بسم الله الرحمن الرحيم

Sudan University of Science and Technology

College of Graduate Studies

Study of Carotid Arteries in Hypertensive Patients Using Color Doppler Ultrasonography

دراسة الشرايين السباتية لمرضي ضغط الدم باستخدام الموجات فوق الصوتية الملونة

A thesis submitted for the award of PhD degree in Diagnostic Medical Ultrasound

By:

Amel Saeed Abdelrahim Elgadal

Supervisor:

Prof. Elsafi Ahmed Abdalla Bala

MSc.PhD Diagnostic Medical Ultrasound

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الاية

قال تعالي :

﴿ شَهِدَ اللَّهُ أَنَّهُ لَا إِلَٰهَ إِلَّا هُوَ وَالْمَلَائِكَةُ وَأُولُو الْعِلْمِ قَائِمًا بِالْقِسْطِ ۚ لَا إِلَٰهَ إِلَّا هُوَ الْعَزِيزُ

الْحَكِيمُ ﴾

سورة آل عمران الاية ﴿١٨﴾

Dedication

To doses of the cup blank to give me a drop of love

To those of the fingers to give us a moment of happiness

To reap the thorns out of my way for me to pave the way science

To heart the great my father

Of whom breastfed of love and healing balm

To the heart as pure whiteness my parents

To my friends, and to all my family

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First and foremost, I would like to express my deepest gratitude to

Prof. Alsafi Abdella Bala, without his help this work could not have been accomplished

I also would like to thank Prof. Mohamed Elfadil for his support and guidance.

Deep thanks to my family for their consistent mental support finally,

I would like to thanks my friend.

Abstract

The objective of this study was to evaluate the carotid arteries in hypertensive patients using color Doppler ultrasonography in order to find quantitative relation between the blood flow indices and the laboratory tests values. This study was carried out in Libyan nationality during the period from 2015 to 2018 in 368 patients (130 were normal and 238 were hypertensive) using grey scale and color Doppler ultrasonography to find the RI of both carotid arteries and intima media thickness, as well as other parameters associated with hypertension.

The results of this study revealed that there is a real difference between the normal and hypertensive patients for all factors except the age and Body Mass Index(BMI), where there was no influential factor that showed inconclusive differences. Using stepwise linear discriminant analysis to classify the data into normal and hypertensive patients, 8 variables were chosen by the program as the most discriminant factors they include: Systolic blood pressure (SBP),Diastolic blood pressure (DBP), (BMI) ,Plasma Total Cholesterol(PTC) Plasma Total Glyceride(PTG) ,Right Intima Media Thickness (RT IMT), Left Intima Media Thickness(LT IMT)and Right Resistive Index (RT RI) the classification accuracy was 100% as well as the sensitivity and specificity. And the generated model that can be used to classify other groups, Systolic and diastolic blood pressure concerning the normal and hypertensive patients showed remarkable differences between the two groups where the values for hypertensive patients in average were apparently exceed that of the normal with a minimum variation that keep the differences between the two groups.

The (PTC) was higher as usual in hypertensive patients than normal and there is a significance differences between the two groups, the intima media thickness for the RT and LT carotid arteries showed that, hypertensive patients were associate with a thicker intima than the normal respondent with considerable variation attributed to hypertensive in respect to the stage of their condition.

المستخلص

دراسة الشريان السباتي في مرضى ارتفاع ضغط الدم باستخدام دوبلر اللون ، وكان الهدف الرئيسي دراسة الشريان السباتي في مرضى ارتفاع ضغط الدم باستخدام لون دوبلر من أجل العثور على العلاقة الكمية بين مؤشرات تدفق الدم وقيم الاختبارات المعملية. أجريت هذه الدراسة على الجنسية الليبية خلال الفترة من 2015 إلى 2018 في 368 مريض (130 طبيعي و 238 ارتفاع ضغط الدم) باستخدام مقياس اللون الرمادي بالموجات فوق الصوتية ولون دوبلر للعثور على الشريان السباتي وسماكة الوسائط الداخلية ، وكذلك المعلمات الأخرى المرتبطة ارتفاع ضغط الدم.

تظهر نتائج هذه الدراسة أن هناك فرقا حقيقيا بين المريض الطبيعي ومريض ارتفاع ضغط الدم لجميع العوامل باستثناء العمر ولم يكن مؤشر كتلة الجسم عاملًا مؤثرًا أظهروا فروقًا غير حاسمة. باستخدام تحليل متسلسل خطي متدرج لتصنيف البيانات في المرضى العاديين وارتفاع ضغط الدم ، تم اختيار 8 متغيرات من قبل البرنامج كعوامل أكثر تميزا تشمل :و التصنيف كانت دقة 100 ٪ وكذلك حساسية وخصوصية. والنموذج المولَّد الذي يمكن استخدامه لتصنيف المجموعات الأخرى ، أظهر ضغط الدم الانقباضي والانبساطي المتعلق بالمرضى العاديين وارتفاع ضغط الدم اختلافات ملحوظة بين المجموعتين حيث كانت قيم المريض المصاب بارتفاع ضغط الدم في المتوسط تتجاوز ، على ما يبدو ، المعدل الطبيعي مع وجود حد أدنى من التباين. التي تحافظ على الاختلافات بين المجموعتين.

كان الكوليسترول الكلي في البلازما أعلى كالمعتاد في مرضى ارتفاع ضغط الدم من المعتاد ، وهناك اختلافات ذات دلالة بين المجموعتين ، وأظهرت سماكة الوسائط البينية في الشريان السباتي ، أن المريض المريض بارتفاع ضغط الدم مع البطانة السميكة أكثر من المستجيب العادي مع اختلاف كبير يعزى إلى ارتفاع ضغط الدم فيما يتعلق بمرحلة حالتهم.

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List of abbreviation

CT	Computed Radiography
MRI	Magnetic Resonance Imaging
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
BMI	Body Mass Index
HR	Heart Rate
PTC	Plasma Total Cholesterol
PTG	Plasma Total Glyceride
RIMT	Right Intima Media Thickness
LIMT	Left Intima Media Thickness
RRI	Right Resistive Index
LRI	Left Resistive Index
AS	Ankylosing spondylitis

Chapter One

Introduction

1.1 Introduction

In recent years, the capabilities of ultrasound flow imaging have increased enormously. Color flow imaging is now commonplace and facilities such as ‘power’ or ‘energy’ Doppler provide new ways of imaging flow. With such versatility, it is tempting to employ the technique for ever more demanding applications and to try to measure increasingly subtle changes in the maternal and fetal circulations. To avoid misinterpretation of results, however, it is essential for the user of Doppler ultrasound to be aware of the factors that affect the Doppler signal, be it a color flow image or a Doppler sonogram. The following describes how these components contribute to the quality of Doppler ultrasound images. Guidelines are given on how to obtain good images in all flow imaging modes. Since color flow imaging provides a limited amount of information over a large region, and spectral Doppler provides more detailed information about a small region, the two modes are complementary and, in practice, are used as such (Carol MR 2005).

Color flow imaging can be used to identify vessels requiring examination, to identify the presence and direction of flow, to highlight gross circulation anomalies, throughout the entire color flow image, and to provide beam/vessel angle correction for velocity measurements. Pulsed wave Doppler is used to provide analysis of the flow at specific sites in the vessel under investigation. When using color flow imaging with pulsed wave Doppler, the color flow/B-mode image is frozen while the pulsed wave Doppler is activated. Recently, some manufacturers have produced concurrent color flow imaging and pulsed wave Doppler, sometimes referred to as *triplex* scanning (Carol MR 2005).

When these modes are used simultaneously, the performance of each is decreased. Because transducer elements are employed in three modes (B-mode, color flow and pulsed wave

Doppler), the frame rate is decreased, the color flow box is reduced in size and the available pulse repetition frequency is reduced, leading to increased susceptibility to aliasing.

Power Doppler is also referred to as energy Doppler, amplitude Doppler and Doppler angiography. The magnitude of the color flow output is displayed rather than the Doppler frequency signal. Power Doppler does not display flow direction or different velocities. It is often used in conjunction with frame averaging to increase sensitivity to low flows and velocities. It complements the other two modes (Table 1.1). Hybrid color flow modes incorporating power and velocity data are also available from some manufacturers. These can also have improved sensitivity to low flow. A brief summary of factors influencing the displays in each mode is given in the following sections. Most of these factors are set up approximately for a particular mode when the application (e.g. fetal scan) is chosen, although the operator will usually alter many of the controls during the scan to optimize the image (Bowman TS 1999).

