

Figure 19 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Age ≤ 30 with regression line.

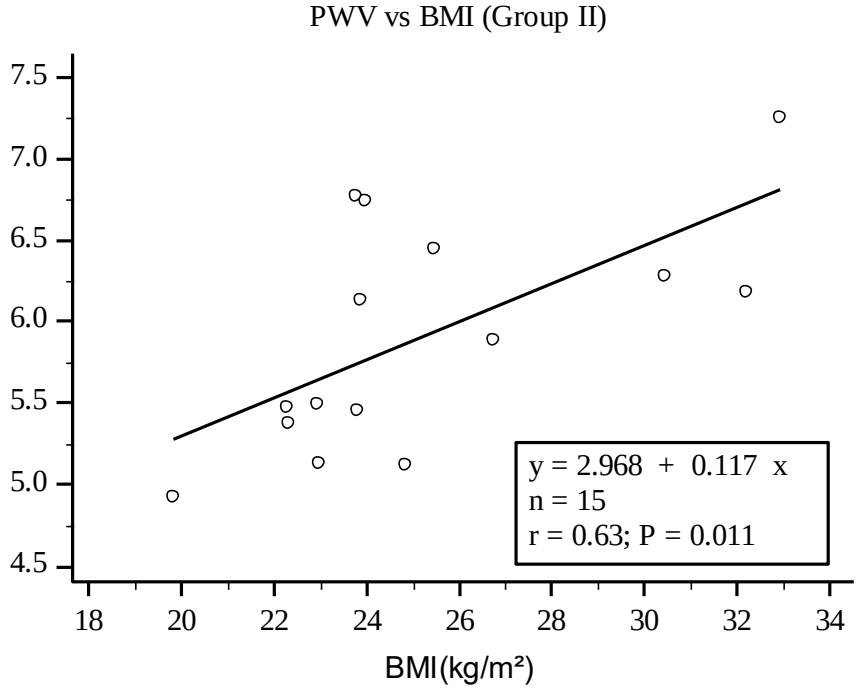

Figure 20 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Age > 30 with regression line.

According to SBP analysis for both two groups, SBP Group I ($r=0.92$, $P<0.001$) and SBP Group II ($r=0.96$, $P<0.001$) highly correlated with PWV and SBP provides sufficient information in the PWV measurements. SBP plays a leading role in the diagnosis of CVDs and shows that PWV results can be used in daily clinical measurements because of its direct association with PWV. Figure 21 and Figure 22 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP with regression line and correlation coefficient for both two age-related groups.

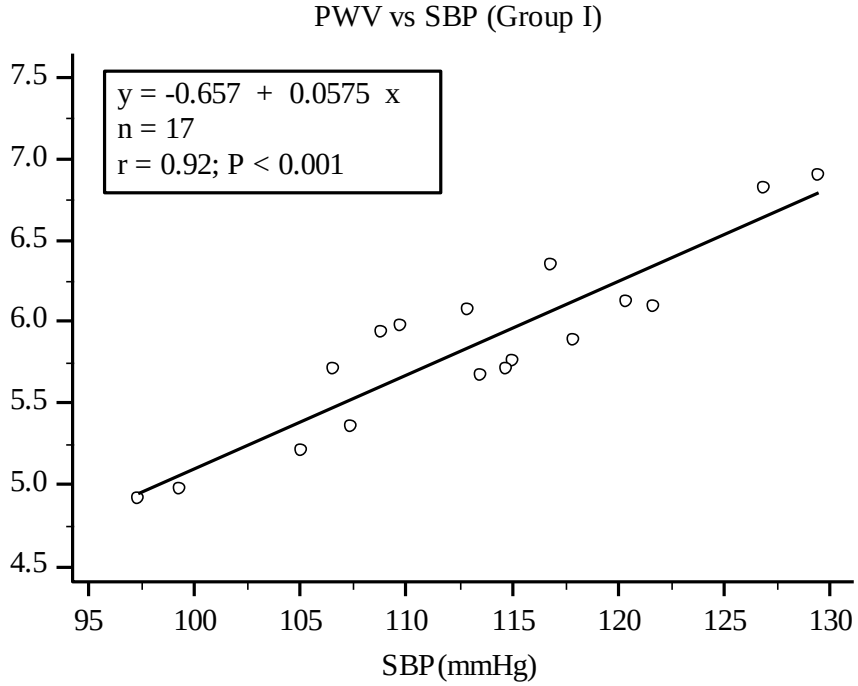

Figure 21 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Age ≤ 30 with regression line.

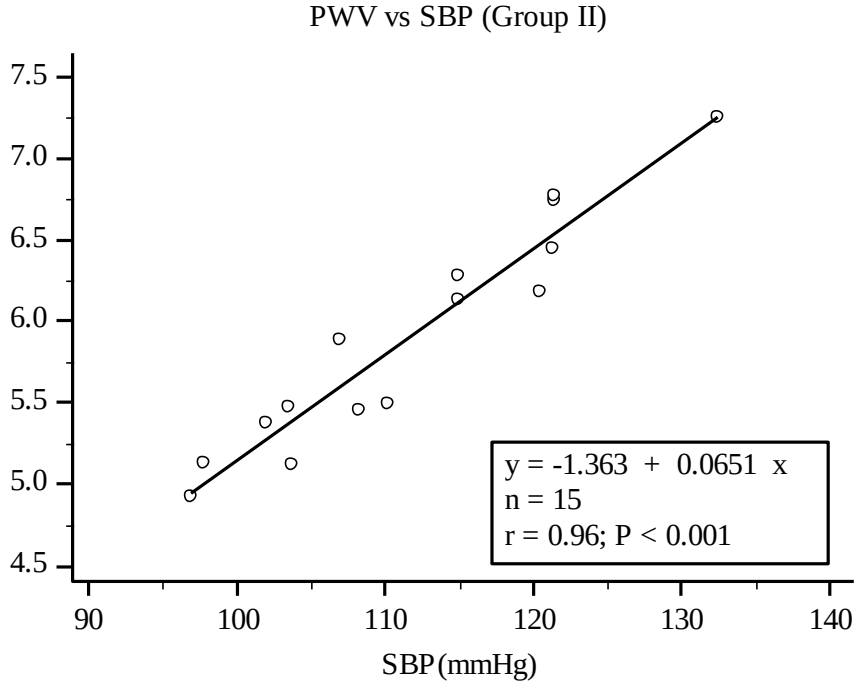

Figure 22 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Age > 30 with regression line.

According to DBP analysis for both two groups, DBP Group I (r=0.38, P=0.130) and DBP Group II (r=0.62, P=0.014) correlated with PWV but they do not give us enough information about CVDs. Figure 23 and Figure 24 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP with regression line and correlation coefficient for both two age-related groups.

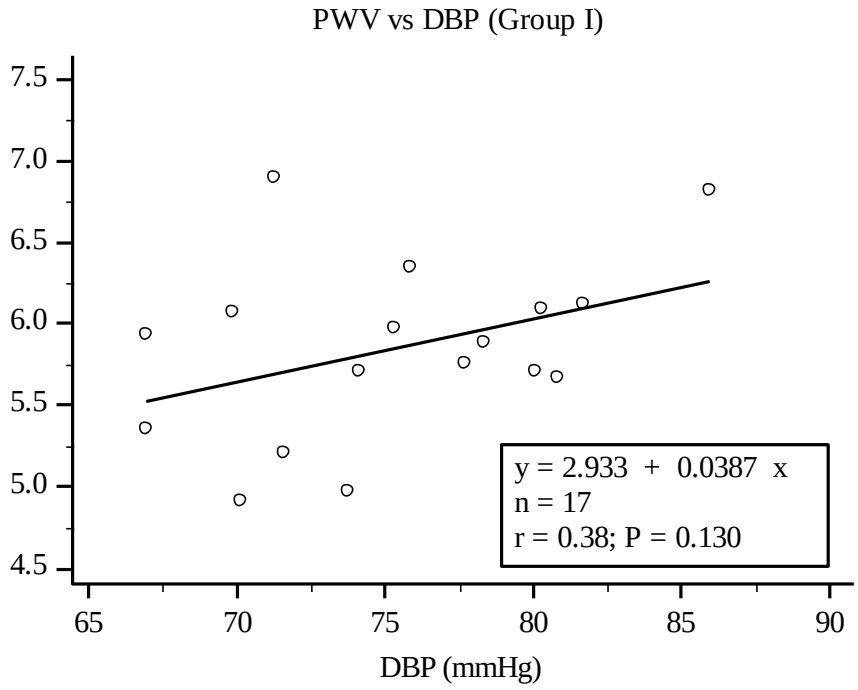

Figure 23 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Age ≤ 30 with regression line.

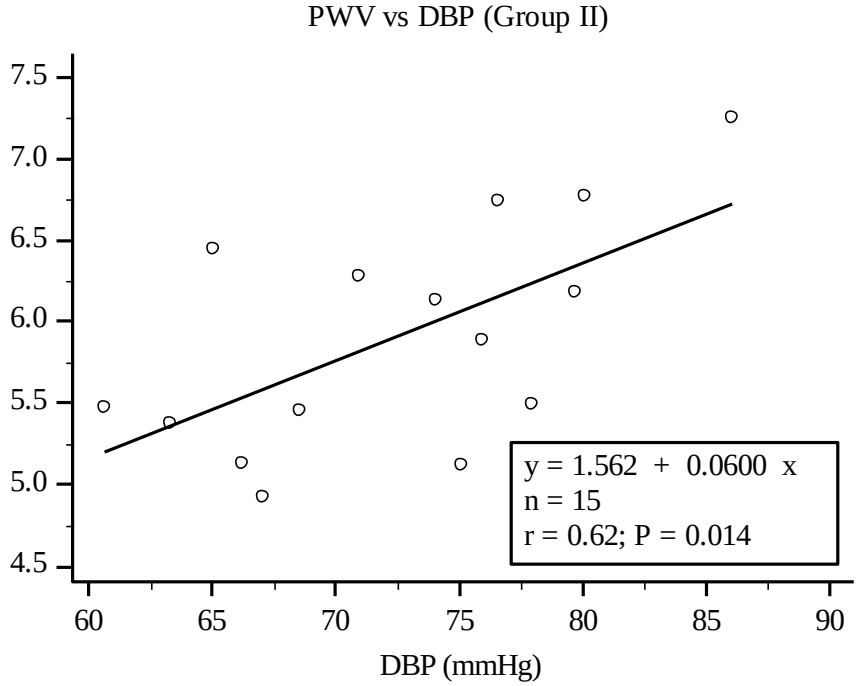

Figure 24 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Age > 30 with regression line.

According to HR analysis for both two groups, HR Group I (r=0.44, P=0.078) and HR Group II (r=0.30, P=0.281) correlated with PWV but they do not give us any information about CVDs. When we analysed the measurement results, the parameter with the least correlation between the BP parameters and the PWV is the heart rate. Figure 25 and Figure 26 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR with regression line and correlation coefficient for both two age-related groups.

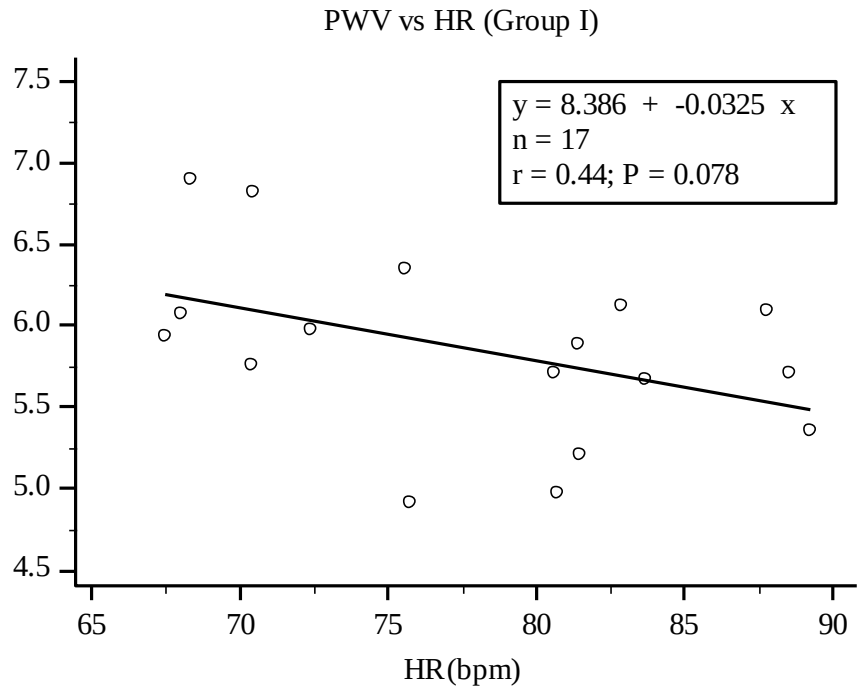

Figure 25 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Age ≤ 30 with regression line.

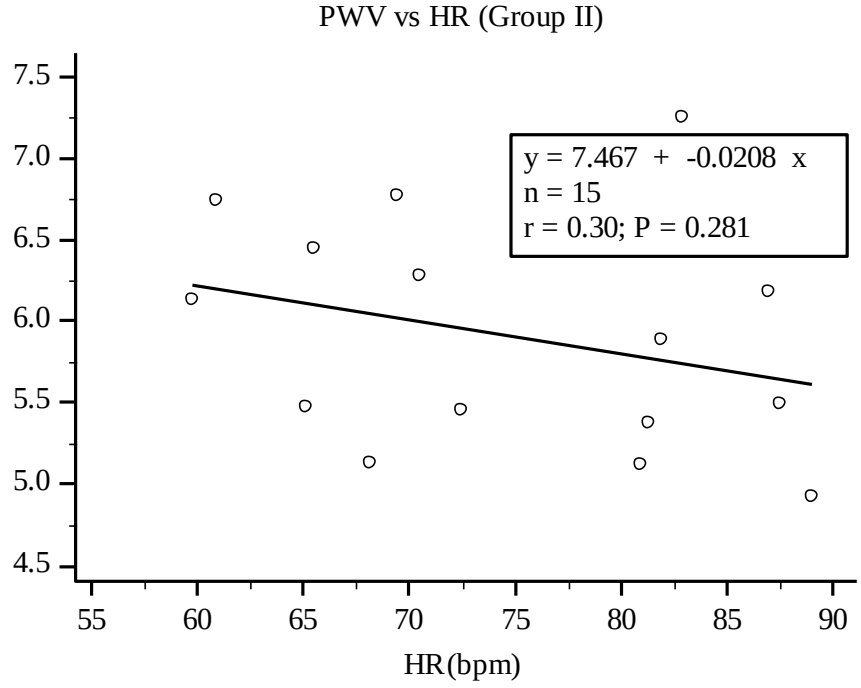

Figure 26 – Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Age > 30 with regression line.

According to PP analysis for both two groups, PP Group I (r=0.81, P<0.001) and PP Group II (r=0.72, P=0.003) highly correlated with PWV but they do not give us enough information about CVDs. Figure 27 and Figure 28 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP with regression line and correlation coefficient for both two groups. When we analysed the graph, Age ≤ 30 groups PP has strongest relationship with PWV than Age > 30 group PP. When assessed according to age, it was found that the PP value was used in PWV assessments in addition to the SBP value.

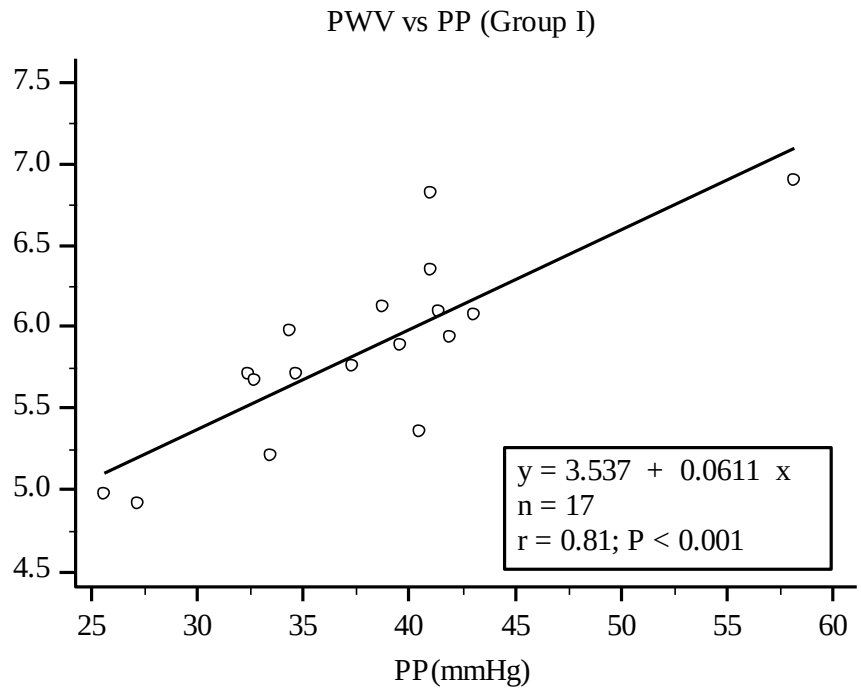

Figure 27 – Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Age ≤ 30 with regression line.

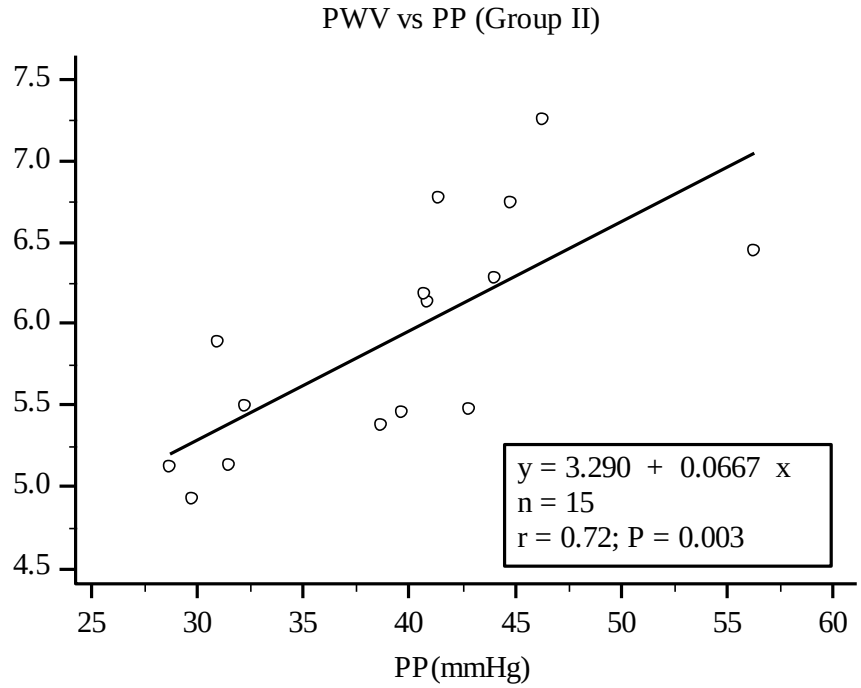

Figure 28 – Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Age > 30 with regression line.

According to MAP analysis for both two groups, MAP Group I (r=0.70, P=0.002) and MAP Group II (r=0.83, P<0.001) highly correlated with PWV and MAP also provides sufficient information in the PWV measurements. When assessed according to age, it was found that the MAP value was used in PWV assessments in addition to the SBP and PP values. However, when examining the other sections, it may not be possible to obtain clear results in daily clinical practice because it does not provide sufficient information in some areas. We can not say that PP and MAP should be used in PWV assessments considering the studies done in the thesis. Figure 29and Figure 30 show the scatter plots of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP with regression line and correlation coefficient for both two age-related groups.

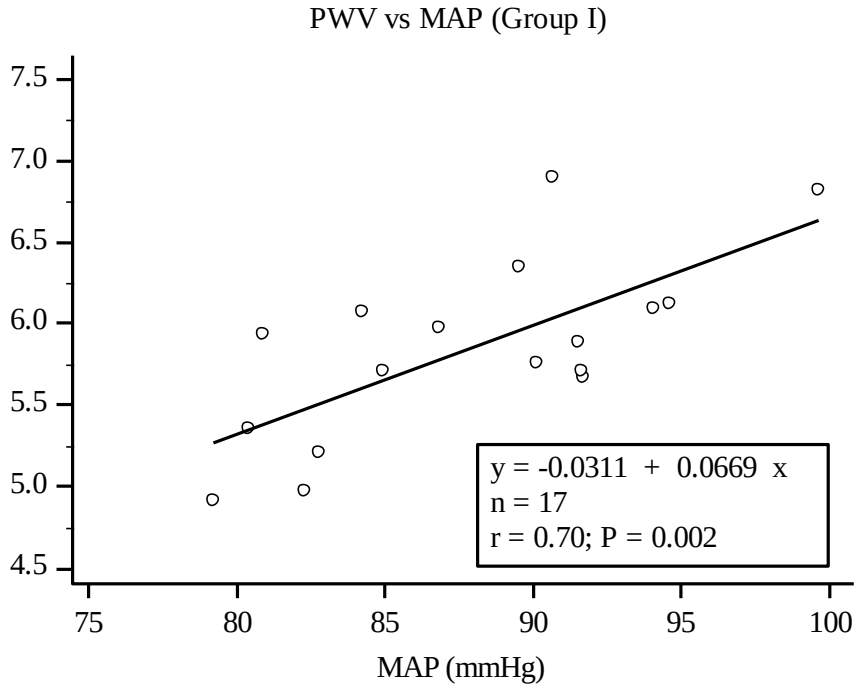

Figure 29 – Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Age ≤ 30 with regression line.

