

Chapter One

Introduction

1.1 Introduction

There are so many fatal diseases attack human body, one of these is a stroke which is considered to be the second top leading causes of deaths worldwide WHO reports(2008). Stroke may result from blockage or rupture of the arteries that supply the brain. Since carotid arteries are the main source of brain supply, this clarifies the importance of studying their abnormality specially the atherosclerosis.

The relationship between extracranial carotid disease and stroke was emphasized since 1914(Singh et al., 2012). Atherosclerosis is a degenerative disease of the arteries resulting in plaques consisting of necrotic cells, lipids, and cholesterol crystals. These plaques can result in symptoms by causing a stenosis, emboli, and thrombosis, Moore (2000). Carotid artery atherosclerosis is a common feature, which is developmentally and anatomically is indistinguishable from atherosclerosis in the other arteries. In population, the main risk factors of carotid artery atherosclerosis are the same as those of other atherosclerotic diseases,(Berglund ,2001).

Smoking represents one of the crucial risk factors for carotid atherosclerosis. The prevalence rate of carotid atherosclerosis increased with age and smoking (Bonithon et al., 1991).Current smoking in Saudi Arabia considered to be of high rate in Saudi males which is about 26.5 % and the tobacco- related health

problems cost 176 billion Dollars per year in KSA. Medhat M.,(2009).This indicates the significance of studies have relation with this problem, like carotid atherosclerotic changes.

Objectives behind this study; To assess the prevalence of carotid atherosclerosis in male Saudi smokers using B- mode & Doppler ultrasound. Moreover to compare this prevalence between elderly and young smokers.

The study will have a significant importance in the smoking quit public program in the KSA. The results of the study have been published as a scientific papers in a peer reviewed journals.

1.2 A stroke:

A stroke is a condition in which the brain cells suddenly die because of a lack of oxygen. This can be caused by an obstruction in the blood flow, or the rupture of an artery that feeds the brain. It is the second cause of death worldwide (WHO, Fact sheet N°310, 2008).

A stroke occurs when the blood supply to part of the brain is suddenly interrupted or when a blood vessel in the brain bursts, spilling blood into the spaces surrounding brain cells. Brain cells die when they no longer receive oxygen and nutrients from the blood or there is sudden bleeding into or around the brain. The

symptoms of a stroke include sudden numbness or weakness, especially on one side of the body; sudden confusion or trouble speaking or understanding speech; sudden trouble seeing in one or both eyes; sudden trouble with walking, dizziness, or loss of balance or coordination; or sudden severe headache with no known cause. There are two forms of stroke: ischemic - blockage of a blood vessel supplying the brain, and hemorrhagic - bleeding into or around the brain(Bethesda, 2011).

Table 1.1 Top leading causes of deaths worldwide (WHO, Fact sheet N°310, 2008).

Worldwide	Deaths in millions	% of deaths
Ischaemic heart disease	7.25	12.8%
Stroke and other cerebrovascular disease	6.15	10.8%
Lower respiratory infections	3.46	6.1%
Chronic obstructive pulmonary disease	3.28	5.8%
Diarrheal diseases	2.46	4.3%
HIV/AIDS	1.78	3.1%
Trachea, bronchus, lung cancers	1.39	2.4%
Tuberculosis	1.34	2.4%
Diabetes mellitus	1.26	2.2%
Road traffic accidents	1.21	2.1%

1.2.1 Prognosis of stroke:

Although stroke is a disease of the brain, it can affect the entire body. A common disability that results from stroke is complete paralysis on one side of the body, called hemiplegia. A related disability that is not as debilitating as paralysis is one-sided weakness or hemiparesis. Stroke may cause problems with thinking, awareness, attention, learning, judgment, and memory. Stroke survivors often have problems understanding or forming speech. A stroke can lead to emotional problems. Stroke patients may have difficulty controlling their emotions or may express inappropriate emotions. Many stroke patients experience depression. Stroke survivors may also have numbness or strange sensations. The pain is often worse in the hands and feet and is made worse by movement and temperature changes, especially cold temperatures.

Recurrent stroke is frequent; about 25 percent of people who recover from their first stroke will have another stroke within 5 years.

An ischemic stroke occurs when an artery supplying the brain with blood becomes blocked, suddenly decreasing or stopping blood flow and ultimately causing a brain infarction. This type of stroke accounts for approximately 80 percent of all strokes. Blood clots are the most common cause of artery blockage and brain infarction. The process of clotting is necessary and beneficial throughout the body

because it stops bleeding and allows repair of damaged areas of arteries or veins. However, when blood clots develop in the wrong place within an artery they can cause devastating injury by interfering with the normal flow of blood. Problems with clotting become more frequent as people age.

Blood clots can cause ischemia and infarction in two ways. A clot that forms in a part of the body other than the brain can travel through blood vessels and become wedged in a brain artery. This free-roaming clot is called an embolus and often forms in the heart. A stroke caused by an embolus is called an embolic stroke. The second kind of ischemic stroke, called a thrombotic stroke, is caused by thrombosis, the formation of a blood clot in one of the cerebral arteries that stays attached to the artery wall until it grows large enough to block blood flow.

Ischemic strokes can also be caused by stenosis, or a narrowing of the artery due to the buildup of plaque (a mixture of fatty substances, including cholesterol and other lipids) and blood clots along the artery wall. Stenosis can occur in large arteries and small arteries and is therefore called large vessel disease or small vessel disease, respectively. When a stroke occurs due to small vessel disease, a very small infarction results, sometimes called a lacunar infarction, from the French word "lacune" meaning "gap" or "cavity."

The most common blood vessel disease that causes stenosis is atherosclerosis. In atherosclerosis, deposits of plaque buildup along the inner walls of large and medium-sized arteries, causing thickening, hardening, and loss of elasticity of artery walls and decreased blood flow. Smoking is one of important controllable risk factor for carotid atherosclerosis.

1.3 Smoking

Smoking represents the most readily preventable risk factor for morbidity and mortality. It's related disease will kill one in any 10 adults globally. By 2030, if current trends continue, smoking will kill one in any 6 people. Around 6 million people may die each year worldwide starting in 2010 because of smoking and tobacco related disease, according to the World Health Organization – including over 438,000 Americans, 650,000 Europeans and 1.2 million people in China (WHO, fact sheet 2002, 2005).

Tobacco use will kill 1 billion people worldwide in the 21st century if current smoking trends continue. 6.6 billion people are on this planet and 1.3 billion are smokers, the International Union against Tuberculosis and Lung Disease (The Union) and the World Lung Foundation (WLF) told the 38th Union World Conference on Lung Health. 66 percent of all smokers live in just 15 countries, according to The Union and the WLF. 1.8 billion young people aged of 10 to 24

smoke cigarettes, according to the World Health Organization. More than 85 percent of these young smokers live in developing countries (WHO). One billion men and about 250 million women use tobacco every day around the world, according to a study presented at the 14th World Conference on Tobacco or Health, Hawkins(2011).

1.3.1 Dangers of smoking:

According to smoking facts, tobacco in a cigarette consists of more than 400 toxic substances and 4,000 chemical compounds. Out of them, the most hazardous substances are tar, which is a carcinogen substance, nicotine that increases cholesterol levels in the body and carbon monoxide, which decreases the amount of oxygen within the body. Nicotine is the most addictive substance in tobacco. Smoking decreases the levels of oxygen reaching tissues, giving rise to different health problems such as stroke, heart attack or miscarriage. It increases cholesterol levels in the blood, increasing the risk of heart attack. Smoking causes damage and constriction of blood vessels, leading to various diseases of blood vessels. Smoking also causes chronic coughing, shortness of breath, premature aging, recurrent infections and reduced overall fitness. Smoking-related deaths are mainly because of heart diseases, cancers and chronic obstructive pulmonary disease (COPD), Jirage (2011).

Other Conditions caused by Smoking: Jirage (2011)

- The chemicals present in tobacco damage the lining of blood vessels and affect the levels of fats in the bloodstream. It increases the risk of atheroma, which is the main cause of heart disease, stroke and aneurysms.
- Smoking affects your oral health. It can stain your teeth and gums. Smoking can give rise to various health problems of gums and teeth, such as swollen gums, loose teeth and bad breath.
- Smoking causes acid taste in the mouth. It can increase the risk of developing mouth ulcers.
- Smoking can give rise to various sexual problems. Couples addicted to smoking are likely to face fertility problems.
- Smoking increases the risk of high blood pressure, which is a risk factor for stroke and heart attacks.
- Smoking worsens asthma by increasing the inflammation of airways.
- Smoking can cause early aging. Due to smoking, the blood supply to the skin is reduced. There is decrease in the levels of vitamin A. Hence, smokers have paler skin and more wrinkles.
- Heavy smoking causes macular degeneration, which results in gradual loss of eyesight. Smokers are at a higher risk for cataract.

- Some other conditions caused by smoking are chest infections, diabetic retinopathy, tuberculosis, multiple sclerosis and Crohn's disease.

1.4 The problem of the study:

Smoking represents a serious issue in Saudi Arabia, a round 26% of the population are smokers. It has been known that smoking may lead to stroke (the second cause of death worldwide)! One of the methods that should follow to decrease the negative effect of this problem, is to prove the direct effect of smoking through scientific studies like this current one.

1.5 Main objectives of the study:

- To evaluate the presence of carotid atherosclerosis in male Saudi smokers using B- mode & Doppler ultrasound.
- To compare the findings between elderly and young smokers.

1.6 Specific objectives of the study:

- To measure the carotid IMT in smokers.
- To check the effect of cigarette's smoking frequency on the presence of carotid atherosclerosis.
- To check the effect of cigarette's smoking duration on the presence of carotid atherosclerosis.
- To check the occurring of atherosclerosis young smokers.

1.7 Significance of the study:

The dissertation will have a significant importance in the smoking quit public program in the KSA. It's results may contribute in health promotion program in Saudi Arabia. A scientific publications have been published in International Scientific Press (UK) and International conference on radiology & imaging – Chicago (USA); as seen in attachments at the end pages.

1.8 Overview of the study:-

This study consist of five chapters with chapter one is an introduction which includes introduction, Stroke & smoking overview, main & specific objectives and significance of the study. Chapter two which Includes theoretical background and literature review about carotid arteries anatomy, atherosclerosis, carotid atherosclerosis diagnostic modalities, Doppler ultrasonography and previous studies in relation with smoking and carotid atherosclerosis. Chapter three which includes materials and methods of the study. Chapter four which Covers presentation of the thesis's results. Finally Chapter five which Includes discussion, conclusion, limitations and recommendations.

Chapter two

Theoretical background & Literature review

2.1 Anatomy of carotid artery:

Arteries are blood vessels that carry blood from the heart throughout the body. They're lined by a thin layer of cells called the endothelium. The endothelium works to keep the inside of arteries toned and smooth, which keeps blood flowing.

The carotid arteries are blood vessels that supply oxygenated and nutrient filled blood to the head, neck and brain. One carotid artery is position on each side of the neck. The right common carotid artery branches from the brachiocephalic artery and extends up the right side of the neck. The left common carotid artery branches from the aorta and extends up the left side of the neck. Each carotid artery branches into internal and external vessels near the top of the thyroid Anson, (1966).

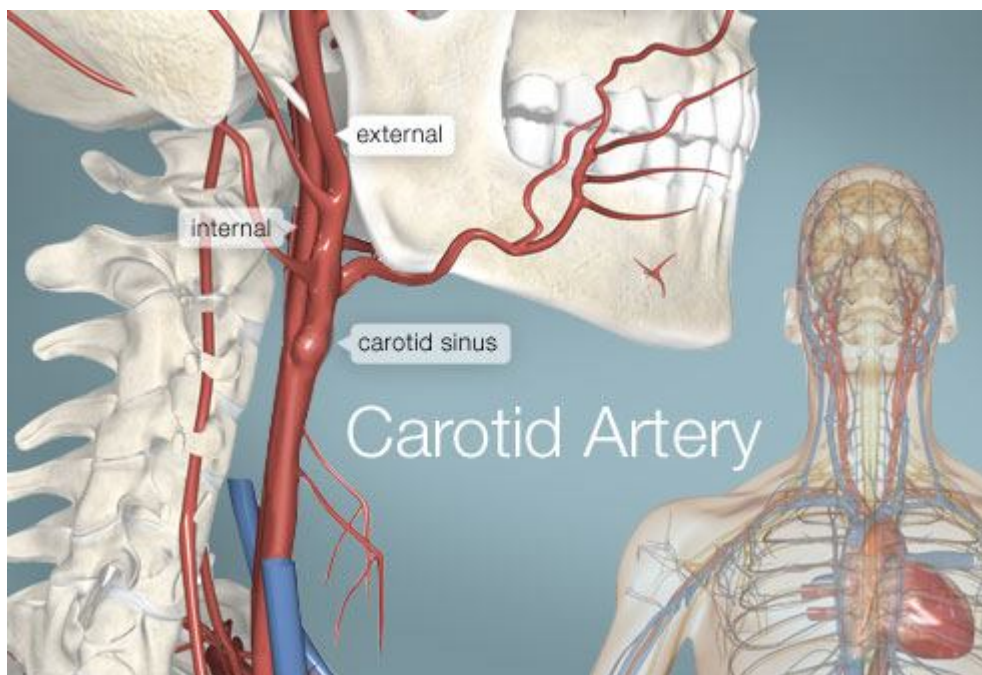


Figure2.1:Carotid artery(WebMD, <http://www.webmd.com/heart/picture-of-the-carotid-artery>)

2.1.1 The common carotid artery: Henry (1918).

The common carotid artery is a paired structure, meaning that there are two in the body, one for each half. The left and right common carotid arteries follow the same course with the exception of their origin. The right common carotid originates in the neck from the brachiocephalic trunk. The left arises from the aortic arch in the thoracic region.