1.2 Problem of the study:

Cholesterol level can be detected by Laboratory test. Color Doppler Ultrasonography is considered a new technology that can detect the blood flow of all arteries. The evaluation of carotid arteries Doppler flow indices is considered as an important issue in patients with vascular diseases. **The questions to be answered:**

1- Can the laboratory findings considered as predictor for the carotid artery Doppler disturbance
2- Can ultrasound be able to evaluate carotid arteries blood flow in hypertensive patients
3- Is there any consistency in the relationship between HTN and the presence of carotid plaque
4- Is there any relation between laboratory results and ultrsonographic findings

1.3 Objectives of the study:

1.3.1 Main Objectives: the main objective of this study to Evaluate of the intimal thickness of the common carotid artery in hypertensive patients in from different regions of Libya.

1.3.2 Specific Objectives

- To determination of the average measurement of the common carotid intimal thickness among hypertensive patients.
- To differentiate between the intimal thickness in hypertensive patients and possible correlation with gender.
- To Differentiate between the intimal thickness in hypertensive patients and possible correlation with age.
- To relation of the intimal thickness to duration of hypertension.

Chapter Two

Theoretical Background

2.1 Principles of Doppler

In recent years, the capabilities of ultrasound flow imaging have increased enormously. Color flow imaging is now commonplace and facilities such as 'power' or 'energy' Doppler provide new ways of imaging flow. With such versatility, it is tempting to employ the technique for ever more demanding applications and to try to measure increasingly subtle changes in the maternal and fetal circulations. To avoid misinterpretation of results, however, it is essential for the user of Doppler ultrasound to be aware of the factors that affect the Doppler signal, be it a color flow image or a Doppler sonogram (Bowman TS 1999).

The following describes how these components contribute to the quality of Doppler ultrasound images. Guidelines are given on how to obtain good images in all flow imaging modes. Competent use of Doppler ultrasound techniques requires an understanding of three key components: The capabilities and limitations of Doppler ultrasound; The different parameters which contribute to the flow display; Blood flow in arteries and veins (Carol MR 2005).

2.1.1 Basic Principles

Ultrasound images of flow, whether color flow or spectral Doppler, are essentially obtained from measurements of movement. In ultrasound scanners, a series of pulses is transmitted to detect movement of blood. Echoes from stationary tissue are the same from pulse to pulse. Echoes from moving scatterers exhibit slight differences in the time for the signal to be returned to the receiver (Figure 2.1). These differences can be measured as a direct time difference or, more usually, in terms of a phase shift from which the 'Doppler frequency' is obtained (Figure 2.1). They are then processed to produce either a color flow display or a Doppler sonogram.

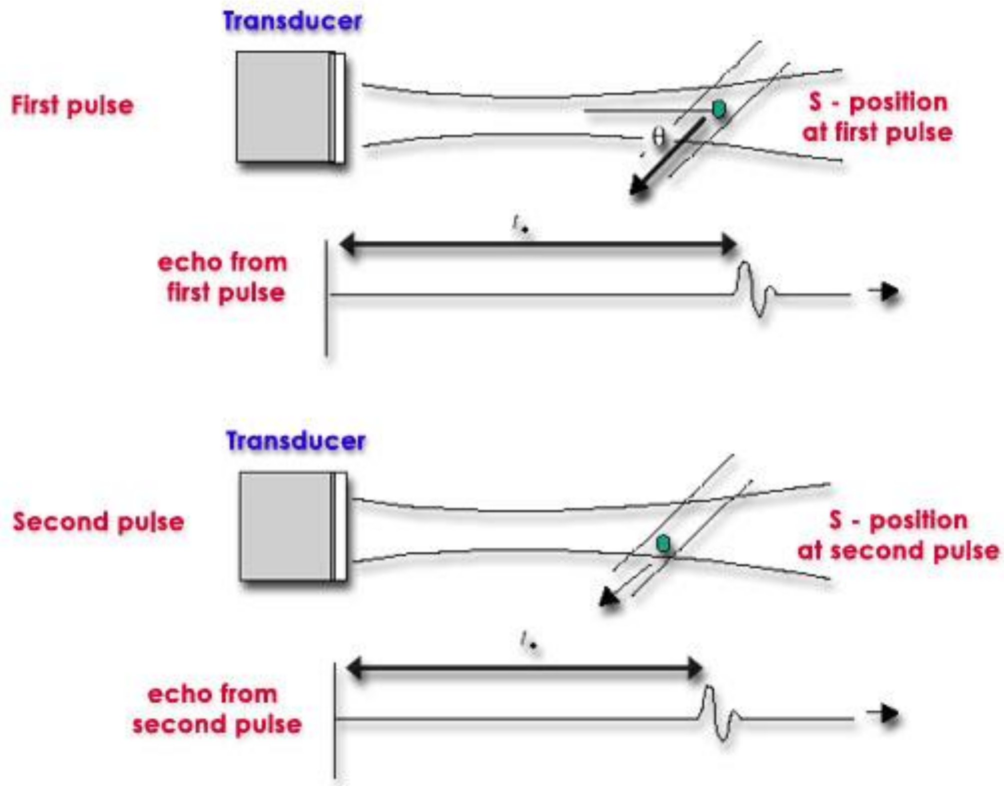


Figure 2.1 Ultrasound velocity measurement. The diagram shows a scatterer S moving at velocity V with a beam/flow angle q. The velocity can be calculated by the difference in transmit-to-receive time from the first pulse to the second *(*t2), as the scatterer moves through the beam.

As can be seen from Figures 2.1 and 2.2, there has to be motion in the direction of the beam; if the flow is perpendicular to the beam, there is no relative motion from pulse to pulse. The size of the Doppler signal is dependent on:

(1) Blood velocity: as velocity increases, so does the Doppler frequency;
(2) Ultrasound frequency: higher ultrasound frequencies give increased Doppler frequency. As in B-mode, lower ultrasound frequencies have better penetration.
(3) The choice of frequency is a compromise between better sensitivity to flow or better penetration;
(4 The angle of insonation: the Doppler frequency increases as the Doppler ultrasound beam becomes more aligned to the flow direction (the angle *q* between the beam and the direction of

flow becomes smaller). This is of the utmost importance in the use of Doppler ultrasound. The implications are illustrated schematically in Figure 2.3.

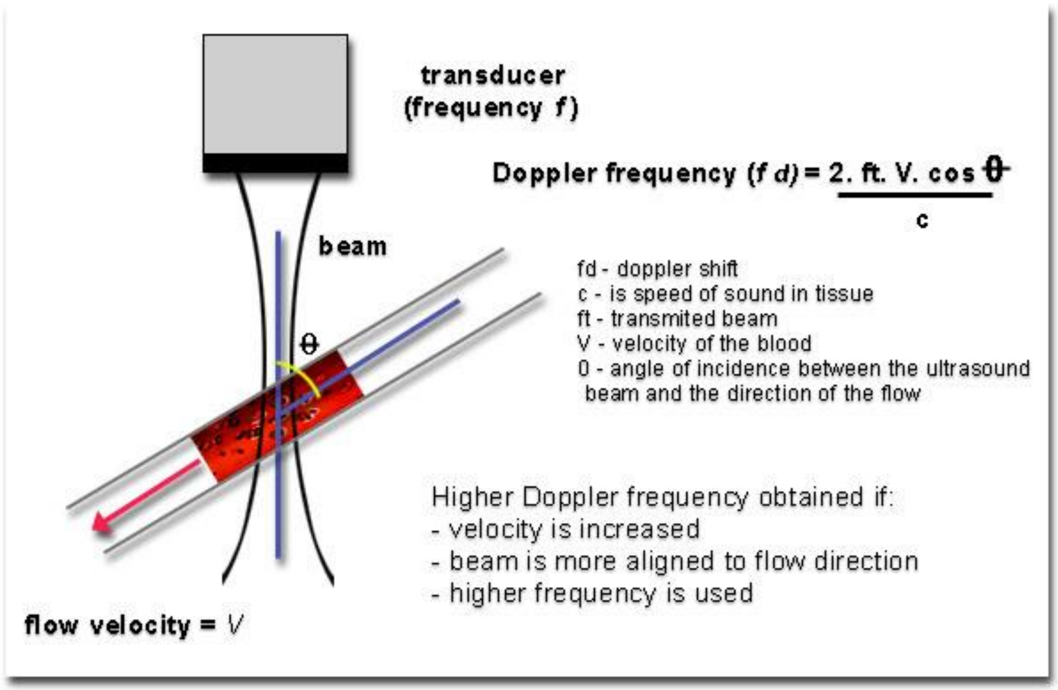


Figure 2.2: Doppler ultrasound. Doppler ultrasound measures the movement of the scatterers through the beam as a phase change in the received signal. The resulting Doppler frequency can be used to measure velocity if the beam/flow angle is known.