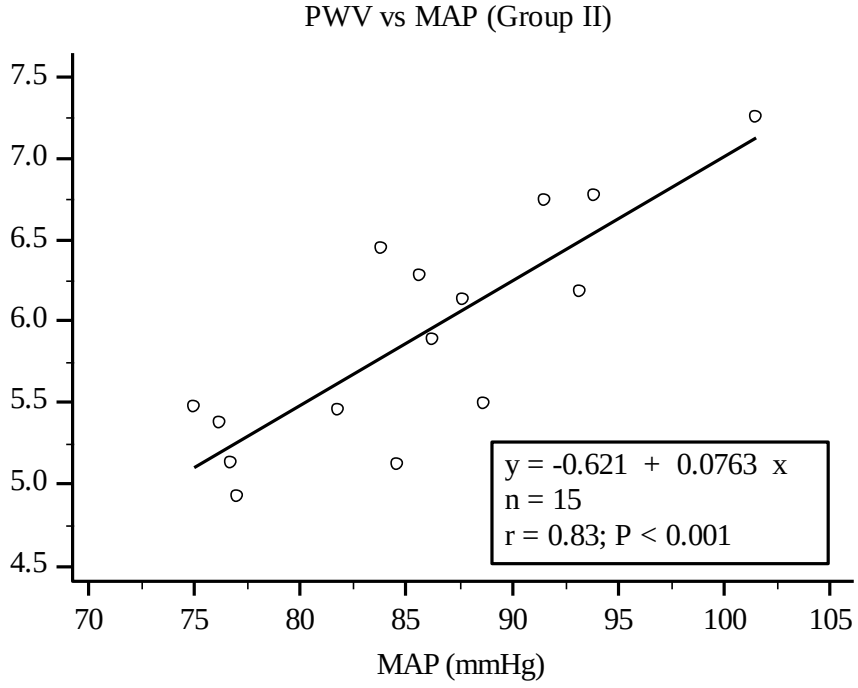

Figure 30 – Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Age > 30 with regression line.

4.3.3 Assessment of Pulse Wave Velocity Measurement Related with Family History

In CVDs, family history and genetic susceptibility are decisive factors in medical literature. People with hypertension and diabetes in the 1st and 2nd degree family members are at much higher risk than those who have no family history [2]. This informant path was asked to determine if there were hypertension and diabetes mellitus in the 1st degree family members, and groups were formed in response to the answers given. Two variant analyzes were grouped under two headings and two groups were separated. The average measurement results are shown in Table 11 for hypertension groups and Table 14 for diabetic groups.

In bivariate analysis, the subtype of hypertension group (Table 12 for group 1 _non-treated hypertension and Table 13 for group 2_treated hypertension), BMI, SBP, DBP, HR, PP and MAP were positively correlated with PWV. Similarly, there was a positive correlation with PWV in the subgroup of diabetics (Table 15 for group 1 _ Non-treated diabetes and Table 16 for group 2 _ Treated diabetes). The relationships between BMI, SBP, DBP, HR, PP and MAP for the two subheadings of PWV are shown in Figures 31-54 respectively.

Table 11 - Measurement Results Related with Treated Hypertension

PARAMETER	GROUP 1	GROUP 2
N	18	14
BMI (kg/m^2)	23.77 ± 2.95	24.32 ± 3.72
SBP (mmHg)	111.56 ± 8.12	113.69 ± 10.4
DBP(mmHg)	73.8 ± 4.9	74.24 ± 7.72
Pulse(bpm)	75.84 ± 8.04	77.3 ± 9.21
Pulse Pressure (PP)	37.76 ± 6.68	39.46 ± 7.77
Mean Arterial Pressure (MAP)	86.39 ± 5.3	87.39 ± 7.9
Pulse Transit Time PTT(ms)	49.31 ± 3.98	47.66 ± 5.16
Brachial to radial distance-D (m)	0.29 ± 0.02	0.28 ± 0.03
Pulse Wave Velocity (PWV) (m/s)	5.86 ± 0.51	5.91 ± 0.71

*Data are mean ± S.D.

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity

Table 12 - Correlation coefficient between pulse wave velocity and blood pressure parameters for Non-treated Hypertension

Parameter	r	P
BMI (kg/m²)	0.35	0.149
SBP (mmHg)	0.90	<0.001
DBP(mmHg)	0.39	0.107
HR (bpm)	0.32	0.191
PP (mmHg)	0.80	<0.001
MAP (mmHg)	0.70	0.001

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

Table 13 - Correlation coefficient between pulse wave velocity and blood pressure parameters for Treated Hypertension

Parameter	r	P
BMI (kg/m²)	0.78	0.001
SBP (mmHg)	0.96	<0.001
DBP(mmHg)	0.56	0.038
HR (bpm)	0.40	0.160
PP (mmHg)	0.73	0.003
MAP (mmHg)	0.79	0.001

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

In the hypertension group analysis, PP and MAP highly correlated with PWV, but the correlation of HR and DBP with PWV decreases. According to results, BMI is related with treated hypertension. In our hypertension-related analysis, the BP parameter, which is directly related to the PWV, was determined to be SBP as it was in the other results. In the light of the information given, PWV analysis helps to be informed about genetic predisposition. The relationships between BMI, SBP, DBP, HR, PP and MAP for the hypertension of PWV are shown in Figures 31-42 respectively.

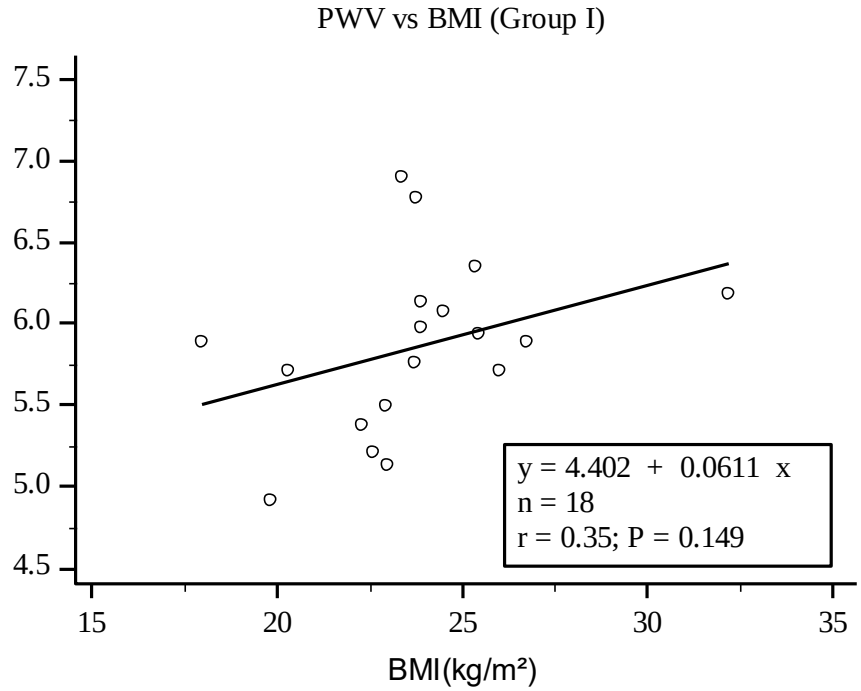

Figure 31 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Non-treated Hypertension with regression line.

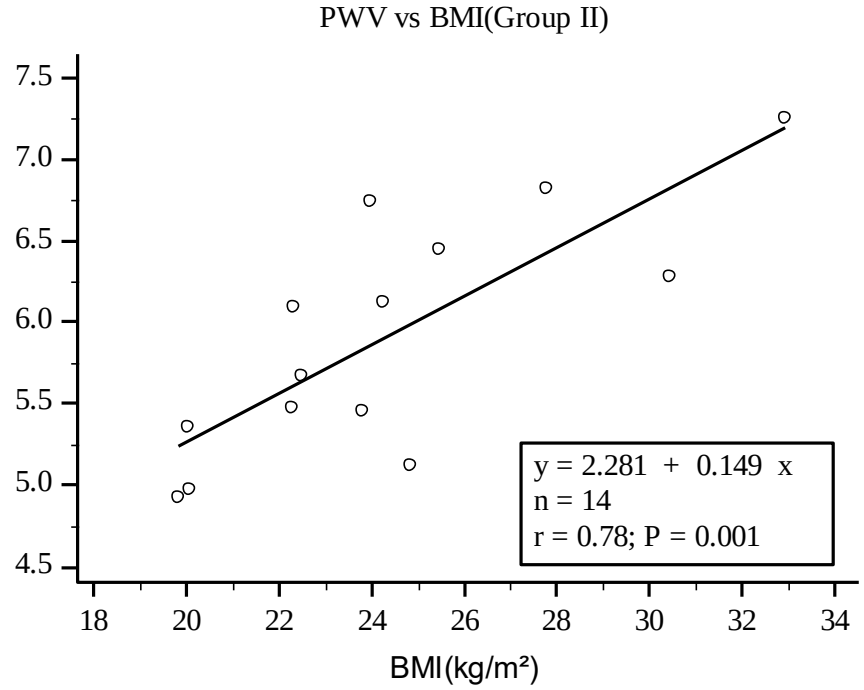

Figure 32 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Treated Hypertension with regression line.

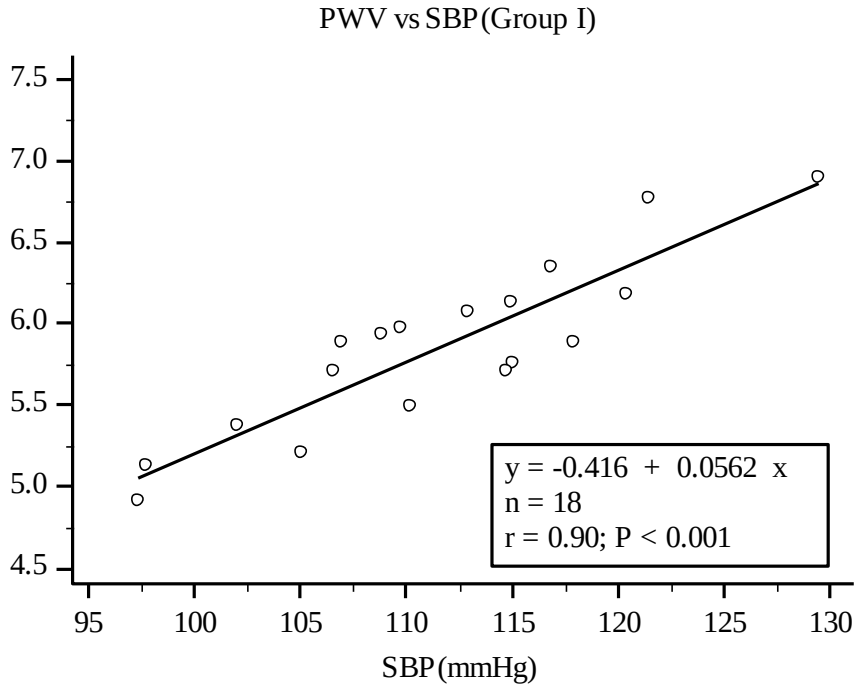

Figure 33 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Non-treated Hypertension with regression line.

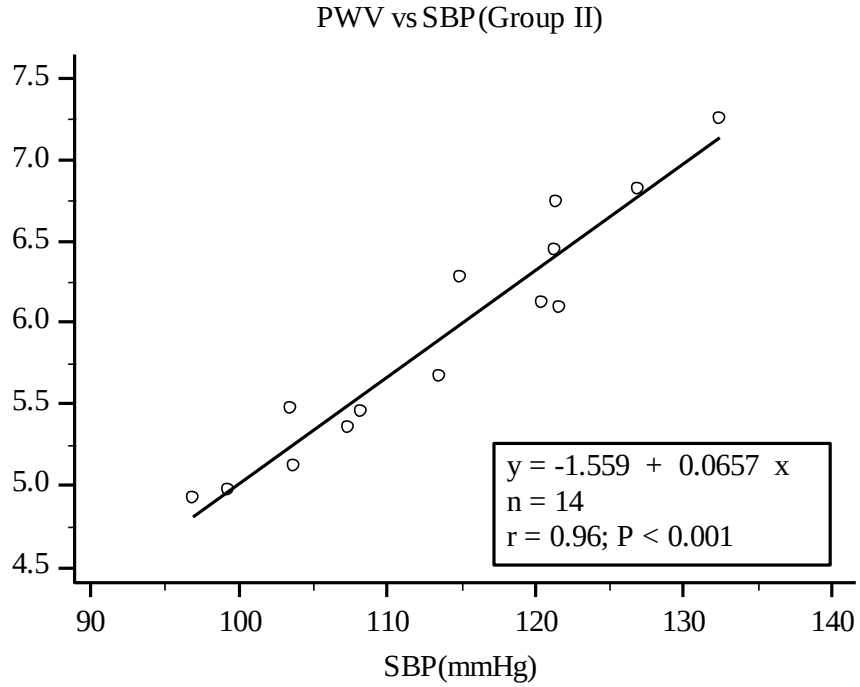

Figure 34 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Treated Hypertension with regression line.

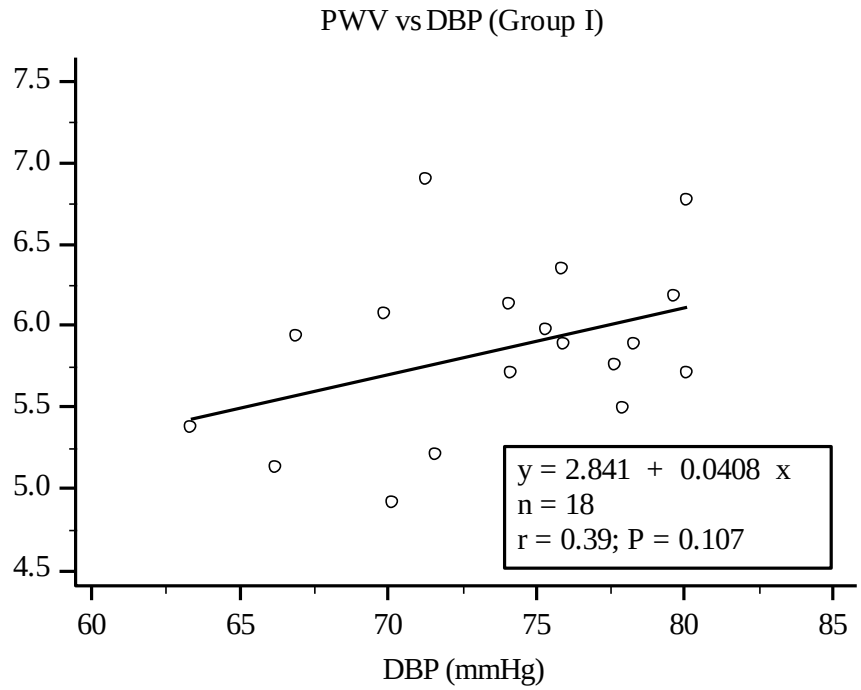

Figure 35 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Non-treated Hypertension with regression line.

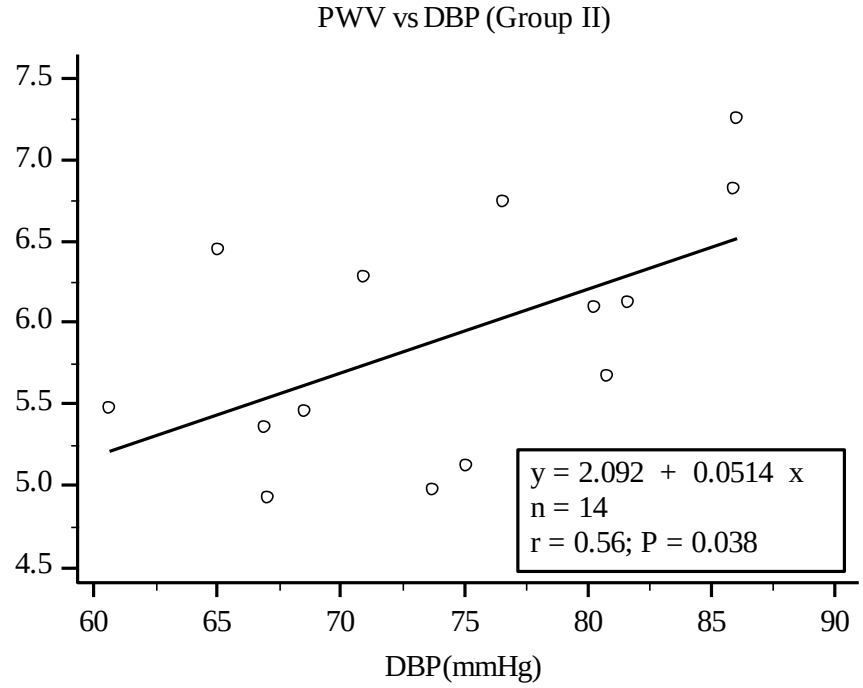

Figure 36 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Treated Hypertension with regression line.

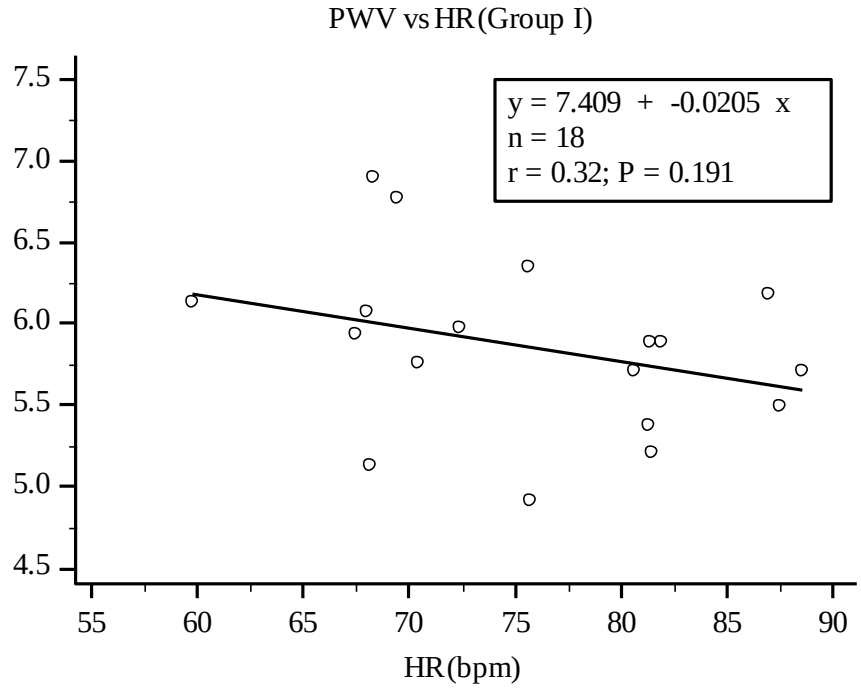

Figure 37 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Non-treated Hypertension with regression line.

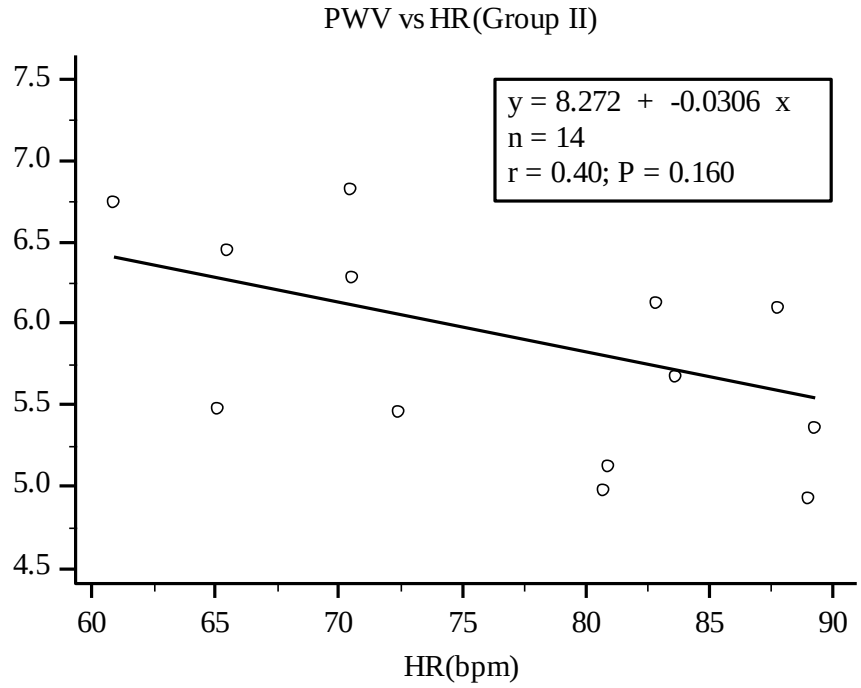

Figure 38 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Treated Hypertension with regression line.