The left common carotid artery can be thought of as having two parts: a thoracic (chest) part and a cervical (neck) part. The right common carotid originates in or close to the neck, so it lacks a thoracic portion.

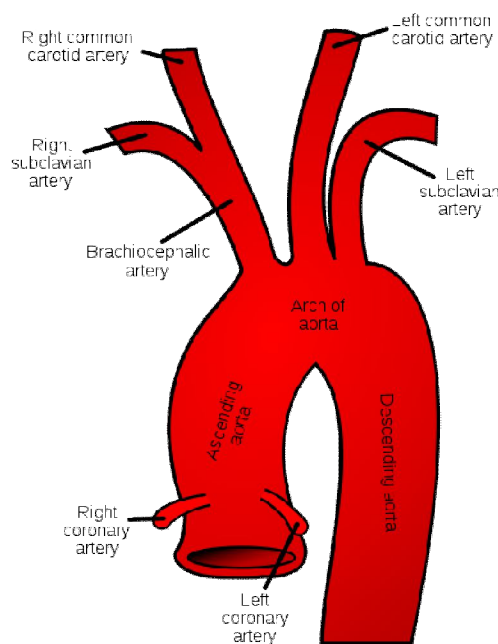


Figure 2.2: The origin of common carotid artery(https://en.wikipedia.org/wiki/Common_carotid_artery)

2.1.1.1 Thoracic part:

Only the left common carotid artery has a substantial presence in the thoracic region. It originates along the aortic arch, and travels upward through the superior mediastinum to the level of the left sternoclavicular joint, where it is continuous with the cervical portion.

2.1.1.2 The cervical portions:

The cervical portions of the common carotids resemble each other so closely that one description will apply to both.

Each vessel passes obliquely upward, from behind the sternoclavicular joint to the level of the upper border of the thyroid cartilage, where it divides.

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.

2.1.2 carotid sheath:

The common carotid artery is contained in a sheath known as the carotid sheath, which is derived from the deep cervical fascia and encloses also the internal jugular vein and vagus nerve, the vein lying lateral to the artery, and the nerve between the

artery and vein, on a plane posterior to both. On opening the sheath, each of these three structures is seen to have a separate fibrous investment.

At approximately the level of the fourth cervical vertebra, the common carotid artery bifurcates into an internal carotid artery (ICA) and an external carotid artery (ECA).

2.1.3 The internal carotid arteries:

The internal carotid arteries take a deeper (more internal) path and they are major arteries of the head and neck that supply blood to the brain and eyes via the carotid canal. There is a left and a right internal carotid artery; each one arises from the corresponding common carotid artery in the neck and divides in the brain into the corresponding anterior cerebral artery and middle cerebral artery.

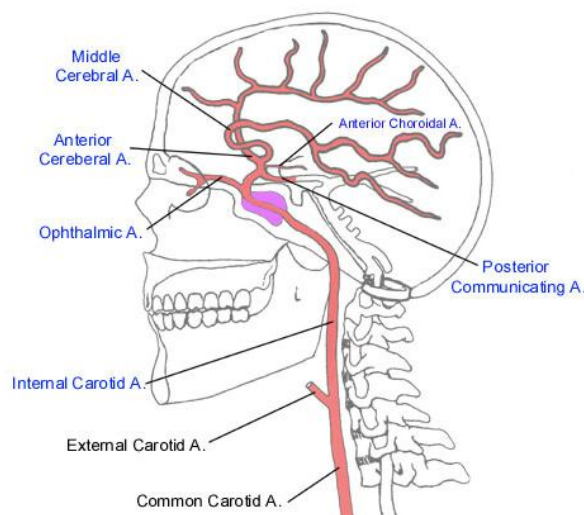


Figure 2.3: Lt. Internal carotid artery(https://en.wikipedia.org/wiki/Common_carotid_artery)

2.1.4 External Carotid Arteries:

The external carotid arteries (Rt. & Lt.) arise from the common carotid artery when it bifurcates into the external and internal carotid artery. They travel more closely to the surface, and send off numerous branches that supply the neck and face (throat, neck glands, tongue, face, mouth, ear, scalp and dura mater of the meninges).

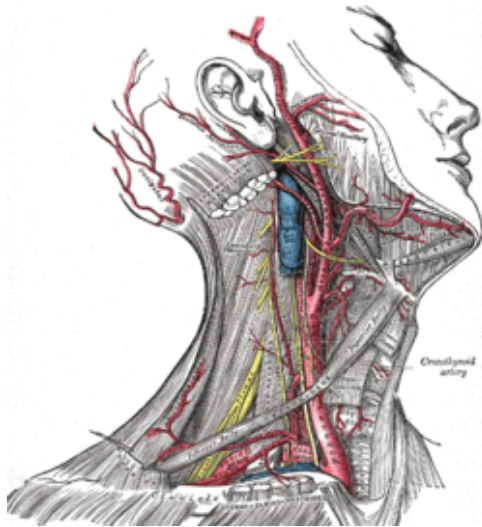


Figure 2.4: Rt. external carotid artery (<http://education.yahoo.com/reference/gray/subjects/subject/143>)

2.2 Atherosclerosis:

Atherosclerosis is a common disorder that specifically affects the medium and large arteries, it's a condition in which fatty material collects along the walls of arteries. This fatty material thickens, hardens (forms calcium deposits), and may

eventually block the arteries. Atherosclerosis is a type of arteriosclerosis, the two terms are often used to mean the same thing (Sarah et al, (2010).

Atherosclerosis starts when high blood pressure, smoking, or high cholesterol damage the endothelium, At that point, cholesterol plaque formation begins, Stein (2010).

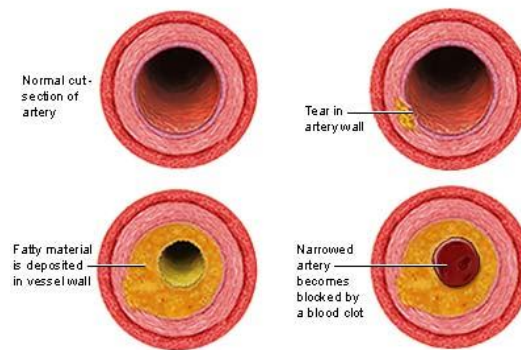


Figure 2.5: development of arterial atherosclerosis(The U.S. National Library of Medicine, www.nlm.org)

2.2.1 Stages of atherosclerosis:

The arterial wall consists of three anatomically distinct layers: intima, media and adventitia, which are separated by two thin elastic layers, inner and outer, respectively. Atherosclerosis is a disease of intima. Atherosclerotic changes in the arterial wall can be divided into five categories. Stage I and II changes include intimal thickening and formation of foam cells (i.e. macrophages with accumulation of cholesterol), stage III pre-atheroma with accumulation of extracellular lipids, stages IV and V plaque (atheroma) formation and stage VI

complicated lesions. Carotid artery atherosclerosis is a common feature, which is developmentally and anatomically is indistinguishable from atherosclerosis in the other arteries. In population, the main risk factors of carotid artery atherosclerosis are the same as those of other atherosclerotic diseases (Berglund et al., 2001).

2.2.2 Causes of atherosclerosis:

This disorder occurs when fat, cholesterol, and other substances build up in the walls of arteries and form hard structures called plaques.

Eventually, the plaques can make the artery narrow and less flexible, making it harder for blood to flow. If the coronary arteries become narrow, blood flow to the heart can slow down or stop. This can cause chest pain (stable angina), shortness of breath, heart attack, and other symptoms.

Pieces of plaque can break off and move through the affected artery to smaller blood vessels, blocking them and causing tissue damage or death (embolization). This is a common cause of heart attack and stroke. Blood clots can also form around a tear (fissure) in the plaque leading to blocked blood flow. If the clot moves into an artery in the heart, lungs, or brain, it can cause a stroke, heart attack, or pulmonary embolism. In some cases, the atherosclerotic plaque is associated with a weakening of the wall of an artery leading to an aneurysm.

2.2.3 Risk factors for Atherosclerosis: Stein (2010).

Atherosclerosis is progressive, but it's also preventable. For example, nine risk factors are to blame for up to 90% of all heart attacks:

- Smoking
- High cholesterol
- High blood pressure
- Diabetes
- Abdominal obesity ("spare tire")
- Stress
- Not eating fruits and vegetables
- Excess alcohol intake
- Not exercising regularly

All of these have something in common, Experts agree that reducing the risk factors leads to a lower risk of cardiovascular disease.

2.2.4 Carotid atherosclerosis: (Karen L et al , 2011).

The symptoms and pathologic substrate of carotid artery atherosclerotic occlusive disease were first described by C Miller Fisher in 1951. He related atherosclerotic disease at the carotid bifurcation to ischemic symptoms in the ipsilateral eye and

brain. The modern era has seen an extraordinary expansion in our approach to the diagnosis and management of patients with carotid artery stenosis.

Stroke, due to atherothrombosis of the extracranial carotid arteries, is caused by a combination of factors involving the blood vessels, the clotting system, and hemodynamics. This interaction explains the mechanism of ischemic stroke in patients with carotid atheroma which may be due to artery-to-artery embolism or low cerebral blood flow.

The classification of symptomatic status of the internal carotid artery, the mechanism of symptom production, and the associated physical signs are reviewed here. Other issues, such as the methods for evaluating carotid stenosis and therapies available for the treatment of carotid artery disease, are discussed separately.

2.2.4.2 Mechanism of symptoms:

Carotid atherosclerosis is usually most severe within 2 cm of the bifurcation of the common carotid artery, and predominantly involves the posterior wall of the vessel. The plaque encroaches on the lumen of the internal carotid artery and often extends caudally into the common carotid artery. An hourglass configuration to the stenosis typically develops with time.

Regardless of their location, carotid plaques were associated with an increased risk of stroke in an observational study of elderly men and women and an increased

risk of mortality in an observational study of elderly men. In addition to a reduction in vessel diameter induced by the enlarging plaque, thrombus can become superimposed on the atheroma which will further increase the degree of stenosis. Thus, the mechanism of stroke may be embolism of the thrombotic material or low-flow due to the stenosis with inadequate collateral compensation.

2.2.4.3 Diagnostic modalities:

As physicians become more willing to trade diagnostic precision for increased patient safety, conventional angiography is losing ground to noninvasive angiography as a means of identifying carotid artery stenosis in patients with cerebrovascular disease. Popular noninvasive modalities include computed tomographic angiography, magnetic resonance angiography (MRA), and carotid duplex ultrasonography (CUS),(Meschia et al., 2007)



Figure 2.6: Computed Tomographic angiography equipment (www.radiologyinfo.org)

2.3 Doppler ultrasound: (Paul L et al., 2006)

An application of diagnostic ultrasound used to detect moving blood cells or other moving structures and measure their direction and speed of movement. The Doppler effect is used to evaluate movement by measuring changes in frequency of the echoes reflected from moving structures.

In many instances, Doppler ultrasound has replaced x-ray methods such as angiography, as a method to evaluate blood vessels and blood flow. Doppler ultrasound permits real-time viewing of blood flow that cannot be obtained by other methods. Doppler ultrasound has proved a boon in all areas of ultrasound, aiding in the evaluation of the major arteries and veins of the body, the heart, and in obstetrics for fetal monitoring.

2.3.1 Types of Doppler Ultrasound:

Color Doppler:

Color Doppler uses a computer to convert the Doppler measurements into an array of colors. This color visualization is combined with a standard ultrasound picture of a blood vessel to show the speed and direction of blood flow through the vessel.

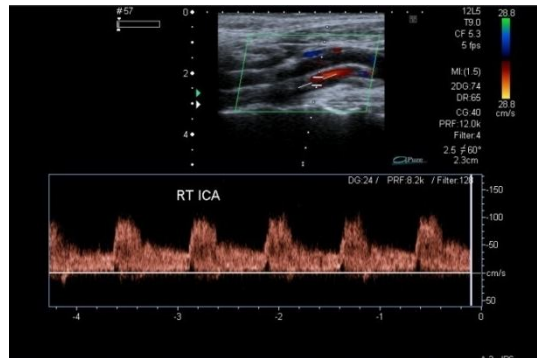


Figure 2.7: Color Doppler with spectral graph

Power Doppler:

Is a newer technique that is more sensitive at detecting blood flow than color Doppler. Power Doppler is able to obtain images that are difficult or impossible to obtain using standard color Doppler and to provide greater detail of blood flow, especially in vessels that are located inside organs.

Although power Doppler may be more sensitive than color Doppler for detection and demonstration of blood flow, power Doppler provides no information about the direction of flow. Color and spectral Doppler both reveal the direction of blood flow which can be valuable information.

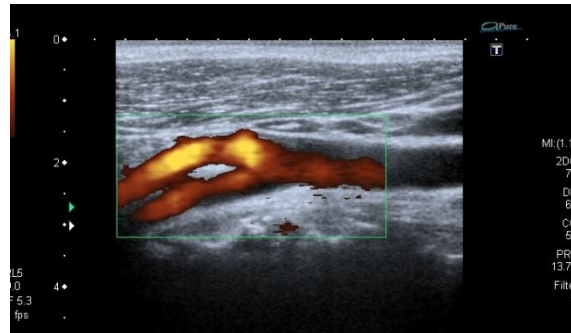


Figure 2.8: Power Doppler flow at Carotid bifurcation

Spectral Doppler:

Instead of displaying Doppler measurements visually as in the color and power Doppler methods, spectral Doppler displays the blood flow measurements graphically, in terms of the distance traveled per unit of time.

2.4.1.a Carotid duplex ultrasonography (CUS) Sandra L.(2001) & Silver (2011).

Carotid duplex ultrasonography is a useful diagnostic tool for assessing cervical carotid artery disease. CUS can be highly reliable with proper technique, has no radiation risk, is well tolerated by all patients including those who are claustrophobic in MRI machines, and has fewer risks than conventional angiography.