All types of Doppler ultrasound equipment employ filters to cut out the high amplitude, low-frequency Doppler signals resulting from tissue movement, for instance due to vessel wall motion. Filter frequency can usually be altered by the user, for example, to exclude frequencies below 50, 100 or 200 Hz. This filter frequency limits the minimum flow velocities that can be measured (Carol MR 2005).

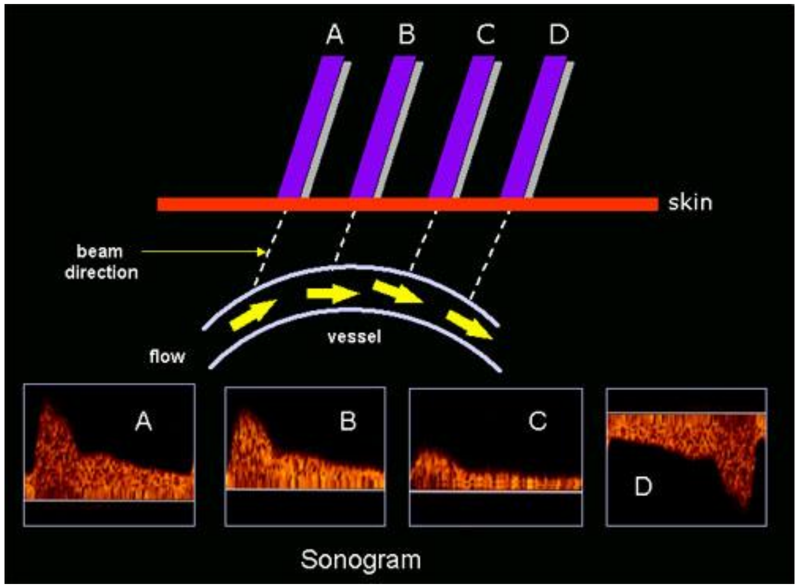
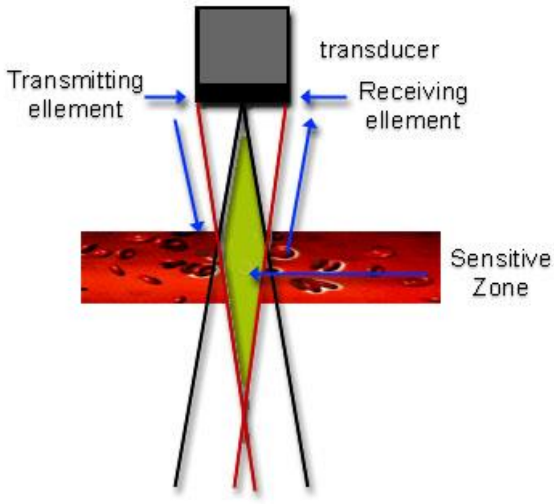
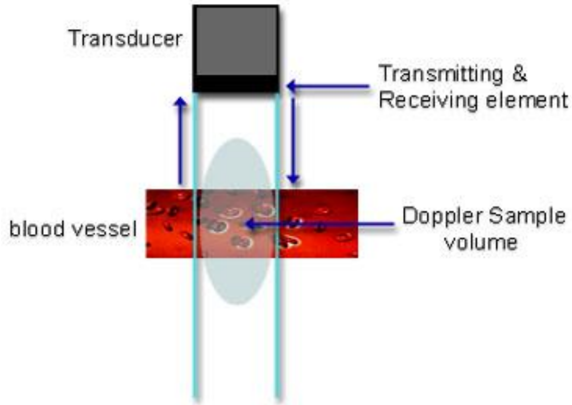


Figure 2.3 - Effect of the Doppler angle in the sonogram. **(A)** higher-frequency Doppler signal is obtained if the beam is aligned more to the direction of flow. In the diagram, beam **(A)** is more ali)gned than **(B)** and produces higher-frequency Doppler signals. The beam/flow angle at **(C)** is almost 90° and there is a very poor Doppler signal. The flow at **(D)** is away from the beam and there is a negative signal.

2.2 Continuous wave and pulse wave

As the name suggests, continuous wave systems use continuous transmission and reception of ultrasound. Doppler signals are obtained from all vessels in the path of the ultrasound beam (until the ultrasound beam becomes sufficiently attenuated due to depth). Continuous wave Doppler ultrasound is unable to determine the specific location of velocities within the beam and cannot be used to produce color flow images. Relatively inexpensive Doppler ultrasound systems are available which employ continuous wave probes to give Doppler output without the addition of B-mode images. Continuous wave Doppler is also used in adult cardiac scanners to investigate the high velocities in the aorta (Bluth EL 2004).





Continuous-wave doppler transducer

Pulsed-wave doppler transducer

Doppler ultrasound in general and obstetric ultrasound scanners uses pulsed wave ultrasound. This allows measurement of the depth (or range) of the flow site. Additionally, the size of the sample volume (or range gate) can be changed. Pulsed wave ultrasound is used to provide data for Doppler sonograms and color flow images (Bluth EL 2004).

2.2.1 Aliasing

Pulsed wave systems suffer from a fundamental limitation. When pulses are transmitted at a given sampling frequency (known as the pulse repetition frequency), the maximum Doppler frequency fd that can be measured unambiguously is half the pulse repetition frequency. If the blood velocity and beam/flow angle being measured combine to give a fd value greater than half of the pulse repetition frequency, ambiguity in the Doppler signal occurs. This ambiguity is known as aliasing. A similar effect is seen in films where wagon wheels can appear to be going backwards due to the low frame rate of the film causing misinterpretation of the movement of the wheel spokes (Bluth el 2004).

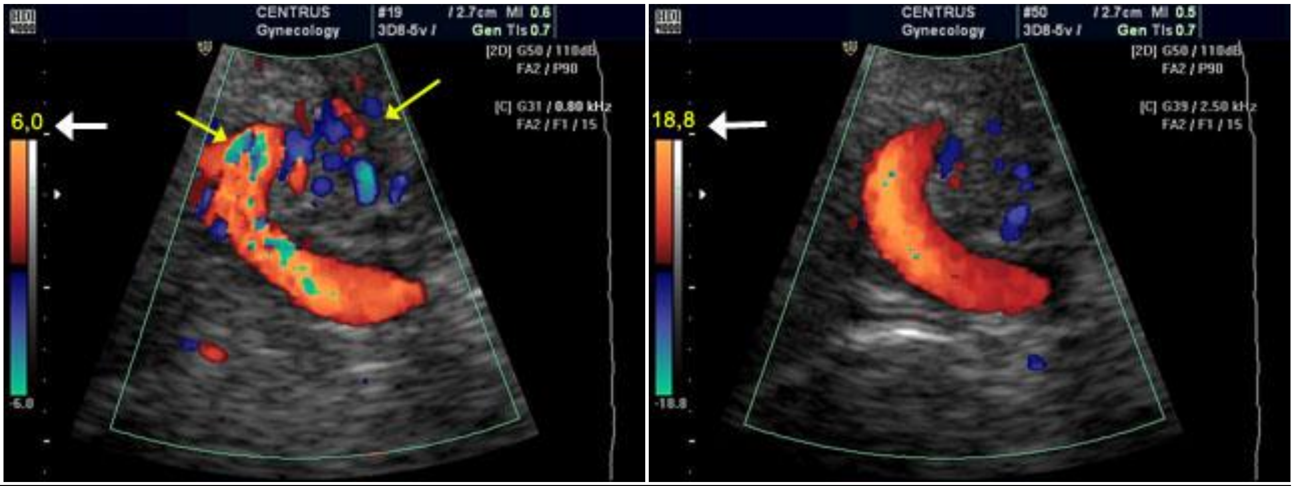


Figure 2.4 : Aliasing of color doppler imaging and artefacts of color. Color image shows regions of aliased flow (yellow arrows). and Reduce color gain and increase pulse repetition frequency