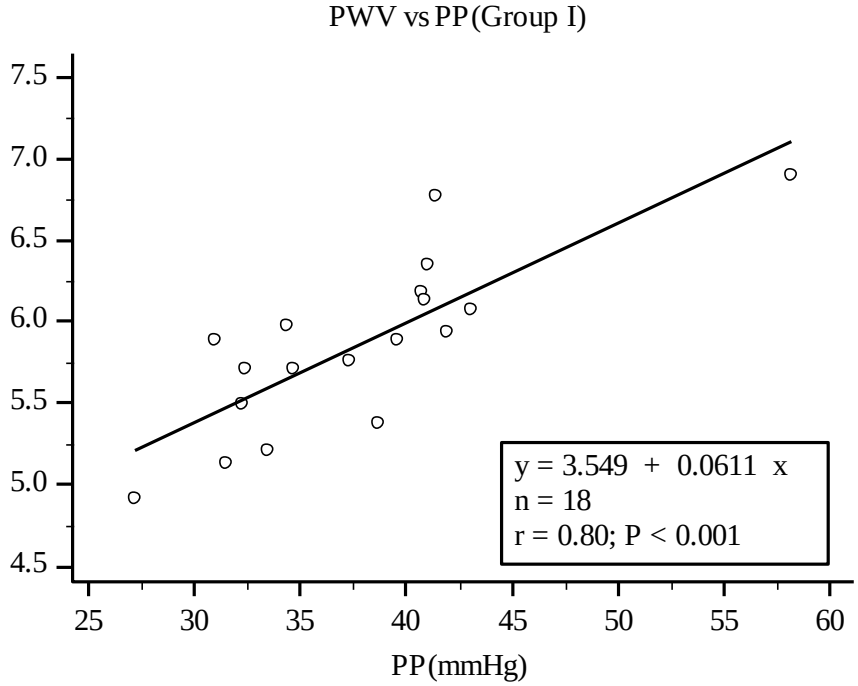

Figure 39 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Non-treated Hypertension with regression line.

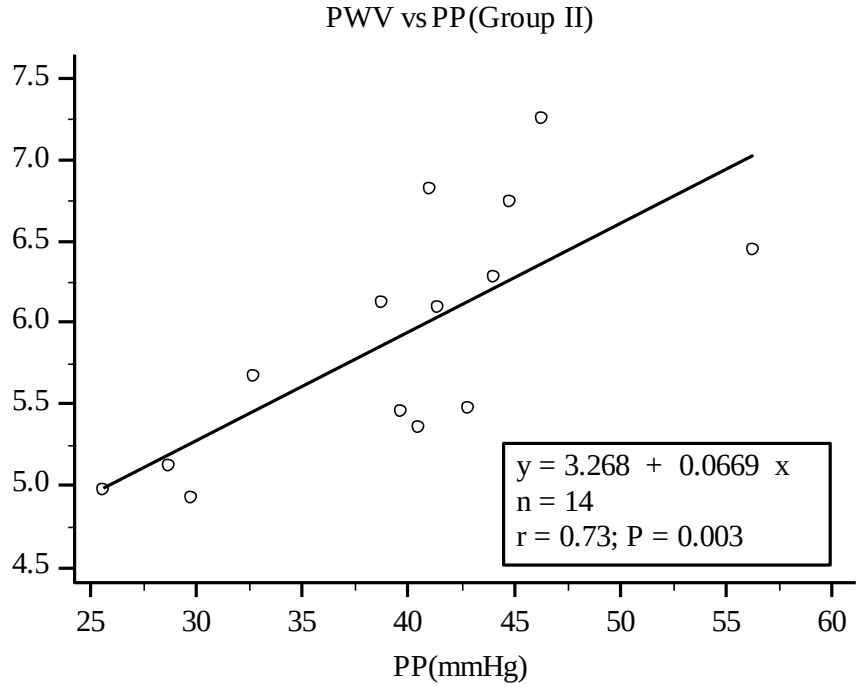

Figure 40 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Treated Hypertension with regression line.

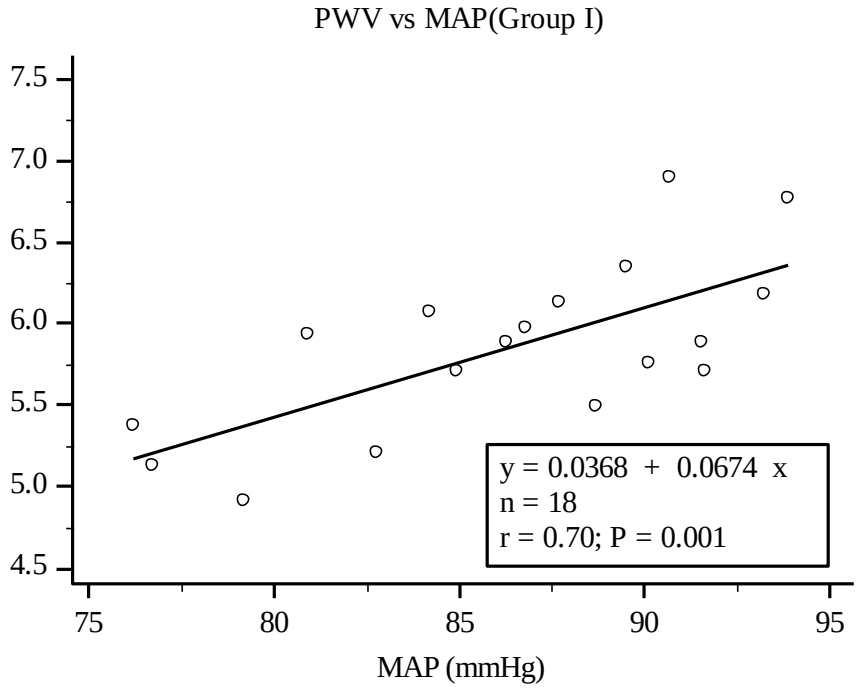

Figure 41 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Non-treated Hypertension with regression line.

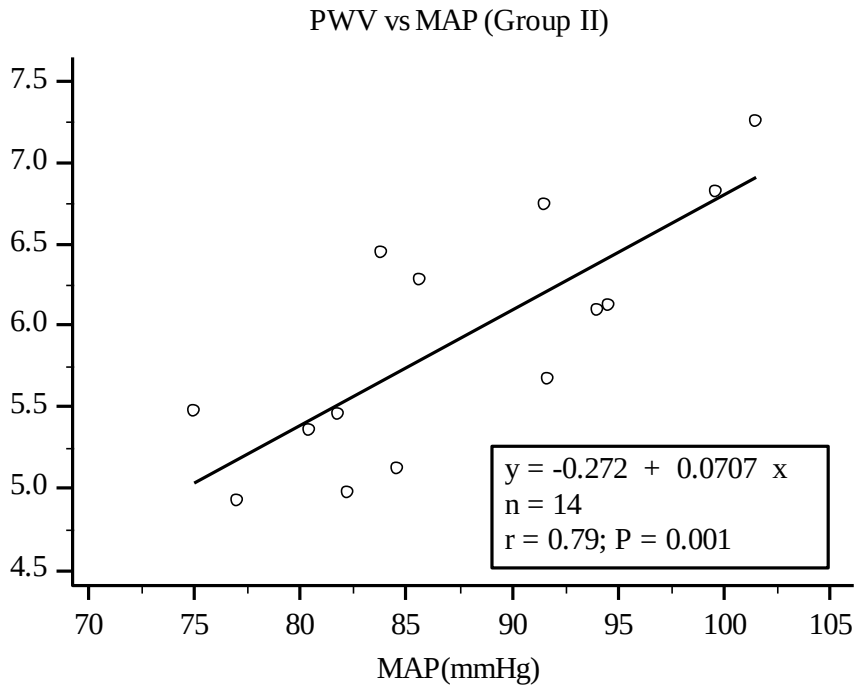

Figure 42 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Treated Hypertension with regression line.

Table 14 - Measurement Results Related with Treated Diabetes

PARAMETER	GROUP 1	GROUP 2
N	22	10
BMI (kg/m^2)	22.96 ± 3.38	24.83 ± 3.03
SBP (mmHg)	111.93 ± 9.13	112.94 ± 9.32
DBP(mmHg)	72.28 ± 5.99	75.33 ± 6.2
Pulse(bpm)	78.42 ± 7.78	74.97 ± 8.91
Pulse Pressure (PP)	39.65 ± 8.42	37.61 ± 6
Mean Arterial Pressure (MAP)	85.49 ± 6	87.86 ± 6.82
Pulse Transit Time PTT(ms)	48.45 ± 4.38	48.7 ± 4.77
Brachial to radial distance-D (m)	0.28 ± 0.03	0.29 ± 0.02
Pulse Wave Velocity (PWV) (m/s)	5.73 ± 0.55	5.99 ± 0.63

*Data are mean ± S.D.
BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity

Table 15 - Correlation coefficient between pulse wave velocity and blood pressure parameters for Non-treated Diabetes

Parameter	r	P
BMI (kg/m²)	0.52	0.012
SBP (mmHg)	0.94	<0.001
DBP(mmHg)	0.46	0.032
HR (bpm)	0.49	0.022
PP (mmHg)	0.75	<0.001
MAP (mmHg)	0.73	<0.001

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

Table 16 - Correlation coefficient between pulse wave velocity and blood pressure parameters for Treated Diabetes

Parameter	r	P
BMI (kg/m²)	0.69	0.026
SBP (mmHg)	0.93	<0.001
DBP(mmHg)	0.63	0.053
HR (bpm)	0.22	0.532
PP (mmHg)	0.91	<0.001
MAP (mmHg)	0.83	0.003

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

In the diabetic group analysis, PP and MAP highly correlated with PWV, but the correlation of BMI, HR and DBP with PWV decreases. In our diabetic-related analysis, the BP parameter, which is directly related to the PWV, was determined to be SBP as it was in the other results. When assessed according to diabetes, it was found that the PP and MAP values were used in PWV assessments in addition to the SBP value. In the light of the information given, PWV analysis helps to be informed about genetic predisposition. The relationships between BMI, SBP, DBP, HR, PP and MAP for the hypertension of PWV are shown in Figures 43-54 respectively.

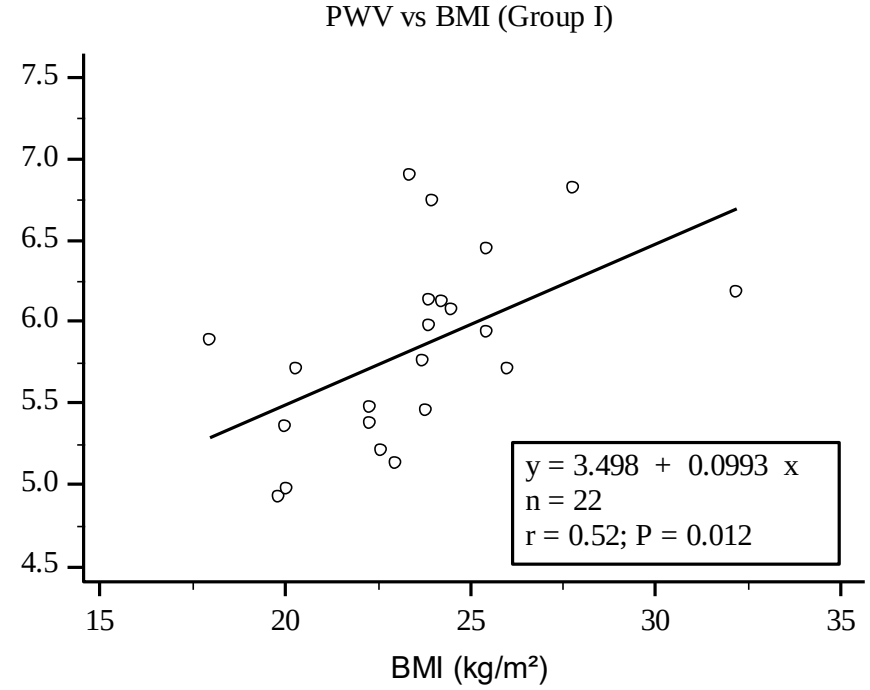

Figure 43 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Non-treated Diabetes with regression line.

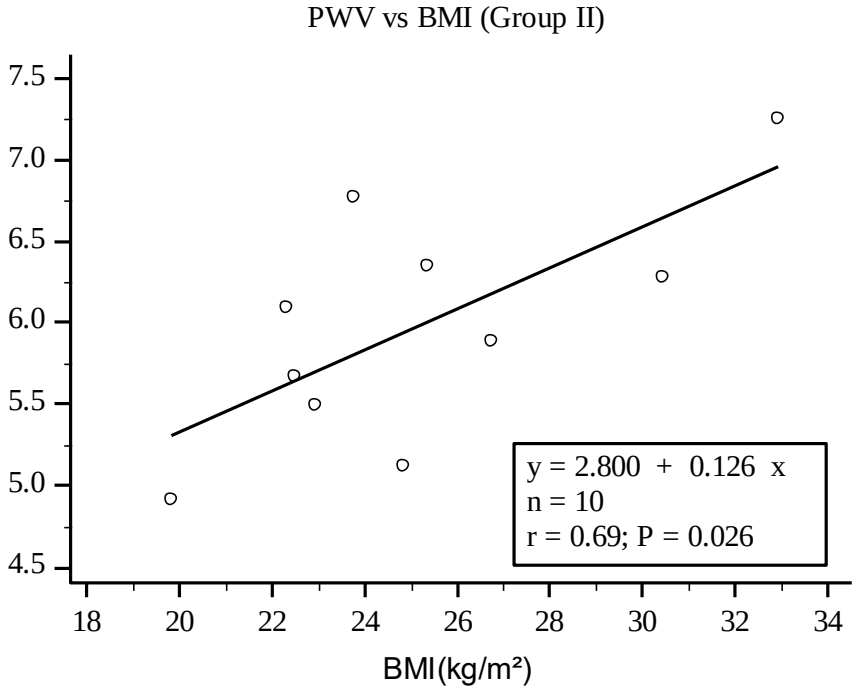

Figure 44 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Treated Diabetes with regression line.

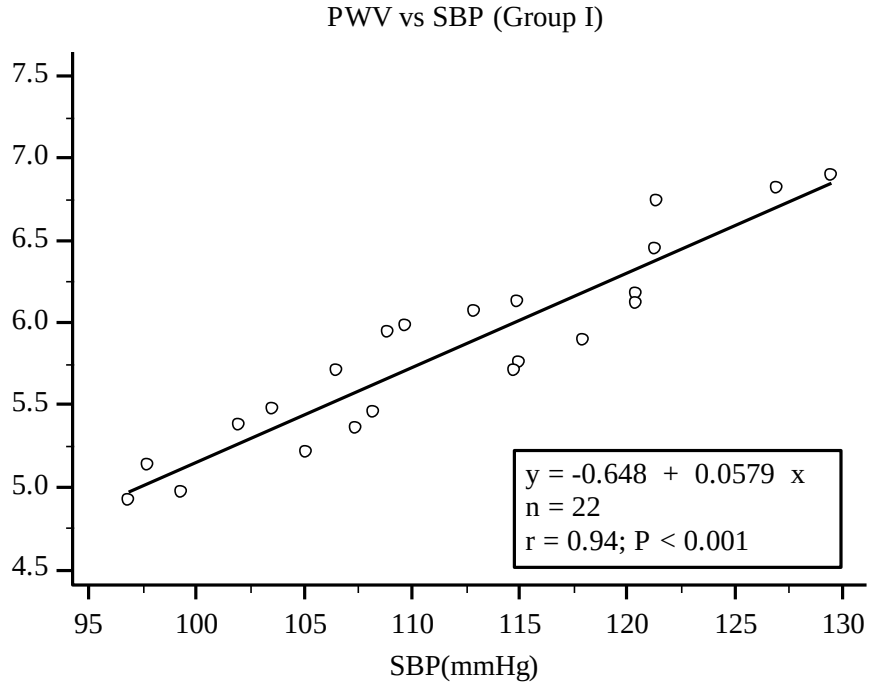

Figure 45 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Non-treated Diabetes with regression line.

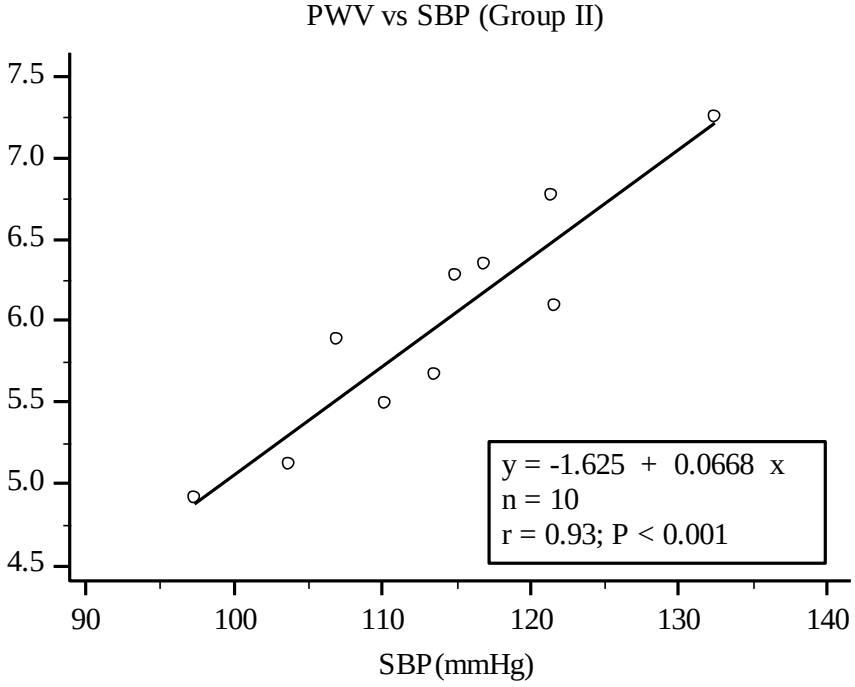

Figure 46- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Treated Diabetes with regression line.

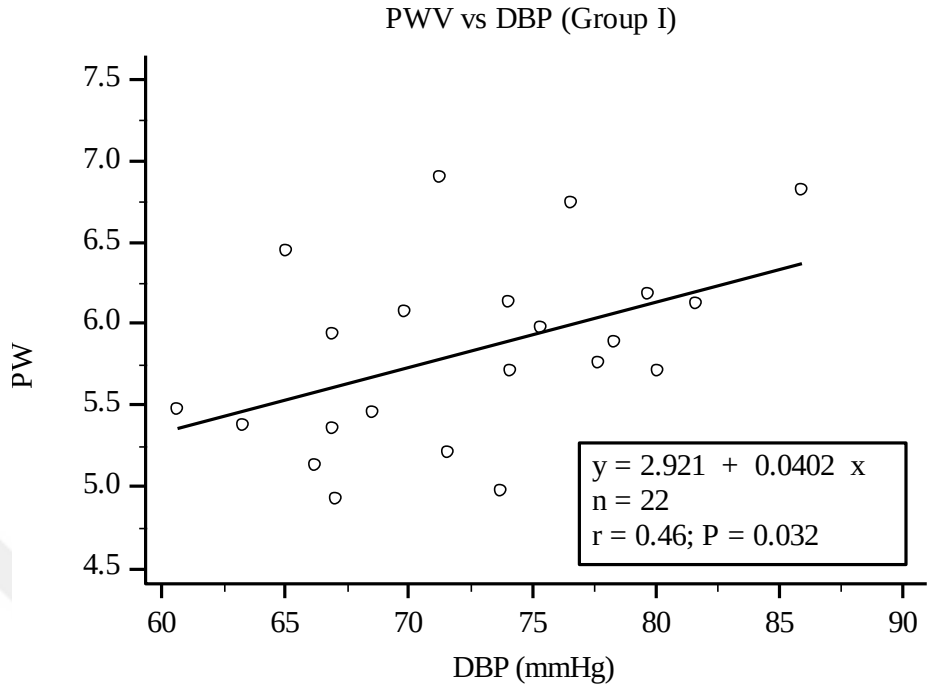

Figure 47- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Non-treated Diabetes with regression line.

