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ULTRASONOGRAPHIC AND COLOR DOPPLER EVALUATION OF CAROTID ARTERY INTIMA MEDIA THICKNESS AND RESISTIVE INDEX IN HYPERTENSIVE PATIENTS COMPARED WITH NORMOTENSIVE, A CROSS SECTIONAL STUDY.

Author - Dr Arjumand Banu .

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Co - author - Dr Nada Mehreen

BACKGROUND

Intima media thickness [IMT] and Resistive index [RI] at common carotid artery are said to reflect the whole body vascular system atherosclerosis. Hypertension is one of the risk factors for atherosclerosis. There are limited numbers of Indian studies assessing these parameters in hypertensive patients.Atherosclerotic cardiovascular sequelae including stroke, coronary disease and peripheral arterial disease, all occur with two-three folds increased frequencies in hypertensive as compared to normotensives of the same age. The development of simple, non-invasive, and inexpensive techniques such as high resolution ultrasound imaging and color Doppler allows the measurement of IMT and RI of carotid artery and thus in early detection of cardiovascular disease.

AIM AND OBJECTIVES OF STUDY:

1.To assess Carotid Intima-media thickness [IMT] and associated Resistive index [RI] changes in hypertensive patients using High frequency ultrasound and Color Doppler.

2.To compare the findings in hypertensive subjects with normotensive subjects.

METHODS:

Cross Sectional study of 50 patients conducted in the department of radio diagnosis at Shadan institute of medical sciences with clinically diagnosed hypertension. The normotensives subjects were students, patient's relatives and clinical staff.

Duration: One year, from 2022 to 2023

Results:

Common carotid artery IMT in normotensives was 0.50mm and 0.49 mm for the right and left sides respectively. RI in normotensive was 0.55 on both the sides. IMT in hypertensives was 0.96mm and 0.97mm for right and left sides respectively. RI in hypertensives was 0.67 on both the sides. So, IMT and RI in hypertensives were significantly increased compared to normotensives.

INTERPRETATION AND CONCLUSION:

Hypertension is a major risk factor for atherosclerosis. Changes in IMT as a morphological parameter and RI as a hemodynamic parameter are said to represent the early atherosclerosis of the vascular system. Our study revealed that IMT and RI of common carotid artery as assessed by high frequency ultrasound and Doppler study respectively, are significantly increased in all hypertensive patients compared with normotensives.

Keywords: B'mode Ultrasonography; Carotid Doppler; Atherosclerosis; Hypertension; Intima media thickness; Resistive index

INTRODUCTION:

Hypertension plays an important and critical role in atherosclerotic related systemic disease, but its impact is greatly influenced by coexistent contributors, particularly abnormalities in blood lipid and glucose metabolism. Hypertension is an independent cause of serious cardiovascular diseases and premature mortality from such diseases. So, comprehensive method is implemented for identification of initial atherosclerotic events in high-risk patients and also in general public so that early preventive measures can be taken.

Atherosclerotic cardiovascular sequelae, including stroke, coronary disease and peripheral arterial disease, all occur with two-three fold frequencies in hypertensives compared to normotensive of the same age. The incidence of every clinical manifestation of cerebrovascular and coronary heart disease is increased in hypertensive patients, and the risk is proportional to the severity of the antecedent hypertension.

Intima - media thickness (IMT) is one of the non-invasive markers of early arterial wall alteration currently available, especially carotid is an important parameter that can be assessed by high resolution sonography in a relatively simple way and represents a safe, precise, inexpensive and reproducible measure. Intima- media thickness [IMT] as morphological value reflects the atherosclerotic process in an indirect manner and this can be assessed as a surrogate marker of generalized atherosclerosis.

Atherosclerosis is a dynamic process is characterized by arterial wall remodelling that may go unnoticed for a lifetime, but may also present as acute vascular disease and become clinically manifest. Because atherosclerosis progresses

over decades, epidemiological studies and intervention trials with clinical endpoints require long-term follow-up, participation of large populations, or both.

The development of non-invasive techniques such as high resolution ultrasound imaging allows the measurement of combined Intima and media thickness [IMT]. The areas open to investigate with high resolution ultrasound technique are mainly carotid and femoral arteries. Many studies have shown that the atherosclerotic process starts to develop in the carotid approximately at the same time as in the aorta, actually preceding plaque occurrence in coronary arteries. It has also been shown that Carotid atherosclerosis is significantly correlated with the extent of coronary artery atherosclerosis suggesting that thickening of Intima media complex only reflects the local morphological alterations in the carotid arteries, but also corresponds to generalized atherosclerosis.

The same applies to the carotid artery distensibility, which diminishes with increasing severity of atherosclerosis. However, assessment of an arterial distensibility requires a relatively arduous procedure and is subject to interobserver and intraobserver variability hemodynamic distensibilities. In contrast, the Resistive index [RI] according to Pourcelot is a hemodynamic parameter that is easily determined by Doppler sonography basically reflecting the vascular resistance, which in turn depends on distensibility of the vessel. So, Intima media thickness [IMT] and Resistive index [RI] are complementary to each other in assessing the atherosclerosis of the vascular system. There are multiple risk factors that are associated with Stroke. They can be classified as modifiable and non-modifiable risk factors. Hypertension which is an independent and modifiable cause of serious cardiovascular diseases plays an important and critical role in atherosclerotic cardiovascular disease. The incidence of every clinical manifestation of cerebrovascular and coronary heart disease is increased in hypertensive patients as compared to the normotensive patients.

AIMS AND OBJECTIVES OF THE STUDY

According to many studies Intima-media thickness [IMT] as a morphological parameter and the resistive index [RI] as a hemodynamic parameter are the surrogate markers of atherosclerosis. However, there are a limited number of Indian studies using these parameters to assess atherosclerosis in hypertensives comparing with normotensives.

Hence this study was carried out,

1. To assess Carotid Intima-media thickness [IMT] and associated Resistive index [RI] changes in hypertensive patients using High frequency ultrasound and color Doppler.
2. To compare the findings in hypertensive subjects with normotensive subjects.

REVIEW OF LITERATURE

ANATOMY

Aortic Arch

The ascending aorta originates from the left ventricle of the heart. The transverse aortic arch lies in the superior mediastinum and is formed as the aorta ascends and curves posteroinferiorly from right to left, above the left main stem bronchus. It descends to the left of the trachea and esophagus. Three main arteries arise from the superior convexity of the arch in its normal configuration. The brachiocephalic trunk (innominate artery) is the first branch, the left common carotid artery the second, and the left subclavian artery the third branch in approximately 70% of cases. The innominate divides into the right common carotid artery, and the right subclavian artery, which gives rise to the right vertebral artery. The left common carotid artery originates slightly to the left of the innominate artery, followed by the left subclavian artery, which gives rise to the left vertebral artery. Anatomic variants of the major arch vessels occur frequently. The most common variant (approximately 10%) is the left common carotid artery forming a common origin with or originating directly from the innominate artery

Common Carotid Artery

Each common carotid artery (CCA) ascends through the superior mediastinum anterolaterally in the neck and lies medial to the jugular vein. The left common carotid is usually longer than the right, because it originates from the aortic arch. In the neck, the carotid artery, jugular vein, and vagus nerve are enclosed in connective tissue called the carotid sheath. The vagus nerve lies between and dorsal to the artery and vein. The common carotid artery usually does not have branches, but occasionally it is the origin to the superior thyroid artery. The termination of the common carotid artery is the carotid bifurcation, which is the origin of the internal carotid artery (ICA) and the external carotid artery (ECA). The CCA bifurcates in the vicinity of the superior border of the thyroid cartilage (approximately C4) in 70% of the cases, and the level of the CCA bifurcations may be asymmetrical. The CCA bifurcation, however, has been described as low as T2 and as high as C1.

Internal Carotid Artery

The internal carotid artery is usually the larger of the CCA terminal branches. The ICA is divided into four main segments: cervical, petrous, cavernous and cerebral. The cervical portion of the internal carotid is evaluated during carotid duplex imaging examinations. The cervical portion of the ICA begins at the common carotid artery bifurcation and extends to the base of the skull. The ICA lies in the carotid sheath and runs deep to the sternocleidomastoid muscle. In the majority of individuals, the internal carotid artery lies posterolateral to the external carotid artery and courses medially as it ascends in the neck. At its origin, the cervical internal carotid artery normally has a slight dilation, termed the carotid bulb and/or the carotid sinus. The cervical ICA usually does not have branches. With age and progressive disease, the cervical ICA may become tortuous, coiled, or kinked.

External Carotid Artery

The external carotid artery originates at the mid-cervical level and is usually the smaller of the two terminal branches of the CCA. Initially, it lies anteromedial to the internal carotid artery, but as the ECA ascends, it courses posterolaterally. In approximately 15% of the population, the external carotid artery originates lateral to the internal carotid artery. This anatomic variation occurs more frequently on the right (3:1). There are eight named branches of the external carotid artery: the superior thyroid, ascending pharyngeal, lingual, facial, occipital, posterior auricular, and the terminal branches, the superficial temporal, and the internal maxillary artery. The abundant number of anastomoses between the branches of the ECA and the intracranial circulation underscore its clinical significance as a collateral pathway for cerebral perfusion when significant disease is present in the internal carotid artery.

Vertebral Artery

The vertebral arteries (VA) are the large branches of the subclavian arteries. Atherosclerotic changes usually occur at the origin of the vertebral arteries. Occasionally the vertebral artery arises directly from the aortic arch (4% of cases on the left side and rarely on the right side). The two vertebral arteries are equal in size in approximately 25% of the cases; therefore, size asymmetry is common. In the majority of the cases, the left vertebral artery is the dominant artery. The vertebral artery can be divided into four segments: the extra vertebral, intervertebral, horizontal, and the intracranial.

The extra vertebral segment is evaluated during the duplex imaging examination. This segment courses superiorly and medially from its subclavicular origin to enter the transverse foramen of the sixth cervical vertebra. The proximal segment of the vertebral artery is approximately 4-5 cm in length and usually there are no branches.

