Chapter One

INTRODUCTION

1.1 Introduction

Diabetes Mellitus (DM) is define as a chronic disease that occur when the pancreas is deficient of insulin or does not produce enough insulin or alternatively when the body cannot effectively use the produced insulin. Insulin is a hormone that regulate blood glucose concentration. Raised blood glucose levels (Hyperglycemia), is a common effect of uncontrolled diabetes and which over times lead to a serious damage to many systems of the body, especially nerves, eyes, kidneys and blood vessels. (www.who.int/mediacenter/factsheets/fs312/en/index.html, 7.11.15)

The number of people with DM is increasing worldwide due to population growth, aging, urbanization, lifestyle modifications and increasing prevalence of obesity and physical inactivity. (www.who.int/mediacenter/factsheets/fs312/en/index.html, 7.11.15)

There are 2 types of Diabetic mellitus:-

Type 1 DM (childhood diabetes – Insulin dependents DM), is characterized by a lack of insulin production, without daily administration of insulin type 1 diabetes is rapidly fatal. The symptoms of type 1 DM include excessive excretion of urine (polyuria), thirsty (polydipsia), constant hunger, weight loss, vision changes and fatigue causing insulin resistance (reduced insulin action). (www.care.diabetesjournal.org, access, 7.11.15)

Type 2 DM (adulthood diabetes or non-Insulin dependents DM), result from insufficient insulin or ineffective of insulin by body's tissues. It is comprises 90% of people with diabetes worldwide and largely triggered by excess body weight and physical inactivity. The symptoms of type 2 DM

similar as Type 1 but often less marker, it may diagnosed several years after onset and it always described in adults but may affect obese children (*Kitabchi et al 2009).*

The classic symptoms of untreated of diabetes mellitus are weight loss, polyuria (increased urination), polydipsia (increased thirsty) and polyphagia (increased hunger). There are some signs and symptoms not specific only to the diabetes mellitus and can make the onset of diabetes mellitus such as blurry vision, headache, slow healing of cuts and itchy skins (www.idf.org/defult/files).

Long term complication of diabetes mellitus include retinopathy with potential loss of vision, nephropathy leading of renal failure, peripheral neveropathy with risk of the foot ulcers, cardiovascular disease and sexual dysfunction (www.idf.org/defult/files).

Diabetes mellitus diagnose by laboratory test by two steps, the first one known as random test or non- fasting test in which the normal level sugar in the blood between 70-----180mm/l, and the second one is fasting test between 70----126mm/l (www.idf.org/defult/files).

The prevention and treatment of diabetes mellitus involve a healthy diet, physical exercise, maintaining a normal body weight and avoiding use of tobacco, diabetes mellitus type one is managed with insulin injection when type two is treated with medication with or without insulin.

Diabetes mellitus consider as vascular disease because of its effect on blood vessels endothelial wall, high blood glucose level over long times lead to damage of the blood vessels (www.idf.org/defult/files).

Cardiovascular disease (CVD) is a group of conditions that include heart disease, stroke and all others diseases of hearts and the arteries, CVD

caused by the buildup of fatty material called atheroma in the main body arteries and lead to narrowing and becoming blocked (atherosclerosis). If the atherosclerosis occur in the coronary artery can cause angina and in severe cases heart attacks and in carotid artery cause stroke (www.merk.com, 12.1.016).

Stroke occur when a waxy substance called plaque builds up inside the carotid artery over time plaque hardens and narrowing and develop to occlusion and cut of the blood to brain cells, when blood cuts for a few minutes, the cells in the brain start to die and this impairs the parts of the body that the brain cells control. Stroke can cause lasting brain damage, long – term disability such as vision, speech problems and paralysis or death (www.merk.com, 12.7.015). Currently DM has reaches epidemic proportions, the World Health Organization (WHO), predict that the current diabetic population of 177 million (estimate 2000), it will increase to 370 million by year 2030, another study has estimated an increase to 2.8% in 2000, raised to 6.4% in 2010 with projection of rise to 7.7% in 2030, from 2012 to 2014 is estimated the mortality of DM is a rise from 1.5 to 4.9 million deaths (www.reproprint.se, access on 12.7.015).

DM is associated with significant morbidity, mortality and economic consequence, in 2002 the USA, the costs associated with diabetes were estimated at 132 billion USD, and data from more than 7000 patients from eight European countries indicate that the mean cost per patients with diabetes was 2928 USD, annually (www.reproprint.se, access on 12.7.015).

The prevalence and incidence rates of DM in Sudan was found 5.5% in northern states and 8% in the capital Khartoum state and it was particularly

high 10.8% in certain community in north states patients. (www.reproprint.se, access on 12.7.015).

The annual costs of DM, in Sudan during childhood was 380 USD, per diabetic child, of which 36% was spent on insulin and for adult 300 USD, which include the costs of drugs and ambulatory care, these costs represents 23% and 9% of incomes of families of the diabetic children and adult patients respectively (www.reproprint.se, access on 12.7.015).

Atherosclerotic carotid arterial disease, account for 15% of all ischemic stroke and TIA, the incidence of carotid artery stenosis for 13 per 100.000 strokes (http://radiopaedia.org, access on 12.7.015).

In human anatomy, the common carotid artery is an artery that supplies the head and neck with oxygenated blood, it divides in the neck to form the internal and external arteries (Ashrafian, 2007).

The left common carotid artery arises from the highest point of the aortic arch, whereas the right common carotid artery arises from the bifurcation of the brachiocephalic (innominate) artery. Both common carotid arteries usually terminate at the upper border of the thyroid cartilage where they bifurcate into internal and external carotid arteries. This bifurcation may occur at a higher or lower level (i.e. close to the mandible or clavicle respectively. The common carotid arteries are posterolateral to the lateral lobes of the thyroid gland and are medial to the internal jugular veins. The common carotid arteries diverge as they ascend along the trachea, thyroid gland and pharynx. They dilate at their bifurcation to form the carotid bulb (Corbett et al, 2005).

Carotid Doppler ultrasound scanning is a painless procedure that measures the amount of blood flow in the carotid arteries with non-invasive procedure and no patient preparation.

It‘s performed with patient lying in the supine position on an examination table, with examiner seated at the patients, the patients head is placed on a small round pad and turned slightly away from the side being scanned. After applying ultrasound gel to the neck, the transducer is placed midway between the clavicle and angle of the law in a transducer plane. The common carotid artery is located and is followed as far as the clavicle will permit (Gilani, 2003).

1.2 Problem of the study:

Diabetes mellitus is consider as a disease of the century, it is spread cross worldwide threaten the people and has high economic costs with dangerous risk to human kinds, because it increase the number of mortality rates due to a serious disease related directly to its impact in the body organ such as stroke, heart disease (angina, heart attack), foot ulcer and arteries/veins diseases (slow blood flow, arteries blockage, blood clot and ischemic disease). The serious risk of diabetes mellitus associated with lack of knowledge for experimental information related to Doppler ultrasound finding of diabetes patients.

1.3 Hypothesis:

Diabetes mellitus is associated with carotid artery intima-media thickening as early indicator of stenotic risk to carotid artery, beside Resistivity Index (RI), Palsatility Index (PI), peak systolic velocity (PSV) and end diastolic velocity (EDV), could show significant changes in common carotid arteries dependent to diabetes mellitus status. The ultrasound brightness mode (B-mode) and pulse wave (PW) Doppler could be used as a couple models for determination of carotid arteries stenotic degree and blood flow velocities.

1.4 Objective of the study:

- To investigate the value of the color Doppler Sonography in detection atherosclerosis of carotid arteries in diabetes mellitus patients.

- To correlate the carotid intima-media thickness (IMT) in diabetic patients.

- To correlate diabetes mellitus duration and carotid arteries diseases.

- To determine the PSV, EDV, RI and ratio of PSV/EDV in the carotid arteries for diabetic patients.

- To compare the results of the study with those available in the literature.

1.5 Thesis outlines:

This thesis will be consists of five chapters. Chapter one will deal with introduction, problems of the study, hypothesis and objectives. Chapter two will shows the literature review, theory of the study and previous studies. Chapter three will shows the methodology of the study. Chapter four will deals with Results and discussion and chapter five will show the conclusion, recommendations, references and appendices.

Chapter Two

Literature Review

Section One

2.1.1 Anatomy

There are six carotid arteries, three in each side of the neck: right and left common carotid arteries, right and left internal carotid arteries and right and left external carotid arteries. The carotid arteries deliver oxygen- rich blood from the heart to the head and brain (Adam, 2010).

Carotid artery is one of several arteries that supply blood to the head and neck. The two common carotid arteries, extend head ward on each side of the neck, the left originates from the arch of the aorta over the heart and the right originates from the brachiocephalic trunk, which is largest branch arise from the right arch of the aorta. Each common carotid artery divides into an external and an internal carotid artery. Each internal carotid artery ascends through the carotid canal in the temporal bone into the cranial cavity. It gives off an ophthalmic branch to eyeball and other contents of the orbit and then divides into the anterior and middle cerebral arteries. The internal carotid arteries, with the vertebral arteries, which are the arteries of primary supply for the brain, are distinguished by lying at some depth from the surface in their course to the organ, by having curves or twists in their course, and by having no larger collateral branches (Britannica, 2010).

The external carotid artery ascends through the upper part of the side of the neck and behind the lower jaw into the parotid gland, where it divides into various branches. The external carotid artery gives off the following

branches: superior thyroid artery to the larynx and thyroid gland, lingual to the tongue and sublingual gland, facial artery to the face, palate, tonsil and sub maxillary gland, occipital artery to the sternomastoid muscle and back of the scalp, posterior auricular artery to the back of the ear and the adjacent part of the scalp, superficial temporal artery to the scalp in the front of the ear and by its transverse facial branch, to the back part of the face, maxillary artery giving muscular branches to the muscles of mastication, meningeal to the dura mater, dental to the teeth and other branches to the nose, palate and tympanum and ascending pharyngeal artery which supplies the pharynx, palate, tonsils and dura mater (Britannica, 2010).

The principal arteries that supply the head and neck are the two common carotid arteries, they ascends in the neck and each divides into two branches, the external carotid artery exterior of the head, the face and the greater part of the neck and the internal carotid supplying to a great extent the parts within the cranial and orbital cavities (Drake et al, 2007).

2.1.2 Arteries:

Arteries are efferent vessels that transport blood away from the heart to the capillary beds. The two major arteries that arise from the right and left ventricles of the heart are the pulmonary trunk and the aorta, respectively. The pulmonary trunk branches, shortly after exiting the heart divided into right and left pulmonary arteries that enter the lungs for distribution. The right and left coronary arteries, which supply the heart muscle, arise from the aorta as it exits the left ventricle (Gartner and Hiatt, 2001).

The aorta, upon leaving the heart course in an oblique posterior arch to descend in the thoracic cavity, where it sends branches to the body wall and viscera, it then enters the abdominal iliac arteries in the pelvic. Three major arterial trunks, the right brachiocephalic artery, the left common

carotid artery and the left subclavian artery arise from the arch of the aorta to supply the superior extremities and the head and neck continued branching of all these arteries into large numbers of smaller and smaller arteries continues until the vessel walls contain a single layer of endothelial cells. The resulting vessels, called capillaries, are the smallest functional vascular elements of the cardiovascular system (Gartner and Hiatt, 2001).

2.1.3 Classification of arteries

Arteries are classified into three major types based on their relative size, morphological characteristics, or both as shown in table 2.1 and figure 2.1. From largest to smallest, they are as follows:

1. Elastic (conducting) arteries.
2. Muscular (distributing).
3. Arterioles.

Table 2.1 illustrates the characteristics of various types of arteries (Gartner and Hiatt, 2001).

Artery	Tunica intima	Tunica media	Tunica adventitia
Elastic artery (conducting) (e.g., aorta)	Endothelium with Weibel-palade bodies, basal lamina, subendothelial layer, incomplete internal elastic lamina	40-70 fenestrated elastic membranes, smooth muscle cells interspersed between elastic membranes, thin external elastic lamina vasa vasorum in outer half.	The layer of fibroelastic connective tissue, vas vasorum, lymphatic vessels, nerve fibers.

Muscle artery (distributing) (e.g., femoral artery)	Endothelium with Weibel-palade bodies, basal lamina, subendothelial layer, thick internal elastic lamina	Up to 40 layers of smooth muscle cells, thick external elastic lamina.	Thin layer of fibroelastic connective tissue, vasa vasorum not very prominent, lymphatic vessels, nerve fibers
Arteriole	Endothelium with Weibel-palade bodies, basal lamina, subendothelial layer not very prominent, some elastic fibers instead of a defined internal elastic lamina	One or two layers of smooth muscle cells	Loose connective tissue, fibers.
Metarteriole	Endothelium, basal lamina	Smooth muscle cells form precapillary sphincter	Sparse, loose connective tissue

2.1.4 General structure of blood vessels:

Most blood vessels have several features that are structurally similar, although dissimilarities exist and are the bases for classifying the vessels into different identifiable groups. For example, the walls of high pressure vessels (e.g., subclavian arteries) are thicker than vessels conducting blood at low pressure (e.g., subclavian veins). However, arterial diameters continue to decrease at each branching, whereas vein diameters increase at each convergence, thus altering the respective layers of the wall of the vessels. Therefore, the descriptions used as distinguishing characteristics for a particular type of artery or vein are not always absolute. Indeed, the

walls of the capillaries and venules are completely modified and less complex compared with those in larger vessels. Generally, arteries have thicker walls and are smaller in diameter than are the corresponding veins. Moreover, in histological sections, arteries are round and usually have no blood in their lumina (Gartner and Hiatt, 2001).

Three separate concentric layers of tissues or tunicas make up the wall of the typical blood vessel as shown in figure 2.2. The inner most layer is the tunica intima, which is composed of single layer of flattened, squamous endothelial cells, which form a tube lining the lumen of the vessel, and the underlying subendothelial connective tissue. The intermediate layer is the tunica media, which is composed mostly of smooth muscle cells oriented concentrically around the lumen. The outer most layer is the tunica adventitia, which is composed mainly of fibroelastic connective tissue arranged longitudinally. The tunica intima houses in its outer mostly layer the internal elastic lamina, a thin band of elastic fibers that is well developed in medium sized arteries. The outer most layer of elastic fibers is external elastic lamina, which is not distinguishable in all arteries (Gartner and Hiatt, 2001).

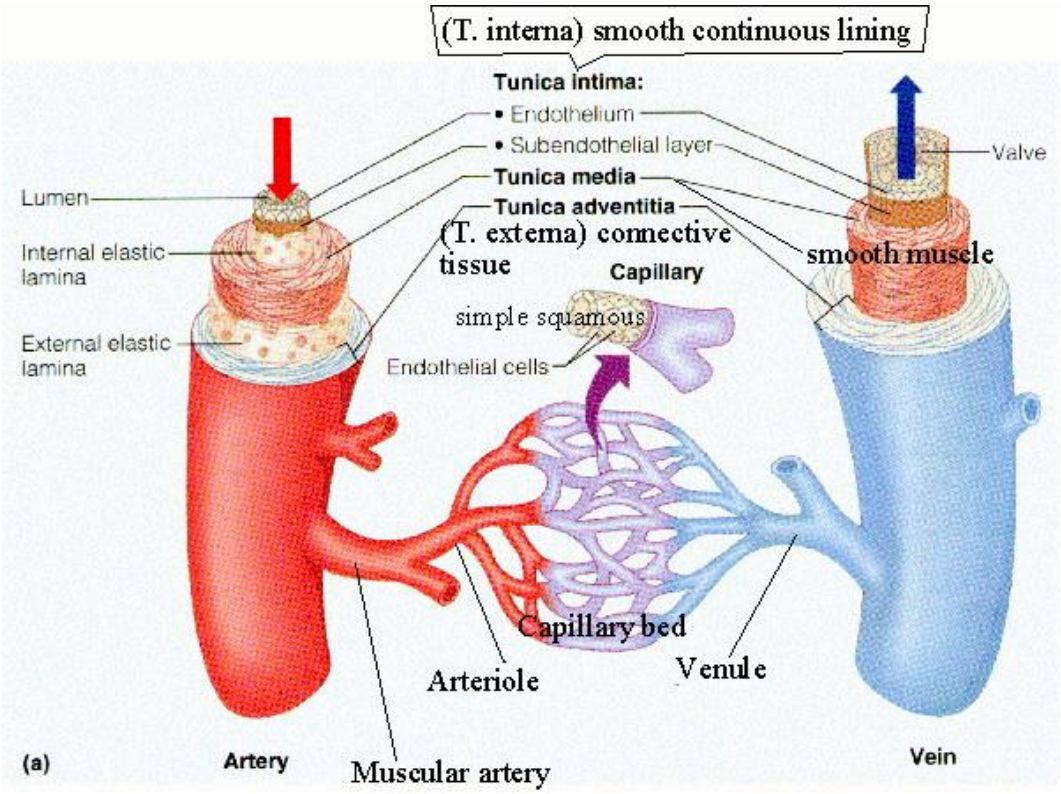


Figure 2.1 demonstrate diagram of a typical artery (www.pinterest.com, access 2.4.015).

2.1.5 Tunica intima:

The endothelial cells, simple squamous epithelium lining the lumen of the blood vessel rest on the basal lamina, These flattened cells are elongated into a sheet such that their long axis of the vessel, which nearly permits each endothelial cell to surround the lumen of a small caliber vessel. In larger bore vessels, several too many individual endothelial cells are required to line the circumference of the lumen. A subendothelial layer lies immediately beneath the endothelial cells, both arranged longitudinally, beneath the subendothelial layer is an internal elastic lamina that is especially well developed in muscular arteries. Separating elastic lamina is composed of elastin, which is a fenestrated sheet that permits the diffusion of substances into the deeper regions of the arterial wall to nourish the cells there (Gartner Hiatt, 2001).

2.1.6 Tunica media:

The tunica media is the thickest layer of the vessel. The concentric cell layer forming the tunica media comprise mostly helically arranged smooth muscle cells. Interspersed within the layers of smooth muscle are some elastic fibers, type III collagen, and proteoglycans. The fibrous elements form lamellae within the ground substance secreted by smooth muscle cells. Larger muscular arteries have an external elastic lamina, which is more delicate than the internal elastic lamina and separates the tunica media from overlying tunica adventitia (Gartner Hiatt, 2001).

Intima-media thickness is defined as a double-line pattern visualized on both walls of the CCAs in a longitudinal echographic image. It is formed by two parallel lines, which represent the leading edges of two anatomic boundaries: the lumen-intima and media-adventitia interfaces (Edoardo et al, 2007).

2.1.7 Tunica Adventitia

Covering the vessel on their outside surface is the tunica adventitia, composed mostly of fibroblasts, type I collagen fibers, and longitudinally oriented elastic fibers. This layer becomes continuous with the connective tissue elements surrounding the vessel (Gartner Hiatt, 2001).

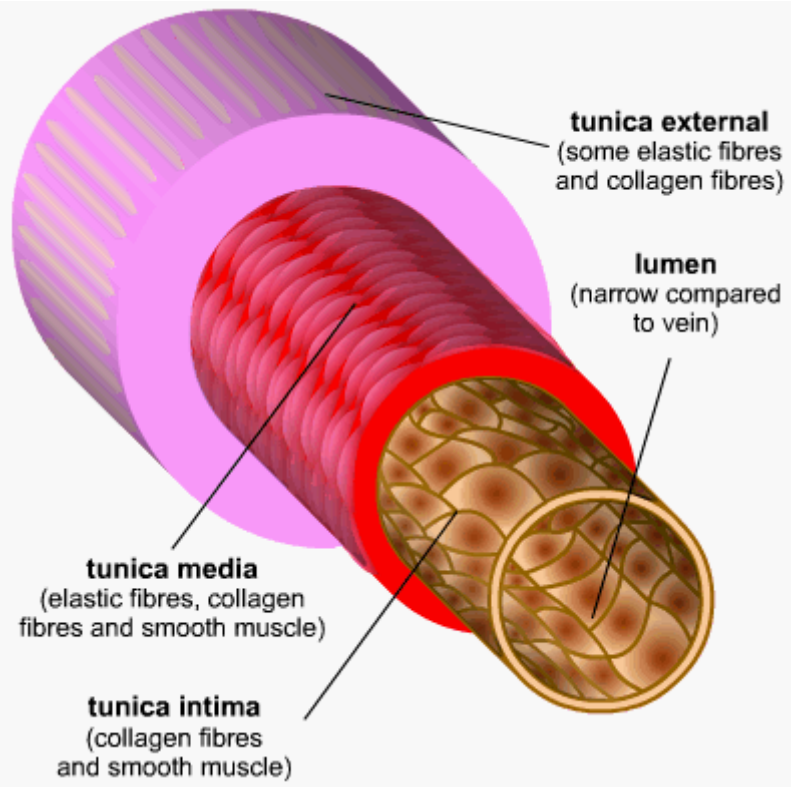


Figure 2.2 shows the three layers of artery (www.s-cool.co.uk, access on 2.4.015)

2.1.8 The common carotid artery

The common carotid arteries differ in length and in their mode of the origin. As shown in Figure 2.3, the right begins at the bifurcation of the innominate artery behind the sternoclavicular joint and is confined to the neck. The left springs from the highest part of the arch of the aorta to the left of, and on a plane posterior the innominate artery, and therefore consists of a thoracic and cervical portion. The thoracic portion of the left common carotid artery ascends from the arch of the aorta through the superior mediastinum to the level of the left sternoclavicular joint, where it is continuous with the cervical portion (Drake et al, 2007).

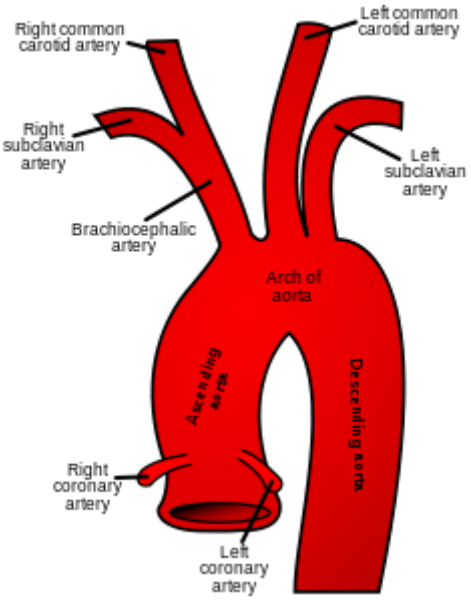


Figure 2.3 demonstrate the origin of the common carotid arteries (www.en.wikipedia.org, access on 2.4.015).

2.1.9 The common carotid artery relations:

In front, it is separate from the manubrium sterni by the Sternohyoideus and Sternothyreoideus, the anterior portions of the left pleura and lung, the left innominate vein, and remains of the thymus, behind, it lies on the trachea, esophagus, left recurrent nerve and thoracic duct. To its right side below is innominate artery, and above the trachea, the inferior thyroid veins and remains of the thymus, to its left side are the left vagus and phrenic nerves, left pleura and lung. The left subclavian artery is posterior and slightly lateral to it. The cervical portions of the common carotids resemble each other so closely that one description will apply to both as illustrate in Figure 2.4, below:

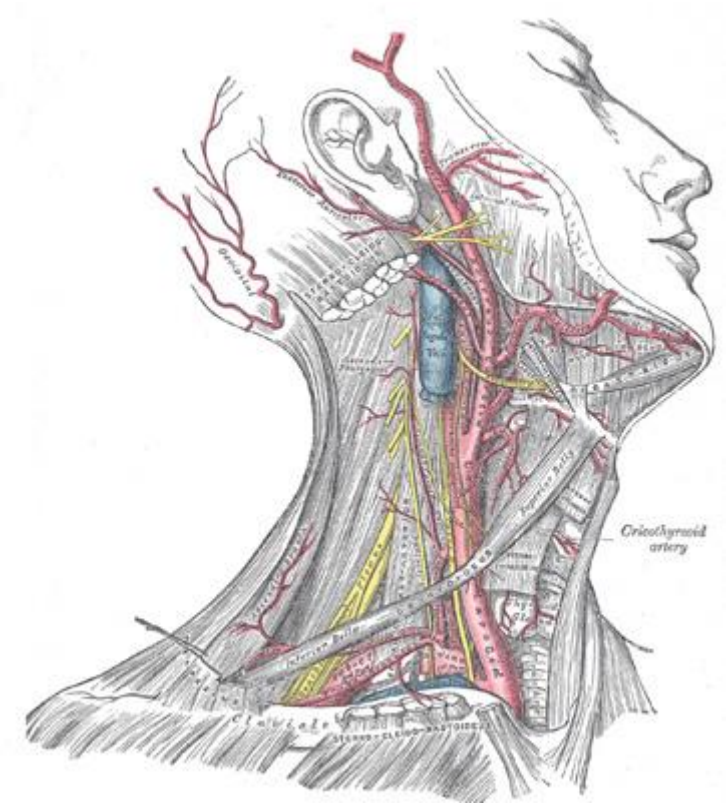


Figure 2.4, Shows superficial dissection of the right side of the neck, showing the carotid and subclavian arteries (www.education.yahoo.com, access on 2.4.015).

Each vessel passes obliquely upward, from behind the sternoclavicular, to the level of the upper border of the thyroid cartilage, where it divides into the external and internal carotid arteries. At the lower part of the neck the two common carotid arteries are separated from each other by a very narrow interval which contains the trachea, but at the upper part the thyroid gland, the larynx and pharynx project forward between the two vessels. The common carotid artery is contained in a sheath, which is derived from the deep cervical fascia and encloses also the internal jugular vein and vagus nerve, the vein lying laterally to the artery, and the nerve between the artery and vein, on a plane posterior to both. On an opening sheath, each of these three structures is seen to have a fibrous investment (Drake et al, 2007).

At the lower part of the neck, the common carotid artery is very deeply seated, being covered by the integument, superficial fascia, platysma, and deep cervical fascia, the sternocleido-mastoieus, Stemohyreoideus and Omohyoideus, in the upper part of its course it is more superficial, being covered merely by the integument, the superficial fascia, platysma, deep cervical fascia, and medial margin of the Sternocleidomastoideus. When the latter muscle is drawn backward, the artery is seen to be contained in a triangular space, the carotid triangle, bounded behind by the Sternocleidomastoideus, above by the Styohyoideus and posterior belly of the Digastricus, and below by the superior belly Omohyoideus. This part of the artery is crossed obliquely, from its medial to its lateral side, by the sternocleidomastoid branch of the superior thyroid artery, it is also crossed by the superior and middle thyroid veins which end in the internal jugular, descending in front of its sheath is the descending branch of the hypoglossal nerve, this filament being joined by one or two branches from the cervical nerves, which cross the vessel obliquely. Sometimes the descending branch of the hypoglossal nerve is contained within the sheath. The superior thyroid vein crosses the artery near its termination, and the middle thyroid vein a little below the level of the cricoid cartilage; the anterior jugular vein crosses the artery just above the clavicle, but is separated from it by the Sternohyoideus and Sternothyreoideus. Behind the artery is separated from the transverse processes of the cervical vertebrae by the Longus coli and Longus capitis, the sympathetic trunk being interposed between it and the muscles. The inferior thyroid artery crosses behind the lower part of the vessel. Medially it is in relation with esophagus, trachea and thyroid gland which overlaps it, the inferior thyroid artery and recurrent nerve being interposed; higher up with the larynx and pharynx. Lateral to the artery are the internal jugular vein and vagus nerve. At the lower part of the neck, the right internal jugular vein diverges from

the artery, but the left approaches and often overlaps the lower part of the artery. Behind the angle of the bifurcation of the common carotid artery is a reddish-brown oval body, known as the glomus caroticum or carotid body (Drake et al, 2007).

The right common carotid artery may arise above the level of the upper border of the sternoclavicular articulation; this variation occurs in about 12 percent of cases. In other cases the artery may arise as a separate branch from the arch of the aorta, or in conjunction with the left carotid. The left common carotid artery varies from in its origin more than the right. In the majority of abnormal cases it arises with the innominate artery; if that artery is absent, the two carotids arise usually by a single trunk. It is rarely joined with the left subclavian, except in cases of transposition of the aortic arch. In the majority of abnormal cases this occurs higher than usual, the artery dividing opposite or even above the hyoid bone; more rarely it occurs below, opposite the middle of the larynx, or the lower border of the carotid cartilage. Very rarely the common carotid ascends in the nick without any subdivision either the external or the internal carotid being wanting and in a few cases the common carotid has been found to be absent, the external and internal carotids arising directly from the arch of the aorta. This peculiarity existed on both sides in some instances, on one side in others (Drake et al, 2007).

2.1.10 The common carotid artery branches

The common carotid usually gives off no branch previous to its bifurcation, when it divided into ICA and ECA figure 2.5, but it occasionally gives origin to the superior thyroid or its laryngeal branch, the ascending pharyngeal, the inferior thyroid or more rarely, the vertebral artery (Drake et al, 2007).

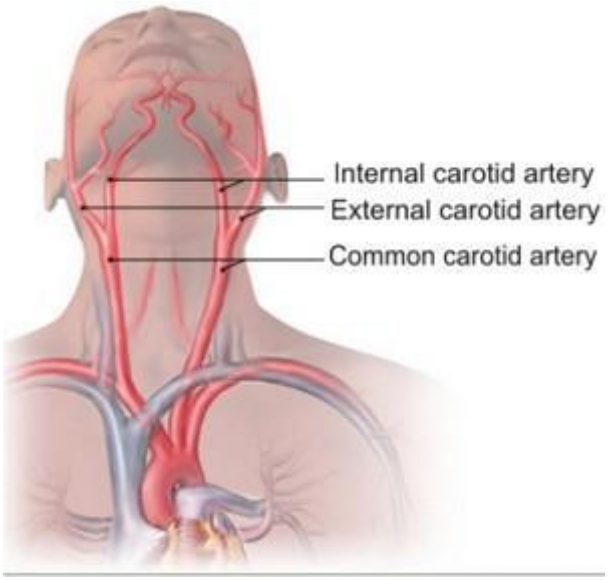


Figure 2.5 shows common carotid and its branches (www.pinterest.com, access on 2.4.015).

2.1.11 Collateral circulation:

After ligature of the common carotid, the collateral circulation can be perfectly established, by the free communication which exists between the carotid arteries of opposite sides, both without and within the cranium, and by enlargement of the branches of the subclavian artery on the side corresponding to that on which the vessel has been tied. The chief communications outside the skull take place between the superior and inferior thyroid arteries, and the profunda cervicis and ramus descends of the occipital, the vertebral takes the place of the internal carotid within the cranium (Drake et al, 2007).

2.1.12 The external carotid artery:

The external carotid artery beings opposite the upper border of the thyroid cartilage and taking a slightly curved course, passes upward and forward and then inclines backward to the space behind the neck of the mandible, where it divides into the superficial temporal and internal maxillary

arteries. It rapidly diminishes in size its course up the neck, owing to the number and large size of the branches given off from it as shown in Figure 2.6. In the child it is somewhat smaller than the internal carotid, but in the adult the two vessels are of nearly equal size. At its origin this artery is more superficial and placed nearer the middle line than the internal carotid and is contained within the carotid triangle (Drake et al, 2007).

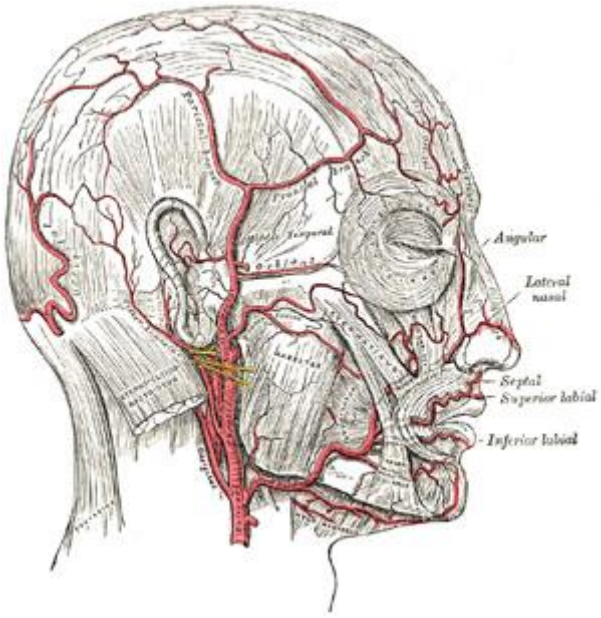


Figure 2.6 illustrates the arteries of the face and scalp related to the external carotid artery (www.education.yahoo.com, 2.4.015).

2.1.13 The external carotid artery relations:

The external carotid artery is covered by the skin, superficial fascia, platysma, deep fascia and anterior margin of the Sternocleidomastoideus; it is crossed by the hypoglossal nerve, by the lingual, ranine, common facial and superior thyroid veins and by the Digastricus and Stylohyoideus, higher up it passes deeply into the substance of the parotid gland, where it lies deep to the facial nerve and junction of the temporal and internal maxillary veins. Medial to it are the hyoid bone, the wall of the pharynx,

the superior laryngeal nerve, and a portion of the parotid gland. Lateral to it, in the lower of the course, is the internal carotid artery. Posterior to it, near its origin, is the superior laryngeal nerve, and higher up, it is separated from the internal carotid by the Styloglossus and Stylopharyngeus, the glossopharyngeal nerve, the pharyngeal branch of the vagus, and part of the parotid gland (Drake et al, 2007).

2.1.14 The external carotid artery branches:

The branches of the external carotid artery as seen in Figure 2.7 may be divided into four sets:

1. The anterior set which includes the superior thyroid artery, lingual artery and external maxillary artery.
2. The posterior set which includes the occipital artery and posterior auricular artery.
3. The ascending set which includes the ascending pharyngeal artery.
4. The terminal set which includes the superficial temporal artery and the internal maxillary artery (Drake et al, 2007).

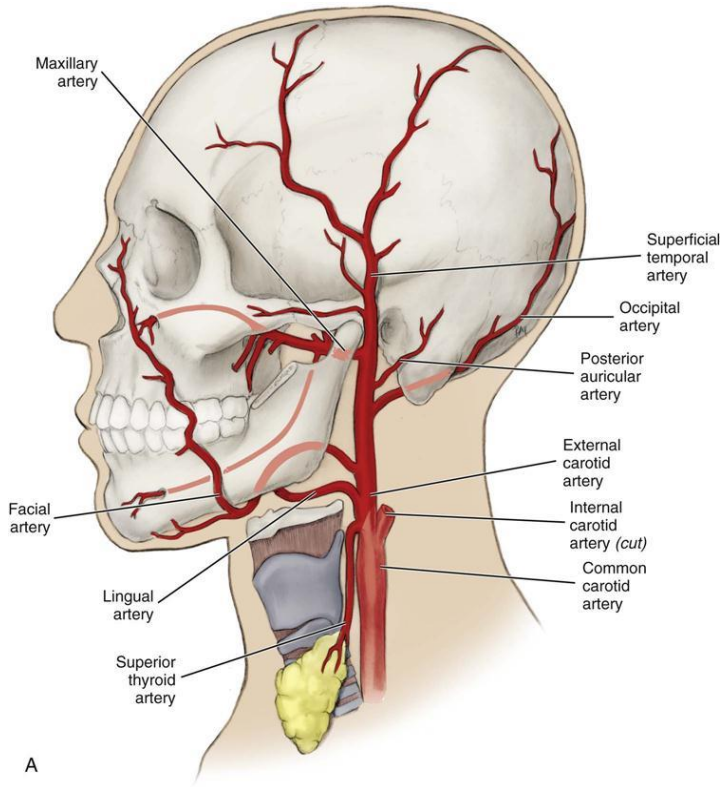


Figure 2.7 shows the branches of the external carotid artery (www. pocketdentistry.com, access on 2.4.015**).**

2.1.15 The internal carotid artery:

The internal carotid artery, Figure 2.8 supplies the anterior part of the brain, the eye and its appendages, and sends branches to the forehead and nose. Its size in the adult is equal to that of the external carotid, though, in the child, it is larger than vessel. It is remarkable for the number of the curvatures that it presents in different parts of its course. It occasionally has one or two flexures near the base of the skull, while in its passage through the carotid canal and long the side of the body of the sphenoid bone it describes a double curvature and resembles the italic letter "S" (Drake et al, 2007).

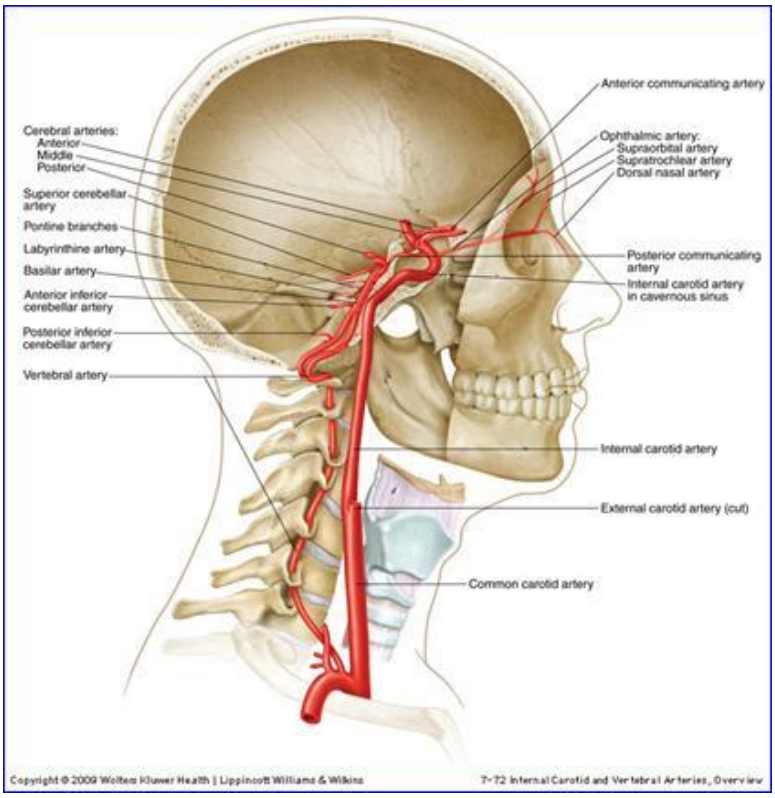


Figure 2.8 determines the internal carotid in the right side of neck (www.duke.edu, access on 2.4.015**).**

2.1.16 The internal carotid artery course and relations:

In considering the course and relations of this vessel it may be divided into four portions: cervical, petrous, cavernous and cerebral as seen in figure 2.9 (Drake et al, 2007).

2.1.17 Cervical portion:

This portion of the internal carotid begins at the bifurcation of the common carotid, opposite the upper border of the thyroid cartilage and runs perpendicularly upward in front of the transverse processes of the upper three cervical vertebrae, to the carotid canal in the petrous portion of the temporal bone. It is comparatively superficial at its commencement, where

it is contained in the carotid triangle and lies behind and lateral to the external carotid, overlapped by the Sternocleidomastoideus, and covered by the deep fascia, platysma and integument, it then passes beneath the parotid gland, being crossed by the hypoglossal nerve, the Digastricus and Stylohyoideus and the occipital and posterior auricular arteries. Higher up it is separated from the external carotid by the Styoglossus and Stylopharyngeus, the tip of the styloid process and the stylohyoid ligament, the glossopharyngeal nerve and pharyngeal branch of the vagus. It is in relation behind with the Longus capitis, the superior cervical ganglion of the sympathetic trunk, and the superior laryngeal nerve, laterally with the internal jugular vein and vagus nerve, the nerve lying on a plane posterior to the artery, medially with the pharynx, superior laryngeal nerve and ascending pharyngeal artery (Drake et al, 2007).

At the base of the skull the glossopharyngeal, vagus, accessory and hypoglossal nerves lie between the artery and the internal jugular vein (Drake et al, 2007).

2.1.18 Petrous portion:

When the internal carotid artery enters the canal in the petrous portion of the temporal bone, it first ascends a short distance, then curves forward and medial ward and again ascends as it leaves the canal to enter the cavity of the skull between the lingual and petrosal process of the sphenoid. The artery lies at first in front of the cochlea and tympanic cavity, from the latter cavity it is separated by a thin bony lamella, which is cribriform in the young subject, and often partly absorbed in old age. Further forward it is separated from the semilunar ganglion by a thin plate of bone which forms the floor of the fossa for the ganglion and the roof of the horizontal portion of the canal. Frequently this bony plate is more or less deficient and then

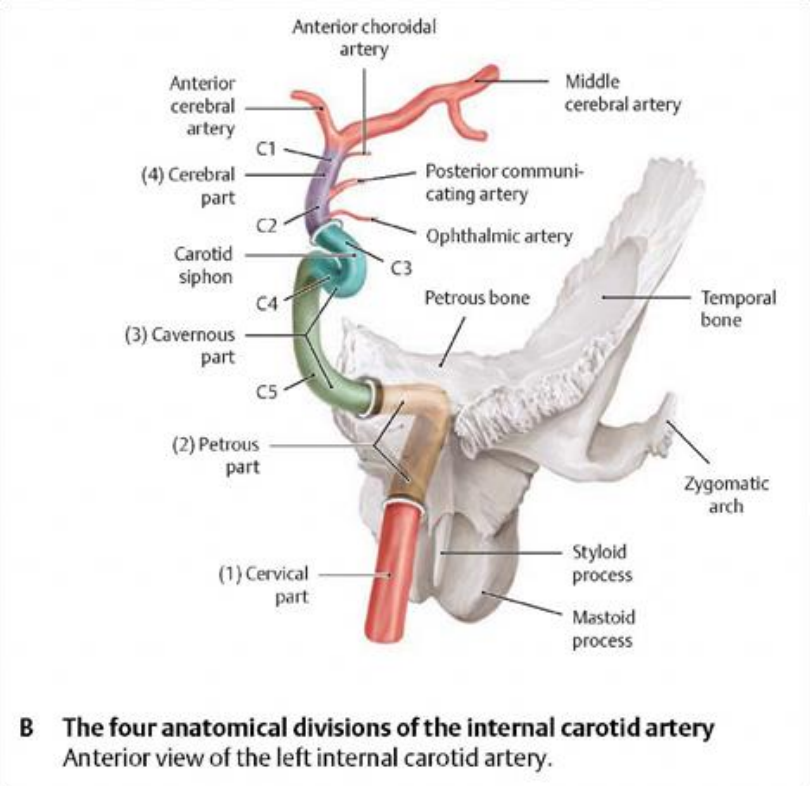
the ganglion is separated from the artery by fibrous membrane. The artery is separated from the bony wall of the carotid canal by a prolongation of dura mater and is surrounded by a number of small veins and by filaments of the carotid plexus derived from the ascending branch of the superior cervical ganglion of the sympathetic trunk (Drake et al, 2007).

2.1.19 Cavernous portion:

In this part of its course, the artery is situated between the layers of the dura mater forming the cavernous sinus, but covered by the lining membrane of the sinus. It at first ascends toward the posterior clinoid process, then passes forward by the side of the body of the sphenoid bone and again curves upward on the medial side of the anterior clinoid process and perforates the dura mater forming the roof of the sinus. This portion of the artery is surrounded by filaments of the sympathetic nerve and on its lateral side is the abducent nerve (Drake et al, 2007).

2.1.20 Cerebral portion:

Having perforated the dura mater on the medial side of the anterior clinoid process, the internal carotid passes between the optic and oculomotor nerves to the anterior perforated substance at the medial extremity of the lateral cerebral fissure, where it gives off its terminal or cerebral branches (Drake et al, 2007).



B The four anatomical divisions of the internal carotid artery
Anterior view of the left internal carotid artery.

Figure 2.9 shows the four anatomical divisions of Lt internal carotid artery (www.sites.google.com, access on 2.4.015).

2.1.21 The internal carotid artery branches:

The cervical portion of the internal carotid gives off no branches. The other portions give off branches as show in Figure 2.10, the branches are:

1. Petrous portion branches are caroticotympanic artery and artery of the pterygoid canal.
2. Cavernous portion branches are cavernous artery, hypophyseal artery semilunar artery, anterior meningeal artery and ophthalmic artery.

3. Cerebral portion branches are anterior cerebral, middle cerebral artery, posterior communication artery and choroidal artery (Drake et al, 2007).

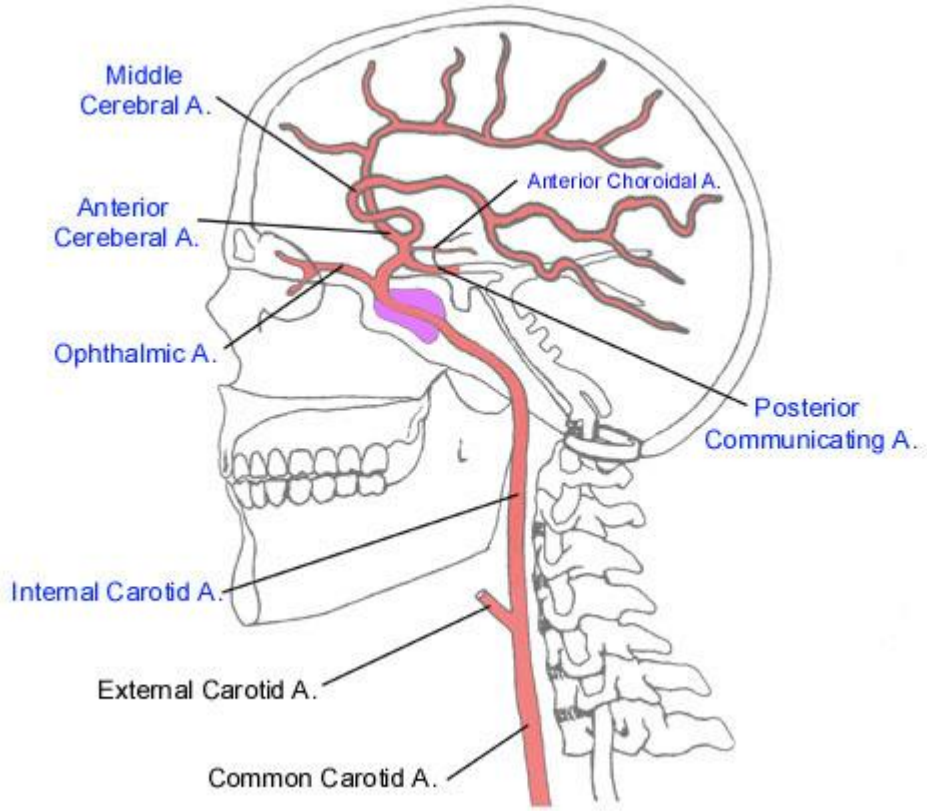


Figure 2.10 shows the branches of internal carotid artery (www.meddean.luc.edu, access on 2.4.015).

2.1.22 The arteries of the brain:

Since the mode of the distribution of the vessels of the brain has an important bearing upon a considerable number of the pathological lesions which may occur in this part of the nervous system, it is important to consider a little more in detail the manner in which the vessels are distributed. The cerebral arteries are derived from the internal carotid and

vertebral, which at the base of the brain from a remarkable anastomosis known as the arterial circle Willis. It is formed in front by the anterior cerebral arteries, branches of the internal carotid, which are connected together by the anterior communicating , behind by the two posterior cerebral arteries, branches of the basilar which are connected on either side with internal carotid by the posterior communicating Figure 2.11 and 2.12. The parts of the brain included within this arterial circle are the lamina terminalis, the optic chiasma, the infundibulum, the tuber cinereum, the corpora mammillaria and the posterior perforated substance (Drake et al, 2007).

The three trunks which together supply each cerebral hemisphere arise from the arterial circle of Willis. From its anterior part proceed the two anterior cerebrals from its antero-lateral parts the middle cerebrals and from its posterior part the posterior cerebrals. Each of these principal arteries gives off origin to two different systems of secondary vessels. One of these is named the ganglionic system and the vessels belonging to it supply the thalami and corpora striata, the other is the carotical system, and its vessels ramify in the pia mater and supply the cortex and subjacent brain substance. These two systems do not communicate at any point of the their peripheral distribution, but are entirely independent of each other and there is between the parts supplies by the two systems a borderland of diminished nutritive activity, where it is softening is especially liable to occur in the brains of old people (Drake et al, 2007).

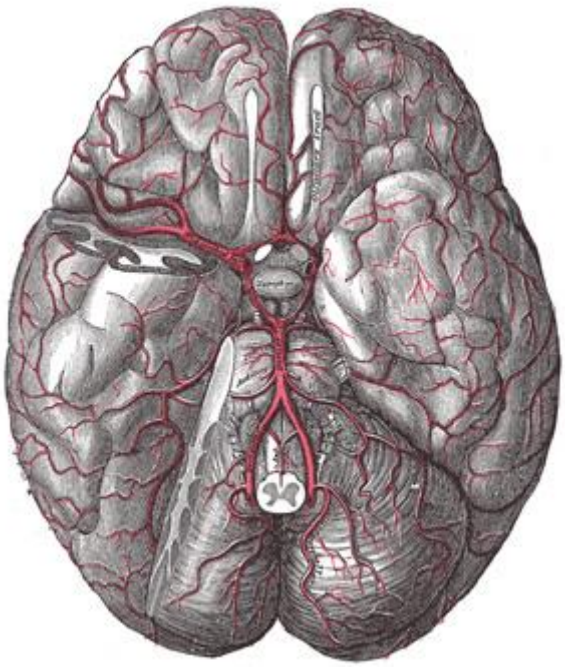


Figure 2.11 shows the arteries of the base of the brain, notice that the temporal pole of the cerebrum and portion of the cerebellar hemisphere have been removed on the right side (www.education.yahoo.com, access on 20.5.015).

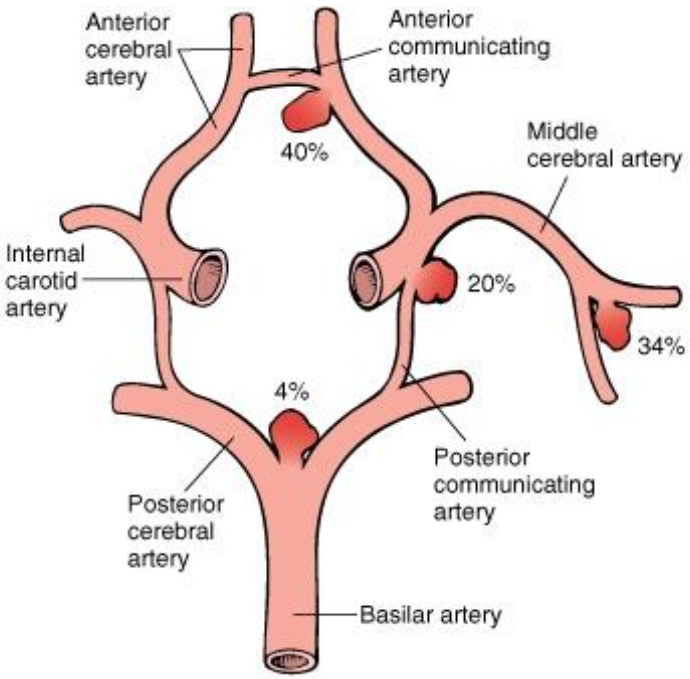


Figure2.12 illustrates the arterial circulation at the base of the brain which known as arterial circle Willis (www.neuroems.com, access on 20.5.015).

2.1.23 The ganglionic system:

All the vessels of this system are given off from the arterial circle of Willis or from the vessels close to it. They form six principal groups, the antero-medial derived from the anterior cerebrals and anterior communicating, the posterior-medial group, derived from the posterior cerebrals and posterior communicating, the right and left antero-lateral groups, derived from the middle cerebrals and the right and left postero-lateral groups, derived from the posterior cerebrals after they have wound around the cerebrals peduncles. The vessels of this system are large than those of the cortical system, vessels which from their origin to their termination neither supply nor receive any anastomotic branch, so that through any one of the vessels only a limited area of the thalamus or corpus striatum can be injected and the injection cannot be driven beyond the area of the part supplied by the particular vessel which is the subject of the experiment (Drake et al, 2007).

2.1.24 The cortical system:

The vessels forming this system are the terminal branches of the anterior, middle and posterior cerebral arteries. They divide and ramify in the substance of the pia mater and give off branches which penetrate the brain cortex perpendicularly. These branches are divisible into two classes along and short. The long or medullary arteries pass through the gray substance and penetrate the subject white substance to the depth 3 or 4 cm, without intercommunicating otherwise than by very fine capillaries and thus constitute so many independent small systems. The short vessels are

confined to the cortex, where they form with long vessels a compact network in the middle zone of the gray substance, the outer and inner zones being sparingly supplied with blood. The vessels of the cortical arterial system are not so strictly terminal as those of the ganglionic system, but they approach are very closely, so that injection of one area from the vessel of another area though possible is frequently very difficult and only is effected through vessels of small caliber. As a result of this obstruction of one of the main branches or its divisions may have the effect of producing softening in a limited area of the cortex (Drake et al, 2007).

2.1.25 Physiology:

The circulatory system is the transport system that supplies oxygen (O2) and substance absorbed from the gastrointestinal tract to the tissues, returns carbon dioxide (CO2) to the lungs and other products of metabolism to the kidneys, functions in the regulation of the body temperature and distributes hormones and other agents that regulate cell function. The blood is the carrier of the substances, is pumped through a closed system of blood vessels by the heart, which in mammals is really two pumps in series with each other, from the left ventricle, blood is pumped through the arteries and arterioles to the capillaries where it equilibrates with the interstitial fluid. The capillaries drain through venules into the veins and back to the right atrium. This is the major (systemic) circulation, from the right atrium blood flows to the right ventricle, which pumps it through the vessels of the lungs (the lesser {pulmonary} circulation) and the left atrium to the left ventricle. In the pulmonary capillaries, the blood equilibrates with the oxygen (O2) and carbon dioxide (CO2) in the alveolar air (Ganong, 1997).

The function of circulation is to service the needs of the tissues to transport nutrients to the tissue, to transport waste product away, to conduct

hormones from one part of the body to another and in general to maintain an appropriate environment in the tissue fluids of the body for optimal survival and function of the cells (Ganong, 1997).

2.1.26 Mechanical events of the cardiac cycle:

Cardiac cycle is the term referring to all or any events related to the flow or blood pressure that occurs from the beginning of one heart beat to the beginning of the next. The frequency of the cardiac cycle is the heart rate. Every single beat of the heart involves five major stages: First, late diastole which is when semilunar valves close, the AV (arterial valve) valves open and the whole heart is relaxed . Second, Atrial systole, when atria is contracting, AV valves open and blood flows from atrium to the ventricle. Third, Isovolumic ventricular contraction, it is when the ventricles begin to contract, AV valves close as well as the semilunar valves and there is no change in volume. Fourth, Ventricular ejection, ventricles are empty, they are still contracting and the semilunar valves are open. The fifth stage is Isovolumic ventricular relaxation, pressure decrease no blood is entering the ventricles then ventricles stop contracting and begins to relax; the semilunar are shut because blood in the aorta is pushing them to shut. Throughout the cardiac cycle the blood pressure increases and decreases. The cardiac cycle is coordinate by a series of electrical impulses that are produced by specialized heart cells found within the sino-arterial s that are produced by specialized heart cells found within the sino-arterial and the atrioventricular node. The cardiac muscle is composed of myocytes which initiate their own contraction without help of external nerves with the exception of modifying the heart beat rate due to metabolic demand. Under normal circumstances each cycle takes approximately one second (Guyton and Hall, 2006).