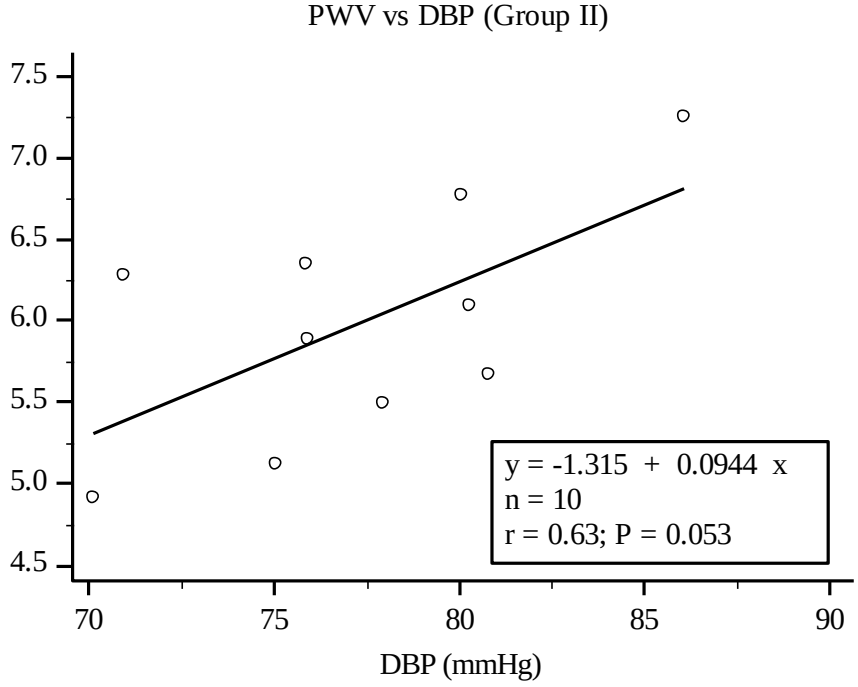

Figure 48- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Treated Diabetes with regression line.

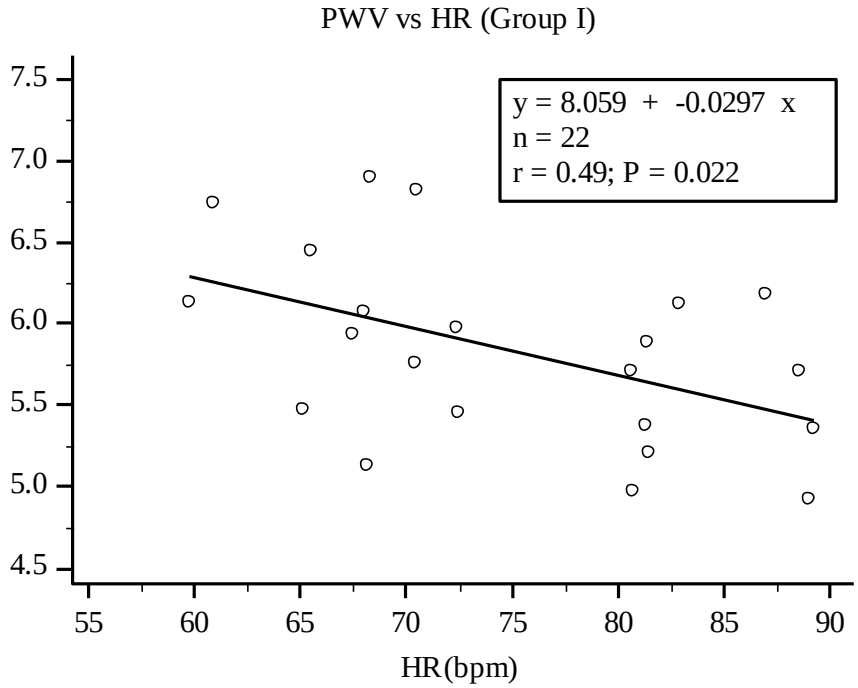

Figure 49- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Non-treated Diabetes with regression line.

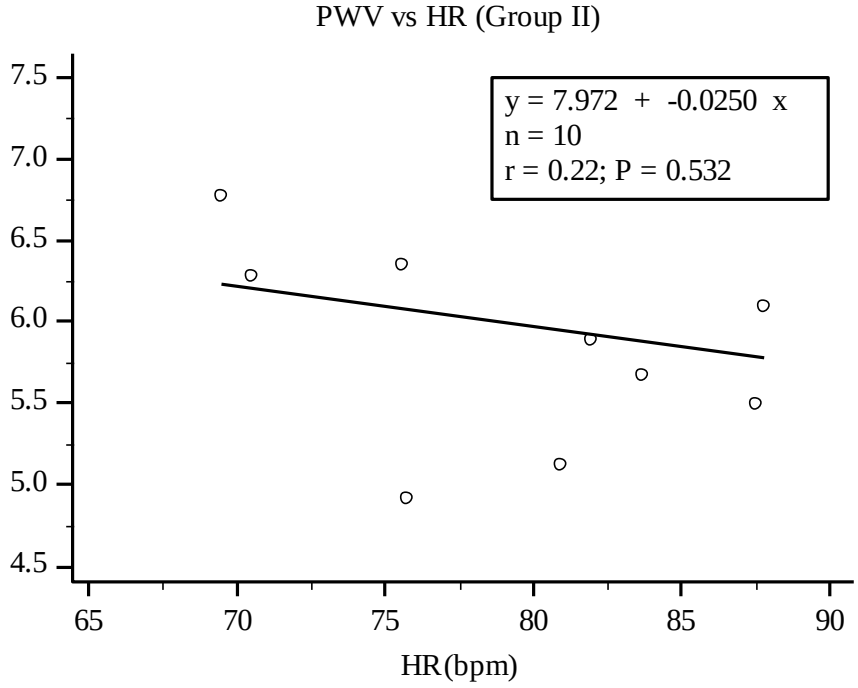

Figure 50- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Treated Diabetes with regression line.

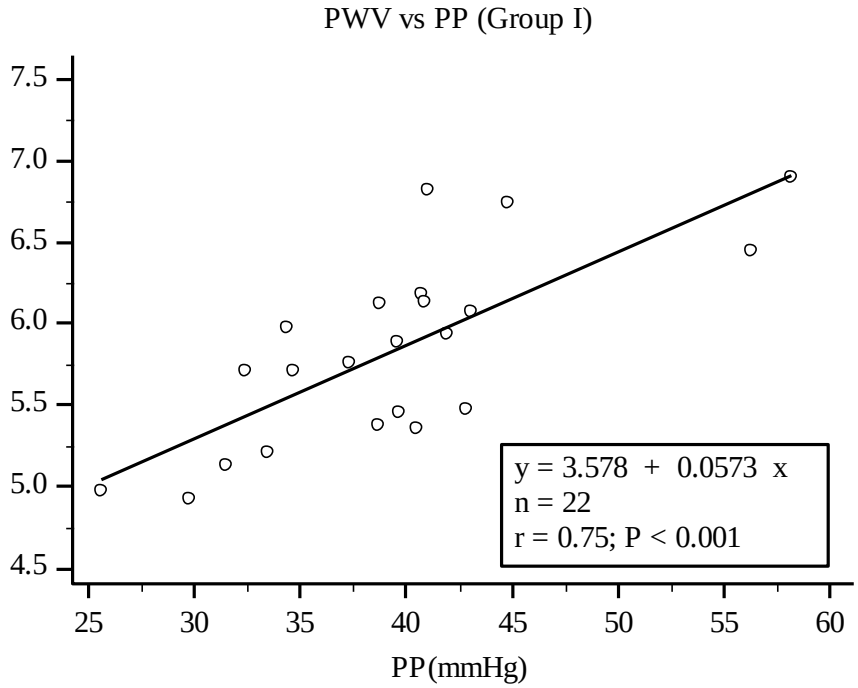

Figure 51- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Non-treated Diabetes with regression line.

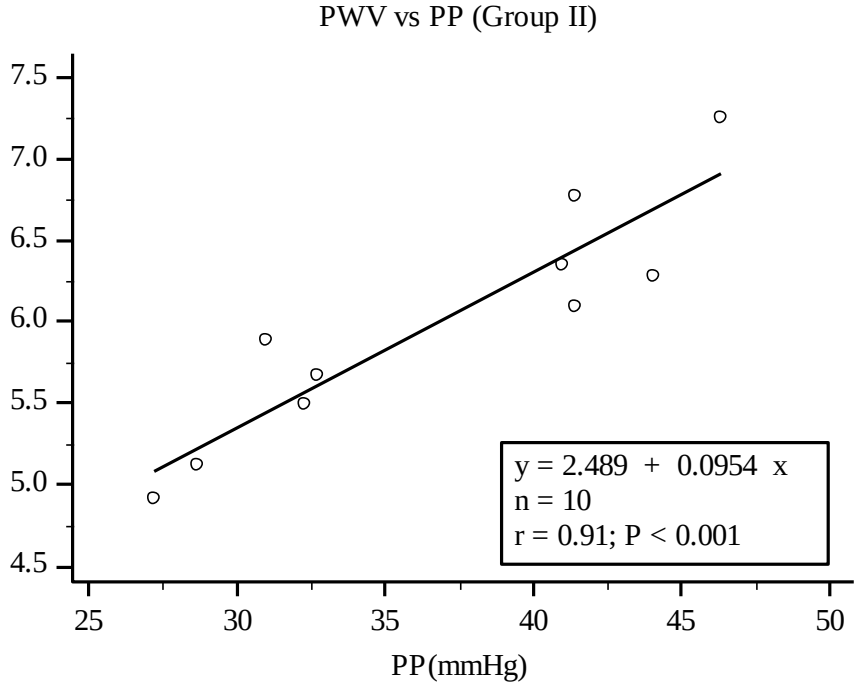

Figure 52- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Treated Diabetes with regression line.

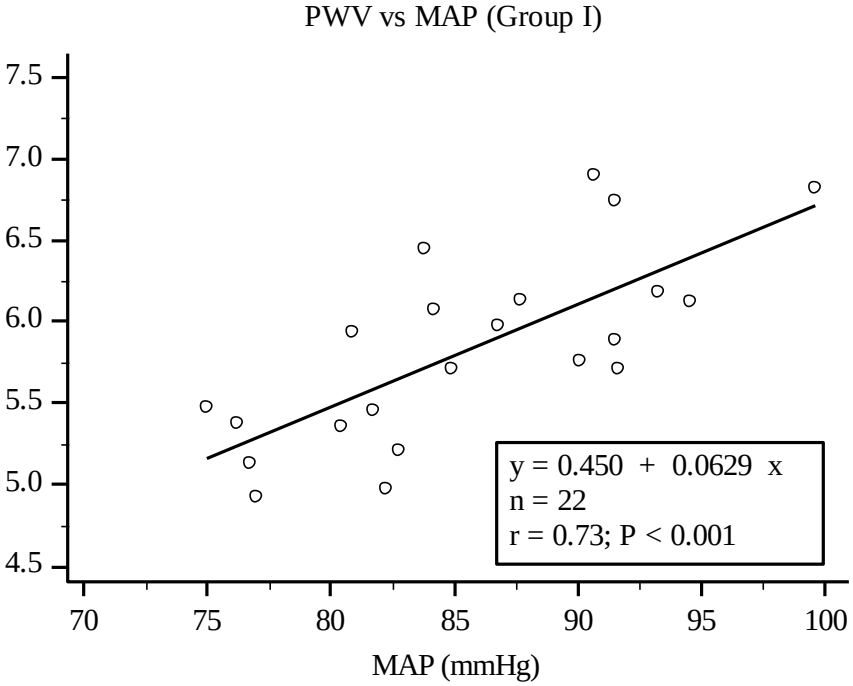

Figure 53- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Non-treated Diabetes with regression line.

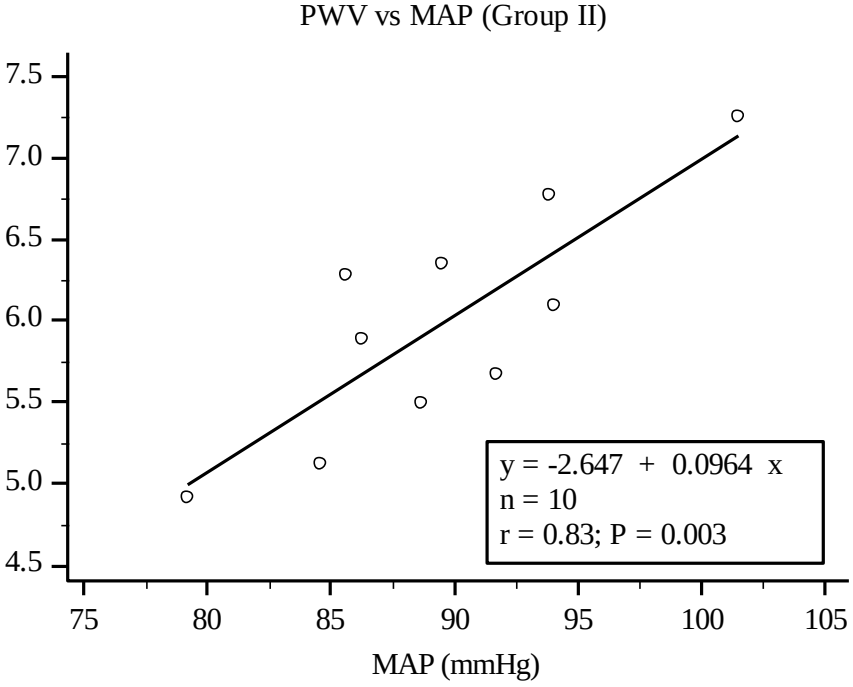

Figure 54- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Treated Diabetes with regression line.

4.3.4 Assessment of Pulse Wave Velocity Measurement Related with Tobacco Using

. Cigarette is a tobacco material and contains tar, nicotine, carbon monoxide. The heart pressures are influenced by the tobacco's content. When heart pressure concentrates, blood pressure can not be pulp to the arteries in a healthy way, causing tension sickness. In this section, the effects of smoking habits on blood pressure parameters and the relation with PWV are examined. All blood pressure measurements of these normotensive individuals were taken at certain intervals of the day, in both left and right arms. The average measurement results are shown in Table 17. In bivariate analysis (Table 18 for group 1 _ non-smoking volunteers and Table 19 for group 2_smoking volunteers), BMI, SBP, DBP, HR, PP and MAP were positively correlated with PWV. The relations of PWV to BMI, SBP, DBP, HR, PP and MAP were displayed in Figures 55 - 66, respectively. SBP, ($r=0.89$, $P<0.001$) for non-smoking volunteers and ($r=0.95$, $P<0.001$) for smoking volunteers remained significantly correlated with PWV according to our measurements. When the PWV and SBP correlations of smokers were examined, it was observed that smokers were higher value than non-smokers.

In the tobacco using group analysis, PP and MAP highly correlated with PWV, but the correlation of BMI, HR and DBP with PWV decreases. According to SBP analysis for both two groups, SBP highly correlated with PWV and SBP provides sufficient information in the PWV measurements. SBP plays a leading role in the diagnosis of CVDs and shows that PWV results can be used in daily clinical measurements because of its direct association with PWV and its also related with tobacco using.

Table 17 - Measurement Results Related with Tobacco Using

PARAMETER	GROUP 1	GROUP 2
N	14	18
BMI (kg/m^2)	24.24 ± 3.69	23.83 ± 2.99
SBP (mmHg)	113.47 ± 8.47	111.74 ± 9.75
DBP(mmHg)	74.4 ± 5.9	73.68 ± 6.57
Pulse(bpm)	75.1 ± 7.43	77.54 ± 9.27
Pulse Pressure (PP)	39.07 ± 6.82	38.06 ± 7.5
Mean Arterial Pressure (MAP)	87.42 ± 6.07	86.37 ± 6.92
Pulse Transit Time PTT(ms)	47.91 ± 4.59	49.12 ± 4.55
Brachial to radial distance-D (m)	0.28 ± 0.02	0.28 ± 0.02
Pulse Wave Velocity (PWV) (m/s)	5.97 ± 0.54	5.81 ± 0.65

*Data are mean ± S.D.

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity

Table 18 - Correlation coefficient between pulse wave velocity and blood pressure parameters for Non-smoking volunteers

Parameter	r	P
BMI (kg/m²)	0.44	0.113
SBP (mmHg)	0.89	<0.001
DBP(mmHg)	0.42	0.133
HR (bpm)	0.31	0.276
PP (mmHg)	0.75	0.002
MAP (mmHg)	0.69	0.006

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

Table 19 - Correlation coefficient between pulse wave velocity and blood pressure parameters for Smoking volunteers

Parameter	r	P
BMI (kg/m²)	0.74	<0.001
SBP (mmHg)	0.95	<0.001
DBP(mmHg)	0.54	0.021
HR (bpm)	0.36	0.140
PP (mmHg)	0.77	<0.001
MAP (mmHg)	0.79	<0.001

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

When assessed according to tobacco using graphs, it was found that the PP and MAP values were used in PWV assessments in addition to the SBP value. However, when examining the other sections, it may not be possible to obtain clear results in daily clinical practice because it does not provide sufficient information in some areas. We can not say that PP and MAP should be used in PWV assessments considering the studies done in the thesis. In the light of the information given, the effects of smoking habit on PWV were examined and the results were indicated with related tables and graphs.

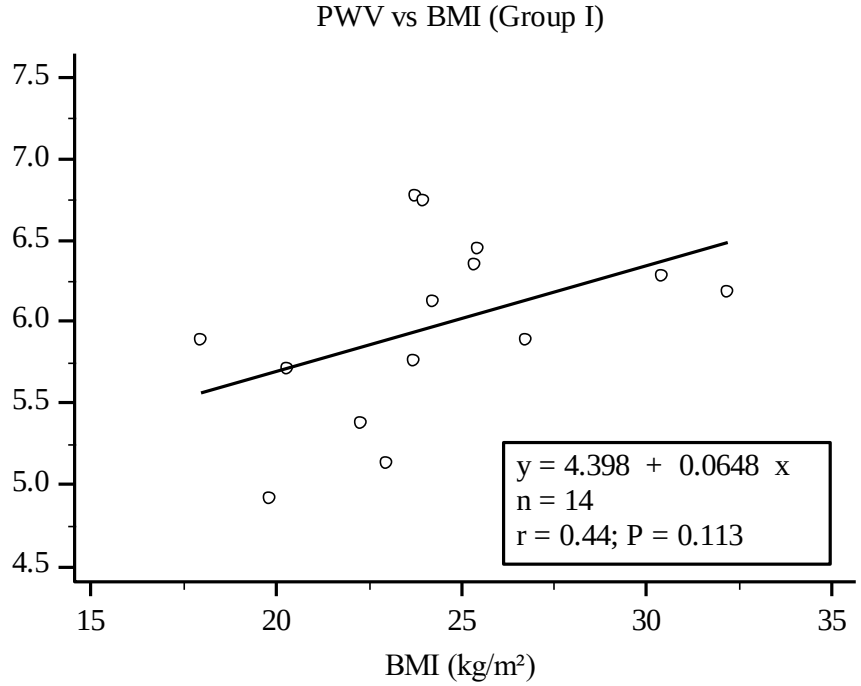

Figure 55 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Non-smoking volunteers with regression line.