Carotid ultrasonography is a 2-step, or duplex, procedure. The 2 steps are as follows:

2.4.1.b Imaging

The extent, location, and characteristics of atherosclerotic plaque in the common carotid artery (CCA) and internal carotid artery (ICA) should be documented with gray-scale imaging. The vessels should be imaged as completely as possible, with caudal angulation of the transducer in the supraclavicular region and cephalic angulation at the level of the mandible. Color Doppler imaging should be performed to detect areas of abnormal blood flow that require Doppler spectral analysis. Pulsed wave (PW) Doppler spectral analysis should be performed, and the velocity of blood flow in the mid-CCA and proximal ICA as well as proximal to, at, and immediately distal to the diseased areas should be measured. Evaluation of the external carotid artery (ECA) should be performed, as it is a source of bruit and differences in the Doppler appearance of the ECA and ICA improve observer confidence that the bifurcation vessels have been correctly identified. Color and PW Doppler imaging of both vertebral arteries should also be performed to rule out the presence of a subclavian steal. The topography of the plaque, velocity information, and interpretation of the results by the radiologist can be conveniently recorded in a standardized format.

- Imaging is accomplished with the brightness-mode (B-mode) technique.
- The image is usually viewed in grayscale, which is a brightness scale.
- Sometimes, color flow information is superimposed on the grayscale image.

By convention, the color of the pulsating artery is red. This is called color Doppler imaging.

Spectral analysis:

- This allows measurement of blood flow velocity.
- A probing cursor is placed in the artery (on the screen), and a signal representing blood flow velocity is generated.
- The signal is both visual and auditory.
- The signal has peaks and ebbs, which correspond to systolic and diastolic blood flow. The peaks and ebbs create the spectrum.

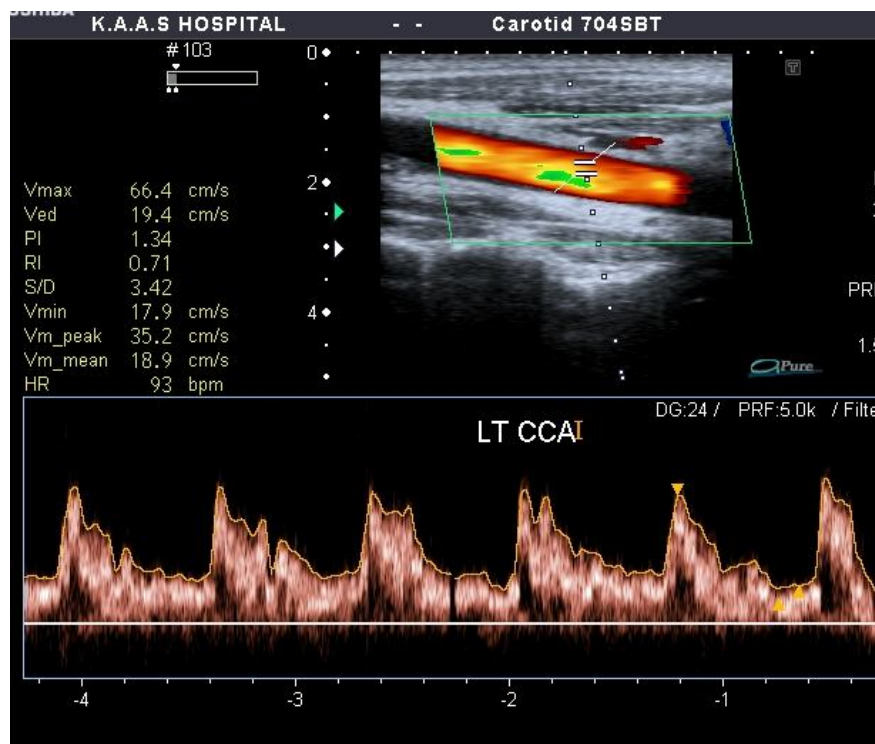


Figure 2.9: Spectral analysis for Lt. CCA.

2.4.2 Physics:

Knowledge of 3 physical properties is helpful in understanding basic carotid ultrasonography:

Pulse-echo technique - Used to image the vessel

- An initial signal (pulse) is generated in the computer, sent through the transducer on the patient's neck, and then bounced off a variety of tissue boundaries.
- The transducer detects a returning signal (echo).
- The direction of the pulse and the time elapsed until the signal return determine the position of the tissue boundary.
- The echogenicity of an object on the image determines its brightness.
- An object that rebounds very little of the pulse, such as the fluid in a cyst, is hypoechoic. An object that rebounds much of the signal, such as heavily calcified plaque, is hyperechoic.

Hemodynamics - Principles of blood movement within an artery

- The velocity changes on spectral analysis reflect changes in hemodynamics.
- An important general rule for CUS is the greater the degree of stenosis, the higher the velocity.

Doppler phenomenon - Used to assess the velocity of blood as it moves past the

probe

- As with the pulse-echo technique, a pulse is emitted from the transducer at a certain frequency.
- When the pulse hits the moving blood, it rebounds back to the probe; however, its frequency is changed.
- The change in frequency (initial frequency minus returning frequency) is known as the Doppler shift. This shift correlates with changes in blood flow velocity.
- An important concept in CUS is that the Doppler shift is dependent not only on the blood velocity and the initial frequency but also on the angle of the probe in relation to the moving blood. This is called angle dependency.

2.4.3 Properties of waves:

Like light, radiation, and audible sound, ultrasound is a wave. The properties of any wave are as follows: $c = f \lambda$ (c = propagation speed of a wave [constant in a given medium], f = frequency, λ = wavelength).

A medium is a conduit through which the wave passes. Examples of media are air, water, and tissue. The value of c for a given wave differs from medium to medium but is always constant in a particular medium. In the context of this discussion, the medium is tissue and the value of c for ultrasound is 1540 m/s (or 1.54 mm/ms). Because c is constant, the wavelength increases as the frequency decreases; the

converse is also true. Frequency is measured in cycles per second, called hertz (Hz). A cycle is one revolution of the wavelength. In CUS, the emitted frequency is millions of cycles per second. Therefore, it is measured in megahertz (MHz) (1 MHz = 1 million cycles/s). During spectral analysis, the Doppler shift is 1000-fold less than the emitted frequency. Therefore, it is measured in kilohertz (kHz) (1 kHz = 1000 cycles/s).

Sometimes, the term spatial pulse length (SPL) is used. It is equal to the number of cycles (n) in a pulse multiplied by the wavelength ($SPL = n \times \lambda$). SPL is important in determining resolution.

2.4.4 Tissue attenuation:

As ultrasound passes through tissue, some of the signal is lost through scattering, reflection, and absorption (conversion to heat). In tissue, attenuation (in decibels [dB]) = $0.5 \times \text{frequency} \times \text{path length}$.

Therefore, the higher the frequency of the machine, the greater the attenuation, and the less can be imaged at a greater distance from the probe. On the other hand, higher frequencies mean shorter wavelengths and better resolutions. Therefore, a trade-off exists in adjusting frequencies.

2.4.5 Hemodynamics:

Blood flow can be laminar, disturbed, turbulent, or plug. In CUS, the first 3 are important. When no stenosis is present, blood flow is laminar. Flow of blood is

even, with the fastest flow in the middle and the slowest at the edges of the vessel. When a small degree of stenosis is present, the blood flow becomes disturbed and loses its laminar quality. Even in normal conditions, such flow can be seen around the carotid bulb. With even greater stenosis, the flow can become turbulent.

Reynolds number determines the level at which turbulent flow occurs. Its derivation is not necessary for routine CUS. The basic equation for flow is $Q = \Delta P / R$ (Q = flow, ΔP = pressure difference, R = resistance). This is known as the law of Poiseuille. Resistance is dependent on vessel length and radius and fluid viscosity, so that $R = 8L \eta / \pi r^4$ (L = length, η = viscosity, r = radius). Thus, in normal hemodynamics, as vessel length increases or as fluid viscosity increases, so does resistance. As vessel radius increases, resistance decreases significantly (by a factor of 4).

2.4.6 Volume flow:

In a stenotic vessel, volume flow remains constant. Volume flow is related to average speed and vessel area according to the following: $Q = v_a \times A$ (Q = volume flow, v_a = average speed, A = vessel area). The continuity rule states that volume flow remains constant regardless of the degree of narrowing.

v_a is proportional to the Doppler shift. Therefore, as vessel diameter (and area) decreases, blood velocity increases to maintain volume flow. The velocity increases by a factor of 2 for every unit decrease in diameter. (The only time

volume flow may not be maintained is with severe stenosis [$>90\%$] when the resistance effect dominates.)

2.4.7 Doppler effect

The Doppler effect is the change in frequency or wavelength due to motion of the wave source, receiver, or reflector of a wave source, as shown below.

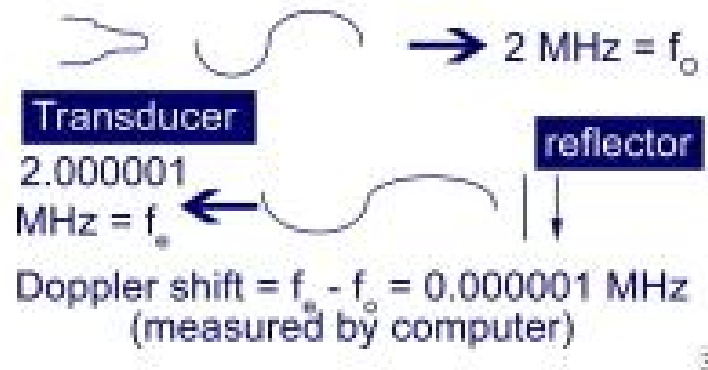


Figure 2.10: The Doppler effect, Silver (2011).

2.4.8 Doppler Equation

US equipment calculates the velocity of blood flow according to the Doppler equation:

$$\Delta f = \frac{2f_0 V \cos \theta}{C},$$

where Δf is the Doppler shift frequency, f_0 is the transmitted ultrasound frequency, V is the velocity of reflectors (red blood cells), θ (theta, also referred to as the Doppler angle) is the angle between the transmitted beam and the direction of blood flow within the blood vessel (the reflector path), and C is the

speed of sound in the tissue (1540 m/sec). Since the transmitted ultrasound frequency and the speed of sound in the tissue are assumed to be constant during the Doppler sampling, the Doppler shift frequency is directly proportional to the velocity of red blood cells and the cosine of the Doppler angle (Roman MJ et al., 2006).

2.4.9 Doppler Angle:

Doppler shift is an angle dependent in CUS. Ordinarily, the computer would use the equation in the previous paragraph to calculate velocity based on Doppler shift. However, 2 adjustments to the equation are made. First, the scatter speed in the denominator is dropped because its speed is negligible compared to that of ultrasound. Second, because the probe cannot be parallel to the arteries in the neck, angle adjustment is required. The correction is based on the cosine of the angle. This is what is meant by angle dependency.

The angle θ affects the detected Doppler frequencies. At a Doppler angle of 0° , the maximum Doppler shift will be achieved since the cosine of 0° is 1. Conversely, no Doppler shift (no flow) will be recorded if the Doppler angle is 90° since the cosine of 90° is 0. The orientation of the carotid arteries may vary from one patient to another; therefore, the operator is required to align the Doppler angle parallel to the vector of blood flow by applying the angle correction or angling the transducer, Hamid R.(2005).

2.4.10 Limitations

Physical challenges such as a short muscular neck, a high carotid bifurcation, tortuous vessels, calcified shadowing plaques, tracheostomy tubes, surgical sutures, postoperative hematoma or bandages, central lines, inability to lie flat in respiratory or cardiac disease or to rotate the head in patients with arthritis, and uncooperative patients may limit the results of carotid US examination.

2.4.11 Artifacts:

At least 18 artifacts have been identified in carotid ultrasound; most of them occur during imaging. The common artifacts include the following:

- Reverberations: If 2 or more reflectors are in the sound path, multiple reflections (reverberations) occur and may result in unreal images on the screen.
- Refraction: A refracting object "bends" the ultrasonic waves so that a reflector is improperly positioned on the screen.
- Shadowing: A strong reflector (e.g., calcified plaque) reduces the quantity of ultrasound that is intended to pass beyond it; the object behind the reflector is "shadowed"; in the case of a plaque, the artifact proves to be helpful in identifying it.
- Enhancing: Enhancing is the opposite of shadowing (eg, gallbladder).

- **Aliasing:** This occurs during spectral analysis and color flow imaging. During spectral analysis, the spectrum is "wrapped" around the screen so that the top of the waveform is seen at the bottom. This problem can be corrected by increasing the pulse repetition frequency (PRF) (aliasing occurs when the highest Doppler shift is greater than half the PRF), increasing the Doppler angle, shifting the baseline, lowering the emitted frequency, or using a continuous wave device.

2.4.12 Instruments:

The principal components of the ultrasound instrument are pictured in the following schematic drawing.

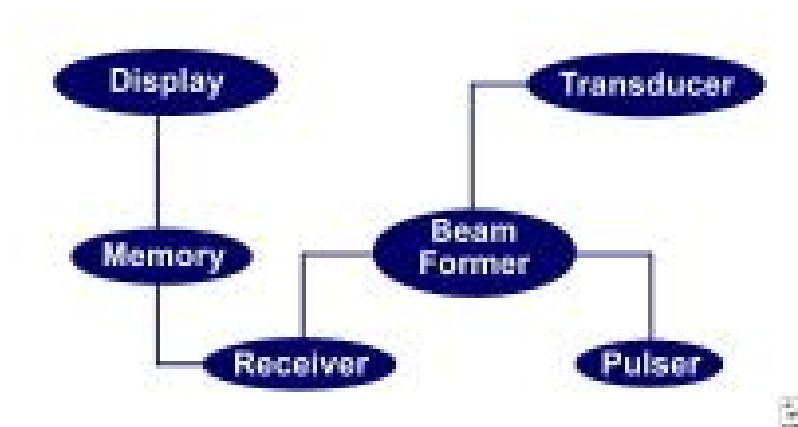


Figure 2.11:Components of a duplex machine , Silver (2011).