2.1.27 Events in the diastole:

Late in diastole, the mitral and tricuspid valve between the atria and ventricles are open and the aortic and pulmonary valves are closed. Blood flows into the heart throughout diastole, filling the atria and ventricles. The rate of filling declines as the ventricles become distended and especially when the heart rate is low the cusps of the atrioventricular valves drift towards the closed position as shown in Figure 2.13 below, the pressure in the ventricles remains low (Ganong, 1997).

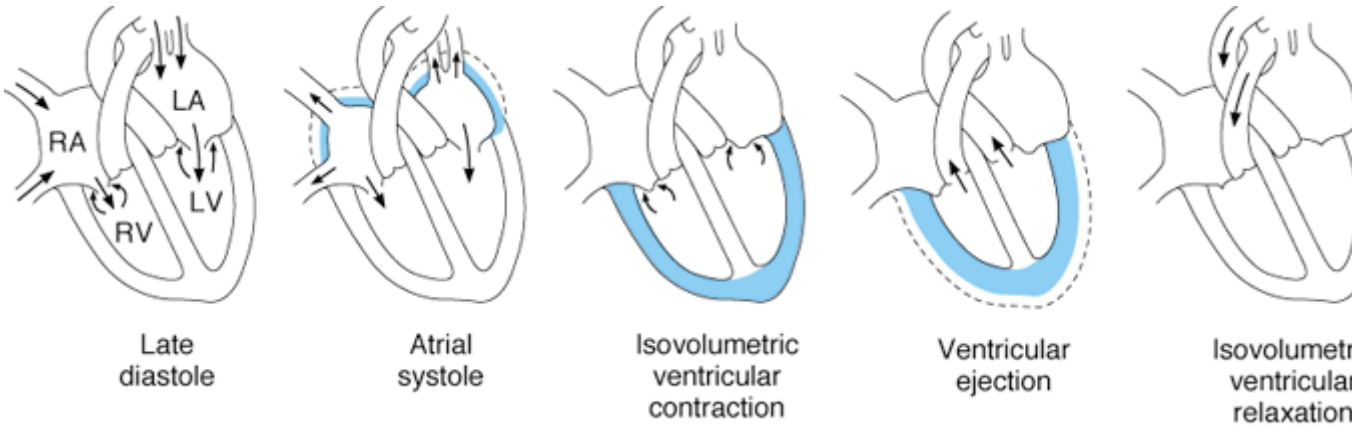


Figure 2.13 shows blood flow in the heart and great vessels during the cardiac cycle, the portion of the heart contracting in each phase are indicating color (Ganong, 1997).

2.1.28 Atrial systole:

Contraction of the atria propels some additional blood into the ventricles, but about seventy percentage of the ventricular filling occurs passively during diastole. Contraction of the atrial muscle that surrounds the orifices of the superior and inferior vena cava and pulmonary veins narrows their orifices and the interia of the blood moving toward the heart tend to keep blood in it, however there is some regurgitation of blood into the veins during atrial systole (Ganong, 1997).

2.1.29 Ventricular systole:

At the start of ventricular systole, the mitral and tricuspid valves close. Ventricular muscle initially shortens relatively little, but intraventricular pressure rises sharply as the myocardium presses on the blood in the ventricle, Figure 2.14. This period of isovolumetric, isovolumic or isometric ventricular contraction lasts about 0.05 second, until the pressures in the left and right ventricles exceed the pressure in the aorta is 80 mm Hg (10.6 KPa), pulmonary artery is 10 mm Hg and the aortic and pulmonary valves open. During isovolumetric contraction, the mitral and tricuspid valve bulge into the atria, causing a small but sharp rise in atrial pressure (Ganong, 1997).

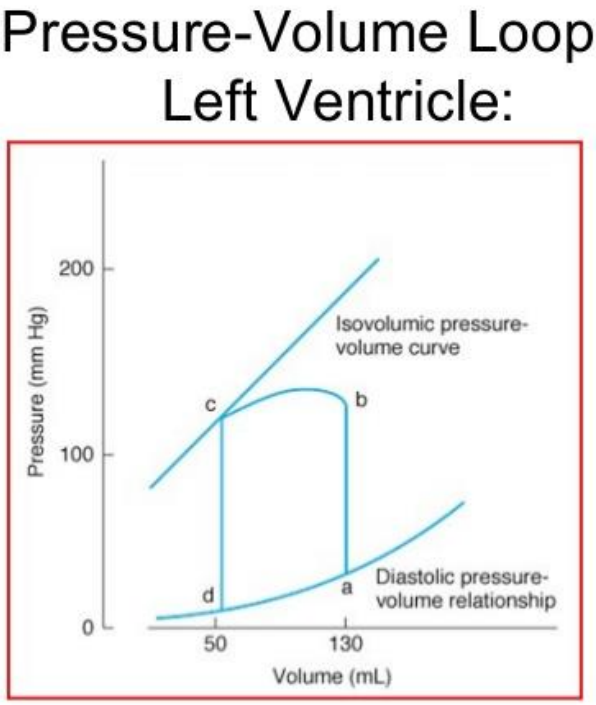


Figure 2.14 shows pressure volume loop of left ventricle during diastole, the ventricle fills and pressure increases from d to a then pressure rises sharply from a to b during isovolumetric contraction and from b to c during ventricular ejection at c, the aortic valves close and pressure falls during isovolumetric relaxation from c back to d (Ganong, 1997).

When the aortic and pulmonary valves open, the phase ventricular ejection begins. Ejection is rapid at first and slowing down as systole progresses. The intraventricular pressure rises to a maximum and then declines somewhat before ventricular systole ends. Peak left ventricle pressure is 2.5 mm Hg or less. In late systole the aortic pressure actually exceeds the ventricular, but for a short period momentum keeps blood moving forward. The tricuspid valves are pulled down by the contraction of the ventricular muscle and atrial pressure drops. The amount of the blood ejected by each ventricle per stroke at rest is 70 to 90 ml, the end diastolic ventricular volume is about 130 ml. Thus about 50 ml of blood remains in each ventricle at the end of the systole (end systole ventricular volume), and the ejected fraction, the percent of the end diastolic ventricular volume that is ejected with each stroke is about 65%. The ejection fraction is a valuable index of ventricular function. It can be measured by injecting radionuclide labeled red blood cells, imaging the cardiac pool at the end of diastole and end of systole (equilibrium dionuclide angiocardiography), and then calculating the ejection fraction (Ganong, 1997).

2.1.30 Early diastole:

Once the ventricular muscle is fully contracted, the ventricular pressures drop more rapidly. This is the period of protodiastole. It lasts about 0.04 second. It ends when the momentum of the ejected blood is overcome and the aortic and pulmonary valves close, setting up transient vibrations in the blood and blood vessel walls. After the valves are closed, pressure continues to drop rapidly during the period of isovolumetric ventricular relaxation. Isovolumetric relaxation ends when the ventricular pressure falls below the atrial pressure and tricuspid valves open, then drop and slowly rises again until the next atrial systole (Ganong, 1997).

2.1.31 Timing:

Although events on the two sides of the heart are similar, they are somewhat asynchronous. Right atrial systole precedes left atrial systole and contraction of the right ventricle starts after that of the left. However, since pulmonary arterial pressure is lower than aortic pressure, right ventricular ejected begins before left ventricular ejection. During expiration, the pulmonary and aortic valves close at the same time, but during inspiration the aortic valves closes slightly before the pulmonary. The slower closure of the pulmonary valve is due to lower impedance of the pulmonary vascular tree. When measured over period of minutes, the outputs of the two ventricles are equal, but transient differences in output during the respiratory cycle occur in normal individuals (Ganong, 1997).

2.1.32 Length of systole and diastole:

Cardiac muscle has the unique property of contracting and repolarizing faster when the heart rate is high and the duration of systole decreases from 0.3 seconds at a heart rate of 65 to 0.16 seconds at a rate of 200 beats per minutes see Table 2.2. The shortening is due mainly to a decrease in the duration of systolic ejection. However, the duration of systole is much more fixed than that of diastole and when the heart rate is increased diastole is shortened to a much greater degree. This fact has important physiologic and clinical implications. It is during diastole that the heart muscle rests and coronary blood flow to the sub-endocardial portions of the left ventricle occurs only during diastole. Furthermore, most of the ventricular filling occurs in diastole (Ganong, 1997).

At heart rates up to 180, filling is adequate as long as there is ample venous return and cardiac output per minutes is increase in rate. However at every high heart rates, filling may be compromised to such a degree that cardiac

output per minutes falls and symptoms of heart failure develop. Because it has a prolonged action potential cardiac muscle is in its refractory period and will not contract in response to a second stimulus until near the end of initial contraction, see Figure 2.15 below. Therefore cardiac muscle cannot be tetanized like skeletal muscle (Ganong, 1997).

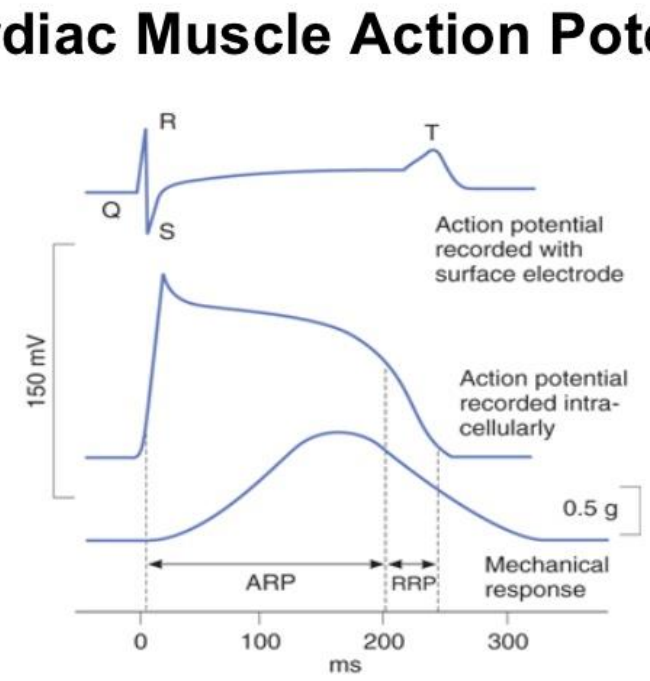


Figure 2.15 illustrate action potentials and contractile response of mammalian cardiac muscle fiber plotted on the time axis where ARP, absolute refractory period, refractory period **(Ganong, 1997).**

Table 2.2 shows the variation in length of action potential and associated phenomena with cardiac rate, all values are in seconds (Ganong, 1997).

Duration	Heart rate 75/min	Heart rate 200/min	Skeletal Muscle
Duration each cardiac cycle	0.80	0.30	
Duration of systole	0.27	0.16	
Duration of action potential	0.25	0.15	0.005
Duration of absolute refractory period	0.20	0.13	0.004
Duration of relative refractory period	0.05	0.02	0.003
Duration of Diastole	0.53	0.14	

2.1.33 Cardiac function curve:

A cardiac function curve is a graph showing the relationship between right arterial pressure (x-axis) and cardiac output (y-axis). Superimposition of the cardiac function curve and venous return curve is used in one hemodynamic model (Brengelmann, 2003).

2.1.34 Shape of curve:

It shows a steep relationship at relatively low filling pressure and plateau, where further stretch is not possible and so increases in pressure have little effect on output. The pressures where there is a steep relationship lie within the normal range of the right atrial pressure (RAP) found in the healthy human during life. This range is about -1 to +2 mmHg. The higher pressures normally occur only in disease, in conditions such as heart failure, where the heart is unable to pump forward all the blood returning to it and so the pressure builds up in the right atrium and the great veins. Swollen neck veins are often an indicator of this type of heart failure (Brengelmann, 2003).

2.1.35 Changes in the cardiac function curve:

In vivo however extrinsic factors such as an increase in activity of the sympathetic nerves and a decrease in vagal tone cause the heart to beat more frequently and more forcefully. This alters the cardiac function curve, shifting it upwards. This allows the heart to cope with the required cardiac output at a relatively low right atrial pressure. We get what is known as a family of cardiac function curves, as the heart rate increases before the plateau is reached and without the RAP having to rise dramatically to stretch the heart more and get the starling effect. In vivo sympathetic outflow within the myocardium is probably best described by the time honored description of the sinoatrial tree branching out to Purkinges fibers. Parasympathetic inflow within the myocardium is probably best described by influence of the vagus nerve and spinal accessory ganglia (Brengelmann, 2003).

2.1.36 Control of blood flow:

Although all blood vessels offer some resistance to the flow of blood, the main resistance lies in the small arteries and arterioles, these vessels are controlled by the local action of the chemical or physical factors, hormones circulating in the blood or by the autonomic nerves that supply them. Although changes in the caliber of resistance vessels tend to change the pressure levels and gradients in the circulation, the mains effect is on blood flow. Blood flow to any tissue is normally regulated by local factors to serve the needs of that tissue but it may be subordinated to supply the needs of the entire body by hormonal or nervous factors (Emslie-Smith et al, 1988).

2.1.37 Local control, effect of metabolism:

Figure 2.16 the effect of temporary occlusion of the circulation on the blood flow in limb. On release of occlusion, the blood flow is raised well above the resting level and then gradually returns towards the resting level (Emslie-Smith et al, 1988).

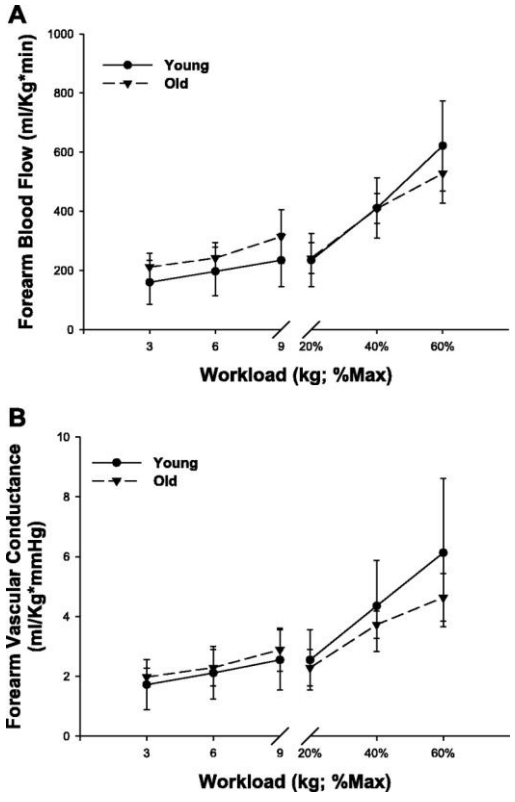


Figure 2.16 determine the change in forearm blood flow and exercise of the forearm muscles (Emslie-Smith et al, 1988).

The increase in blood flow after occlusion is known as reactive hyperaemia. The excess blood flow after release is sometimes referred to as the blood flow repayment for the blood flow debt incurred during occlusion. Though this is not a precise relationship, increasing the period of occlusion tends to increase both the intensity and duration of the reactive hyperaemia. Reactive hyperaemia is caused by a local mechanism since it is confined to those tissues whose circulation has been reduced. It is not mediated by vasomotor nerves since it is unaffected by severance of the autonomic nerves to limb. A similar increase in blood flow is seen after a period of exercise in a limb. When the exercise stops the blood flow is increase greatly above the resting level and then falls in an exponential fashion towards the resting level. This phenomenon is called exercise hyperaemia. Like reactive hyperaemia reactive it is confined to the exercising tissues and still occurs after section of the autonomic nerves to the tissue. The intensity of the exercise hyperaemia is related to the severity and duration of the exercise. In both exercise and reactive hyperaemia the increase in blood flow is thought to be due to an increased concentration of metabolites in the tissues, which can cause blood vessels dilate. In the case of circulatory arrest, metabolism continues to produce metabolites even when blood flow is stopped. So the concentration of metabolites and hence the vasodilatation in the tissue increases in the period of circulatory arrest. When the circulation is re-established, the increased blood flow through the dilated vessels washed away the metabolites in an exponential manner until their concentration in the tissues, and thus the blood flow that occurs in muscles during exercise is not adequate supply the needs of the increased metabolism. Metabolites

therefore accumulate in the tissues and the resulting vasodilatation is responsible for hyeraemia that follows exercise. When the raised blood flow has cleared the axcess of metabolites the blood flow returns to normal (Emslie-Smith et al, 1988).

It is the local control of resistance blood vessels by metabolites that ensures that the blood supply to the tissues is precisely regulated to meet their metabolic needs. If heart muscle has to do more work, the increase local metabolism that this entails increased production of metabolites and hence local coronary blood flow. The parts of the heart muscle that undergo the greatest increases in work get the greatest increases in blood flow. The occurrence of metabolic hyperaemia is most evident in tissues such as muscle and liver where blood flow is mainly determined by metabolic needs. In tissues such as skin and kidney, where blood flow is related to functions other than metabolism, metabolic hyperaemia is less evident (Emslie-Smith et al, 1988).

2.1.39 Local control, effect of local temperature:

If the hand or foot is put into water at 45C the blood flow through the part increases several fold. The increase is restricted to the part that is immersed. It is independent of the autonomic nerve supply since it can occur even the part is denervated. This vasodilatation serves to protect the extremity from the damaging effect of heat. If the extremity is immersed in water at 45C with the circulation occluded, it becomes painful as the tissue temperature rises. The vasodilatation that normally occurs tends to keep the tissues relatively cool by increasing their perfusion with blood at central body temperature. Since heat causes vasodilatation in denervated tissues it is likely that its effect is a direct local one on the smooth muscle in the walls of the arterioles. In intact tissues the stimulating effect of heat

on local tissue metabolism may contributed to the dilatation. The immersion of an extremity in moderately cold water normally causes vasoconstriction, which reduces the loss of the heat from the blood to the environment. An extremity exposed to near freezing temperature for example 0 C to 4. The local blood flow falls to about zero initially and the part becomes painful. Blood flow then starts to rise rapidly to a value well above resting level (Emslie-Smith et al, 1988).

At this time pain disappears. After another short interval flow falls again and pain reappears. This cyclic pattern of blood flow persists while the immersion in ice containers. It is referred to as cold include vasodilatation (Emslie-Smith et al, 1988).

2.1.40 Local control, effect of transmural pressure:

The pressure difference across the wall of a blood vessel is measured by subtracting the external tissue pressure from the intravascular pressure. It is referred to as the transmural pressure cause local changes in the arterioles. As the transmural pressure in the vessels rises, one would expect the arterioles to dilate due to distension and the blood flow to increase. However, as Figure 2.17 shows this expectation is not fulfilled. If the arterial pressure is raised above the normal value of about 100 mm Hg, blood flow rises only very slowly, at a high critical pressure, it rises sharply. The fact that flow does not change very much when the pressure is elicits an increase in vascular resistance. The large increase in flow at high pressures is thought to be due to the distending forces overcoming the vasoconstrictor response. If the pressure is lowered below normal, the blood flow at first does not fall proportionately this indicates that a fall in transmural pressure decreases the vascular resistance. However, at very low perfusion pressures the flow stops even while there is still a positive

perfusion pressure head. This closure of the vessels below a certain critical transmural pressure is known as critical closure (Emslie-Smith et al, 1988).

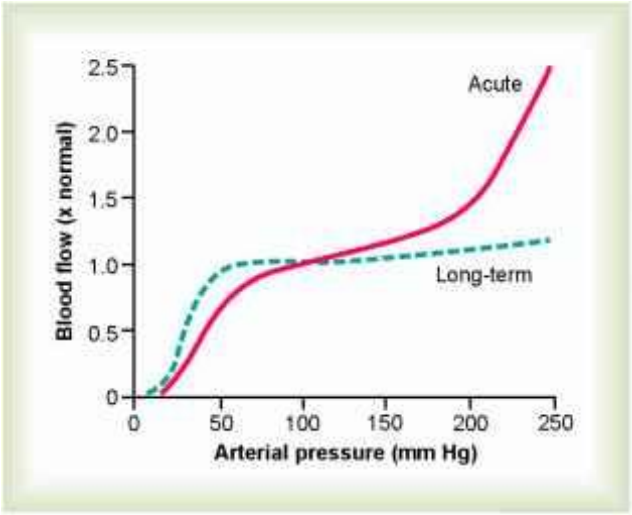


Figure 17–4

Figure 2.17 determine the effect of arterial pressure on blood flow, broken line shows the relation that would be expected if the blood vessels behaved as right tubes (Emslie-Smith et al, 1988).

2.1.41 Local control, effect of oxygen partial pressure in pulmonary alveoli:

As mentioned earlier, oxygen lack is thought to be one of the factors responsible for vasodilatation in active tissues. However, when the pressure of oxygen in the alveoli of one part of the lungs falls, vasoconstriction occurs in the blood vessels perfusing that part. In this situation hypoxia acts as a vasoconstrictor agent. This response ensures that blood is not sent to poorly ventilated alveoli and so helps to maintain the normal ventilation to perfusion ratio in the lungs (Emslie-Smith et al, 1988).

2.1.42 Nervous control, vasoconstrictor nerves:

This nerves when are stimulated causes blood vessels to contract. Impulses reaching their terminals release noradrenalin, which excites the smooth muscle in the walls of the blood vessel. The central origin of the vasoconstrictor nerve impulses can be traced in animals by marking sections through the brain stem at various levels. A large number of cells and fibers in the medulla are concerned with transmission of impulses to blood vessels and this area is called the vasomotor center. Afferent impulses to blood vessels are constantly reaching the vasomotor center from all parts of the body, especially from the pressor receptor in the carotid sinus and aortic arch and from the cardiac and respiratory centers in the medulla itself, efferent impulses are thus initiated or modified and appropriate adjustment made in the circulatory system via the sympathetic nervous system. In disease of afferent nervous system, as for example in the neuropathy of diabetes mellitus, relax alterations of vascular tone may disturb (Emslie-Smith et al, 1988).

The vasoconstrictor impulses pass down from the medulla into the cord and leave by the anterior spinal roots of the thoracic and upper lumber part of the cord. The fibers pass by way of the white rami communicants to the sympathetic ganglia (preganglionic fibers) as shown in Figure 2.18 here new fibers (postganglionic fibers) arise, some going straight to the main blood vessels, others returning to the mixed spinal nerves, to be carried in them to the blood vessels in the periphery (Emslie-Smith et al, 1988).

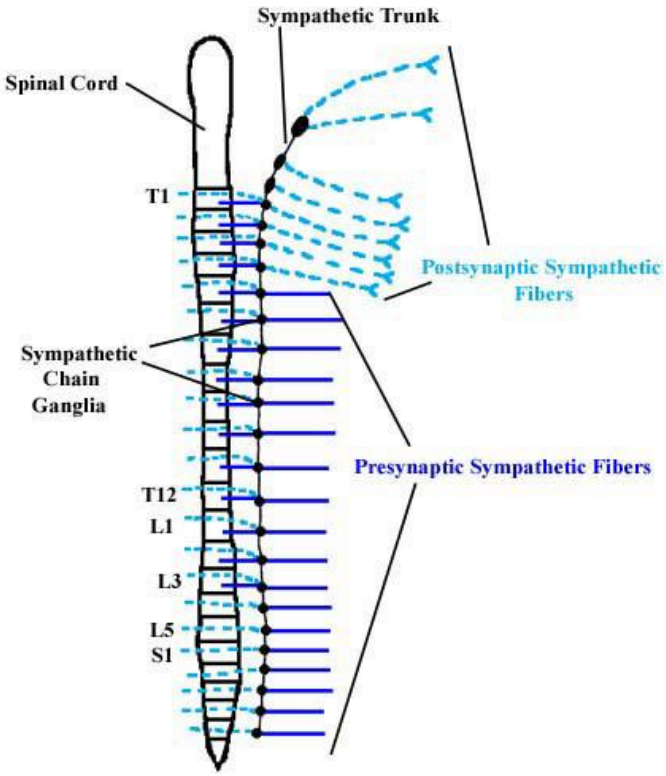


Figure 2.18 shows pathways of sympathetic fibers from lateral horn of the gray matter of the spinal cord (Emslie-Smith et al, 1988).

The frequency of impulses in vasoconstrictor nerve is usually quite low compared with that in somatic motor fibers. It has been shown that almost complete vasoconstriction is produced when vasoconstrictor nerves are stimulated at rates of about eight impulses per second. The resting level of vasoconstrictor tone could be mimicked by about one impulse per second. In somatic fibers, maximum contractions of skeletal muscle are achieved with impulse frequencies of about 50 per second (Emslie-Smith et al, 1988).

2.1.43 Nervous control, vasodilator nerves:

These are nerves which, when stimulated cause dilatation of the blood vessels they innervate. They are thought to do this by releasing a vasodilator substance such as acetylcholine at their nerve endings.

Vasodilator nerve fibers occur in both sympathetic and parasympathetic systems (Emslie-Smith et al, 1988).

2.1.44 Vasomotor reflexes, thermoregulatory reflexes:

When a subject is heated by immersing, his hands in warm water, the blood flow to his hands increases. This is reflex mediated by release of sympathetic vasoconstrictor tone since it does not occur if the sympathetic nerves to the hand are cut if the vasoconstrictor fibers are selectively blocked. A similar release of vasoconstrictor tone occurs in other extremities, such as the ears, nose and lips. Vasodilatation also occurs in the skin of other parts of the body, but this is the result of activity in the sympathetic cholinergic nerves. The dilation may be secondary to the release of bradykinin-forming enzyme by active sweat glands, which have sympathetic cholinergic innervations. Reflex vasodilatation in response to body heating is not seen vascular beds such as muscle, which lie deep to the skin. Skin vasodilatation, by raising skin temperature normally leads to increased heat loss from the body (Emslie-Smith et al, 1988).

If the body is closed, a reflex increase in vasoconstrictor tone occurs in most of the skin areas of the body. The vasoconstrictor, by decreasing skin temperature and therefore the temperature gradient between the body and the environment, helps the body conserve heat. The coordinating centers for these reflexes are thought to lie in the hypothalamus. The centers are controlled not only by change in the temperature of the blood impinging upon them but also by afferent impulses travelling from thermo-receptors in the heated parts (Emslie-Smith et al, 1988).

2.1.45 Vasomotor reflex, blood shift reflexes:

Many stimuli, which have in common the effect of shifting blood towards or away from the chest, can produce reflex alterations in vasoconstrictor tone. These reflex changes are most evident the blood vessels of the muscle and also can be observed in skin. Tilting a person into the foot down position, the application of negative pressure to the lower part of the body, breathing at positive pressure, all tend to shift blood away from the chest towards the feet. These stimuli are associated with a reflex increases in vasoconstrictor tone in muscle blood vessels. Titling a person into the foot up position, the application of positive pressure to the lower limbs and squatting all tend to move blood towards the chest and result in reflex vasodilatation (Emslie-Smith et al, 1988).

The efferent limb of these reflexes is composed of sympathetic vasoconstrictor fibers. The reflex changes are not seen in sympathectomised tissues. Neither the location nor the nature of receptors concerned in the afferent limb of the reflexes is known. The receptors may be one of the large numbers of stretch receptors that have been identified in the walls of the low pressure vessels in the thorax. The baroreceptors in the arterial system do not have much effect on vasoconstrictor tone in man. When blood pressure at the carotid sinus is altered in man the changes in blood flow in the limbs are small and can be explained by the changes that occur in arterial pressure (Emslie-Smith et al, 1988).

2.1.46 Vasomotor reflexes, chemoreceptor reflexes:

As mentioned earlier, the effect of carbon dioxide on the blood vessels is to dilate them. However, when carbon dioxide is breathed by man in high concentration a reflex increases in peripheral vascular resistance occurs in the muscles. This is mediated by way of sympathetic vasoconstrictor

fibers. If these fibers are blocked peripheral vasodilatation occurs when high concentrations of carbon dioxide are breathed (Emslie-Smith et al, 1988).

Carbon dioxide is thought to act directly on the vasomotor center in the medulla but it probably acts on the peripheral chemoreceptor also. Severe oxygen lack also produces some reflex increase in peripheral resistance but its effect is small relative to that of carbon dioxide (Emslie-Smith et al, 1988).

2.1.47 vasomotor reflexes, exercise reflexes:

When a subject exercises his muscle, strong local vasodilatation is brought about by metabolites in the active muscle. However, in other tissues, such as the muscles that are not taking part in the exercise, there is a reflex vasoconstriction. Figure 2.19 shows the changes that occurred when a subject exercised his legs on a bicycle ergometer. Blood pressure and heart rate rose. Blood flow rose in the forearm, the sympathetic nerves of which had been blocked, probably because the increase in the arterial blood pressure drove more blood through the tissue. However, in the normally innervated forearm, the blood flow fell slightly in spite of the rise in mean arterial pressure. This showed that the peripheral vascular resistance in the forearm rose reflexly during leg exercise. This reflex helps to redistribute blood from the non-active to the active muscle during exercise. The efferent limb of the reflex consists of sympathetic vasoconstrictor fibers but the nature and location of the receptors on the afferent limb and reflex center are not known. If all the sympathetic vasoconstrictor fibers are blocked pharmacologically, exercise cannot be sustained for long. The peripheral vasodilatation produced by the exercises such as a fall in total

peripheral resistance that the arterial pressure falls dramatically and unconsciousness ensues (Emslie-Smith et al, 1988).

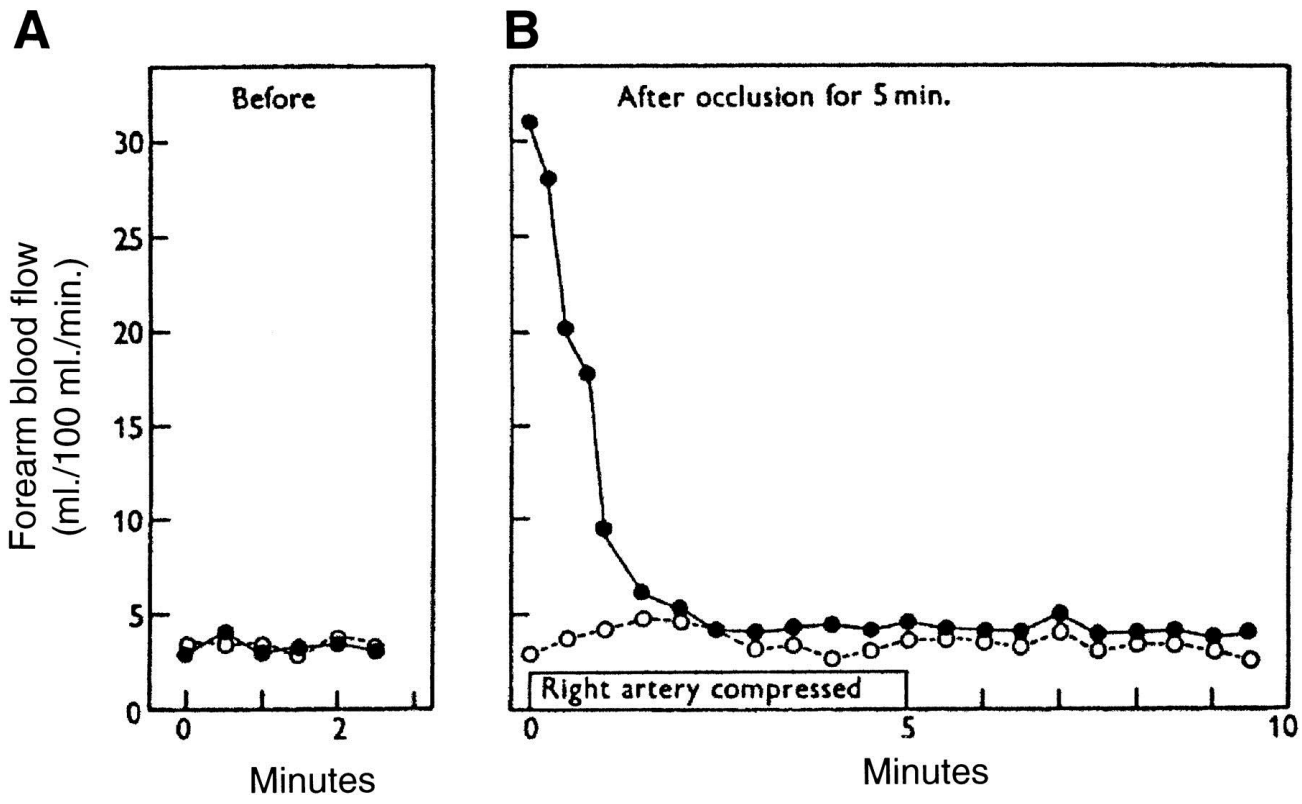


Figure 2.19 illustrates the effect of deep nerve block on forearm blood flow and forearm vascular resistance during 5 minute leg exercise, nerve blocked forearm (•), normal forearm (°), (Emslie-Smith et al, 1988).

2.1.48 Vasomotor reflexes, emotional reflexes:

When a subject is frightened or given difficult mental arithmetic to do, vasodilatation occurs in muscle. This response is reduced or abolished by blocking the sympathetic nerves supplying the tissue and by atropine. These results indicate that sympathetic cholinergic vasodilator nerves are involved in the response. It is likely also that adrenaline released from the adrenal medulla contributes to the response (Emslie-Smith et al, 1988)

2.1.49 Vasomotor reflexes, lung inflation reflexes:

Taking a deep breath causes a reflex vasoconstriction in the skin of the peripheral parts in man. It does not occur if the sympathetic fibers have been served. In fact, a large number of relatively trivial stimuli, such as sudden noise, a pinch or the inflation of a cuff on arm, can cause well marked reflex vasoconstrictor in the hand. The muscles of blood vessels are not involved in these responses. Some of these responses from part of the altering reaction in man but their physiological significance are obscure (Emslie-Smith et al, 1988).

2.1.50 Hormonal control, adrenaline and noradrenaline:

When the splanchnic nerves are stimulated the initial rise of blood pressure is probably due to vasoconstriction in the abdominal organs. This is followed about half a minute later by a second rise due to the liberation of adrenaline and noradrenaline from the adrenal medulla. A similar effect is described in asphyxia. Again, when the pressure in the carotid sinus is reduced the rise of arterial blood pressure that follows is due partly to the reflex activity of the vasoconstrictor nerves and partly to liberation of adrenaline and noradrenaline. Liberation of these hormones also occurs in flight or fight reactions or when the subject is exposed to emotional stress. Adrenaline causes constriction in the cutaneous and other vessels, however, at the same time the blood vessels of the skeletal muscles dilated to that the total peripheral resistance is slightly (Emslie-Smith et al, 1988).

The increased cardiac output must therefore be responsible for the rise in systolic pressure, the man blood pressure may not be altered. Injection of

noradrenaline is not followed by an initial fall in arterial pressure and the rise in systolic pressure is greater than that after adrenaline. In spite of the reduction in cardiac output brought about through the aortic and carotid sinus reflexes the mean blood pressure rises (Emslie-Smith et al, 1988).

2.1.51 Hormonal control, angiotensin, kinis, kistamine and prostaglandin:

Angiotension stimulates the production of aldosterone and therefore tends to increase the volume of the extracellular fluid and the blood volume. The kinis may take part in the vasodilatation associated with the activity of all tissue, not only glandular tissue. Histamine has very pronounced effects on the circulation, it cause vasodilatation of the resistance vessels, flushing of the skin and a fall in arterial pressure. It also increases the permeability of the capillaries, which then permit loss of protein and fluid from the circulation. Where in prostaglandins there is no agreement on their normal role in regulating the circulation (Emslie-Smith et al, 1988).

2.1.52 Pathology:

Vascular disorders are responsible for more morbidity and mortality than any other category of human disease. Among them, arterial diseases are the most important. They achieve this unviable preeminence by narrowing vessels and thus producing ischemia of tissues perfuse by such vessels, damaging the endothelial lining and thus promoting intravascular thrombosis, a process that contributes to critical ischemia of vital organs such as the heart and brain, weakening the walls vessels, predisposing to dilation or possibly rupture, and contributing to the pathogenesis of the

some of the most common disease in humans namely atherosclerosis, hypertension and diabetes (Kumar et al, 1997).

Different pathologies are associated with arterial function disturbance which include:

1. Arteriosclerosis
2. Hypertension and hypertensive disease
3. Vasculitis: polyarterities nodosa, Wenger's granulomatosis, microscopic polyangitis (microscopic polyarteritis, hypersensitivity, vasculitis), temporal (giant cell, cranial), arteritis, Takayasu's arteritis (pulseless disease), Kawasaki's disease (mucocutaneous lymph node syndrome) and thromboangitis obliterans (Buerger's disease).
4. Aneurysms: atherosclerotic (abdominal) and aneurysms.
5. Neoplasm (Tumors).

   The most important arterial disorder which shows good relation with diabetes mellitus as a causing factor and related to this research is the arteriosclerosis, so this is why there is more concentration upon it compare to the other arterial pathologies (Kumar et al, 1997).

2.1.53 Arterial disorders:

Arteriosclerosis is the term for three patterns vascular disease, all of which cause thickening and inelasticity of arteries:

1. The dominant pattern is atherosclerosis, characterized by the formation of intimal fibro fatty plaques that often have a central core

rich lipid hence the term "atherosclerosis" derived from the Greeks term athera, which meaning "gruel or porridge" (Kumar et al, 1997).

2. The second morphologic form arteriosclerosis is rather trivial Monckeberg's medial calcific sclerosis, characterized by calcifications in the media of muscular arteries. It is usually encountered in medium sized muscular arteries in persons older than 50 years. The calcifications take the form of irregular medial plates or discrete transverse rings: they create nodularity on palpation and are readily visualized radiographically. Occasionally the calcific deposits undergo ossification. Since these medial lesions do not encroach on the vessel lumen, medial calcific sclerosis is largely of anatomic interest alone; however, arteries so affected may also develop atherosclerosis (Kumar et al, 1997).

3. Disease of small arteries and arterioles (arteriolosclerosis) is the third pattern. Small vessel sclerosis is most often associated with hypertension and diabetes mellitus. There are two anatomic variants, hyaline and hyperplastic, depending on the cause and rate of progression of disease. Both cause thickening of vessel walls with luminal narrowing and may in the aggregate induce ischemic injury to tissues or organs. Since the lesions are often associated with hypertension, here we will consider only atherosclerosis, which is so clearly the most important form that is often loosely referred as arteriosclerosis (Kumar et al, 1997).

2.1.54 Atherosclerosis (AS):

No disease in the developed countries is responsible for more deaths, has stimulated more research and has engendered more controversy about how best to control it than atherosclerosis (AS). Basically it is characterized by intimal plaques called atheromas that protrude into the lumen, weaken the underlying media and undergo a serious of complications. AS alone accounts for more than half of all deaths in the western world. Although any artery may be affected, the major targets are the aorta, the coronary and cerebral arteries. Coronary AS induces ischemic heart disease (IHD) and when the arterial lesions are complicated by thrombosis the most serious form of IHD, myocardial infarction (IM), which alone is responsible for 20% to 25% of all deaths in the United States. Atherothrombotic disease of the cerebral vessels is the major cause of brain infarcts or strokes of the most common cause of neurologic disease. In addition, AS often produces critical ischemia of the intestines and lower extremities and is major cause of abdominal aortic aneurysms (abdominal dilations) that sometimes rupture to produce massive fatal hemorrhage. The disease begins in early childhood and progresses slowly over decades. Thus, in some sense AS is a pediatric case and if its toll is to be reduced, measures must be dilated early before it rears its ugly head and provokes one it's unfortunate consequences (Kumar et al, 1997).

2.1.55 Atherosclerosis, risk factors:

The prevalence and severity of the disease and therefore the age when it is likely to cause tissue or organ injury, are related to a number of factors, some constitutional and therefore immutable but others acquired and potentially controllable. The constitutional factors include age, sex and familial background (Kumar et al, 1997).

1. Age: is a dominant influence, although early lesion of AS appear in childhood, clinically significant disease as judged by the death rates from IHD, rises with each decade, even in advanced age. For example from 40 to 60 age there is a greater than five-fold increase in the incidence of MI (Kumar et al, 1997).

2. Gender: Other factors being equal, males are much prone to AS than females. Females are more or less sheltered from advanced disease-producing AS until menopause, so MI is uncommon in premenopausal women unless they are predisposed by diabetes or some unusual (possibly familial) form of hyperlipidemia or have severe hypertension, between ages 35 and 55 years, the mortality rate from IHD for white women is one fifth that for white men. After menopause protection slowly dwindles, until the frequency of MI becomes the same in both sexes by the seventh to eighth decade of life (Kumar et al, 1997).

3. Familial Predisposition: There is a well-defined familial predisposition to AS and IHD. In some instances it relates to familial clustering of other risk factors, such as hypertension and diabetes. In other instance, it involves well defined hereditary genetic derangements in lipoprotein metabolism that result in excessively high blood lipid levels. The prototype of these conditions is familial hypercholesterolemia, but in addition there are a growing number of familial dyslipoproteinemias many of which result from mutations that yield detective apolipoproteins. Recall that these are proteins bound to the various blood lipid fractions, which have many functions, among them activating or inhibiting particular enzymes facilitating transmembrane transport of certain lipoproteins and serving as ligands to high-affinity cellular receptors

that guide the lipoproteins to specific sites of catabolism (Kumar et al, 1997).

There are four major acquired risk factors that are least in some part amenable to control:

1. Diabetes mellitus with this disease, the body's blood sugar level is too high because the body doesn't make enough insulin or doesn't use its insulin properly. People who have diabetes are four times more likely to have AS than people who don't have diabetes, also the incidence of MI is twice as high in diabetics as in nondiabetics. There is also an increased risk of stroke and even more striking (Kumar et al, 1997).

2. Hypertension is a major risk factor for AS at all ages and may well be more important than hypercholesterolemia after age 45. Men age 45 to 62 whose blood pressure exceeds 160/95 mm Hg have more than fold greater risk of IHD than those with blood pressures of 149/90 mm Hg or lower. Both systolic and diastolic levels are important in increasing risk (Kumar et al, 1997).

3. Hyperlipidemia is virtually universally acknowledged to be the major risk factor for AS. Most of the evidence specifically implicates hypercholesterolemia. But hypertriglyceridemia may also play a role although it is not as significant as hypercholesterolemia. Recall from an earlier discussion that the various classes of blood lipids are transported as lipoproteins complex to specific a proteins (Kumar et al, 1997).

4. Smoking another important risk factor is thought to account for the relatively recent increase in the incidence and severity of AS in women. When one or more packs of cigarettes are smoked per day

for several years the death rate of IHD increased by up to 200%. Cessation of smoking reduces this increased risk in time (Kumar et al, 1997).

While other factors are sometimes referred to as minor or "soft" risk factors because they are associated with a less pronounced and difficult-to-quantitate risk. These include:

1. Insufficient regular physical activity (Kumar et al, 1997).
2. Competitive stressful life style with "type A" personality behavior (although this is controversial) (Kumar et al, 1997).
3. Obesity (Kumar et al, 1997).
4. The use of oral contraceptives (Kumar et al, 1997).
5. Hyperuricemia (Kumar et al, 1997).
6. High carbohydrate intake (Kumar et al, 1997).
7. Hyperhomocysteinemia, it recently received increased attention and a role of homocysteine as a deleterious agent in AS is currently pursued. In closing this discussion of risk factors, it is important to note that multiple factors impose more than an effect. When three risk factors are present (e.g. hyperlipidemia, Diabetes mellitus and smoking), the heart attack rate is seven times greater than when none present. Two risk factors increase the risk fourfold. However the converse is equally important. AS may develop in the absence of any apparent risk factors, so even those who live "the prudent life" and have no apparent genetic predispositions are not immune to this killer disease (Kumar et al, 1997).

2.1.56 Atherosclerosis, pathogenesis:

Understandably, the commanding importance of AS has stimulated enormous efforts to discover its cause and a number of hypotheses for its pathogenesis have been proposed. The currently favored theory and the one receiving the greatest attention is the response-to-injury hypothesis as shown in figure 2.17 below.

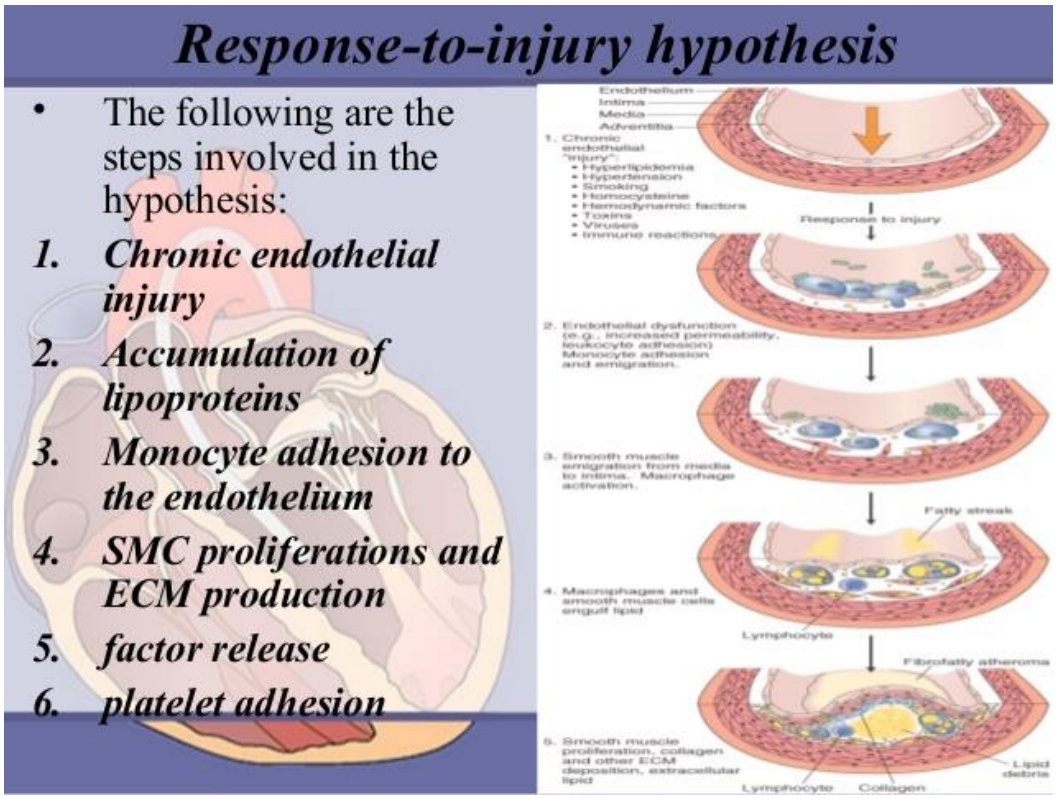


Figure 2.20 determine the artery response to injury theory of atherogensis, where ECM is extracellular matrix (Kumar et al, 1997).

It best accommodates the various risk factors discussed. Central to this thesis are the following features:

1. The development of focal areas of chronic endothelial injury usually with resulting increased endothelial permeability or other evidence of endothelial dysfunction (Kumar et al, 1997).

2. Increased insudation of lipoproteins into the vessel wall, mainly low-density lipoprotein (LDL) or modified LDL with its high cholesterol content and also very low-density lipoprotein (VLDL) levels (Kumar et al, 1997).

3. A series of cellular interactions in these foci of injury involving endothelial cells (ECs), monocytes/macrophages, T lymphocytes and smooth muscles cells (SMCs) of intimal or medial origin (Kumar et al, 1997).

4. Proliferation of smooth muscle cells in the intima with formation of extracellular matrix by the SMCs (Kumar et al, 1997).

2.1.57 Atherosclerosis, clinical significance:

The clinical implications and potential consequences of AS have already been amply emphasized. Understandably, then intensive efforts are under way to devise means to reduce its toll. These involving primary prevention programs for person who have never suffered atherosclerotic event, aimed to preventing or delaying the formation atheromatous plaques or possibly causing regression in persons who have never suffered an acute atherosclerotic event and secondary prevention programs intended to prevent recurrence of acute atherosclerotic events of MI. The media are filled with advice (some of it quite sound) on primary prevention. Weight reduction by control of total calorie intake coupled with increased exercise, moderation of alcohol consumption and most importantly lowering blood cholesterol levels particularly LDL and VLDL, while increasing high density lipoprotein HDL. Thus the great current interest in replacing

saturated fats (red meat, eggs, butter and other fat-laden dairy products) with mono- or polyunsaturated fats such as are in olive, corn and safflower oils and omega-3 fatty acids derived from fish. Such methods are not always successful in lowering high blood levels of cholesterol and therefore there is growing interest in the use of lipid-lowering drugs particularly in patients with genetic hyperlipidemia (Kumar et al, 1997).

Although the controversy persists most of the evidence indicates that treatment of hypercholesterolemia whether by diet or drugs reduce the mortality rate from IHD. Moreover, it is also hoped that lipid-lowering regimens will favor the regression of already developed atherosclerotic plaques as has been documented in animals. In addition several angiographic studies in humans suggest that lipid-lowering diets retard the progression of coronary artery narrowing and even reduce the size of plaques. Analogously secondary prevention programs based on attempts to lower blood lipid levels and prevent thrombotic complications using antiplatelet drugs have successfully reduced the frequency of recurrent myocardial infarcts. Despite the encouraging results a minority of investigators decay the preoccupation with blood lipids, pointing out that the pathogenesis of this disease is undoubtedly multifactorial. However if we wait until all the pieces of the puzzle have been put together, thousands of possibly preventable deaths may have occurred (Kumar et al, 1997).

2.1.58 Polyarteritis nodosa:

Polyarteritis nodosa is a rare autoimmune disease (immune system attacking its own body) featuring spontaneous inflammation of the arteries (arteritis). Because arteries are involved the disease can affect any organ of the body. The most common areas of involvement include the muscles,

joints, intestines (bowel), nerves, kidneys and skin. Poor function or pain in any of these organs can be a symptom. Poor blood supply to the bowels can cause abdominal pain, local bowel death and bleeding. Fatigue, weight loss and fever are common (Emedicine, 2010)

Polyarteritis nodosa is most common in middle-age people. Its cause is unknown, but it has been reported after hepatitis B infection. Polyarteritis is not felt to be an inherited condition. The diagnosis is supported by tests that indicate inflammation including elevation of blood sedimentation rate and C –reactive protein. The white blood cell count and platelet count can elevated, while the red blood count is decreased (anemia). Hepatitis B virus testing (for either antigen or antibody) can be found in 10%-20% of patients with polyarteritis nodosa. Urine testing can show protein and red blood cells in the urine. In patients with nerves affected, nerve function tests are abnormal (Emedicine, 2010).

The diagnosis of Polyarteritis nodosa is confirmed by a biopsy of involved tissue that reveals the inflamed blood vessels (vasculitis). Examples of tissues that are sometimes biopsied include nerves, muscle, kidney and bowel. Vasculitis of the bowel and kidneys can often be detected with an angiogram such as x-ray testing while contrast "dye" is infused into the blood vessels (Emedicine, 2010).

The American College of Rheumatology criteria for the classification of Polyarteritis nodosa in 1990, for classification purposes a patient has Polyarteritis nodosa if he at least has three of the following ten criteria are present:

1. Weight loss greater than/equal to 4 kg.
2. Livedo reticularis (a mottled purplish skin discoloration over the extremities or torso).

3. Testicular pain or tenderness (occasionally a site biopsied for diagnosis).
4. Muscle pain, weakness, or leg tenderness.
5. Nerve disease (either single or multiple).
6. Diastolic blood pressure greater than 90mm Hg (high blood pressure).
7. Elevated kidney blood tests (BUN greater than 40 mg/dl or creatinine greater than 1.5 mg/dl).
8. Hepatitis B virus tests positive (for surface antigen or antibody).
9. Arteriogram (angiogram) showing the arteries that are dilated (aneurysms) or constricted by the blood vessel inflammation.
10. Biopsy of tissue showing the arteritis (typically inflamed arteries).

Polyarteritis is a serious illness that can be fatal. Treatment is directed toward decreasing the inflammation of the arteries by suppressing the immune system. Medications used to treat Polyarteritis nodosa include high-dose intravenous and oral cortisone medications such as prednisone as well as immunosuppressive drugs such as cyclophosphamide (Cytoxan) or azathioprine (Imuran). When hepatitis B is present in patients with Polyarteritis, antiviral medications (such as vidarabine and interferon alpha) are used as primary treatments. Some studies have used various combinations of antiviral medications, plasma exchange and immunosuppressive drugs (Emedicine, 2010).

2.1.59 Takayasu's arteritis:

Takayasu's arteritis is a chronic inflammatory disease of the large arteries usually affecting the aorta and its large branches and the pulmonary arteries. It is one of the vasculitis and can manifest systemically involving any or all of the major organ systems, the brain is a prime target. Takayasu's arteritis is an inflammatory disease of large and medium size arteries, with a predilection for the aorta and its branches. Advanced lesions demonstrate a pancreatitis with intimal (Emedicine, 2010).

Lesions produced by the inflammatory process can be stenotic, occlusive or aneurysmal. All aneurysmal lesions may have areas of arterial narrowing. Vascular changes lead to the main complications including hypertension, most often due to renal artery stenosis or more rarely stenosis of the suprarenal aorta, aortic insufficiency due to aortic involvement, pulmonary hypertension and aortic or arterial aneurysm. Congestive heart failure is a common finding more than dilated cardiomyopathy, myocarditis and pericarditis. In patients in whom the pulmonary artery is involved the right artery appears to be affected more than the left, with patients developing pneumonia, interstitial pulmonary fibrosis and alveolar damage. Other pathophysiologic consequences include hypotensive ischemic retinopathy, vertebrobasilar ischemia, microaneurysms, carotid stenosis, hypertensive encephalopathy and inflammatory bowel disease. Rarely Takayasu's arteritis has also associated with glomerulonephritis, systemic lupus, polymyositis, polymyalgia rheumatic, rheumatoid arthritis, still disease and ankylosing spondylitis (Emedicine, 2010).

Because Takayasu's arteritis is rare, data of on mortality and morbidity are limited. The site of lesions and degree of involvement determine the extent and the clinical severity. A National Institutes of Health study of 60

patients with Takayau's arteritis prospectively demonstrates a 3% mortality rate. This result was similar to data from Japan and China but markedly different from other reports (which reported mortality as high as 3.5%). Such disparity may reflected differences in access to care, definitions of disease activity and indications for treatment (Emedicine, 2010).

The same National institute of Health study showed that 20% of patients had a monophasic illness which was self - limiting, they did not require immunosuppressive treatment. In the remaining 80% of patients who did not have a monophasic illness and experienced one exacerbation, immunosuppressive therapy resulted in remission in 60% of these, one half experienced relapse after immunosuppressive therapy was stopped. The overall morbidity depends on the severity of the lesions and their consequences (Emedicine, 2010).

2.1.60 Thromboangitis obliterans (Buergers disease):

Buerger disease, is a nonatherosclerotic vascular disease also known as thromboangitis obliterans characterized by the absence or minimal presence of atheromas, segmental vascular inflammation, vasooclusive phenomenon and involvement of small and medium sized arteries and veins of the upper and lower extremities. The condition is strongly associated with heavy tobacco use and progression of the disease is closely linked to continued use. The typical presentations are rest pain, unremitting ischemic ulcerations and gangrene of the digits of hands and feet, as the disease evolves the patients may require several surgical amputations (Emedicine, 2010).