ANATOMY OF EXTRACRANIAL CAROTID ARTERIAL SYSTEM

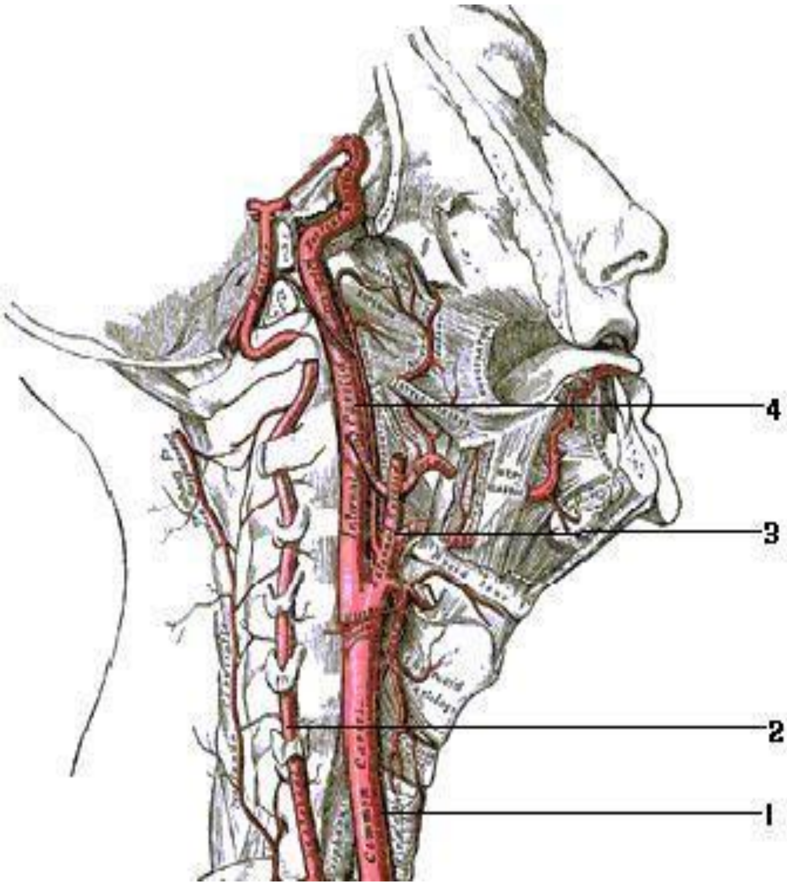


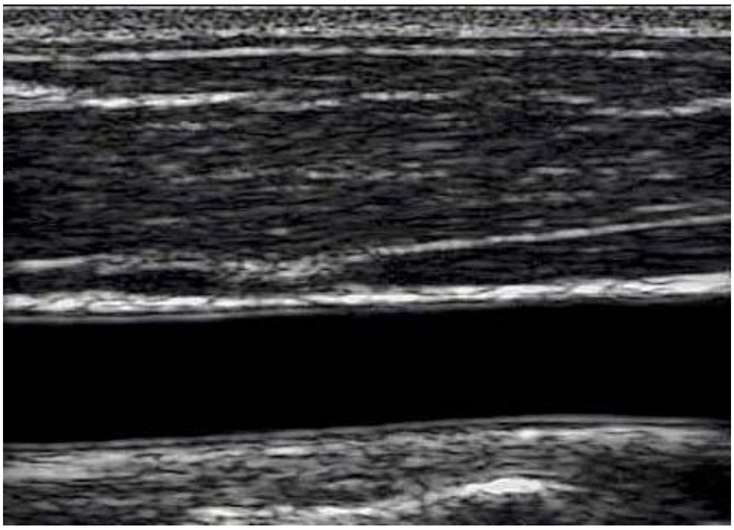
Fig: 1 Anatomy of Extra cranial Carotid Arterial System

1-Common carotid artery, 2-Vertebral artery, 3-External carotid artery 4-Internal carotid artery

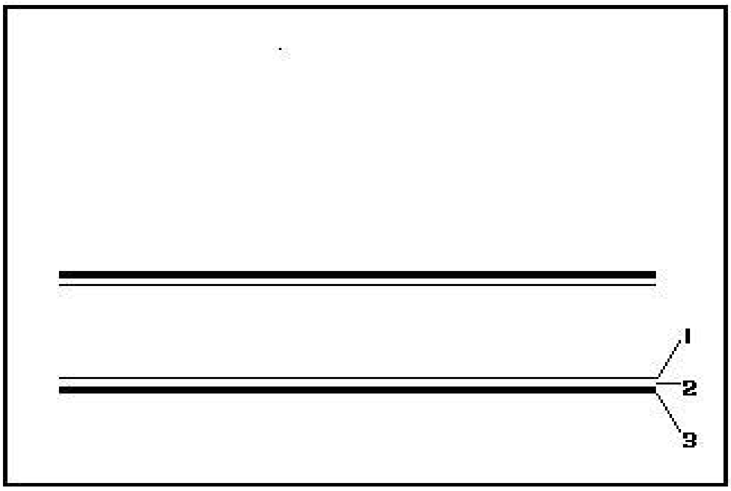
Normal Sonological Anatomy of Common Carotid Artery

The wall of carotid artery consists of three distinct layers. The inner most layer is the intima, or epithelial lining of the artery. The middle layer is media, or muscular layer, which gives the artery its stiffness, elasticity and strength. The outer layer is the adventitia, which is composed of loose connective tissue. All the three layers are represented on ultrasound images. The intima and adventitia produce parallel echogenic lines, with an intervening echo void area that represents the media. The intimal reflection should be straight, relatively thin and parallel to adventitial layer. Significant undulation and thickening of the intima indicates plaque deposition or more rarely, fibromuscular hyperplasia. Observing intimal reflection on longitudinal images ensures that the image plane passes through the vessel diameter. Similarly, in transverse section, visualization of the intima indicates that the image plane is perpendicular to the vessel axis. Histological studies have shown that the thickness of the media and adventitia are more accurately depicted on ultrasoun images.

Normal Sonological Anatomy of Common Carotid Arterial Wall



A-ULTRASOUND IMAGE



B-PICTORAL REPRESENTATION

1=Intima 2=Media 3=Adventitia 1+2=Intima-media thickness [IMT]

Fig-2: Normal Sonological Anatomy of Common Carotid Arterial Wall

PATHOPHYSIOLOGY OF CAROTID ATHEROSCLEROSIS

The word Atherosclerosis is derived from the Greek words 'athero' meaning gruel or paste and 'sclerosis' meaning hardness. The pathogenesis of atherosclerosis is not clear but involves a complex series of events with the formation of atherosclerotic plaque as the end result. Atherosclerotic changes in the arterial wall can be divided into five categories. Stage I and II changes include intimal thickening and formation of foam cells (i.e. macrophages with accumulation of cholesterol), stage III preatheroma with accumulation of extracellular lipids, stages IV and V plaque (atheroma) formation and stage VI complicated lesions.

The most important mechanism by which essential hypertension acts as a cardiovascular risk factor is the induction of atherosclerosis. However, the pathological events leading from high BP to atherosclerotic lesions are still to be fully clarified. It is well documented that functional or morphological alterations of endothelial cells appear to be critical to the evolution, progression, and clinical manifestation of atherosclerotic vascular disease. The mechanism through which a dysfunctioning endothelium could promote atherosclerosis is related to the evidence that endothelial dysfunction is caused by an alteration in the L-arginine–NO pathway, leading to a reduction of NO bioavailability. NO [Nitric oxide] is a potent vasodilator and also an endogenous inhibitor of platelet aggregation, vascular smooth muscle cell growth and migration, leukocyte adhesion, and adhesion molecule expression. This alteration in the L-arginine– NO pathway may reduce this potentially antiatherosclerotic activity. This dysfunctioning endothelial cell attracts leukocytes and vascular smooth muscle cells, which accumulate and proliferate in the arterial wall resulting in increased intima-media thickness. This increased wall thickness may impair diffusion of endothelial vasoactive substances to smooth muscle cells, thereby impairing endothelium-dependent vasodilatation. Further, endothelial dysfunction is also associated with monocyte/macrophage infiltration and production of prostanoids such as thromboxane A_2, which causes vasoconstriction and platelet aggregation, causing further changes of atherosclerosis. Moreover, endothelial dysfunction has also been documented in the presence of different cardiovascular risk factors involved in the pathogenesis of atherosclerosis itself, such as hypertension, aging, menopause, diabetes mellitus and smoking.

Atherosclerosis is a systemic disease affecting the entire arterial tree mainly affecting large and medium-sized arteries like extracranial, cerebral, coronary, and lower extremity arteries, which have the most clinical significance. It causes gradual hardening and narrowing of the arteries which in turn causes restriction of blood flow to end organs. Known risk factors that contribute to the development of atherosclerosis include hypertension, high low-density lipoprotein cholesterol (LDL- C), low high-density lipoprotein cholesterol (HDL-C), genetics, smoking, diabetes mellitus, obesity (abdominal, visceral), diet, physical inactivity, and environmental factors. Hypertension by itself is an independent risk factor for atherosclerosis and in combination with hypercholesterolemia; however, it is a potent promoter of atherogenesis.

The Curie brothers were the first scientists to demonstrate the direct piezoelectric effect utilizing quartz crystals in 1888. Crystals would expand and contract and were both users and receivers of sound. This physical phenomenon made possible the generation & detection of high frequency mechanical pressure waves. This high frequency mechanical pressure wave more than 20,000 Hz is called ultrasound.

Piezoelectric effect refers to the application of an electric field to a crystal, which causes a realignment of the internal dipole structure. This realignment results in crystal lengthening or contraction, converting electrical energy into kinetic or mechanical energy. This is how ultrasound transducers produce sound waves.

The reverse of the piezoelectric effect results from realignment results in crystal lengthening or contraction, converting electrical energy into kinetic or mechanical energy. This is how ultrasound transducers produce sound waves.

Real time ultrasound came into vogue in tardy sixties. A real time ultrasound transducer can produce multiple frames in a very short time. Because of the short assiduousness of vision, a flicker free exhibit requires at least 16 frames per second, which was possible with real time ultrasound.

Later, with the introduction of linear phased array transducer, which is different from the earlier model and is capable of imaging superficial structures helped in producing a highly focused beam with superior resolution. Again with the introduction of transducers with smaller diameter crystals the resolution improved because of higher frequency.

Christian Doppler formulated the principle that there is a change in the frequency of a wave for an observer moving relative to the source of the wave. Doppler effect named in his honour. The first practical use of this principle was made during World War II for the detection of enemy submarines in the sea bed.

The Doppler principle was first described by Christian Andreas Doppler in Austria in 1842. Medical applications of the Ultrasonic Doppler techniques were first implemented by Shigeo Satomura and Yasuhara Nimura at the Institute of Scientific and Industrial Research in Osaka, Japan in 1955 for the study of cardiac valvular motion and pulsations of peripheral blood vessels.

Color Doppler was introduced in medical practice effectively in mid-1980. Since then it has undergone tremendous change and is now established as an effective non-invasive technique to study the characteristics of blood flow in the blood vessels.

Pignoli P, *et al*. in 1986 showed that, by mode imaging of internal + medial thickness did not differ significantly from the intimal + medial thickness measured on pathologic examination. With respect to the accuracy of measurements obtained by B mode imaging as compared with pathologic findings, we found an error of less than 20% for measurements in 77% of normal and pathologic aortic walls. In addition, no significant difference was found between B mode determined intimal + media thickness in the common carotid arteries evaluated in vitro and that determined by this method in the vivo in young subjects, indicating that B mode imaging represents an useful approach for the measurement of internal + medial thickness of human arteries in vivo.

Many studies are based on the neckartery ultrasonography use both near wall and far wall measurements while the near wall intima media thickness (IMT) may be very hard to define, due to the echogenic structure of adventitia in comparison to the far wall, where the media- adventitia interface is usually easy to detect.