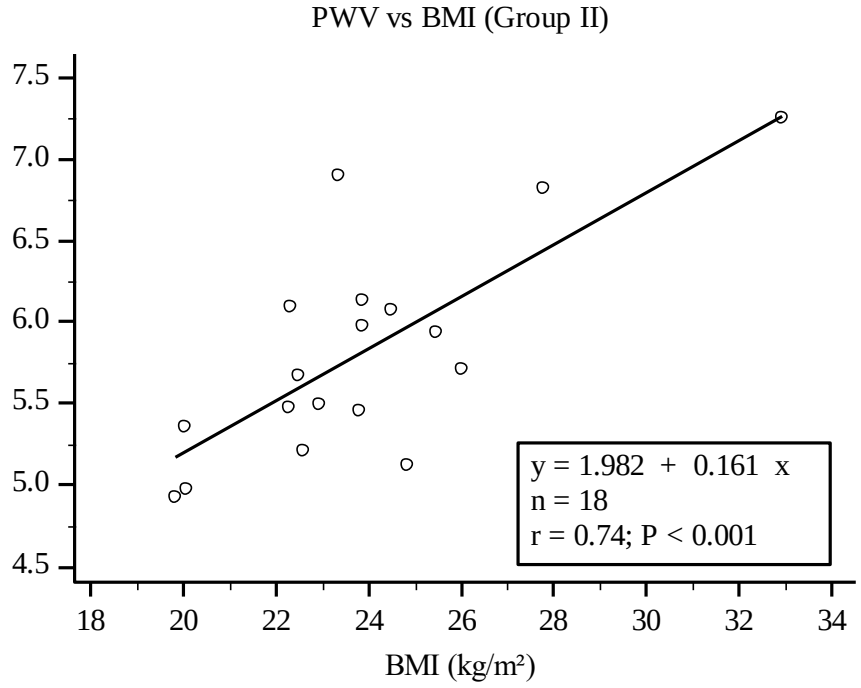

Figure 56 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Smoking volunteers with regression line

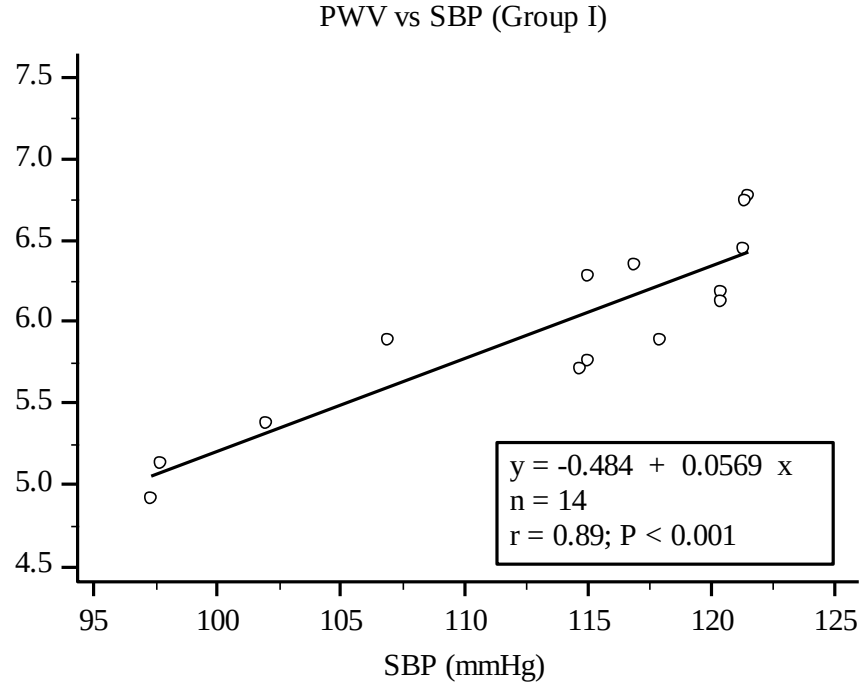

Figure 57 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Non-smoking volunteers with regression line.

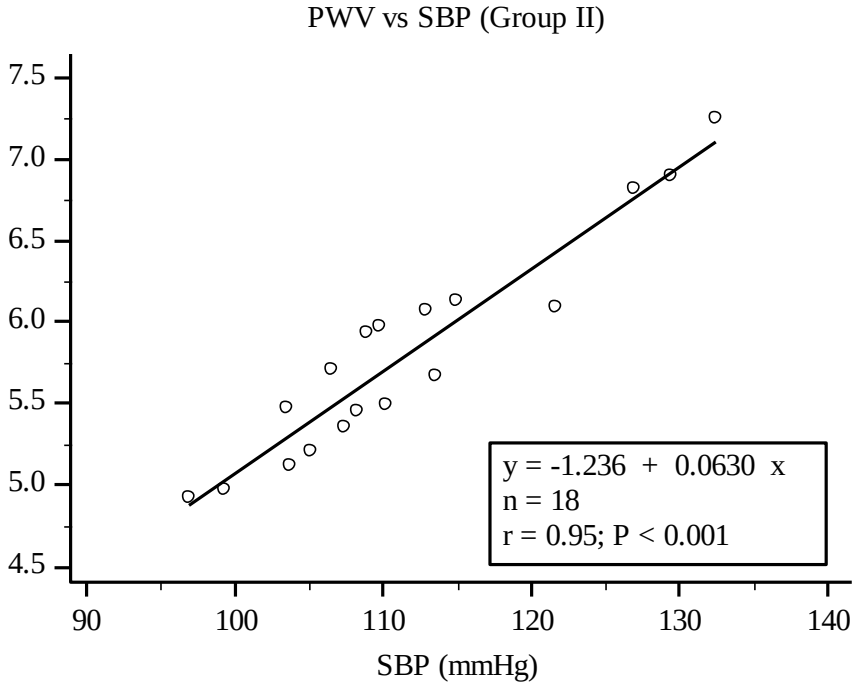

Figure 58 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Smoking volunteers with regression line.

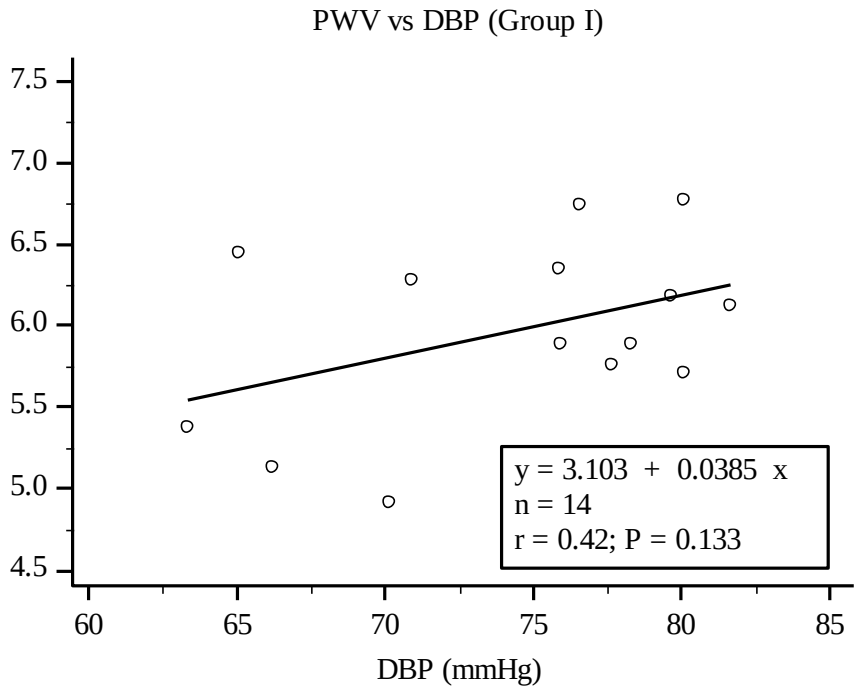

Figure 59 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Non-smoking volunteers with regression line.

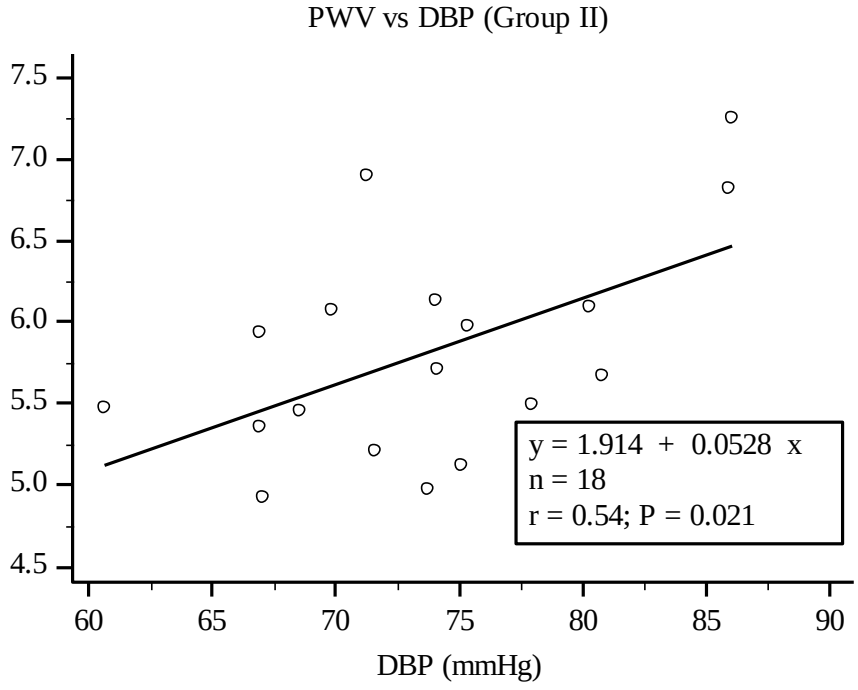

Figure 60 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Smoking volunteers with regression line.

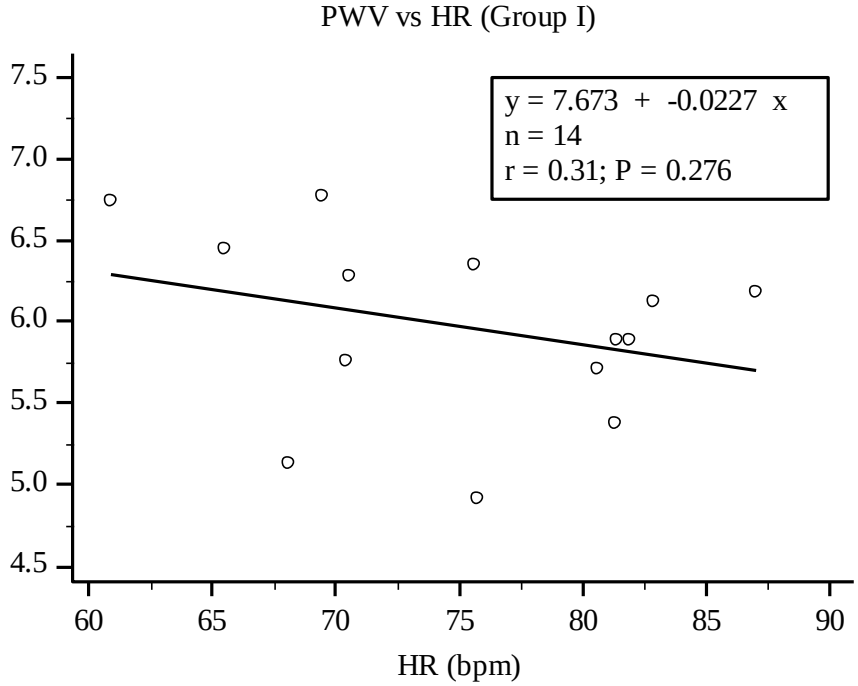

Figure 61 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Non-smoking volunteers with regression line.

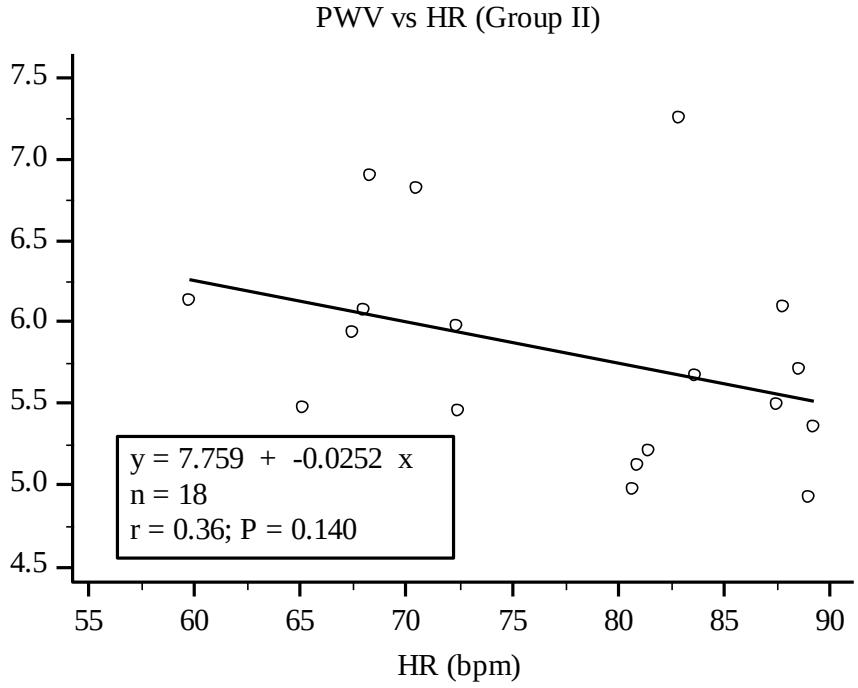

Figure 62 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Smoking volunteers with regression line.

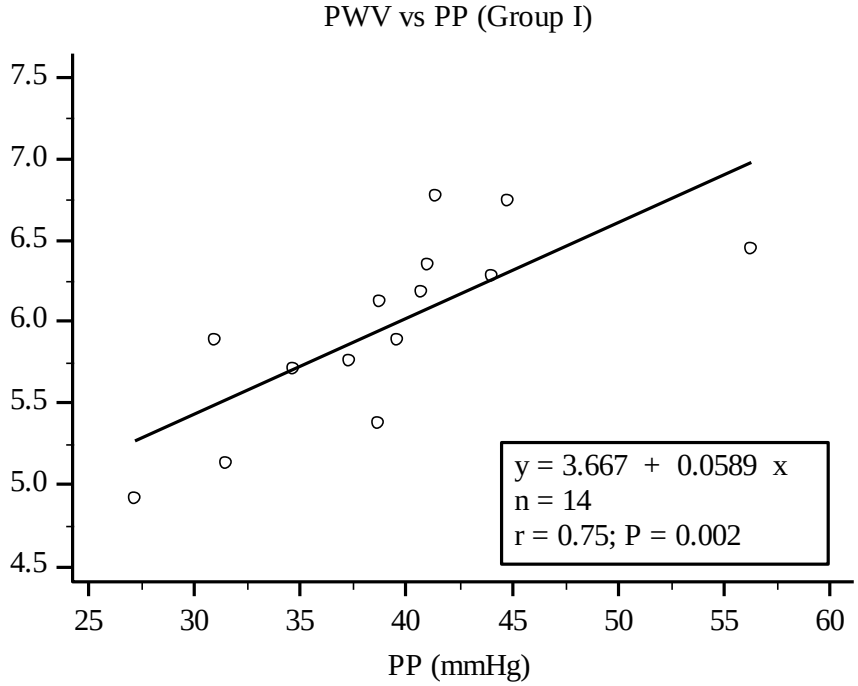

Figure 63 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Non-smoking volunteers with regression line.

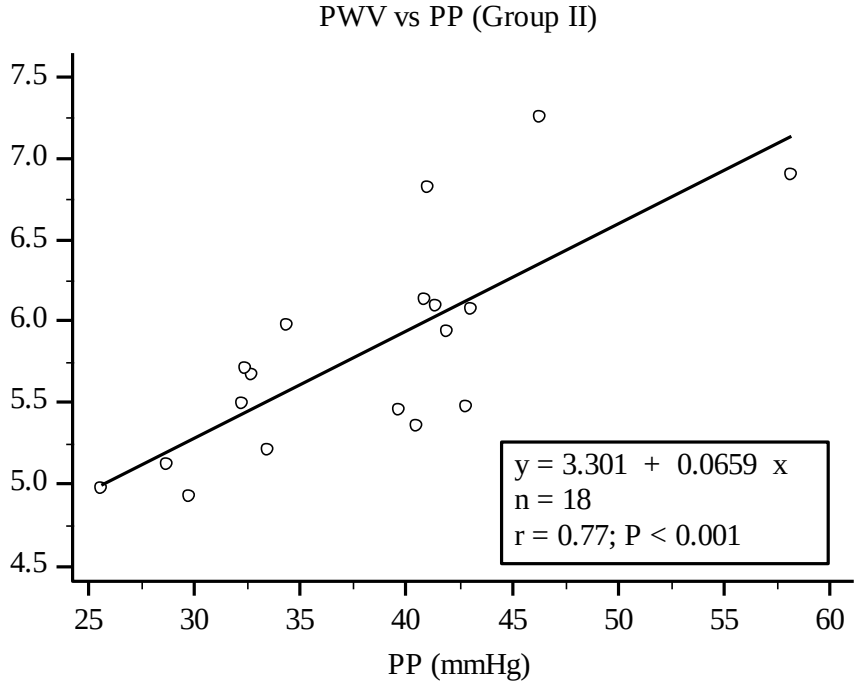

Figure 64 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Smoking volunteers with regression line.

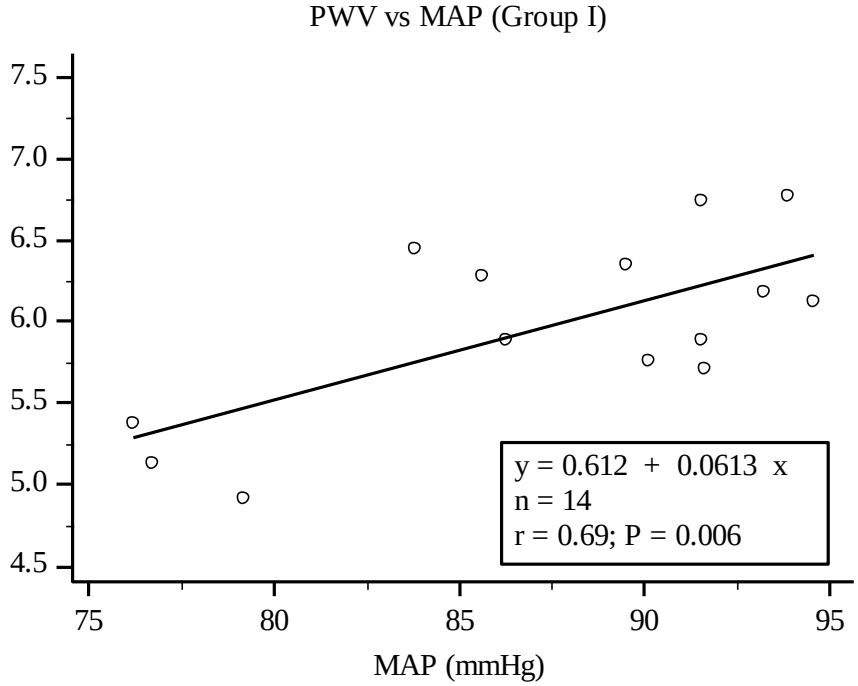

Figure 65 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Non-smoking volunteers with regression line.

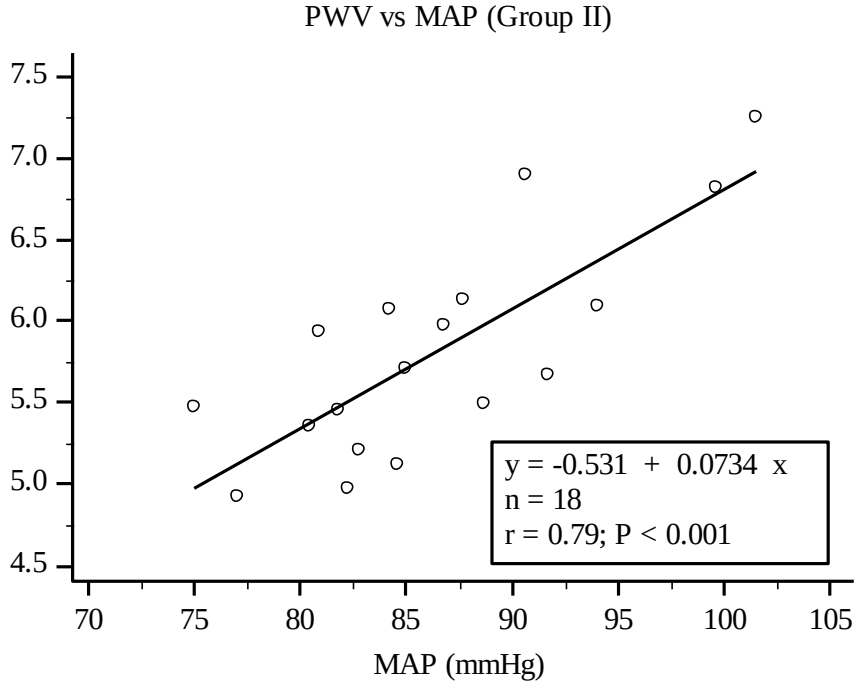

Figure 66 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Smoking volunteers with regression line.

4.3.5 Assessment of Pulse Wave Velocity Measurement Related with Physical Activity

In recent years, many studies have been carried out on the level of physical activity and health effects in our daily lives and people are trying to gain consciousness. The World Health Organization and the World Heart Foundation anticipate that 8,000 steps per day will protect our health and prevent CVDs [1]. In this part of our study, volunteers were asked daily physical activity levels and three different groups were formed as low, medium and high levels according to the answers given. All blood pressure measurements of these normotensive individuals were taken at certain intervals of the day, in both left and right arms. The average measurement results are shown in Table 20. In bivariate analysis, BMI, SBP, DBP, HR, PP and MAP were positively correlated with PWV. The relations of PWV to BMI, SBP, DBP, HR, PP and MAP were displayed in Figures 67–84, respectively.

In the physical activity related group analysis, PP and MAP highly correlated with PWV, but the correlation of BMI, HR with PWV decreases. According to SBP analysis for both two groups, SBP highly correlated with PWV and SBP provides sufficient information in the PWV measurements. When assessed according to related graphs, it was found that the PP and MAP values were used in PWV assessments in addition to the SBP value. However, when examining the other sections, it may not be possible to obtain clear results in daily clinical practice because it does not provide sufficient information in some areas. We can not say that PP and MAP should be used in PWV assessments considering the studies done in the thesis.