The disease mechanism underlying Buerger disease remains unclear but a few observations have led investigators to indicate an immunologic phenomenon that leads to vasodysfunction and inflammatory thrombi.

Patients with the disease show hypersensitivity to intradermally injected tobacco extracts have increased cellular sensitivity to type I and III collagen have elevated serum anti-endothelial cell antibody titers and have impaired peripheral vasculature endothelium-dependent vasorelaxation. Buerger disease is relatively less common in people of northern European descent, Natives of India and Japan. The Buerger disease is more common in males (male-to- female ratio 3:1) and most patients with Buerger disease are aged 20-45 years (Emedicine, 2010).

2.1.60 Carotid surgery

Carotid endarterectomy is the surgical procedure during which the carotid artery is opened, and the atherosclerotic plaque and fatty material deposited on the inside of the artery wall are removed, figure 2.21 (Nemes B, 2010). The Carotid endarterectomy (CEA) was introduced in the 1950s as a treatment option for carotid stenosis, but it was not considered as gold standard for treatment of carotid occlusive disease until two major randomized trials comparing CEA to medical therapy proved its effectiveness. These two multicenter trials were the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST) which enrolled patients with symptomatic carotid stenosis (Nemes B, 2010).

In the NASCET study, the absolute risk reduction of any ipsilateral stroke for patients with ≥70% stenosis at 2 years was 15.9%. There was no significant benefit for patients with less than 70 percent stenosis. In the final ECST analysis, the absolute risk reduction at 3 years was 11.6%, which is similar to the reduction in major stroke or death at 2 years reported for NASCET patients with ≥70 % stenosis (Nemes B, 2010).

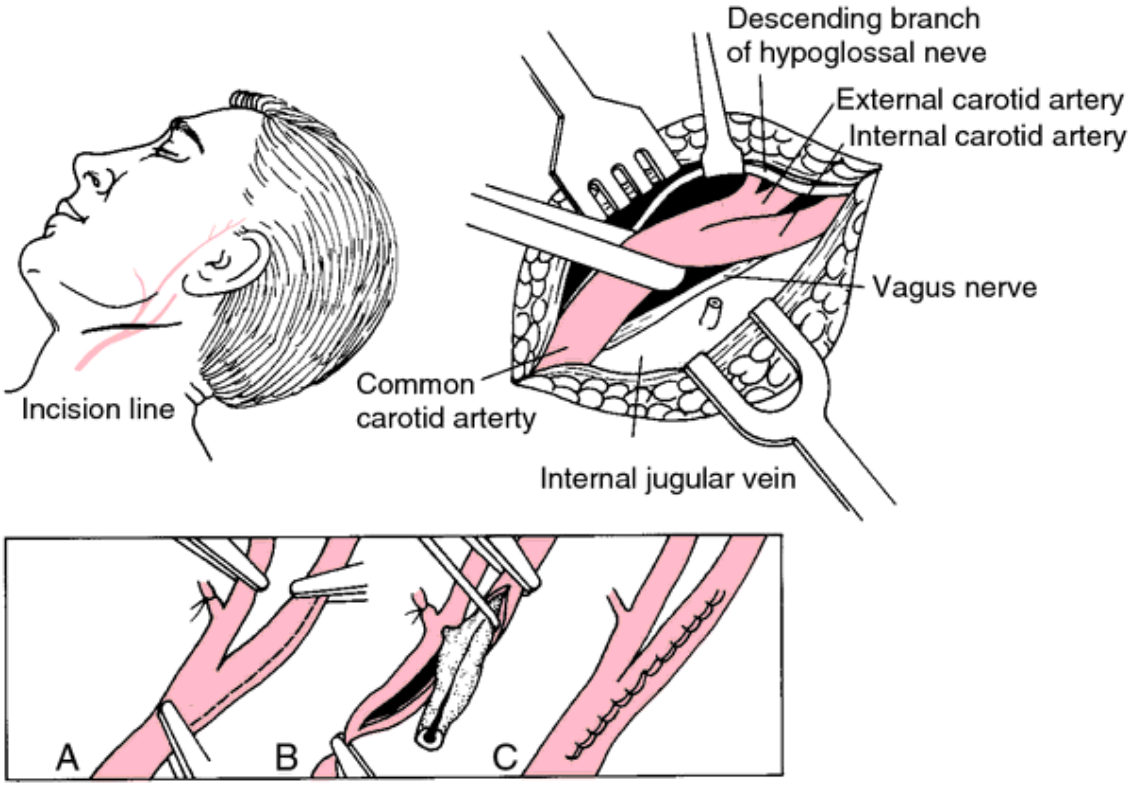


Figure 2.21 shows the procedure of the endarterectomy (www.medical-dictionary.thefreedictionary.com, access on 2.8.015)

2.1.61 Carotid Stenting

Angioplasty of the carotid artery was first performed in 1980, stenting helps exclude the plaque material from the circulation as seen in figure 2.22, to prevent embolization and promote the formation of a smooth neointimal layer **(**Nemes B, 2010).

Endovascular revascularization of carotid occlusive disease offers a less invasive treatment; several trials have compared CEA and carotid stenting. The Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) suggested that angioplasty and surgery are equally effective in preventing stroke and the death and disabling stroke rate is the same following angioplasty and surgery **(**Nemes B, 2010).

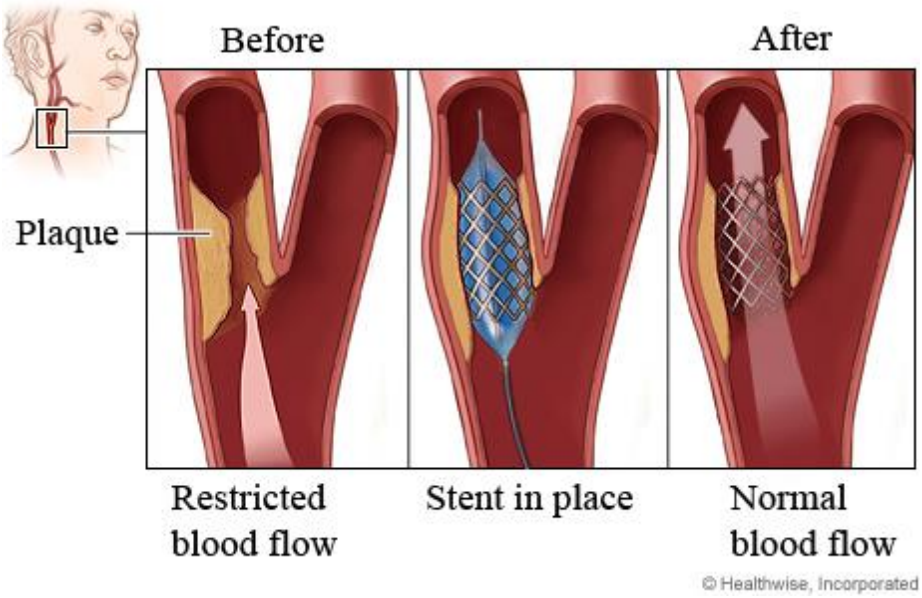


Figure 2.22 the procedure of stenting in the proximal of ICA (www.myhealth.alberta.ca, access on 2.8.015).

Chapter Two-Section Two

Ultrasound Studies

2.2.1 Doppler:

Doppler is a major component of ultrasound imaging especially in the investigation of cardiac and peripheral vascular disease. Modern Doppler systems are sophisticated and can provide accurate information about the effects of disease on blood flow. Our knowledge of blood flow is helpful in understanding the effects of certain disease on organ function and can help the physician in the management and treatment of patients (Corbett et al, 2005).

2.2.2 Nature of the Doppler shift:

2.2.2.1 Doppler shift for audible sounds:

Whenever there is relative motion between a sound source and a listener the frequency heard by the listener differs from that produced the source. The perceived frequency is either greater or less than that transmitted by the source, depending on whether the source and the listener are moving toward or away from one to another. This change in the perceived frequency relative to the transmitted frequency is called Doppler shift. In general a Doppler shift can occur for a moving source and stationary listener, a moving listener and stationary source, or moving source and moving listener (Zagzebski, 1996).

Most researchers are familiar with the Doppler effects occurring when automobile truck or other motor vehicle sounds its horns as it passes us. If the horn is sounding continuously its pitch seems to drop abruptly just as the vehicle passes and as the vehicle approaches the listener, the Doppler

shift results in the perceived pitch of the horn being higher than that actually transmitted. Similarly, the perceived frequency is lower than that transmitted as the vehicle recedes. The very noticeable drop in pitch as the vehicle passes is just the transmitted between the two conditions (Zagzebski, 1996).

Another way to experience a Doppler shift is to be a listener travelling towards or away from a stationary source. A listener moving towards a stationary sound source hears a higher frequency while a listener moving away hears a lower frequency than the transmitted frequency (Zagzebski, 1996).

2.2.2.2 Doppler shift in medical ultrasound:

In medical ultrasound we get Doppler shifts when echo signals are picked up from moving reflectors. In figure 2.23 a stationary transducer is sending sound waves to the right and receiving echoes from reflector. The emerging echo pattern from the reflector varies depending on whether the reflector is stationary or moving. Slightly higher frequencies are received from a reflector moving towards the transducer than from a stationary reflector while the opposite is true for a reflector moving away from the transducer. The Doppler effects actually is manifested twice in the production of an echo from a moving reflector. First the reflector plays the role of a moving "listener" as it travels towards or away from the ultrasound transducer. The ultrasound waves that reflector encounters are thus initially Doppler shifted. The reflector subsequently acts as a moving "source" as it sends echoes back towards the transducer. This result in an additional shift in the frequency of the waves compared to transmitted frequency. The Doppler frequency is the different between the frequency

of the incident ultrasound beam and that of the received echoes (Zagzebski, 1996).

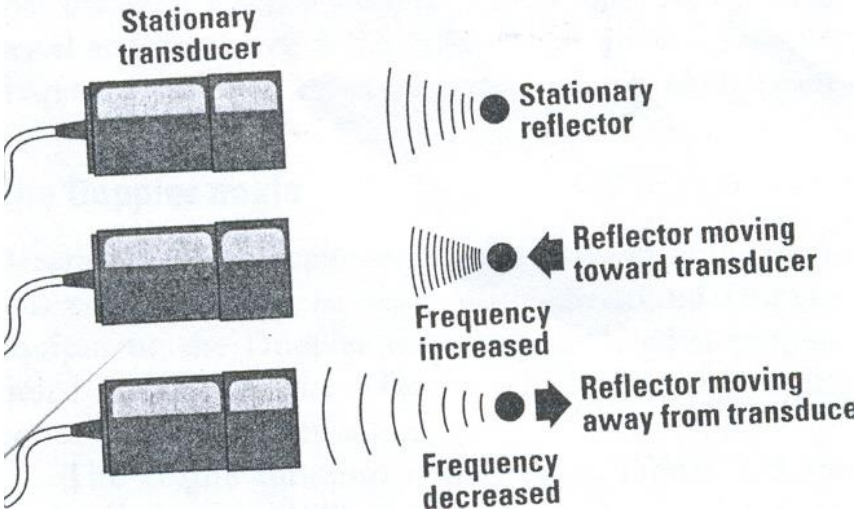


Figure 2.23 shows Doppler shift in medical ultrasound where the frequency of echoes from a stationary reflector is the same as that produced by the transducer, slightly higher frequency echoes result if the reflector moves towards the transducer and slightly lower frequencies occur for reflectors moving away (Zagzebski, 1996).

2.2.2.3 The Doppler equation:

Doppler equipment is commonly used for detecting and evaluating blood flow in arteries and veins. A typical arrangement is shown in Figure 2.22 below. The ultrasonic transducer is placed in contact with the external skin surface and the ultrasound beam directed toward the vessels. The beam is at an angle Θ with respect to the axis of the vessel. Red blood cells flowing in the vessels scatter ultrasound waves giving rise to echo signals. In most instruments the echo signals are detected by the transducer used to produce the incident beam. Because the scatters are moving the frequency of the return echo signals is Doppler shifted. The Doppler frequency is given by equation 2.1:

$$f_d = \frac{2f_0 v \cos\theta}{c}$$

Where:

- fd = Doppler shifted frequency
- fo = transducer frequency
- v = blood velocity
- θ = beam flow angle
- c = speed of sound in tissue (1540 m/s)

In many situations we use Doppler equipment to estimate reflector velocities. As equation 2.1 indicates to the Doppler frequency which is in turn in a direct proportional to the reflector velocities. When the reflector velocity doubles the Doppler frequency doubles as well and when it halves the Doppler frequency halves. Equation 2.1 also indicates that the Doppler frequency depends on the frequency of the incident ultrasound beam. The Doppler frequency obtained from the red cells within a vessel when using a 10 MHz beam is twice that obtained when a 5 MHz bean is used for the same vessel and geometry (Zagzebski, 1996).

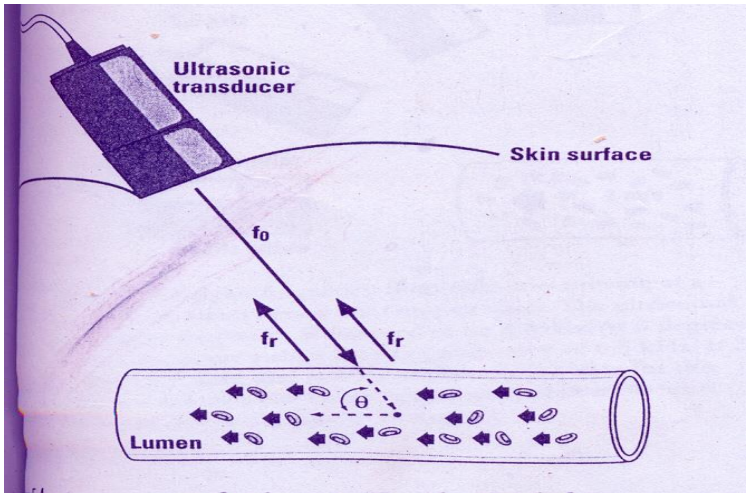


Figure 2.24 shows arrangement for detecting Doppler signals from vessel, where Θ is the Doppler angle (Zagzebski, 1996).

2.2.2.4 The Doppler angle:

In description of the Doppler angle, the angle Θ in Figure 2.24 is called the Doppler angle. With ultrasound Doppler equipment, the Doppler frequency detected is proportional not only to the reflector velocity but also to the cosine of the Doppler angle. The cosine function is plotted in Figure 2.25 for angles from 0 to 180 degrees. It varies from 1 for 0 degree angle to 0 for 90 degrees to -1 at 180 degrees.

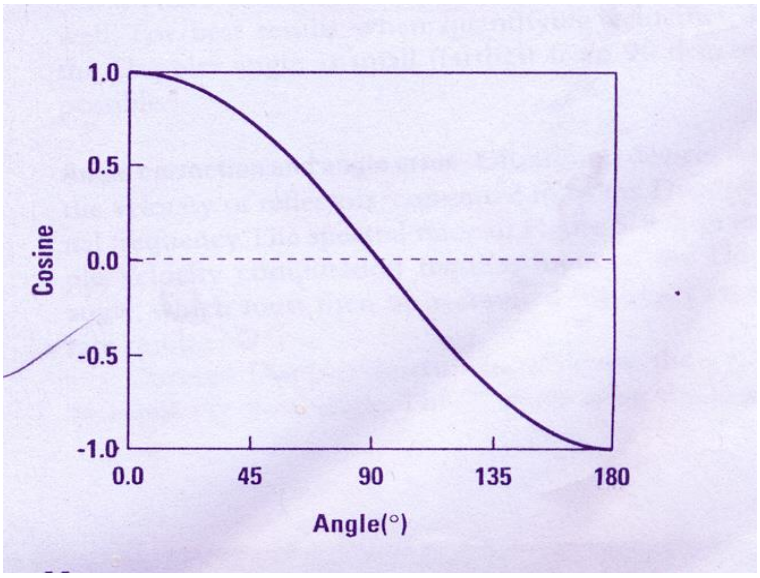


Figure 2.25 shows the changes according to cosine function for angles from 0 up to 180 degrees (Zagzebski, 1996).

Looking closely at Figure 2.25, a 0-degree Doppler angle corresponds to reflectors moving directly towards the transducer while a 180-degree Doppler angle means the reflectors are moving directly away from the transducer. If the Doppler angle is 90-degree reflectors are moving perpendicular to the ultrasound beam (Zagzebski, 1996).

The effect of Doppler angle on the Doppler frequency for a given reflector velocity where the given example assumes that the reflectors are moving at a speed of 1 m/s and that the ultrasound frequency is 5-MHz, Doppler frequencies for different Doppler angles, determined by the location of the ultrasound transducer are presented (Zagzebski, 1996).

Finally at 90-degrees when the ultrasound beam is perpendicular to the reflector direction the detected frequency is 0-Hz because there is no Doppler shift (Zagzebski, 1996).

If the incident beam angle is greater than 90-degrees to the flow, the cosine of the angle is negative this corresponds to the flow directed away from the transducer, the frequency of echo signals from moving reflectors is now

lower than Fo, the transmitted frequency. Most equipment detects the magnitude of Doppler frequency, so the Doppler signals sound the same as for signals from flow directed towards the transducer. Notice, the transducer beam orientation that provides the best B-mode image detail of a vessel wall, that is perpendicular beam incidence, results in the favorable Doppler signals from the lumen of the vessel. In practice the transducer beam is usually oriented to make a 30 to 60-degree angle with the lumen of vessel when the vessel runs nearly parallel to the skin surface. If the Doppler angle is greater than 60-degree, Doppler shift signals can usually be detected, however it becomes difficult to quantify the Doppler angle introduce large uncertainties in the reflector velocities as the Doppler angle approaches 90 degrees and also transducer related spectral broadening results in uncertainties in the peak Doppler frequencies (Zagzebski, 1996).

2.2.3 Continuous wave Doppler instruments:

2.2.3.1 Continuous wave Doppler system description:

Continuous wave (CW) Doppler instruments are the simplest and often the least expensive Doppler devices available. A simplified block diagram is presented in Figure 2.26. A CW transmitter continuously excites the ultrasonic transducer with a sinusoidal electrical signal. This produces a sound wave of frequency Fo.

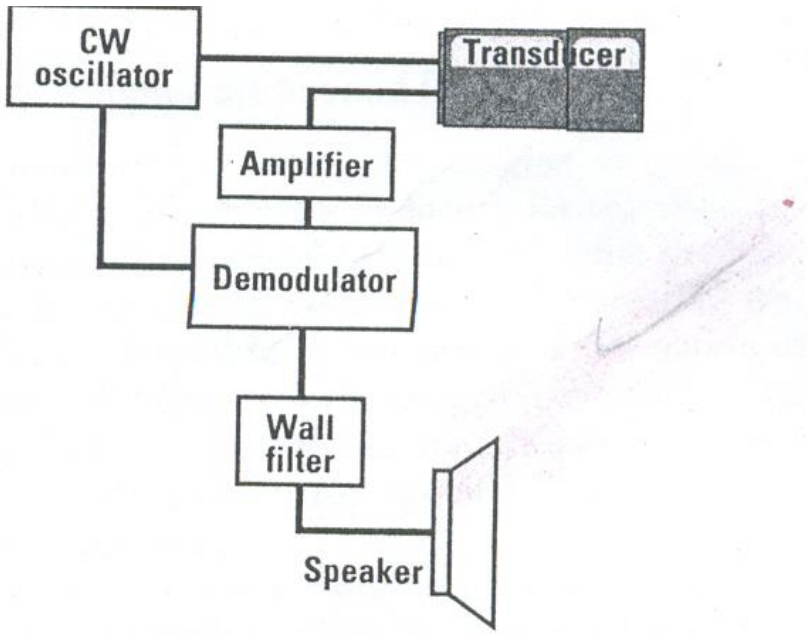


Figure 2.26 schematic showing parts of a CW (continuous-wave) Doppler instrument (Zagzebski, 1996).

Echo signals resulting from reflection and scattering return to the transducer creating an electrical signals that is applied to the receiver amplified. The signals is boosted in strength and then applied to the demodulator. Here the echo signals are multiplied with a reference signal derived from the transmitter, producing a complicated product. The product contains a mixture of signals, one whose frequency is equal to the sum of the reference frequency and the return echo signal frequency and another that is equal to the difference between the reference frequency and the return frequency. The "difference frequency" signal is the Doppler signal that we are after. It is isolated by electronically filtering away all of the high frequencies in the complicated product. The result is that only low frequency Doppler shift signals emerge in the output (Zagzebski, 1996).

High frequency signals are removed in the demodulator. Further filtering is applied after this stage to remove the very low frequency Doppler signals originating from slowly moving reflector, such as vessels walls. This filter

is usually called a wall filter and is adjusted by the operator. The wall filters available on most Doppler instruments preferentially removed low frequency Doppler signals from display. As the wall filter setting or the "filter" setting is adjusted upward, more of the Doppler signal from the baseline is lost. The filtered output Doppler signal may be applied to a loudspeaker or headphone for interpretation. The signals also can be recorded on audio tape or applied to a spectral analysis system (Zagzebski, 1996).

Continuous wave Doppler instruments range in complexity from simple, pocket-tape instruments to units that are part of large "duplex" scanners. Operator controls available on a continuous wave Doppler instrument vary with the degree of complexity of the unit. Typically the following are available:

1. Transmit power control, this varies electrical power applied to the ultrasound transducer and hence varies the amplitude of the transmitted beam. Higher power output setting result in larger amplitude echo signals picked up by the transducer and they also result in greater acoustic exposure to patients.

2. Receiver sensitivity or gain control, this adjusts the amount of amplification or gain of the receiver amplifier.

3. Loudness or volume control, this allows adjustments of the gain of the audio amplifier section of the instrument.

4. Wall filter control, adjusts the low frequency cutoff of the output Doppler signals. Signals whose frequencies are lower than this cutoff are eliminated from the display.

Some combination of the first three controls generally is available to allow the operator to vary the sensitivity of the Doppler instrument. Most Doppler units have a wall filter adjust (Zagzebski, 1996).

2.2.3.2 Continuous wave Doppler transducer:

Most continuous wave Doppler instruments employ separate transducer elements for transmitting and receiving. The reason for this is that since the transducer transmits sound wave continuously, weak echo signals picked up by the transducer would be overwhelmed by the transmit signal if the same element were used for both transmitting and receiving. Thus one element is used for continuous transmitting while the other is used for receiving. This could be done using separate elements in the array of a duplex scanner. More commonly, stand –alone transducer are used in continuous wave Doppler (Zagzebski, 1996).

The stand-alone transducer design for continuous wave Doppler is illustrated in Figure 2.27 each element is cut in the shape of a semicircle and the elements are titled slightly as shown in Figure 2.27. The beam patterns of the transmitting and receiving transducer are thus made to cross. The region of beam overlap is the most sensitive area of this type of transducer and scatters that happen to be within this region yield the largest amplitude Doppler signals. Transducer may be designed emphasized signals from any depth by appropriate choice of beam overlap or beam focal distance. Since a continuous wave Doppler transducer does not produce short duration pulse, steps taken to dampen the ringing of the element that are common to pulsed transducers do not need to be taken. It may be advantageous, however to add quarter-wave matching layers to improve the sensitivity of the probe (Zagzebski, 1996).

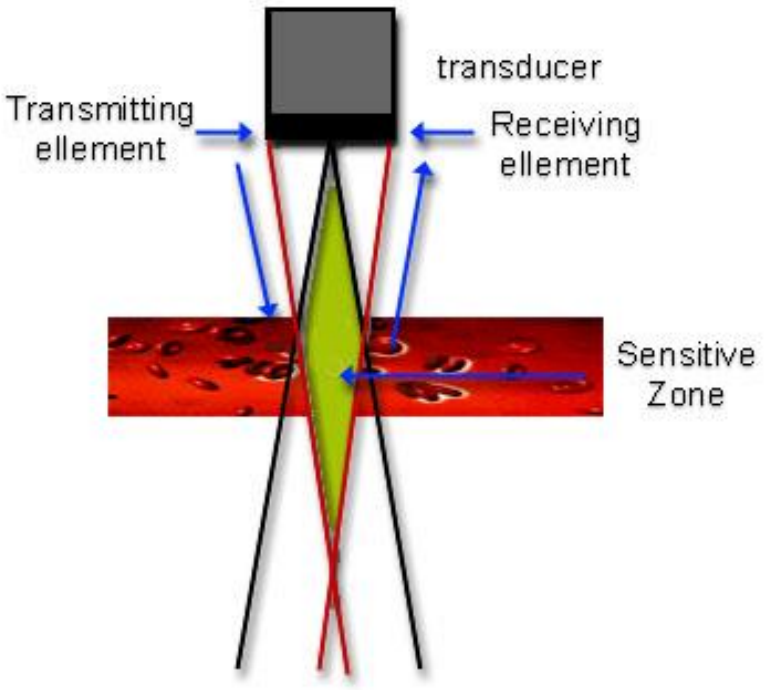


Figure 2.27 shows CW Doppler transducer containing two piezoelectric elements. One element continuously transmits ultrasound waves and other continuously detects echoes (Zagzebski, 1996).

2.2.4 Choice of Doppler ultrasound frequency:

Choice of operating frequency for a modality was the result of a trade-off between the desire to obtain high resolution (which improves with increasing frequency) and the need to obtain adequate penetration of the ultrasound beam (which decrease with increasing frequency). These trade-offs also are factors in determining the best frequency for specific applications of Doppler instruments. However factors in addition to attenuation play a role in the signals strength in Doppler ultrasound. Since the source of Doppler ultrasound signal is blood, the scatters are small (Rayleigh scatters). The intensity of scattered signals for Rayleigh scatters increases with the frequency raised to the fourth power. It would thus seem

reasonable to use a high ultrasound frequency to increase the intensity of echo signals scattered from blood (Zagzebski, 1996).

As the frequency increases the rate of beam attenuation also increases. In selecting the optimal frequency for detecting blood flow these competing processes must be balanced and the choice is related to the depth of the vessel of interest. For small superficial vessels where attenuation from overlying tissues is not significant, Doppler probes operating in the 8 to 10 MHz frequency range are common. Frequencies as low as 2-MHz is sometimes used where significant ranges and large amounts of attenuation are present. In instruments that provide combined B-mode image and Doppler operating mode, it is not unusual to have different ultrasound frequencies applied for each mode. For example a 7.5 MHz B-mode image might be combined with Doppler processing done at 5 MHz to optimize the detect ability of the Doppler signals from all depth of interest. The echoes originating from stationary structures displayed in B-mode are of significant greater amplitude than those from blood so greater amounts of beam attenuation can be tolerated for their detection than for detection of signals from blood (Zagzebski, 1996).

2.2.5 Directional Doppler:

In a simple "non-directional" Doppler instrument the output Doppler signals are identical for reflectors moving at a fixed speed, say 50 cm/s towards the transducer or away from the transducer. In other words a non-directional Doppler instrument con not distinguish whether the Doppler shift in the returning echoes is positive or negative. In some applications only the presence of flow or the relative speed of reflectors needs to be detected and simple processing without this directional information will

do. However in many situations the direction of flow also is important requiring directional Doppler circuitry (Zagzebski, 1996).

2.2.7.1 Pulsed Doppler

With continuous wave Doppler instruments reflectors and scatter anywhere in the beam of the transducer can contribute to the Doppler signal. Pulsed Doppler provides the ability to select Doppler signals from specific depths. The region from which the signals are selected is called the sample volume. When combined with steerable Doppler beams on duplex scanners, pulsed Doppler enables the precise selection of the depth and angle of the sample volume (Zagzebski, 1996).

2.2.7.2 Pulsed Doppler circuitry:

Pulsed Doppler is somewhat like pulse echo ultrasound in that in that sounds are produced by the transducer at regular intervals. A transmitter as shown in Figure 2.28 applies a transmit pulse to the transducer; this pulse has a well-defined frequency. Some pulsed Doppler instruments allow the operator to vary the pulse duration that is the number of cycles in the pulse, in order to vary the sensitivity. More cycles in the pulse results in improve sensitivity and better performance of the Doppler circuitry. This is done at the expense of somewhat greater exposure to the patient and poorer axial resolution (Zagzebski, 1996).

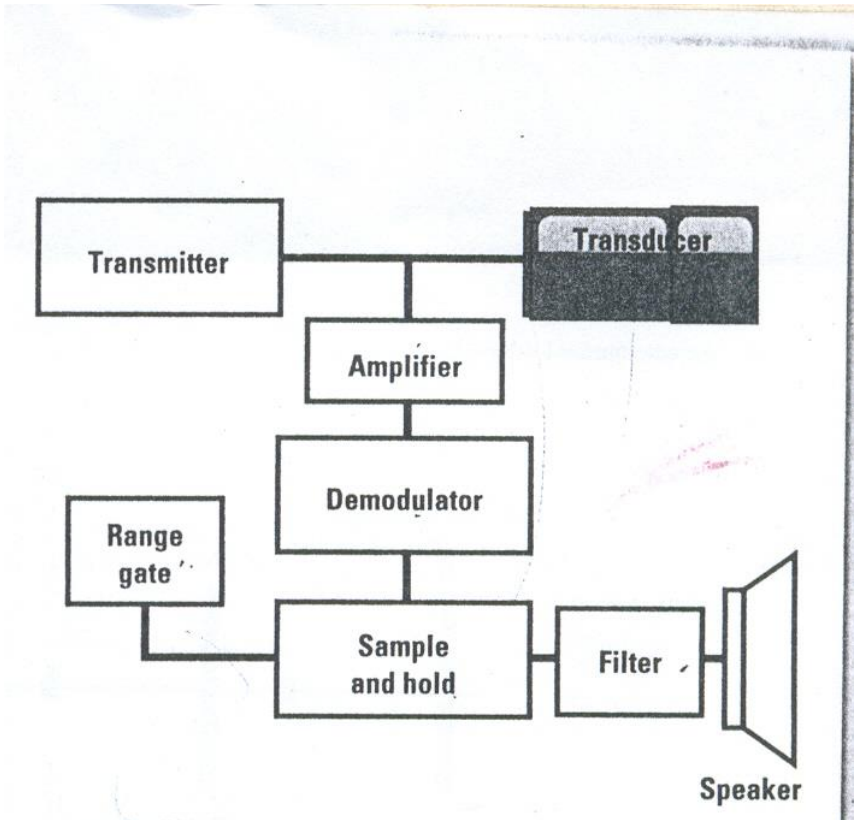


Figure 5-16. Pulsed Doppler instrument. Following each transmit

Figure 2.28 shows pulsed Doppler instrument. Following each transmit pulse echoes are amplified and Doppler processed in the demodulator so the signals depends both on the echo amplitude and the phase a segment of the signal from a fixed depth is selected by the range gate/sample and hold system (Zagzebski, 1996).

Amplification and demodulation of the echo signals occur, analogous to continuous wave Doppler. The output Doppler demodulator depends not only on the amplitude of echoes from reflectors, but also on the precise phase of the echo signals. An operator adjusted "range gate" isolates signals from desire depth. These are stored temporarily in the sample and hold unit. Awaiting the outcome of another transmit pulse. If reflectors within the gated volume are moving echoes collected during the subsequent pulse echo sequence are of slightly different phase. This difference will show up during Doppler processing in the Doppler signal

from the gated volume is built up gradually in the sample and hold unit (Zagzebski, 1996).

2.2.7.3 Size of the pulsed Doppler sample volume:

The sample volume size indicated in Figure 2.29 is determined by two factors. The ultrasound beam width, in the scan plane and perpendicular to the scan plane, determines the cross sectional area of the sample volume. Thus a more tightly focused ultrasound beam results in a smaller beam area and narrower sample volume (Zagzebski, 1996).

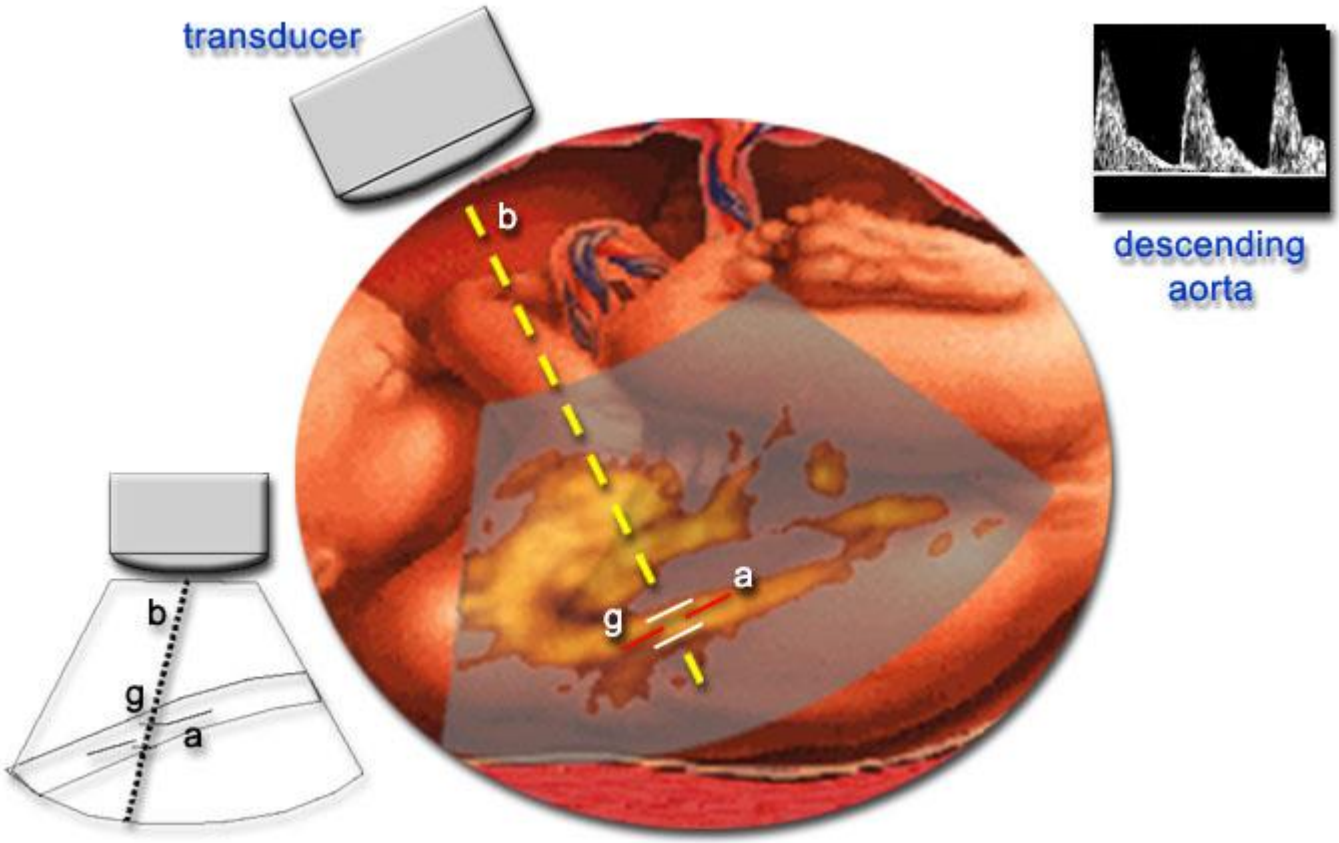
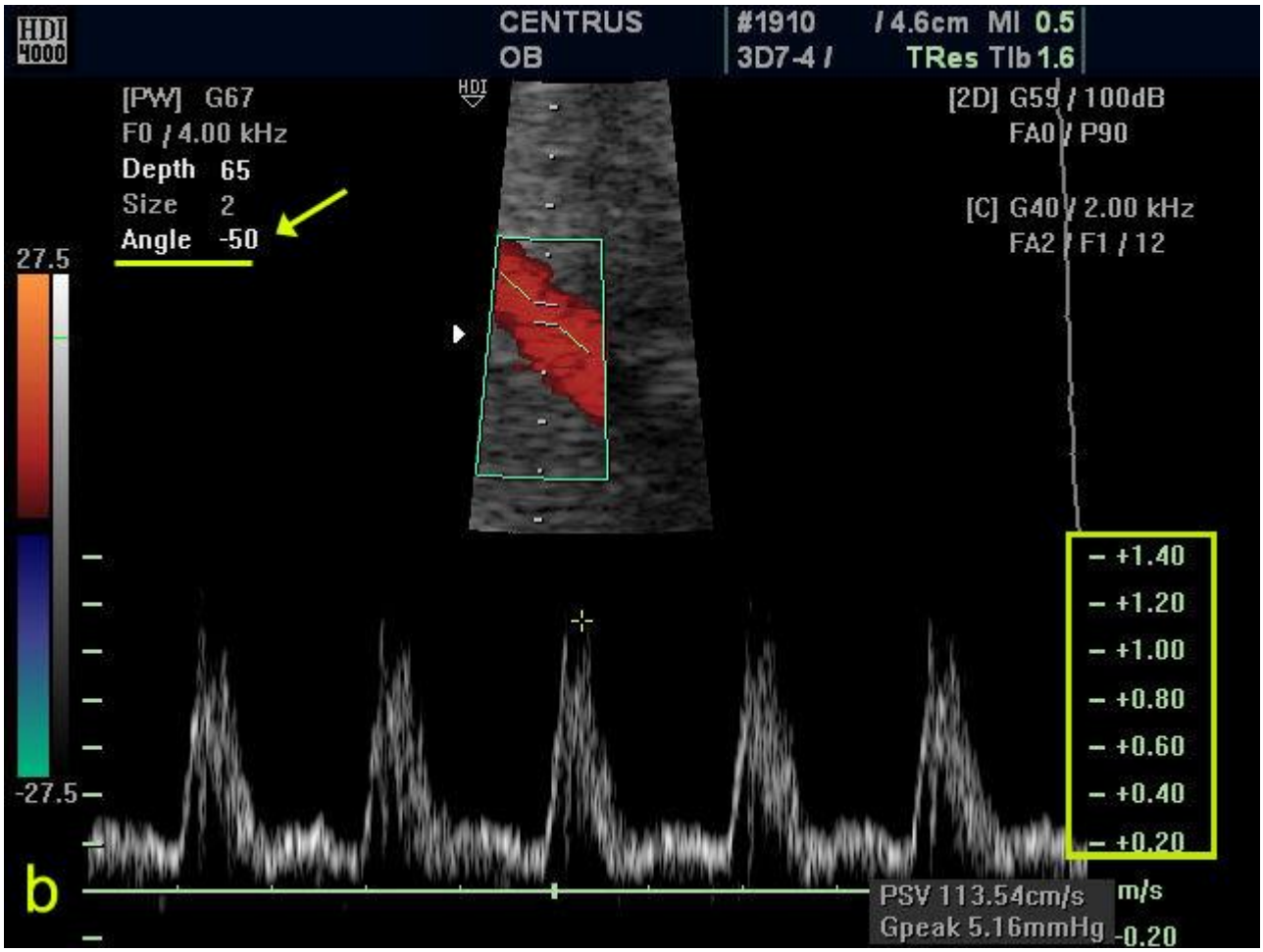


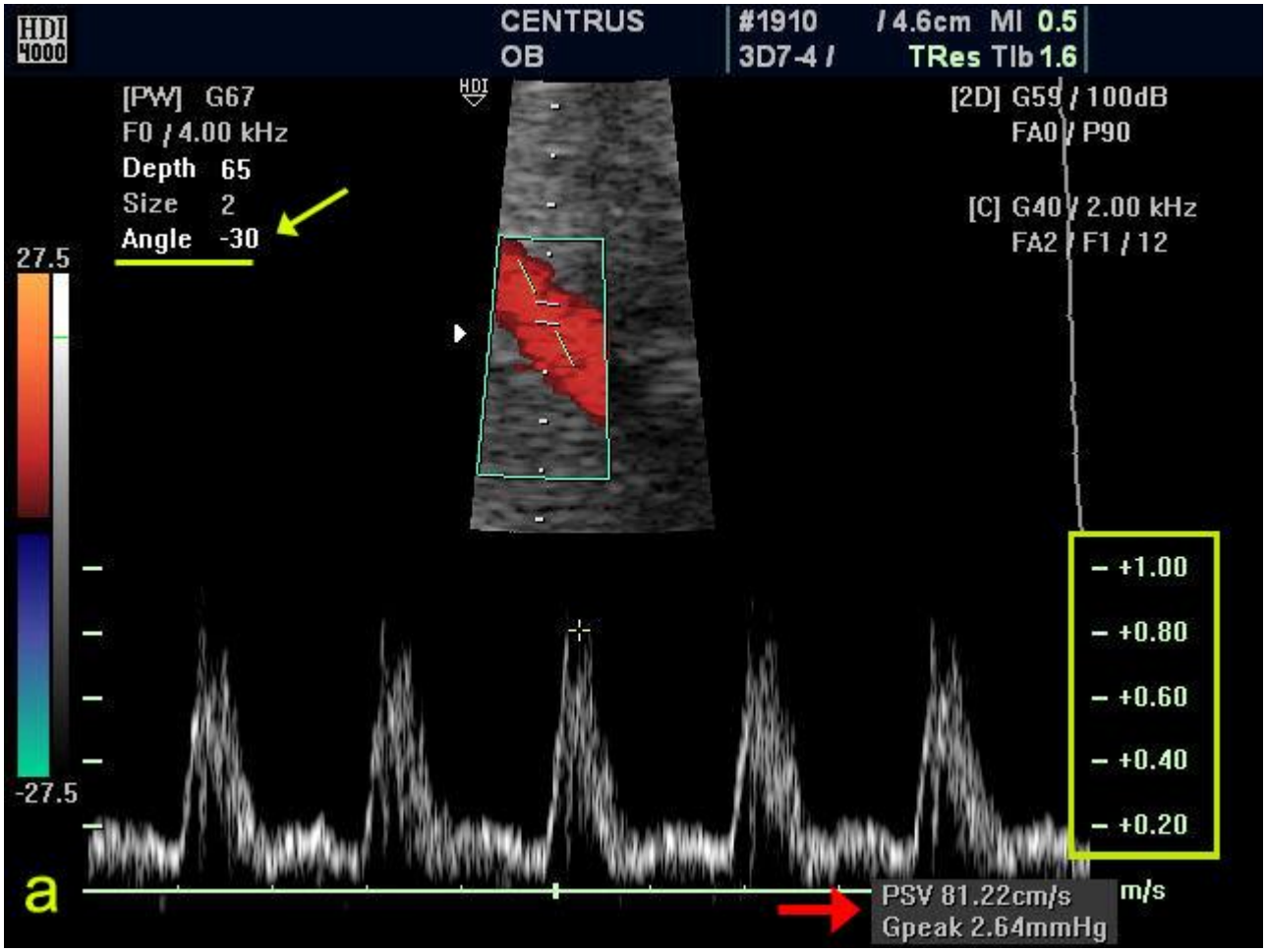
Figure 2.29 illustrate pulsed Doppler sample volume in descending aorta, where b is direction of the Doppler beam, g is sample volume and a is angle correction (Zagzebski, 1996).

The axial length of the sample volume is determined by the pulse duration and by the sample gate size. Most instruments provide a control so that the operator can adjust the gate size (Zagzebski, 1996).

Increase the gate size, increase the volume from which Doppler signals are picked up. This is easily demonstrated using a flow phantom as shown in Figure 2.30. When a narrow gate is used figure 2.30, A, and is centered in the middle of the vessel, a very narrow range of velocities is picked up, as shown by the velocity traces on the bottom. When a larger gate is used Figure 2.30, B, and a larger range of velocities is picked up (Zagzebski, 1996).



A



B

Figure 2.30, A and B shows control of sample volume size by varying the gate size of pulsed Doppler instrument (Zagzebski, 1996).

2.2.7.4 Pulsed Doppler controls:

Operator controls on pulsed Doppler instruments, in addition to those already mentioned for continuous wave Doppler units include the following:

1. Range gate position, the operator can place the range gate at various depths. With duplex instruments the operator can also place it at various positions in the B-mode field.

2. Gate or sample volume size, increasing the range gate accepts Doppler signals from longer axial region.

3. Pulse duration which appear on some instruments.

4. Flow angle cursor, for duplex instruments the angle cursor is positioned by the operator so that it follows the perceived direction of flow. The instrument then makes an angle correction to the velocity display (Zagzebski, 1996).

2.2.8 Duplex Instruments:

A pulse echo scanner and a Doppler instrument provide complementary information in that the scanner can best outline anatomical details whereas a Doppler instrument yields information regarding flow and movement patterns. Duplex ultrasound instruments are real-time B-mode scanners image obtained with a duplex scanner is used to localize areas where flow will be examined using Doppler. The area to be studied in pulsed Doppler mode is selected on the B-mode image with a "sample volume" or "sample gate" indicator, Figure 2.31. The cursor position is controlled by the operator. Many duplex instruments allow the operator to indicate the direction of low with respect to the ultrasound beam direction by adjusting an angle cursor. This is necessary to estimate the reflector velocity from the frequency of the Doppler signal. During duplex scanning, the ultrasound transducer assembly and the instrument "time-share" between pulse echo and Doppler mode. The extent of this time sharing is often under operator control directly or indirectly. Thus some instruments allow the operator to specify the rate at which the B-mode image is update while in the Doppler mode. This may range from 7 to 10 times per seconds to no updating at all. Of course, the more frequently the B-mode image is update, the more certain the operator determine the exact location of the

sample volume during a Doppler study, an important consideration especially for smaller vessels (Zagzebski, 1996).

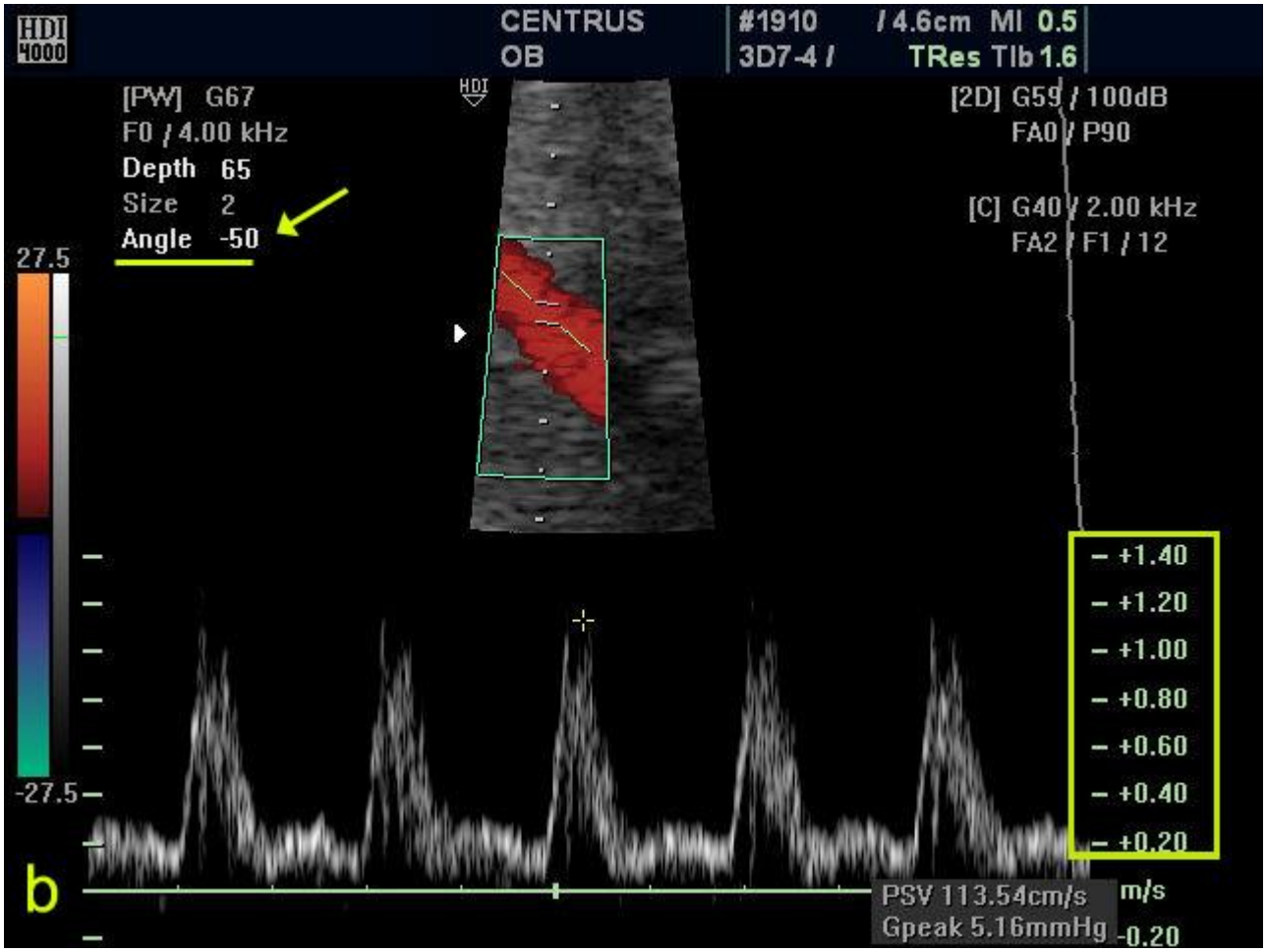


Figure 2.31 shows ultrasound B-mode image of a Doppler phantom (top) along with a spectral Doppler trace (bottom) where the vertical scale in the spectral Doppler trace indicates velocity in meters per second (m/s), operator positioned angle cursor is located in the middle of the gated region. The cursor is aligned along the assumed axis of the vessels (Zagzebski, 1996).

2.2.9 Transducer for duplex:

Both mechanical scanners and array transducer assemblies are used as duplex scanners. Mechanical sector scanners provides the ability to incorporate annular array transducer for an improve slice thickness over

the image. However, phased linear and curvilinear arrays offer other advantages for duplex scanning, especially in the flexibility in switching between Doppler and real time B-mode. Because there are no moving parts in the transducer assembly the array scanning instrument can quickly automatically shift between steering the beam toward the sample volume in Doppler mode and then back to B-mode to build up part of the B-mode image, then back to Doppler mode and so on. Thus B-mode image updating may be more rapid when studies are done in a combined B-mode scan and pulsed Doppler mode (Zagzebski, 1996).

2.2.10 Doppler spectral analysis:

2.2.10.1 Characteristics of flow in vessels:

Doppler signals from flowing blood may be complicated because of the nature of the flow patterns encountered by the sound beam. Sometimes the flow is parabolic or laminar as shown in Figure 2.32. Blood cells move fastest along the axis of the vessel, the velocity drops to zero at the vessel wall. Laminar flow is often considered an ideal condition that slow to moderately fast flow reaches if there are no abrupt discontinuities in the flow such as caused by turns and obstructions. In large vessels such as the aorta the flow may take on a more blunt profile. Here the flow profile is constant across the vessel, near the wall the flow decrease to zero again. Finally, a turbulent flow as might be caused by a blockage or narrowing is shown in C of Figure 2.32. The actual velocity profile across any vessel depends on a number of factors including the diameter of the vessel, the mechanical properties of blood, the flow velocity and the time. If echo signals are detected simultaneously from across the vessel, a range of Doppler frequencies is present in the signal. The number of different frequencies depends on the distribution of velocities present, the transducer

beam width and the size of the Doppler sample volume if pulsed Doppler is employed. A quantitative analysis showing the distribution of frequencies is done by spectral analysis (Zagzebski, 1996).

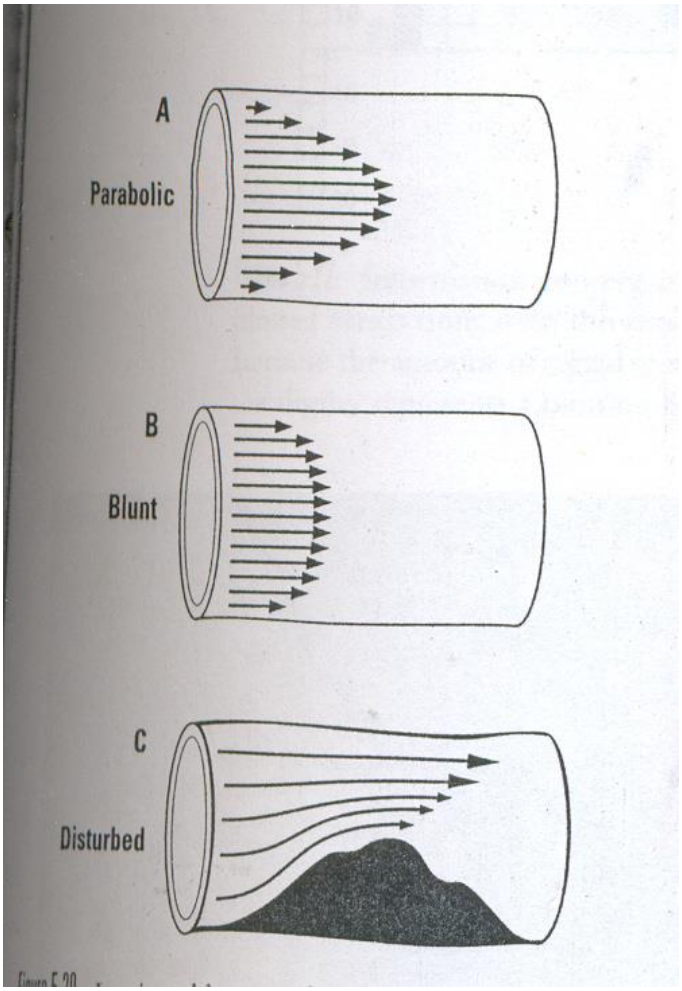


Figure 2.32 illustrate laminar, blunt and turbulent flow patterns (Zagzebski, 1996).