Wong *et al*. in 1993 and Wikstrand & Wendelhag in 1994 concluded that only the far wall Intima media thickness [IMT] can be measured by ultrasonography and if near wall measurement are used, however these measurements should be presented separately.

Ultrasound overestimated the thickness of the intima and adventitia and underestimated the thickness of the media. For combined intima-media thickness, the differences between histology and imaging were insignificant, averaging 4% for the carotid artery and 9% for the femoral artery in the far-wall projection. In the near-wall projection, sonographic intima-media thickness was 20% less than that determined histologically.

A disease progression is directly related to the severity of atherosclerotic changes. The rate of disease progression and regression seems to be quite variable according to the methods used to assess carotid atherosclerosis. Most of the previous studies used either angiography or duplex scanning or continuous wave Doppler and gave very conflicting results.

Intima media thickness [IMT] has been shown to be associated with hypertension, age, plasma LDL cholesterol level and smoking. Lipid and lipoproteins greatly affect the impact of hypertension on the pace of atherogenesis. Carotid arteries provide a "window" to the coronary arteries and both have similar risk factors.

Carotid atherosclerosis provides a window to the degree of coronary atherosclerosis in an individual. Carotid IMT is considered an independent predictor of future cardiovascular events, including heart attacks, cardiac death, and stroke.

The intimal-medial thickness was defined as the distance between the medial- adventitial interface and the luminal-intimal interface. The intimal-medial thickness was measured on the central portion of a longitudinal B-mode scan visualizing the mid and distal CCA (generally, about 2 cm below the beginning of the dilatation of the distal CCA).

The intimal-medial thickness was defined as the distance between the medial- adventitial interface and the luminal-intimal interface. The intimal-medial thickness was measured on the central portion of a longitudinal B-mode scan visualizing the mid and distal CCA.

Atherosclerosis is a disorder of the intima, an increase in the Intima media thickness [IMT] of the carotid arteries measured by ultrasonography is considered to reflect early signs of atherosclerotic process. Association between increased intimal- medial thickness and increased levels of cardiovascular risk factors has been studied.

Increased Intima media thickness [IMT] has been shown to be successfully reduced by lipid-lowering therapy.

In a Finnish study by Salonen & Salonen in 1991, for each millimeter increase of Intima media thickness [IMT] the risk of acute coronary event raised 2-14 folds, although the mean follow-up was about one year.

Lemne C *et al.* showed that Intima media thickness [IMT] is increased in hypertensives compared with age and sex matched normotensives and there is powerful evidence to link blood pressure to clinical cardiovascular pathology. They also showed that hypertension predisposes both sexes to ischemic infarction of the myocardium both in elderly and young age groups, and isolated systolic hypertension is associated with a greater than two fold risk of cardiovascular disease.

High-resolution carotid duplex scanning has been widely recognized as a non- invasive, reproducible, and accurate method of evaluating CCA atherosclerosis. The sensitivity of duplex scanning in the detection of carotid stenosis is high (88% to 95%); the accuracy of duplex (79% to >90%) was established by a blind comparison with angiography.

Carola Lemne, MD *et al* in 1999 concluded that Intima media thickness [IMT] is increased even in borderline hypertensives.

The Rotterdam Study in 1997 which was prospective study showed significant relationship between Intima media thickness [IMT] and the risk of stroke and myocardial infarction. The mean duration of follow-up was 2.7 years.

Simons PC *et al.* [SMART study] in 1999 and many previous studies showed that similar to increased carotid Intima media thickness [IMT] its distensibility diminishes with increasing severity of atherosclerosis suggesting correlation between Intima media thickness [IMT], distensibility and atherosclerosis.

However, assessment of arterial distensibility requires a relatively arduous procedure and is subjected to interobserver and intraobserver variability of up to 19%.

In contrast, the Resistive index (RI) according to Pourcelot is a hemodynamic parameter that is easily determined by Doppler sonography and basically reflects vascular resistance.

Ishimura *et al.* demonstrated correlation between the Intima media thickness [IMT] of the CCA and the Resistive index [RI] in the renal parenchyma indicating that the Resistive index [RI] of CCA could be used to assess atherosclerosis.

Beat Frauchiger, MD *et al*. in 2001 concluded that the RI of the carotid artery can be assessed as a surrogate marker of generalized atherosclerosis complementary to Intima media thickness [IMT], and compared with other indirect measurements of atherosclerosis e.g., distensibility, the ease with which Resistive index [RI] data are obtained is striking.

Recently an Indian study by Adaikkappan M *et al.* in 2002 yielded similar results as previous studies and concluded that, Intima media thickness of Common carotid artery is significantly increased in hypertensives when compared to normotensives.

Measurement of carotid intima-media thickness (CIMT) with B-mode ultrasound is a non-invasive, sensitive, and reproducible technique for identifying and quantifying atherosclerotic burden and CVD risk. It is a well-validated research tool that has been translated increasingly into clinical practice for predicting future risks.

MATERIALS AND METHODS

Type of Study

Our study was Clinical Cross Sectional Study.

Source of Data

Data for the study was collected from the patients referred to the Department of Radio diagnosis at the Shadan institute of medical sciences with clinically diagnosed hypertension. The normotensive subjects were students, patient's relatives and clinical staff.

Study Period

The study was performed for the period of one year from 2022 to 2023 excluding the period of data analysis and write-up.

Method of Collection of Data

A structured, pre-prepared case a pro forma (CP) was used to enter the clinical history, physical examination findings, investigations-hematological, urinary and duplex sonography findings.

Total number of subjects selected for the study was 50. We selected 25 hypertensive patients aged between 35-55 years and 25 normotensive subjects of the same age group. All 25 normotensives were eligible for examination.

Hypertension was defined according to the criteria established by the seventh Joint National Committee on Detection, Evaluation, and Treatment of high blood pressure.

Blood pressure measurements were performed with a mercury sphygmomanometer with a standardized fashion cuff size adjusted to the circumference of the right arm. The arm with the cuff was placed at the level of the heart. After 5 minutes of rest in the supine position, three consecutive brachial artery blood pressure measurements were recorded at one minute interval. Then another three blood pressure measurements were recorded at one-minute intervals with the patient standing. The mean value of the three supine blood pressure measurements was used for the analysis. Systolic and diastolic blood pressures were defined according to Korotkoff sounds I and V respectively. Hypertension was defined as blood pressure ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic.

Height was measured to the nearest centimeter without shoes. Weight was measured to the nearest 0.1 kg on a lever balance with the subject in light underwear without shoes. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters) squared.[33] Data on alcohol use and smoking was obtained by self-reported questionnaire. Secondary forms of hypertension were excluded as follows: Renovascular disease was excluded in most cases by renal artery color Doppler, renal parenchymal diseases were ruled out by the normality of serum creatinine levels and urine examination, primary aldosteronism was ruled out by the absence of hypokalaemia, pheochromocytoma was ruled out by the absence of an adrenal or abdominal mass on sonography. Diabetes mellitus was ruled out by measuring RBS. Plasma lipid profile was also performed to assess the cholesterol level.

Inclusion Criteria

Hypertensive group-All male and female patients suffering from primary hypertension without any symptoms and within the age group between 35-55years. Normotensive group-All male and female subjects without hypertension and within the age group between 35-55years.

Exclusion Criteria

All hypertensive patients and normotensive subjects with history of secondary hypertension, diabetes mellitus, smoking, alcoholism and postmenopausal women.

Technique of Carotid Duplex Sonography

In the study, we used volusion GE scanner with 7.5-10 MHZ linear array transducer. After explaining the procedure to the patient, the patient was made to lie in a supine position and chest being elevated with a pillow and the head being turned to the opposite side of the carotid artery under examination.

The probe was placed on the medial side of the sternocleidomastoid to identify the carotid artery and examined in transverse and longitudinal view starting from the origin to its bifurcation. Then the internal carotid artery was examined both in transverse and longitudinal starting from bifurcation to the maximum length it was traceable. The proximal part of external carotid artery was examined in both transverse and longitudinal plane. All arteries were carefully examined with regard to wall changes. Normal carotid artery wall shows two parallel echogenic lines separated by hypoechoic region. These lines can be better appreciated at CCA. The inner echogenic line represents the intima and the outer echogenic line represents adventitia.

The central hypoechoic region represents the media. The I-M thickness [IMT] was defined as the distance between the leading edge of the lumen-intima echo and the leading edge of the media-adventitia echo. Plaques were screened for in the common, internal, and external carotid arteries and any stenosis was graded according to Washington criteria.

Measurement of Intima Media Thickness [IMT]

The measurement was done in an optimal longitudinal freeze-frame image by manual cursor placement. The far wall of the common carotid artery (CCA) at 0.5-1 cm proximal to carotid bulb was used for measurement of Intima media thickness [IMT]. The optimum magnification was used for Intima media thickness [IMT] measurement. On the basis of previous descriptions, the leading edge of vascular lumen-intima echoes was selected as the internal measurement site and the leading edge of the media-adventitia echo as the external limit. The measurement was repeated twice on the same site and then performed in the same way three times at the corresponding opposite site. Then, mean of right, left and combined measurements were taken separately for further calculations. There were no exclusions with regard to the Intima media thickness [IMT] measurements.

Measurement of Resistive index [RI]

The wall filter setting was 50-100 Hz and the Doppler frequency of 3.5- 5 MHz. The pulsed-Doppler volume was carried out in the distal CCA 0.5- 1cm proximity to the bulb region with a maximum Doppler angle of 60° with a sampling volume of approximately half of the vascular diameter. The maximum systolic and minimum diastolic flow rates were determined and Resistive index [RI] was calculated automatically in a cycle by means of inbuilt software. The measurement was then repeated twice. The same was repeated on the left side for three times. Then mean of left, right and combined measurements were taken separately for further calculations.

The RI was calculated as follows:

$$\frac{Peak\ Systolic\ Velocity - Minimum\ Diastolic\ Velocity}{Peak\ Systolic\ Velocity}$$

Finally, the curves and graphs of the Intima media thickness [IMT] and Resistive index [RI] calculations are based on bilateral measurements of Common carotid artery in 25 hypertensives and 25 normotensive subjects.

The examination was done free of cost for which permission was obtained from the Department. Static images of positive sociological findings were recorded using the inbuilt DICOM facility within the equipment, free of cost for which prior permission was obtained from the Department.

Statistical Methods

The chi - square test has been used to find the significance of proportions of hypertensives in different age groups. The student't' test has been used to find the significance of Blood Pressure parameters and Intima media thickness [IMT] between normotensive and hypertensives.

The Mann Whitney U test has been used to find the significance of the resistive index between normotensive and hypertensives. Pearson correlation co- efficient has been used to find the degree of relationship between blood pressure parameters and the Intima media thickness [IMT] and Resistive index [RI] for the normotensives and hypertensives. Student't' test has been used to test the significance of Pearson correlation co-efficient.