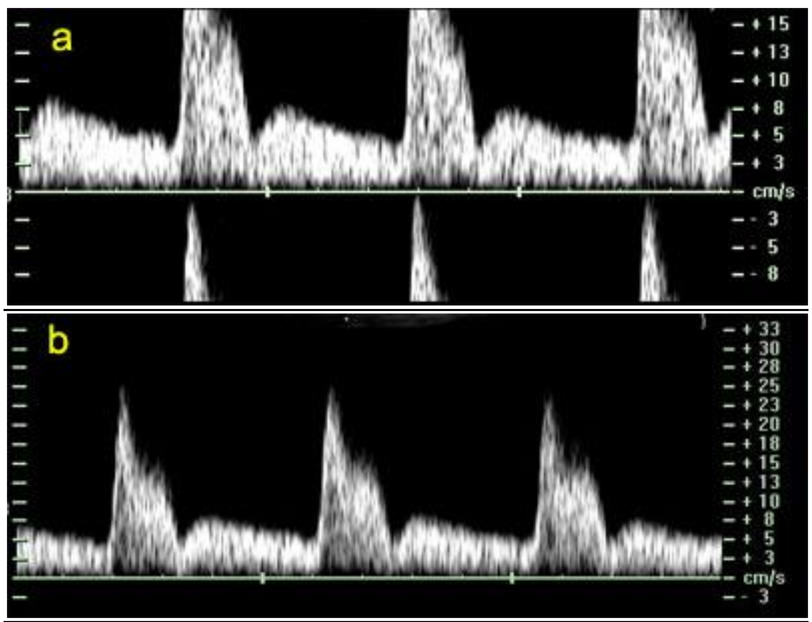


Figure 2.5 (a,b): Example of aliasing and correction of the aliasing. (a) Waveforms with aliasing, with abrupt termination of the peak systolic and display this peaks bellow the baseleineSonogram clear without aliasing. (b) Correction: increased the pulse repetition frequency and adjust baseline (move down)

The pulse repetition frequency is itself constrained by the range of the sample volume. The time interval between sampling pulses must be sufficient for a pulse to make the return journey from the transducer to the reflector and back. If a second pulse is sent before the first is received, the receiver cannot discriminate between the reflected signal from both pulses and ambiguity in the range of the sample volume ensues. As the depth of investigation increases, the journey time of the pulse to and from the reflector is increased, reducing the pulse repetition frequency for unambiguous ranging. The result is that the maximum **fd** measurable decreases with depth (Bluth et al 2004).

Low pulse repetition frequencies are employed to examine low velocities (e.g. venous flow). The longer interval between pulses allows the scanner a better chance of identifying slow flow. Aliasing will occur if low pulse repetition frequencies or velocity scales are used and high velocities are encountered (Figure 1.4, 1.5 and 1.6). Conversely, if a high pulse repetition frequency is used to examine high velocities; low velocities may not be identified.

Figure 2.6 (a,b): Color flow imaging: effects of pulse repetition frequency or scale. (above) The pulse repetition frequency or scale is set low (yellow arrow). The color image shows ambiguity within the umbilical artery and vein and there is extraneous noise. (b) The pulse repetition frequency or scale is set appropriately for the flow velocities (bottom). The color image shows the arteries and vein clearly and unambiguously.

2.3 Ultrasound flow modes

Since color flow imaging provides a limited amount of information over a large region, and spectral Doppler provides more detailed information about a small region, the two modes are complementary and, in practice, are used as such.

Color flow imaging can be used to identify vessels requiring examination, to identify the presence and direction of flow, to highlight gross circulation anomalies, throughout the entire color flow image, and to provide beam/vessel angle correction for velocity measurements. Pulsed wave Doppler is used to provide analysis of the flow at specific sites in the vessel under investigation. When using color flow imaging with pulsed wave Doppler, the color flow/B-mode image is frozen while the pulsed wave Doppler is activated. Recently, some manufacturers have produced concurrent color flow imaging and pulsed wave Doppler, sometimes referred to as *triplex* scanning (Firas et al 2011).

When these modes are used simultaneously, the performance of each is decreased. Because transducer elements are employed in three modes (B-mode, color flow and pulsed wave Doppler), the frame rate is decreased, the color flow box is reduced in size and the available pulse repetition frequency is reduced, leading to increased susceptibility to aliasing.

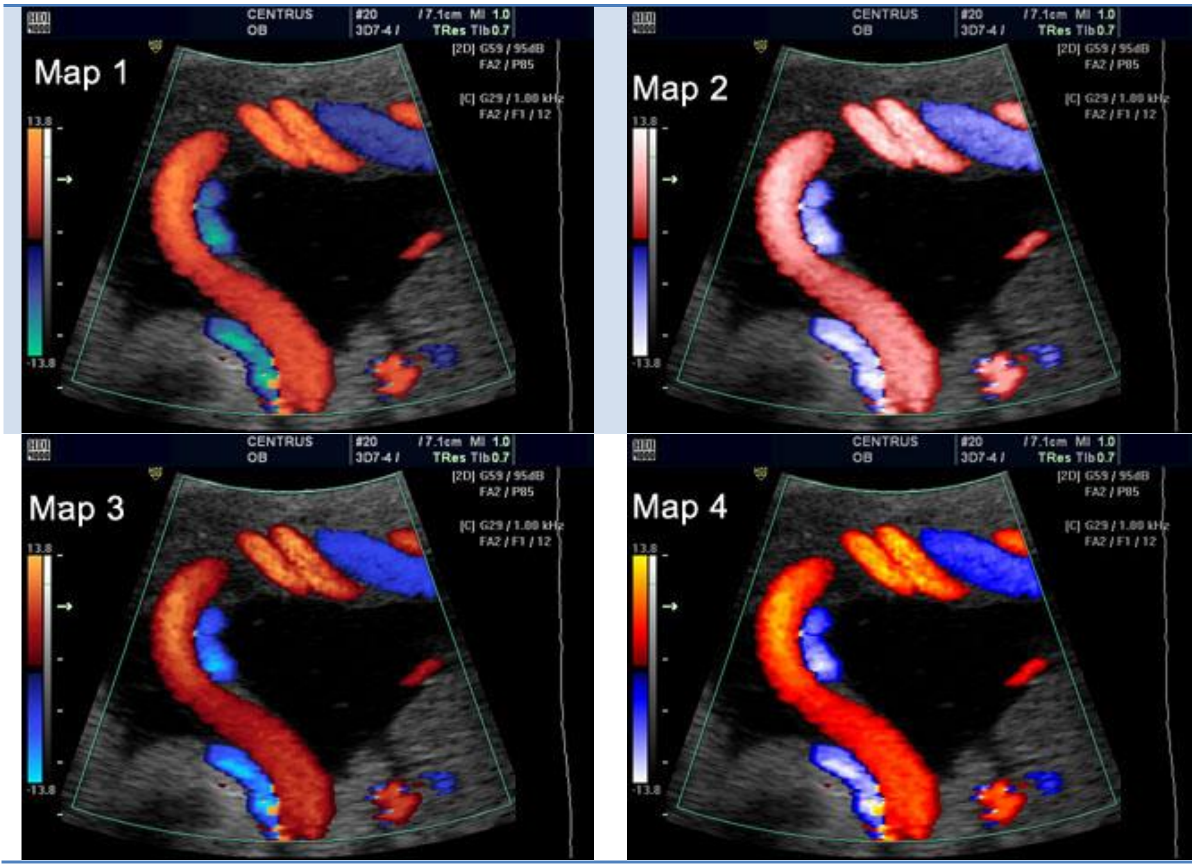
Power Doppler is also referred to as energy Doppler, amplitude Doppler and Doppler angiography. The magnitude of the color flow output is displayed rather than the Doppler frequency signal. Power Doppler does not display flow direction or different velocities. It is often used in conjunction with frame averaging to increase sensitivity to low flows and velocities. It complements the other two modes (Table 1.1). Hybrid color flow modes incorporating power and velocity data are also available from some manufacturers. These can also have improved sensitivity to low flow. A brief summary of factors influencing the displays in each mode is given in the following sections. Most of these factors are set up approximately for a particular mode when the application (e.g. fetal scan) is chosen, although the operator will usually alter many of the controls during the scan to optimize the image.