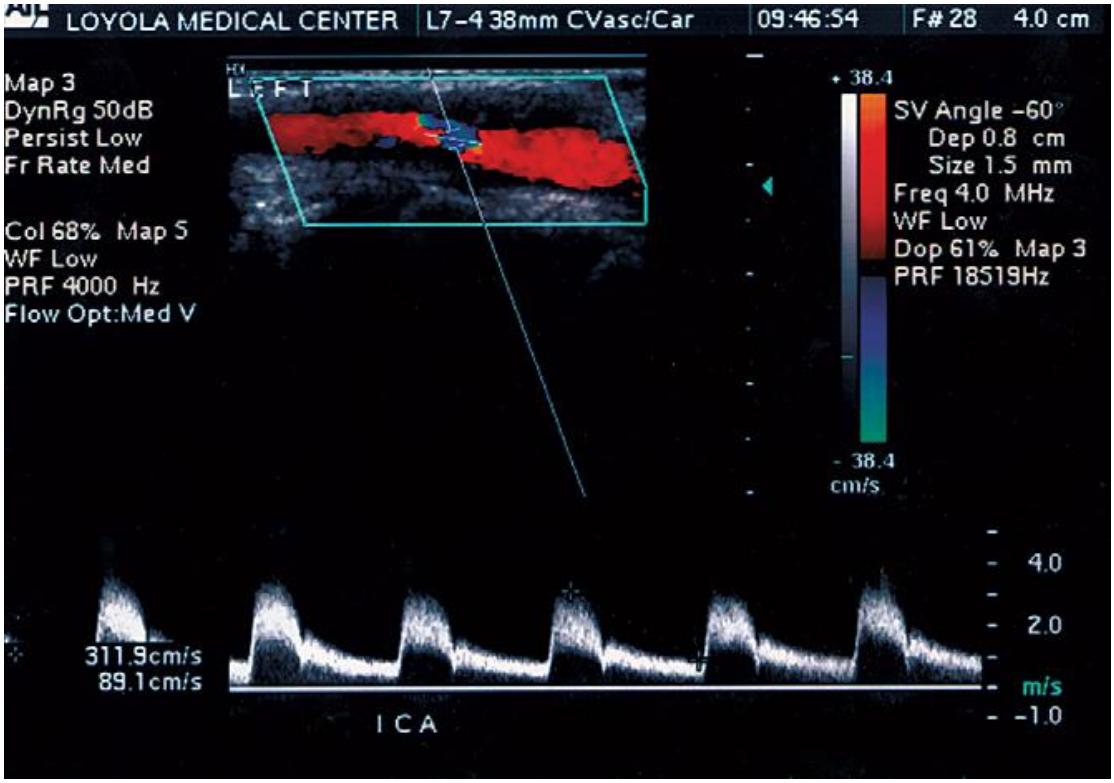
2.2.10.2 Spectral analysis:

Spectral analysis is a process by which a complex signal is broken down or analyzed into simple frequency components. In physics and engineering the most common way to do spectral analysis is to use a process called Fourier analysis. A commonly used device that performs the spectral analysis in ultrasound instruments is a fast Fourier transform (FFT)

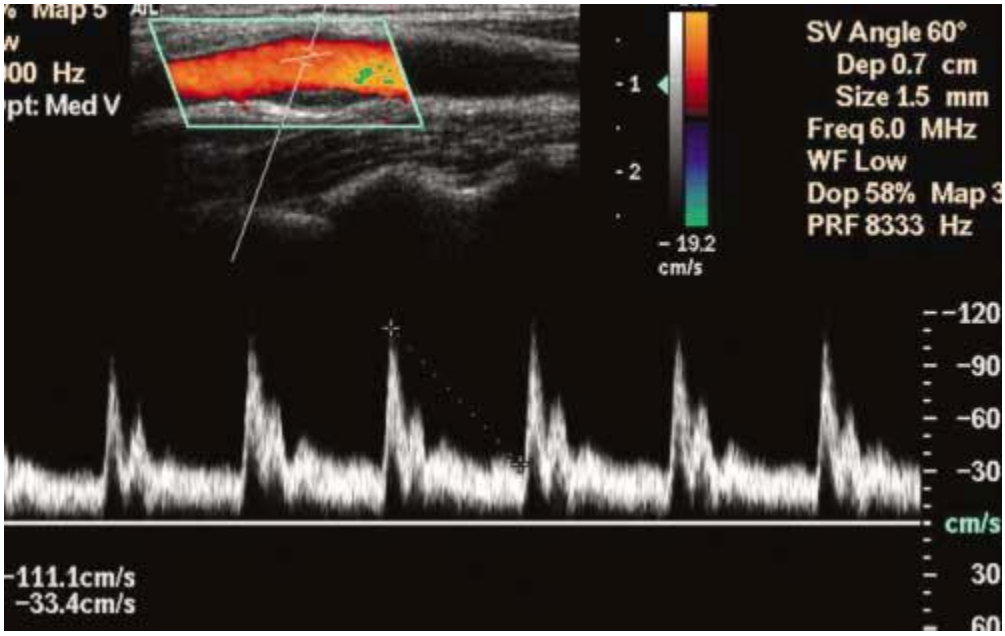
analyzer. The FFT instrument along with a display screen allows the amount of Doppler signal present at different frequencies to be displayed as a function time. The FFT operates serially on small 1 to 5ms segments of the Doppler signal. The signal segment is converted to digital format "digitized" in an analog-to- digital (A/D) converter and is then sent to the spectral analyzer. The analyzer produces a record showing the relative amount of signal with each of several discrete frequency bins. Then operate on another signal segment and so on, producing a continuous display (Zagzebski, 1996).

2.2.10.3 Information on the spectral display:

The Doppler spectral display provides a readout of the distribution of frequencies and hence reflector velocities contributing to the signal. Velocity versus time flow patterns for arteries and many large veins have been established. Deviations of these patterns from normal are evaluated using spectral Doppler. The example in Figure 3.33 is for a normal carotid artery and one that has a stenosis, where the sample volume was placed at the distal margin of the stenotic region. Other important characteristics of flow pattern may also be gleaned from the spectral display. For example with pulsed Doppler and a short sample volume gate positioned in the center of a vessel, a narrow band Doppler frequency spectral display is usually obtained in Figure 2.34 (Zagzebski, 1996).



A



B

Figure 2.33 shows spectral Doppler tracing for a normal right internal carotid artery (RICA), (A) an ICA artery a stenosis where is the peak systolic velocity is 312 cm/s and (B) in normal ICA the peak velocity during systole is 111cm/s (Zagzebski, 1996).

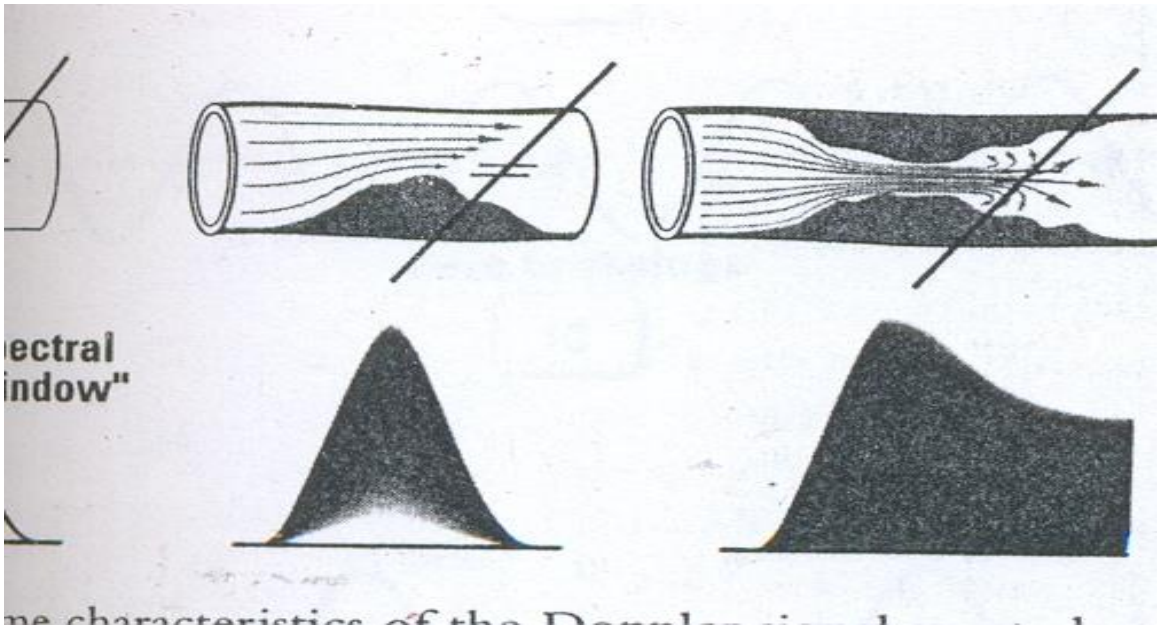


Figure 2.34 shows some characteristics of the Doppler signal spectral display for different flow condition, left diagram presents a normal spectrum with the gate selecting a very narrow range of velocities that contribute to the signal, open region within the spectral envelope during peak flow is called the spectral window, partial or total fill of the spectral window occurs with turbulence seen in the two panels on the right (Zagzebski, 1996).

The area beneath the peak of the spectral trace is called the spectral window, partial or total fill-in of the spectral window can occur in the presence of turbulence. These disturbances in the Doppler spectrum are also called spectral because they are related to a wider range of Doppler frequencies from the sample volume. The presence of obstructions may sometimes be detected from the spectrum. If the vessel is large compared to the sample volume, a fairly narrow velocity ranged is sampled. This results in a narrow frequency band and the spectral window on the display. In presence of mild or several turbulence caused by obstruction, this spectral window is filled in partially or entirely Figure 2.35 (Zagzebski, 1996).

Some instruments display additional information related to the instantaneous distribution of velocities in the spectrum. The "mean" Figure 2.35 is the average value of all signals in the spectrum at any given time. An example is shown in Figure 2.36 where the mean frequency trace is superimposed on spectral trace from the carotid artery. The "mode" is the

most likely velocity, or the value in the spectrum that is the whitest shade of gray, this correspond the most prevalent red blood cell velocity in the sample volume. The spectral "width" indicates the range of Doppler frequencies and hence reflector velocities contributing to the Doppler signal and the peak which is the top of the spectral envelope (Zagzebski, 1996).

Various parameters have been derived from the Doppler spectrum to quantify important properties of the flow. For example the pulsatility index PI as seen in Figure 2.37 and Figure 2.36, is defined by equation 2.2

$$PI = \frac{Max - Min}{Mean}$$

Where max and min refer to the peak systolic and minimum diastolic velocities, respectively during the cardiac cycle (Zagzebski, 1996).

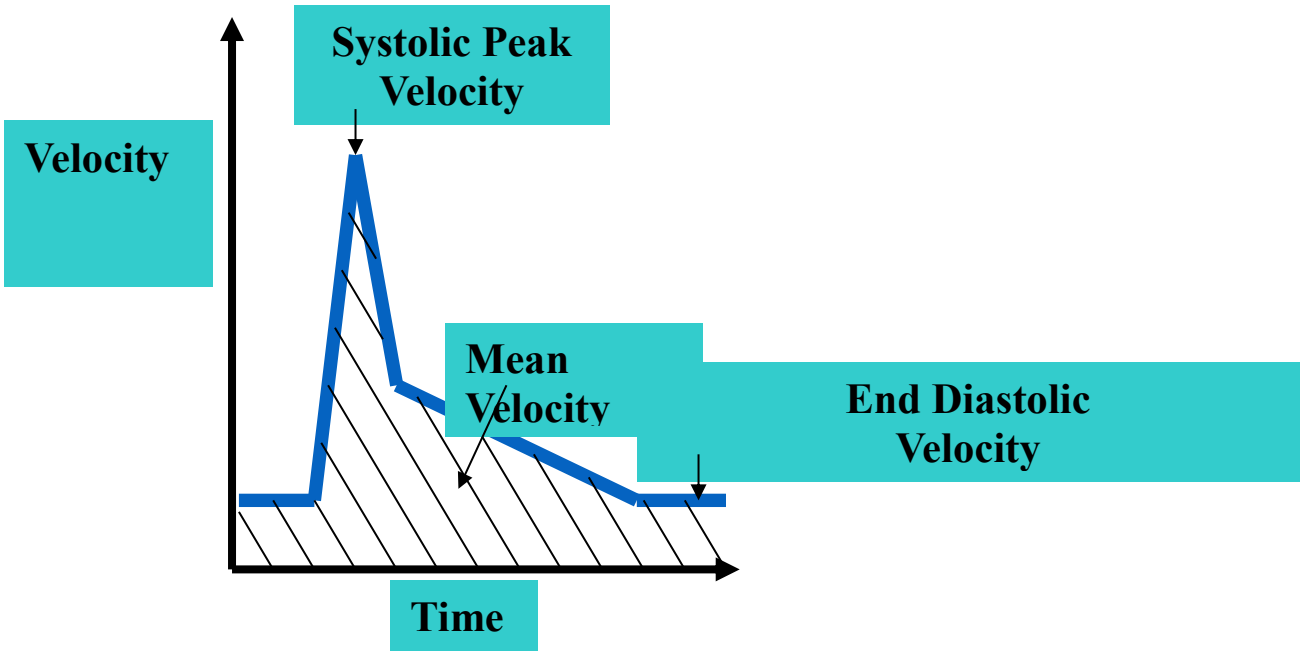


Figure 2.35 determine definition of the peak, mean and diastolic velocities on a Doppler spectral display (Zagzebski, 1996).

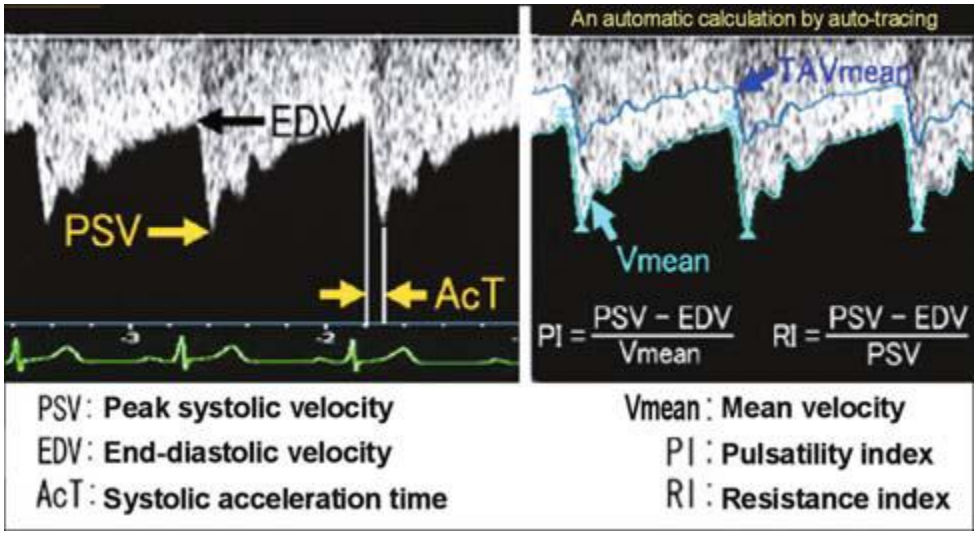


Figure 2.36 shows spectral Doppler display with calculated mean velocity (Zagzebski,1996).

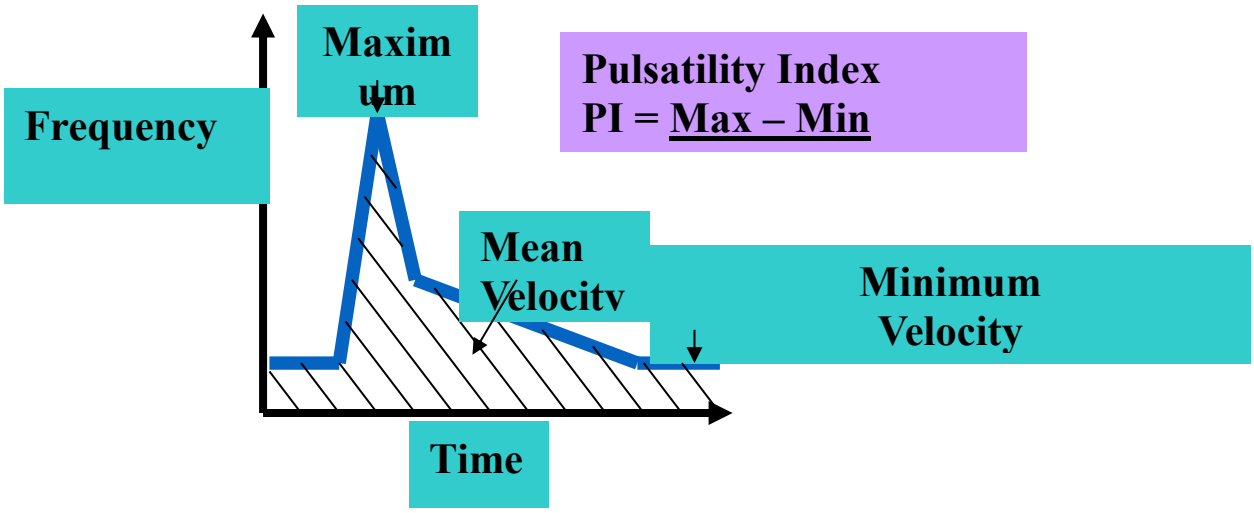


Figure 2.37 shows how calculated Pulsatility Index (Zagzebski, 1996).

These quantities are obtained from the spectral display as shown in Figure 2.38 and Figure 2.36. The average value during the cardiac cycle either must be obtained by the operator tracing the mean spectral waveform or for some instruments by algorithms in the instrument. A similar index the resistivity index does not require estimates of the mean velocity during the cardiac cycle but only maximum and minimum values. It is defined by equation 2.3

$$RI = \frac{Max - Min}{Max}$$

An advantage of these parameters is that they provide data on the relative resistance to flow of the vascular bed, they do this without the need to quantify velocities and flow absolutely, where angle correction must provide. Angle correction may be impossible especially in situations where the vessel lumen cannot be visualized such as in the kidney (Zagzebski, 1996).

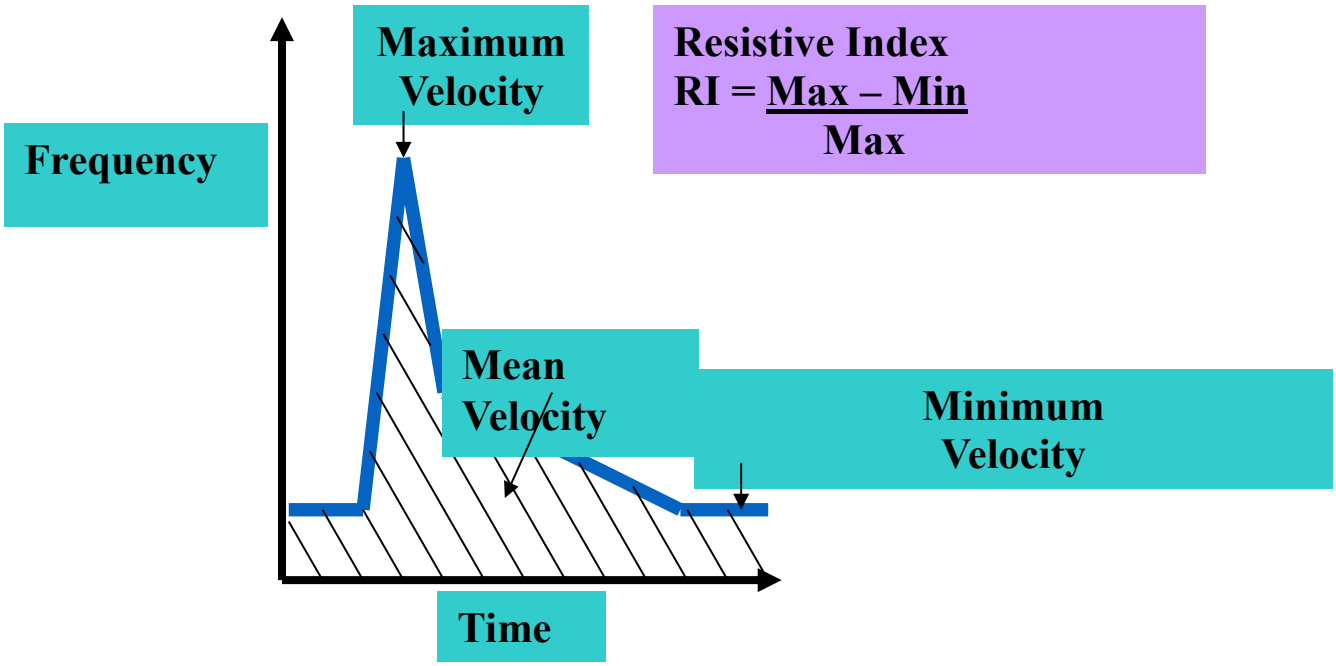


Figure 2.38 determine the parameters used to calculated the Resistivity index, RI (Zagzebski, 1996).

In general PI values greater than 1.2 are consider high and values below 0.8 are considered low also RI values greater than 0.7 are interpreted as high and values less than 0.4 are considered low. Also the systolic/diastolic (S/D) ratio (sometimes called the A/B ratio), can used to describe the shape of flow waveforms in a quantitative way as defined in equation 2.4 and seen in Figure 2.39 (Zagzebski, 1996).

Equation 2.4

$$\text{A/B ratio} = \frac{\text{Max}}{\text{Min}}$$

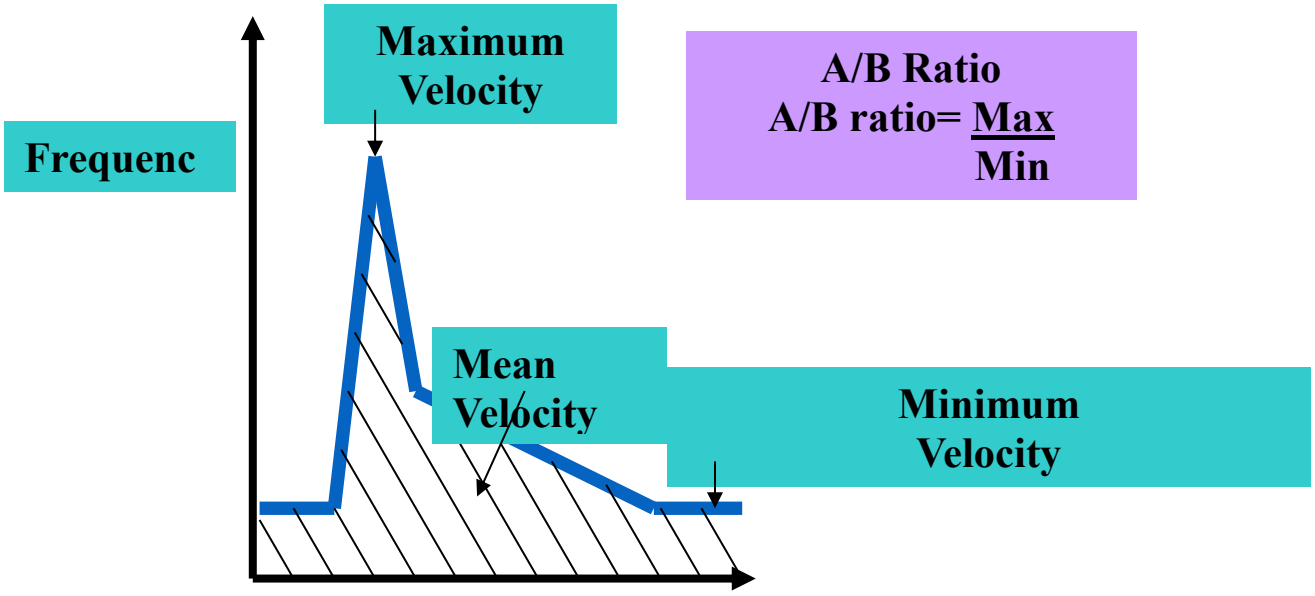


Figure 2.39 determine the parameters used to calculated the systolic/diastolic, A/B (Zagzebski, 1996).

2.2.11 Aliasing and the Nuquist frequency:

2.2.11.1 Sampling the Doppler signal:

With a pulsed instrument the output Doppler signal is built up discrete "pieces", one piece being added each time a pulse is launched and echo signals are detected from the sample volume. We say that the Doppler signal is "sampled" rather than recorded continuously. Sampling in somewhat like a strobe light illuminating a dancer on stage. If the strobe frequency is high enough, the movements of the dancer may be followed easily but if the strobe flashes are too slow the audience only sees a jerky, discontinuous movement. In pulsed Doppler each time a pulsed is launched by the transducer and an echo from moving reflectors detected a

sample of Doppler signal is stored in the sample and hold unit. The frequency of a pulsed Doppler instrument is equal to the pulse repetition frequency (PRF) in Doppler mode (Zagzebski, 1996).

In any situation where sampling occurs the greater the sampling frequency in comparison to the actual frequencies present, the better the rendition of that signal after it has been sampled. This illustrated in Figure 2.40 where a sine wave signal (solid line) is shown sampled at a fairly high rate (arrows). The lower curve is the resultant sample version of the signal. It is fairly easy to appreciate the original signal with the sampling conditions in this example; the sine wave corresponds to the actual Doppler signal, the arrows to individual pulses transmitted and echoes picked up by the transducer and the dotted line on the PRF, limiting the sampling frequency. For pulsed Doppler instruments the upper limit of the PRF is established by the fact that a sound pulse takes a small but measurable amount of time to travel to the sample volume and return. Before a pulse is launched by the sample volume, if the waiting time between pulses in insufficient "range ambiguities" arise rang ambiguities are uncertainties in the actual range from which Doppler signals occur (Zagzebski, 1996).

At the very least the PRF on the instrument must be great enough to the sample the Doppler signal at least two times for each cycle of the Doppler signals. If the PRF is less than twice the frequency of the maximum Doppler (FD) signal frequency, the aliasing will occur. Aliasing is production of art factual, lower frequency components in the signal spectrum when the pulse repetition frequency of the instrument is less than two times the maximum frequency of the Doppler signal. The condition when the PRF equals 2FD, known as the Nyquist sampling rate. It defines a minimum sampling rate is below the Nyquist rate, the signal can be determined unambiguously (Zagzebski, 1996).

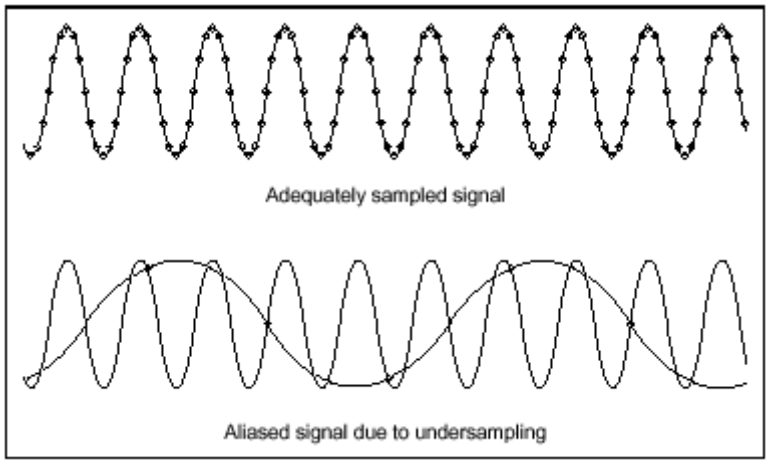
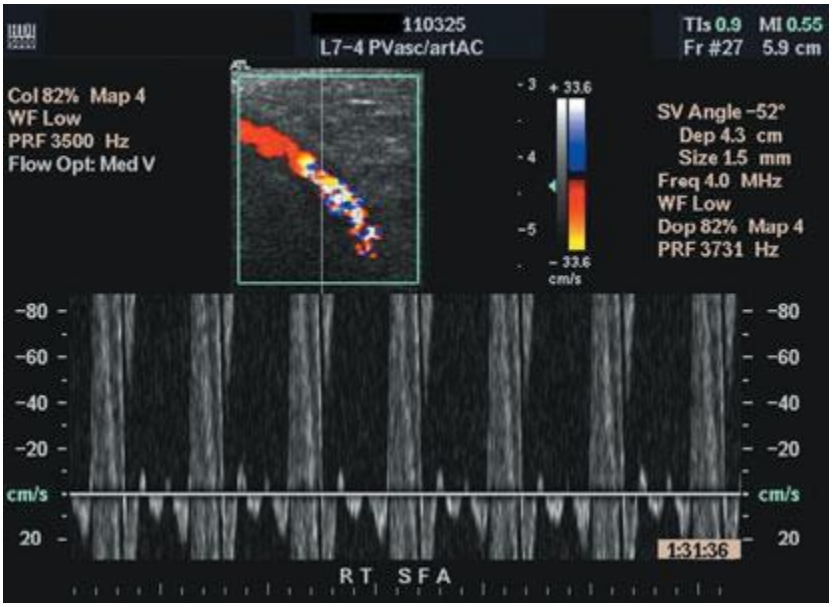


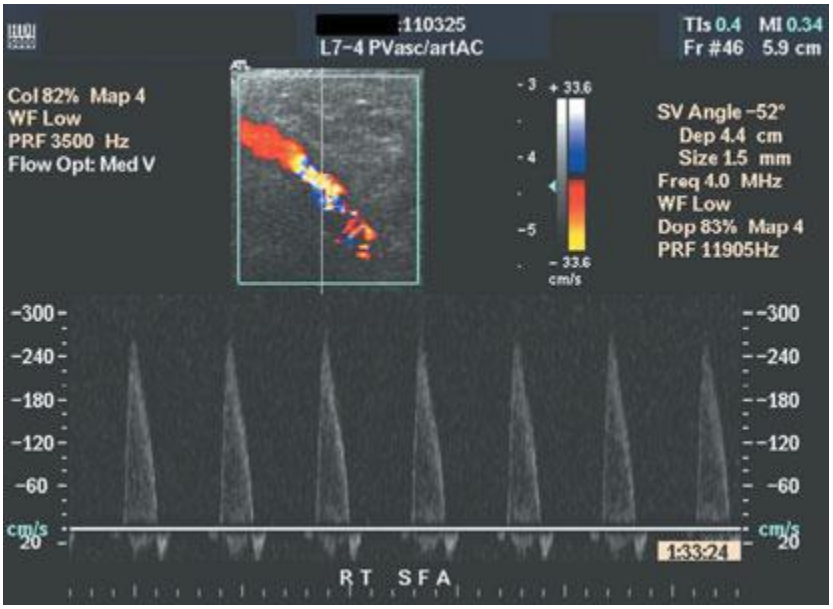
Figure 2.40 illustrate sampling a signal (www.ni.com, access on 20.5.015).

2.2.11.2 Aliasing:

The production of aliasing is occurring when the PRF is less than twice the frequency of the maximum Doppler signal frequency. Aliasing is manifested in three ways on pulsed Doppler instrument equipped with a spectral display. First the display "wraps around" producing an apparent reversal of the flow direction Figure 2.41. Second the audible Doppler signal exhibits a noticeable loss of high frequencies as the frequency exceeds the maximum. Third the audible Doppler signal also sounds as though flow reversals occurs (Zagzebski, 1996).



A



B

Figure 2.41A, shows manifested of aliasing on a spectral Doppler display the spectrum "wraps around" from the top to the bottom of the display, producing an apparent reversal of flow even through flow does not reverse itself the high frequencies are converted to low frequencies on the display where in B the elimination of aliasing is by increasing the velocity scale

and the Doppler instrument automatically increases the PRF when the operator changes the scale setting (Zagzebski, 1996).

2.2.11.3 Elimination aliasing:

The most straight forward way to eliminate aliasing when it occurs is to adjust the velocity or frequency scale on the Doppler spectral display as shown in Figure 2.41**,** B. Most instruments have the PRF of the pulsed Doppler unit linked to the scale setting. As the scale setting is increased, the PRF is automatically increased to satisfy the Nyquist rate for the maximum scale setting. If the spectral scale is at its maximum setting another method to eliminate the appearance of aliasing is to adjust the spectral baseline, Figure 2.42. If neither of these methods succeeds, aliasing may sometimes be eliminated by using a lower frequency ultrasound transducer. Another possible method is to locate a widow to the region of interest for which the incident sound beam angle is closer to 90 degrees (Zagzebski, 1996).

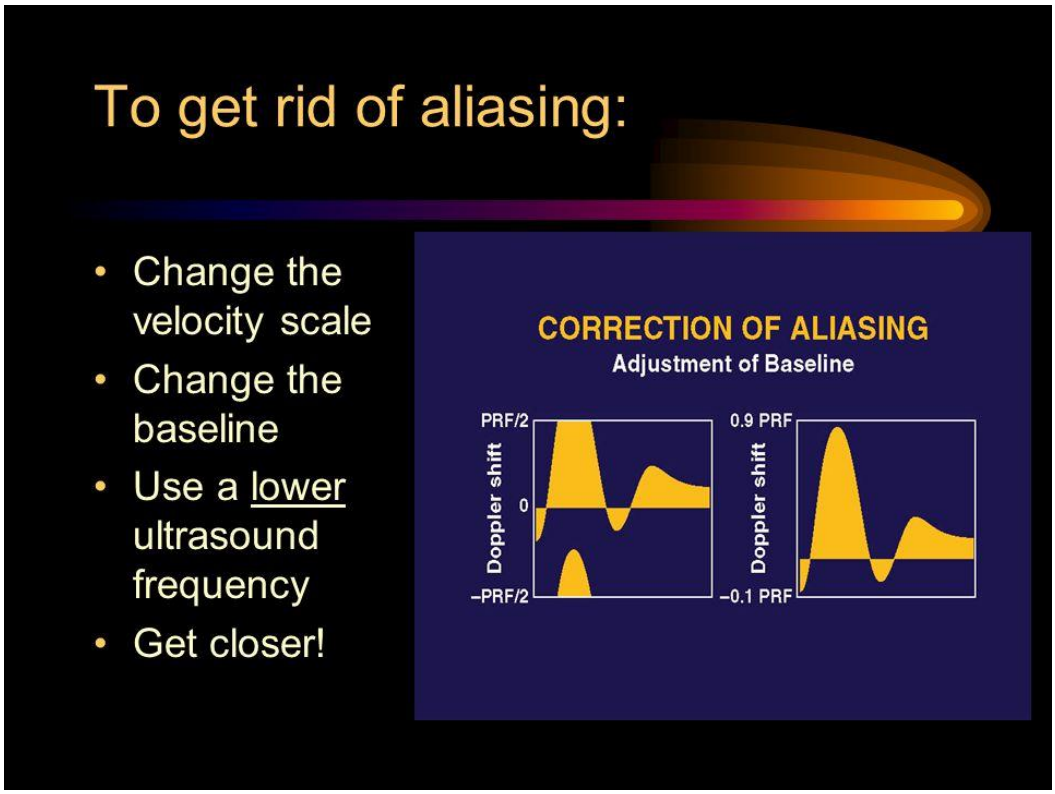


Figure 2.42 shows how to rid the aliasing (Zagzebski, 1996).

2.2.12 Poiseuile's law and equation:

The most important law governing the flow of fluids through cylindrical tubes is called Poiseuile's law which relates velocity and flow volume in the following equation 2.5:

$$V=Q/A$$

Where V is the velocity (cm/sec), Q is the volume flow (cm^3/sec) and A is the cross sectional area of a vessel (cm^2) (Zagzebski, 1996).

Poiseuile's law tells us several important points about blood flow:

1. Flow velocity in a tube (vessel) is directly related to the volume of fluid and inversely related to tube area. Thus, the higher the flow volume, the greater the flow velocity and smaller the vessel, the higher the velocity (assuming other factors remain constant) (Corbett et al, 2005).

2. Flow volume is the product of flow velocity and vessel area and directly proportional to these two factors. It is important to note that flow volume in different segments of the vessel remains the same. This occurs because fluid cannot be created or destroyed as it flows through the vessel. It is the velocity that changes as the blood passes through different segments of the vessel (Corbett et al, 2005).

If this were the only relationship between velocity and flow then the velocity in capillaries would be incredibly high a second equation 2.6 accounts for low velocity within the tiny capillaries:

$$V_1/V_2=V_1/V_2$$

The velocity at any point in the circulatory system is dependent not only on cross sectional area but also on the magnitude of the blood flow (Q), and the magnitude of flow (Q) depends on many factors including pressure gradient, the properties of the fluid and the dimensions of the entire circulatory system. We have already discussed how the pressure gradient changes in the circulatory system, thus accounting for the low flow velocity in the capillary (Corbett et al, 2005).

Poiseuille's law describes the "viscous" or frictional loss of energy that occurs with changing vessel area and is modeled on continuous (non pulsatile) laminar flow of a simple fluid in a rigid of uniform size. Fortunately, it also applies to the flow of blood in the circulatory system which can be pulsatile and in compliant vessels of varying dimensions (Corbett et al, 2005).

Poiseuille's equation 2.7

$$Q = \frac{\Delta P \pi r^4}{8 \eta l}$$

Where Q is the volume flow rate $P_1 - P_2$ is the pressure different (from proximal to distal end of tube), r is the radius of the vessel, L is the length of the vessel and n is the viscosity of the fluid and is the constant of proportionality (Corbett et al, 2005).

Poiseuille's law states that flow (Q) varies directly as the pressure different ($P_1 - P_2$) and the 4^{th} power of the radius of the vessel, and various inversely as the length of the vessel and the viscosity of the blood. Note $P_1 - P_2$ may be substituted as the change in pressure. We can prove a few relationships by examining Poiseuille's equation including:

1. As the pressure differences the flow increases.

2. As the vessel diameter increases the flow rate increases.
3. As the length of the vessels increases the flow rate decreases.
4. As the viscosity of the fluid increases the flow rate decreases.

The most important relationship to be drawn from Poiseuille's equation is the relationship of the radius of the vessel to flow science volume flow is proportional to the 4^{th} power of the radius. Even small change in the cross sectional area of a vessel results in large changes in flow. Also another important relationship from Poiseuille's equation that is:

$$\text{Pressure} = \text{flow} \times \text{resistance} \qquad 2.8$$

Resistance (R) may be defined as the ratio of the pressure drop $(P_1 - P_2)$ to flow (Q), as determine in equation 2.8

$$R = P_1 - P_2/Q \qquad 2.9$$

For example a 10% decrease in the radius of a vessel results in a 35% decrease in flow and a 50% decrease in vessel radius results in 95% decrease in flow (Corbett et al, 2005).

2.2.13 Stenosis Degree:

Carotid artery stenosis is usually caused by an atherosclerotic process and is one of the major causes of stroke and transient ischemic attack (TIA), most common sites of symptomatic stenosis are carotid bulb and the proximal segment of ICA, only measurement the high grade stenosis with ignored lesser degrees of stenosis because it are rarely subjected to endarterectomy. The degree of stenosis is expressed as a percentage reduction in vessel diameter and according to it determine whether a patient go to endarterectomy (htt://radioaedia.org, access on 10.3.016).

There are three methods used to percent and evaluate the degree of the stenosis as seen in figure 2.43 and figure 2.44 below:

1/ NASCET (North American Symptomatic Carotid Endareterectomy Trial) =

(diameter of internal carotid artery above stenosis) − (diameter on nonstenotic internal carotid artery at point of maximum stenosis) / ×100% (diameter of internal carotid artery above stenosis)

As seen in Equation2.10

NASCET = d−a/ d ×100 (figure 2.43) 2.10

NASCET = C−A/ C ×100 (figure 2.44)

2/ ECST (European Carotid Surgery Trial) =

(diameter of normal lumen of internal carotid artery at bifurcation before development of stenosis) −(diameter of nonstenotic internal carotid artery at point maximum stenosis)) / (diameter of likely normal lumen of internal carotid artery at bifurcation before development of stenosis) × 100%

As seen in Equation 2.11

ECST = b−a / b ×100 (figure 2.43) 2.11

ECST = B−A / B ×100 (figure 2.44)

3/ CC method (Common Carotid) = (diameter of common carotid artery)− (diameter of nonstenotic internal carotid artery at point maximum stenosis)) / (diameter of common carotid artery) × 100%

As seen in Equation 2.12

ECST = c−a / c ×100 (figure 2.43) 2.12

ECST = D−A / D ×100 (figure 2.44)

(www.meducator3.net access on 10.3.016).

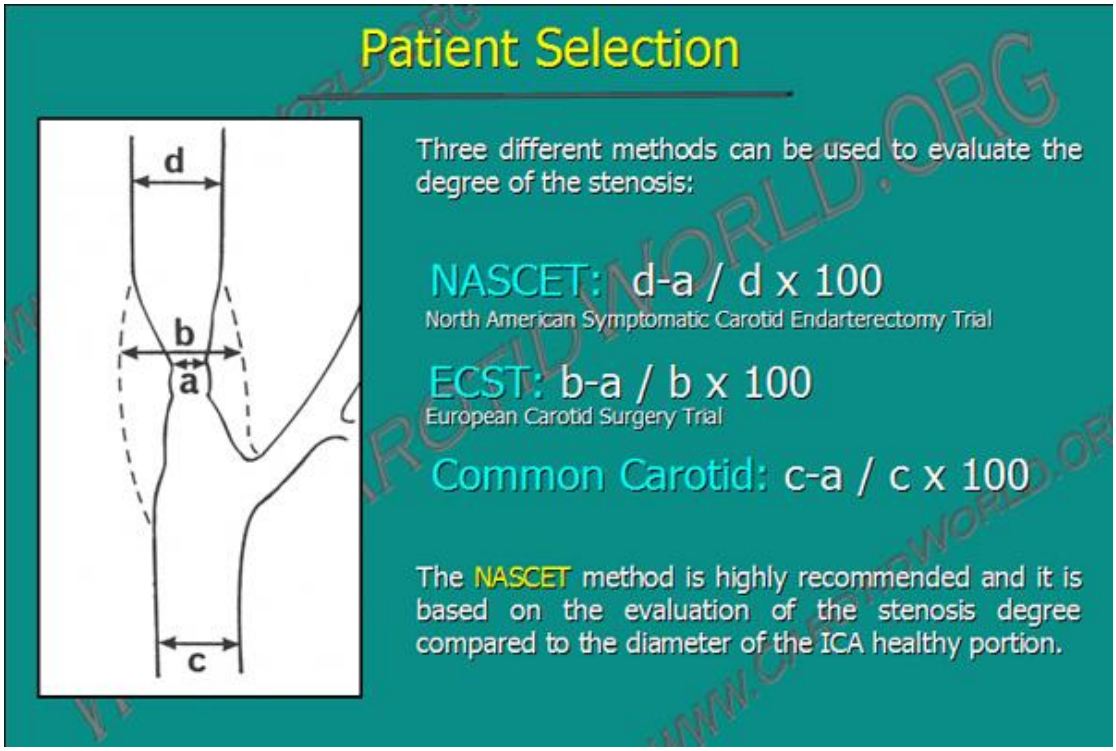


Figure 2.43 shows three different methods used to evaluate the degree of stenosis (www.carotid world.org, access on 10.3.016).

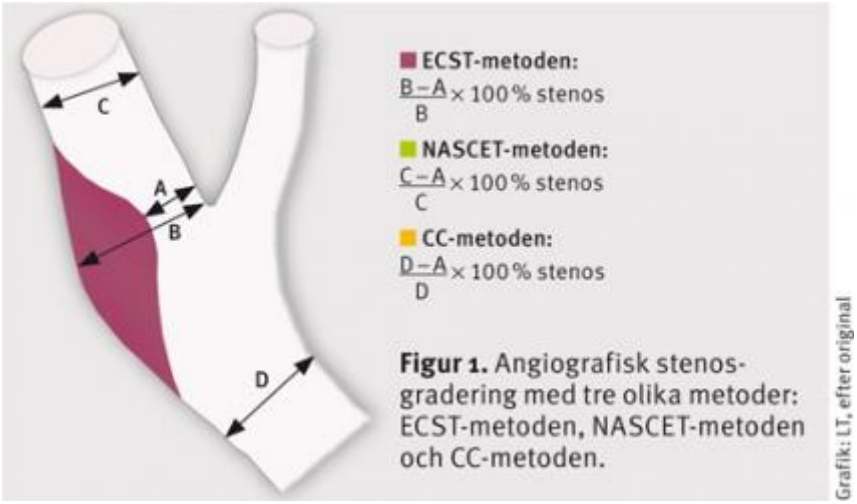


Figure 2.44 shows three different methods used to evaluate the degree of stenosis (www.meducator3.net access on 10.3.016).

2.2.14 Stenosis Severity Calcification:

The stenosis severities calcified as its percentage to mild, moderate and sever as seen in table (www.meducator3.net access on 10.3.016).

Table 2.3 shows stenosis percentage associated with severity calcified (www.meducator3.net access on 10.3.016).

Stenosis	Stenosis Severity
0 - 29%	ECST mild
30 - 69%	ECST moderate
70 - 99%	ECST severe

2.2.15 Comparison of Different Measure

The percent stenosis by ECST criteria =

= (0.6 * (percent stenosis by NASCET method)) + 40%

The percent stenosis by CC criteria =

= (0.6 * (percent stenosis by NASCET method)) + 40% (Rothwell et al, 1994)

Table 2.4 approximate equivalent degrees of internal carotid artery stenosis used in NASCET and ESCT according to recent direct comparisons (www.meducator3.net access on 10.3.016).

NASCET (% stenosis)	ECST (% stenosis)
30	65
40	70
50	75
60	80
70	85
80	91
90	97

2.2.16 Plaques Morphology:

Not only the degree of stenosis can lead the patients to endarterectomy, but also the carotid plaque ultrasonic morphology or characterization can emphasis the risk of stroke and clinical significance (Sabetai, 2000).

The morphological variables are grouped in two categories:

1/ plaque surface configuration (smooth or ulcerated)

The ultrasonic characteristics of the plaque surface classified as regular when the blood lesion interface is smooth and unbroken or irregular when a break in the echo-reflective surface of the lesion is observed or the surface is uneven as seen in figure 2.45 and 2.46(Sabetai, 2000).

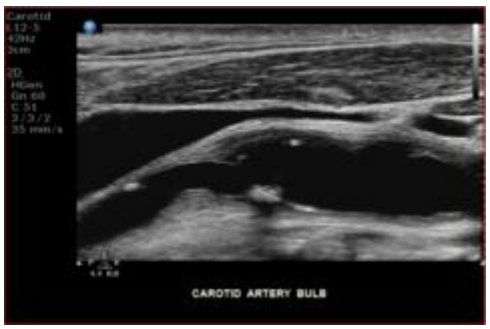


Figure 2.45 shows regular smooth calcified plaque in artery Bulb (www.slideshare.net, access on 12.1.016).

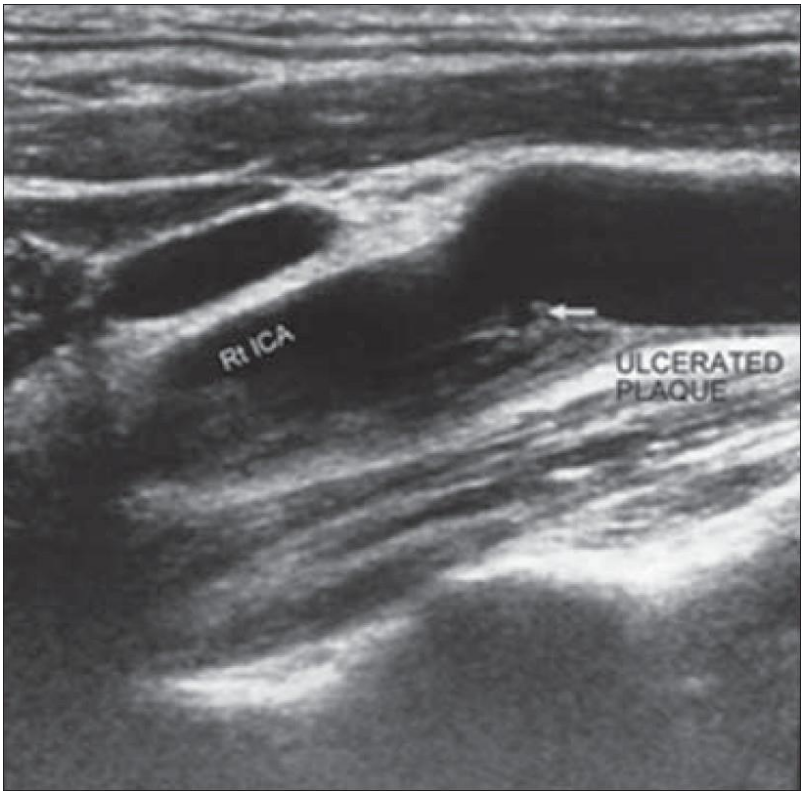


Figure 2.46 shows irregular ulcerated plaque (www.slideshare.net, access on 12.1.016).

The color Doppler flow add more classified to plaque morphology such as the definition of plaque ulceration, which appear as plaque niche filled with reversed flow on longitudinal and transverse views as seen in figure 2.47 (O'Donnell Jr et al, 1985).

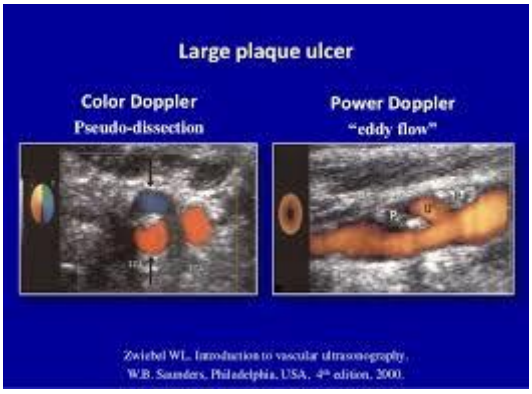


Figure 2.47 shows plaque ulceration (www.slidesshare.net, access on 12.1.016).

2/ Plaque Internal Stricture:

The early systems classified the carotid plague according into internal surface into calcified, dense (high level echoes) and soft (low level echoes) as seen in figure 2.48 (G. Geroulakos, M.M. Sabetai, 2000).

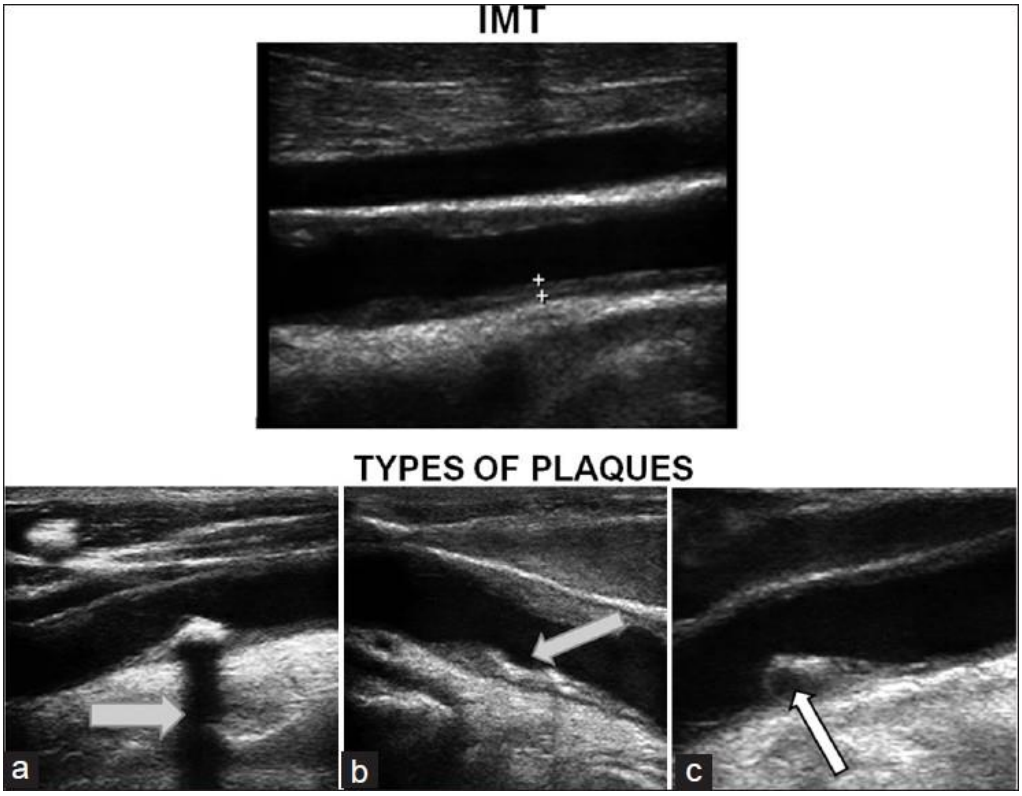


Figure 2.48 shows classification of the carotid plaque due to internal surface, a is calcified, b dense and c is soft (www.annalsofian.org, access on 12.1.016).

Another classification introduces two new types:

1/ Homogenous:

Defined as plaque with uniform high or medium level echoes with histological fibrous lesion as seen in figure 2.49, figure 2.50 and figure 51.

2/ Heterogeneous:

Defined as plaque with high, medium and low level echoes and histologically contained variables amounts of intra-plaque such as hemorrhage, lipids and cholesterol crystals as seen in figure 2.49, figure 2.50 and figure 2.51 (Sabetai, 2000).

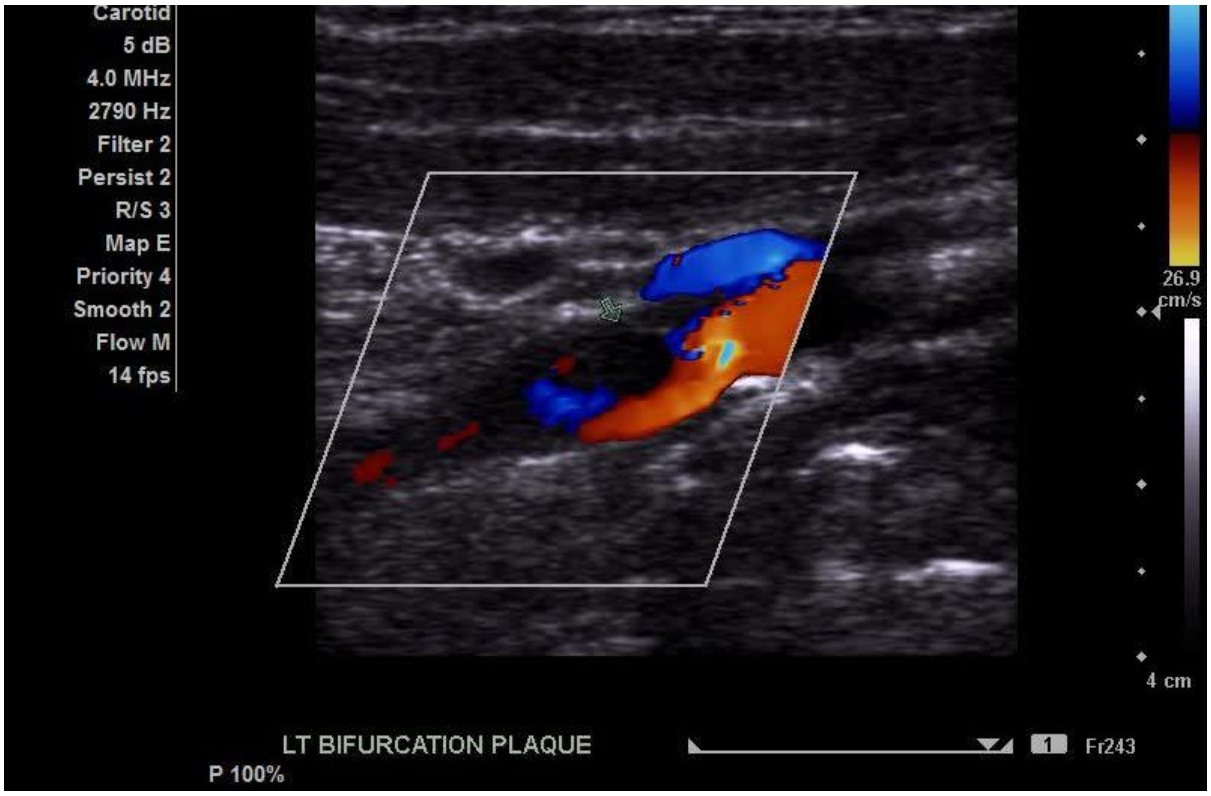


Figure 2.49 shows homogenous echolucent plaque at Lt Carotid artery bifurcation (www.vascularmedicinelab.com, access on 12.1.016).