The Statistical software, namely SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Figure 3. Volusion GE – Ultra Sound Machine

Sample size of Estimation

Data for the study will be collected from the patients referred to department of radio diagnosis at the Shadan Institute of Medical Sciences with clinically diagnosed hypertension. The normotensives subjects were students, patient’s relatives and clinical staff.

Sample Size:

Prevalence of hypertension in Indian population from previous studies was found to be 25-44%. Thus Formula for sample size calculation is

$$\text{Sample size(n)} = \frac{Z^2_{\sigma/2}\, x P x Q}{d^2}$$

Where, n is the sample size,

p is the prevalence-25%

q is the 100-p value-75% d is the error taken-10%

$Z^2_{\sigma/2}$ –90% of confidence interval-1.64 Sample size(n)= $(1.64)^2$x0.25x0.75

$(0.1)^2$

The sample size of my study will be taken as 50, 25 hypertensive patients and 25 normotensive subjects.

Inclusion Criteria:

Hypertensive Group: All male and female patients suffering from primary hypertension without any symptoms and within age group between 35-55 yrs.

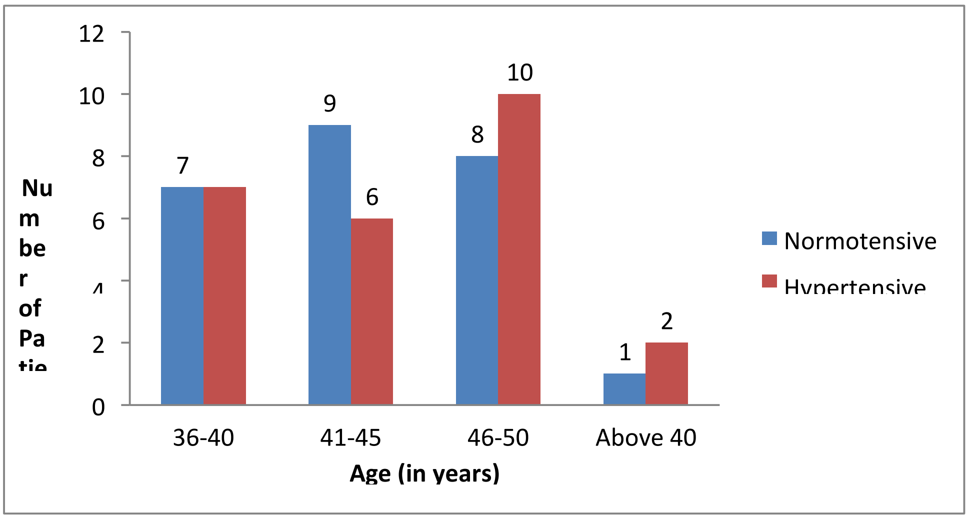
Normotensive group: All male andfemale subjects without hypertension within age group between 35-55 yrs.

RESULTS

Table 1: Age distribution of normotensives and Hypertensives (n=50).

Age (in years)	Normotensive	Hypertensive	Total	p value
36-40	7	7	14	0.764
	28.0%	28.0%	28.0%	
41-45	9	6	15	
	36.0%	24.0%	30.0%	
46-50	8	10	18	
	32.0%	40.0%	36.0%	
Above 40	1	2	3	
	4.0%	8.0%	6.0%	
Total	**25**	**25**	**50**	
	100.0%	**100.0%**	**100.0%**	

Graph 1. Age distribution of Normotensives and Hypertensives (n=50)

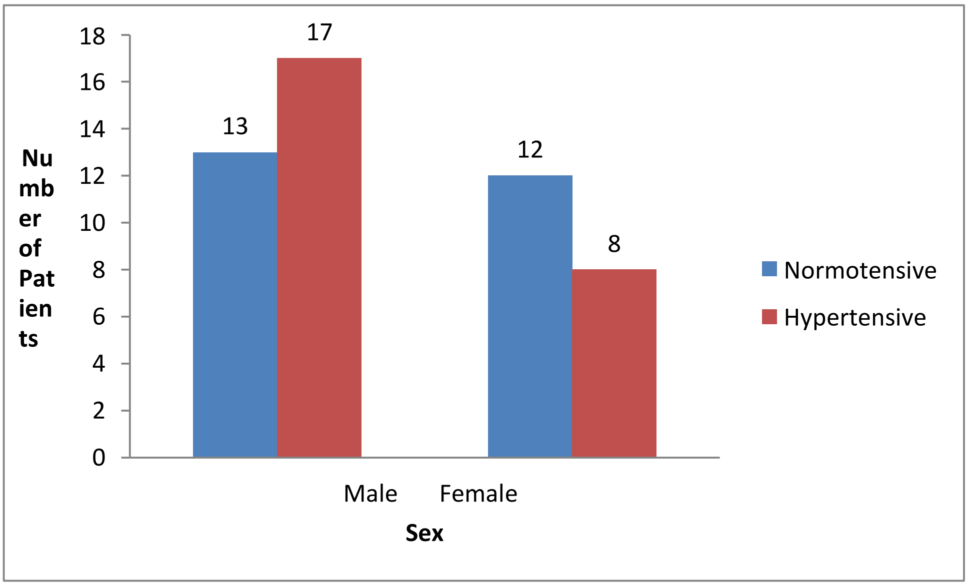


Age distribution of the subjects is shown in Table 1 and Graph 1. Both hypertensives and normotensive groups were proportionately distributed.

Table 2. Sex distribution of Normotensives and Hypertensives (n-50).

Sex	Normotensive	Hypertensive	Total	p value
Male	13	17	30	0.248
	52.0%	68.0%	60.0%	
Female	12	8	20	
	48.0%	32.0%	40.0%	
Total	25	25	50	
	100.0%	100.0%	100.0%	

Graph 2. Sex distribution of Normotensives and Hypertensives (n-50).



Sex distribution of hypertensive and normotensive groups are shown in Table 2 and Graph 2. Both hypertensives and normotensive groups were proportionately distributed.

Table 3. Demographic Data of two groups.

Demographic characteristics	Normotensive	Hypertensive	p value
Age	43.68±4.68	44.60±4.63	0.488
HR	78.40±5.5.57	80.40±5.03	0.189
BMI	23.04±1.59	23.16±1.43	0.781
TC	146.56±6.62	169.64±4.62	<0.01
TG	114.48±8.19	171.12±3.92	<0.01

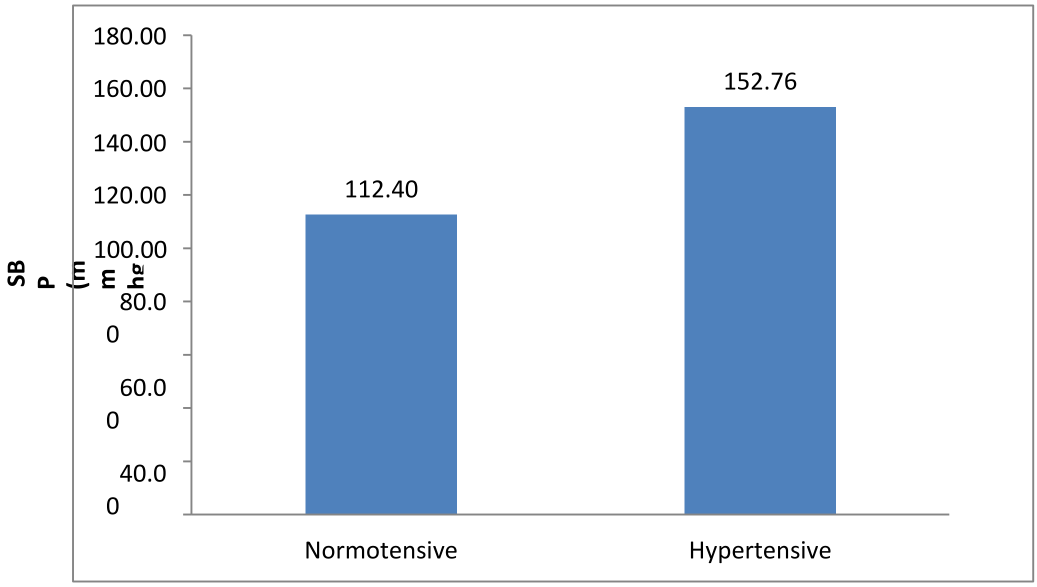
HR-Heart rate; BMI-Body mass index; TC-Plasma total cholesterol; and TG- Plasma triglycerides.

Mean±SD is reported.

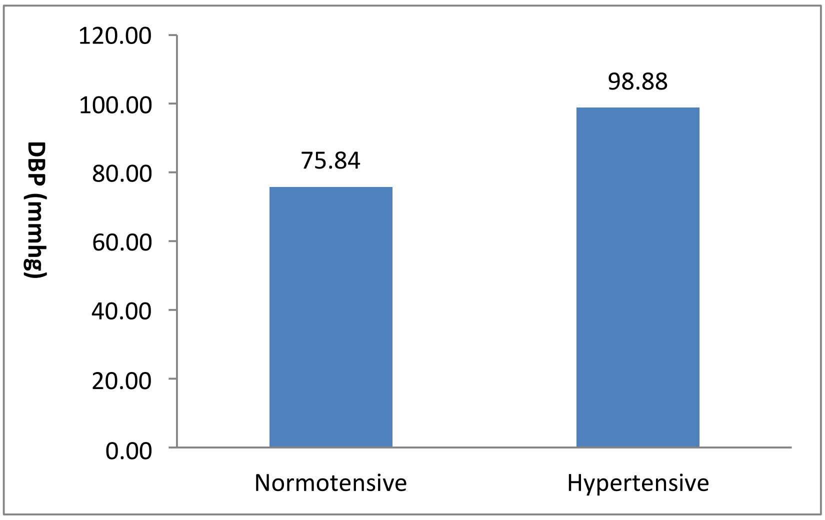
Table 4. Blood Pressure parameters in normotensives and Hypertensives

Blood Pressure	Normotensive (Mean ± SD)	Hypertensive (Mean ± SD)	Student t
Systolic	112.40±7.14	152.76±4.61	<0.01
Diastolic	75.84±5.06	98.88±3.17	<0.01
MAP	88.04±5.44	116.76±3.23	<0.01

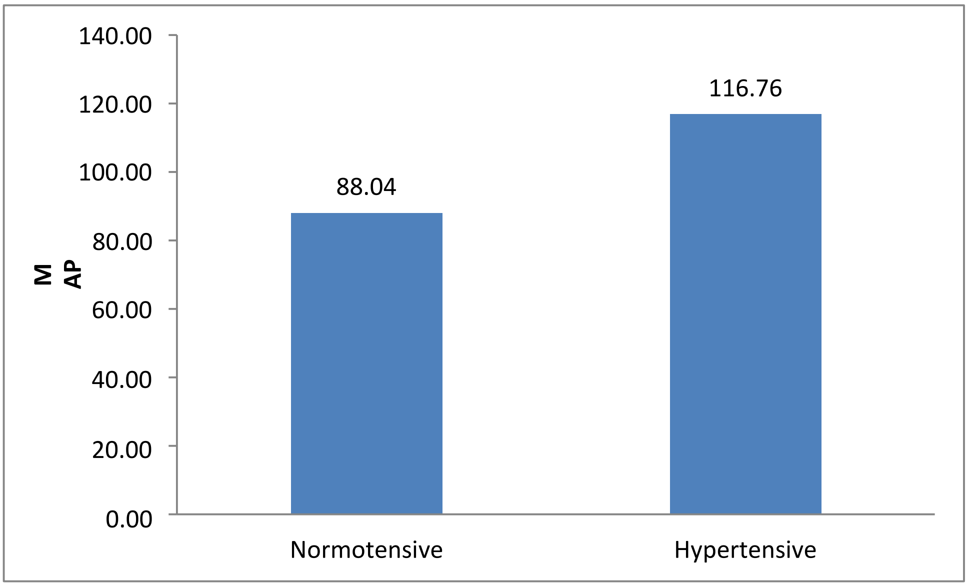
Graph 3a-Systolic blood pressure parameter in normotensives and Hypertensives.