Table 2.1 - Flow imaging modes
Spectral Doppler
• Examines flow at one site • Detailed analysis of distribution of flow • Good temporal resolution – can examine flow waveform • Allows calculations of velocity and indices

Color flow

- Overall view of flow in a region
- Limited flow information
- Poor temporal resolution/flow dynamics (frame rate can be low when scanning deep)
- color flow map (different color maps)
- direction information
- velocity information (high velocity & low velocity)
- turbulent flows

COLOR FLOW MAPS (DIRECTIONAL)



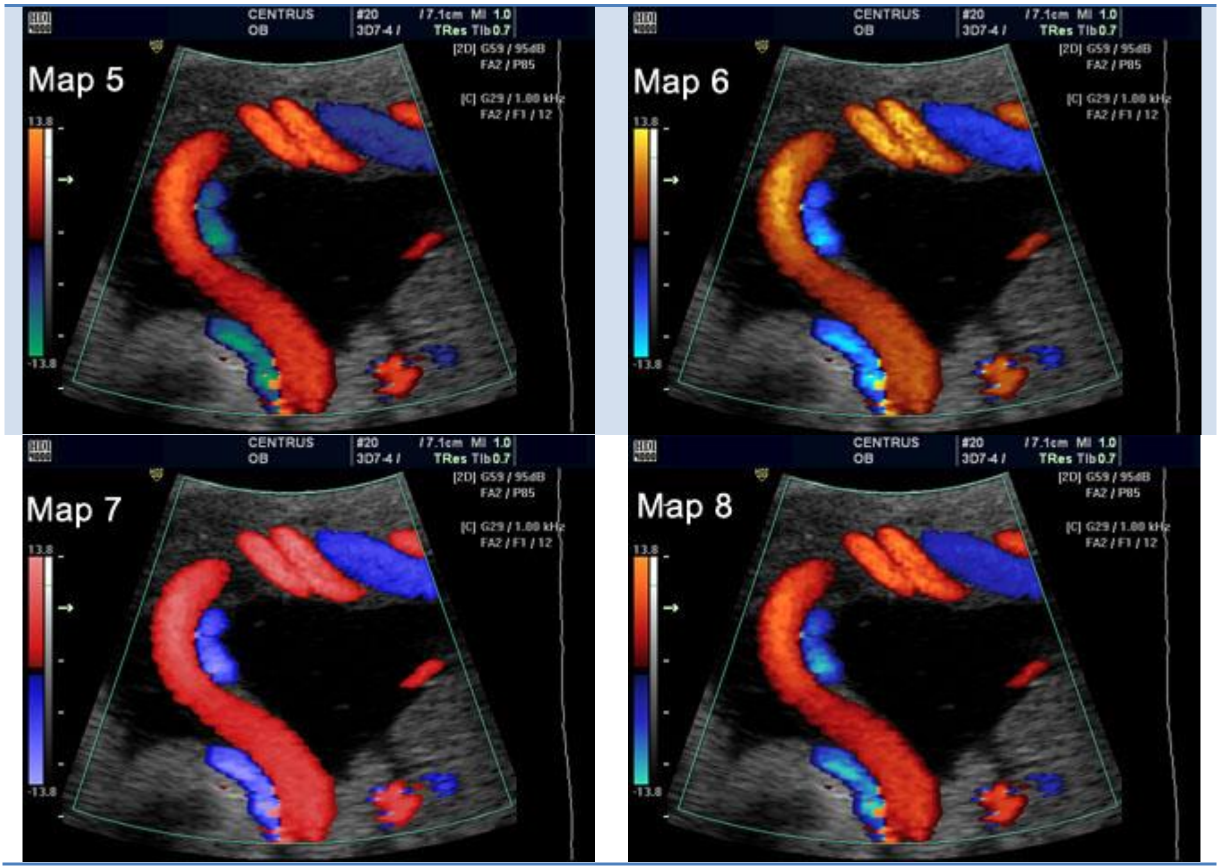


Figure 4.7 show Power/energy/amplitude flow ensitive to low flows

- No directional information in some modes
- Very poor temporal resolution
- Susceptible to noise

Although color flow imaging uses pulsed wave ultrasound, its processing differs from that used to provide the Doppler sonogram. Color flow imaging may have to produce several thousand color points of flow information for each frame superimposed on the B-mode image. Color flow imaging uses fewer, shorter pulses along each color scan line of the image to give a mean frequency shift and a variance at each small area of measurement. This frequency shift is displayed as a color pixel. The scanner then repeats this for several lines to build up the color image, which is superimposed onto the B-mode image. The transducer elements are switched rapidly between B-mode and color flow imaging to give an impression of a combined simultaneous image. The pulses used for color flow imaging are typically three to four times longer than those for the B-mode image, with a corresponding loss of axial resolution (Firas et al 2011).

Assignment of color to frequency shifts is usually based on direction (for example, red for Doppler shifts towards the ultrasound beam and blue for shifts away from it) and magnitude (different color hues or lighter saturation for higher frequency shifts). The color Doppler image is dependent on general Doppler factors, particularly the need for a good beam/flow angle. Curvilinear and phased array transducers have a radiating pattern of ultrasound beams that can produce complex color flow images, depending on the orientation of the arteries and veins. In practice, the experienced operator alters the scanning approach to obtain good insonation angles so as to achieve unambiguous flow images. The controls that affect the appearance of the color flow image are summarized in Table 1.2. The main factors include:

(1) ***Power and gain****:*Color flow uses higher-intensity power than B-mode. Attention should be paid to safety indices. Power and gain should be set to obtain good signal for flow and to minimize the signals from surrounding tissues.

(2) ***Frequency selection****:* Many scanner/transducer combinations permit changes of frequency. High frequencies give better sensitivity to low flow and have better spatial resolution. Low frequencies have better penetration (Figure 1.5) and are less susceptible to aliasing at high velocities.

(3) ***Velocity scale/pulse repetition frequency****:* Low pulse repetition frequencies should be used to examine low velocities but aliasing may occur if high velocities are encountered (Figure 1.7a,b).

(4) *Region of interest:* Because more pulses are needed to look at flow than for the B-mode image, reducing the width and maximum depth of the color flow area under investigation will usually improve frame rate and may allow a higher color scan line density with improved spatial resolution (Figure 1.9).

(5) *Focus:* The focus should be at the level of the area of interest. This can make a significant difference to the appearance and accuracy of the image (Figure 2.7).

Table 2.2 - Factors affecting colour flow image
Main factors
Power: transmitted power into tissue*
Gain: overall sensitivity to flow signals
Frequency: trades penetration for sensitivity and resolution*
Pulse repetition frequency (also called scale): low pulse repetition frequency to look at low velocities, high pulse repetition frequency reduces aliasing*
Area of investigation: larger area reduces frame rate*
Focus: color flow image optimized at focal zone*
Other factors
Triplex color: pulse repetition frequency and frame rate reduced by need for B-mode/spectral pulses
Persistence: high persistence produces smoother image but reduces temporal resolution*
Pre-processing: trades resolution against frame rate*
Filter: high filter cuts out more noise but also more of flow signal*
Post-processing assigns color map/variance*
*Settings appropriate for specific examinations assigned by set-up/application keys

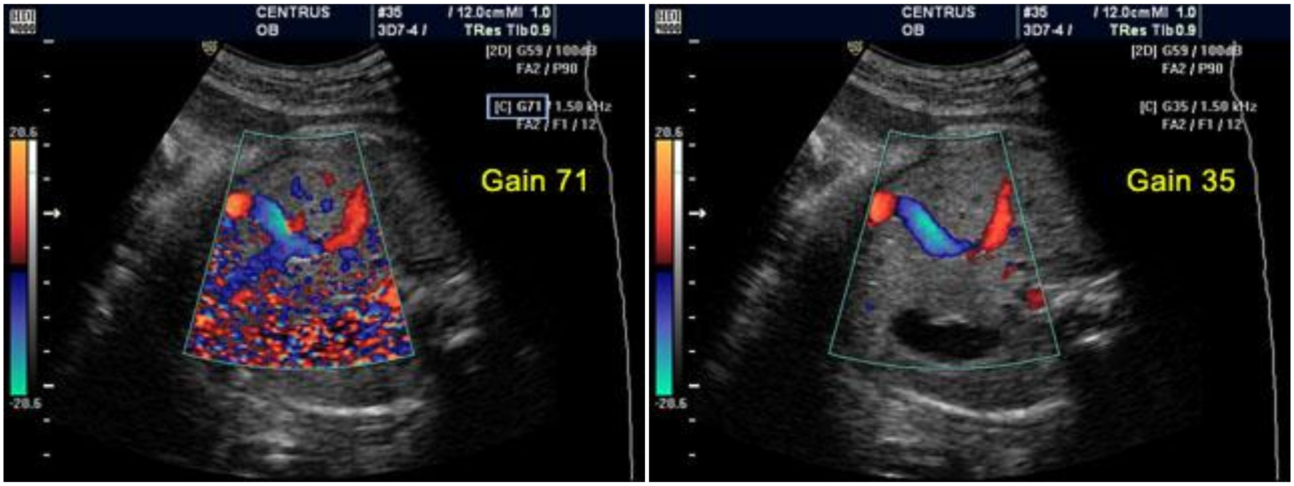


Figure 2.8 : Setting the color gain to minimize the signals (artefacts) from surrondng tissue, on left color gain = 71, then on right decreasing the color gain to 35