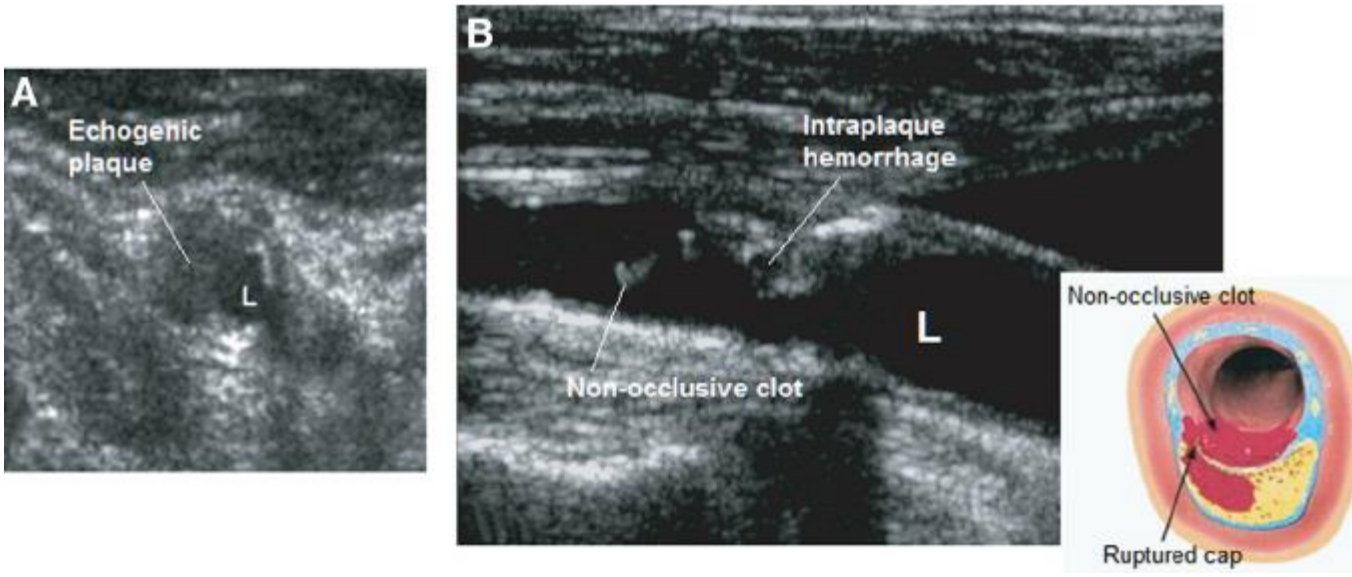


Figure 2.50 shows heterogeneous plaque with intra-plaque hemorrhage (www.researchgate.net, access on 12.1.016).

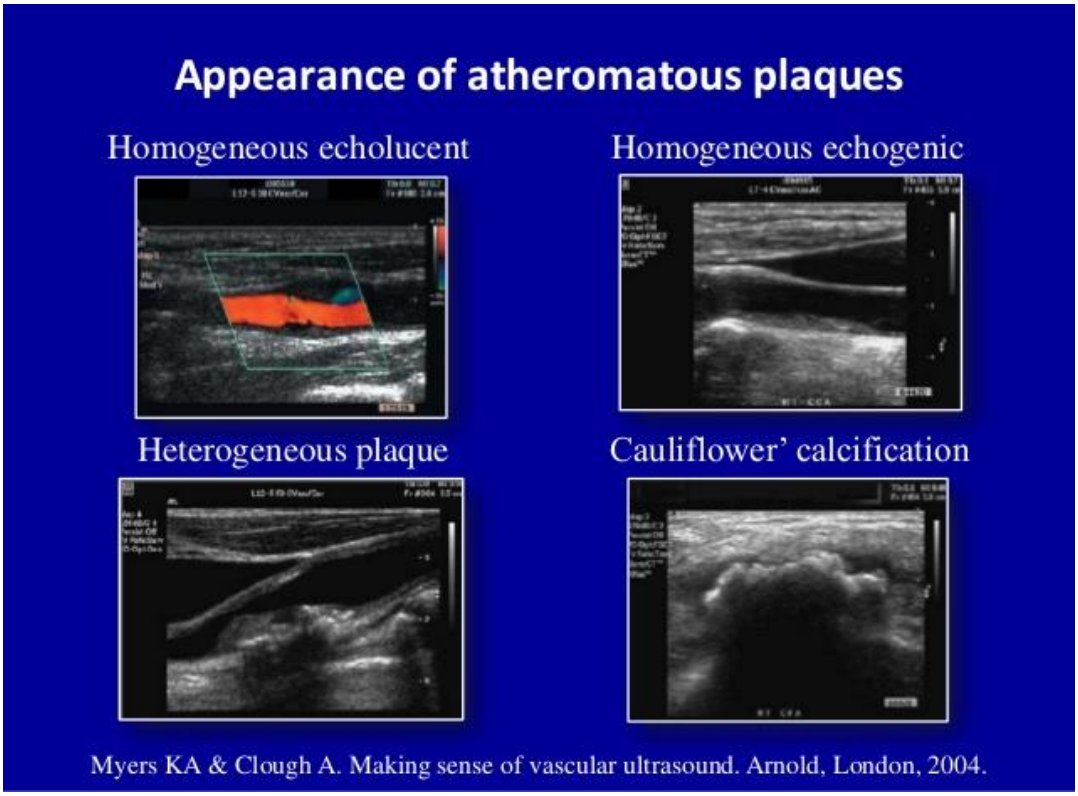


Figure 2.51 shows homogeneous and heterogeneous plaques (www.slidesshare.net, access on 12.1.016)

Chapter Two – Section Three

Previous Studies

Regarding the issue of Diabetes Mellitus effects in the common carotid arteries, many authors and ultrasound practitioners have wrote bout. They agree that there are obvious effect in common carotid arteries such as atherosclerosis, emphysema, coronary artery disease, heart attack and increased blood pressure. In general the influence of diabetes mellitus in arteries has been cited by many authors, however the influence of common carotid arteries with diabetes mellitus which is under focus in this research which also has been considered by many researchers to highlight it is response to diabetes mellitus in different aspects as follows:

- **(Garg S et al)(2016)** carried out study to evaluate the prevalence of atherosclerosis, haemodynamic and morphological change that take place in carotid arteries with risk factor (DM, Hypertension and coronary artery disease) and determine the association of risk factors with carotid abnormalities, examined 1043 patients by Doppler ultrasonography to measure CCA, IMT, ICA IMT and percent stenosis. They found that the prevalence of sever stenosis >70% was low while the prevalence of mild stenosis <50% was quite high. In all age groups, stenosis was more prevalence and more sever in men as compared to women and DM shows the strongest positive correlation with all three measure of interest.

- **(Alonso N et al) (2015)** they designed compared study between patients with type2 diabetes mellitus and diabetic retinopathy without cardiovascular events and normal renal function with patients without diabetic retinopathy to test the concept that say

the type 2 diabetes mellitus and diabetic retinopathy increased atherosclerotic burden. A total of 312 with type 2 DM (153 of them had diabetic retinopathy) were examined by ultrasound to measure IMT and plaque in CCA, Bifurcation and ICA. The result shows that the percentage of carotid plaques and prevalence of plaque in type 2 DM patients with diabetic retinopathy was higher than in type 2 DM patients without diabetic retinopathy (68% vs. 52.2%) and (44% vs.21.4%) respectively.

- **(Liapis ch et al) (2000)** carried out study to assess the incidence and rate of progression of ICA stenosis to determine the related risk factors DM, HT and stroke, 442 carotid arteries with varies degree of stenosis examined by color Doppler ultrasonography every 6 months, 134 (30%) of these arteries were diabetes mellitus, 248 (56%) hypertension and 90 (20%) stroke. They found that the progression of ICA stenosis occurred in 19% of cases and the mean progression rate in these cases was 15% annually and was correlated with coronary artery disease and plaque characterizations.

- **(MU Yu-ming et al) (2005)** establish study to investigate the effect of diabetes and diabetes associated with hyperlipiodemia on the atherosclerosis of carotid arteries using color Doppler ultrasonography in 131patients, included 33 diabetes patients (DM), 55 diabetes associated with hperlipiodemia patients (DH) and 40 controlled subjects. They were examined by Doppler ultrasonography to measure CCA IMT, IMT of bifurcation (BIMT), RI and PI. They found that the IMT was higher in DM and DH group than that in the control group, with highest in DH

among three groups. Compared with controlled group the PSV/EDV and volume were lower and RI and PI were higher in DM and DH groups.

- **(Mustsumoto et al) (2008)** carried out study to investigate the serum level of apolipoprotein B concentrations and insulin resistance can be good markers of carotid atherosclerosis in patients with type 2 DM, the 66 type 2 DM patients with carotid atherosclerosis compared with 6 patients in 66 ages. They found that the combination of apolpoprotein B concentration and insulin resistance is a superior marker of carotid atherosclerosis in patients with type 2 DM (90.9%).

- **(Boseuski M et al) (2009)** run out study to define the risk factors for developing of carotid artery disease among 30 patients with type 2 DM and absent vascular disease (60% were women and 40% of them were men) and the carotid arterial disease was define if carotid plaque or stenosis >50% presented. They found that the development of carotid arterial disease was registered in 43% of patients and progression of carotid IMT was found in 62.5% of patients.

- **(O'Donnel et al) (1983)** compared B-mode ultrasound and selection arteriography with pathologic specimens obtained from 89 carotid endarterectomies, while arteriography detected only 16 of 27 ulceration plaque with sensitivity 59% and B-mode ultrasound did better24 of 27 with sensitivity 89%. Also the two imaging compared specificity while arteriography has 73% the B-mode ultrasound get 89%

- (**Comerota et al) (1990)** demonstrated that the degree of stenosis significantly affects diagnostic sensitivity. B-mode sensitivity for the presence of ulceration plaques were 77% in plaques with less than 50% stenosis and only 41 in plaques with greater than 50% stenosis. The corresponding figures for arteriography were 77% and 48% respectively.
- **(Sitzer M et al) (1996)** recently more study of 43 consecutive patients with greater than70% internal carotid artery stenosis, plaque surface abnormalities were detected by Duplex imaging evaluation of the corresponding endarterectomy specimens. The sensitivity of Duplex imaging in detecting surface ulceration was only 33%.
- **(Hochanomiz J et al) (2009)** carried out study to provide normal reference values of ratio of blood flow velocity in ICA to those in CCA using color Doppler ultrasonography, the aim of this study to provide reference data for the V(ICA)/V(CCA) ratio for the PSV,EDV and mean velocity (MV) in 343 healthy subjects divided into 3 groups, group I < 40 years, group II 40 – 60 years and group III > 60 years and examined by color Doppler ultrasonography, they found that the values of the PSV(ICA)/PSV(CCA) as follows:

  In women group I = 0.8(0.48- 1.14)

  In women group II = 0.88(0.36 – 1.4)

  In women group III = 0.9 (0.36 – 1.4)

  In men group I = 0.65 (0.32 – 0.98)

  In men group II = 0.72 (0.37 – 1.05)

  In men group III = 0.91 (0.27 – 1.56)

The ratio of PSV increased with age in men and its values were significantly higher in women than in men in the age group I and group II.

- **(Ostling G et al) (2007)** study the increased echolucency of carotid plaques in patients with type 2 DM, the aim of the study to evaluate whether patients with type 2 DM have different plaque echogenicity (47 patients) than do non-diabetic subjected (51 patients), both with carotid artery plaque in different echogenicity assessed by quantitatively on B-mode ultrasound o images by standardized gray-scale median values. They found that Gray-scale median values were significantly lower, indicating more echolucent plaques, in patients with type 2 diabetes compared with non-diabetics (37.0±14.8 vs. 45.5±15.4, *P*=0.007).
- **(Akasaka et al) (2010)** investigated the atherosclerosis in patients with different vascular disease (353 patients), classified as 92 patients with coronary artery disease, 62 cerebral vascular disease, 104 with peripheral arterial disease. They were examined by ultrasound to clarify whether the accumulation of vascular disease affects the IMT. They found that the maximum IMT of the carotid artery expanded with increasing numbers of vascular disease as follows:

  No vascular disease --- (1.1 +/- 0.51)

  One vascular disease --- (1.38 +/- 0.63)

  Two vascular diseases --- (1.69 +/- 0.65)

  Three vascular diseases --- (2.1 +/- 0.67) and the accumulation of vascular disease independent on the types of the vascular lesion lead to acceleration of the carotid atherosclerosis.

- Early detection of atherosclerosis in type 2 DM patients by endothelial dysfunction and IMT have consider by **(Ifrim S and Vasilesu R) (2004)**, the aim of the study was to evaluate whether peripheral endothelial function and CCA IMT are impaired in type 2 DM patients with inadequate glycemic control, 20 cases examined by ultrasound 10 as controlled group and 10 patients with type 2 DM. They found that the IMT was significantly increased in DM patients.
- **(Soldatos S et al) (2011)** was carried out study comprehensively characteristics of large artery biomechanical puporties and examine their relationship to cardiac function in patients with type 2 DM, 55 individuals with type 2 DM compared with 66 healthy controlled group to assess the carotid pulse wave velocity and cardiac augmentation index, they found that the pulse wave velocity was higher when compared with the healthy population while carotid augmentation index was not different between two group.
- Additional study was carried out by **(Danese et al) (2006)** which about the influence of Hypertension and DM in the sites of atherosclerotic plaques in carotid arteries beside to verify if the anatomical site of plaque influence plaque morphology and vulnerability. They found that a significant association between type 2 and the presence of non-ulceration plaque.
- **(Hirano M et al) (2008)** carried out study to clarify the relation between the measurement of IMT and plaque in 50 patients with DM, 25 of them with type 1 DM and rest with type 2 DM, the study revealed that the highest percentage of plaque was found in type 2 DM which is (29.6%) and lowest in type 1.

- **(Stion C et al) (2014)** demonstrated study to assess the prevalence of carotid atherosclerosis, intra plaque neo-vascularization and plaque ulceration in 51 asymptomatic patients with DM using ultrasound. The revealed 90% (46) patients had subclinical atherosclerotic plaques with a median plaque thickness (2.4cm) beside 88% 0f patients the plaque had an ulceration surface.
- **Ahmed Z, (2006),** carried out study to evaluate and compare the Carotid artery IMT in patients with type 2 DM and control group using color Doppler sonography. The study revealed that the IMT in DM group was significantly higher (0.75 ± 0.148 SD mm) than that in the non-DM group (0.59 ± 0.154 SD mm) and routine sonographic evaluation of carotid arteries in DM type 2 patients is helpful in identifying patients with substantial atherosclerotic burden .

Chapter Three

Methodology

3.1 Type of the study:

This prospective study was done at Khartoum State which is deal with patients suffering from DM, present to ultrasound department in Ribat Hospital.

3.2 Population of the study:

Patients with DM, present to ultrasound department in Ribat Hospital between 11/2014 to 11/2016.

3.3 Sample selection:

The Sample size consisted of 200 patients with DM, who fulfilled inclusion criteria, were selected from inpatient and outpatient.

3.3.1 Inclusion criteria:

- Age: Patients of all age groups.
- Sex: Both male and female patients.
- Patients with DM

3.3.2 Exclusion criteria:

- Patients with hypertension
- Smoker patients
- Patients with history of endarterectomy and stenting.

3.4 Tools and equipment:

The common carotid arteries duplex examination should be performed only with appropriate instrumentation. The current standard of practice in this research includes the following tools and equipment which used

effectively and accurately to give the desired expected results, planed previously in the hypothesis and objective articles in chapter one.

3.4.1 Ultrasound system:

The applied Ultrasound unit was a Siemens, Soniline G 60S, as seen in figure 3.1.

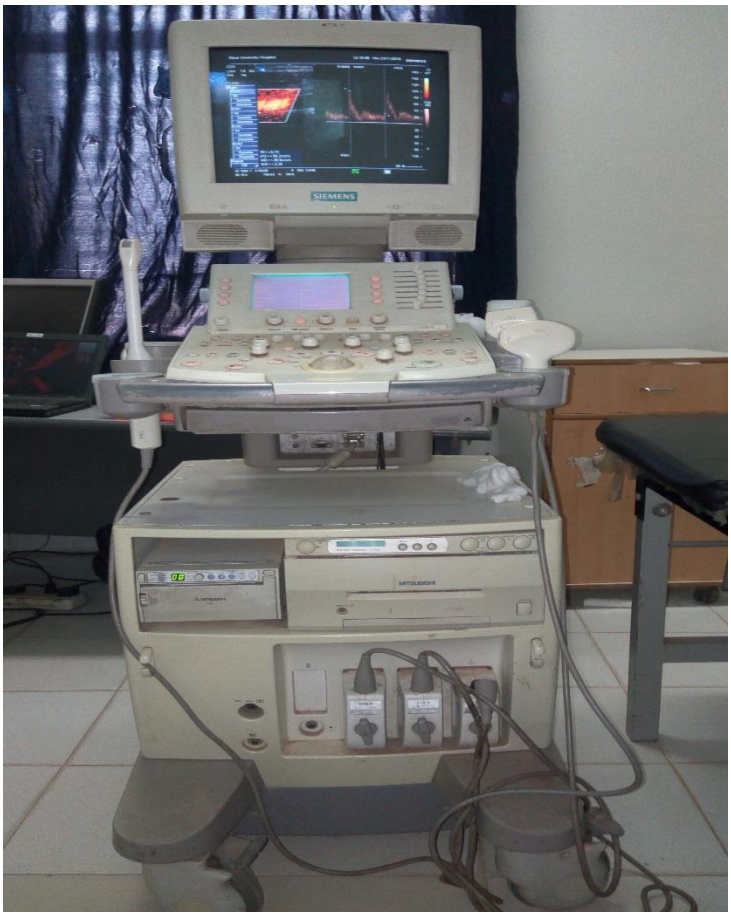


Figure 3.1 shows Siemens, Sonoline, G 60S, Ultrasound machine which was used in the research.

3.4.2 Ultrasound transducer :

The applied Ultrasound transducer was a linear probe with a frequency of 7 – 10 MHz,

3.5 Patient preparation:

The common carotid arteries for the Sudanese diabetic patients have been scanned without previous preparation; only a short orientation about the exam was given to the patient.

3.6 Method of the study:

3.6.1 Examination protocol:

An examination or the techniques protocol established within Ultrasound Department to ensure that common carotid arteries Sonography is performed consistently, comprehensively and accurately. These techniques may be modified to match the needs of specific patients. In all cases, however the protocol should meet or exceed the standards established

3.6.2 Patient position:

The sample under study has been scanned to visualize the common carotid arteries, internal and external carotid arteries, in the supine position with knee support, with the examiner seated at the patients head. The neck scanning was enhanced by titling and rotating the head away from the side being examined as in Figure 3 with possible adjustment for the position of the head and neck during the examination to facilitate visualization of the common carotid arteries.

3.6.3 Transducer position:

Several transducer positions were used in this research to examine the common carotid arteries in long – axis (longitudinal) planes as Illustrated in Figure 3.2 a and b, below. Generally the posterolateral and far – posterolateral are most useful for showing the carotid bifurcation and the ICA but in some cases, an anterior or lateral approach works best. The far posterolateral approach often provides the best images of the distal reaches of the ICA. To use this view effectively it is necessary to turn the patient's head far to the contralateral side and to place the transducer posterior to the sternomastoid muscle.

The short axis (transverse) view of the carotid artery was obtained from an anterior and lateral or posterolateral approach depending on which best shows the vessels.

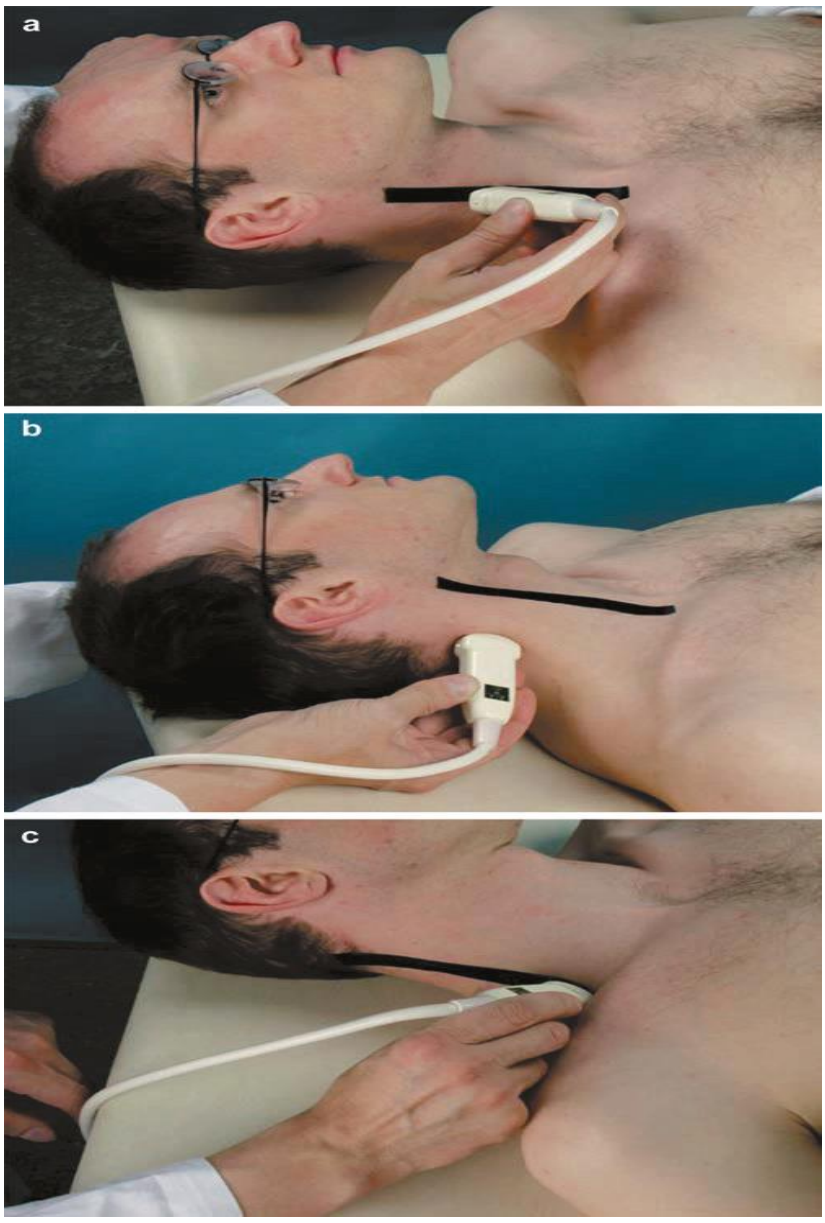


Figure 3.2 illustrate transducer positions for duplex carotid ultrasound examination, a is anterolateral probe position and b is posterolateral position (Schäberle, 2011)

The intima-media thickness (IMT) in (mm) which is defined as the distance between the media–adventitia interface and the lumen–intima interface was calculate by measure the distance between the two echogenic interface using ultrasound brightness mode (B-mode) one cm before bifurcation with value up to 0.9 mm consider as normal (Mancia G et al, 2007). The

caliper as well measuring one cm before bifurcation for CCA and one cm after bifurcation for ICA and ECA from outer border of anterior wall of CAs to outer border of posterior wall. The following values consider as normal measurement for the calipers (6.3---7 mm) for CCA, (4.1---5.5 mm) for ICA and (3.5---5 mm) for ECA (Touboul PJ et al, 2005). then power Doppler (PD) to assess the present of flow, followed by pulse wave Doppler (PW) modes were applied for spectral analysis determination the values of peak systolic velocity (PVS) in cm/sec and end diastolic velocity (EDV) in cm/sec, resistive index (RI), pulsatility index (PI), PSV/EDV ratio (A/S) and PSV ICA/CCA ratio for each artery respectively. The normal value of PSV is up to (125 cm/s), EDV is up to (40 cm/s) and less than 2 mm for PSV ICA/CCA ratio, while the RI calculated by PSV-EDV/PSV, PI by PSV-EDV/MV and MV is mean velocity which is calculated by PSV+ 2 EDV/3 (Polak JF et al, 1989).

The obtained numerical values of the above different Doppler parameters were taken from the middle part of each artery because flow pattern seems to be steady and uniform, which actually help in avoiding any misleading or wrong values. In addition using Doppler angle of 60 degree or less help in making Doppler signal waveform stronger and clear.

3.7 Data analysis:

Data were analyzed by using SPSS program and Excel 2013, the results were presented in form of graphs and tables.

3.8 Ethical consideration:

- No identical or individual details were published.
- No information or patient details will be disclosed or used for other reasons than the study.

Chapter Four

Results

The following chapter will deal with all results related to influence of DM among Sudanese sample on the carotid arteries specially the caliper, IMT, PSV, EDV, RI, PI and PSV ratio of ICA/CCA, according to patients' age and duration of DM.

Table 4.1 Distribution of study sample according to Participant's sex

Gender	Frequency	Percent (%)
Male	112	56.0
Female	88	44.0
Total	200	100.0 (%)

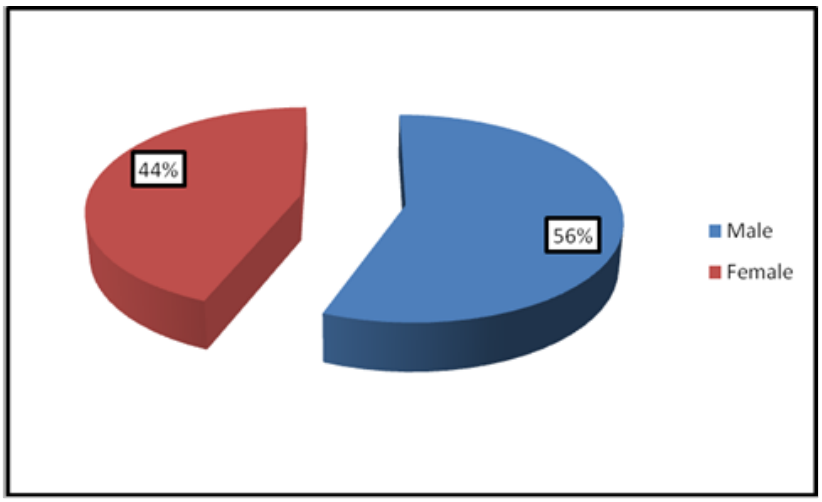


Figure 4.1 Distribution of study sample according to Participant's sex

Table 4.2 shows distribution of diabetes mellitus type.

Type of DM	Frequency	Percentage
Type 1	108	54%
Type 2	92	46%

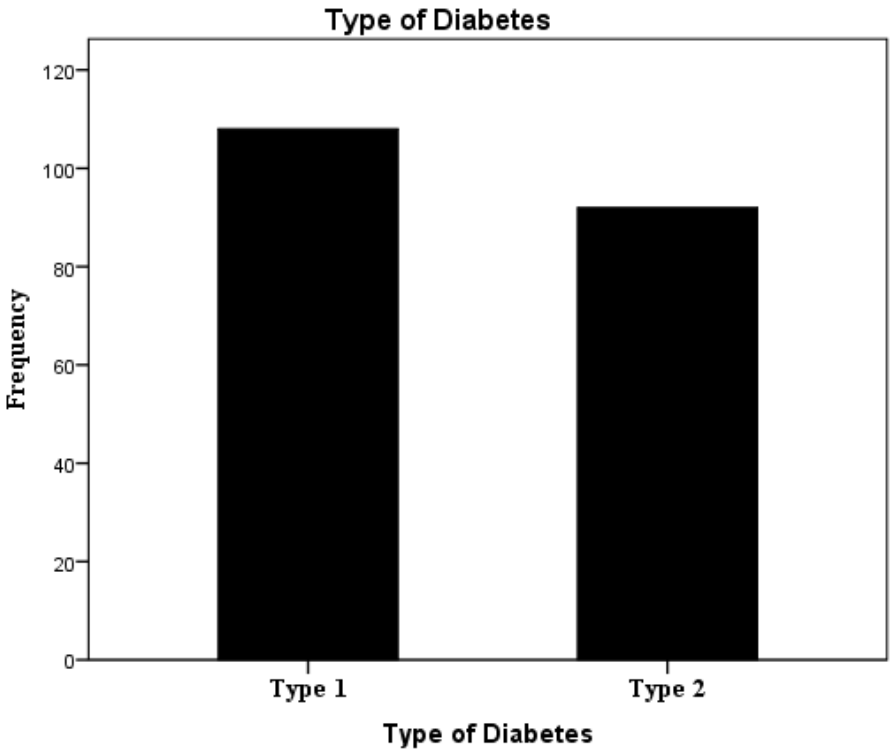


Figure 4.2 shows the frequency of diabetes mellitus type

Table 4.3 shows the frequency of treatment type for DM.

Type of treatment	Frequency	Percentage
Tabs	51	25.5%
Insulin Injection	103	51.5%
Diet Control	46	23%

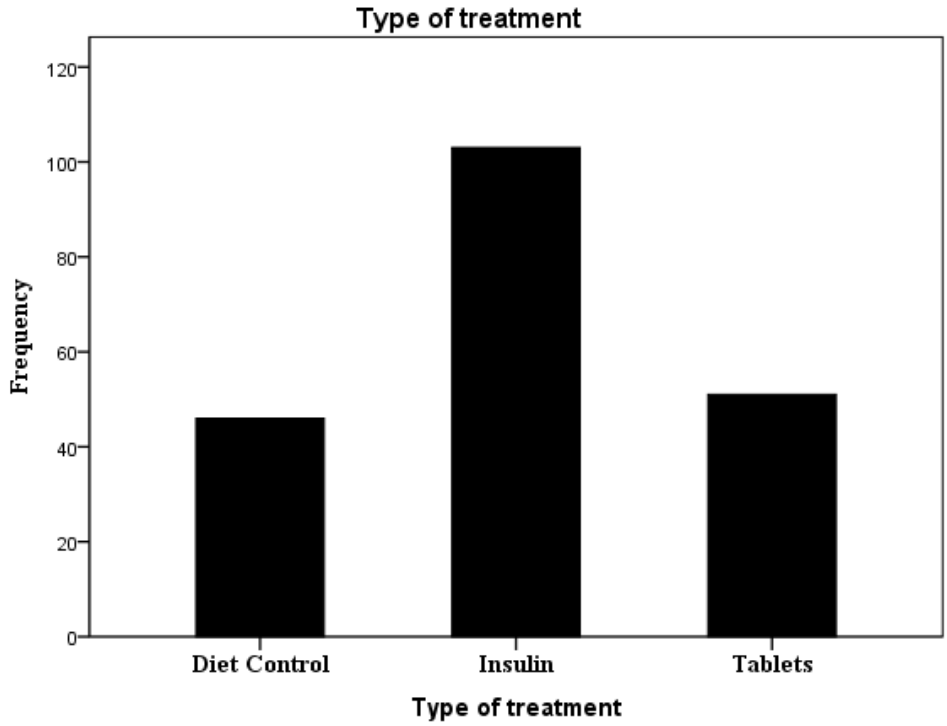


Figure 4.3shows the frequency of treatment type of DM.

Table 4.4 shows the frequency of occupation in DM paients.

	Frequency	Percentage
Employed	123	61.5%
Un-employed	77	38.5%
Total	200	100%

Figure 4.4 shows the frequency of ocuupation in DM patients.

Table 4.5 Distribution of study sample according to Participant's age

Age	Frequency	Percent (%)
30-39	24	12.0
40-49	65	32.5
50-59	67	33.5
60-69	33	16.5
≥70	11	5.5
Total	200	100.0 (%)

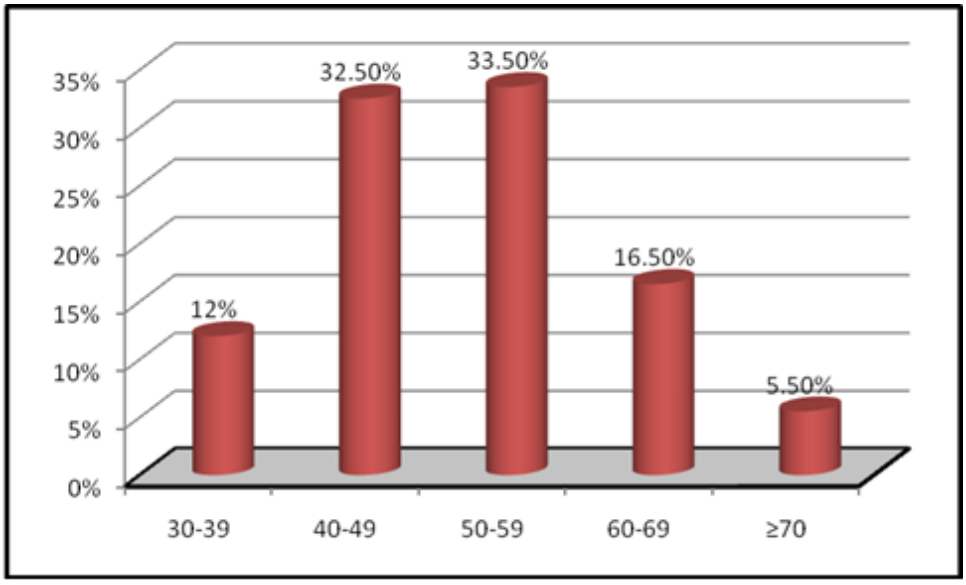


Figure 4.5 Distribution of study sample according to Participant's age

Table 4.6 shows the Mean and Std.Deviation of different variables

	N	Minimum	Maximum	Mean	Std. Deviation
Age	200	30.00	73.00	51.5300	9.64491
Duration	200	1.00	20.00	7.0400	3.53992
THA	200	1.00	2.00	1.9950	.07071
RT CCA ((Caliper	200	4.00	9.00	6.4485	1.13881
IMT	200	1.20	1.90	1.5175	.18443
PSV	200	47.00	155.40	76.2190	17.02649
EDV	200	13.80	47.20	24.0050	6.78805
RI	200	.07	.92	.6828	.07843
PI	200	1.00	3.00	1.9778	.29016
S/D Ratio	200	2.00	7.60	3.2985	.83296
RT ICA ((Caliper	200	.00	7.00	5.0630	.91746
PSV	200	44.20	101.50	67.4320	12.41981
EDV	200	14.60	38.70	22.6320	4.76919
RI	200	.00	.86	.6569	.09494
PI	200	.64	5.00	1.9682	.42526
S/D Ratio	200	2.20	4.60	3.0113	.44708
ICA PSV/CCAPSV	200	.39	84.00	2.3487	10.18700
RT ECA ((Caliper	200	3.00	7.60	4.4920	.69516
PSV	200	38.80	105.60	62.6830	10.94978
EDV	200	.00	39.20	21.3420	5.08423
RI	200	.00	71.00	1.0087	4.97447
PI	200	1.00	3.00	2.0345	.31537

S/D Ratio	200	2.00	5.90	2.9750	.45362
LT CCA ((Caliper	200	4.90	9.50	7.4975	1.08306
IMT	200	1.40	2.10	1.7025	.15480
PSV	200	48.20	150.20	73.9505	14.02492
EDV	200	15.00	46.60	24.6165	6.03087
RI	200	.51	.94	.6725	.05934
PI	200	1.20	3.00	2.0334	.26416
S/D Ratio	200	2.00	6.00	3.0786	.62296
LT ICA ((Caliper	200	4.00	8.00	5.4355	.78567
PSV	200	44.20	136.20	65.5670	13.39904
EDV	200	15.00	42.40	22.1695	5.58015
RI	200	.46	.87	.6655	.05407
PI	200	1.00	3.00	2.0057	.31728
S/D Ratio	200	1.80	5.00	3.0140	.48816
ICA PSV/CCAPSV	200	.35	5.30	.9276	.37701
LT ECA ((Caliper	200	3.30	7.30	4.8240	.77694
PSV	200	42.60	101.00	61.7300	11.21015
EDV	200	14.50	35.00	20.7550	4.33470
RI	200	.55	.87	.6670	.04640
PI	200	1.20	2.60	2.0160	.22627
S/D Ratio	200	2.20	5.30	3.0080	.43379

Table 4.7 shows the Mean and Std.Deviation in Rt CCA according to Participant's Gender.

	Gender	N	Mean	Std. Deviation
RT CCA Caliper	Male	112	7.565	1.1072
	Female	88	7.491	1.1575

Table 4.8 shows the Mean and Std.Deviation in Rt ICA according to Participant's Gender.

	Gender	N	Mean	Std. Deviation
RT ICA Caliper	Male	112	5.864	1.0206
	Female	88	5.899	.7701

ble 4.9 shows the Mean and Std.Deviation in Lt CCA and ICA according to Participant's Gender.

	Gender	N	Mean	Std. Deviation
LT CCA Caliper	Male	112	7.618	1.0199
	Female	88	7.557	1.0266
LT ICA Caliper	Male	112	5.8813	.87853
	Female	87	5.9115	1.03726

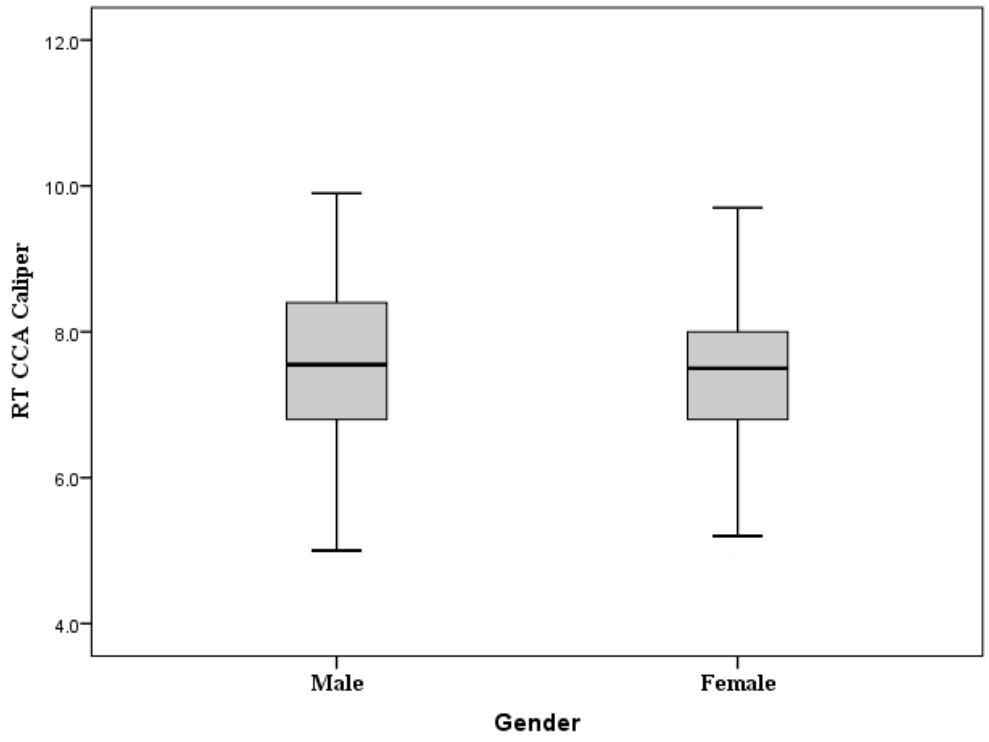


Figure 4.6 Shows Compare the Caliper of Rt CCA in study sample according to Participant's gender

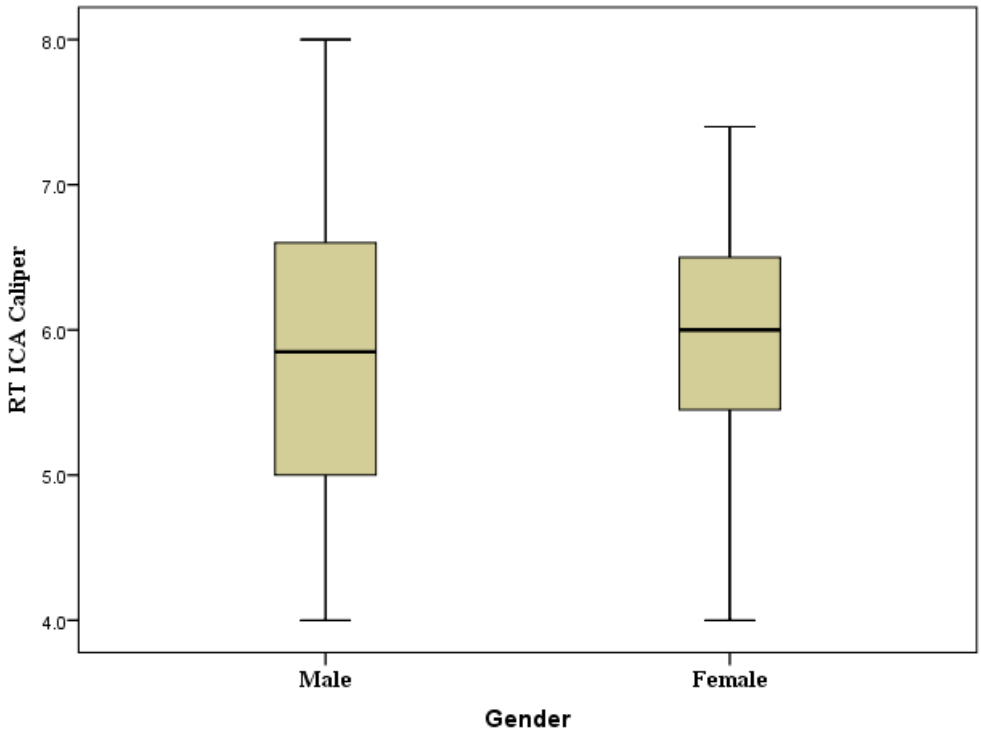


Figure 4.7 Shows Compare the Caliper of Rt ICA in study sample according to Participant's gender.

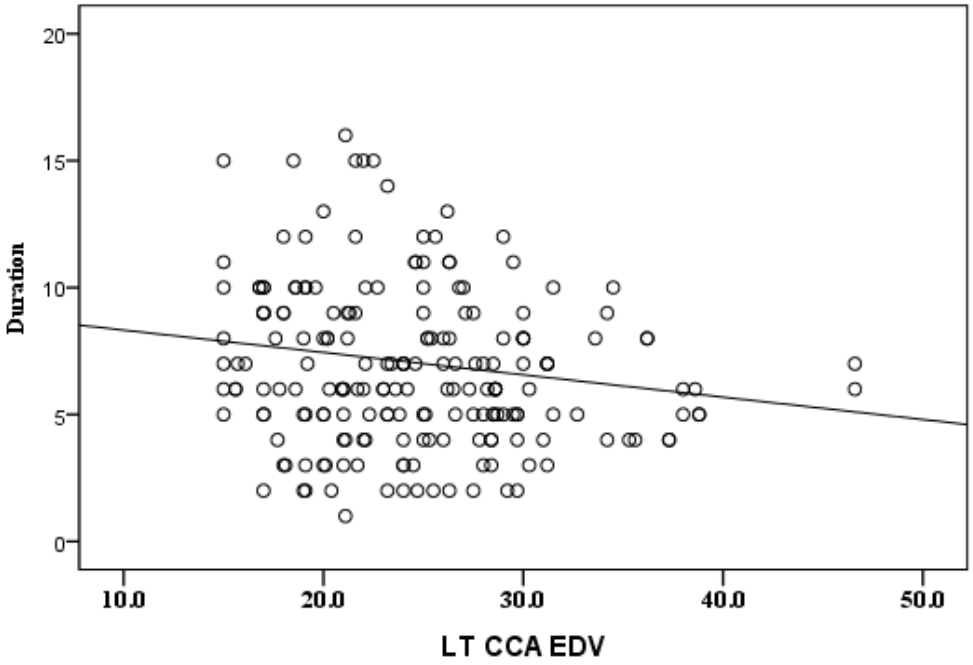


Figure 4.8 Correlation between Duration of Diabetes and EDV in Lt CCA.

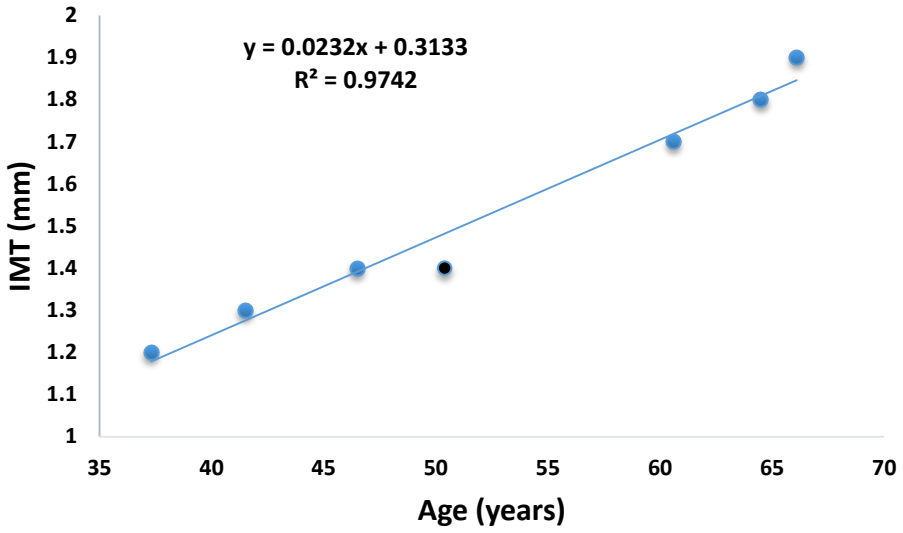


Figure 4.9 shows the correlation between IMT and age in Rt CCA.

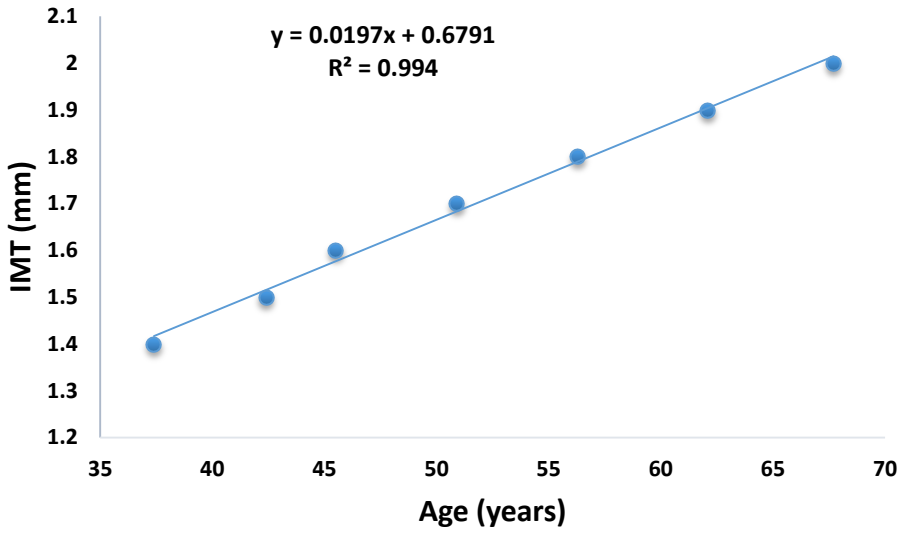


Figure 4.10 shows the correlation between IMT and age in Lt CCA.

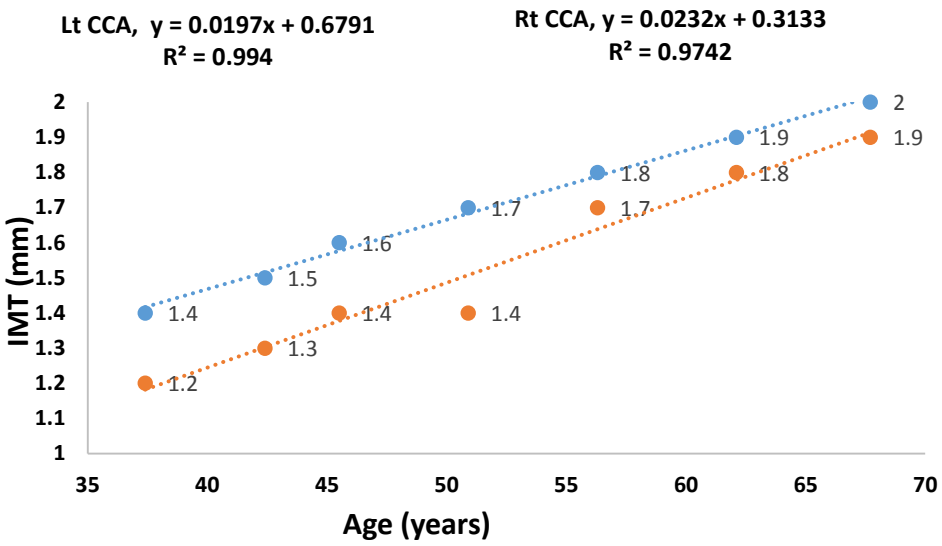


Figure 4.11 shows Compare the IMT in Rt and Lt CCA according to age.

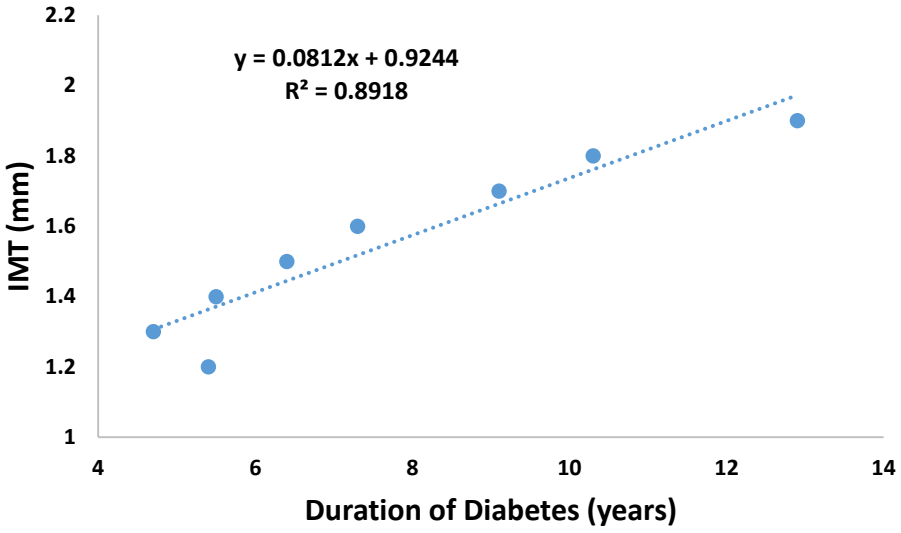


Figure 4.12 shows the correlation between IMT and Duration of Diabetes in Rt CCA.

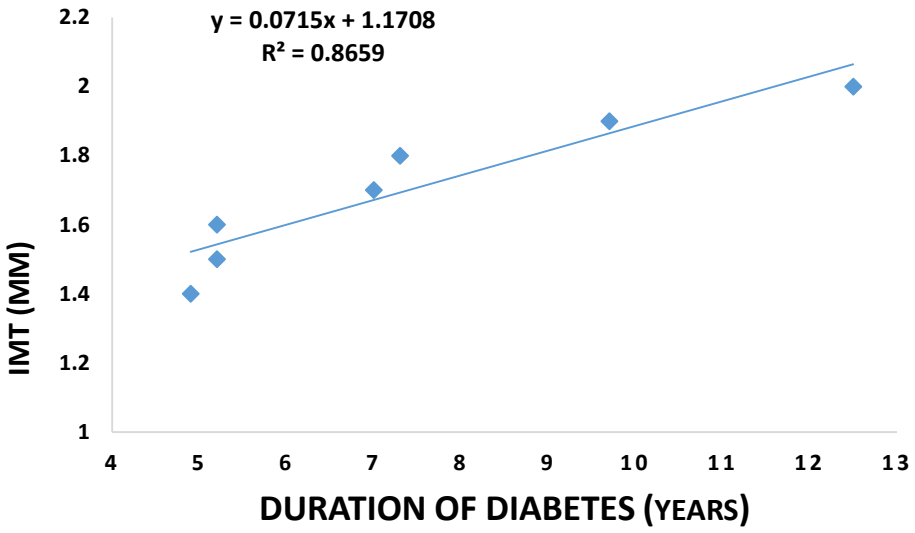


Figure 4.13 shows the correlation between IMT and Duration of Diabetes in Lt CCA.

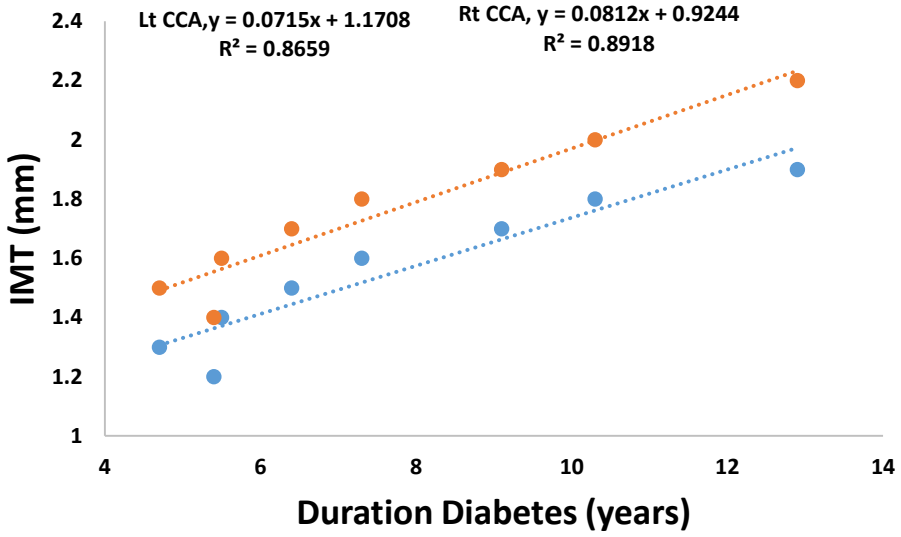


Figure 4.14 shows Compare the IMTin Rt and Lt CCA according to duration of diabetes.

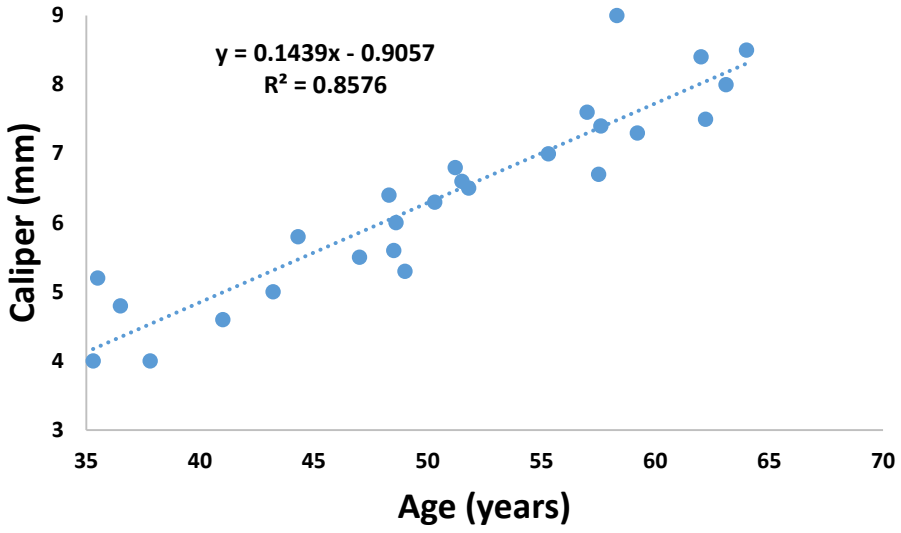


Figure 4.15 shows the Correlation between Caliper and age in Rt CCA.