Graph 3b-Diastolic blood pressure parameter in Normotensives and Hypertensives



Graph 3c-Mean arterial pressure parameter in Normotensives and Hypertensives



Different blood pressure parameter status in hypertensive and normotensive groups is shown in Table 4 and Graphs 3. Compared to normotensives, hypertensives showed significantly higher systolic BP, diastolic BP and Mean arterial pressure [MAP].

Table 5 .Effect of Hypertension on Intima media thickness [IMT]

M-IMT	Normotensive	Hypertensive	P Value
LEFT	0.54 ± 0.118	0.98 ± 0.097	< 0.01
RIGHT	0.53 ± 0.113	1.00 ± 0.106	< 0.01
COMBINED (Average)	0.54 ± 0.119	1.00 ± 0.096	< 0.01

M – IMT – Mean Intima Media Thickness

Graph 4. Effect of Hypertension on Intima media thickness [IMT].

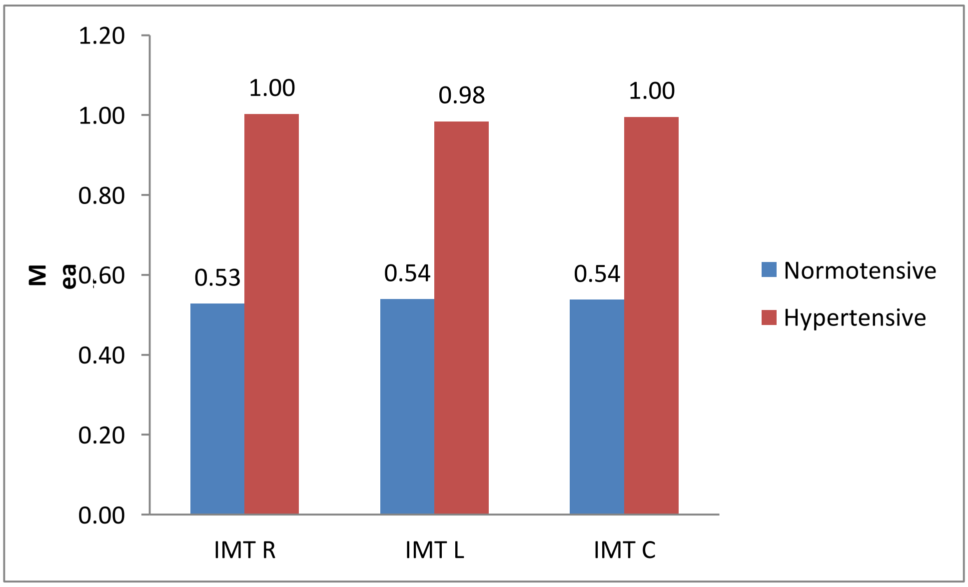


Table 5 and Graph 4 shows the Mean Intima media thickness [M-IMT] measurement of right side, left side and combined values of both sides in hypertensives and in normotensives. There is highly significant increase in Intima media thickness [IMT] on both sides in hypertensives compared to normotensive.

Table 6.Effect of Hypertension on Resistive index [RI].

M-RI	Normotensive	Hypertensive	P Value
LEFT	0.57 ± 0.051	0.69 ± 0.035	$P < 0.01$
RIGHT	0.56 ± 0.043	0.69 ± 0.032	$p < 0.01$
COMBINED (Average)	0.57 ± 0.045	0.679 ± 0.032	$p < 0.001$

M – RI Mean Resistance Index

Graph 5. Effect of Hypertension on Resistive index [RI].

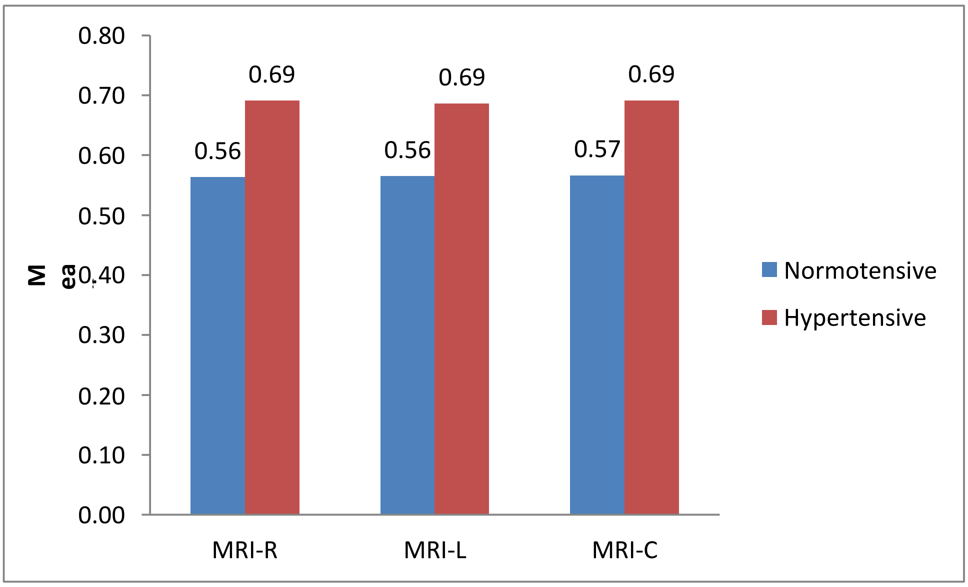


Table 6 and Graph 5 shows Mean Resistive index [M-RI] of right side, left side and combined value of both sides in normotensives and hypertensives. There is highly significant increase in Resistive index [RI] on both sides in hypertensives compared to normotensives.

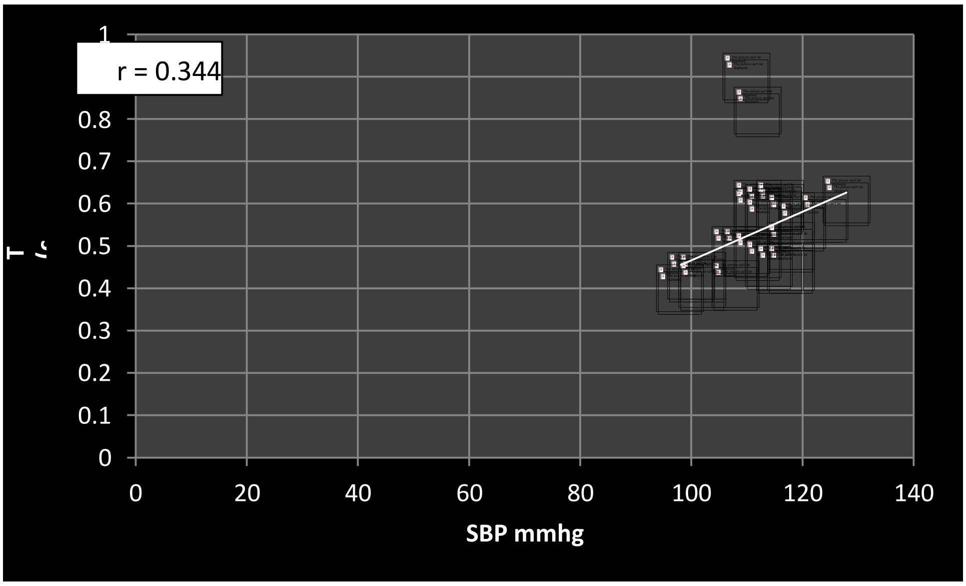
Table 7. Relationship between blood pressure parameters and IMT and RI in both groups

Blood Pressure	**Normotensive (Pearson correlation)**		**Hypertensive (Pearson Correlation)**	
Status	IMT	RI	IMT	RI
Systolic	0.344	-0.011	0.562**	0.440*
	0.093	0.960	0.003	0.028
Diastolic	0.493*	0.266	0.403*	0.377
	0.012	0.198	0.046	0.063
MAP	0.471*	0.174	0.529**	0.462*
	0.017	0.405	0.007	0.020

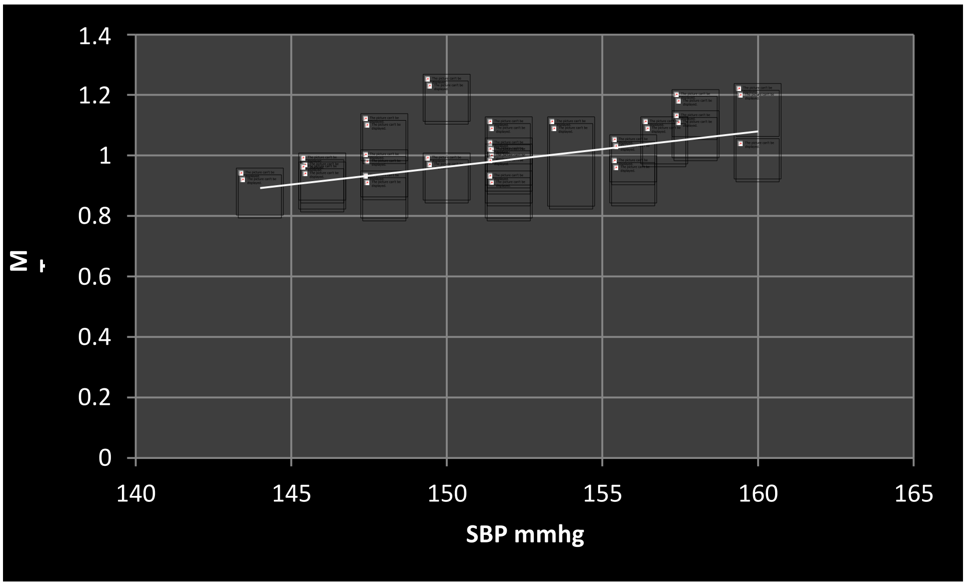
* Significance at 5% ** Significance at 1%