Pulsar: The pulser generates short electrical pulses, which are converted to ultrasonic waves in the transducer. To image deeper structures, the PRF is set

lower to allow the transducer more "listening" time. The shorter the pulse, the better the axial resolution. The narrower the pulse, the better the lateral resolution. Damping and using higher frequencies shorten the pulse. Axial resolution is equal to half of the SPL.

Beam former: The beam former controls the shape and direction of beam, known as focusing and steering. The beam former can be mechanical or electronic. Mechanical beam formers operate via an oscillatory mechanism. Electronic beam formers may be linear-switched arrays or linear-phased arrays. Focusing the beam narrows the pulse, which improves lateral resolution. Lateral resolution is equal to pulse width.

Transducer: The transducer contains the damping element, piezoelectric crystal (converts electric energy to ultrasonic waves), and the matching layer. The damping element is behind the crystal. It acts to reduce the pulse length and to improve lateral resolution. The matching layer is in front of the crystal. It reduces reflection of ultrasound at the transducer surface, improving ultrasonic transmission. Gel is applied to improve ultrasonic transmission. Even a very thin layer of air can reflect virtually all ultrasound. High frequency transducer is used in carotid arteries.

Receiver: The receiver amplifies (increases small signals), compensates (equalizes signals that are at different distances from the transducer), compresses

(reduces the brightness scale to that which is visible to the eye), demodulates (changes bidirectional signals and smoothens), and rejects (gets rid of ambient noise).

Memory: Memory often is coded in binary.

Display: The display comprises a series of lines representing adjacent scan lines. The varieties of scanning formats are unlimited. The most commonly used methods are linear (rectangular) and sector (pie shaped). Deeper scanning theoretically requires that fewer scan lines be made available in order to maintain a real-time display. Alternatively, the number of scan lines can be preserved at the cost of a slower real-time display.

2.4.13 Technique:

An ultrasound examination may be performed in many ways. Recommended techniques include the following:

After entering the patient's required data into the computer, take a focused history, ask the patient to lie supine, and choose a conventional starting site (right or left - most use right).

Have the patient's head turned contralateral to the side being tested, place a towel on clothing for protection, apply gel liberally to the transducer or neck, and start the scan transversely from the proximal common carotid artery (CCA) moving distally.

Note the carotid bifurcation, look for plaques, attempt to characterize the nature of the plaque, and switch to the sagittal view; by convention, the patient's head is at the left on the screen, and images at the top of the screen are closest to the transducer; color may be used at this point to identify flow within the artery and potential areas of high velocity.

The on-screen probe is placed in the artery parallel to vessel walls; make sure to correct for excessive angles. The "gate" is the width of the listening window; the larger the gate, the more likely that signal will be detected. However, the trade-off is increased noise. Perform spectral analysis and find the highest velocity or frequency.

The procedure is done in the CCA, internal carotid artery (ICA), and external carotid artery (ECA); at least 2 or 3 spectral analyses of each vessel should be obtained. Color imaging and power Doppler may be used but may not necessarily provide additional information. After assessment of the arterial circulation, assess the vertebral circulation. Usually, the C4-C6 segment is accessible; to find the vertebral artery, angle the transducer laterally and inferiorly and identify the presence and direction of flow; velocity measurements may also be obtained.



Figure 2.12:Ultrasound machine (<http://www.howstuffworks.com>)

Sample Volume Box and Angle Correction:

The US machine calculates the velocity from the Doppler shift frequency reflected from red blood cells within the sample volume box. In most cases, sonographers will experience some uncertainties in estimating the flow angle and positioning the sample volume box. If the Doppler angle is small ($<50^\circ$), this uncertainty leads to only a small error in the estimated velocity.

If Doppler angles of 50° or greater are required, then precise adjustment of the angle correct cursor is crucial to avoid large errors in the estimated velocities. The Doppler angle should not exceed 60° , as measurements are likely to be

inaccurate. Our preferred angle of incidence is $45^{\circ} \pm 4$. Consistent use of a matching Doppler angle of incidence for velocity measurements in the CCA and ICA reduces errors in velocity measurements attributable to variation in θ . Incorrect assignment of the Doppler angle of incidence with the direction of blood flow is a common source of operator error.

The optimal position of the sample volume box in a normal artery is in the mid lumen parallel to the vessel wall, whereas in a diseased vessel it should be aligned parallel to the direction of blood flow. In the absence of plaque disease, the sample volume box should not be placed on the sharp curves of a tortuous artery, as this may result in a falsely high velocity reading. If the sample volume box is located too close to the vessel wall, artificial spectral broadening is inevitable.

Spectral Broadening:

Spectral broadening results from turbulence in the blood flow. Spurious spectral broadening can result from a large Doppler angle, a large sample volume box (>3.5 mm), a sample volume box located close to the vessel wall, or a high PW Doppler gain setting. The size of the sample volume box (also known as the gate) is normally kept between 2 and 3 mm. If the gate is too small (<1.5 mm), the Doppler signal may be missed. Increasing the gate is helpful in searching for

trickle flow or trying to obtain a Doppler signal behind a shadowing calcified plaque.

Color Doppler Parameters:-

Color is a display of the reflected Doppler frequencies from red blood cells.

Color Doppler Sampling Window: The color Doppler sampling window (also known as the color box) is positioned over the artery to be interrogated. The size of the color Doppler sampling window is adjusted to include all regions of interest. Adjustment of the angle of incidence can be achieved by changing pre-set color box angles from left to center or right, as well as angling the transducer to ensure that the Doppler angle of incidence is less than 60° to the direction of blood flow.

Color Velocity Scale Control: The color velocity scale is the most important parameter of the carotid US color Doppler setup. The color velocity scale is an operator-defined range of velocities that requires adjustment, analogous to the window width and level of a gray-scale image. It is not synonymous with the pulse repetition frequency (PRF), but the PRF is related to the velocity scale setting, so that increasing the velocity scale increases the PRF and vice versa . The image frame rate may appear slow if a very low color velocity scale is applied, since the PRF decreases and the time between transmit pulses in a pulse packet increases.

If the velocity of blood flow exceeds $\frac{1}{2}$ the PRF (Nyquist limit), then the direction and velocity are inaccurately displayed and flow appears to change direction (aliasing). Aliasing can be advantageously used to demonstrate high or low flow and turbulence. If the color velocity scale is set below the mean velocity of blood flow, aliasing throughout the vessel lumen makes it impossible to identify the high-velocity turbulent color jet associated with a tight stenosis. Conversely, if the color velocity scale is set significantly higher than the mean velocity of blood flow, aliasing may disappear, resulting in a missed stenosis.

In a near occlusion, blood flow velocity may be slower than the usual color velocity scale range thresholds, resulting in a false-positive appearance of an occlusion. In this setting, the area of interest should be re-evaluated by using very low color velocity settings (<15 cm/sec) to enhance detection of trickle flow in a near occlusion. If this setting does not reveal detectable flow, contrast material-enhanced imaging (computed tomographic [CT] angiography, gadolinium-enhanced magnetic resonance [MR] angiography, or conventional angiography) may be required to differentiate near occlusion from total occlusion.

In a normal carotid US examination, the color velocity scale should be set between 30 and 40 cm/sec (mean velocity). In a diseased artery, however, the color velocity scale should be shifted up or down according to the mean velocity of blood flow to demonstrate aliasing only in systole.

Color Gain Control: The color gain should be set so that color just reaches the intimal surface of the vessel. If the color gain setting is too low, trickle flow may go undetected. If a high color gain setting is applied, “bleeding” of the color into the wall and surrounding tissues may limit visualization of the plaque surface and may result in misalignment of the angle correction with the direction of blood flow during a PW Doppler examination. Although measurement of the intima-media thickness and the initial survey should always be performed on a gray-scale image, color bleeding artifact may mask the eddy flow at the surface of an ulcerated plaque.

2.4.14 Vessels identification:

Identify common carotid artery through the following:

- Pulsatile walls
- Smaller caliber than jugular vein
- Systolic peak and diastolic endpoints in between that of external and internal carotid arteries on spectral analysis

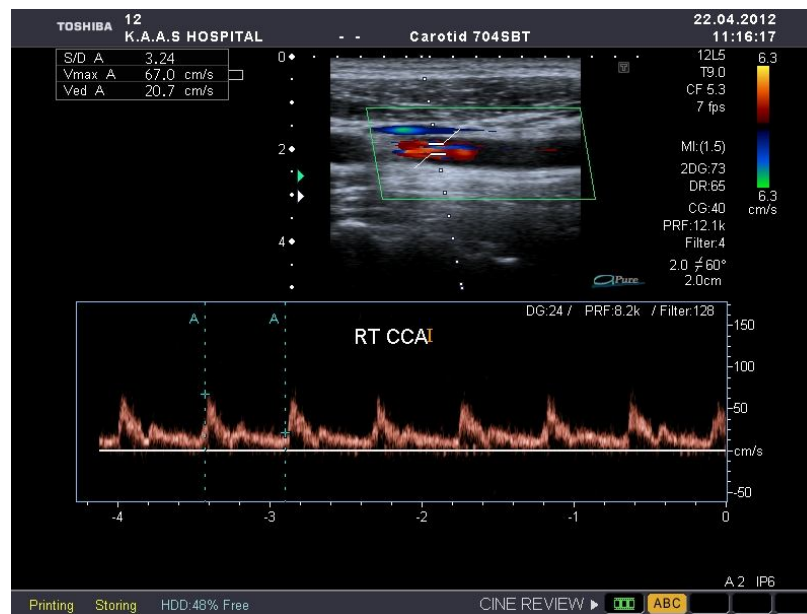


Figure 2.13: Common carotid with spectral analysis

Distinguishing internal and external carotid arteries:

- ECA has smaller caliber. Typical carotid bifurcation seen on grayscale.
- ICA is often posterolateral to ECA.
- ECA may have superior thyroid artery branch coming off.
- ECA has virtually no diastolic flow (high resistance vessel) on spectral analysis.
- ECA shows positive "temporal tap" (undulations in waveform with tapping of temporal artery).

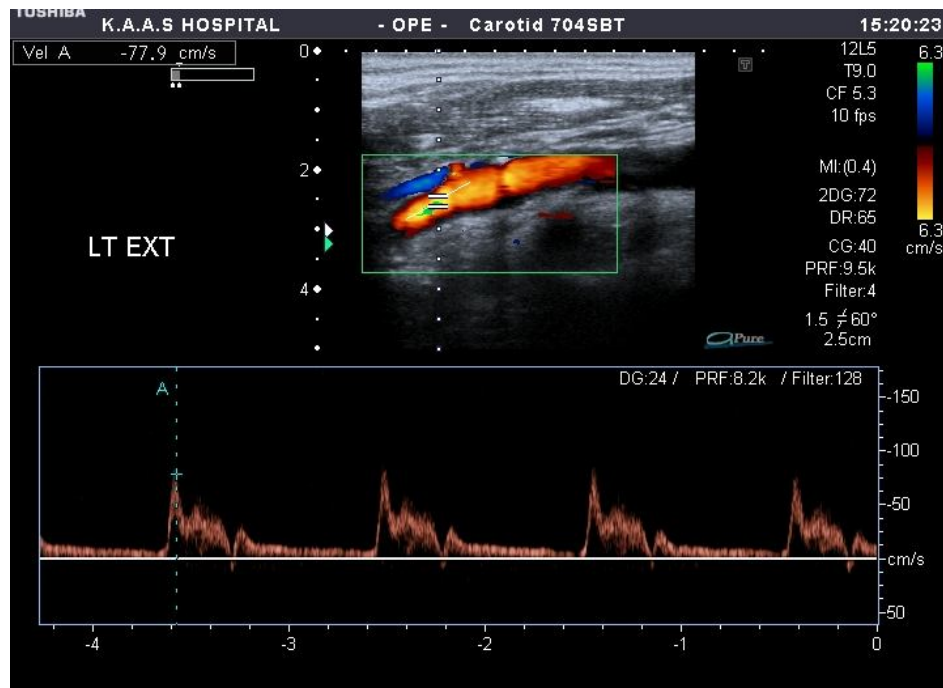


Figure 2.14: External carotid artery as seen on spectral analysis. Note the absence of flow in diastole and the sharp upstroke in systole.

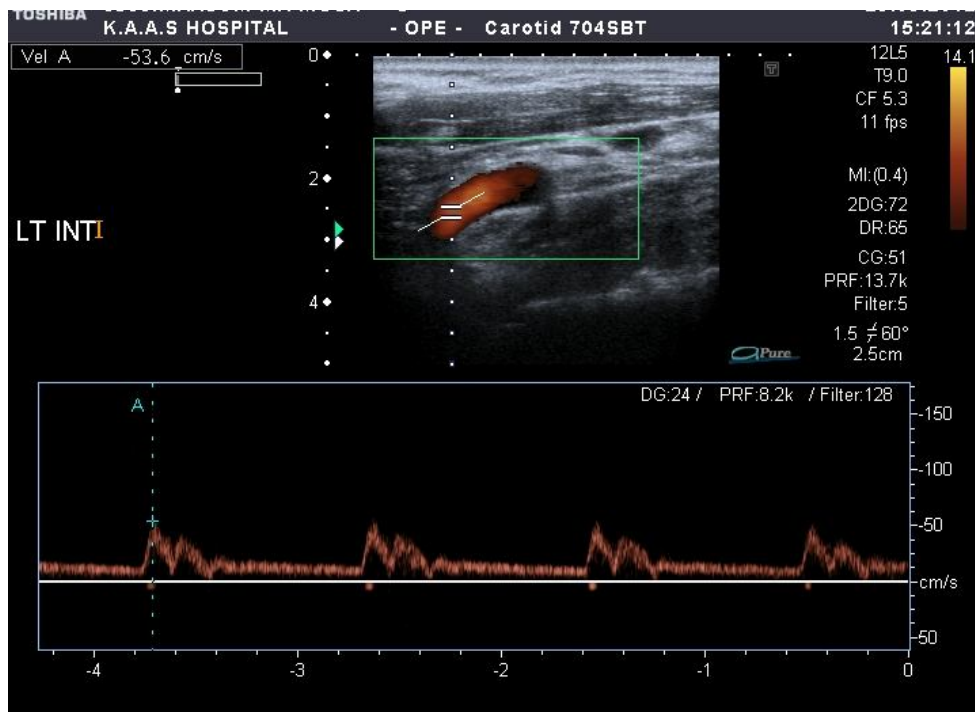


Figure 2.15: Internal carotid artery as seen on spectral analysis. Note that flow is discontinuous through diastole.