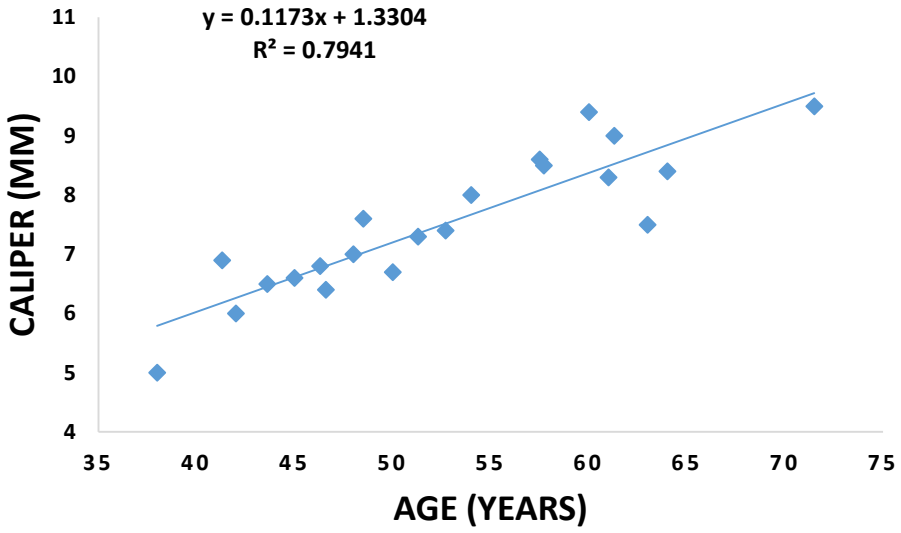


Figure 4.16 shows the Correlation between Caliper and age in Lt CCA.

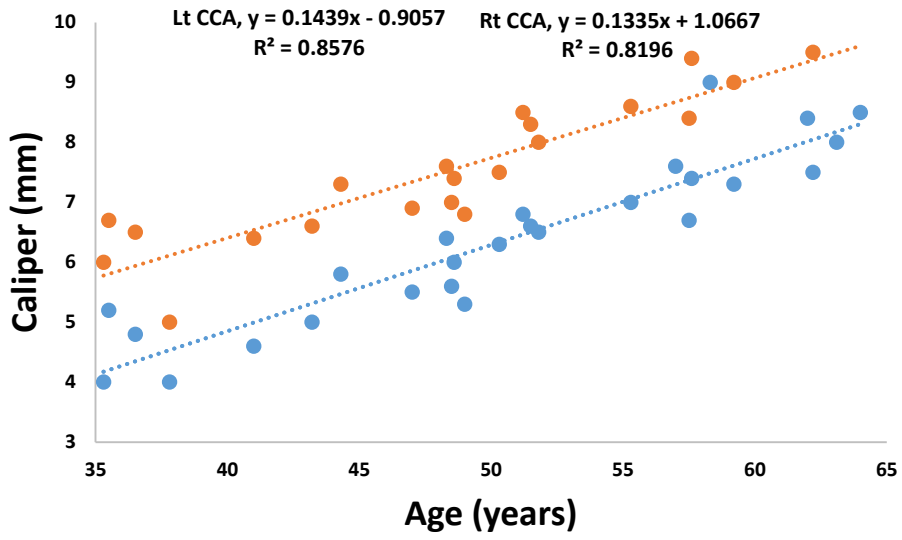


Figure 4.17 shows Compare of Caliper in Rt and Lt CCA according to age.

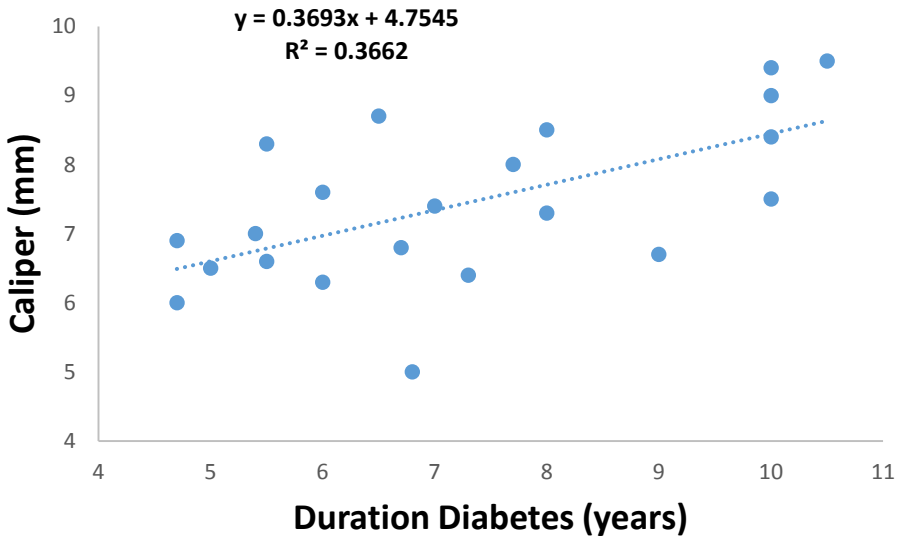


Figure 4.18 shows the Correlation between Caliper and Duration of Diabetes in Rt CCA.

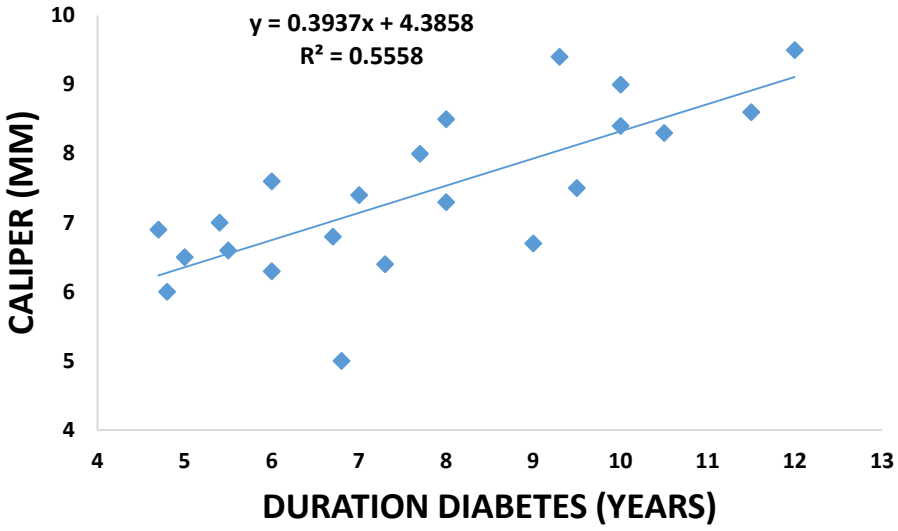


Figure 4.19 shows the Correlation between Caliper and Duration of Diabetes in Lt CCA.

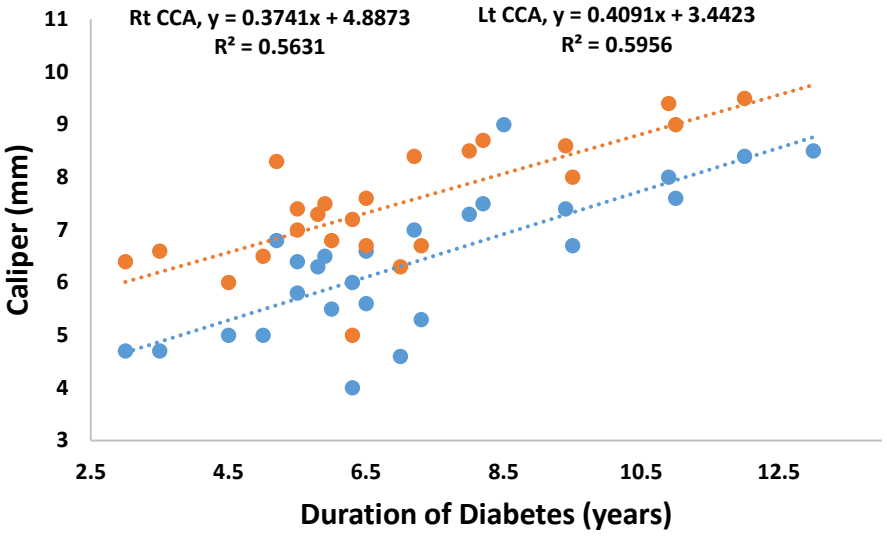


Figure 4.20 shows Compare of Caliper in Rt and Lt CCA according to duaration of diabetes.

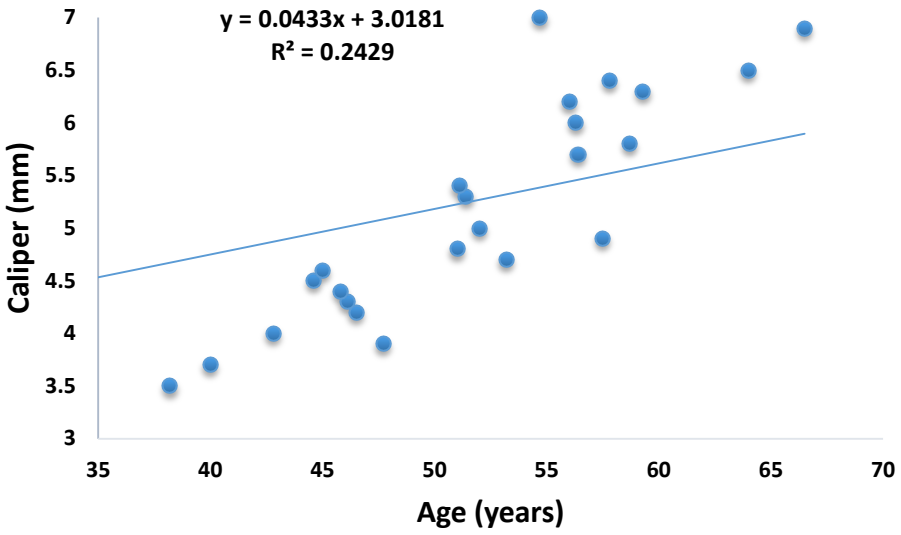


Figure 4.21 shows the Correlation between Caliper and age in Rt ICA.

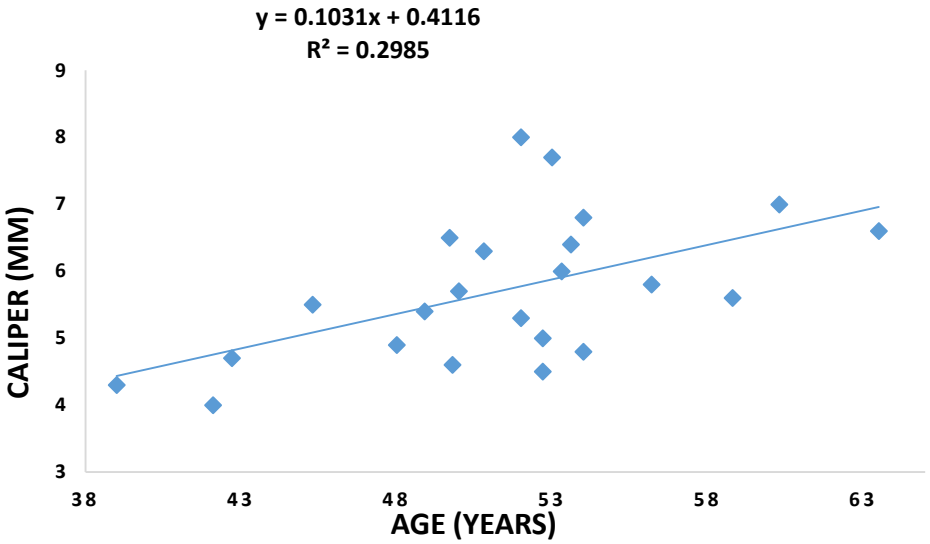


Figure 4.22 shows the Correlation between Caliper and age in Lt ICA.

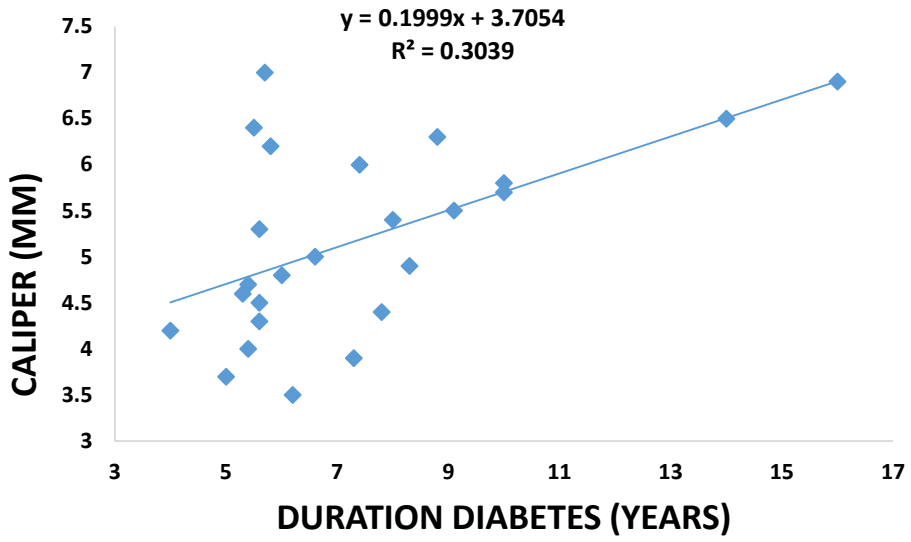


Figure 4.23 shows the Correlation between Caliper and Duration Diabetes in Rt ICA.

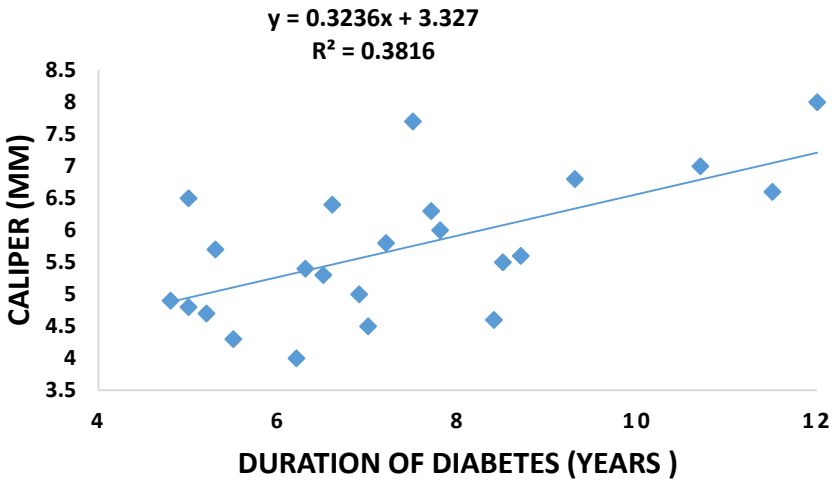


Figure 4.24 shows the Correlation between Caliper and Duration of diabetes in Lt ICA.

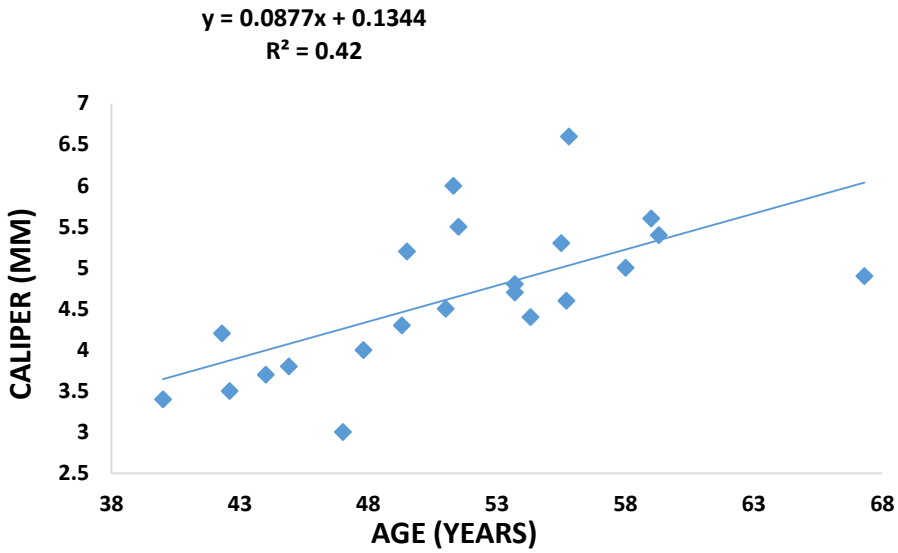


Figure 4.25 shows the Correlation between Caliper and age in Rt ECA.

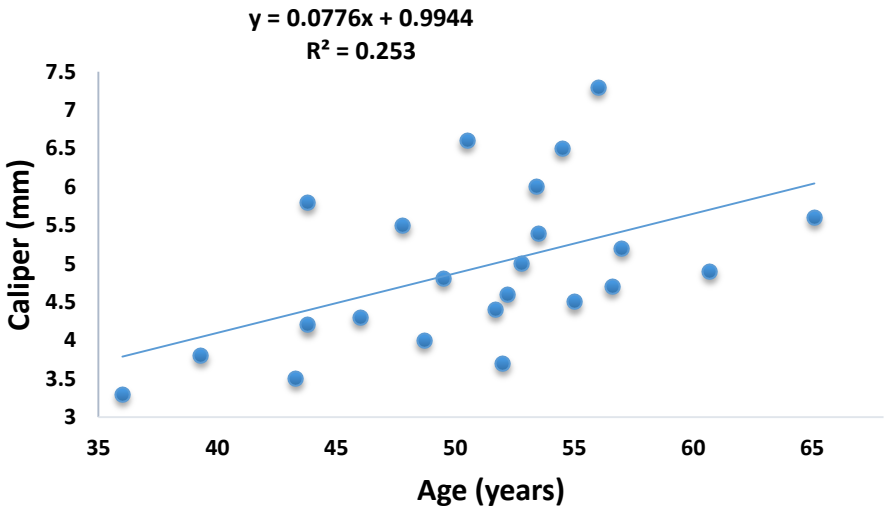


Figure 4.26 shows the Correlation between Caliper and age in Lt ECA.

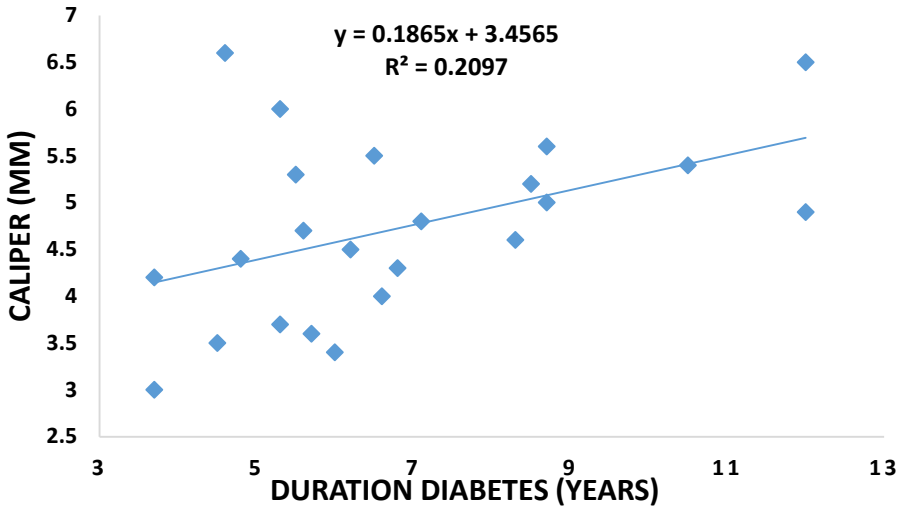


Figure 4.27 shows the Correlation between Caliper and Duration of Diabetes in Rt ECA.

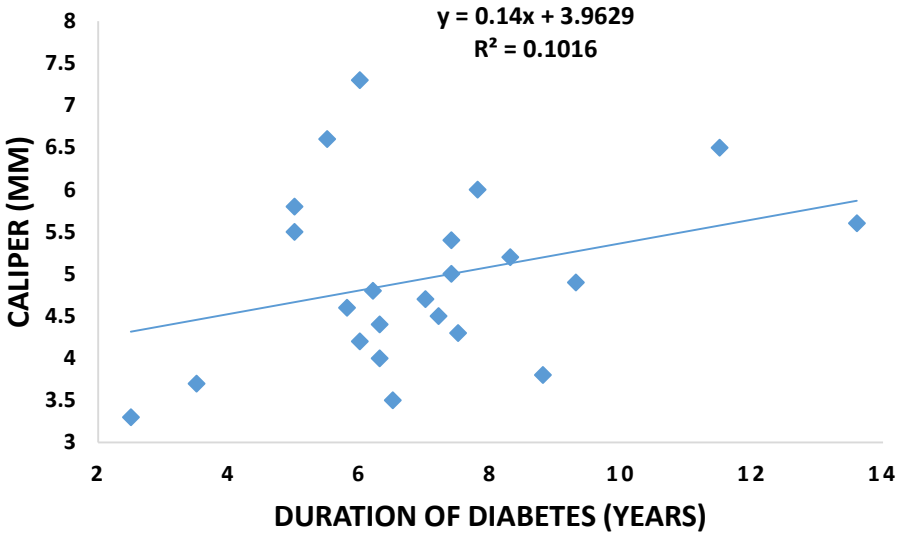


Figure 4.28 shows the Correlation between Caliper and Duration of Diabetes in Lt ECA.

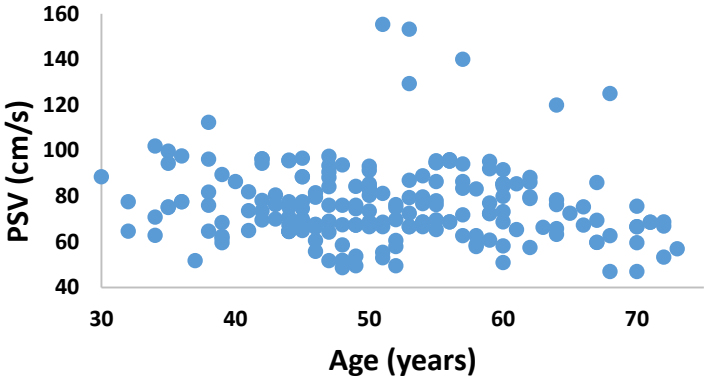


Figure 4.29 Shows no Correlation between PSV and Age in Rt CCA.

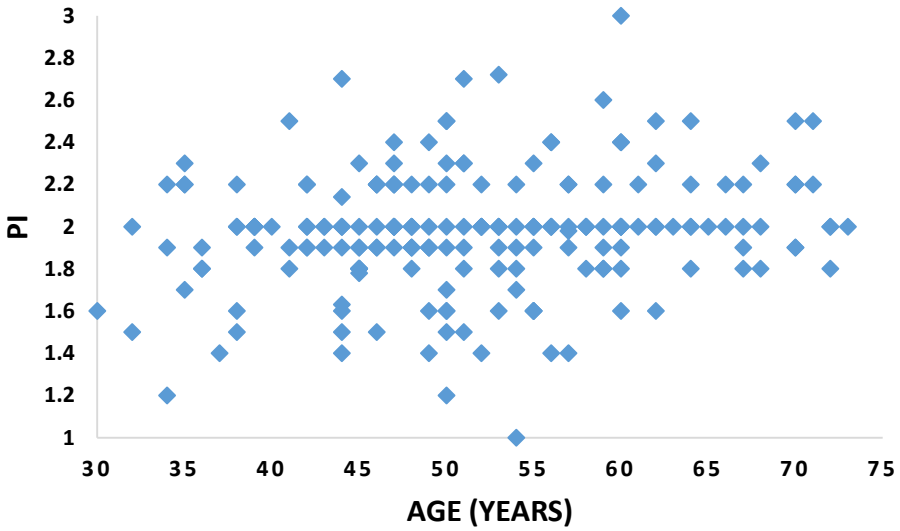


Figure 4.30 Shows no Correlation between PI and Age in Rt CCA.

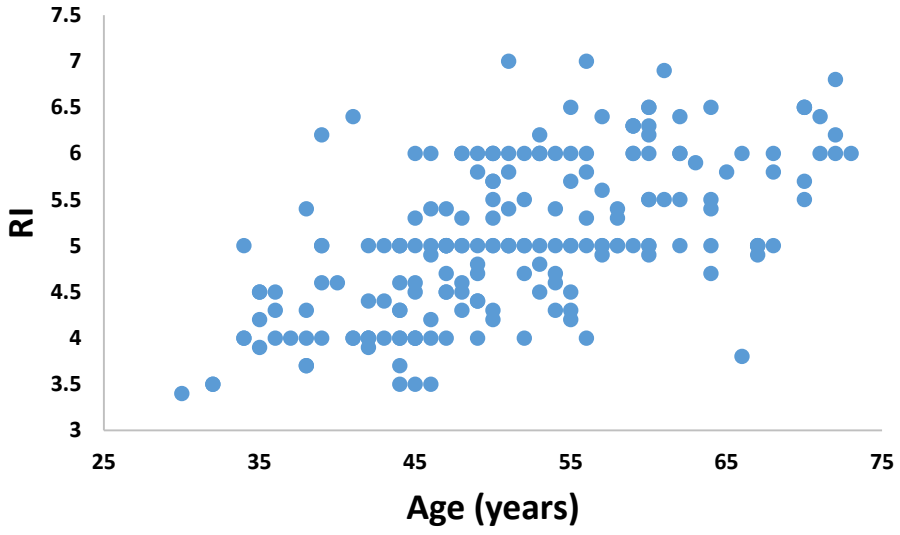


Figure 4.31 Shows no Correlation between RI and Age in Rt ICA.

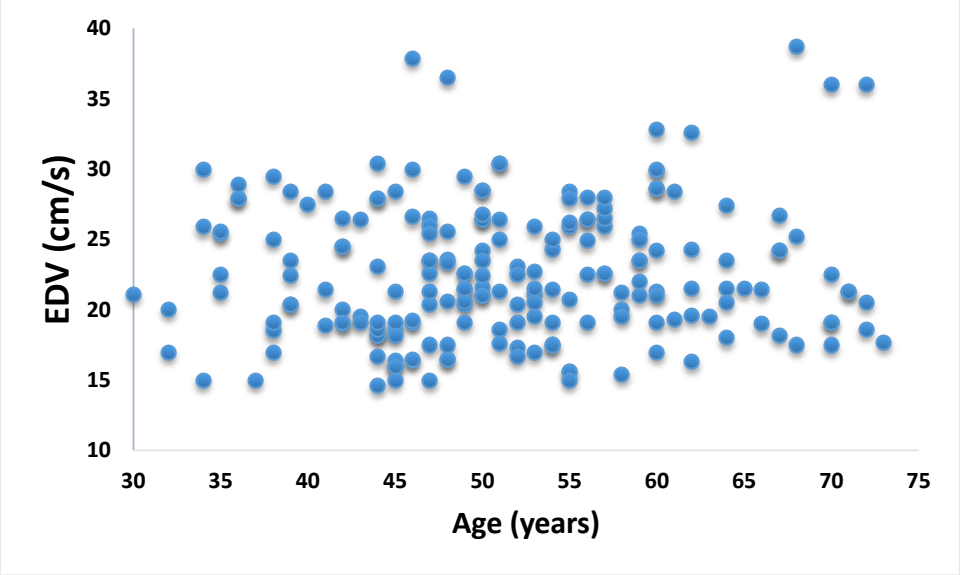


Figure 4.32 Shows no Correlation between EDV and age in Rt ICA.

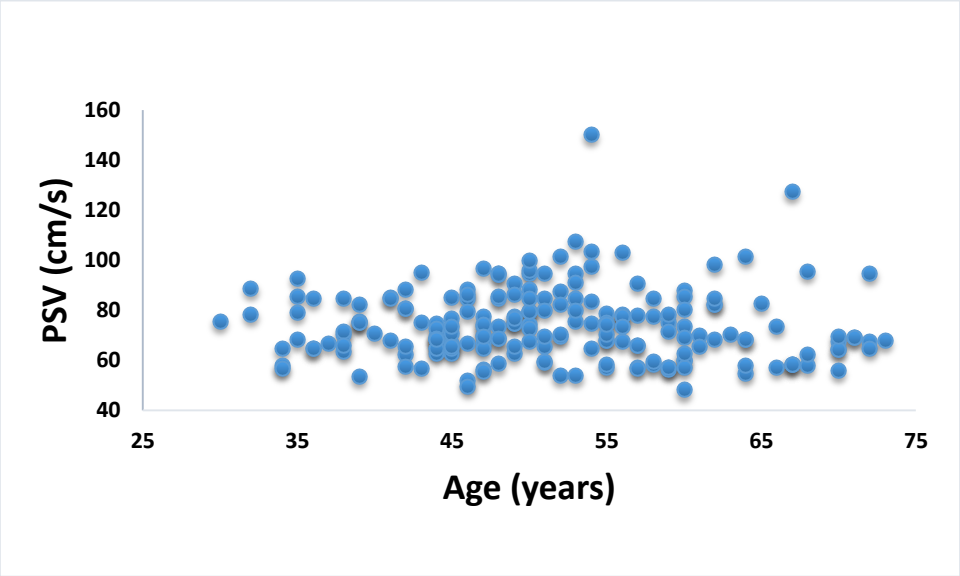


Figure 4.33 Shows no Correlation between PSV and age in Lt CCA.

Figure 4.34 Shows no Correlation between EDVand age in Lt CCA.

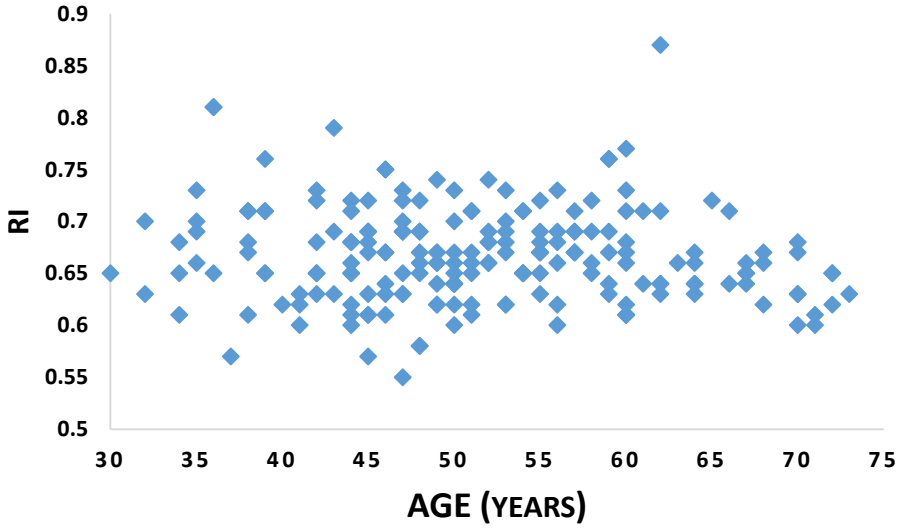


Figure 4.35 Shows no Correlation between RI and age in Lt ECA.

Table 4.10 shows the frequency of Plaques in sample study.

	Frequency	Percentage
Plaque	**6**	**3%**
Non-Plaque	**197**	**97%**

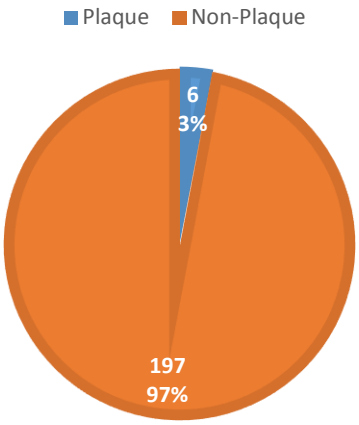


Figure 4.36 **shows the frequency of Plaques in sample study**.

Table 4.11 shows the site of Plaques in CAS

	Plaque	Percentage
Rt CCA	3	50%
Lt CCA	2	33%
Lt ICA	1	17%

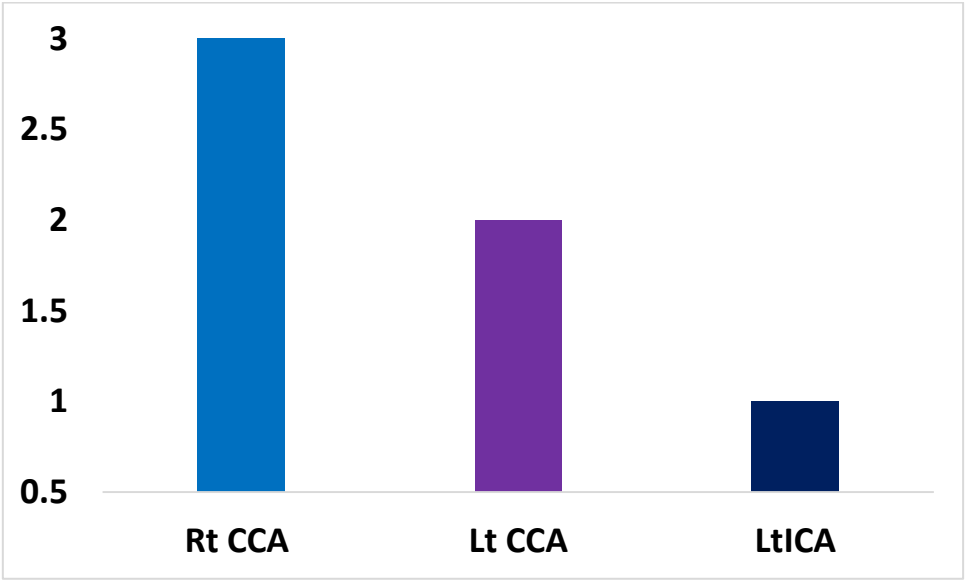


Figure 4.37 shows the sites of Plaques in CAS

Table 4.12 shows the charactristics of Plaques in CAs

	Measurement	Morphology	Stenotic %	PSV	EDV	RI	A/S Ratio
Rt CCA	5.3×8.3 mm	Calcified	56%	140 cm/s	44 cm/s	0.69	3.2
Rt CCA	3.3×7.3 mm	Ulcerated	72%	155 cm/s	45.6cm/s	0.71	3.4
Rt CCA	3.5×4.7 mm	Calcified	64%	153.3 cm/s	47.2 cm/s	0.69	3.3
Lt CCA	5.9×4.7 mm	Heterogonous	76%	158.2 cm/s	46.6 cm/s	0.73	3.4
Lt CCA	3×6.4 mm	Calcified	35%	127.4 cm/s	42 cm/s	0.69	3
Lt ICA	4.3×6.9 mm	Ulcerated	55%	136.2 cm/s	42.4 cm/s	0.69	3.2

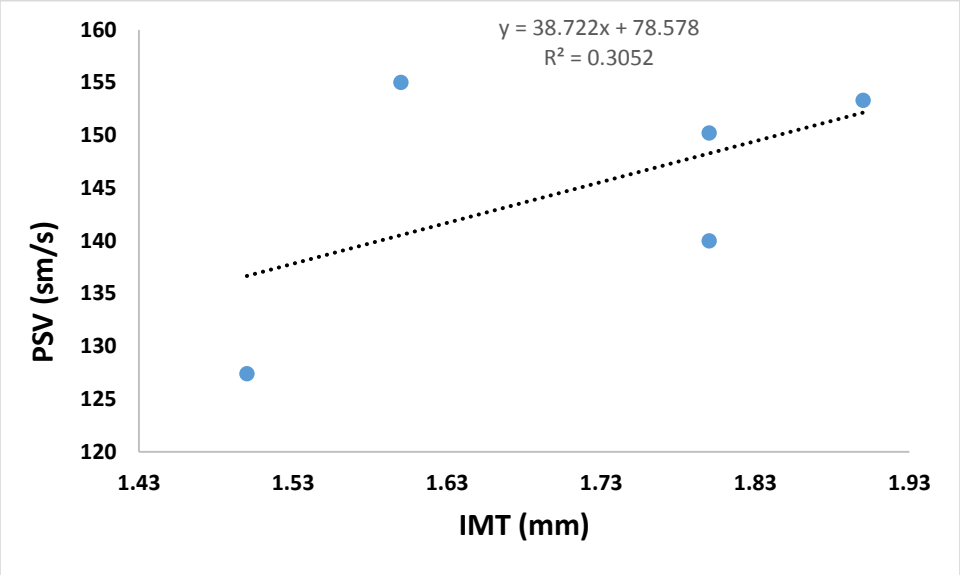


Figure 4.38 Correlation between IMT and PSV in Patient with plaques

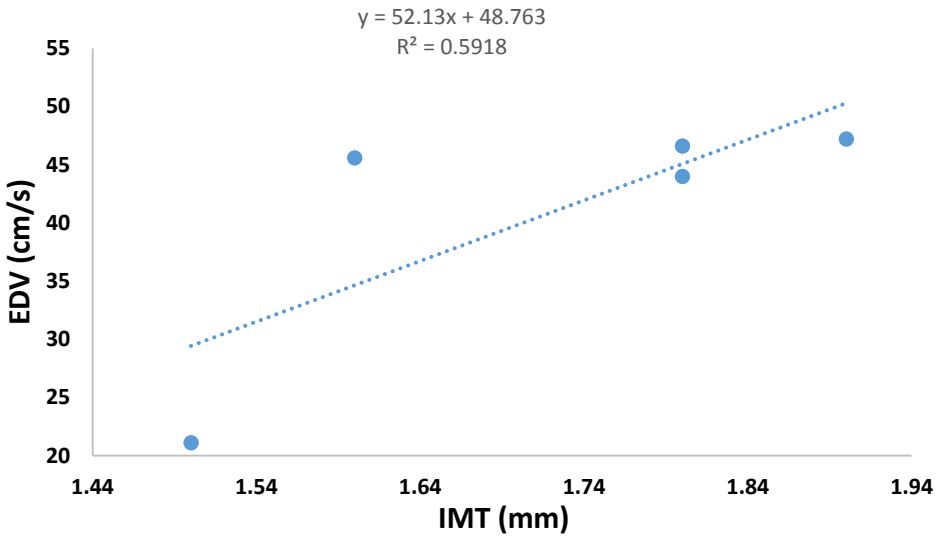


Figure 4.39 Correlation between IMT and EDV in Patient with plaques

Table 4.13 shows the correlations between different variables in Lt CCA.

	LT CCA IMT	LT CCA PSV	LT CCA EDV	LT CCA RI	LT CCA PI	LT CCA S/D Ratio
LT CCA IMT	1	.116	.264**	-.223**	.250**	-.164*
		.101	.000	.001	.000	.020
	200	200	200	200	200	200
LT CCA PSV	.116	1	.678**	.076	.217**	.157*
	.101		.000	.284	.002	.026
	200	200	200	200	200	200
LT CCA EDV	.264**	.678**	1	-.520**	.597**	-.587**
	.000	.000		.000	.000	.000
	200	200	200	200	200	200
LT CCA RI	-.223**	.076	-.520**	1	-.569**	.784**
	.001	.284	.000		.000	.000
	200	200	200	200	200	200
LT CCA PI	.250**	.217**	.597**	-.569**	1	-.493**
	.000	.002	.000	.000		.000
	200	200	200	200	200	200
LT CCA S/D Ratio	-.164*	.157*	-.587**	.784**	-.493**	1
	.020	.026	.000	.000	.000	
	200	200	200	200	200	200

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

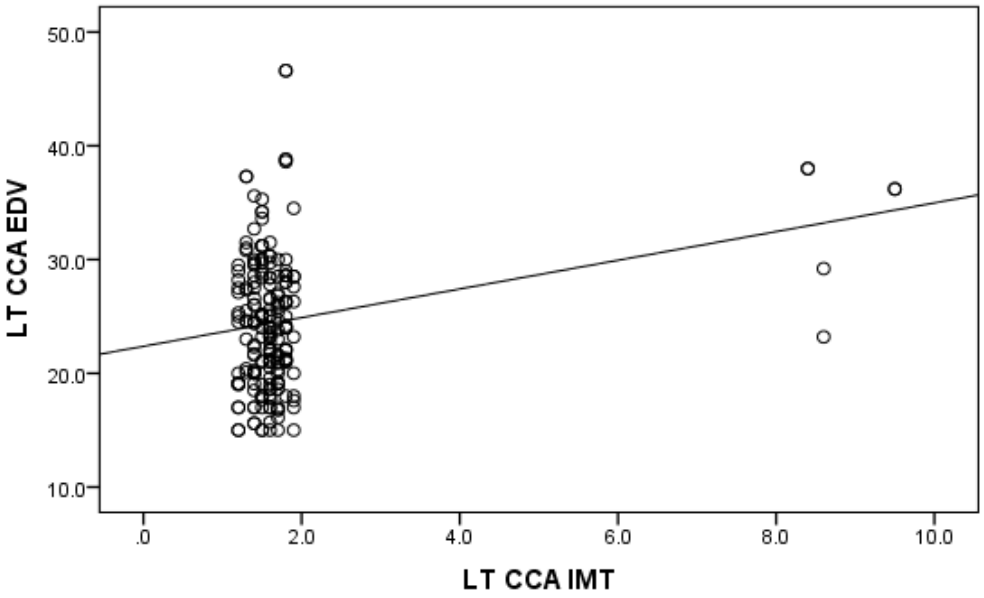


Figure 4.40 Correlation between EDV and IMT in Lt CCA.

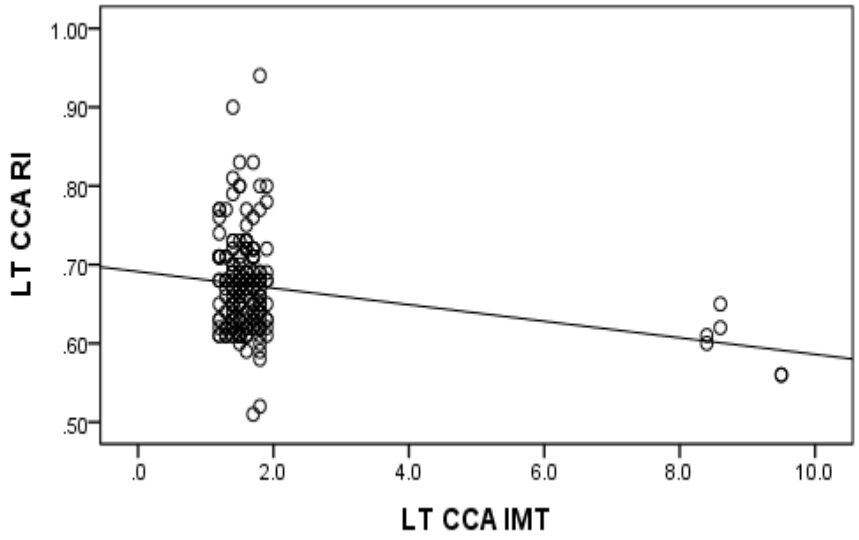


Figure 4.421 Correlation between RI and IMT in Lt CCA.

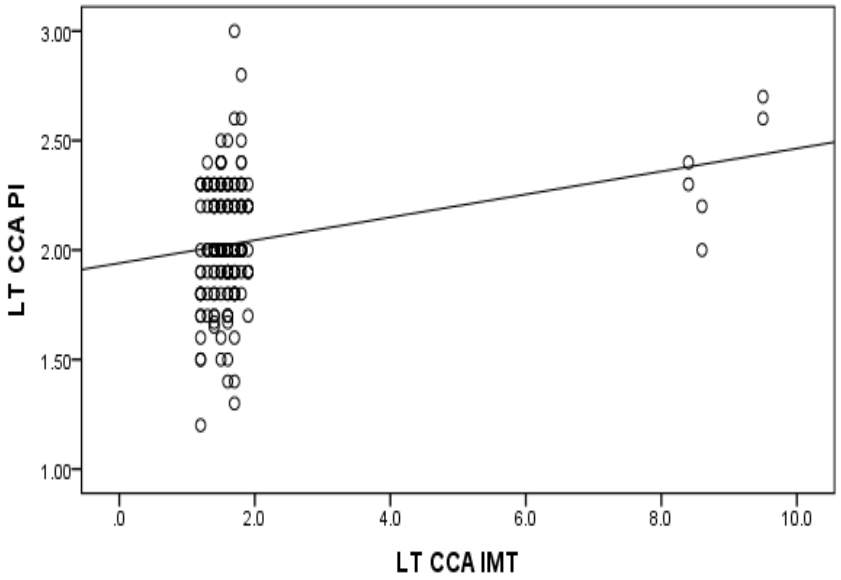


Figure 4.42 Correlation between PI and IMT in Lt CCA.

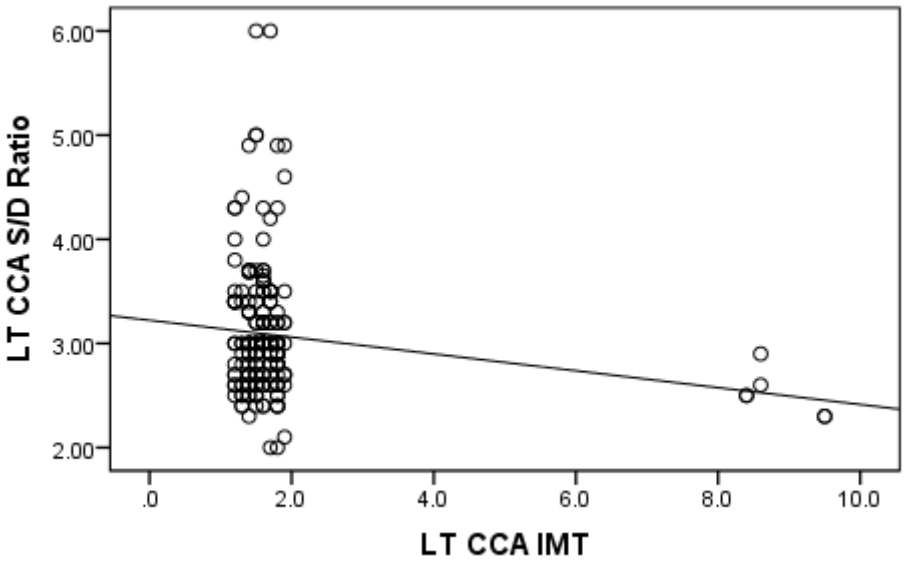


Figure 4.43 Correlation between S/D Ratio and IMT in Lt CCA.

Table 4.14 shows correlation between Rt and Lt ICA/CCA PSV Ratio

		LT ICA PSV/LT CCA PSV Ratio	RT ICA PSV/RT CCA PSV Ratio
ICA PSV/LT CCA PSV Ratio	Pearson Correlation	1	1.8*
	Sig. (2-tailed)		.011
	N	200	200

*. Correlation is significant at the 0.05 level (2-tailed).

Chapter Five

5.1 Discussion

Diabetes Mellitus is a metabolic disease which has an influence impact on most body organs. This study is looking for ultrasound finding of Carotid arteries in Sudanese diabetes patients, two hundred patients were investigated by high frequency gray scale and Doppler ultrasonography to evaluate the carotid arteries plaques in diabets mellitus patients.

Table and Figure 4.1 shows the sample distribution according to gender, which shows that there were 112 male patients which constitute 56% from study sample and 88 (44%), female this prevalence is in line with study carried out by (Kristine F,2008) to calrify gender prevalence in type 2 diabetes mellitus, she found that the prevelance is higher in men than women and this mainly caused by more sedentary lifestyle particulary among men resulting in increased obsity, while table and Figure 4.2 reveal the frequency of diabetes type, which was 108 patients in type one (54%) and type two 92 patients (46%). Table and figure 4.5 shows frequency of sample study in age group as following: in first age group (30-39) there were 24 patients (12%), (40-49) there were 65 patients (32.5%), (50-59) there were 67 patients (33.5%), (60-69) there were 33 patients is (16.5%) and ≥ 70 there were 11 ptients (5.5%).

Figures 4.10 and 4.11 shows the correlation between the IMT in mm and age in year among Sudanese diabetic patients for Rt and Lt common carotid arteries, in Rt CCA the in IMT as seen in the figure 4.10 is 1.2 mm in first age group (35-40), 1.3 mm in (40-45), 1.4 mm in (45-50), 1.5 mm in (50-55). 1.6 mm in (55-60), 1.7 mm in (60-65) and 1.8 mm in (65-70), while in Lt CCA 1.4 mm, 1.5 mm, 1.6 mm, 1.7 mm, 1.8 mm, 1.9 mm and 2mm in the same age group respectively. From this values notice that value of IMT is increment by +0.2 mm every decade. The correlation between IMT and the age of diabetic patients was given by the following equation: $y = 0.0232x + 0.3133$ for Rt CCA and $y = 0.0197x + 0.6791$ for Lt CCA, where y refers to age and x refers to IMT in both equation. Various studies have explored that the IMT directly correlated with increasing age even among healthy individuals (Lorenz M, 2006), and diabetes mellitus has great relation with the increment of the IMT within the carotid arteries lumen, such IM thickening is due to adherence of circulating monocytes to the endothelium, migration into the subendothelium and subsequent formation of foam cells which are principal initial events in the development of atherosclerosis (Eigenbrodt et al., 2007),

Figure 4.11 shows that the IMT for the Lt CCA is greater than in the Rt CCA with a value of +0.1 mm which is based on the basic thickness of the Lt CCA that is usually thicker than the Rt CCA as has been stated by

(Edoardo et al, 2007) study in which they found that the Lt CCA thickness is 1.02 ± 0.21 mm and the Rt is 0.98 ± o.18 mm among male while among female for Lt CCA thickness is 0.92 ± 0.19 mm and the Rt CCA thickness is 0.90 ± 0.18 mm, this due to Lt CCA consider as main artery as it arise directly from Aortic Arch while Rt CCA is a branche arise from brachiocephalic trunk.

The values of CIMT (in mm) observed at CCA for diabetic participants according to duration of diabetes group (4 – 6) were 1.2, 1.3, 1.4 mm, (6 – 8) were 1.5, 1.6 mm, (8 – 10) was 1.7mm, (10 – 12) was 1.9 mm, for Rt CCA, while in Lt CCA, (4 – 5) was 1.4 mm, (5 – 6) were 1.5 mm, 1.6 mm, (7 – 8) were 1.7 mm, 1.8 mm, (9 – 10) was 1.9 mm and (12 – 13) was 2mm, as are shown in Figures 4.12, 4.13. This results reveal that IMT is significantly correlated to duration of diabetes. Aside from age as a variable that can influence IMT, the duration of diabetes is a relevant factor for IMT increase, this result totally consistent with (Kamile G et al, 2008) study which reveal that in patients with DM CIMT is higher than in the control group and each increment in its value is related with diabetes microvascular complications and duration of diabetes (Gul et al., 2010), and due to adherence of circulating monocytes to the endothelium then immigration into the sub-endothelium and subsequent formation of foam cells which are principle initial events in an increase IMT value DM

patients (Eigenbrodt et al., 2007). Longer disease duration of diabetes might enhance its metabolic effects on the vascular system and result in earlier onset and accelerated progression of atherosclerosis. However, with increasing duration other classical cardiovascular risk factors may play an additional role in diabetic (Pezeshki Rad et al, 2014). As the overlap between age and duration of diabetes, the IMT more great in the Lt CCA than in Rt CCA as seen in Figure 4.14.

Many study confirmed an association between CCAs diameters and prevalent and incident cardiac events with evidence of independence from many traditional risk factors when diameter was evaluated. CCA diameter is easily assessed by B-mode ultrasound and is related to many atherosclerosis risk factors (Jensen K et al, 1999) and diameter is an important correlate of cardiac events, independent of IMT (Marsha E et al, 2007).

Figures (4.15), (4.16), (4.21), (4.22), (4.25) and (4.26), shows the correlation between calipers and age in Rt CCA, Lt CCA, Rt ICA, Lt ICA, Rt ECA and Lt ECA respectively while figures (4.18), (4.19), (4.23), (4.24), (4.27) and (4.28) shows the correlation between calipers and duration of diabetes in Rt CCA, Lt CCA, Rt ICA, Lt ICA, Rt ECA and Lt ECA respectively. All figures showed that the calipers positively correlated with patient's age and duration of diabetes. This results consistent with (Schmit A, et

al, 1999), study which showed that arterial wall enlarged with age and (Marsh E, et al, 2007), in his study found that CAs diameter complemented IMT for discrimination of risk factors of carotid events and both IMT and diameter are so effective in men but in women diameter is stronger than IMT. This prove that the CAs diameter can be a good marker as IMT in assessment early progression of carotid plaques, because arterial diameter occurs early in atherosclerosis (Landy A, et al. 2004) and exaggerated in the presence of vulnerable plaques (Kichel S, et al, 1999) and (Merono P, et al, 2002).

Calipers data revealed that the caliper for the Lt CCA is greater than in the Rt CCA which is based on the basic thickness of the Lt CCA that is usually thicker than the Rt CCA as has been stated by (Edoardo et al, 2007), in their study in which they found that the Lt CCA thickness is greater than in the Rt CCA (4.17) and (4.20) and expressed by this equations $y = 0.1335x + 1.0667$ for Rt CCA and $y = 0.1439x - 0.9057$ for Lt CCA where y refers to caliper and x refers to age, $y = 0.3741x + 4.8873$ for Rt CCA and $y = 0.4091x + 3.4423$ for Lt CCA where y refers to caliper and x refers to duration of diabetes.

Furthermore the study reveal that no correlation between age and duration of diabetes with Doppler parameters in healthy participates, in contrast in plaque conditions as seen in figure 4.36 and table 4.11 which were revealed

that 6 participates shows plaques 3 in Rt CCA, 2 in Lt CCA and 1 in Lt ICA (Figure 4.37), the IMT shows positive correlation with PSV as seen in figure 4.38 while figure 4.39 shows the positive correlation between EDV and IMT, Several studies have shown that carotid artery degree of stenosis is a critical parameter in the evaluation of stroke risk (Warlow C et al, 1998). . Many trials showed that the risk of ischemic events increases with the degree of stenosis and can be markedly reduced with endarterectomy or carotid artery stenting (Warlow C et al, 1998). Table 4.12 shows stenotic degree which were showed that the degree of stenosis arises with increase of PSV, this result in line with (Grant et al, 2003) in his study which reveal that PSV value rises in direct proportion to the degree of stenosis. Recently new parameters other than degree of stenosis have been shown to be important markers for the stratification of the risk of stroke, although the degree of stenosis is still considered the leading parameter for choosing a specific option (Eliasziw M et al, 1994), which is The plaque morphology, such as the echogenicity of the plaque, the surface, presence of ulceration, as well as the presence of plaque and stenosis, is important for predicting future cardiovascular events, (Park AE et al, 1998) and The plaque surface can be described as smooth, irregular, or ulcerated. Plaque ulceration is associated with an increased risk of stroke (Eliasziw M et al, 1994), table 4.12 shows the description of plaques which were 2 calcified and 2 ulcerated while one mixed (heterogeneous).

The PSV ICA/CCA ratio consider as important marker for carotid arteries atherosclerosis which less than 2 consider as normal. Table 4.14 showed the values of PSV ICA/CCA ratio which were high in Rt CCA than in Lt CCA due to the number of plaques were more in RT CCA.

5.2 Conclusion:

The outcomes of this study suggest that gray scale and Doppler ultrasound are a good tool to evaluate and assessment carotid arteries in diabetic patients and predict the degree and severity of atherosclerosis. Statistically IMT and carotid calipers showed strong positive correlation with age and duration of diabetes and they consider as a good marker of subclinical atherosclerosis. IMT values and diameter of carotid arteries tends to be larger in Lt side of the neck than the Rt neck. While there is no correlation between PSV, EDV, RI and PI with age and duration of diabetes in healthy participates but in plaques conditions there is a linear correlation between PSV, EDV and IMT.