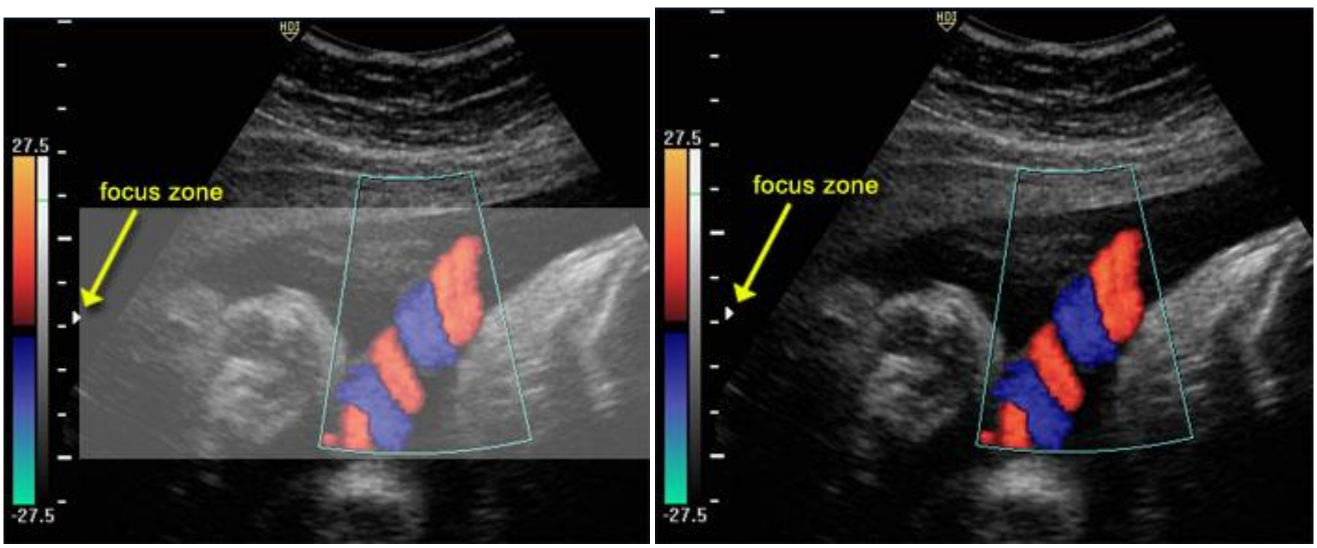


Figure 2.9 : Set the focus at the region of interest, and also could use more than one focal zone.

In practice, the operator will make many changes to the controls and will try different probe positions to optimize the image. Practical guidelines are given in Table 2.3.

Table 2.3: Color flow imaging: practical guidelines
(1) Select the appropriate applications/set-up key. This optimizes parameters for specific examinations
(2) Set power to within fetal study limits. Adjust color gain. Ensure focus is at the region of interest and adjust gain to optimize color signal
(3) Use probe positioning/beam steering to obtain satisfactory beam/vessel angle
(4) Adjust pulse repetition frequency/scale to suit the flow conditions. Low pulse repetition frequencies are more sensitive to low flows/velocities but may produce aliasing. High pulse repetition frequencies reduce aliasing but are less sensitive to low velocities
(5) Set the color flow region to appropriate size. A smaller color flow 'box' may lead to a better frame rate and better color resolution/sensitivity

2.4 Spectral or pulsed wave doppler

Pulsed wave Doppler ultrasound is used to provide a sonogram of the artery or vein under investigation (Figure 2.12). The sonogram provides a measure of the changing velocity throughout the cardiac cycle and the distribution of velocities in the sample volume (or gate) (Figure 2.11). If an accurate angle correction is made, then absolute velocities can be measured. The best resolution of the sonogram occurs when the B-mode image and color image are frozen, allowing all the time to be employed for spectral Doppler. If concurrent imaging is used (real-time duplex or triplex imaging), the temporal resolution of the sonogram is compromised (Firas et al 2011).

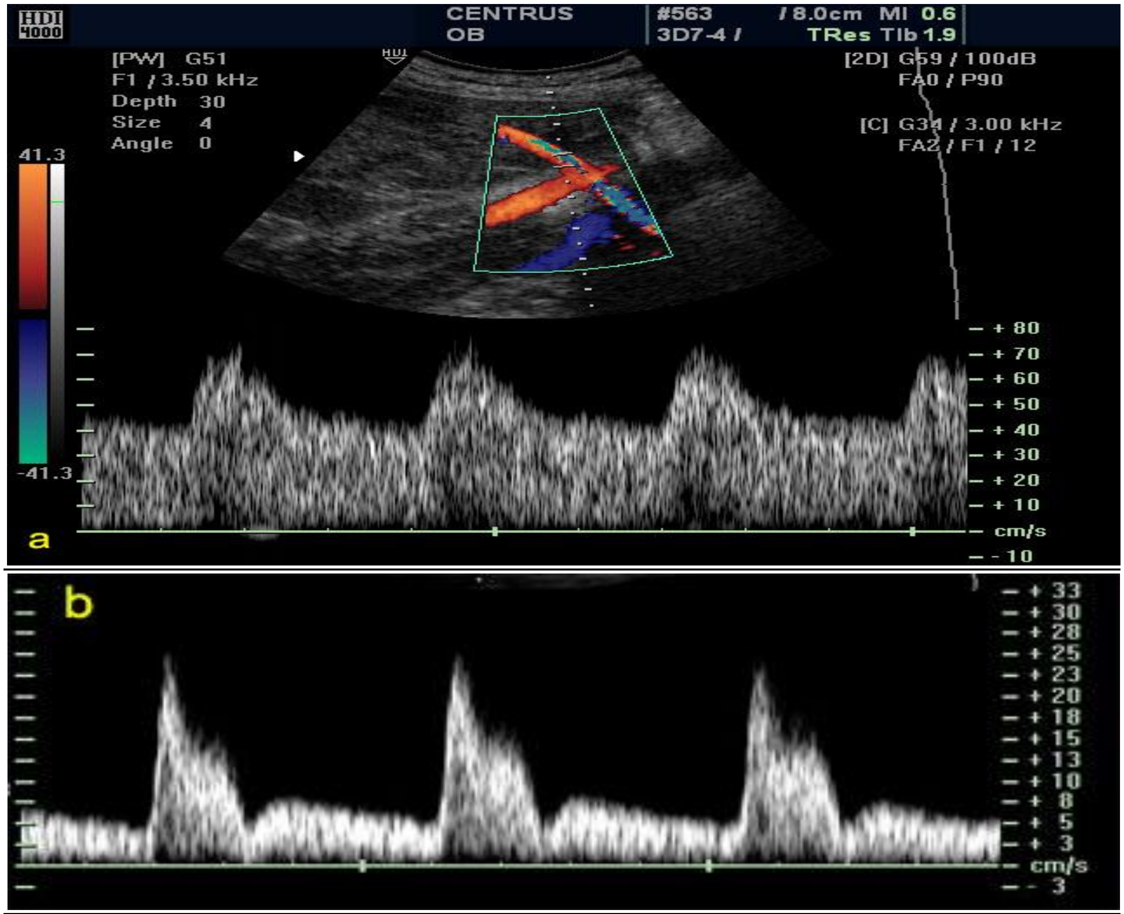


Figure 2.10 (a,b): Doppler spectra of uterine artery flow. (a) The color flow image allows beam/flow angle visualization. The sonogram shows high velocities throughout the cardiac cycle, indicating low distal resistance. (b) The sonogram shows a pulsatile flow waveform with low diastolic velocities. This is indicative of high distal resistance.