Identifying the vertebral arteries:

- With probe parallel to carotid, angle the probe laterally and inferiorly.
- Look for vertebral body processes that appear as hypoechoic transverse bars.
- The vertebral artery runs perpendicular to vertebral processes.

2.4.15 Determining Degree of Stenosis:

While some ultrasonographers attempt to characterize the degree of stenosis based on visual characteristics alone (similar to the North American Symptomatic Carotid Endarterectomy Trial method of angiographic estimation), estimation of stenosis solely based on this criterion is not reliable.

Commonly used methods of acoustic estimation of the degree of stenosis include the following:

- Measurement of peak systolic velocities (PSV) and end diastolic velocities
- Measurement of ratios (eg, ICA PSV/CCA PSV)

Some laboratories characterize degree of stenosis in terms of exact percentages. A range (eg, 50-69% stenosis) is probably more accurate. The ranges and measurements vary from laboratory to laboratory. Factors that affect measurements include the equipment used, the person performing the ultrasound, and the sites sampled for measurement (eg, the distal ICA often has higher

velocities than the proximal ICA). When possible, laboratories should perform their own correlations with angiographic measurements for quality control.

A consensus conference in 2003 of the Society of Radiologists in Ultrasound recommended the following criteria for estimating stenosis:

Normal: ICA PSV < 125 cm/s and no plaque or intimal thickening is visible.

- < 50% stenosis: ICA PSV < 125 cm/s and plaque or intimal thickening is visible.
- 50-69% stenosis: ICA PSV is 125-230 cm/s and plaque is visible.
- >70% stenosis to near occlusion: ICA PSV >230 cm/s and visible plaque and lumen narrowing are seen.
- Near occlusion: A markedly narrowed lumen is seen on color Doppler ultrasound.
- Total occlusion: No detectable patent lumen is seen on grayscale ultrasound, and no flow is seen on spectral, power, and color Doppler ultrasound.

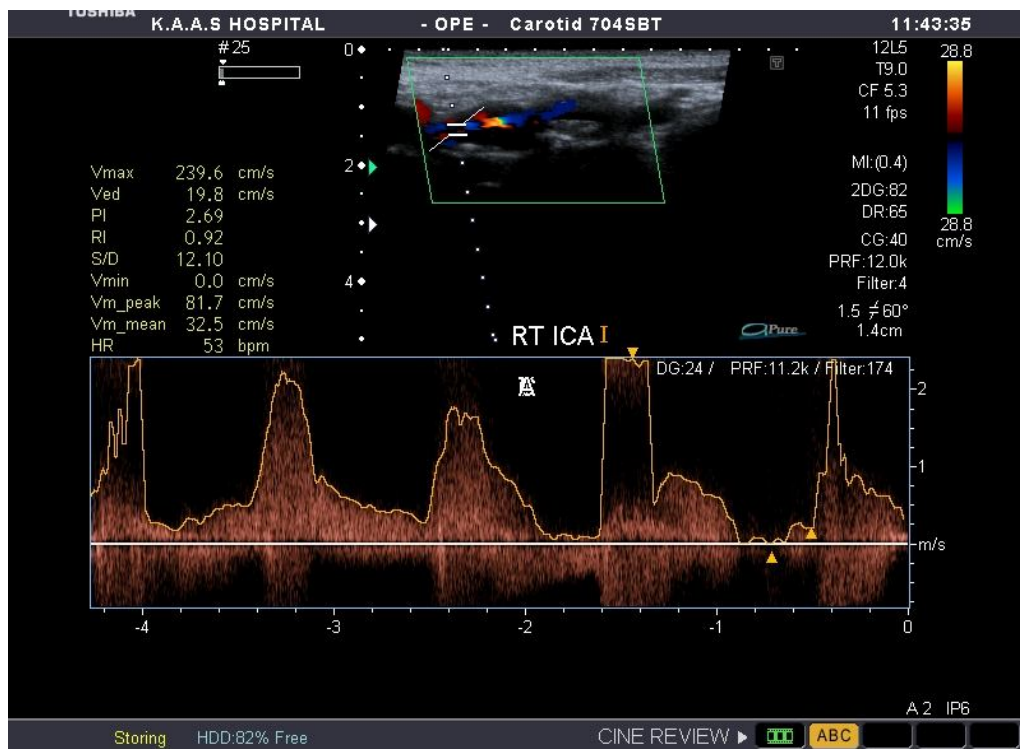


Figure 2.17: Moderate-grade stenosis as seen on spectral analysis. Note the high frequencies and velocities (239 cm/s systolic).

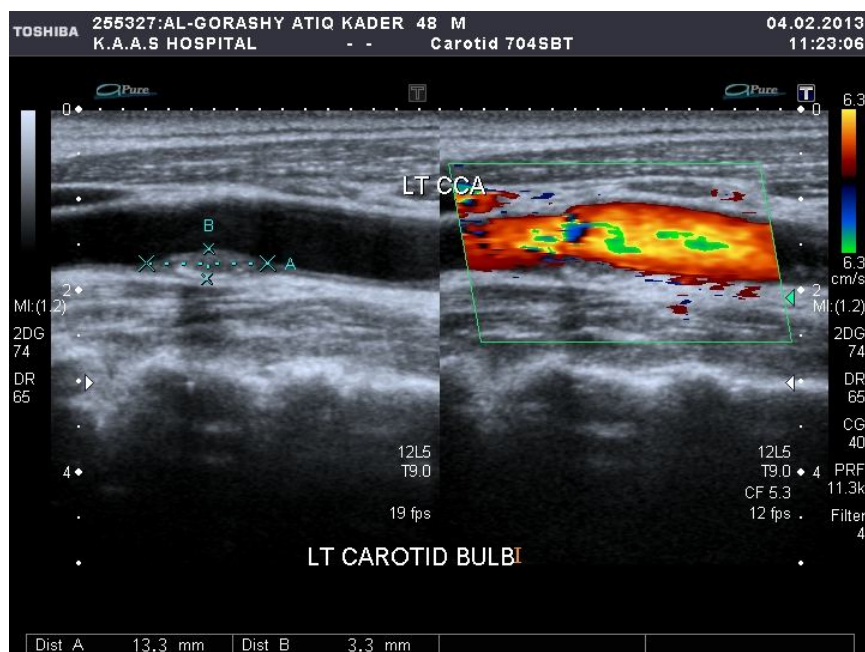


Figure 2.18 Carotid plaque at left carotid bulb.

With stenosis over 90% (near occlusion), velocities may actually drop as mechanisms that maintain flow fail. Ratios may be particularly helpful in situations in which cardiovascular factors (poor ejection fraction) limit the increase in velocity. In such cases, ICA/CCA ratios above 3 may signify significant stenosis.

With normal cardiovascular function and normal velocities, changes in ratios should be interpreted with caution.

2.4.16 Intima-Medial Thickness measurement:

An early sign of atherosclerosis is hypertrophy of the arterial wall. Increased intima-media thickness (IMT) is a non-invasive marker of arterial wall alteration, which can easily be assessed in the carotid arteries by high-resolution B-mode ultrasound. There are important differences in B-mode measurements of carotid IMT between laboratories. These might concern on IMT image acquisition (in relation to the segment and/or the wall of measure) as well as determination of the echo boundary defining the IMT interfaces and the difference in relationship between anatomic and sonographic structures of the near and far arterial wall. Measurements derived from the near wall reflect thickness of a part of media and intima influenced by sonographic artefacts, rather than that of the total intima-media complex.

Two main approaches are used for measuring IMT: 1) manual measurement at multiple extracranial carotid sites in near and far walls, and 2) automated computerized measurement, restricted to the far wall of the distal common carotid artery. Intra- and inter-observer variabilities have been found to vary in manual measurements between 0.09 to 0.13 mm and 0.12 to 0.18 mm (absolute differences). The best reproducibility of manual IMT-measurements is found at the far wall of the common carotid artery 1 cm from the bulb in the site of two parallel wall contours without local thickening. For automated measurements lower intra- and inter-observer variabilities have been reported. IMT of the common carotid artery is strongly influenced by age. For younger age groups (20 to 30 years) mean IMT values of 0.5 mm have been reported, while IMT values of 0.9 mm have been found for older subjects (60 to 70 years). (Ludwig M et al., 2003).

The American Society of Echocardiography and the Society for Vascular Medicine and Biology issued a report in 2006 recommending a standard technique for measuring IMT. The main recommendations were in carotid artery imaging protocol: (1) use end-diastolic (minimum dimension) images for IMT measurements; (2) provide separate categorization of plaque presence and IMT; (3) avoid use of a single upper limit of normal for IMT because the measure varies with age, sex, and race; and (4) incorporate lumen measurement, particularly when serial measurements are performed, to account for changes in

distending pressure. The recommendation acknowledges that protocols may vary in the number of segments where the IMT is measured, whether the near wall is measured in addition to the far wall, and whether IMT measurements are derived from B-mode or M-mode images, depending on the application (Roman MJ et al., 2006).

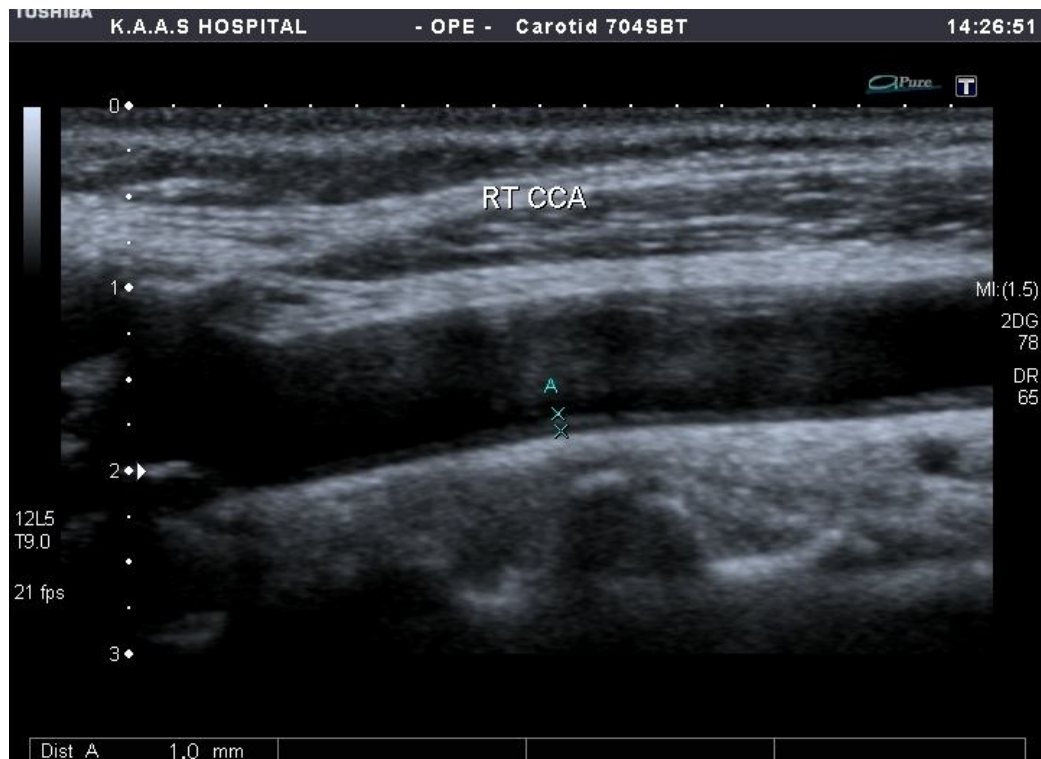


Figure 2.19 Measuring the Intima-media thickness in the Rt. CCA. Gray-scale.

2.5 Previous studies:

Regarding Carotid atherosclerosis in relation with the risk of smoking, there are some sonographic studies were conducted to cover part of this issue; In a retrospective study,(Abdalla et al., 2010) showed that atherosclerotic carotid artery disease prevalence was 41% of the study population, in the form of intimal thickening in (17.6%), <50% stenosis in (20.8%), 50–69% stenosis in 81 (1.7%), $\geq 70\%$ stenosis in 38 (0.8%) and occlusion of internal carotid artery in 3 (0.06%) patients.

Alegre (2008) proposed that, the frequency of carotid atherosclerosis and intima-media thickness was, respectively, 52 and 30.2%. There was an association between atherosclerosis types and age (≥ 64 years), stroke, obesity and smoking. When only carotid stenosis $\geq 60\%$ was considered, there was an association with age (≥ 64 years), carotid occlusion and coronary disease. Intima-media thickness was associated with age (≥ 64 years).

(Djoussé et al., 2002) registered that the prevalence odds ratios for carotid atherosclerosis were 1.7 and 1.9 for current smokers of 1 to 20 cigarettes per day, and current smokers of >20 cigarettes day, respectively (P=0.0018 for trend).