Table 20 - Measurement Results Related with Physical Activity

PARAMETER	GROUP 1	GROUP 2	GROUP 3
N	13	14	5
BMI (kg/m^2)	23.9 ± 3.47	23.42 ± 2.97	24.32 ± 1.58
SBP (mmHg)	112.25 ± 8.83	111.27 ± 9.28	114.95 ± 9.83
DBP(mmHg)	74.63 ± 6.95	74.23 ± 5.56	70.65 ± 5.7
Pulse(bpm)	78.07 ± 7.77	75.42 ± 9.3	73.5 ± 6.82
Pulse Pressure (PP)	37.62 ± 5.57	37.04 ± 5.94	44.29 ± 10.9
Mean Arterial Pressure (MAP)	87.17 ± 7.16	86.57 ± 6.44	85.42 ± 5.24
Pulse Transit Time PTT(ms)	48.23 ± 5.02	48.78 ± 4.53	49.67 ± 3.7
Brachial to radial distance-D (m)	0.28 ± 0.02	0.28 ± 0.02	0.3 ± 0.03
Pulse Wave Velocity (PWV) (m/s)	5.86 ± 0.58	5.81 ± 0.65	6.08 ± 0.53

*Data are mean ± S.D.

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity

Table 21 - Correlation coefficient between pulse wave velocity and blood pressure parameters for Low Level Physical Activity

Parameter	r	P
BMI (kg/m²)	0.69	0.009
SBP (mmHg)	0.92	<0.001
DBP(mmHg)	0.56	0.044
HR (bpm)	0.11	0.732
PP (mmHg)	0.78	0.002
MAP (mmHg)	0.74	0.004

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

Table 22 - Correlation coefficient between pulse wave velocity and blood pressure parameters for Middle Level Physical Activity

Parameter	r	P
BMI (kg/m²)	0.62	0.018
SBP (mmHg)	0.94	<0.001
DBP(mmHg)	0.71	0.005
HR (bpm)	0.46	0.102
PP (mmHg)	0.81	<0.001
MAP (mmHg)	0.86	<0.001

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

Table 23 - Correlation coefficient between pulse wave velocity and blood pressure parameters for High Level Physical Activity

Parameter	r	P
BMI (kg/m²)	0.18	0.770
SBP (mmHg)	0.94	0.017
DBP(mmHg)	0.02	0.973
HR (bpm)	0.73	0.164
PP (mmHg)	0.84	0.075
MAP (mmHg)	0.60	0.281

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

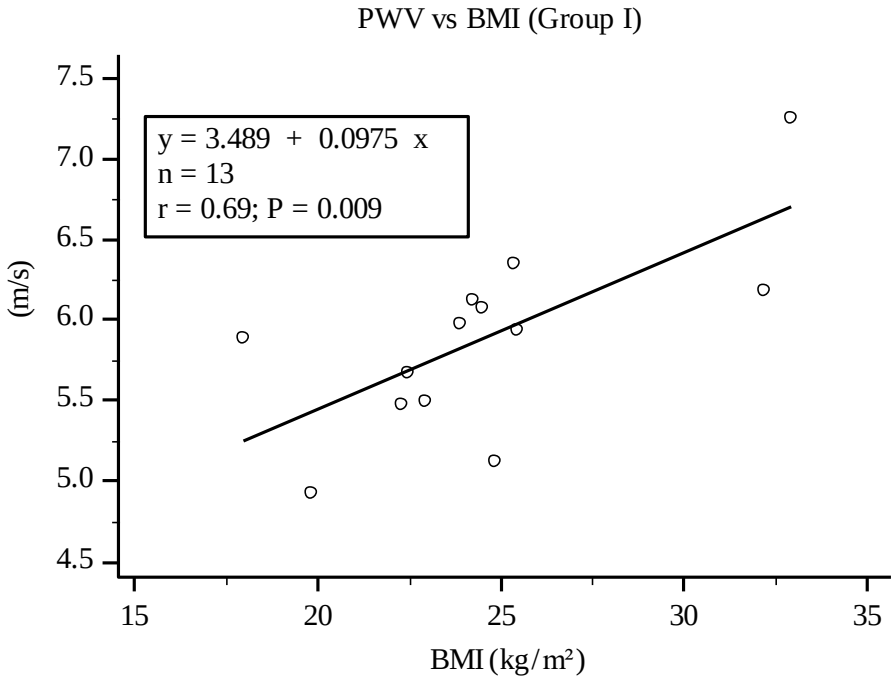

Figure 67 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Low Level Physical Activity with regression line.

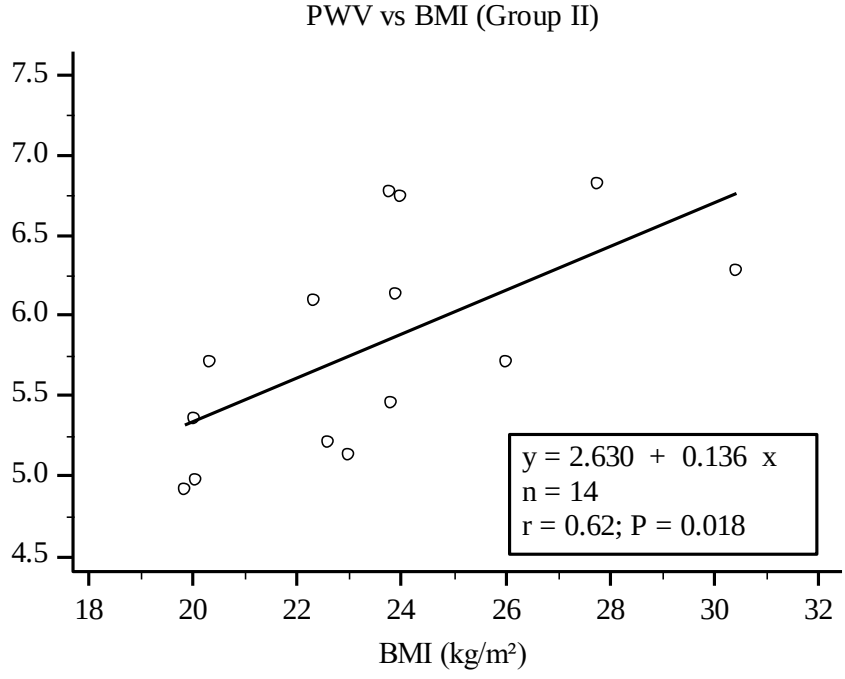

Figure 68- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for Middle Level Physical Activity with regression line.

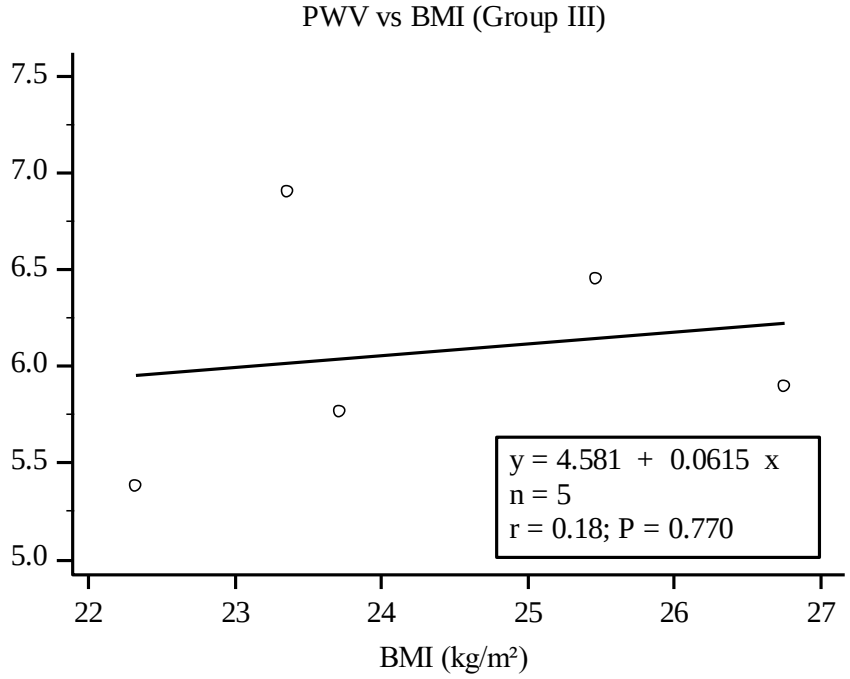

Figure 69- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI for High Level Physical Activity with regression line.

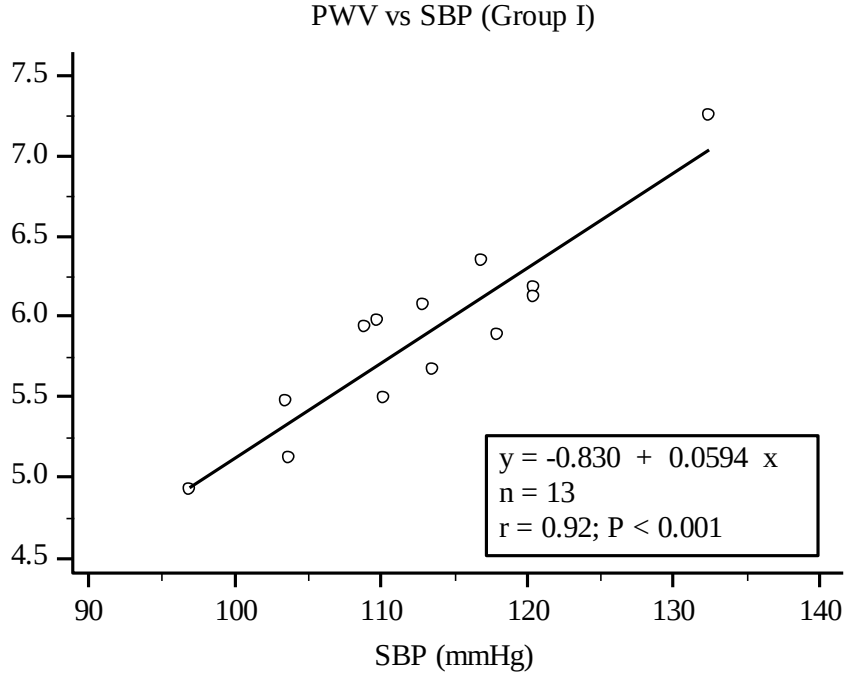

Figure 70- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Low Level Physical Activity with regression line.

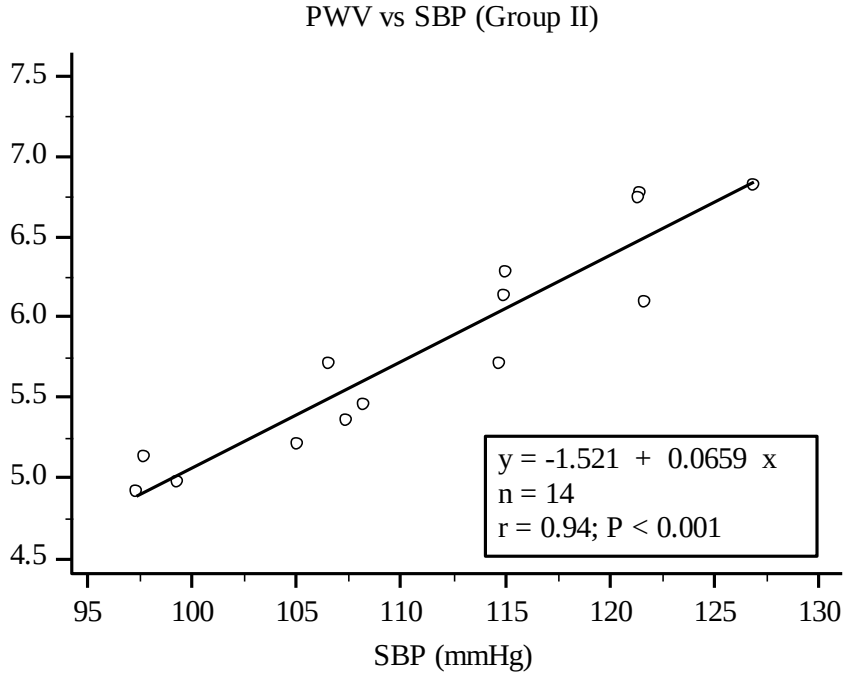

Figure 71- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for Middle Level Physical Activity with regression line.

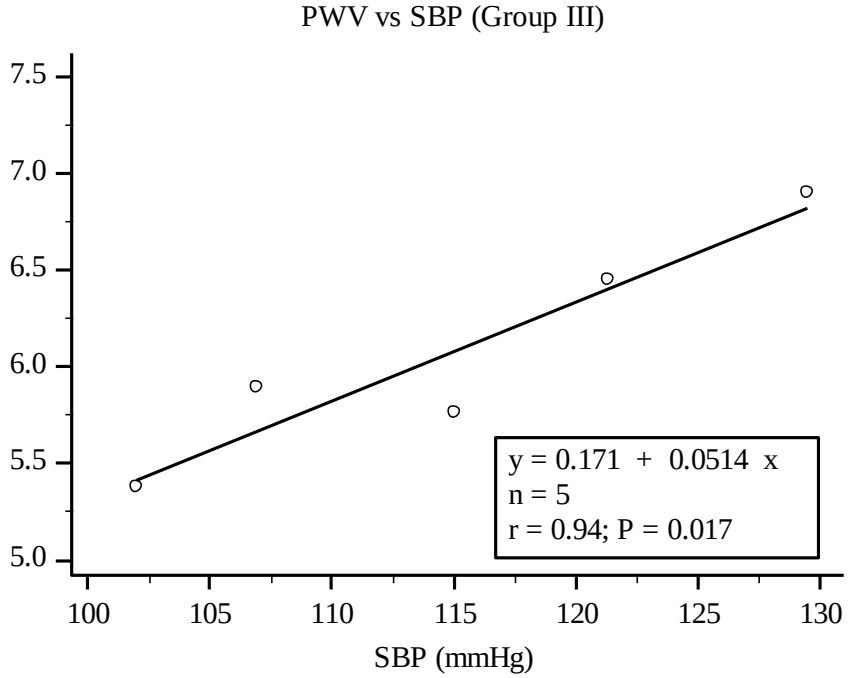

Figure 72- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP for High Level Physical Activity with regression line.

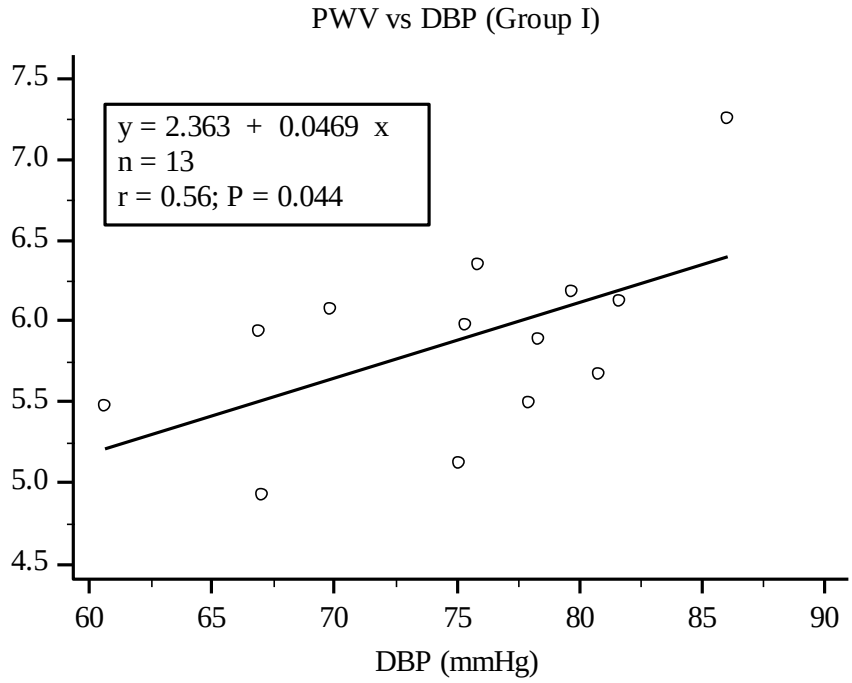

Figure 73- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Low Level Physical Activity with regression line.

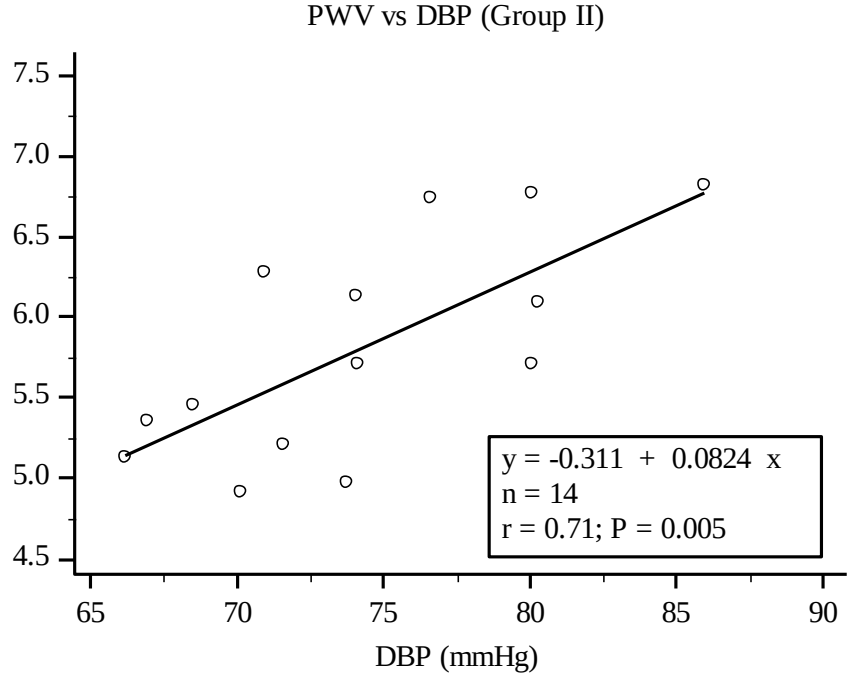

Figure 74- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for Middle Level Physical Activity with regression line.

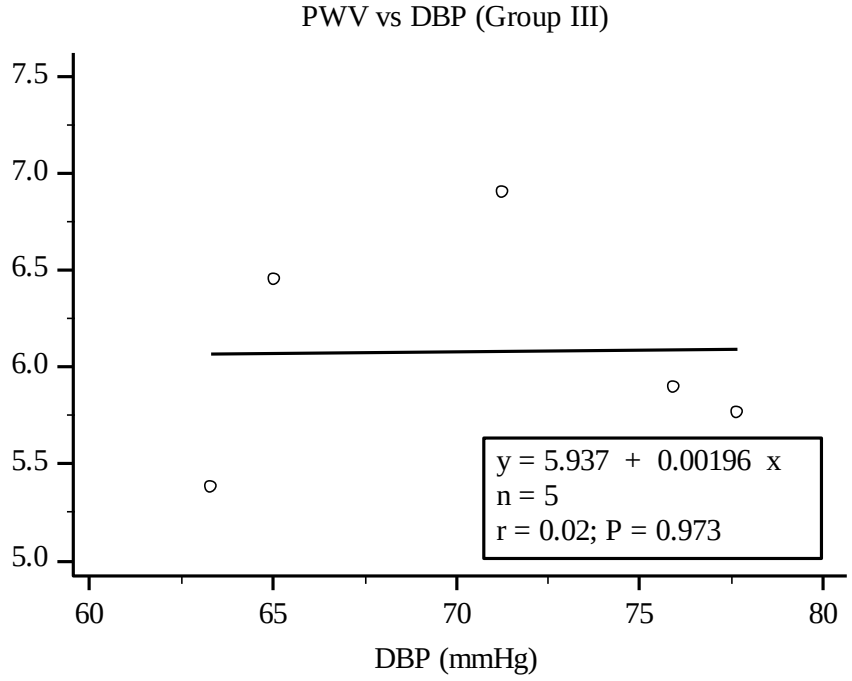

Figure 75- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP for High Level Physical Activity with regression line.