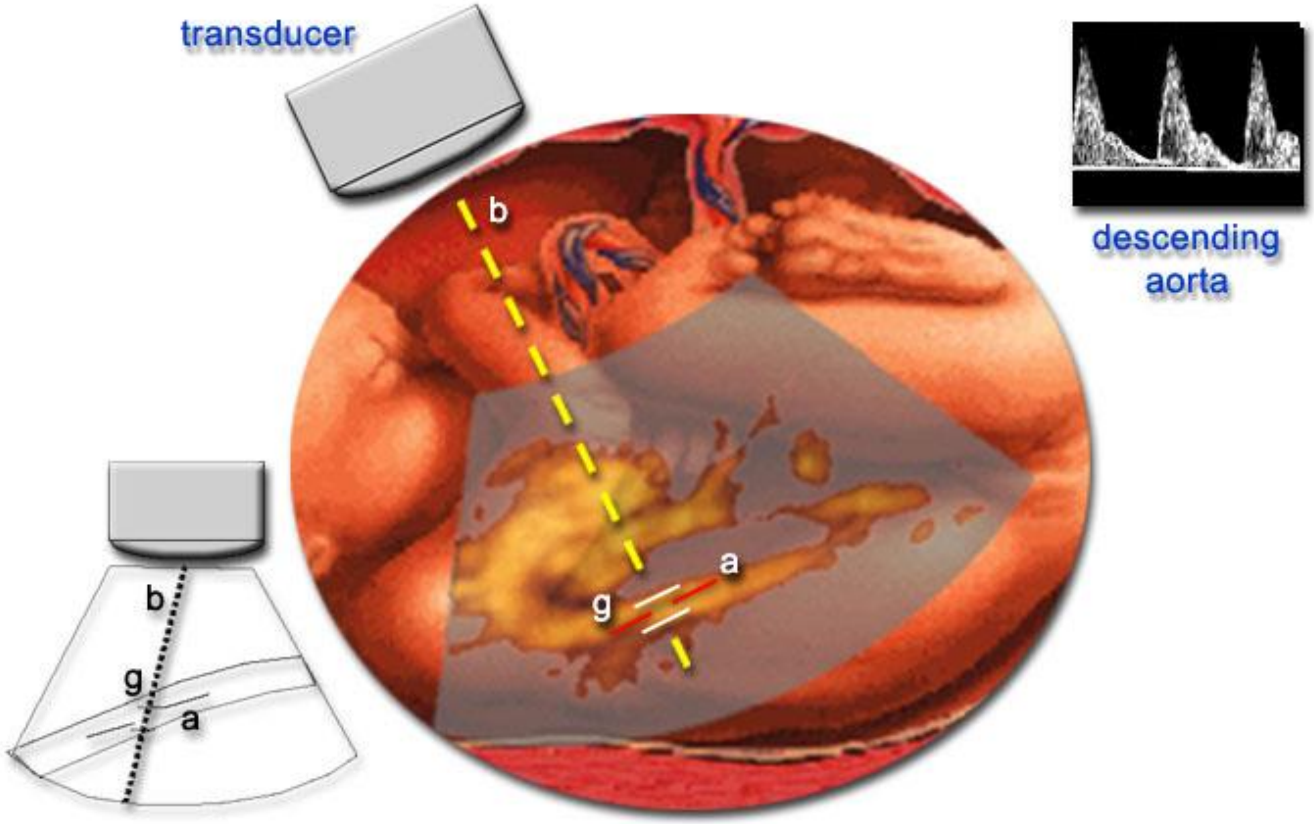


Figure 2.11: Setting up the sample volume ; Sonogram of the descending aorta. With the angle correction the peak velocities could be measured. (b) - direction of the Doppler beam (g)gate or sample volume
(a) angle correction

The controls that affect the appearance of the sonogram are summarized in Table 1.4. The main factors include:

(1) ***Power and gain****:* Pulsed wave Doppler uses higher intensity power than B-mode. Attention should be paid to safety indices. Power and gain should be set so that clear signals are obtained

(2) ***Velocity scale/pulse repetition frequency:*** Low pulse repetition frequencies should be used to look at low velocities but aliasing may occur if high velocities are encountered.

(3) ***Gate size:*** If flow measurements are being attempted, the whole vessel should be insonated. A large gate may include signals from adjacent vessels (Figure 1.13).

Table 2.4 - Factors affecting the spectral Doppler image

Main factors

Power: transmitted power into tissue*

Gain: overall sensitivity to flow signals

Pulse repetition frequency (also called scale): low pulse repetition frequency to look at low velocities, high pulse repetition frequency reduces aliasing*

Gate size*

Beam steering can allow improved beam/flow angle for better accuracy of velocity

calculation*

Live duplex/triplex spectral resolution constrained by need for B-mode/color pulses

Other factors

Gate: sharpness of resolution*

Filter: high filter cuts out more noise but more of flow signal*

Post-processing: assigns brightness to output*

*Settings appropriate for specific examinations assigned by set-up/application keys

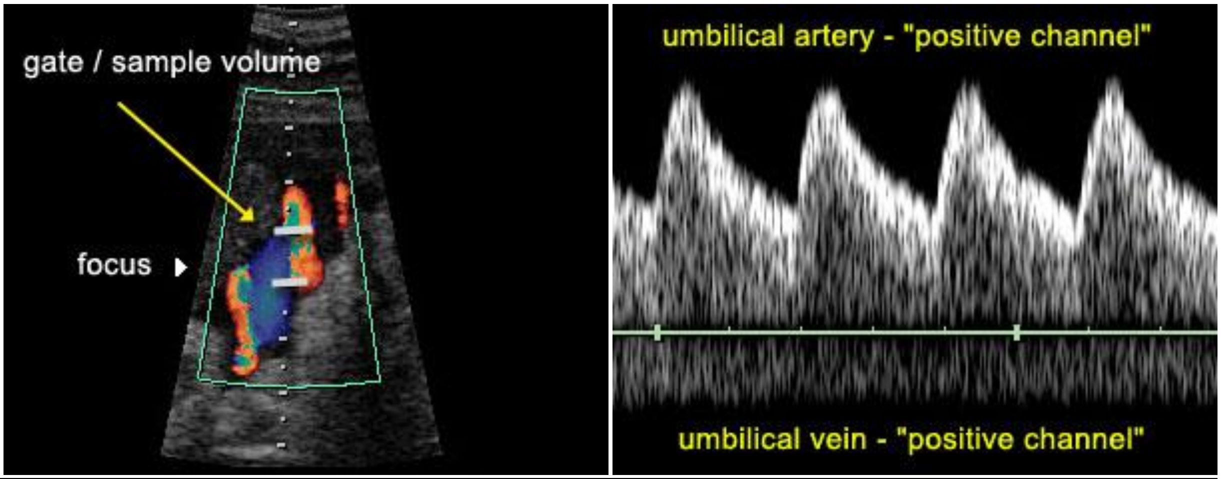


Figure 2.12: Umbilical cord displaying umbilical artery (red) and umbilical vein (blue), the gate or sample volume include both signals (left). Sonogram of the umbilical artery and vein (right). Guidelines for a practical approach to obtain good-quality spectral images are given in Table 2.5 .

Table 2.5: Spectral Doppler imaging: practical guidelines
(1) Set power to within fetal study limits
(2) Position the pulsed wave Doppler cursor on the vessel to be investigated
(3) Adjust gain so that the sonogram is clearly visible and free of noise
(4) Use probe positioning/beam steering to obtain a satisfactory beam/vessel angle. Angles close to 90° will give ambiguous/unclear values. The beam/vessel angle should be 60° or less if velocity measurements are to be made
(5) Adjust the pulse repetition frequency/scale and baseline to suit flow conditions. The sonogram should be clear and not aliased
(6) Set the sample volume to correct size. Correct the angle to obtain accurate velocities. Use the B-mode and color flow image of the vessel to make the angle correction

2.5 Blood Flow Measurements

Velocity Measurement: Theoretically, once the beam/flow angle is known, velocities can be calculated from the Doppler spectrum as shown in the Doppler equation. However, errors in the measured velocity may still occur. Sources of error can be broadly divided into three categories

(1) Errors can arise in the formation of the Doppler spectrum due to:

Use of multiple elements in array transducers; Non-uniform insonation of the vessel lumen; Insonation of more than one vessel; Use of filters removing low-velocity components.

(2) Errors can arise in the measurement of the ultrasound beam/flow velocity angle

Use of high angles ($q > 60^o$) may give rise to error because of the comparatively large changes in the cosine of the angle which occur with small changes of angle (Figure 2.14).

The velocity vector may not be in the direction of the vessel axis.

(3) Errors can arise in the calculation packages provided by the manufacturers for analysis of the Doppler spectrum (for instance, of intensity weighted mean velocity).

While efforts can be made to minimize errors, the operator should be aware of their likely range. It is good practice to try to repeat velocity measurements, if possible using a different beam approach, to gain a feel for the variability of measurements in a particular application. However, even repeated measurements may not reveal systematic errors occurring in a particular machine.

(b) The effort applied to produce accurate velocity measurements should be balanced against the importance of absolute velocity measurements for an investigation

(c) Changes in velocity and velocity waveform shape are often of more clinical relevance when making a diagnosis. In this and other cases, absolute values of velocity measurement may not be required.