5.3 Recommendations:

The researcher has come out with following proposed future's researches:

1. Evaluation of carotid arteries in patients of hypertensive and diabetes mellitus with gender in different age groups 18-40, 40-70 and more than 70 years.

2. Studying of diabetic effects in internal carotid and intra-cranial arteries as an extension for current study.
3. Studying of diabetic effects in common carotid and in coronary arteries.
4. Establish normal parameters of IMT, calipers of carotid arteries in healthy participates in different age groups.
5. Application of ultrasound in obesity, body mass index and race and how they effect carotid arteries.

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Appendices:-

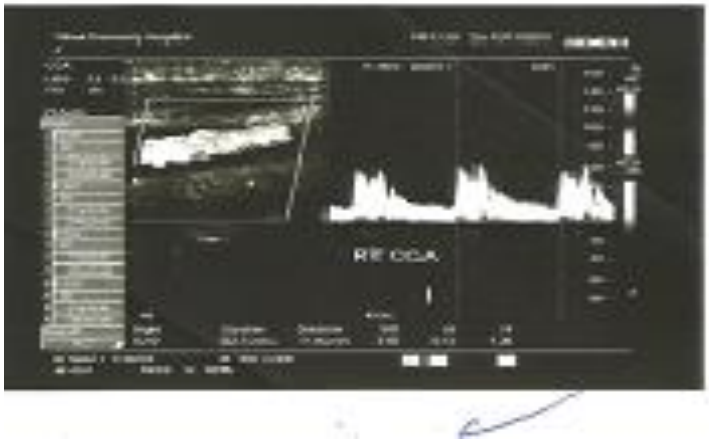

Figure 1 Rt CCA-male-57 year's diabetic patient with normal Doppler parameters.

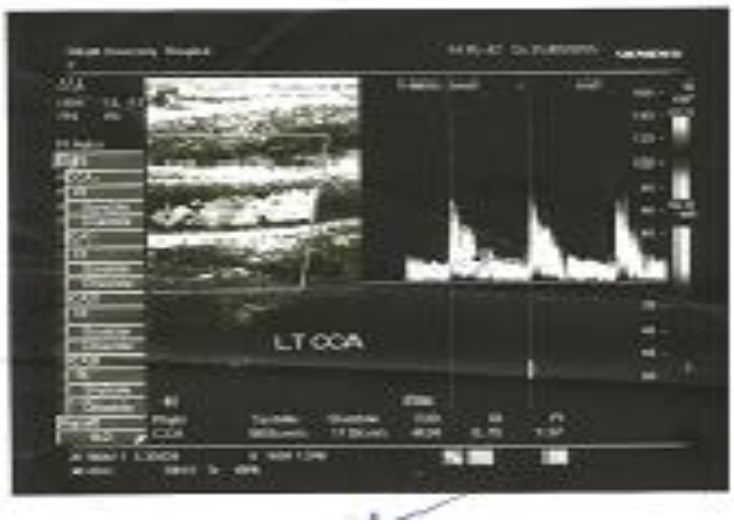

Figure 2 Lt CCA- female- 44 years diabetic patient with normal Doppler parameters.

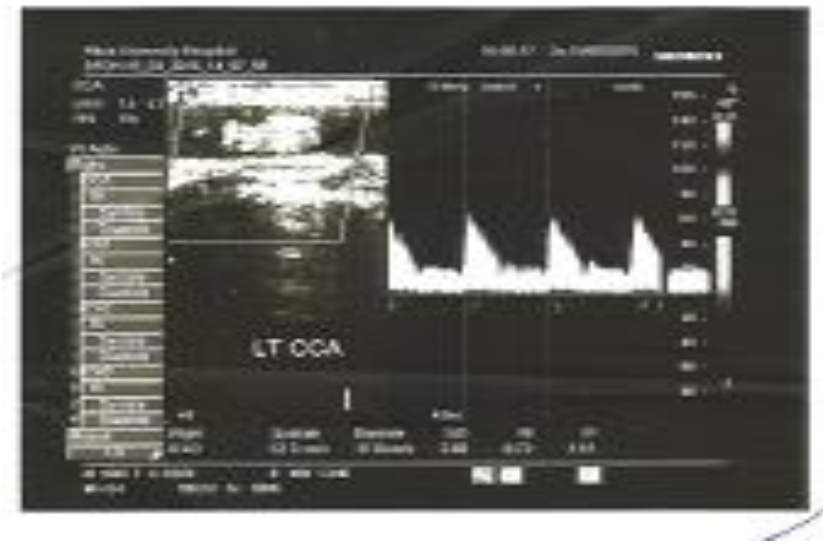

Figure 3 Lt CCA- female- 60 years diabetic patient with normal Doppler parameters.

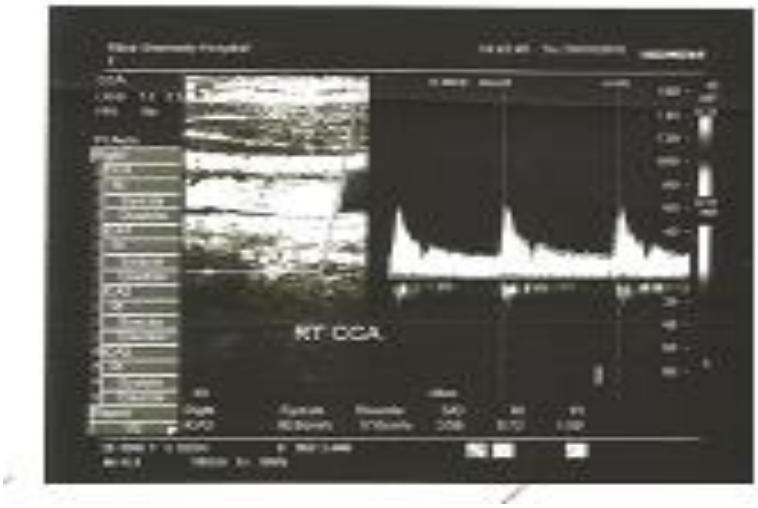

Figure 4 Rt CCA-male-57 years diabetic patient with normal Doppler parameter.

Figure 5, Rt CCA-male-54 year's diabetic patient with normal Doppler parameters.

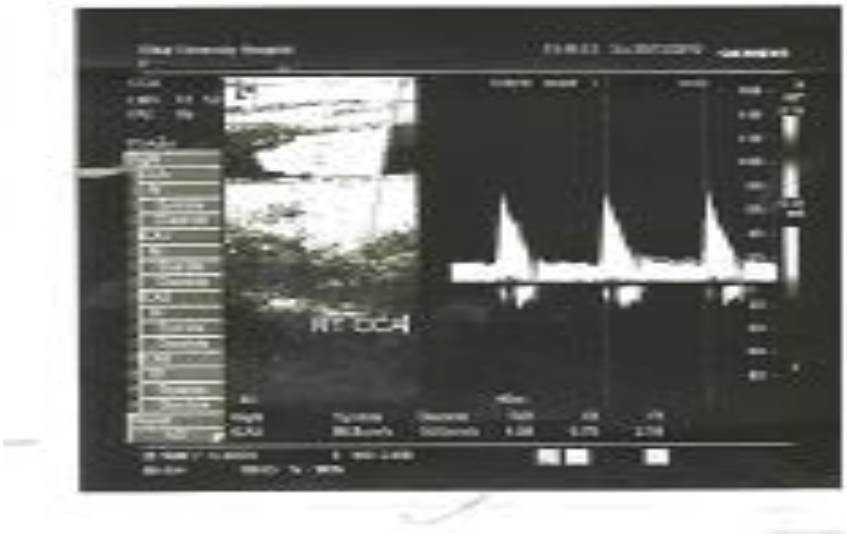

Figure 6, Rt CCA- female- 45 years diabetic patient with normal Doppler parameters.

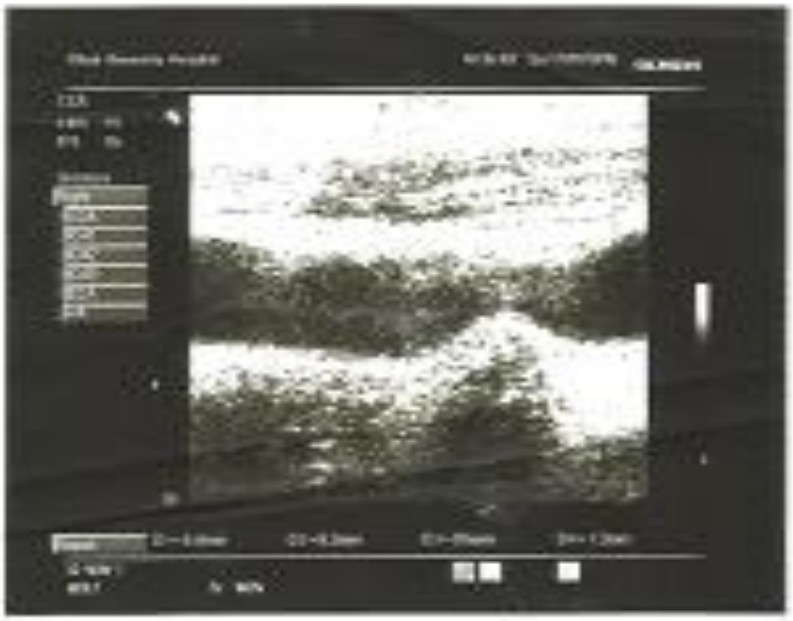

Figure 7, Rt CCA-male- 57 years diabetic patient with calcified plaque (4×8 mm).

Figure 8, Lt CCA-male-57 year's diabetic patient with ulcerated plaque (4.7×7.8 mm).

Figure 9, Rt CCA-female- 44 years diabetic patient with normal Doppler parameters.

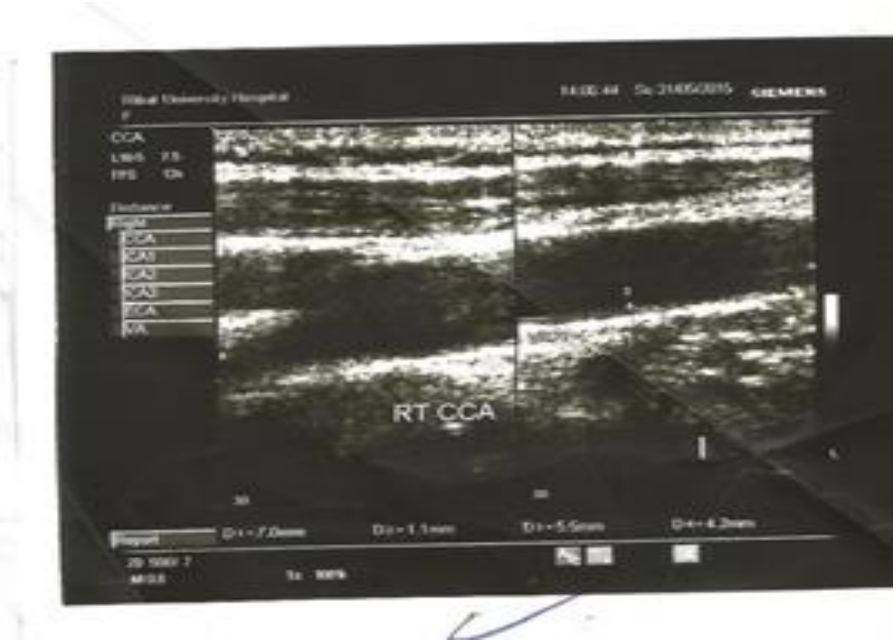

Figure 10, Rt CCA- female- 44 years diabetic patient shows IMT, caliper and bifurcation.

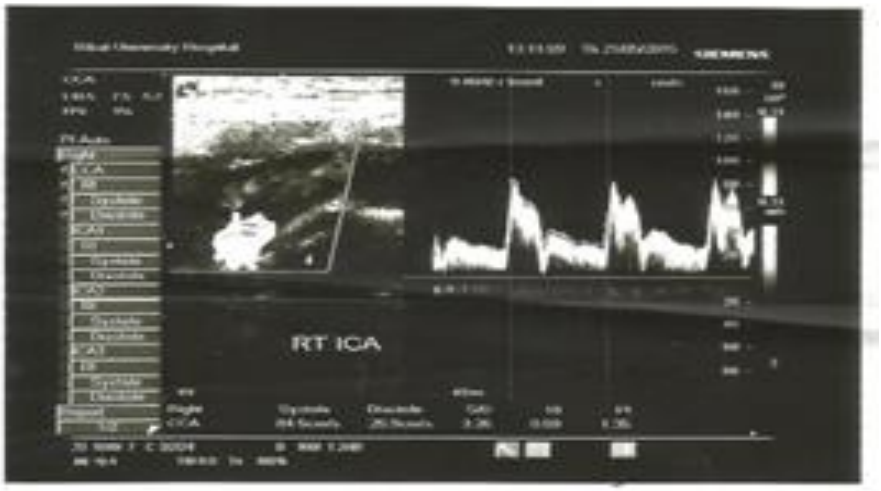

Figure 11, Rt ICA-male- 53 years diabetic patient with normal Doppler parameters.

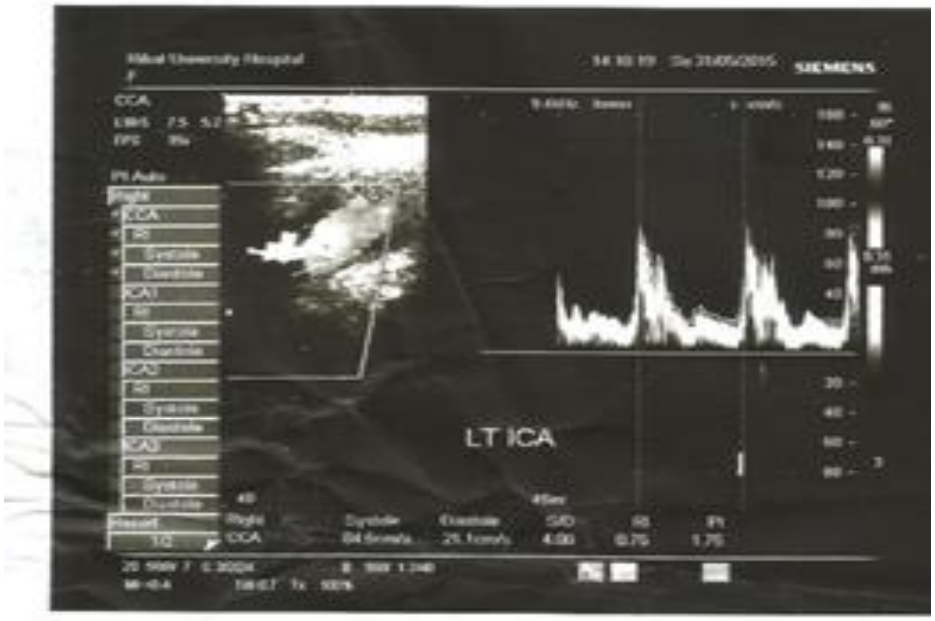

Figure 12, Lt ICA-female- 44 years diabetic patient with normal Doppler parameters.

Figure 13, Lt ICA-male- 68 years diabetic patient with normal Doppler parameters.

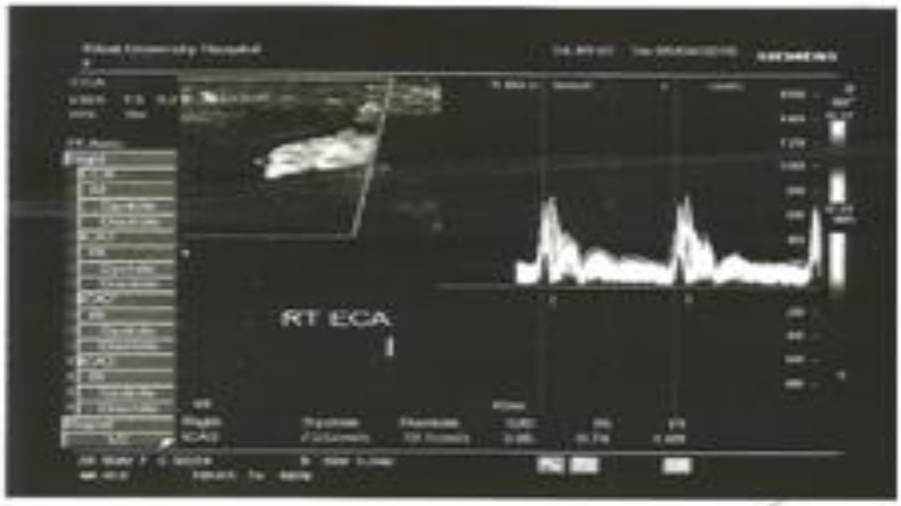

Figure 14, Rt ECA- male- 44 years diabetic patient with normal Doppler parameters.

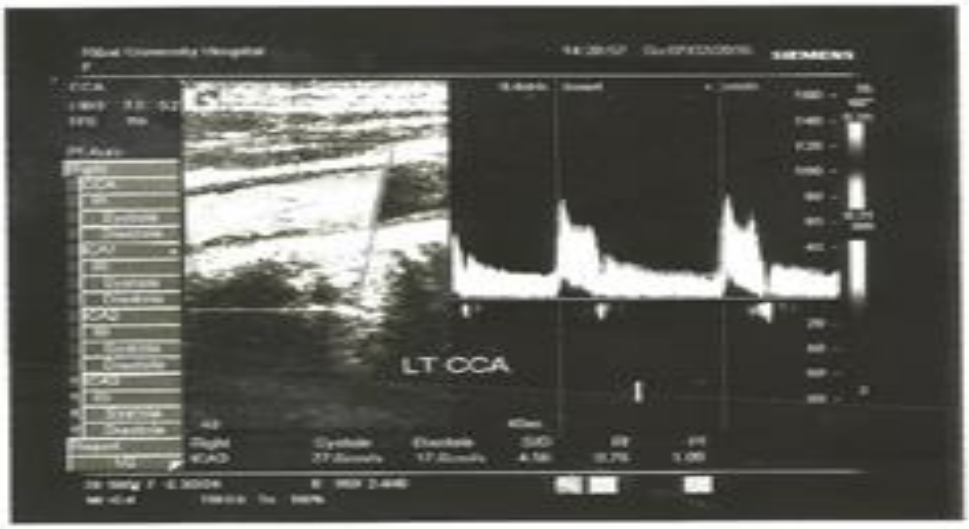

Figure 15, Lt CCA-male- 58 years diabetic patient with normal Doppler parameters.

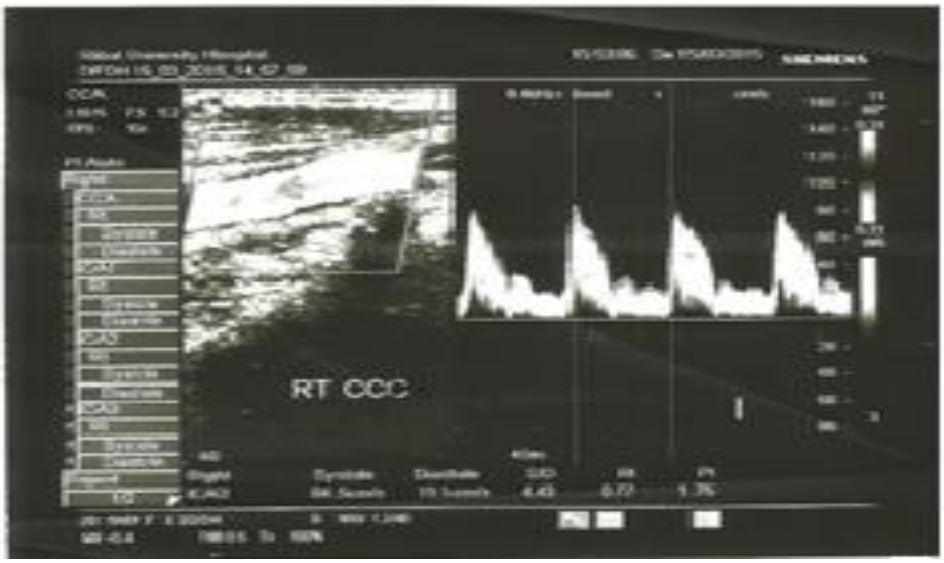

Figure 16, Rt ICA-female- 60 years diabetic patient with normal Doppler parameters.

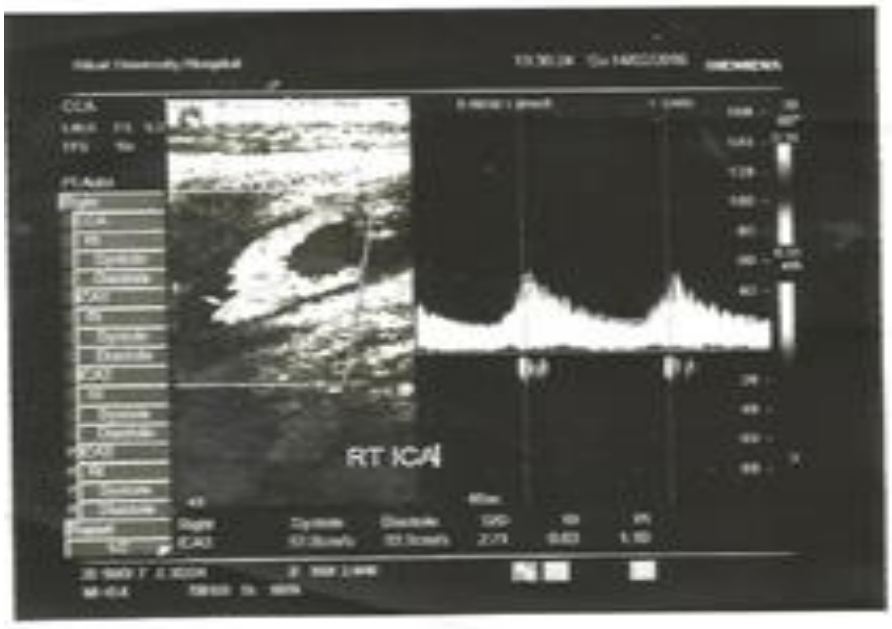

Figure 17, Rt ICA-female- 54 years diabetic patient with normal Doppler parameters

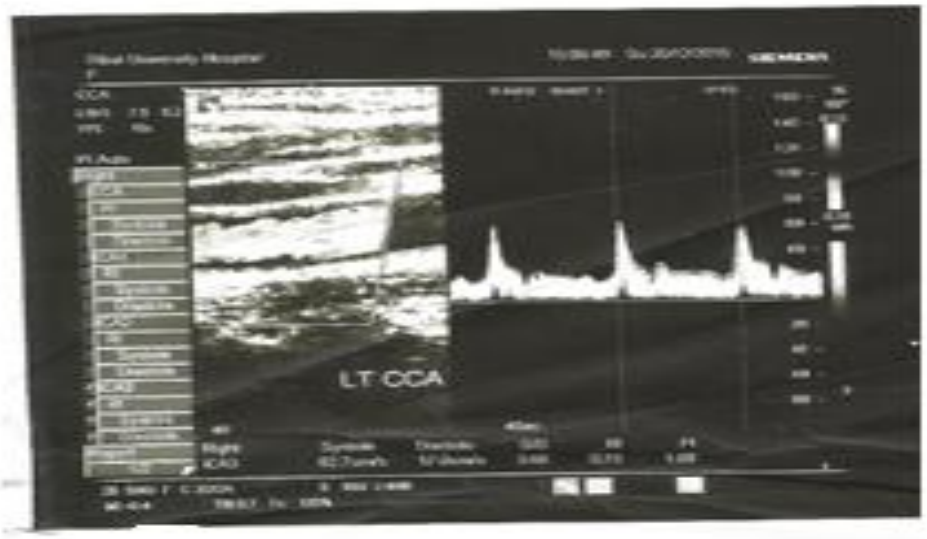

Figure 18, Lt CCA- male- 45 years diabetic patient normal Doppler parameters.

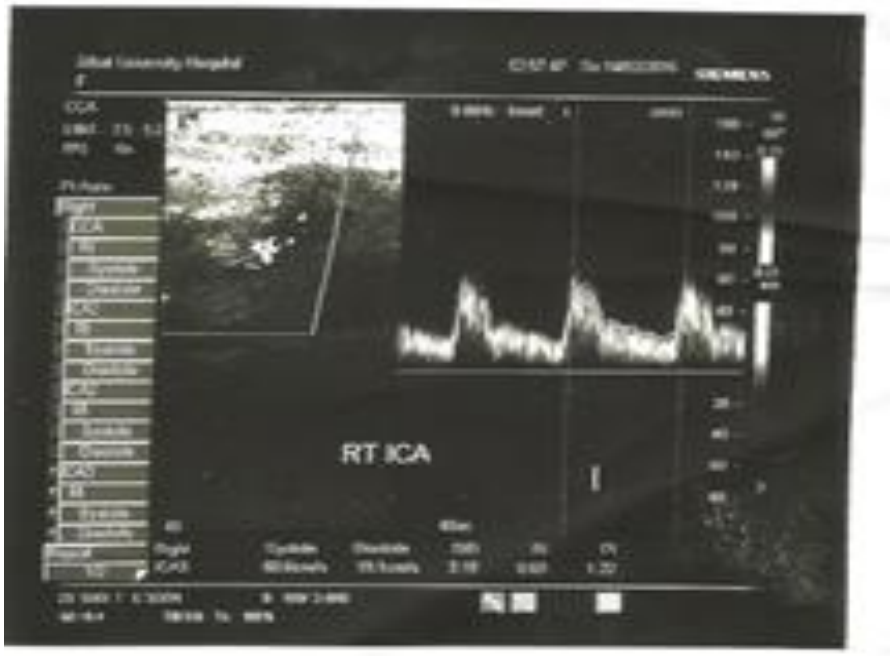

Figure 19, Rt ICA-male- 46 years diabetic patient with normal Doppler parameters.

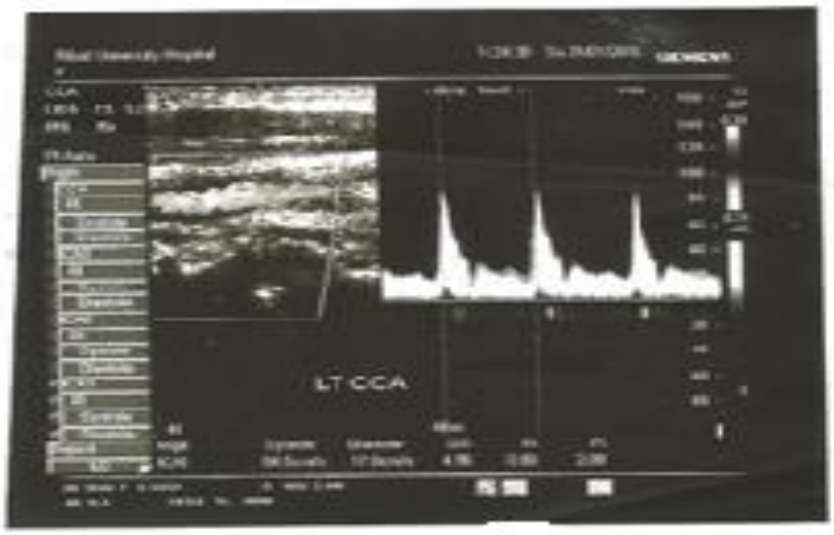

Figure 20, Lt CCA-male- 61 years diabetic patient with normal Doppler parameters.

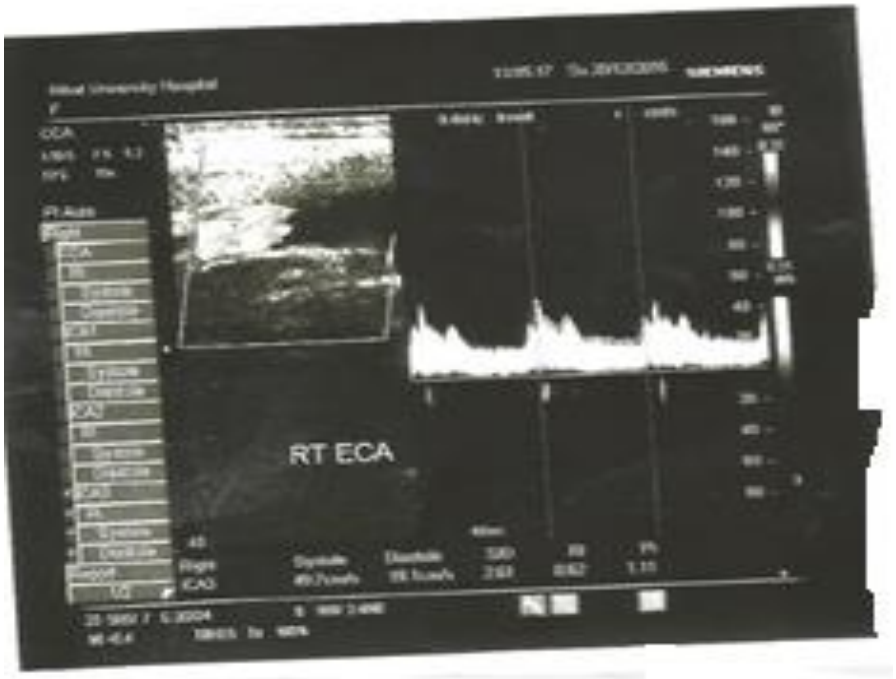

Figure 21, Rt ECA-male- 38 years diabetic patient with normal Doppler parameters.

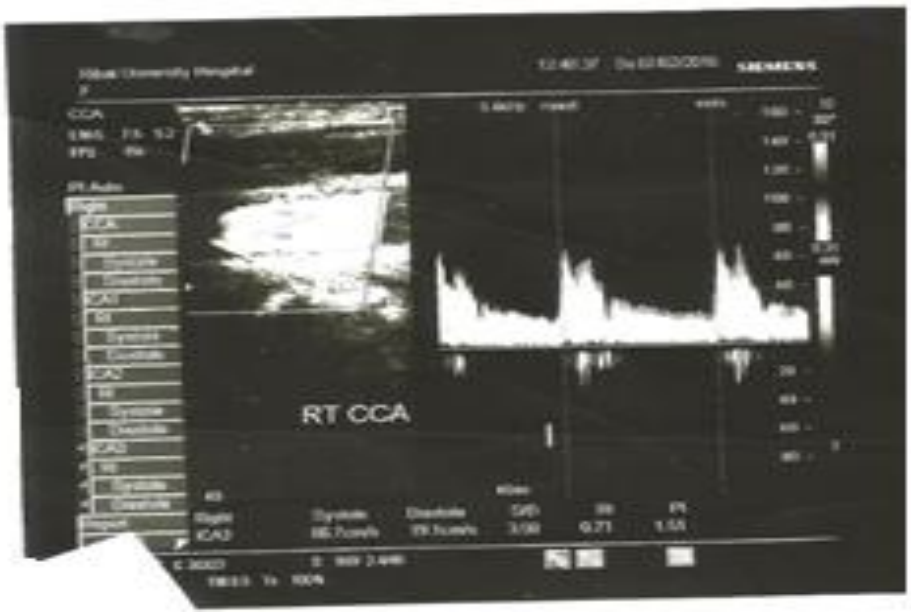

Figure 22, Rt CCA- female- 58 years diabetic patient with normal Doppler parameters.

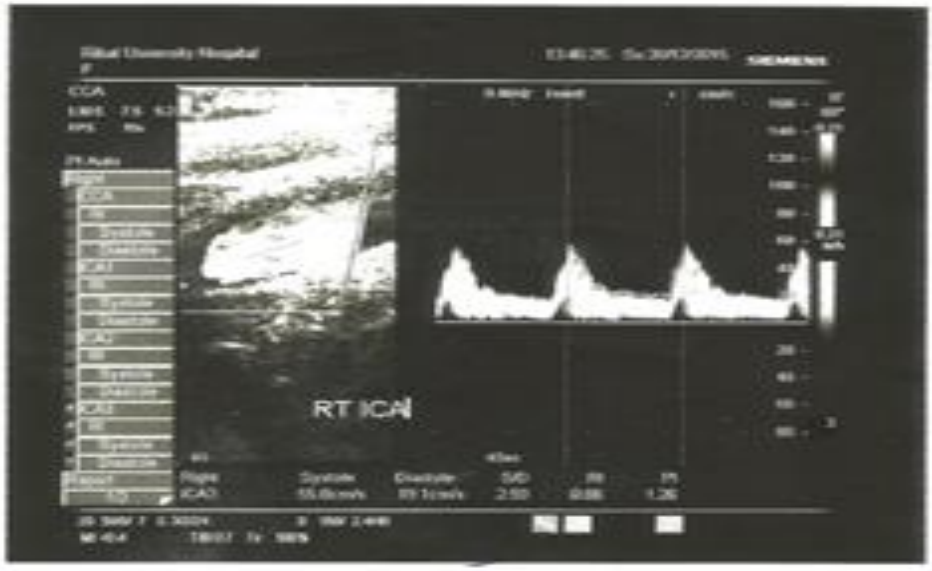

Figure 23, Rt ICA-female- 45 years diabetic patient with normal Doppler parameters.

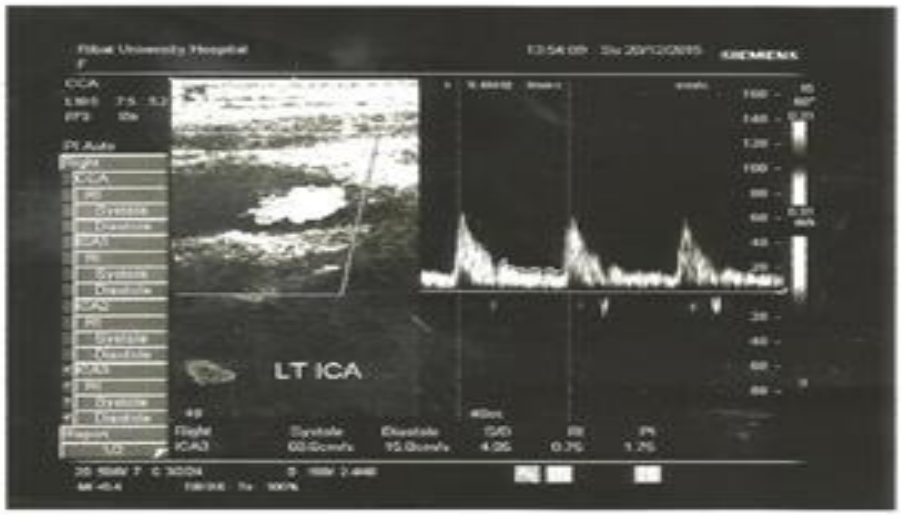

Figure 24, Lt ICA-male- 60 years diabetic patient with normal Doppler parameters.

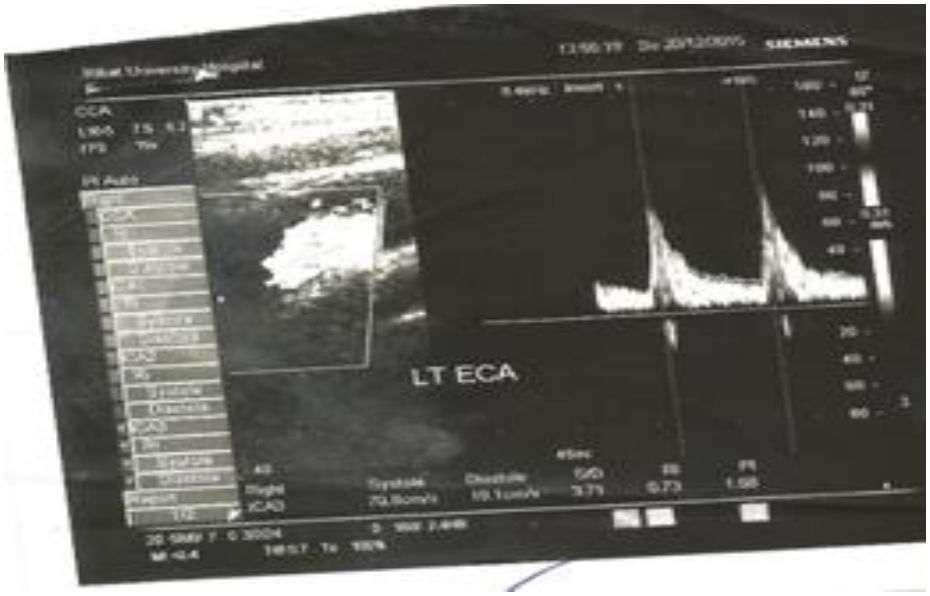

Figure 25, Lt ECA- female- 60 years diabetic patient normal Doppler parameters.

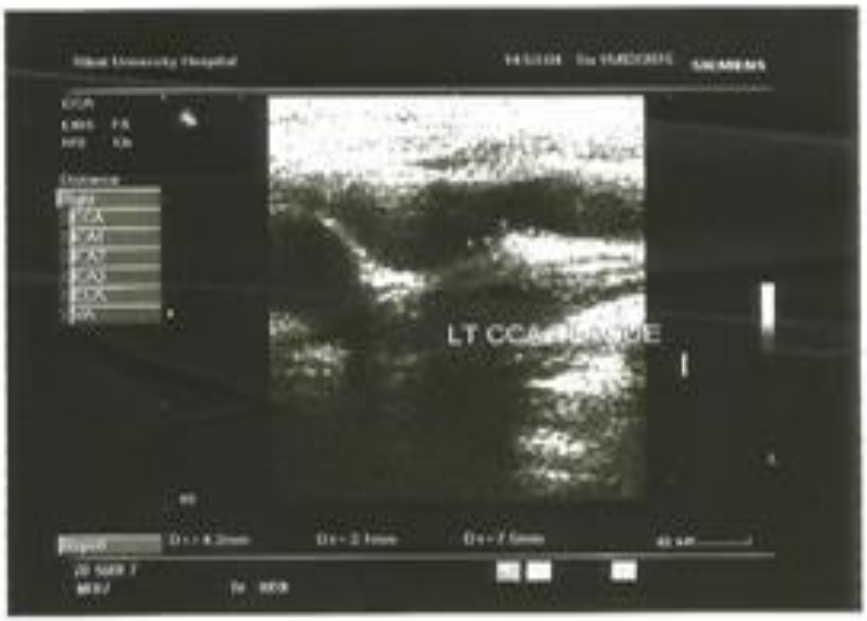

Figure 26, Lt CCA-female- 58 years diabetic patient with calcified plaque.

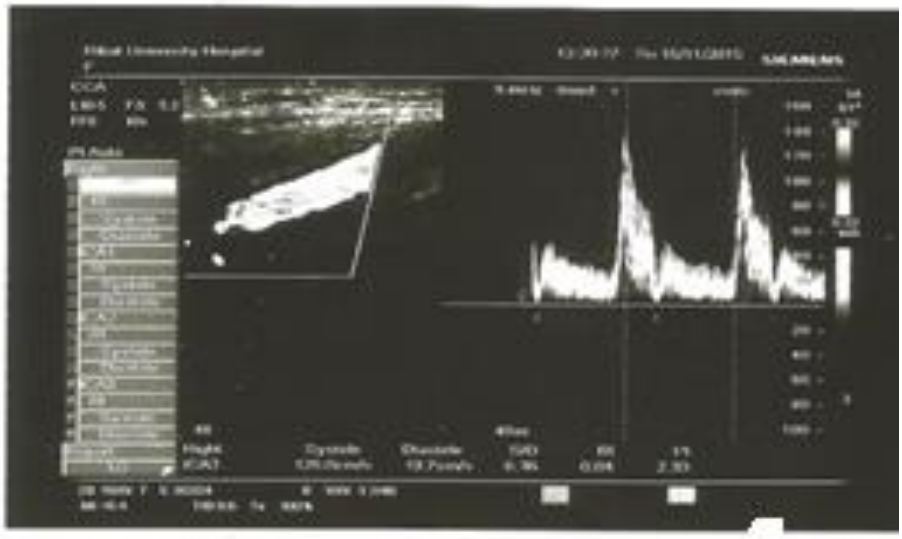

Figure 27, Rt CCA-male- 68 years diabetic patient with normal Doppler parameters.

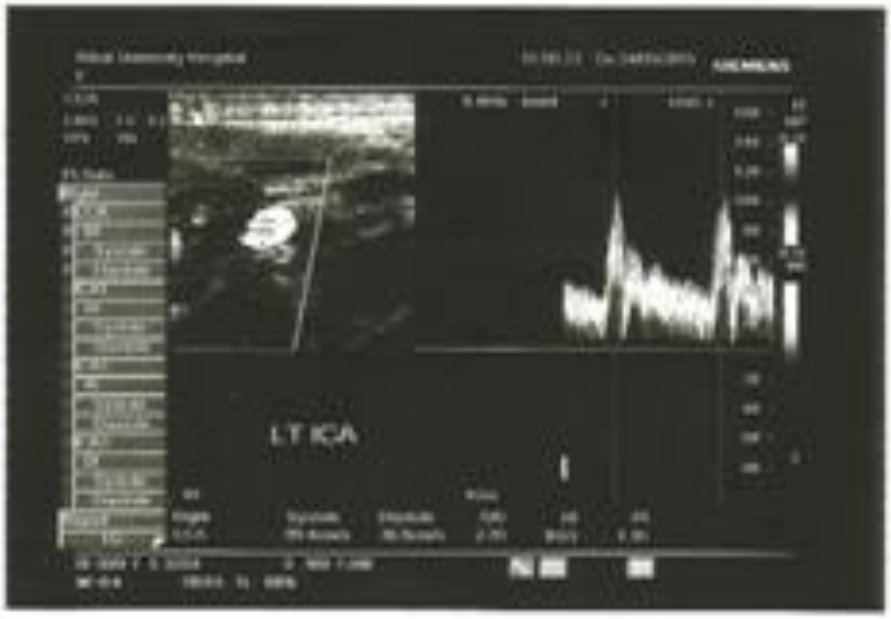

Figure 28, Lt ICA-female- 68 years diabetic patient with normal Doppler parameters.

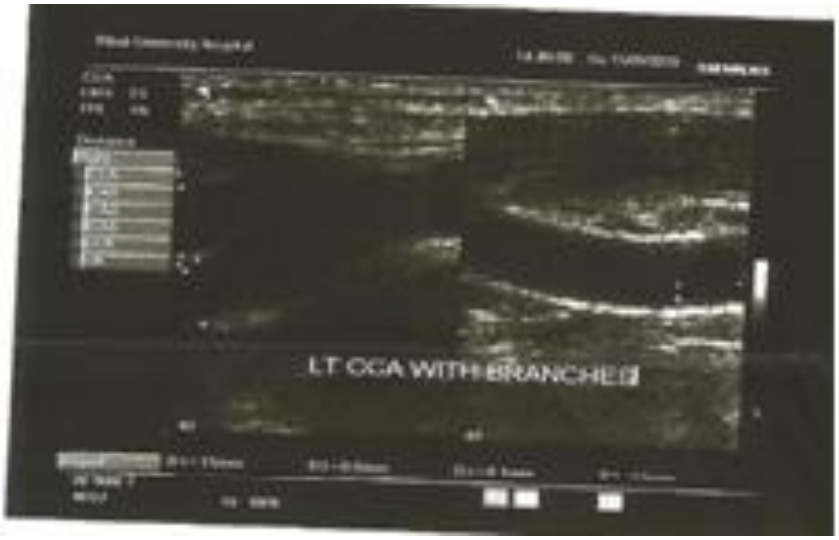

Figure 29, Lt CCA- female- 51 years diabetic patient shows IMT and Calipers of ICA and ECA.

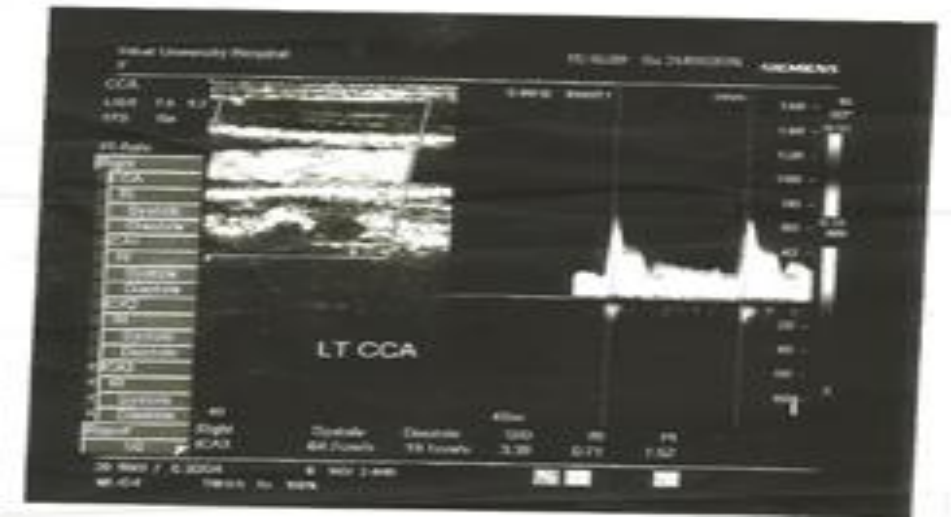

Figure 30, Lt CCA-female- 58 years diabetic patient with normal Doppler parameters.

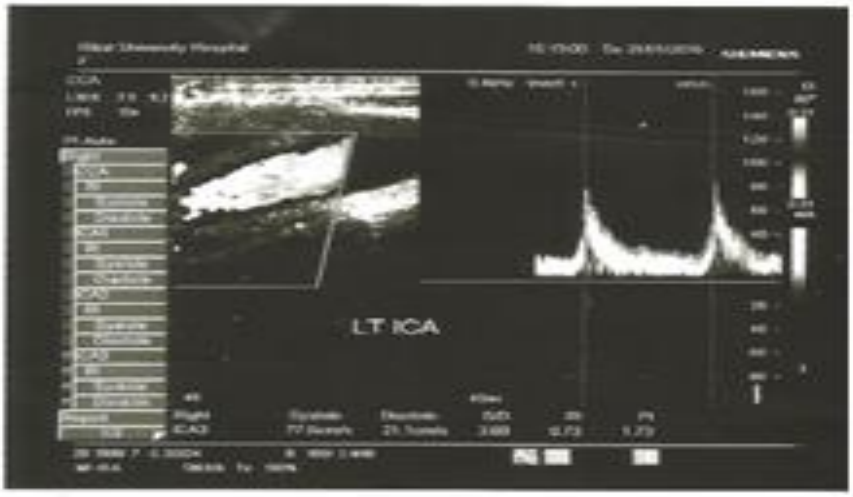

Figure 31, Rt CCA-male- 68 years diabetic patient with normal Doppler parameters

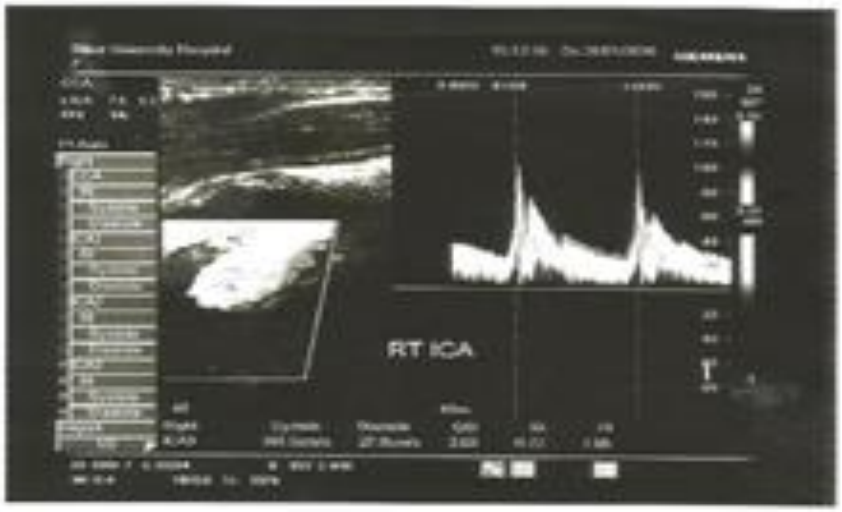

Figure 32, Rt ICA-female- 65 years diabetic patient with normal Doppler parameters.

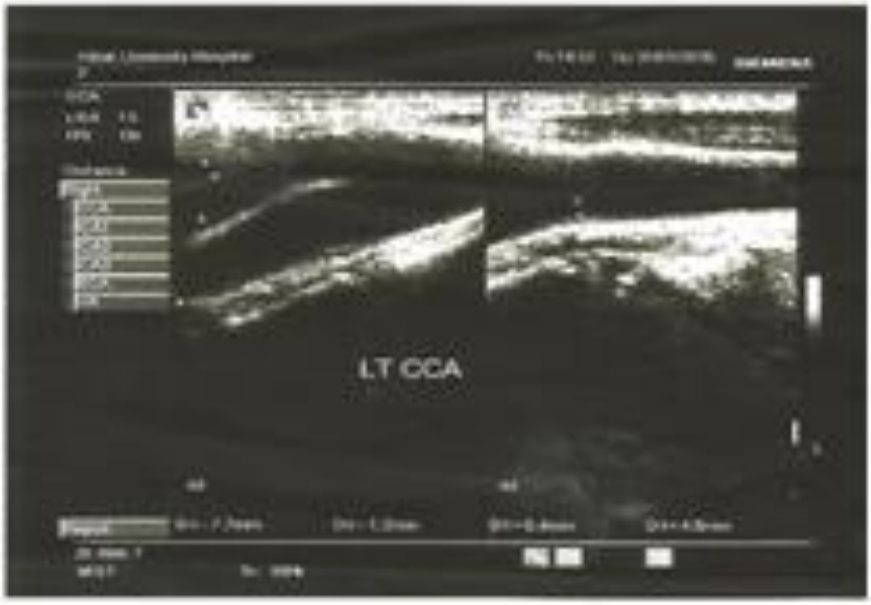

Figure 33, Lt CCA- female- 50 years diabetic patient shows IMT and Calipers.

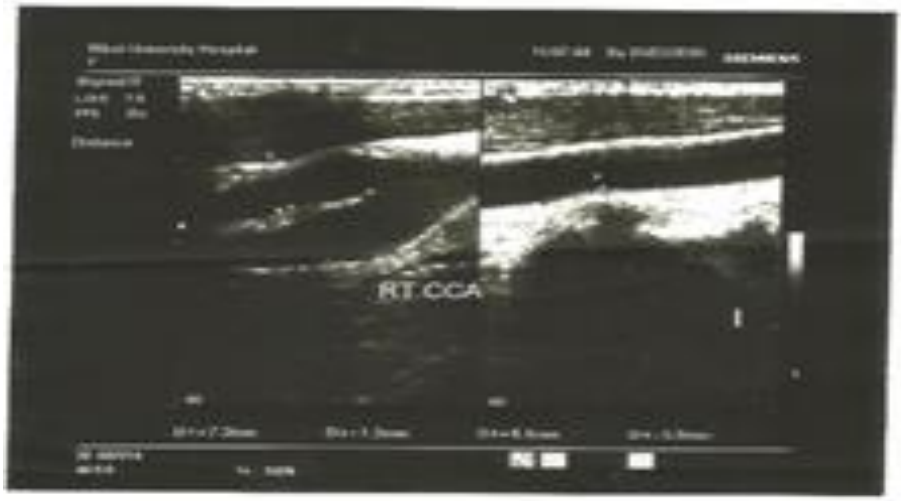

Figure 34, Rt CCA-male- 36 years diabetic patient shows IMT and Calipers.

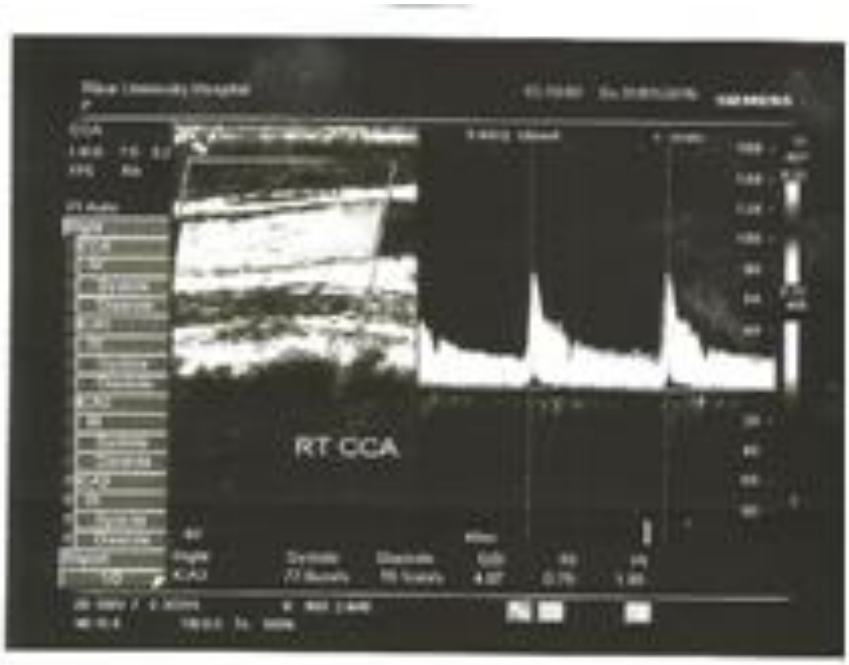

Figure 35, Rt CCA-male- 36 years diabetic patient with normal Doppler parameters.

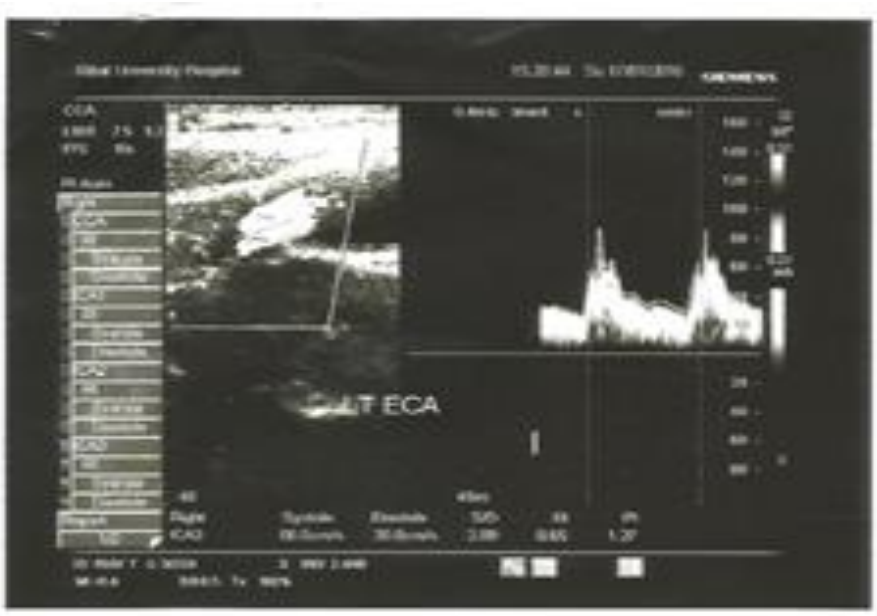

Figure 36, Rt ECA-male- 49 years diabetic patient with normal Doppler parameters.