Graph 6.Relationship between Systolic blood pressure and IMT in both groups

Graph 6a. Normotensive

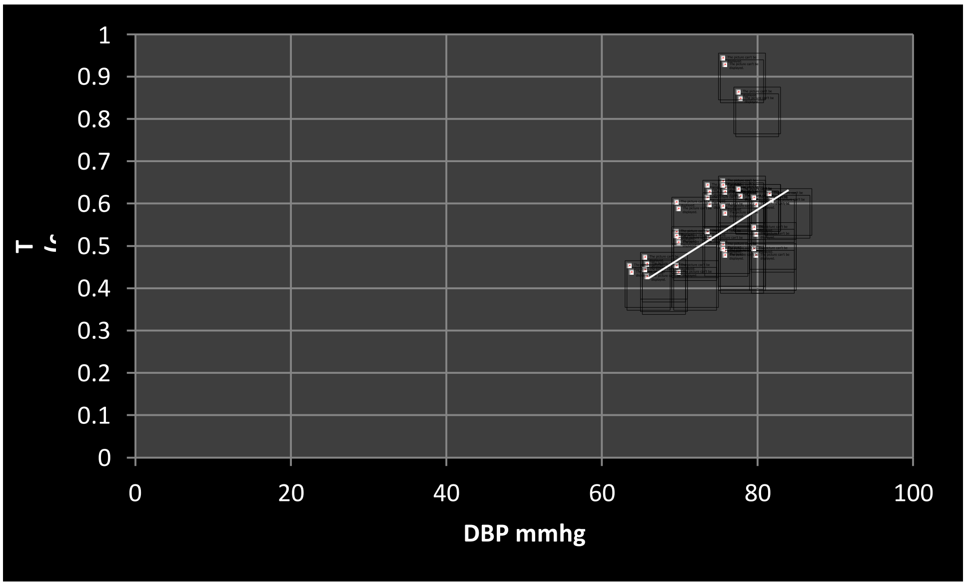


Graph 6b. Hypertensive

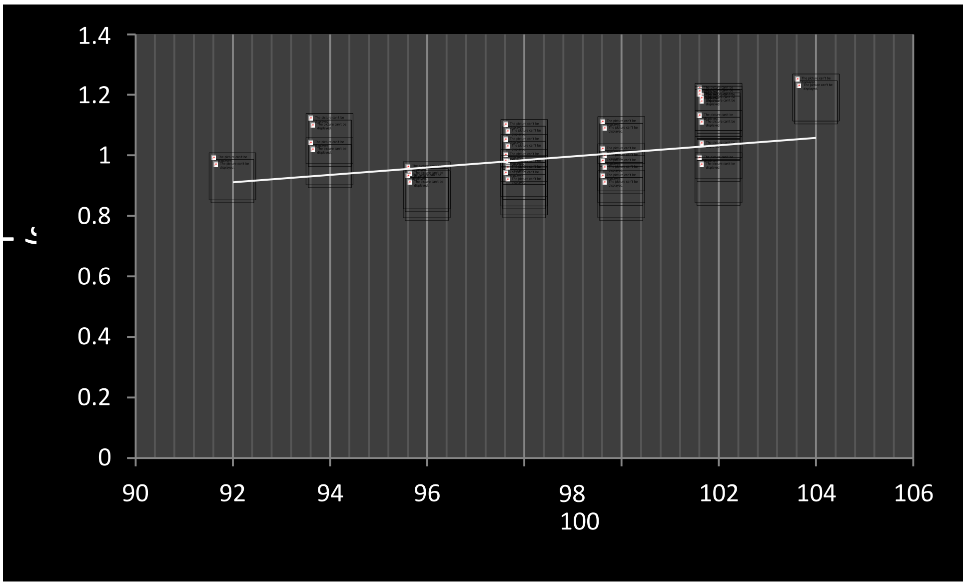


Graph 7.Relationship between Diastolic blood pressure and IMT in both groups.

Graph 7a. Normotensive

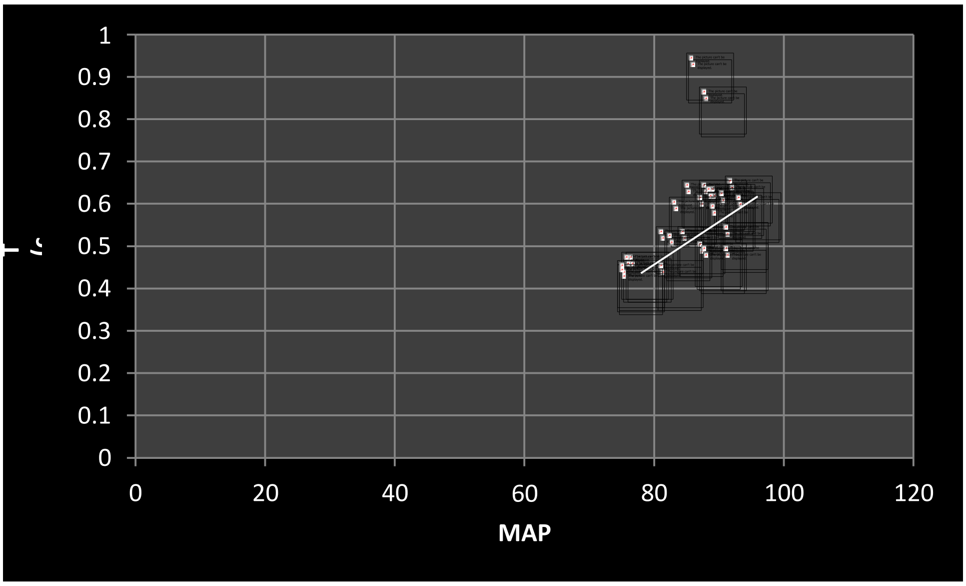


Graph 7b. Hypertensive

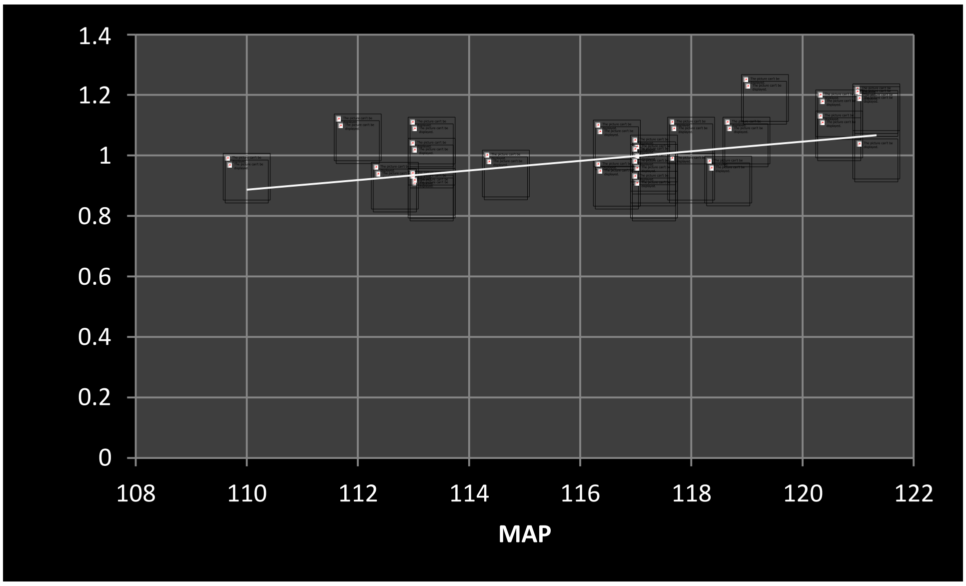


Graph 8.Relationship between Mean arterial pressure and IMT in both groups.