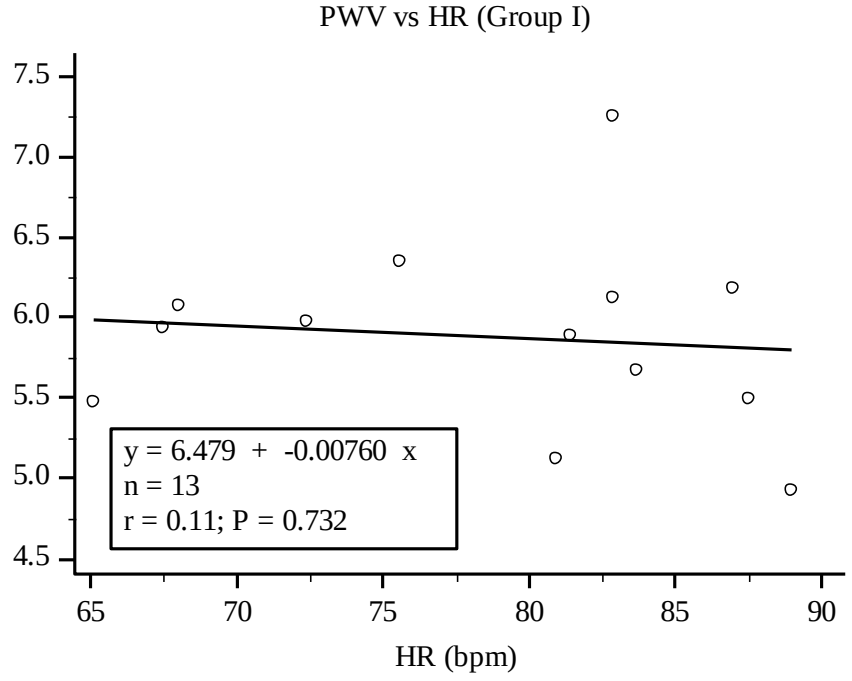

Figure 76- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Low Level Physical Activity with regression line.

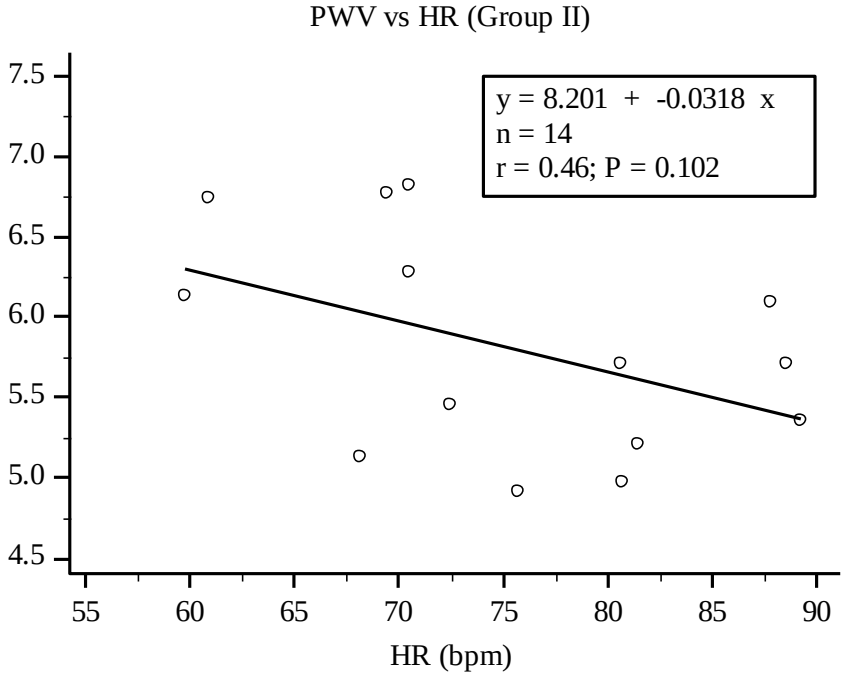

Figure 77- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for Middle Level Physical Activity with regression line.

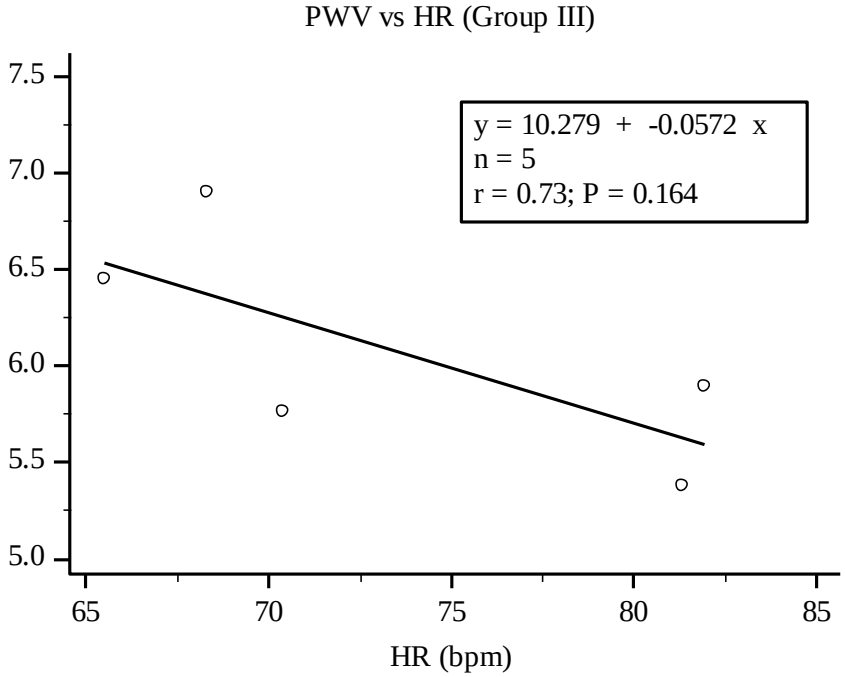

Figure 78- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR for High Level Physical Activity with regression line.

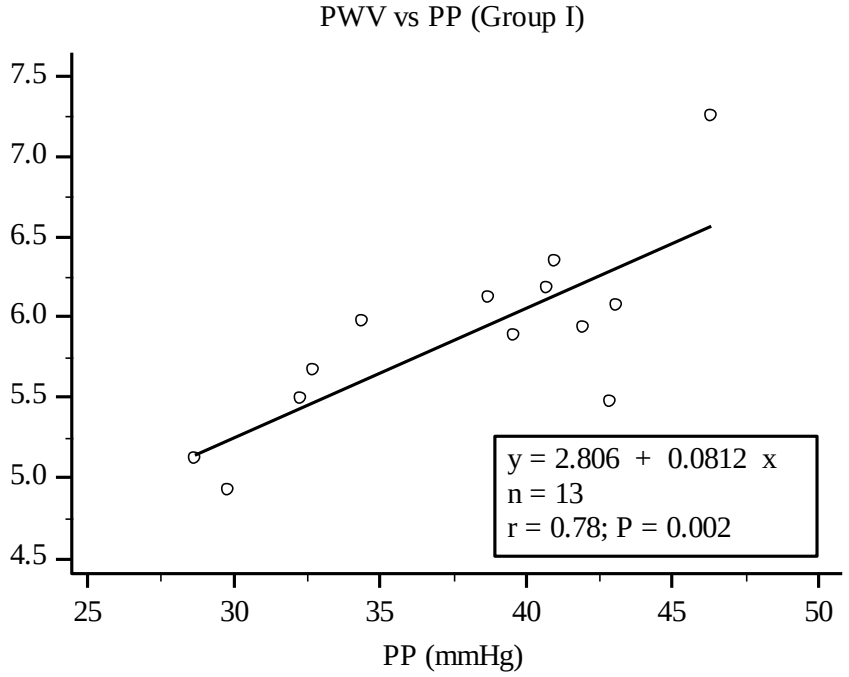

Figure 79- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Low Level Physical Activity with regression line.

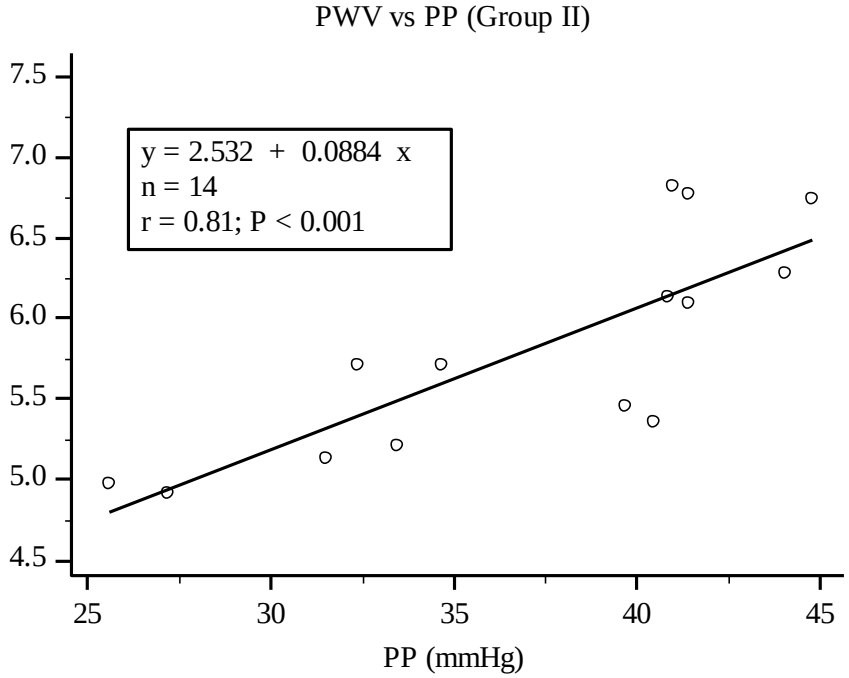

Figure 80- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for Middle Level Physical Activity with regression line.

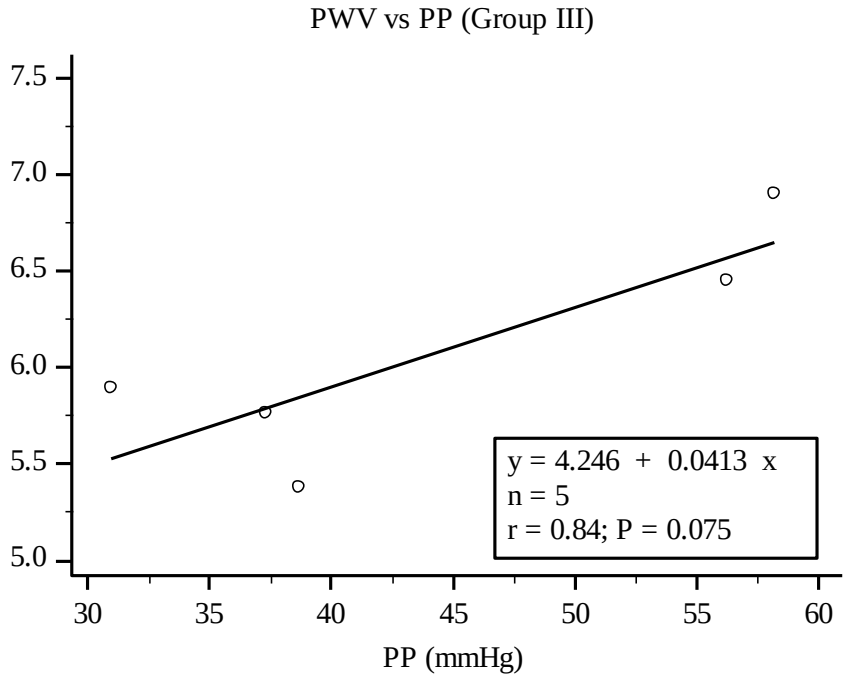

Figure 81- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP for High Level Physical Activity with regression line.

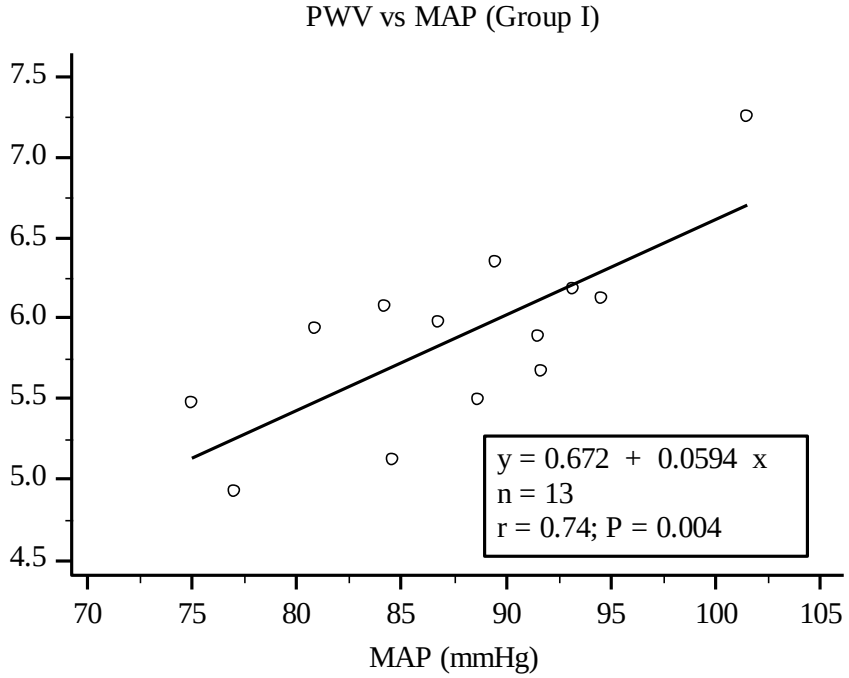

Figure 82- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Low Level Physical Activity with regression line.

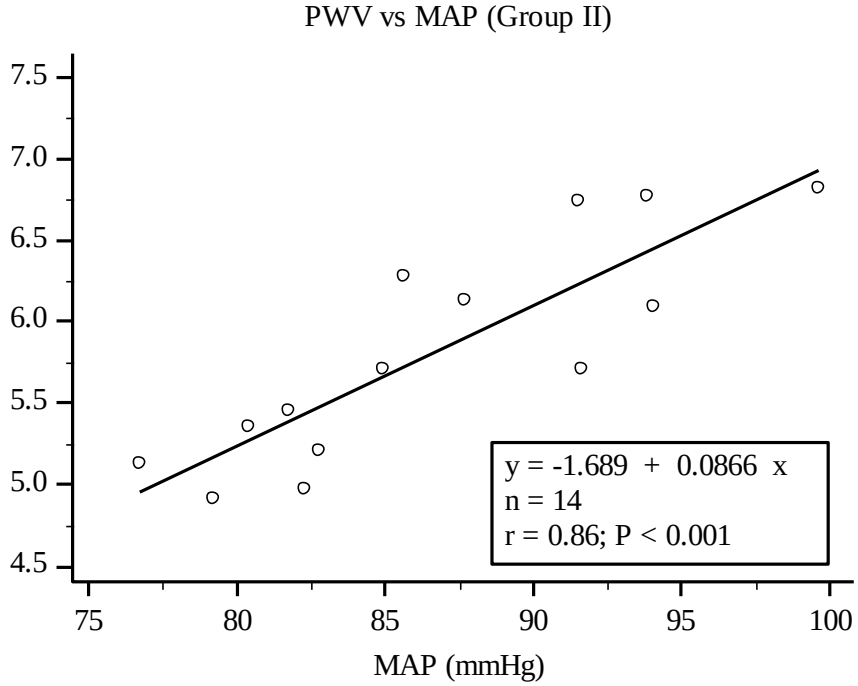

Figure 83- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for Middle Level Physical Activity with regression line.

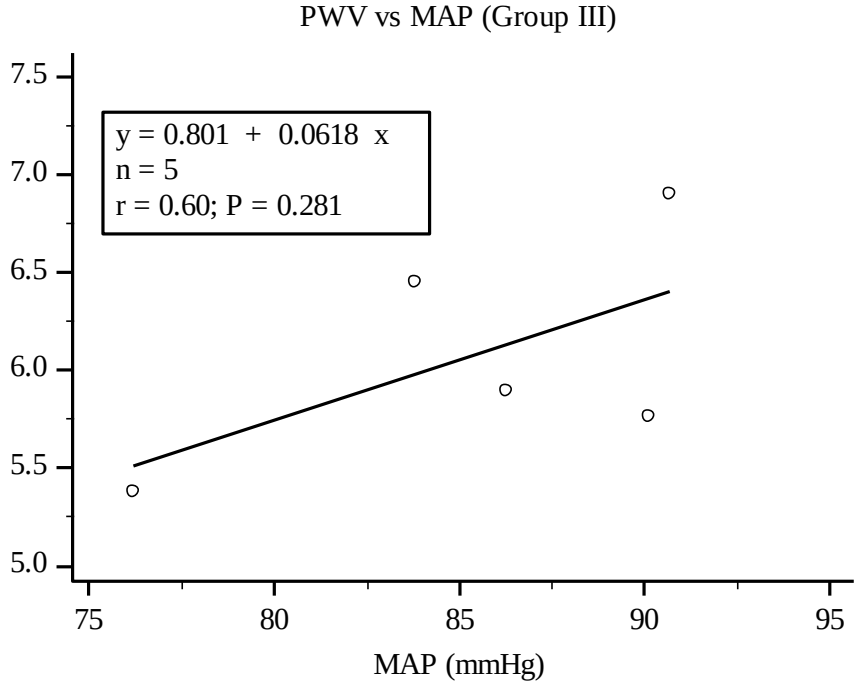

Figure 84- Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP for High Level Physical Activity with regression line.

CHAPTER V

RESULTS & DISCUSSIONS

5.1 Results

The main characteristics of the study group classified by gender are shown in Table 4. All blood pressure measurements of these normotensive individuals were taken at certain intervals of the day, in both left and right arms. The average measurement results are shown in Table 24. In bivariate analysis (Table 25), BMI, SBP, DBP, PP and MAP were positively correlated with PWV. Besides, HR was negatively correlated with PWV. The relations of PWV to BMI, SBP, DBP, HR, PP and MAP were displayed in from Figure 85 to Figure 90**,** respectively. SBP ($r=0.93$, $P<0.001$) remained significantly correlated with PWV according to our measurements.

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

Table 24 – Average Measurement Results of the Volunteers

Parameter	Group 1	Group 2	Total
N	15	17	32
Gender (M/F)	F	M	-
Height (m)	1.65 ± 0.05	1.79 ± 0.08	1.72 ± 0.1
Body Mass (kg)	61.07 ± 10.34	81.47 ± 10.76	71.91 ± 14.67
BMI (kg/m²)	22.48 ± 3.24	25.36 ± 2.76	24.01 ± 3.32
SBP (mmHg)	110.12 ± 8.15	114.59 ± 9.65	112.5 ± 9.25
DBP(mmHg)	75.3 ± 5.07	72.84 ± 7	73.99 ± 6.29
Heart Rate (HR) (bpm)	82.06 ± 5.57	71.55 ± 7.76	76.48 ± 8.6
Pulse Pressure (PP)	34.82 ± 5.14	41.75 ± 7.25	38.5 ± 7.23
Mean Arterial Pressure (MAP)	86.91 ± 5.78	86.76 ± 7.22	86.83 ± 6.58
Pulse Transit Time PTT (ms)	48.13 ± 3.9	49 ± 5.11	48.59 ± 4.61
Brachial to radial distance-D (m)	0.26 ± 0.01	0.3 ± 0.02	0.28 ± 0.02
Pulse Wave Velocity (PWV) (m/s)	5.52 ± 0.43	6.19 ± 0.57	5.88 ± 0.61

*Data are mean ± S.D.

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity

Table 25 - Correlation coefficient between pulse wave velocity and blood pressure parameters for total volunteers.

Parameter	r	P
BMI (kg/m²)	0.60	<0.001
SBP (mmHg)	0.93	<0.001
DBP (mmHg)	0.50	0.004
HR (bpm)	-0.36	0.045
PP	0.76	<0.001
MAP	0.75	<0.001

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, Heart rate; PP, pulse pressure; MAP, mean arterial pressure; PTT, pulse transit time; D, distance between brachial to radial; PWV, pulse wave velocity.

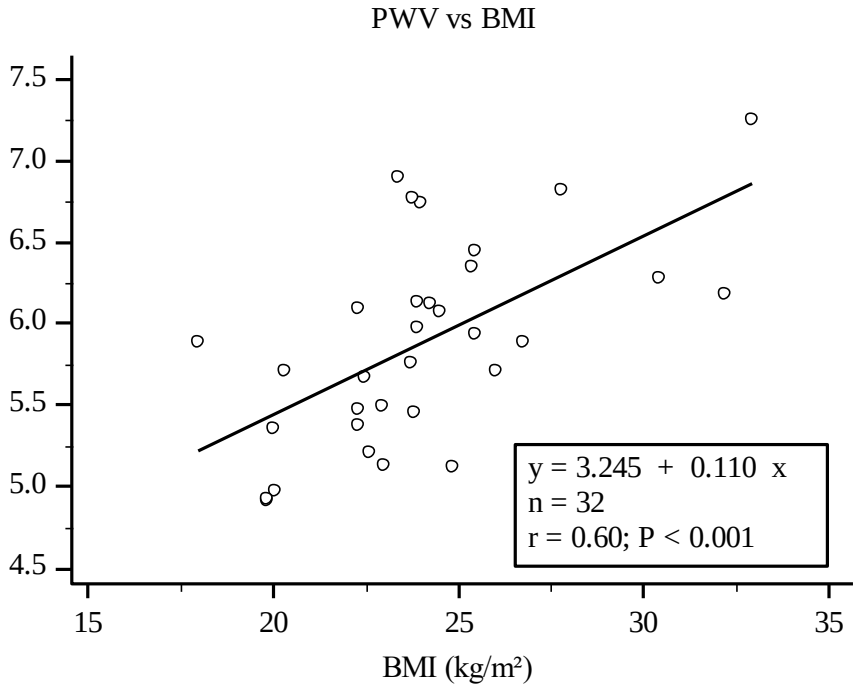

Figure 85 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs BMI with regression line (r=0.60, P<0.001).