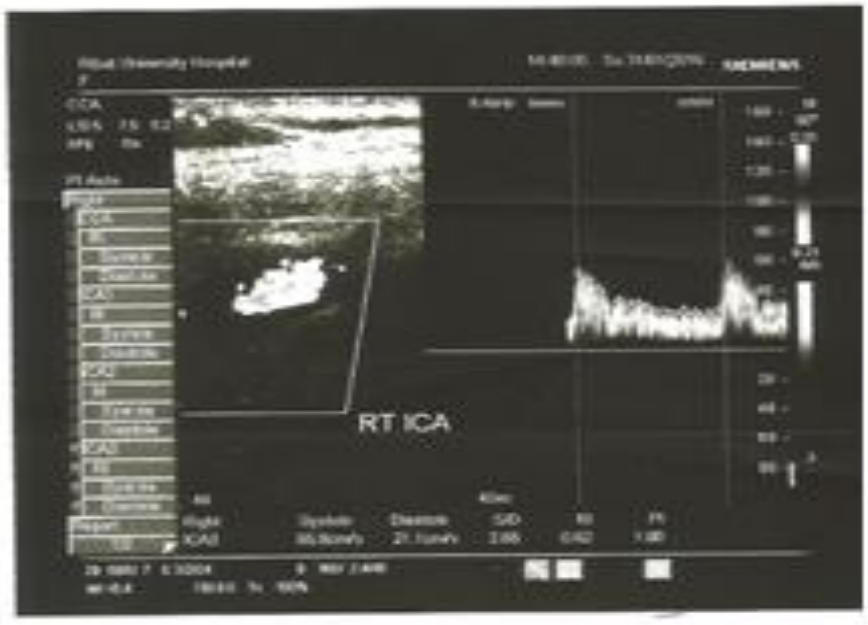

Figure 37, Lt ICA- male- 57 years diabetic patient with normal Doppler parameters.

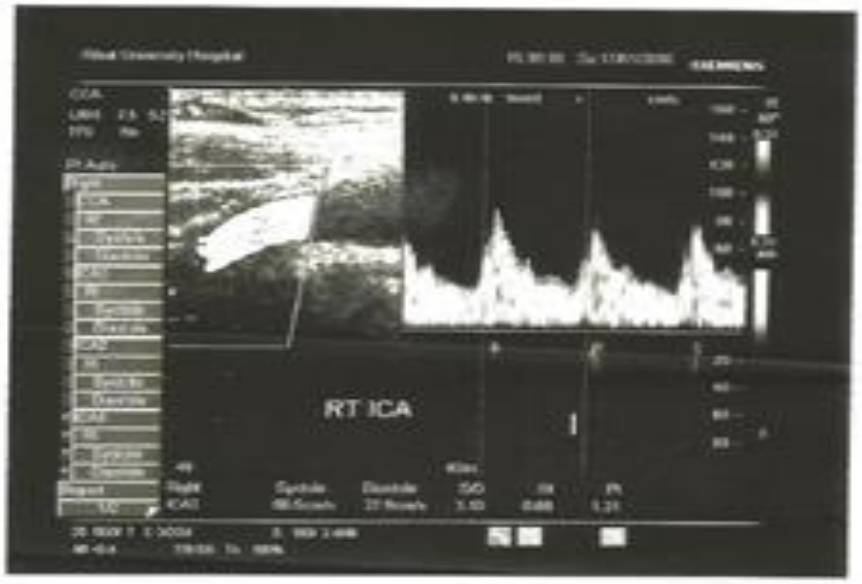

Figure 39, Rt ICA-male- 49 years diabetic patient with normal Doppler parameters.

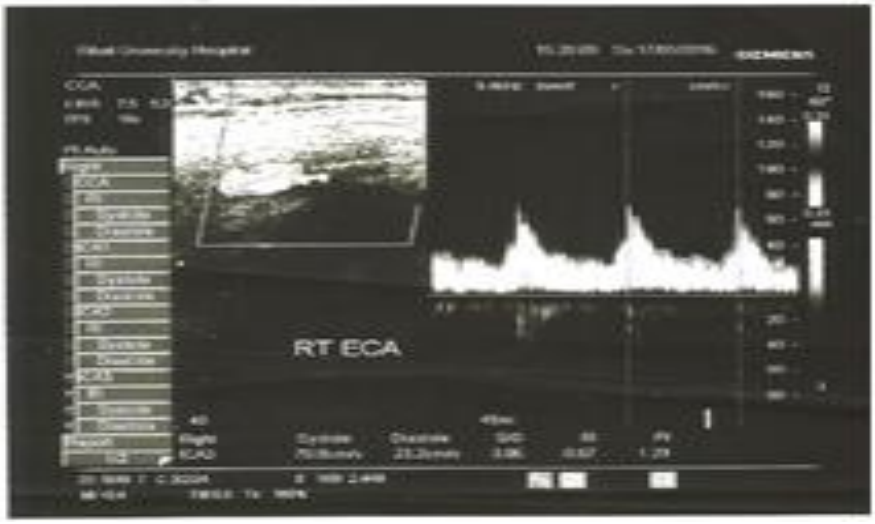

Figure 40, Rt CCA-male- 49 years diabetic patient with normal Doppler parameters.

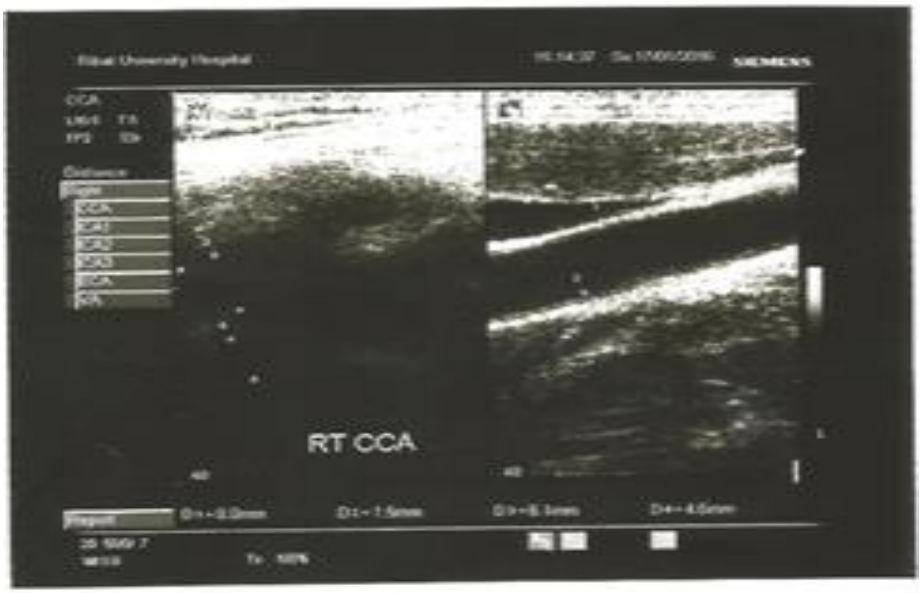

Figure 41, Rt CCA-male- 49 years diabetic patient with shows IMT.

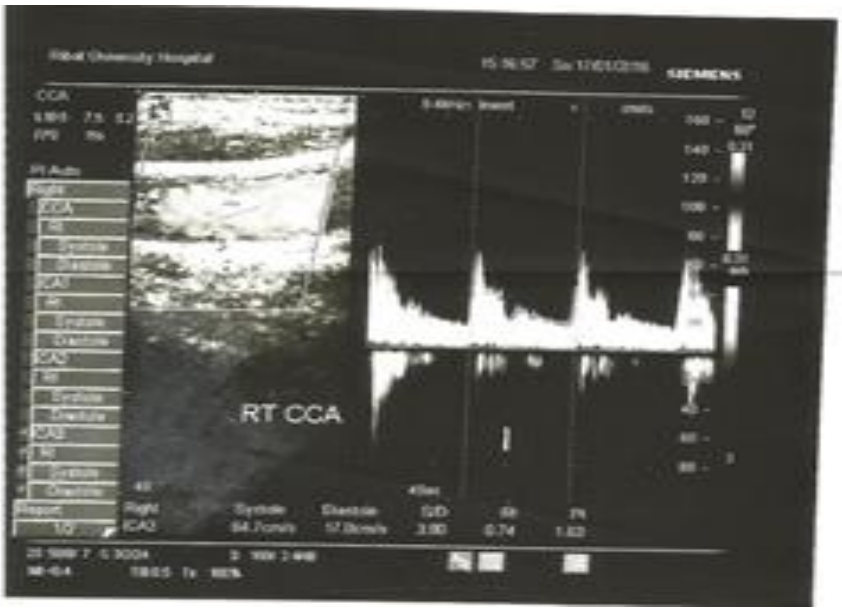

Figure 42, Rt CCA- male- 49 years diabetic patient normal Doppler parameters.

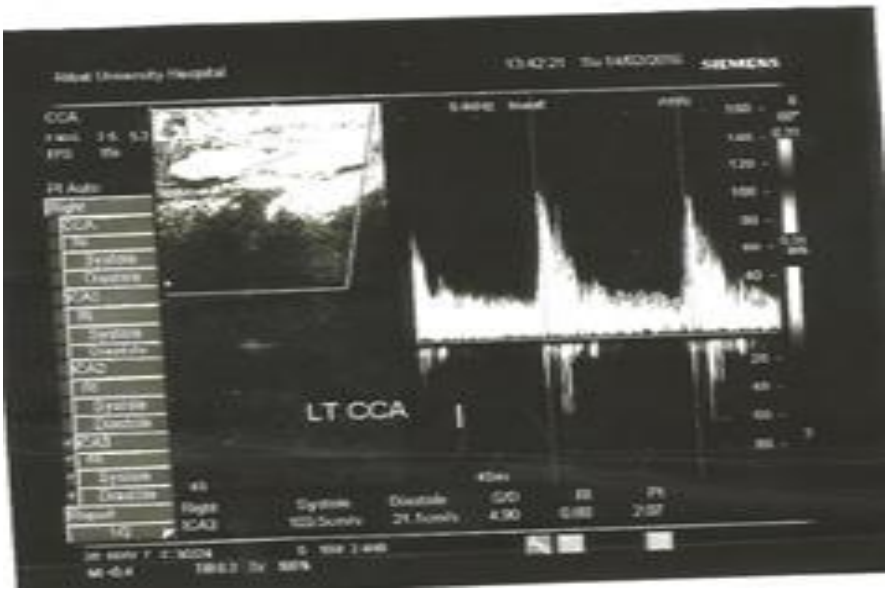

Figure 43, Lt CCA-female- 54 years diabetic patient normal Doppler parameters.

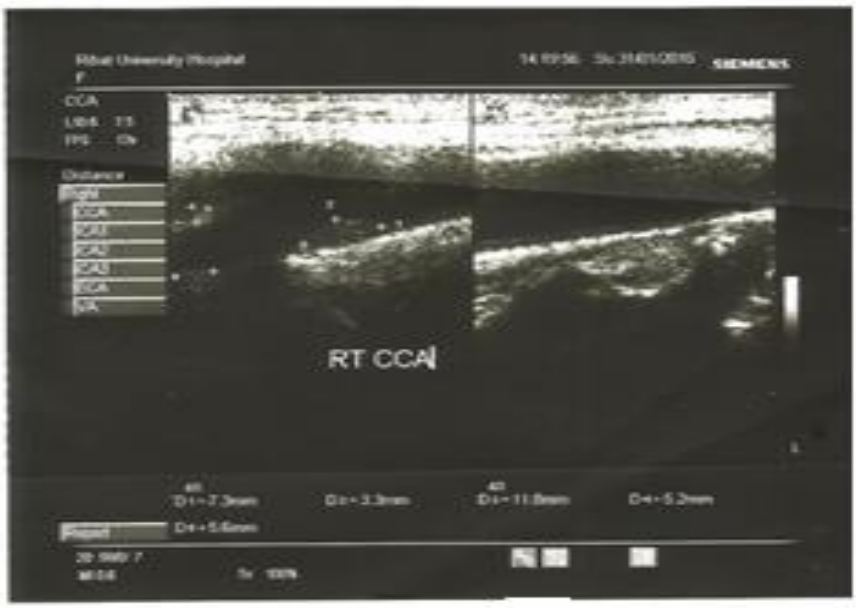

Figure 44, Rt CCA-female- 53 years diabetic patient shows hypoechoic plaque.

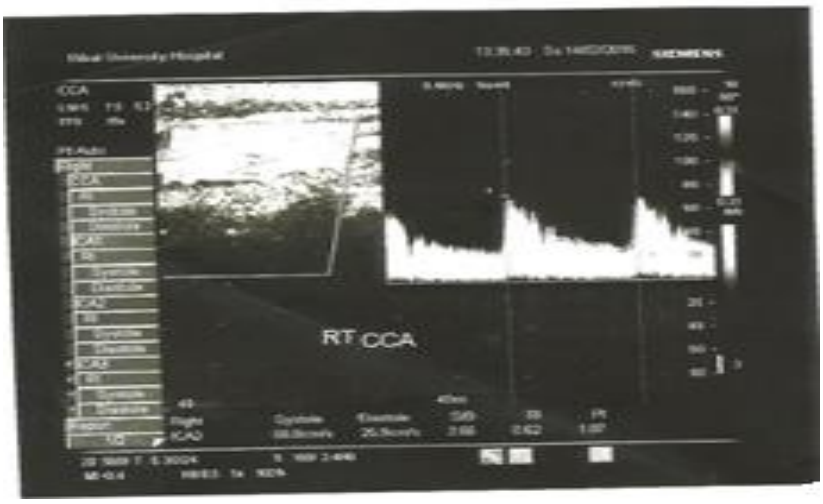

Figure 45, Rt CCA-female- 54 years diabetic patient with normal Doppler parameters.

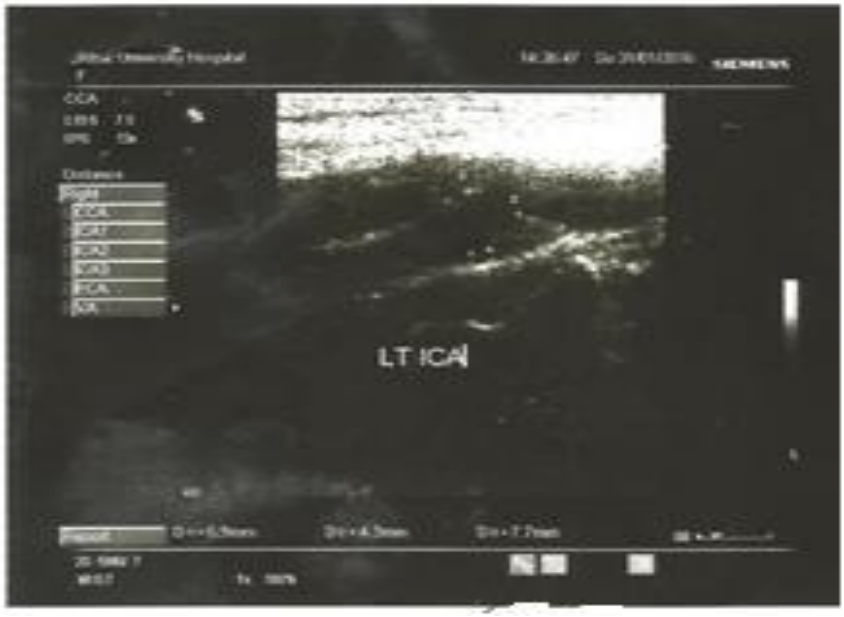

Figure 46, Lt ICA- male- 54 years diabetic patient shows ulcerated plaque.

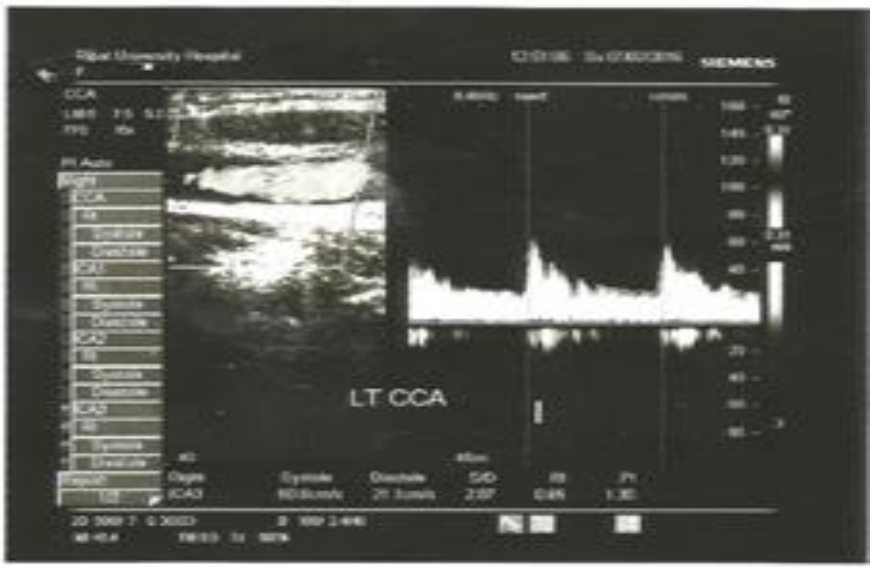

Figure 47, Lt CCA-female- 47 years diabetic patient with normal Doppler parameters.

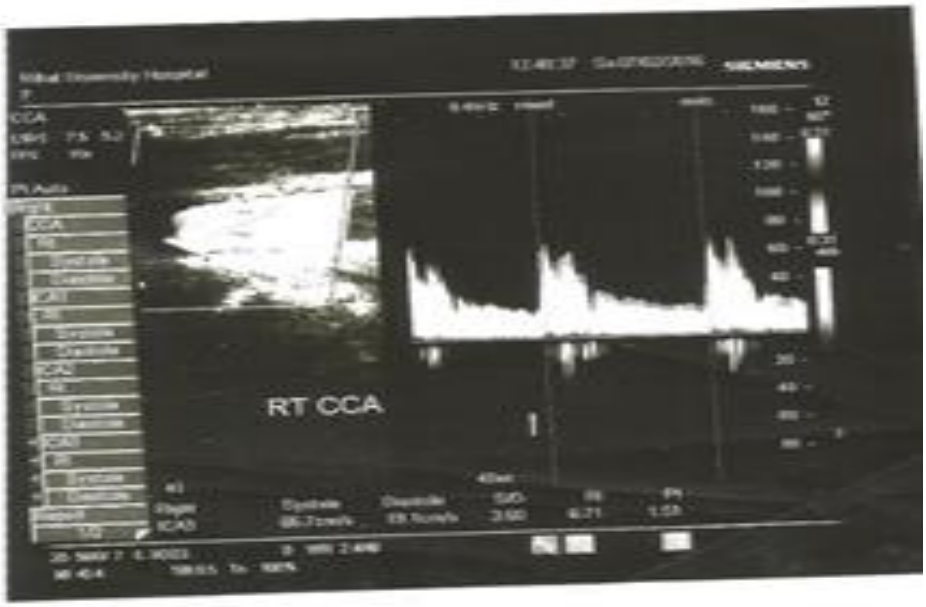

Figure 48, Rt CCA-female- 52 years diabetic patient with normal Doppler parameters.

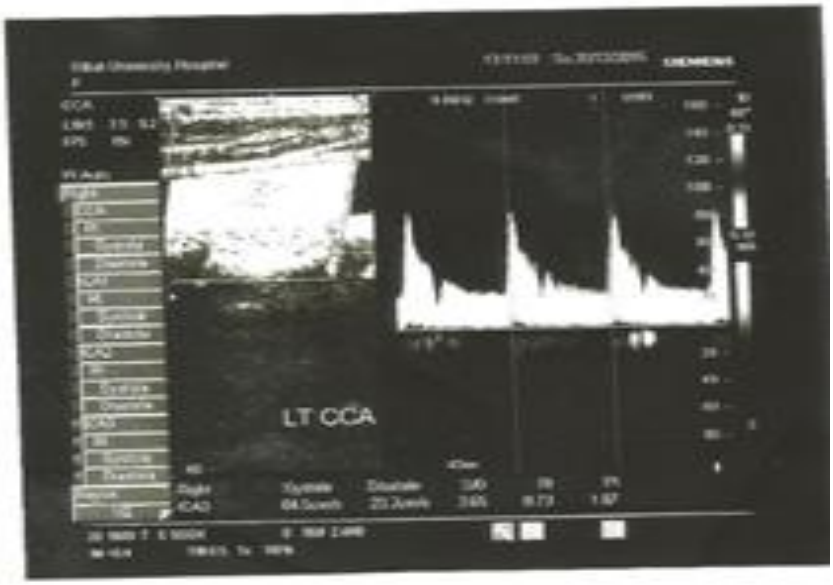

Figure 49, Lt CCA-female- 38 years diabetic patient with normal Doppler parameters.

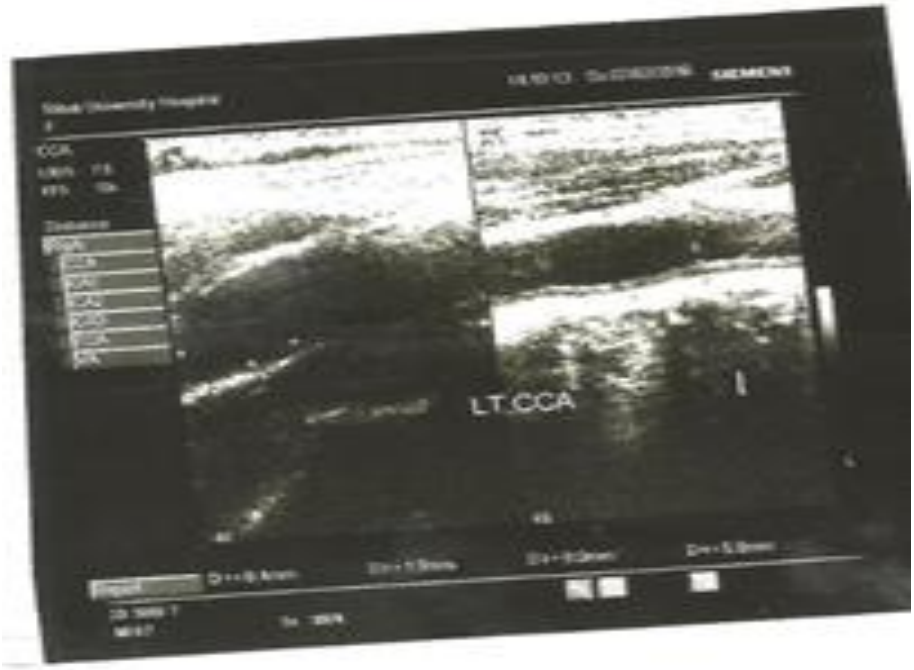

Figure 50, Lt CCA- male- 58 years diabetic patient shows IMT and Calipers.

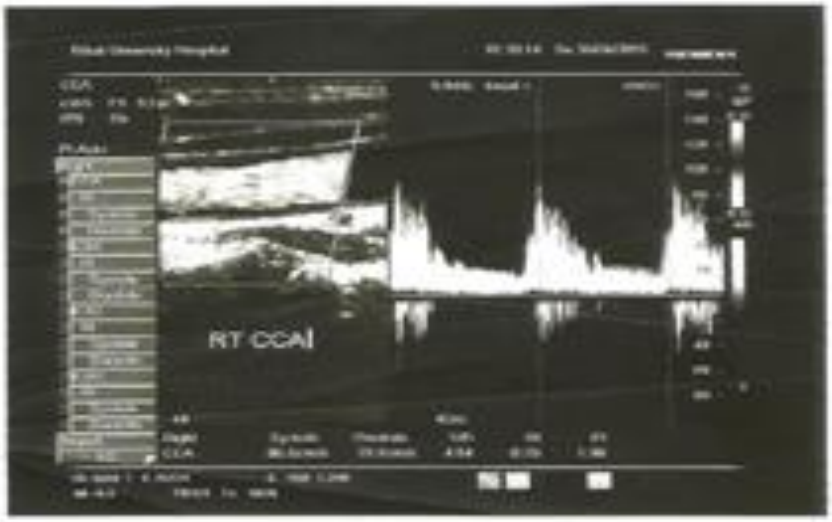

Figure 51, Rt CCA-female- 48 years diabetic patient with normal Doppler parameters.

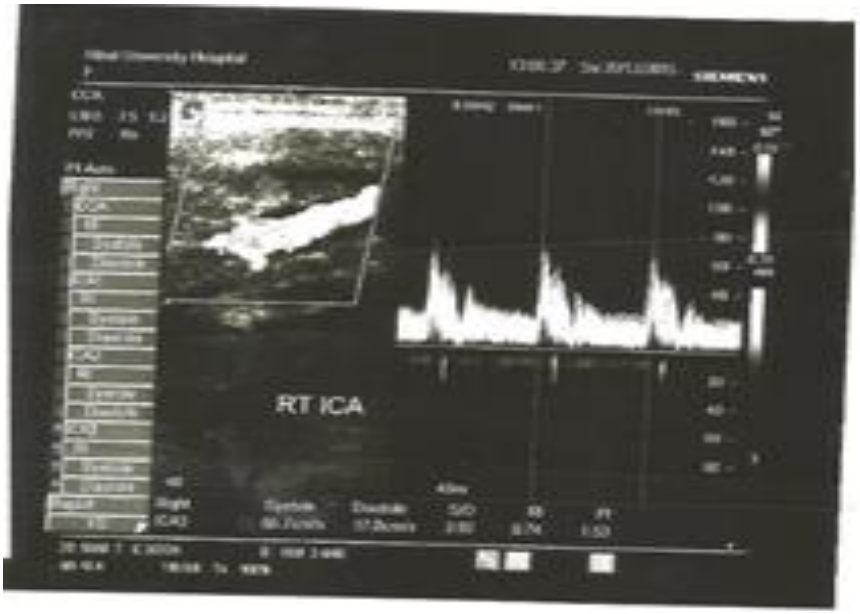

Figure 52, Rt ICA-male- 38 years diabetic patient with normal Doppler parameters.

Figure 53, Rt CCA-male- 52 years diabetic patient shows IMT, Calipers and bifurcation.

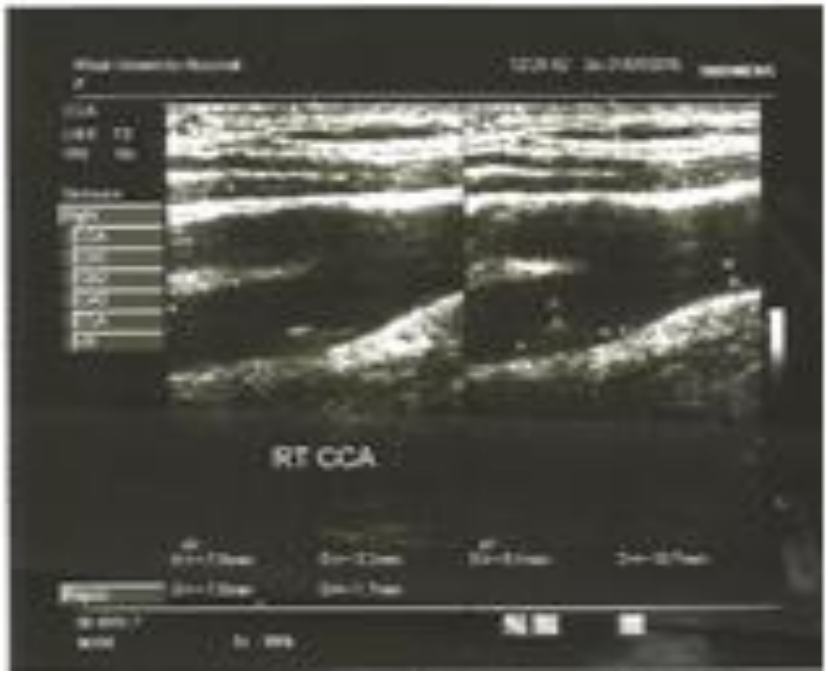

Figure 54, Rt CCA- male- 67 years diabetic patient shows ulcerated plaque at bifurcation.

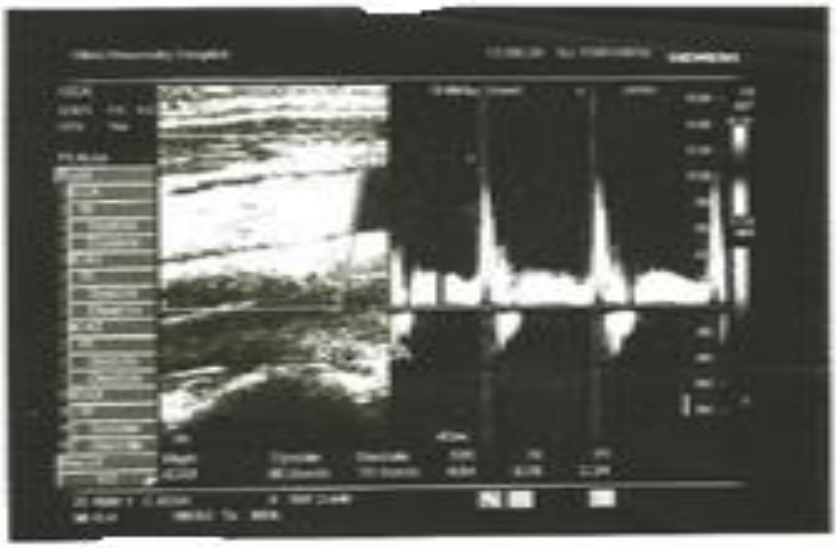

Figure 55, Rt CCA-female- 62 years diabetic patient with normal Doppler parameters.

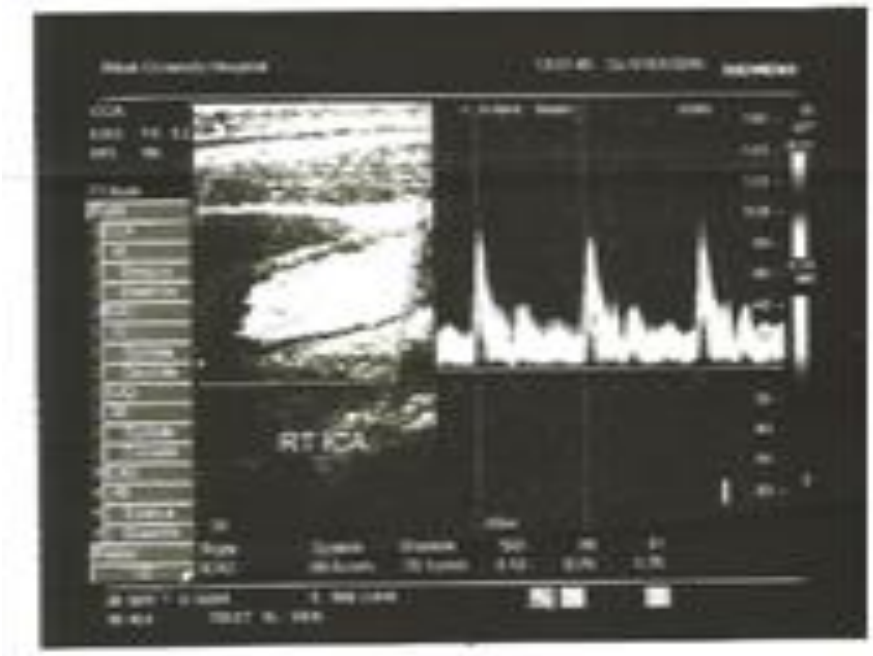

Figure 56, Rt ICA-male- 62 years diabetic patient with normal Doppler parameters.

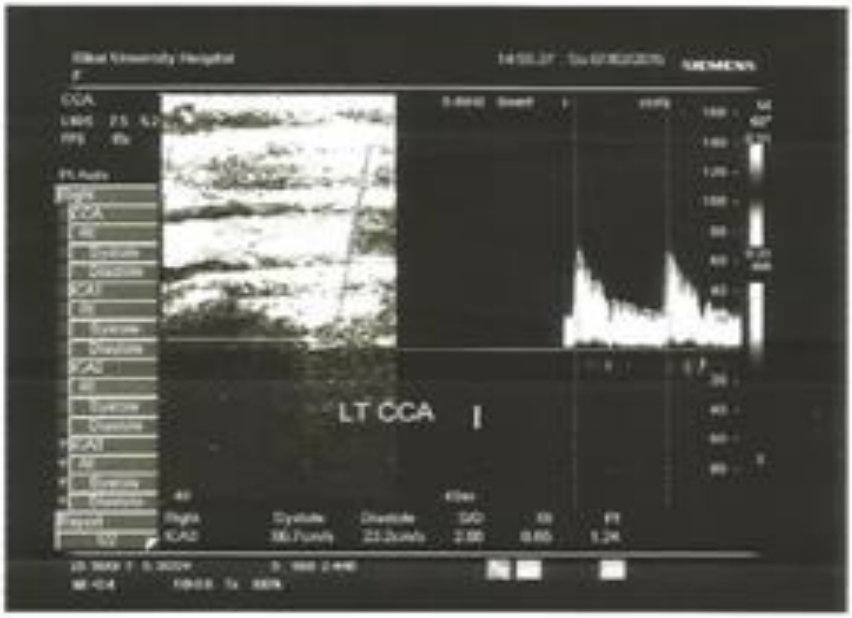

Figure 57, Lt CCA-female- 45 years diabetic patient with normal Doppler parameters.

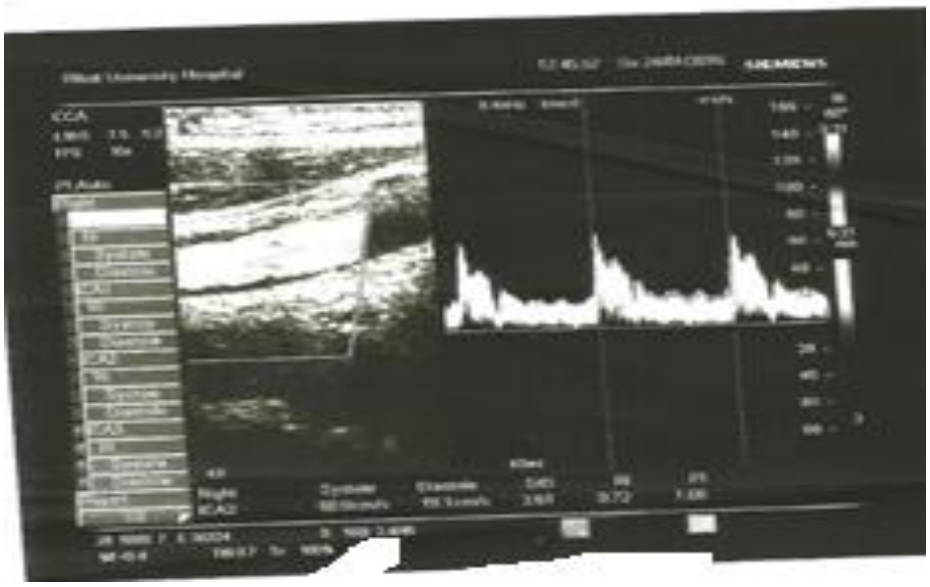

Figure 58, Rt CCA- male- 55 years diabetic patient with normal Doppler parameters.

Figure 59, Rt ICA-female- 50 years diabetic patient with normal Doppler parameters.

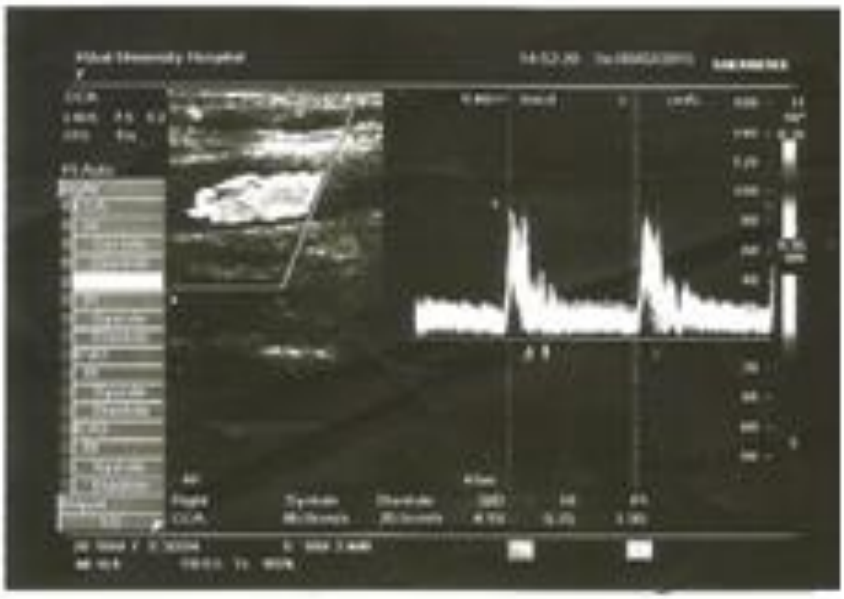

Figure 60, Rt CCA-female- 51 years diabetic patient with normal Doppler parameters.

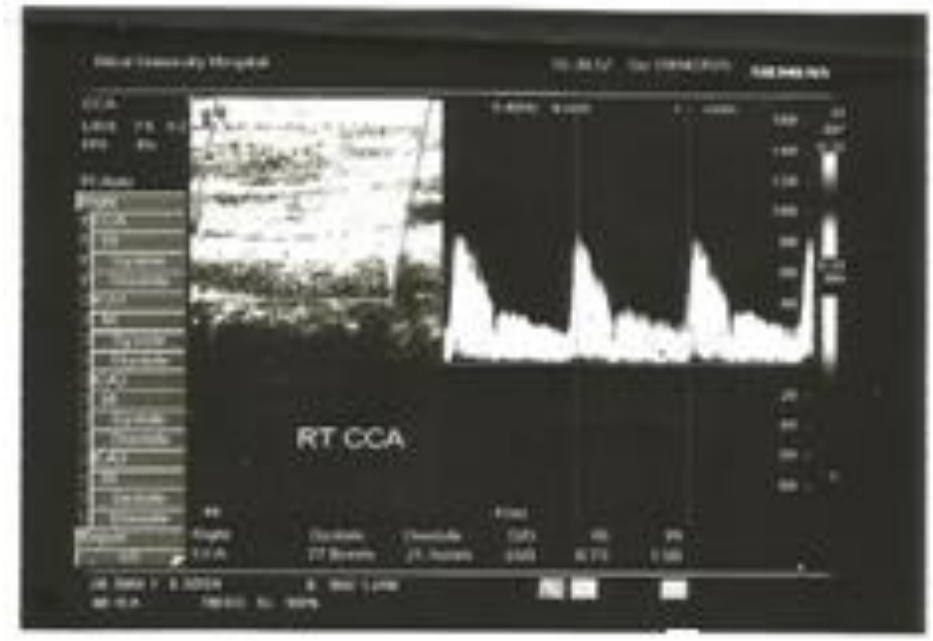

Figure 61, Rt CCA-female- 53 years diabetic patient with normal Doppler parameters.

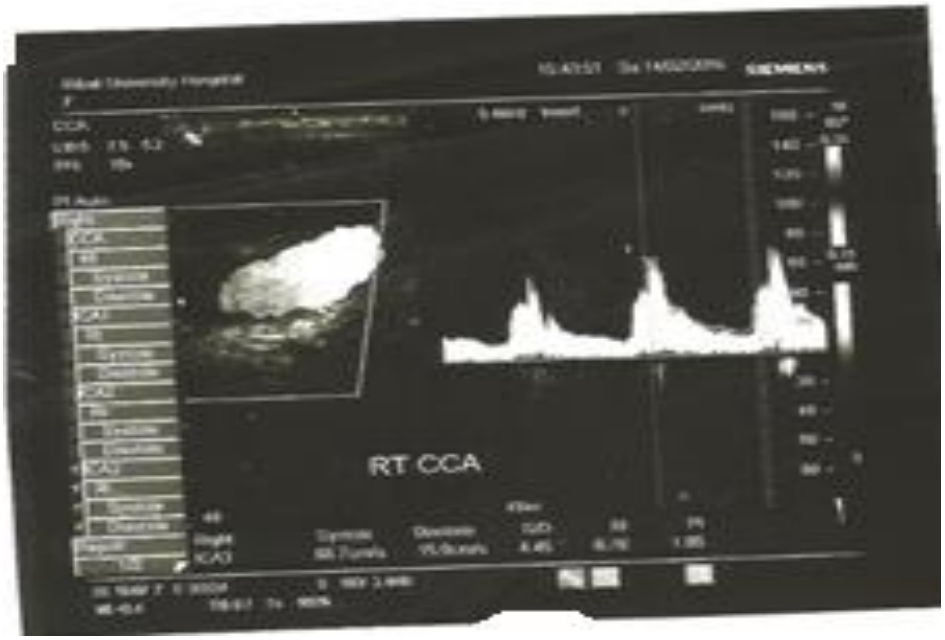

Figure 62, Rt CCA- female- 50 years diabetic patient with normal Doppler parameters.

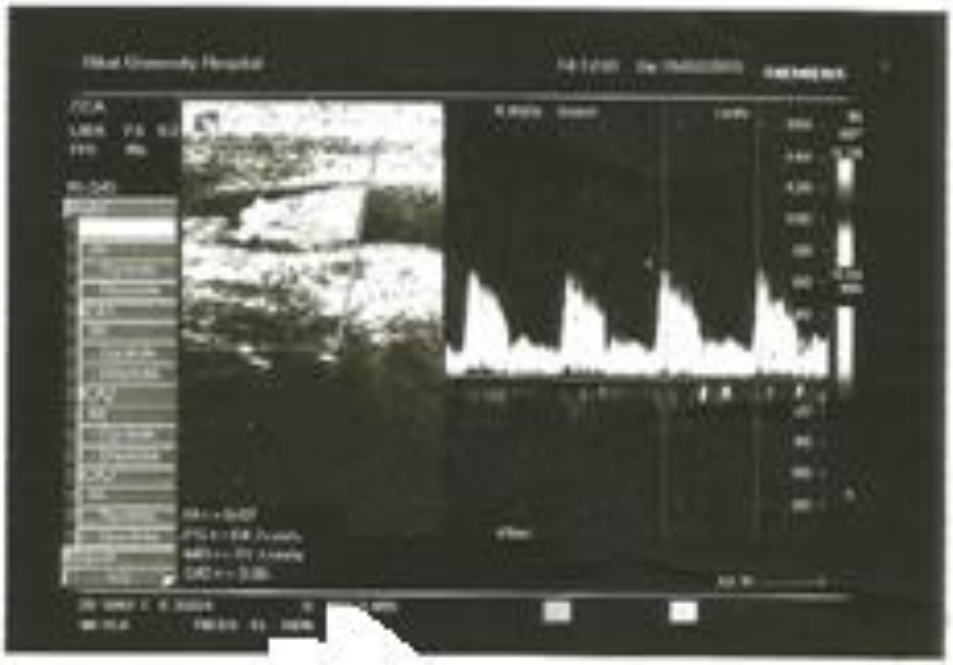

Figure 63, Rt CCA-female- 32 years diabetic patient with normal Doppler parameters.

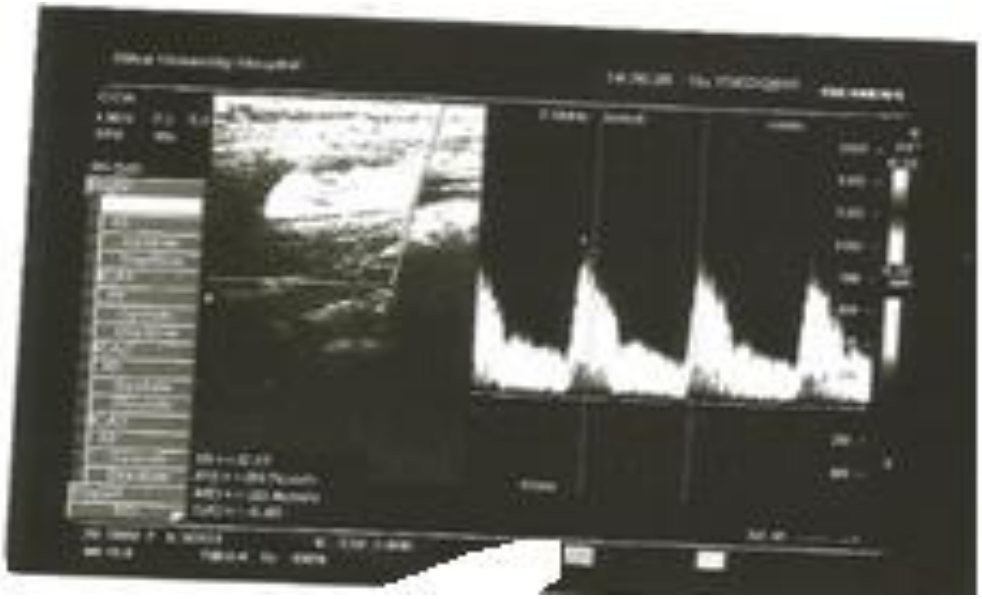

Figure 64, Lt CCA-female- 51 years diabetic patient with normal Doppler parameters.

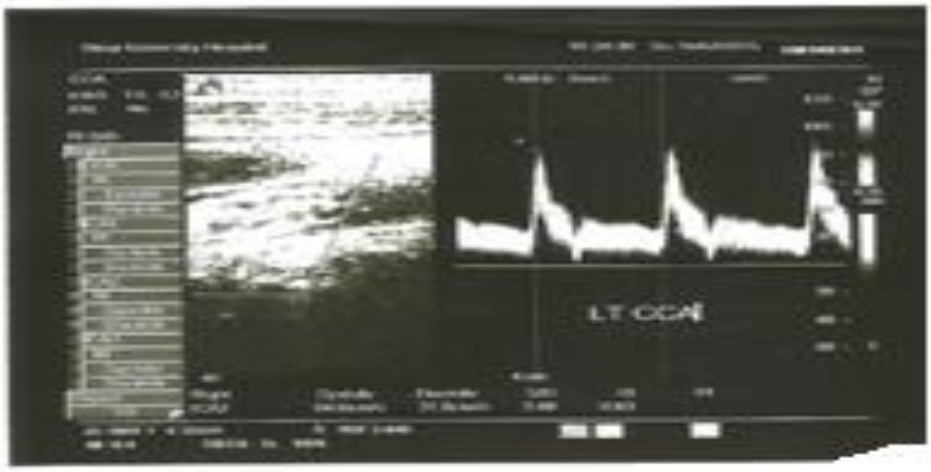

Figure 65, Lt CCA- male- 41 years diabetic patient with normal Doppler parameters.

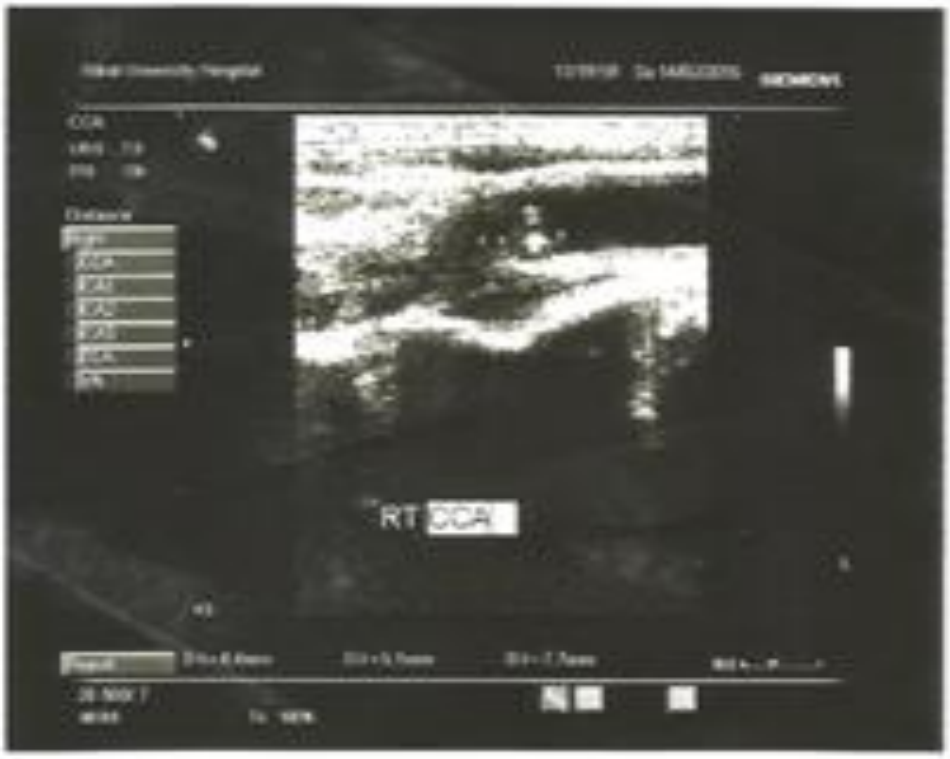

Figure 66, Rt CCA-male- 60 years diabetic shows heterogonous plaque.

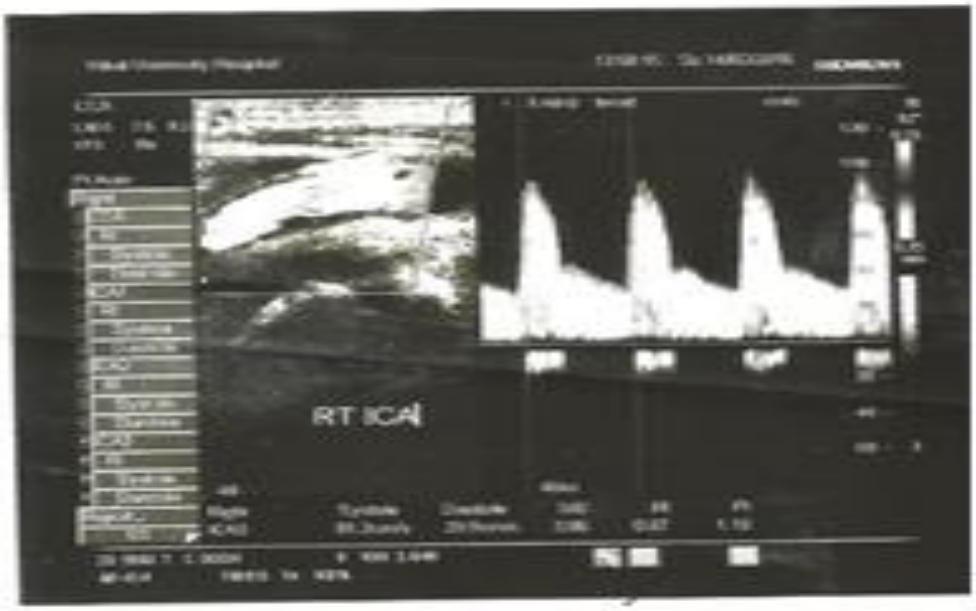

Figure 67, Lt ICA-male- 60 years diabetic patient with normal Doppler parameters.

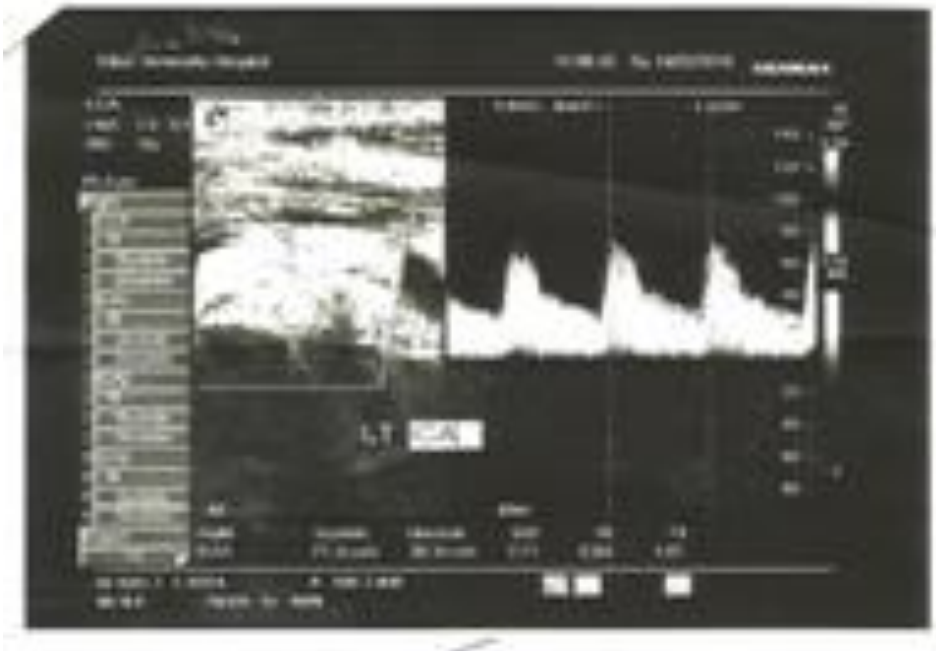

Figure 68, Rt ICA-female- 48 years diabetic patient with normal Doppler parameters.

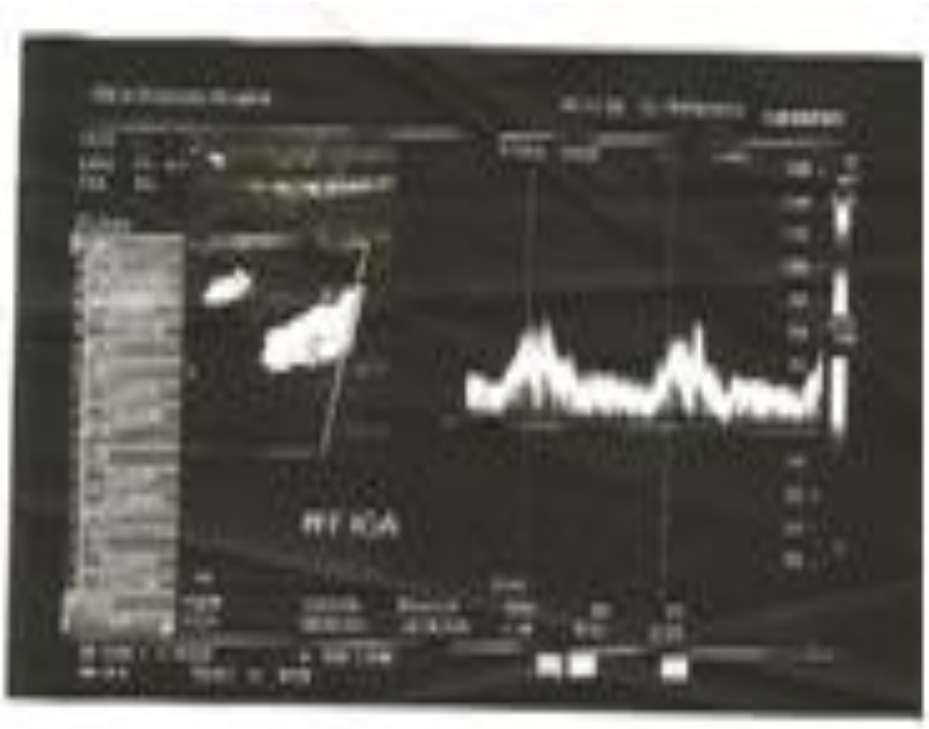

Figure 69, Lt ICA-male- 62 years diabetic patient with normal Doppler parameters.