(Fan,et al., 2006) showed that Intima-media thickness of common carotid artery (CCA-IMT) and its components (echogenic and echolucent layers) in current

smokers was associated with thicker echogenic layer than never smokers. The study of (Lassila et al., 1997) concluded that the mean IMT was 0.76 ± 0.11 mm, and 50% of the population had at least one focal plaque. Smoking had the strongest association with the presence of plaque. (Dempsey et al., 1992) showed that increase in age is associated with smaller increases in plaque thickness.

(Kwon et al., 2009) showed that the Carotid plaque was identified in 30.3% the study population. Carotid plaque was located at the common carotid artery (24.0%), carotid bulb (72.7%), and at both sites (3.4%).

Carolyn (2005) suggested that the acute smoking causes Hemodynamic Alterations in the Common Carotid Artery.

Chapter three

Materials and methods

3.1 Materials:

ACUSONX300 ultrasound machine with 7MHz linear transducer was used in the study. B- mode and color Doppler ultrasonography measurements was applied to examine all participants. A questionnaire and data sheet were used to collect the data of the study.

3.2 Methods:

In an observational case control study, which conducted through Feb. 2011 to June 2013 at king Abdul- Aziz Specialty Hospital in KSA. The populations are Saudi smokers, the sample size was 121participants (92 smokers and 29 were control group). Inclusion criteria was male Saudi smokers. Exclusion criteria included patients with coronary artery or cardiac diseases. High blood cholesterol level, obesity and hypertension were considered factors. The sampling technique used was systemic simple convenient sampling to select all the study population.

The technique was used to examine carotid arteries of all participants is laying them in supine position, with the head rotated opposite to the interested side. After applying ultrasound gel along the sternocleidomastoid muscle border on the neck, the transducer was placed above the clavicle. Both saggital and transverse views was applied to assess all variables. The study variables were; CCA Intima-

media thickness, peak systolic velocity & maximum end-diastolic velocity of CCA, ICA and ECA.

The standard site of measurements for measuring blood velocities in CCA, ICA and ECA through the spectral Doppler was according to the below protocol;

From the upper CCA 2-3 cm below the bifurcation; ICA 1-2 cm above the pulb; ECA from the lower part. The sample volume is set about one-third of the total diameter and placed in the centre of the vessel (Paul L Allan et al., 2006).

The standard reference for measuring the stenosis was as follow; Sandra L.(2001).

< 50%	when Psv is < 125 cm/sec
50% - 79%	when Psv is > 125 cm/sec
80% - 99%	when Edv is >140% cm/sec
Occlusion	when there is no signal

The guided reference for CCA IMT was as following; IMT is considered normal when it is (less than 1.0 mm), moderate thickness is considered when the IMT is

(less than 2.0 mm), and signs of carotid plaque when (IMT is more than 2.0 mm). (Duplyakov Dmitry et al., 2003).

3.3 Data collection:

Information about smoking was obtained by a questionnaire. All participants were asked if they had ever smoke and if so; whether they were current smokers or not. The type and frequency of smoking per day was also registered for current smokers. The participants were classified into two groups according to the frequency range of smoking per day (from 1 to 20 or >20 cigarettes per day).

The sonographic data was obtained through direct ultrasound scanning of carotid arteries for the participants bilaterally(both smokers and control group).

3.3 statistical analysis:

SPSS 16.0 For Windows Evaluation Version statistical system was used in analyzing the processes of the findings. T-tests & Scattered plots were applied to achieve the statistical values of relation between smoking and the presence of carotid atherosclerotic changes.

3.4. Ethical considerations:

Special consideration was given to the right of confidentiality and anonymity for all participants. Anonymity was achieved by using number for each participant to provide link between the collected information and the participants.

In addition confidentiality was obtained by making the collected data accessible only to the researcher and the supervisor. Justice and human dignity was considered by teaching the selected participants equally when offering them an opportunity to participate in the research. The participants are free to decide whether to participate or not. The diagnostic tool used to perform the study was ultrasound which is safe and has no known harmful side effects to the participants. Permission for conducting the study was obtained from the King Abdul-Aziz specialty hospital director.

Chapter four

Results

4. Results:

121 participants were included in the study (92 smokers and 29 were control group). The mean age was 40.8 ± 21.5 (Table 4.5) (range from 19 to 100 years old). 71.7 of the participants smoke cigarettes (Table 4.6). Table 4.3 summarizes the status of smokers 89.1% were smokers only, 7.6% of the smokers were hypertensive and 2.2% were of high cholesterol level and 1.1% were diabetic. Table 4.1 summarizes the frequency of carotid plaques which was 22.8% (of 92). The detail of this prevalence was as follow; 9.5% in participant with high cholesterol level, 33% in hypertensive and 57.5 in participants under the risk of smoking only. Figure 4.1 summarizes the comparison between presence of plaques in participants smoke ≤ 20 cigarettes per day and those who smoke > 20 cigarettes per day, the higher percentage of plaques was in the group that smoke > 20 cigarettes per day. Tables 4.7 & 4.8 summarize the statistical analysis for the association between duration and frequency of smoking with the presence of plaques, which indicated strong association between duration of smoking and the presence of plaques, $P = .000$. There is also statistical association between age and presence of plaques ($P = .000$). Moreover there is statistical association between duration of smoking and the increase in plaque size.

Table 4.4 summarizes the frequency of stenosis, 18.4% (of 92) had stenosis. 13% had stenosis $< 50\%$ and 5.4% had stenosis from 50 – 79%. While 2.2% (of 92)

had total occlusion. Scattered plot showed that there is linear association between the duration of smoking and the percentage of carotid stenosis, which increases by 0.34%/ year (Figure4.8). Scattered plot showed that there is linear association between the frequency of smoking and the percentage of carotid stenosis, which increases by 0.31%/ frequency (Figure4.9).

The mean thickness of IMT in smokers was $.88 \pm .4$ mm (Table4.5). While it was .5 mm in control group. There is statistical association between the plaque and the increase in IMT, ($P = .000$)(Tble4.8).

Figure2 summarizes the representative comparison between blood velocities in young smokers and young control group (19 to 29 years old), through hemodynamic assessment of carotid PSV. The mean PSV in smokers were 60.5, 57.4 , 76.0 in CCA, ICA and ECA respectively. For the control group the PS velocities were 58.1, 55.6 and 68.4 in CCA, ICA and ECA respectively.

Scattered plot showed that there is linear association between the duration of smoking and the increase of carotid PSV, which increases by 0.62/year(Figure4.10). Scattered plot showed that there is linear association between the duration of smoking and the increase of carotid EDV, which increases by 0.65/year (Figure4.11).

Figure 4.4 through 4.7 show the representative B-mode images of plaques, increase IMT and Doppler spectral analysis.

Table 4.1:Shows the frequency of plaques in smokers

Plaque	Frequency	Percent
None	71	77.2
present	21	22.8
Total	92	100.0

Table 4.2:Shows the frequency of plaques/ sites

Plaque	Frequency	Percent
None	71	77.2
bifurcation	6	6.5
CCA	5	5.4
ICA	7	7.6
Bifurcation & CCA	1	1.1
Bifurcation & ICA	2	2.2
Total	92	100.0

Table 4.3: Shows the status of the participants.

Status	Frequency	Percent
Normal smokers	82	89.1
Hypertensive smokers	7	7.6
High Cholesterol smokers	2	2.2
Diabetic smokers	1	1.1
Total	92	100.0

Table 4.4: Shows the frequency of stenosis in the participants.

Status of stenosis	Frequency	Percent
No stenosis	73	79.3
Stenosis < 50%	12	13.0
Stenosis between 50 - 79%	5	5.4
Total occlusion	2	2.2
Total	92	100.0

Table 4.5: Shows the mean of study variables.

Variable	Mean±SD
Age (years old)	40.8±21.5
Smoking duration (year)	19.2±15.6
Size of plaque (mm)	8.2±21.5
Stenosis %	11.1±22.5
IMT	0.88±0.4

Table 4.6:Shows the frequency of type of smoking.

Type of smoking	Frequency	Percent
Cigarette	66	71.7
Shisha	16	17.4
both	10	10.9
Total	92	100.0

Table 4.7:Shows cross- tab of plaques and the mentioned variables.

Plaques		Mean	Std. Deviation	Std. Error Mean
Age	none	33.915	18.7721	2.2278
	present	64.333	11.3461	2.4759
Smoking duration	none	18.268	16.4247	1.9493
	present	22.143	12.1585	2.6532
Frequency of smoking	none	10.871	11 .6207	1.3889
	present	25.238	11.9704	2.6122
Stenosis	none	1.872	9.4742	1.1244
	present	42.357	25.8498	5.6409
IMT	none	.7663	.37129	.04406
	present	1.2548	.26921	.05875
PSV	none	60.713	18.4774	2.1929
	present	85.410	50.1139	10.9357
EDV	none	14.725	6.7963	.8066
	present	26.005	28.6410	6.2500

Table 4.8:Shows T-test for the relation of plaques and mentioned variables.

t-test presence of plaque	t-test for Equality of Means	
	t	Sig. (2-tailed)
Age	7.038	.000
Smoking duration	1.001	.319
Smoking frequency	4.935	.000
Stenosis	11.031	.000
IMT	5.599	.000
PSV	3.464	.001
EDV	3.074	.003

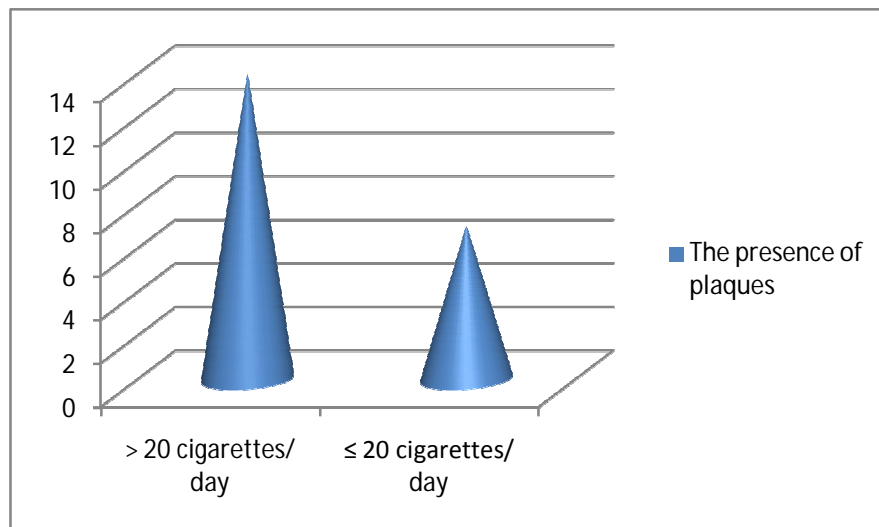


Figure 4.1. Shows the presence of plaque in relation with the frequency of smoking in the participants.

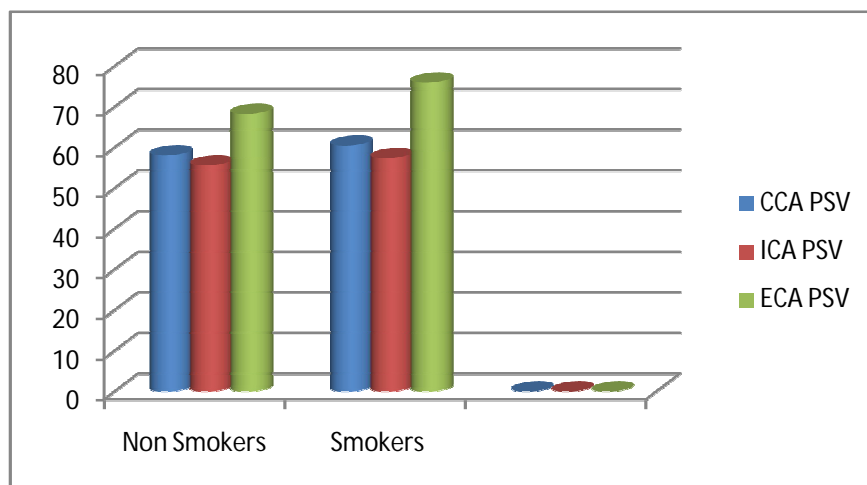


Figure 4.2. Shows a representative comparison of carotid artery velocities between the control group and smokers. Note the increase velocities in smokers.

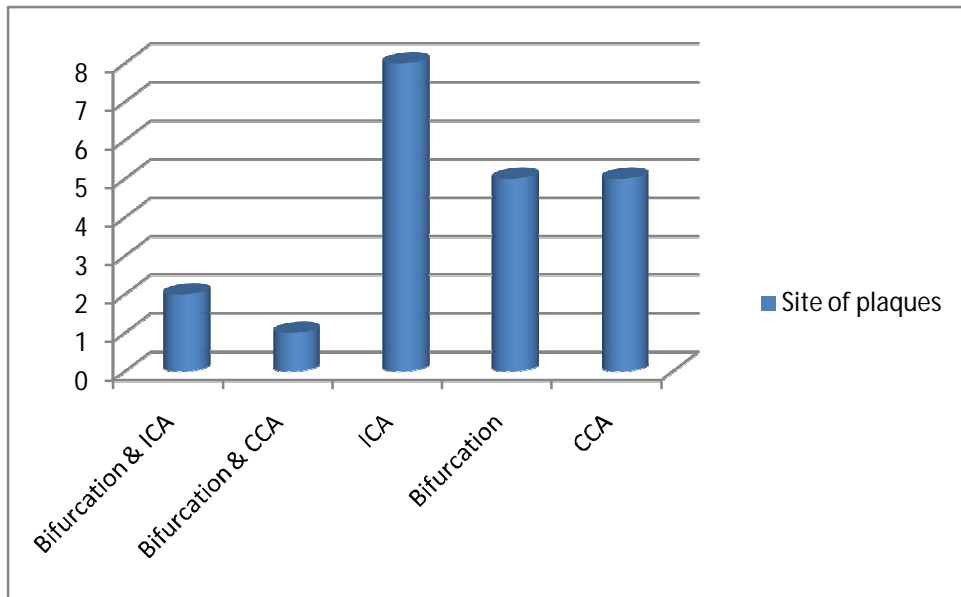


Figure 4.3. Shows the site of plaques distribution.