Graph 8a Normotensive

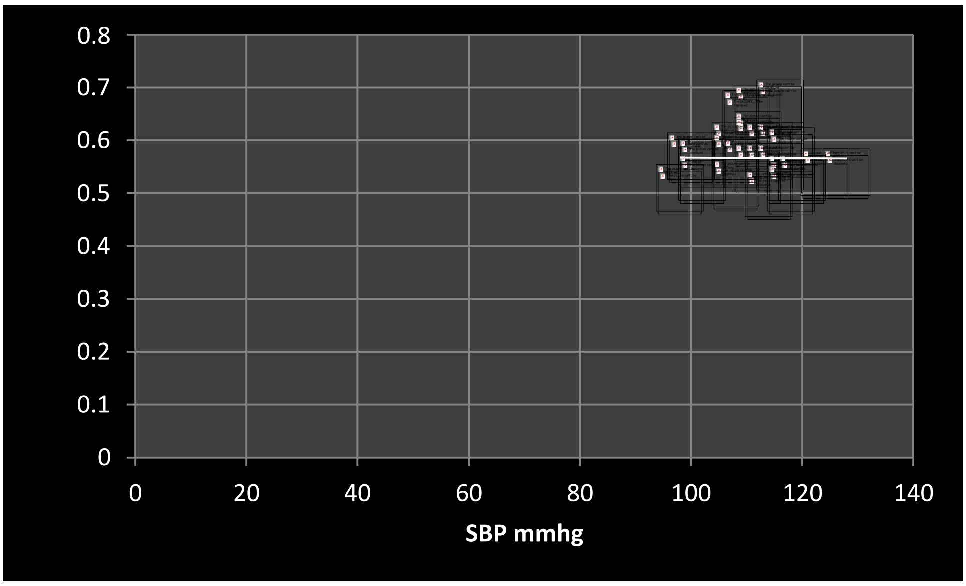


Graph 8b Hypertensive

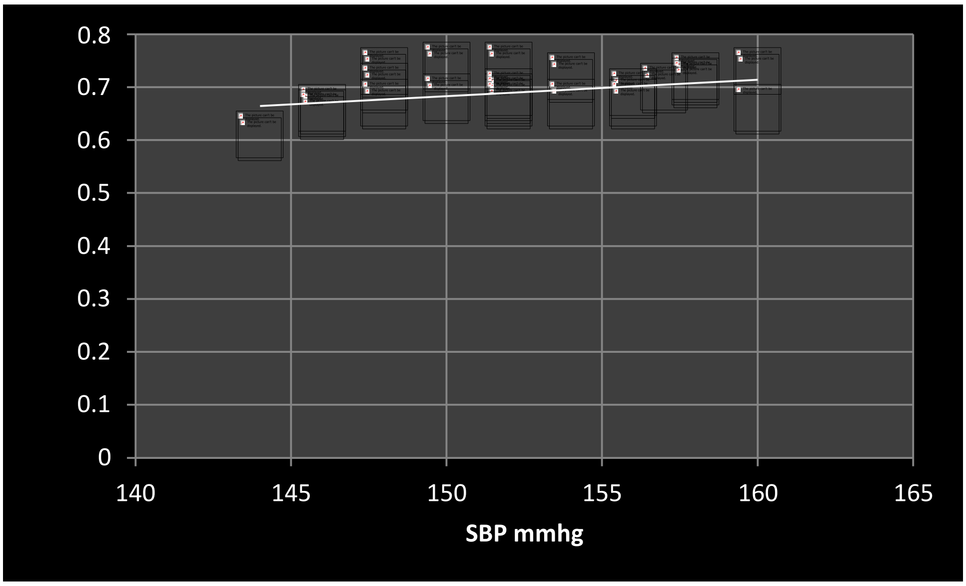


Graph 9.Relationship between systolic blood pressure and RI in both groups

Graph 9a Normotensive

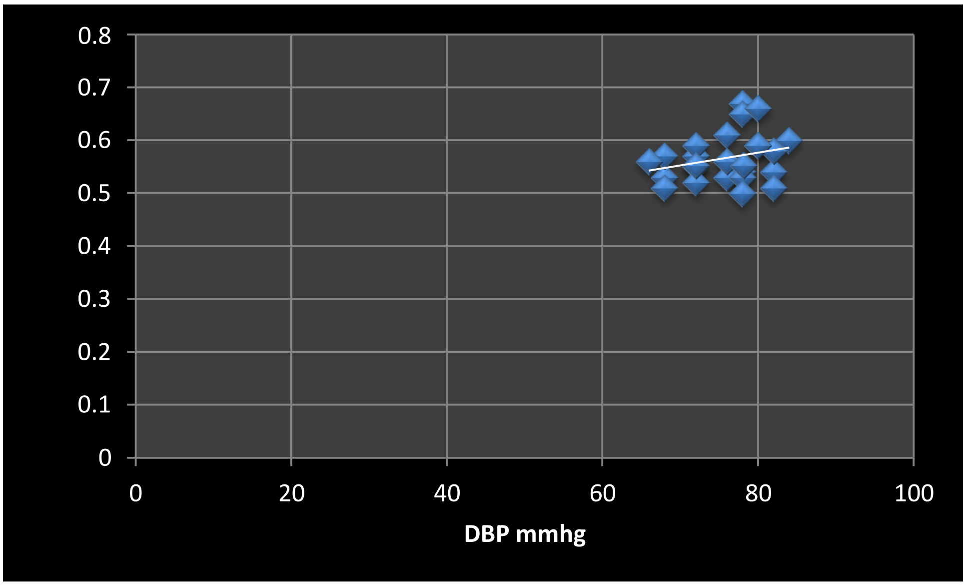


Graph 9b Hypertensive

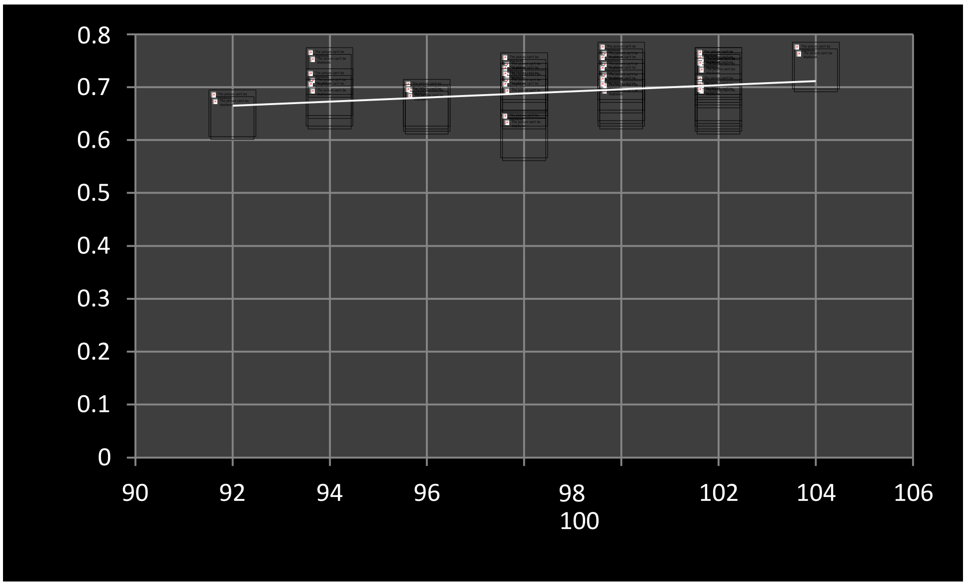


Graph 10.Relationship between diastolic blood pressure and RI in both groups.

Graph 10a. Normotensive

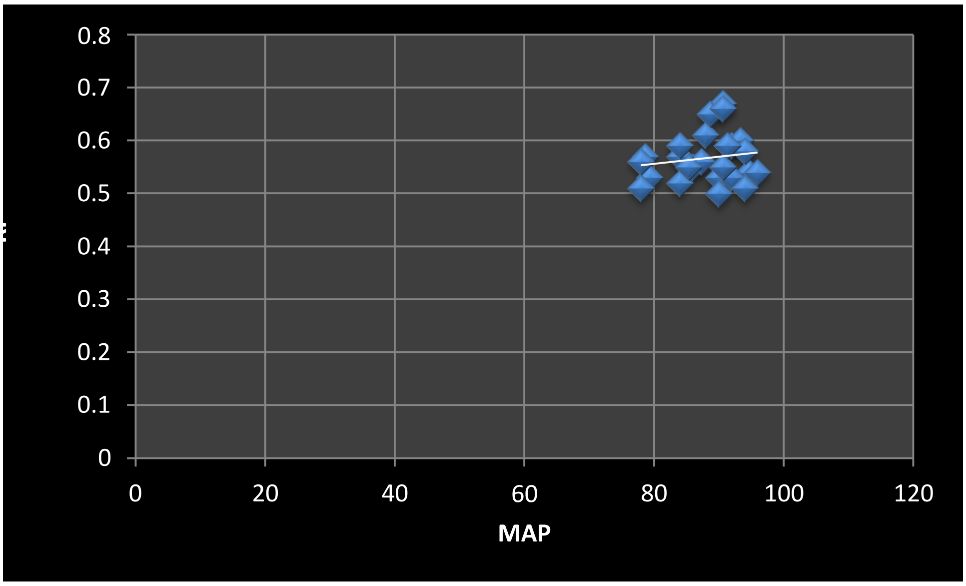


Graph 10b. Hypertensive

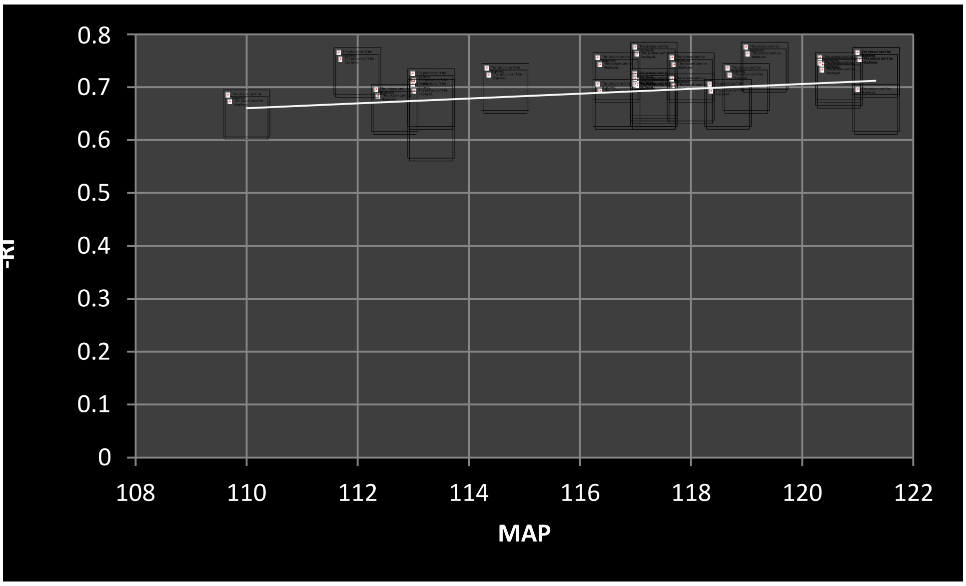


Graph 11**.** Relationship between Mean arterial pressure and RI in both groups.

Graph 11b. Normotensive



Graph 11b. Hypertensive



MAP in mmHg

Table 7 and Graphs 6 to Graph 11 shows relationship between various blood pressure parameters and Intima media thickness [IMT] and Resistive index [RI] in normotensive and hypertensive group. There is highly significant correlation between Systolic blood pressure [SBP], Diastolic blood pressure [DBP] and Mean arterial pressure [MAP] with IMT and RI.

In present study, the mean Intima media thickness [IMT] measurement in hypertensives was 1.00± 0.096 with a P value of <0.01. The mean Resistive index [RI] in hypertensives in our study is 0.679± 0.032 with the P value of <0.01 [highly significant].

DISCUSSION

Our study was a clinical cross sectional study conducted on total number of 50 patients, including equal numbers of hypertensive and normotensive subjects to know the effect of hypertension on Intima media thickness [IMT] and Resistive index [RI] of the carotid arteries which can be effectively done using high frequency ultrasound and Color Doppler sonography.

All the patients were scanned for both right and left CCA, ICA and ECA. B- mode, color mode and spectral wave features were studied. High-frequency transducer for imaging of carotid vessels and color flow imaging and spectral wave pattern is must for proper interpretation and diagnosis of pathology.

Main role of carotid doppler examination is detection of occlusive atherosclerotic plaques in the common carotid artery and bifurcation of common carotid artery into internal and external carotid arteries. The accurate diagnosis of critical stenosis (more or equal to 70% decrease in diameter) is important because these are the patients who carry increased risk of cerebral infarction.

Clinical Background and Significance of the Study:

Hypertension has been recognized as a strong risk factor for atherosclerotic cardiovascular diseases. Isolated systolic hypertension and isolated borderline hypertension are associated with a higher risk of cardiovascular disease and subclinical atherosclerotic disease.[36] Mechanisms by which hypertension predisposes to atherosclerosis may include endothelial dysfuncion, hyperinsulinemia, hemodynamic stress, and multiple metabolic alterations. Impaired production of endothelium-derived relaxing factor and increased activity of endothelium-derived contractile substances have been demonstrated.

In addition, endothelium importantly determines vascular tone through the release of different relaxing and constricting factors that modulate the contractile activity of the underlying smooth muscle, endothelial injury releases certain substances which enhance smooth muscle cell proliferation with internal wall thickening and proteoglycan accumulation accelerates atherosclerosis. Increased flow velocity and wall shear stress, barotruama are considered to be the important factors that caused hypertension induced Intima media hypertrophy and thickness.

The gradual narrowing and hardening of the arteries has dramatic effects on arterial resistance and blood flow. Resistance increases when radius decreases, as friction of blood flow against vessel wall increases. Development of a plaque also deforms the endothelial wall, increasing turbulent flow and increasing resistance. The hardening of the arterial walls increases resistance to flow, as vessel walls lose their distensibility. Atherosclerosis is a generalized process that significantly involves the coronary, cerebral, and peripheral arteries, which are of clinical importance.