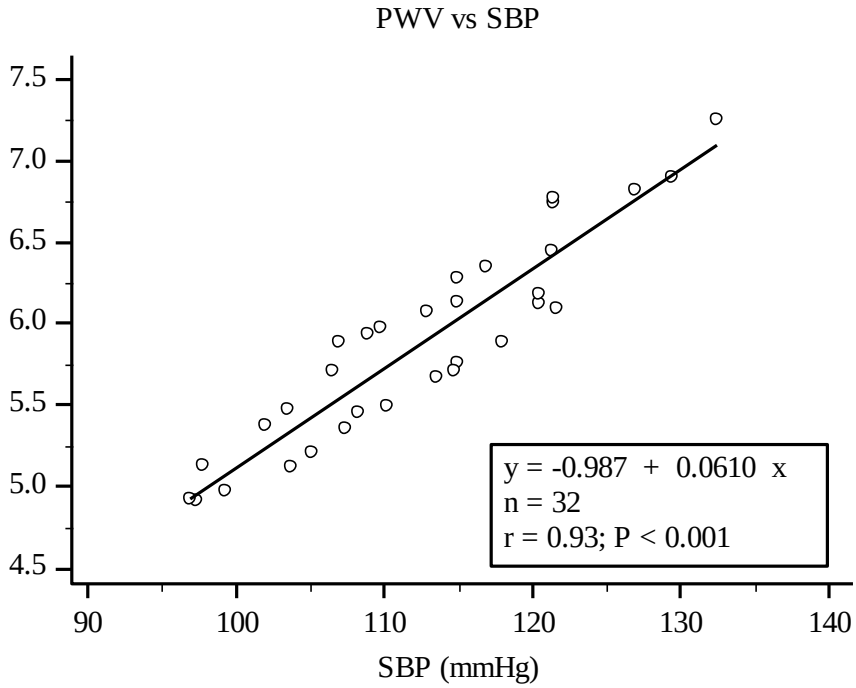

Figure 86 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs SBP with regression line (r=0.93, P<0.001).

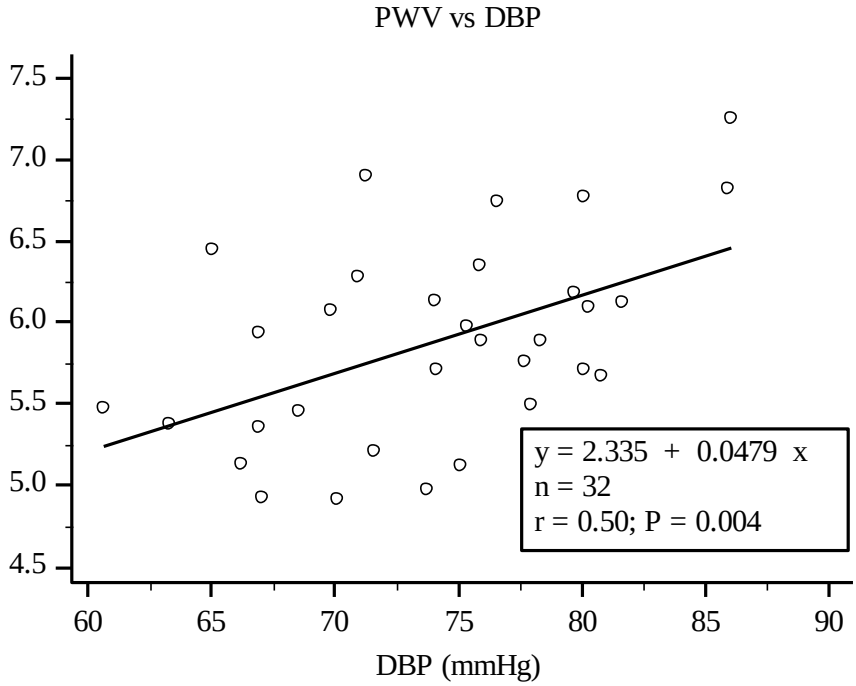

Figure 87 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs DBP with regression line (r=0.50, P=0.004).

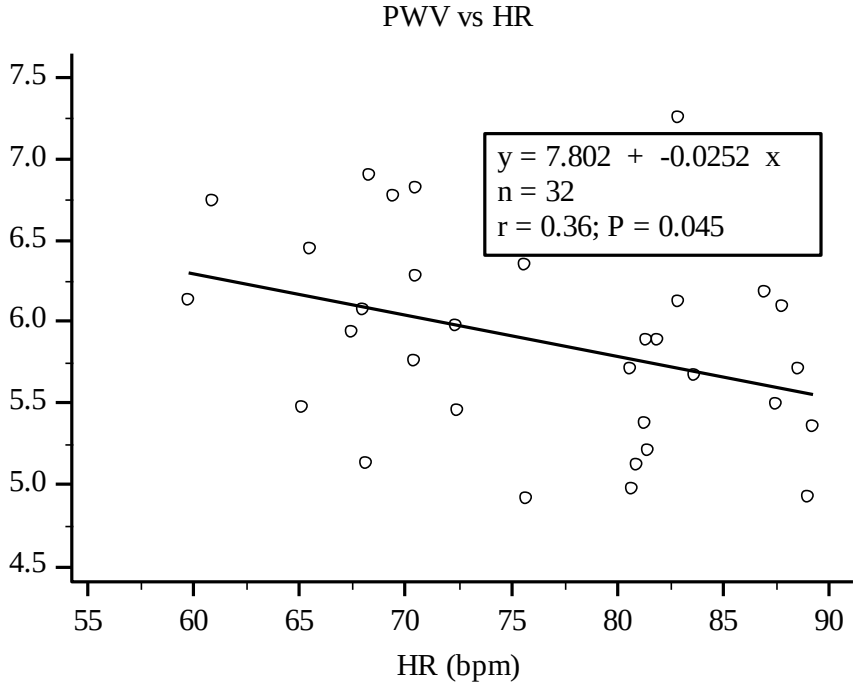

Figure 88 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs HR with regression line (r=0.36, P=0.045).

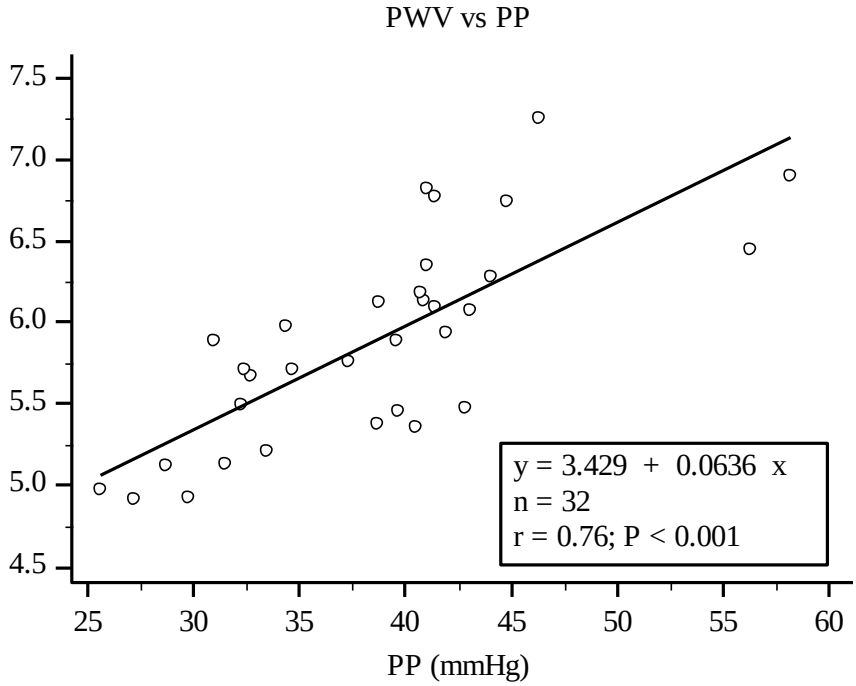

Figure 89 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs PP with regression line (r=0.76, P<0.001).

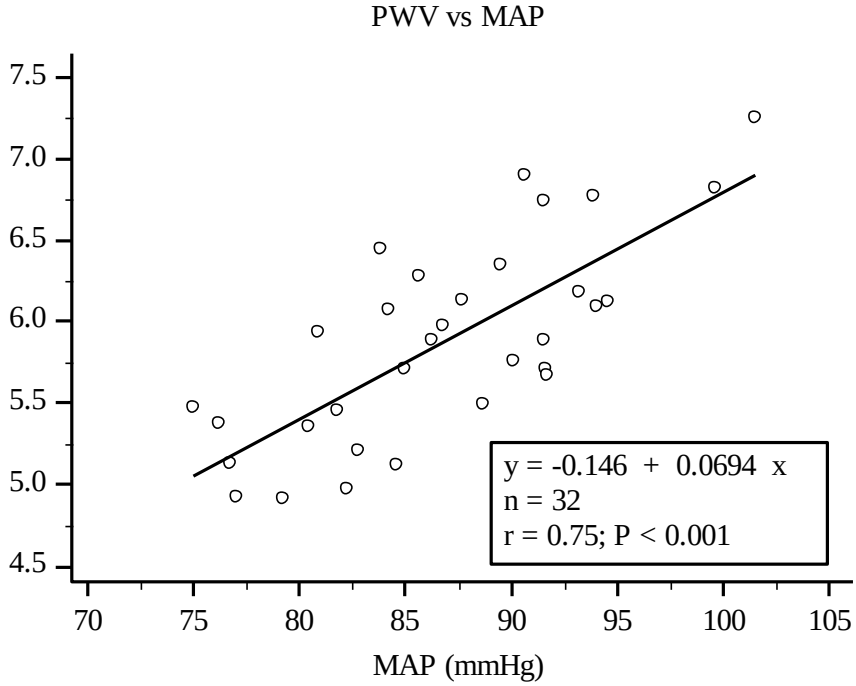

Figure 90 - Scatter plot of PWV calculated by dividing brachial radial distance by brachial radial pulse transit time vs MAP with regression line (r=0.75, P<0.001).

In the analysis, PP (r=0.76, P<0.001), MAP (r=0.75, P<0.001) and BMI (r=0.60, P<0.001) highly correlated with PWV, but the correlation of HR (r=0.36, P=0.045) and DBP (r=0.50, P=0.004) with PWV decreases. In our study, it is suggested that the SBP had more effect on PWV than the other clinical parameters.

We will analyze the relationship between the average PWV values and separation into family history, gender, age, tobacco used and physical activity related groups in discussion part.

5.2 Discussions

One of the main findings of this study is that PWV, which is a sign of arterial stiffness, is a linear relationship with SBP when all the volunteers' measurements are taken into consideration, so PWV value can be considered as an independent risk factor for blood pressure monitoring in healthy subjects.

Another main finding is that PWV is a decisive factor as an independent variable in the outcomes that occur when volunteers are based on family histories. It is seen that the average of the PWV values is higher in the related individuals as seen in the results.

PWV is an independent method for monitoring SBP under daily clinical conditions. SBP, DBP, PP, MAP and HR measurement were determined for PWV evaluation and the relation between PWV. No clear correlation was found with all measurements except SBP measurements. It was found that there is a linear correlation between PWV and SBP.

PWV is an independent method for monitoring possible CVDs in individuals with CVDs in the family history. Based on the answers of volunteer participants, PWV values of individuals without hypertension and diabetes mellitus in their family history were found to be lower than individuals with these diseases among their first-degree relatives. The high PWV of individuals with a disease in their family members may open the way for PWV to be used as an independent factor in assessing the likelihood of people having CVDs in clinical treatments.(Table 26, Table 27)

Table 26 - Family History Related Changes in Pulse Wave Velocity -Treated Hypertension

Parameter	Group 1	Group 2
N	14	18
Pulse Wave Velocity (PWV) (m/s)	5.86 ± 0.51	5.91 ± 0.71

*Data are mean ± S.D.
Treated hypertension; cardiovascular disease in first degree relative aged 75 years or less. Group 1, without family history; Group 2, with family history.

Table 27 - Family History Related Changes in Pulse Wave Velocity -Treated Diabetes

Parameter	Group 1	Group 2
N	22	10
Pulse Wave Velocity (PWV) (m/s)	5.73 ± 0.55	5.99 ± 0.63

*Data are mean ± S.D.
Treated diabetes; cardiovascular disease in first degree relative aged 75 years or less. Group 1, without family history; Group 2, with family history.

Gender related evaluation. It should be considered that there may be differences in values depending on gender difference during PWV assessment in future projects. When the difference of PWV values on gender constituting the main group of our measurements was evaluated, it was seen that the PWV value varied depending on gender and the PWV value of female volunteers was lower than male volunteers (Table 28).

Table 28 - Gender Related Changes in Pulse Wave Velocity

Parameter	Group 1	Group 2
N	15	17
Pulse Wave Velocity (PWV) (m/s)	5.52 ± 0.43	6.19 ± 0.57

*Data are mean ± S.D.

Group 1, Female; Group 2, Male.

Aged related evaluation. In order to observe the correlation between PWV and age, a total number of 32 participants aged between 23 and 41 years were separated into two groups; group 1 was composed 30 years old and young people and group 2 was older than 30 years old. It was observed that the PWV value increased as the average age of the individuals increased. The average measurement results are shown in Table 29.

Table 29 - Aged Related Changes in Pulse Wave Velocity

Parameter	Group 1	Group 2
N	17	15
Pulse Wave Velocity (PWV) (m/s)	5.85 ± 0.54	5.91 ± 0.68

*Data are mean ± S.D.

Group 1 ≤ 30, Group 2 > 30.

Tobacco used related evaluation. Under ideal conditions, BP and PWV values should be measured over the period of time when people do not use tobacco products. In order to observe the effects of tobacco use, participants were divided into two groups

as smokers and non-smokers. When evaluated based on the measurement results, the average PWV of tobacco users was found to be lower.

Table 30 - Tobacco Used Related Changes in Pulse Wave Velocity

Parameter	Group 1	Group 2
N	14	18
Pulse Wave Velocity (PWV) (m/s)	5.97 ± 0.54	5.81 ± 0.65

*Data are mean ± S.D.

Group 1, non-smoking population; Group 2, smoking population.

Physical activity related evaluation. In future projects, it is desirable that volunteers define daily living physical activity levels as low, medium, and high in order to generate baseline data. Although there was no linear relationship was observed with PWV from this study, when evaluated with brPTT results, there was an increase in PTT values in direct proportion to physical activity levels.

Table 31 - Physical Activity Related Changes in Pulse Wave Velocity & Pulse Transit Time

Parameter	Group 1	Group 2	Group 3
N	13	14	5
Pulse Transit Time PTT(ms)	48.23 ± 5.02	48.78 ± 4.53	49.67 ± 3.7
Pulse Wave Velocity (PWV) (m/s)	5.86 ± 0.58	5.81 ± 0.65	6.08 ± 0.53

*Data are mean ± S.D.

Group 1, low level; Group 2, middle level; Group 3, high level.

Study limitations. It was observed that the volunteers who were participating in measurements can be considered as healthy when their health histories were taken into consideration; which limits the generalization of our findings to other populations on behalf of the new generation of noninvasive methods those we are implementing. One of the goals of non-invasive PWV measurement methods is to develop a system that is not dependent on any transfer function or transitional model, which helps to reduce error factor in signal detection. Moreover, this method does not involve any human interaction. However, in this study, the PWV is calculated with related to PTT and distance between brachial to radial artery and depend on operator & function to obtain results.

Design effects. Although daily clinical trials target BP results in the diagnosis of normotensive individuals at risk of hypertension and genetic risk, our results show that PWV may be used as an additional tools in evaluating BP. Moreover, it is observed that the new non-invasive design is suitable for daily clinical applications because it is a simpler, inexpensive and effective method than the other invasive and noninvasive methods of measurement. Future studies are needed to directly measure the parameters and transform them into an operator independent system without intermediate model or function for the system development and adaptation of daily clinical routines.

CHAPTER VI

CONCLUSION

In this thesis, a new non-invasive measurement method and analysis for PWV BP measurement were presented. As a result of this study, PWV measurement suggests a method to monitor SBP under daily clinical conditions. The results show a direct correlation between the SBP and PWV with the golden standard of BP measurement.

In addition, when the genetic susceptibilities of the individuals participating in the measurements were evaluated, PWV was found to be higher in people with high BP family history and people with frequent encounter of diabetic individuals in their family tree.

In conclusion, since SBP, high BP and diabetic evaluations are directly related to cardiovascular morbidity and mortality [35], our findings indicate that PWV can be used as a screening tool to identify SBP values in daily practice and to identify normotensive individuals at genetic risk by targeting for pharmacological and non-pharmacological interventions thanks to continuous monitoring.

Although the PWV measurement is performed with the technique used in this study, the PTT value is directly determined on the pulses coming from the used system and the PWV value is calculated with related to PTT and distance between brachial to radial artery.

In the future work, it is planned to develop smart algorithms to increase the

accuracy of measurements. The aim of these algorithms will be measuring the variables directly without using any transfer function or transitional model which would help to reduce error factor in signal detection, as well as, eliminating the need of an operator. Moreover, in order to make it a more viable system, the continuous-time measurement battery life time needs to be optimized to extend the current single charge life time of a single day (target measurement rate of 1sample/10 mins).

CHAPTER VII

APPENDIX

All specs are taken from the supplier websites [36, 37].

7.1 Omron M7 Intelli IT Electronic Sphygmomanometers

Table 32 - Specification of Electronic Sphygmomanometer

Product category	Electronic Sphygmomanometers
Product description	Automatic Upper Arm Blood Pressure
Monitor Model (code)	M7 Intelli IT (HEM-7322T-E)
Display	LCD digital display
Measurement method	Oscillometric method
Transmission method	Bluetooth® Version 4.0 (Low Energy support)
Wireless communication	Frequency range: 2.4 GHz (2400 - 2483.5 MHz) Modulation: GFSK Effective radiated power:
Measurement range	Pressure: 0 to 299 mmHg Pulse: 40 to 180 beats / min.
Accuracy	Pressure: ±3 mmHg Pulse: ±5% of display reading
Inflation	Fuzzy-logic controlled by electric pump
Deflation	Automatic pressure release valve
Memory	100 measurements with date and time

Rating	DC6V 4W
Power source	4 “AA” batteries 1.5V or optional AC adapter (AC ADAPTER-S, INPUT AC100-240V 50/60Hz 0.12A) (AC ADAPTER-UK, INPUT AC100-240V 50/60Hz 15VA)
Battery life	Approx. 1000 measurements (using new alkaline batteries)
Applied part	Type BF
Protection against electric shock	Internally powered ME equipment (When using only the batteries) Class II ME equipment (Optional AC adapter)
Operating conditions	+10°C to +40°C / 30 to 85% RH / 700 to 1060hPa
Storage / Transport conditions	-20°C to +60°C / 10 to 95% RH / 700 to 1060hPa
IP classification	IP 20
Weight	Monitor: Approx. 390g without batteries Arm cuff: Approx. 163g
Dimensions	Monitor: Approx. 124 (w) mm × 90 (h) mm × 161 (l) mm Arm cuff: Approx. 145 mm × 532 mm (air tube: 750 mm)
Cuff circumference	22 to 42 cm
Cuff / Tube material	Nylon, polyester, polyvinyl chloride
Contents	Monitor, arm cuff, instruction manual, storage case, battery set, blood pressure pass, setup instructions

7.2 Tektronix MDO3012 Mixed Domain Oscilloscope

Table 33 - Specification of Mixed Domain Oscilloscope

	MDO3012
Analog channels	2
Analog channel bandwidth	100 MHz
Rise time (typical, calculated)	4 ns
(10 mV/div setting with 50 Ω input termination)	
Sample rate (1 ch)	2.5 GS/s
Sample rate (2 ch)	2.5 GS/s
Sample rate (4 ch)	-
Record length (1 ch)	10 M
Record length (2 ch)	10 M
Record length (4 ch)	-
Digital channels with MDO3MSO option	16
Arbitrary Function Generator outputs with MDO3AFG option	1
Spectrum analyzer channels	1
Standard spectrum analyzer frequency range	9 kHz - 100 MHz
Optional spectrum analyzer frequency range with MDO3SA option	9 kHz - 3 GHz

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VITA

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