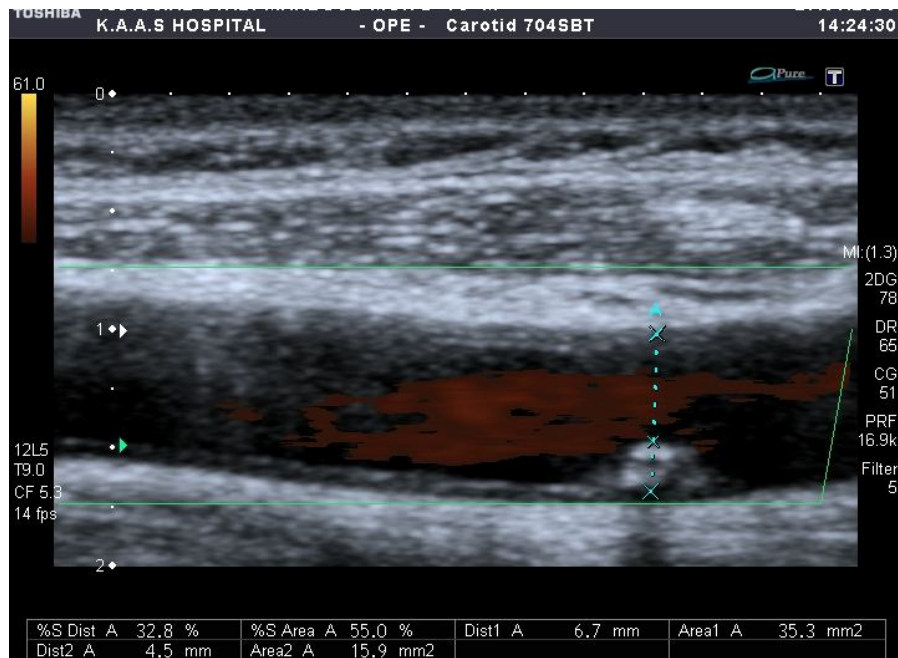
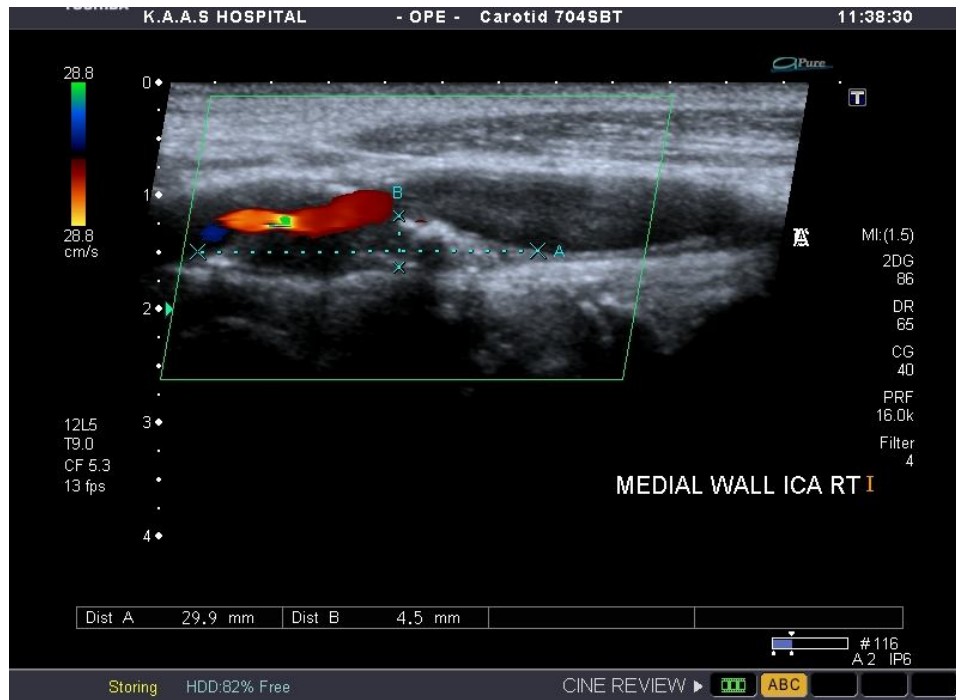


Figure 4.4. Shows echogenic plaque in ICA.

a.



b.

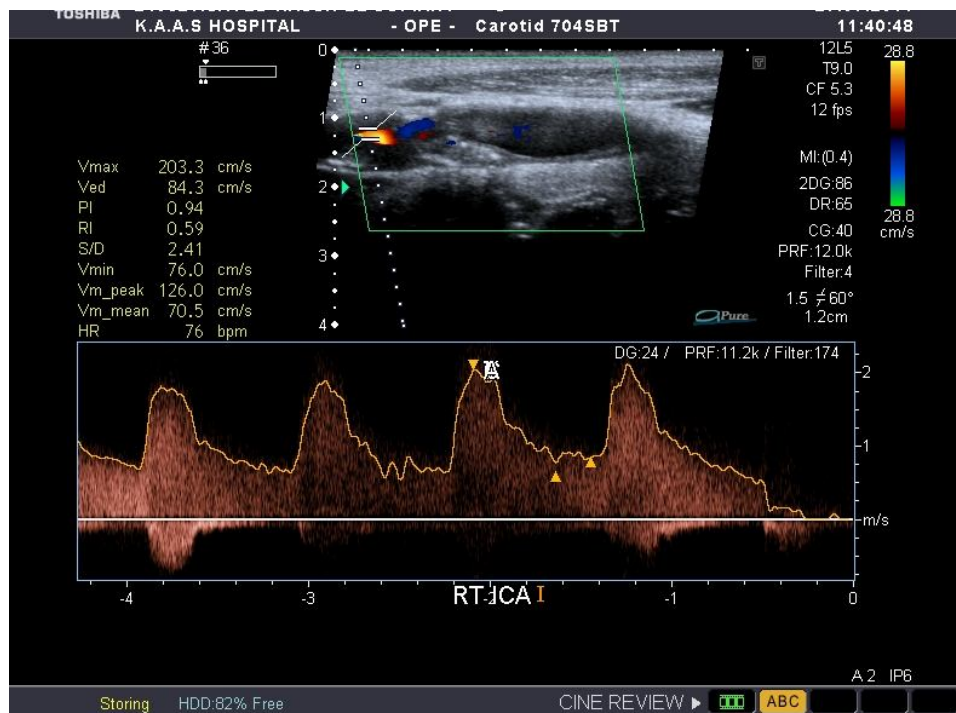
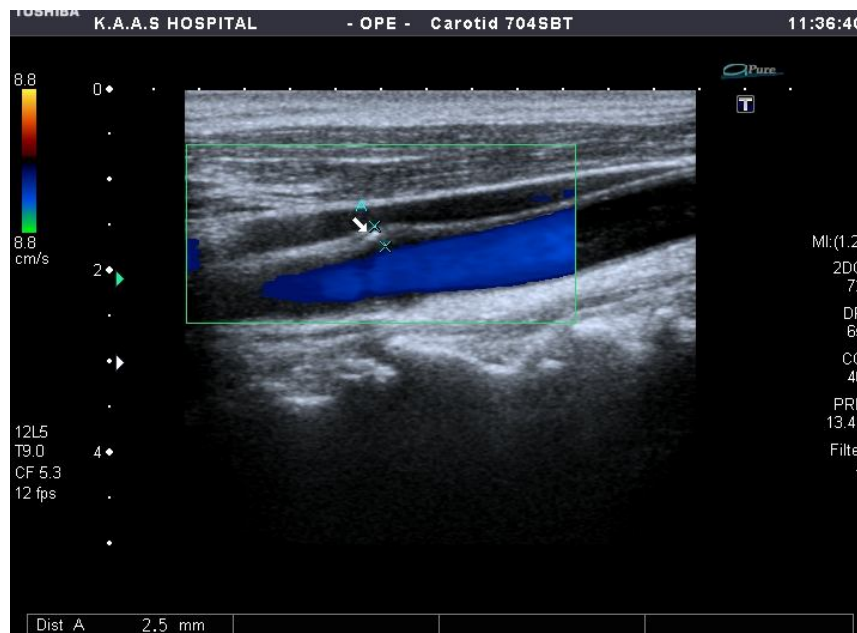


Figure 4.5. Shows internal carotid plaque and stenosis in 55 years old heavy smoker: a. B- mode image with mixed echotexture plaque in ICA. b. Spectral Doppler analysis shows increased carotid velocities with sign of (50% - 79%) stenosis.

a.



b.

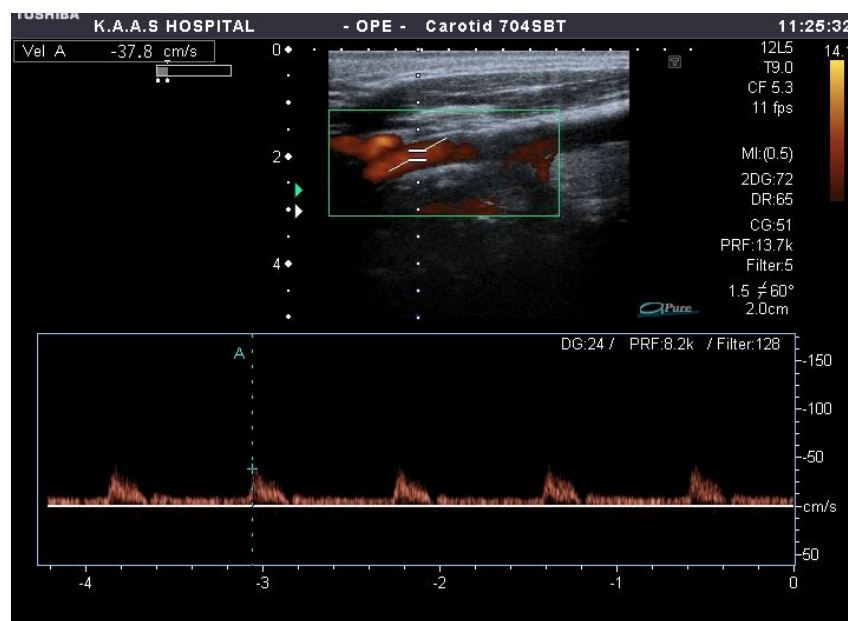
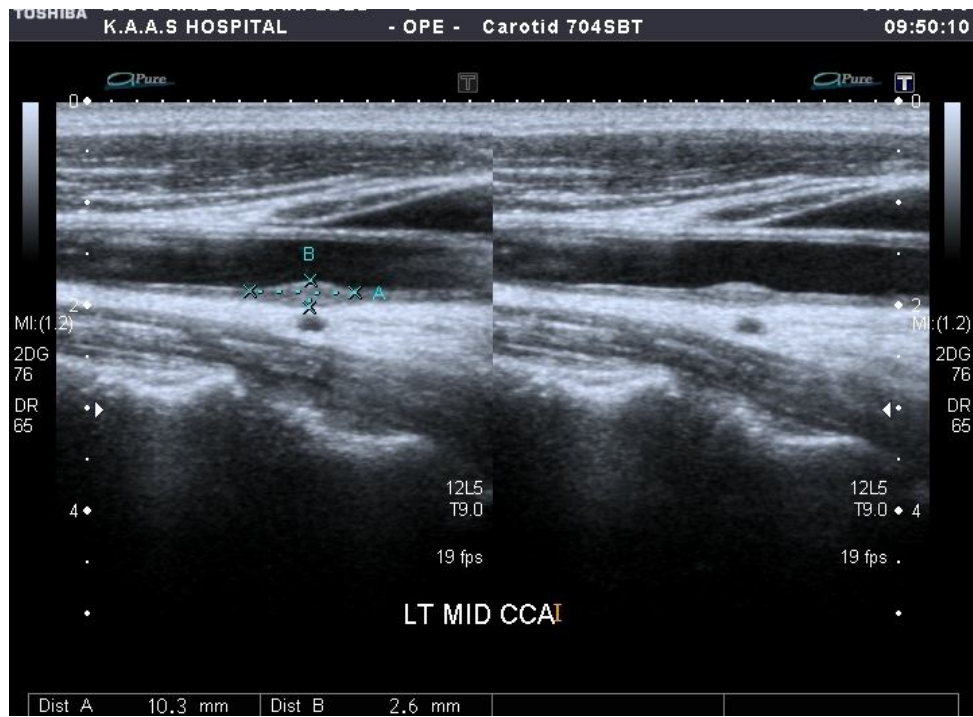


Figure 4.6. a. B- mode image shows Increased IMT with focal calcification in ICA of 49 years old smoker. b. Spectral Doppler analysis shows normal velocity in the same participant.

a.



b.