Clinical manifestations tend to coexist, and the presence of one manifestation increases the likelihood of developing others because, major risk factors tend to affect all arterial territories. Also, clinical atherosclerosis in one area may directly predispose the patient to the occurrence of atherosclerosis in other vascular territory.

Carotid artery intima-media thickness is a simple, non-invasive and reproducible clinical tool to evaluate atherosclerosis and predict coronary artery disease in Indian subjects. In Western countries like United States**,** atherosclerosis is the leading cause of illness and death. In the United States alone, it caused almost 1 million deaths in 1992 twice as many as from cancer and 10 times as many as from accidents.

Despite significant medical advances, atherosclerotic coronary artery disease such as myocardial infarction and atherosclerotic cerebrovascular disease such as stroke are more responsible for more deaths than all other causes combined.

Intima medial thickness in diabetes is more than non-diabetic patients. Diabetes and age are the most important risk factors associated with increased intima medial thickness in this South Indian cohort.

The risk factors for CAD that are unique to Asian Indians are low HDL cholesterol (good cholesterol), high LDL cholesterol (bad cholesterol), high triglycerides, central obesity-Insulin resistance syndrome.

It was found from many studies that

1. Asian Indians have the highest risk of CAD and it also starts at an early age.
2. The hospitalization rate of CAD among Asian Indians in US is 4 times higher than Caucasians, Japanese and Filipinos and 5 times higher than Chinese.
3. Asian Indian women are also at high risk of CAD and its sequel.
4. Earliest identification and aggressive treatment of CAD is very important to prevent morbidity and mortality that results from this major killer disease.

So, the challenge for all health care professionals is to implement a comprehensive method for identification of initial atherosclerotic events in high risk patients and also in general public so that more vigorous preventive measures can be taken. For this, various non-invasive markers of early arterial wall alteration are currently available such as the arterial wall thickening and stiffening, endothelial dysfunction and coronary artery calcification. Of them, Intima media thickness (IMT) of large artery walls, especially carotid, can be assessed by B-Mode ultrasound in a relatively simple way and represents a safe, inexpensive, precise and reproducible measure.

Intima media thickness [IMT] is thus far the best-studied sonographic parameter. An increase in IMT in relation to vascular risk factors or manifestation of atherosclerosis has been demonstrated many times. In clinical practice the measurement of Intima media thickness [IMT] is done as a routine investigation.

Kablak-Ziembicka *et al.* concluded that IMT increases with advancing CAD, patients with mean IMT over 1.15 mm have a 94% likelihood of having CAD, and the coexistence of CAD with severe stenosis of aortic arch arteries is relatively high and was found in 16.6% of patients with three vessel CAD.

The predictive value of Intima media thickness [IMT] with regards to cardiovascular complications has been established in several prospective studies and suggests that the intima media thickness [IMT] measurement might participate in future in the stratification of cardiovascular risk of asymptomatic patients in primary prevention.

Increased IMT complex reflects overall generalized atherosclerosis. The same applies to CCA distensibility, which diminishes with increasing severity of atherosclerosis. A correlation between Intima media thickness [IMT], distensibility, and atherosclerosis have recently been shown. Measurement of Intima media thickness [IMT] enabled a better discrimination of high- and low-risk patients compared with distensibility.

In contrast, the Resistive index (RI) according to Pourcelot is a hemodynamic parameter that basically reflects vascular resistance and is easily determined by Doppler sonography. In the renal arteries, the Resistive index [RI] has been studied thoroughly as a surrogate marker of atherosclerotic alterations. Ishimura *et al.* previously demonstrated correlation between the Intima media thickness [IMT] of the CCA and the Resistive index [RI] in the renal parenchyma.

The CCA is suitable for such examinations since the Doppler sonographic properties of CCA are similar to those of renal arteries like low-resistance bed to a highly constant Resistive index. This relationship could indicate that the Resistive index [RI] of CCA could be used to assess atherosclerosis and many studies has addressed the possible correlation between carotid RI and the degree of atherosclerosis. The drawback of measuring only the intima media thickness [IMT] measurement is that it is more prone for intraobserver and interobserver variability and the marked side differences that increase with higher values.

However, this is not the problem with the intima media thickness [IMT] combined with Resistive index [RI]. Because, when the resistive index [RI] and Intima media thickness [IMT] measurements are compared, the essential advantages of the former are; the easier data acquisition by the use of simple duplex apparatus, the tendency to have less interobserver and intraobserver variability and the smaller side difference.

Our study included a total of 50 subjects, which were grouped into two; hypertensive and normotensive group. Hypertensives were the patients attending the outpatient of medicine department for follow-up and without any symptoms. The normotensives were the patient’s relatives, students and clinical staff. We investigated them to rule out the presence of other risk factor for atherosclerosis. Patients with other known risk factor for atherosclerosis and secondary hypertension were excluded from the study. Both groups were comparable to each other in age, sex, BMI, heart rate and the absence of other predisposing factors for atherosclerosis. However, systolic blood pressure, diastolic blood pressure and mean arterial pressure, LDL cholesterol and Triglyceride level was significantly higher in hypertensive patients. We examined bilateral common carotid arteries of all patients with duplex sonography and Intima media thickness [IMT] and Resistive index [RI] were assessed.

By measuring Intima media thickness [IMT] and Resistive index [RI] we assessed both morphological and hemodynamic [physiological] changes. We assessed Intima media thickness [IMT] from the distal common carotid artery proximal to carotid bulb. Although, some authors have found an even better correlation with the degree of atherosclerosis when using Intima media thickness [IMT] values for the combination of ICA and CCA values, we have restricted ourselves to the determination of Intima media thickness [IMT] in the CCA. Because the intima media thickness [IMT] measurements in the ICA have a massive scatter and Intima media thickness [IMT] measurement of CCA is easier to obtain, more reliable, and have been proved by many studies. Resistive index [RI] was also assessed at the same site. The results obtained were analyzed statistically.

The results got in our study definitely showed that there is highly significant [P<0.001] increased in Intima media thickness [IMT] and Resistive index [RI] of CCA in hypertensives compared with normotensive.

The Pearson correlation test was used to show the relationship between blood pressure parameters [SBP, DBP and MAP] with Intima media thickness [IMT] and Resistive index [RI] values of CCA. It showed highly significant [significance at 1%] relationship between hypertension and Intima media thickness [IMT] and Resistive index [RI] values of CCA. The results of our study closely correlate with the results of other previous studies.

In our study, the mean Intima media thickness [IMT] measurement in hypertensives was 1.00± 0.096 with a P value of <0.01. The mean Resistive index [RI] in hypertensives in their study was 0.699+/-0.143 and in our study, the mean value in hypertensives was 0.679± 0.032 with the P value of <0.01 [highly significant]. Our study showed significantly higher LDL and triglyceride levels in hypertensives, which was also seen in their study. The role of hypertension in the development of LDL cholesterol and triglycerides mediated atherosclerosis measured by Common carotid artery Intima media thickness [IMT] was confirmed by the study of Sun *et al.* in 2000. They observed that elevated LDL cholesterol and triglycerides were associated with increased IMT in higher blood pressure after adjustment for the other risk factors. This supports the response-to-injury model of hypertension-induced atherosclerosis. Another explanation for the Intima media thickness [IMT] thickening along with increased LDL cholesterol and triglyceride levels occurring in hypertensives was suggested to be adaptive thickening of the intima and the media. Such thickening is characterized by remodelling to counteract the rise in wall tension observed as medial hypertrophy in the presence of hypertension. In contrast, maladaptive thickening involving monocyte recruitment and lipid accumulation in the intima occurs in the high BP trial group, in which endothelial damage is more likely to be sufficient to initiate atherogenesis.

These findings were supported in the ACAPS study, where the effect of the lipid-lowering lovastatin intervention was larger in hypertensive patients than in the non hypertensive group.

CONCLUSION

The carotid arteries are among the vessels that are prone to develop atherosclerotic lesions in the presence of risk factors for example hypertension. Atherosclerotic plaques start in the Carotids at approximately coinciding as in the aorta, actually preceding the Plaque occurrence in coronary arteries.

Ultrasonography is an easy, safe accurate, quick and inexpensive method of investigation of vessel wall changes in atherosclerosis. An increase in thickness of the Intima media complex is said to anticipate the earliest morphological changes that occur in the vessel distinguish atherosclerosis. These changes credible, clearly visualized with high-resolution sonography and Intima media thickness [IMT] conceivable accurately measured. Alteration in the vessel wall also causes alteration in hemodynamic of the vascular system.

High-resolution sonography using extremely high frequency transducers gives a superb resolution of vessel wall layers, namely, intima, media and adventitia conceivable clearly visualized. Color Doppler gives accurate hemodynamic information within the blood vessels. Resistive index [RI] is the most widely studied hemodynamic parameter that shows alteration in its value again Intima media thickness [IMT] as the atherosclerosis progresses.

So, IMT gives morphological information and RI gives hemodynamic information in atherosclerosis of the blood vessels. Moreover, when both parameters are studied together they are less prone for interobserver and intraobserver variability and will be more accurate.

Our study revealed that IMT and RI of CCA were significantly increased in all hypertensive patients compared to normotensive, and it is ideal to assess both IMT and RI together. IMT gives morphological information and RI gives hemodynamic information in atherosclerosis of the blood vessels. When both parameters are studied together they are less prone for interobserver and intraobserver variability and will be more accurate.

Our study showed that extremely high frequency ultrasound and Color Doppler perhaps effectively common study both IMT and RI of CCA together which are significantly increased in hypertensive patients. Our study results closely correlate with the results of previous Indian and Western studies and show full is ideal to assess both IMT and RI together.

Early identification of atherosclerosis using these parameters should prompt early incorporation of lifestyle modification in these patients, which would definitely help in reducing the cardiovascular mortality.

SUMMARY

Hypertension is one of the most important and independent risk factor atherosclerotic changes in the vascular system of human body. Elevated blood pressure is one of the major killers throughout the world and Asians are more prone for atherosclerosis compared to western world. So, it's very important to implement a comprehensive method for early identification of atherosclerotic changes in high risk patients and also in general population so that early preventive measures can be taken. Various non-invasive markers of early arterial wall alteration are currently available. Of them, Intima-media thickness (IMT) and Resistive index (RI) of large artery walls, especially carotid are the important parameters that can be assessed by Duplex sonography in a relatively simple way and represents a safe, inexpensive, precise and reproducible measure. Intima-media thickness [IMT] as morphological value and Resistive index [RI] as a hemodynamic value reflects the atherosclerotic process in an indirect manner and these can be assessed as a surrogate marker of generalized atherosclerosis. In our study these parameters were assessed in Common carotid arteries of hypertensives and normotensives, and the results were compared. Results showed statistically significant increase in Intima media thickness [IMT] and Resistive index [RI] values in hypertensives compared to normotensives as concluded by other previous Indian and foreign studies.

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