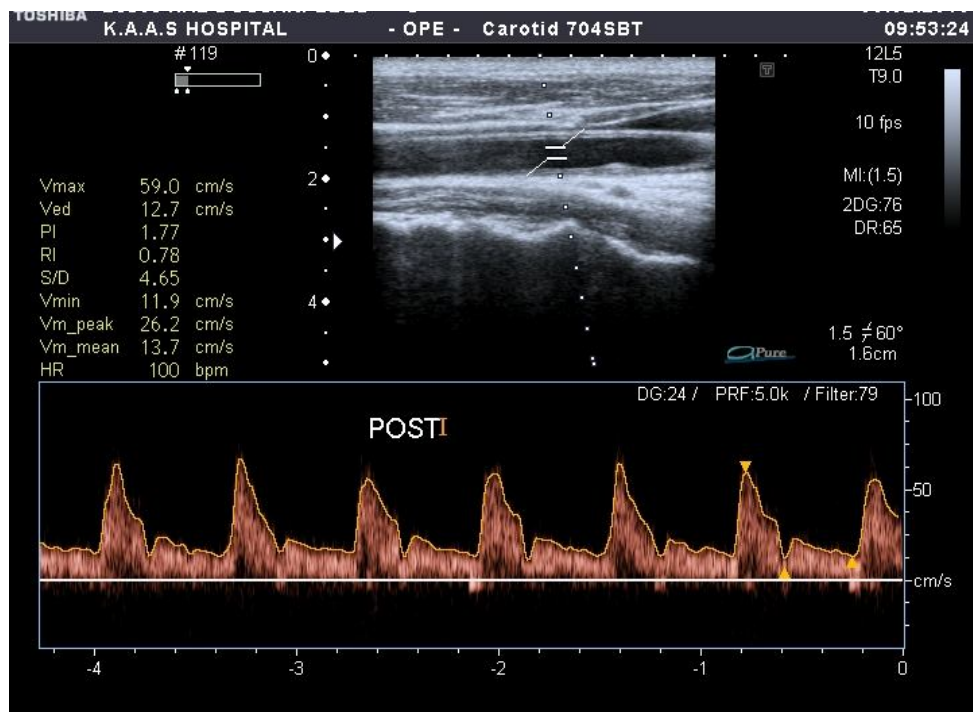


Figure 4.7 .a. B- mode image shows CCA plaque in 59 years old smoker. b. Shows Doppler spectral analysis of CCA in the same participant, no stenosis.

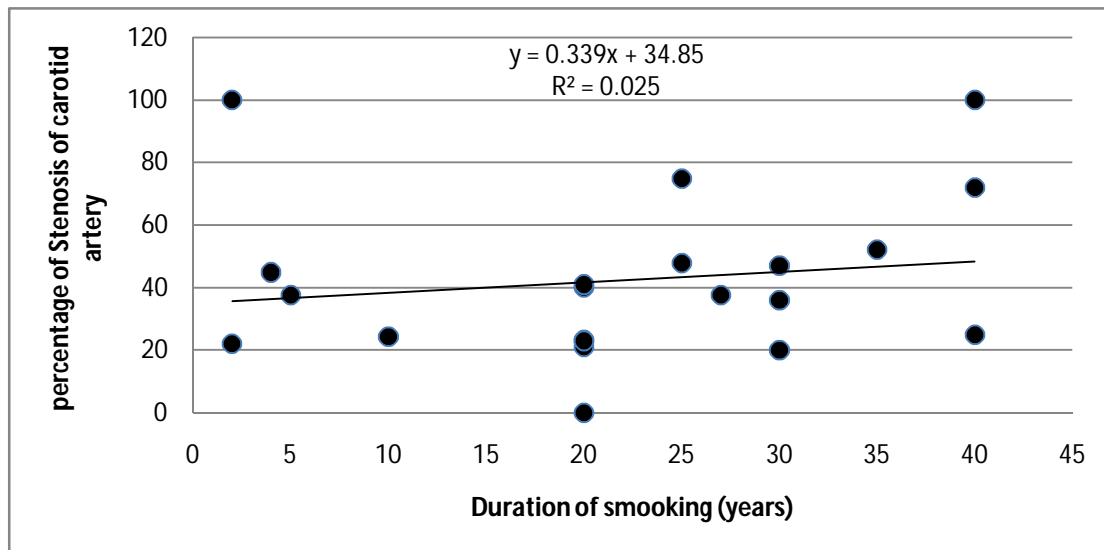


Figure 4.8: Scatter plot for the relationship between the duration of smoking & Carotid stenosis

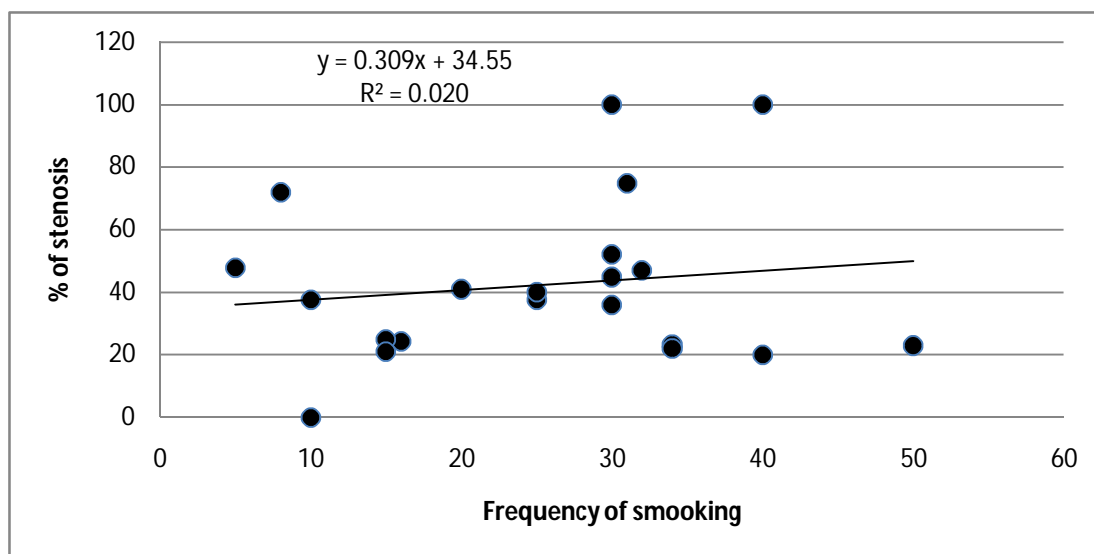


Figure 4.9: Scatter plot for the relationship between the frequency of smoking & Carotid stenosis.

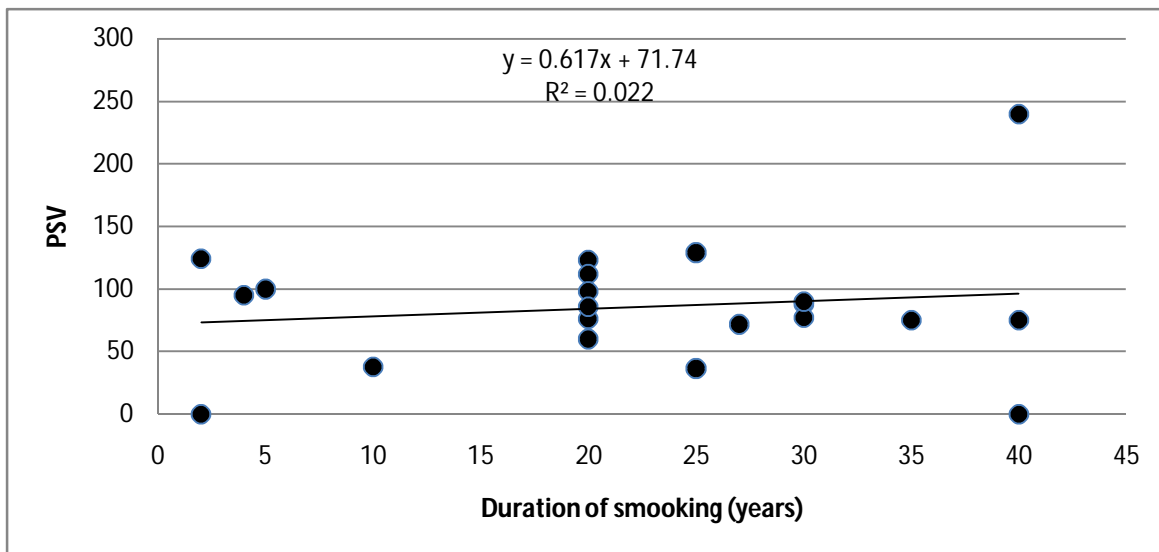


Figure 4.10: Scatter plot for the relationship between the duration of smoking & Carotid PSV

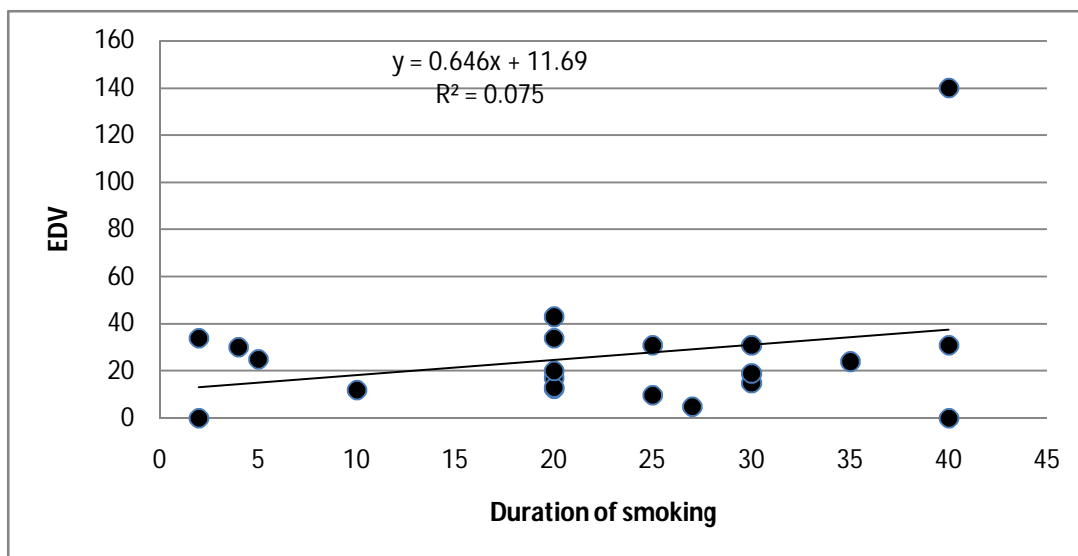


Figure 4.11: Scatter plot for the relationship between the duration of smoking & Carotid EDV

Chapter five

Discussion & conclusion

5.1 Discussion

Carotid atherosclerosis may have association with smoking and ischemic arterial diseases. This is beside other risk factors such as; age, gender, systemic hypertension, obesity. This study aimed to evaluate the association of carotid atherosclerosis with smoking in Saudi smokers.

The study assured that there is strong statistical significant association between the smoking and the occurring of carotid plaques, $P = .000$ (Table 4.8). The frequency of plaques in participants smoke > 20 cigarettes per day was the higher frequency (Figure 4.1). These findings were totally agree with (Lassila et al., 1997) results who showed that smoking had a strong association with the presence of plaque. Also agree with (Djoussé et al., 2002) results who suggested that the prevalence odds ratios for carotid atherosclerosis were 1.7 and 1.9 for current smokers of 1 to 20 cigarettes per day, and current smokers of >20 cigarettes day, respectively.

Previous author has suggested that the presence of carotid atherosclerosis is associated with age ≥ 64 years old (Alegre (2008), that is in contrast to the results of this study, summarized in figures 4.5 and 4.7, which showed plaques in ages less than 64 years old.

Regarding the size of plaque this study assured that there was association between the duration of smoking and age with increases in plaque thickness (Tables 4.7).

These finding confirm the results of (Dempsey et al., 1992) who reported that increase in age is associated with smaller increases in plaque thickness.

The results of this study showed that smoking has effects on hemodynamic in carotid artery (Figures 4.2, 4.10 and 4.11) these findings match Carolyn (2005) results who suggested that the acute smoking causes Hemodynamic Alterations in the Common Carotid Artery.

The study findings assured that there is strong association between the frequency of smoking and the increase thickness of IMT ($P = .000$) (Table 4.8). These findings agree with (Fan, et al., 2006) who showed that IMT of common carotid artery (CCA-IMT) and its components (echogenic and echolucent layers) in current smokers was associated with thicker echogenic layer than never smokers. Some previous authors have proposed that carotid bifurcation is the common site of plaques (Rubba et al., 2001), this study findings showed that the ICA carotid is the common site of plaques (Figure 4.3).

5.2 Conclusion:

The main objectives of the study were to evaluate the presence of carotid atherosclerosis in male Saudi smokers using B- mode & Doppler ultrasound and to compare the findings between elderly and young smokers. chapter one contains an introduction, Stroke & smoking overview, main & specific objectives and significance of the study. Chapter two includes theoretical background and literature review about the carotid arteries anatomy, atherosclerosis, carotid atherosclerosis diagnostic modalities, Doppler ultrasonography and previous studies in relation with smoking and carotid atherosclerosis. Chapter three includes materials and methods of the study. Chapter four covers presentation of the thesis's results. Chapter five includes discussion, conclusion, limitations and recommendations.

The study concluded that smoking is an important effective risk factor for the carotid atherosclerosis. Duration of smoking increases the percentage of carotid stenosis by 0.34%/ year and the frequency of smoking increases the percentage of carotid stenosis by 0.31%/ frequency. Regarding the hemodynamic of carotid artery, smoking increases the carotid PSV by 0.62/year and increases carotid EDV by 0.65/year. In addition this study proved that smoking is associated with an early carotid atherosclerosis in young smokers < 54years old.

5.3 Limitations:

The study was restricted only in male Saudi smokers, because it is difficult to be performed in female Saudi population due to the culture in this country. The sample volume was 121, if there was a possibility to include both male and female it would be great and helpful in conducting the study on a large population.

5.4 Recommendations:

The researcher recommend that intensive awareness against smoking in the KSA. is needed. Moreover further studies in the same field were needed. Conducting the study in both male and female Saudi smokers will be more effective. During the upcoming studies the researcher recommend to use a wide range of participants. Calibrated ultrasound machines were recommended to be used in studying carotid disorders.

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Attachments