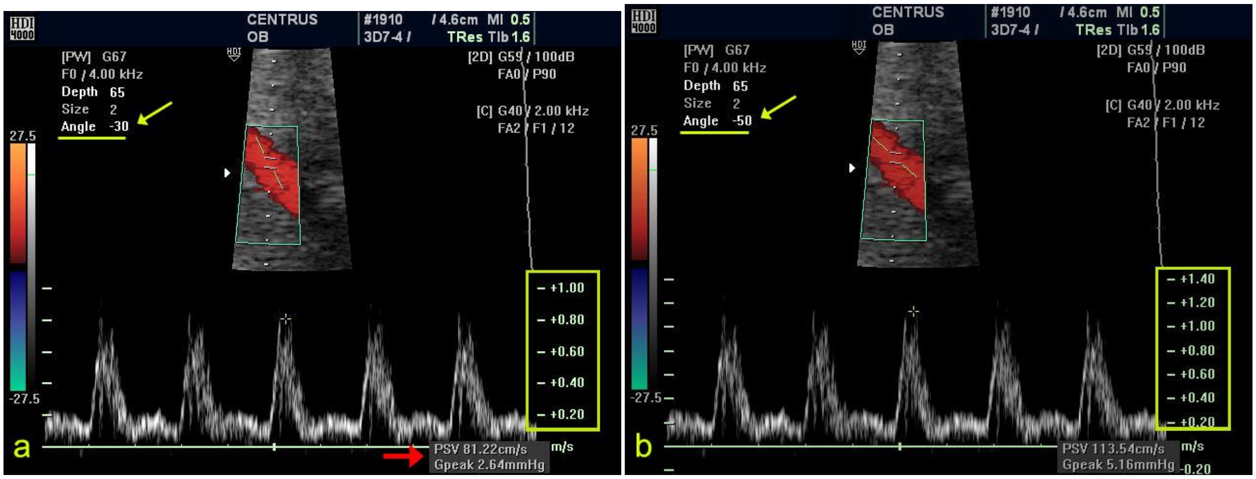


Figure 2.14: Effect of high vessel/beam angles. (a) and (b) A scan of fetal aortic flow is undertaken at a high beam/vessel angle. Beam/flow angles should be kept to to 60° or less. A hudge discrepancy is observed when use unapropiate angles > 60°. If absolute velocities are to be measured, beam/flow angles should be kept to 60° or less.

Calculation of absolute flow: Total flow measurement using color or duplex Doppler ultrasound is fraught with difficulties, even under ideal conditions [5]. Errors that may arise include:

1- Those due to inaccurate measurement of vessel cross-sectional area, for example the cross-sectional area of arteries which pulsate during the cardiac cycle;

2- Those originating in the derivation of velocity (see above).

These errors become particularly large when flow calculations are made in small vessels; errors in measurement of diameter are magnified when the diameter is used to derive cross-sectional area. As with velocity measurements, it is prudent to be aware of possible errors and to conduct repeatability tests (Rothwell PM et al 2000).

Flow wave form analysis: Non-dimensional analysis of the flow waveform shape and spectrum has proved to be a useful technique in the investigation of many vascular beds. It has the advantage that derived indices are independent of the beam/flow angle.

Changes in flow waveform shape have been used to investigate both proximal disease (e.g. in the adult peripheral arterial circulation) and distal changes (in the fetal circulation and uterine arteries). While the breadth of possible uses shows the technique to be versatile, it also serves as a reminder of the range of factors which cause changes to the local Doppler spectrum. If waveform analysis is to be used to observe changes in one component of the proximal or distal vasculature, consideration must be given to what effects other components may have on the waveform (Rothwell PM et al 2000).

Flow wave form shape: Indices of measurement, Many different indices have been used to describe the shape of flow waveforms. Techniques range from simple indices of systolic to diastolic flow to feature extraction methods such as principal component analysis. All are designed to describe the waveform in a quantitative way, usually as a guide to some kind of classification. In general, they are a compromise between simplicity and the amount of information obtained.

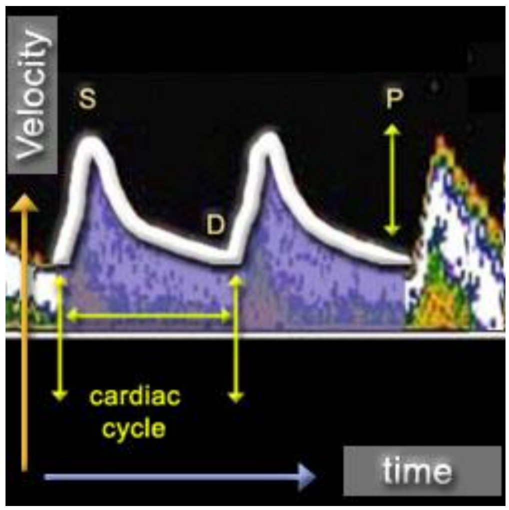


Figure 2.15: Arterial velocity sonogram (waveform)

The relative merits of indices used in uterine arteries have been discussed elsewhere. Commonly used indices available on most commercial scanners are:

(1) Resistance index (RI) (also called resistive index or Pourcelot's index);

(2) Systolic/diastolic (S/D) ratio, sometimes called the A/B ratio;

(3) Pulsatility index (PI).

These indices are all based on the maximum Doppler shift waveform and their calculation is described in Figure 12. The PI takes slightly longer to calculate than the RI or S/D ratio because of the need to measure the mean height of the waveform. It does, however, give a broader range of values, for instance in describing a range of waveform shapes when there is no end-diastolic flow.

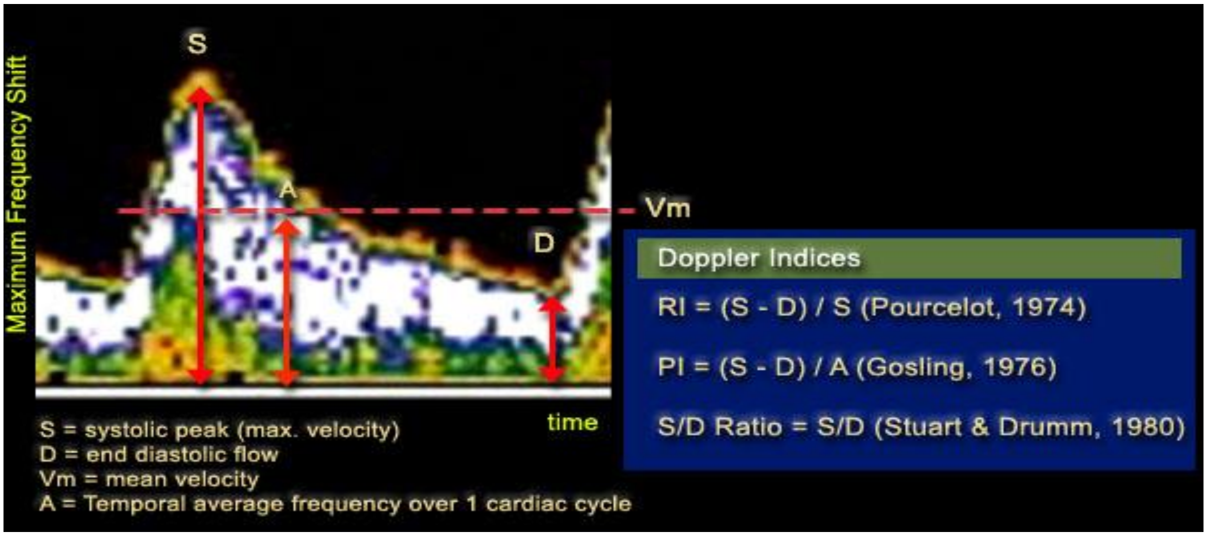


Figure 2.16 - Flow velocity indices

In addition to these indices, the flow waveform may be described or categorized by the presence or absence of a particular feature, for example the absence of end-diastolic flow and the presence of a post-systolic notch (Rothwell PM et al 2000).

Generally, a low pulsatility waveform is indicative of low distal resistance and high pulsatility waveforms occur in high-resistance vascular beds (Figure 1.8), although the presence of proximal stenosis, vascular steal or arteriovenous fistulas can modify waveform shape. Care should be taken when trying to interpret indices as absolute measurements of either upstream or downstream factors. For example, alterations in heart rate can alter the flow waveform shape and cause significant changes in the value of indices.

2.6 Histology of blood vessels

2.6.1 General Concept:

The blood vessels are made of three layers, called from the luminal side outward, the tunica intima, the tunica media and the tunica adventitia. These three layers are analogous to the endo-, myo- and epicardium, respectively. The thickness of these three layers varies greatly depending upon the size and type of vessel (large, medium & small arteries and veins; capillaries). [1]

- The tunica intima consists of an endothelium (present in all vessels) and any subendothelial connective tissue that may be present (highly variable depending on vessel). The endothelium of vessels entering or leaving the heart is continuous with that of the heart.

- The tunica media is the layer of concentrically-arranged smooth muscle, the autonomic control of which can alter the diameter of the vessel and affect the blood pressure. Smooth muscle cells (in contrast to cardiac and skeletal) have secretory capabilities, and (depending on the vessel), the tunica media contains varying amounts of collagen fibres, elastic fibres, elastic lamellae, and proteoglycans secreted by the smooth muscle cells. The tunica media of arteries is larger than that of veins of similar size.
- The tunica adventitia is made chiefly of longitudinally arranged collagen fibres. It tends to be much larger in veins than arteries.

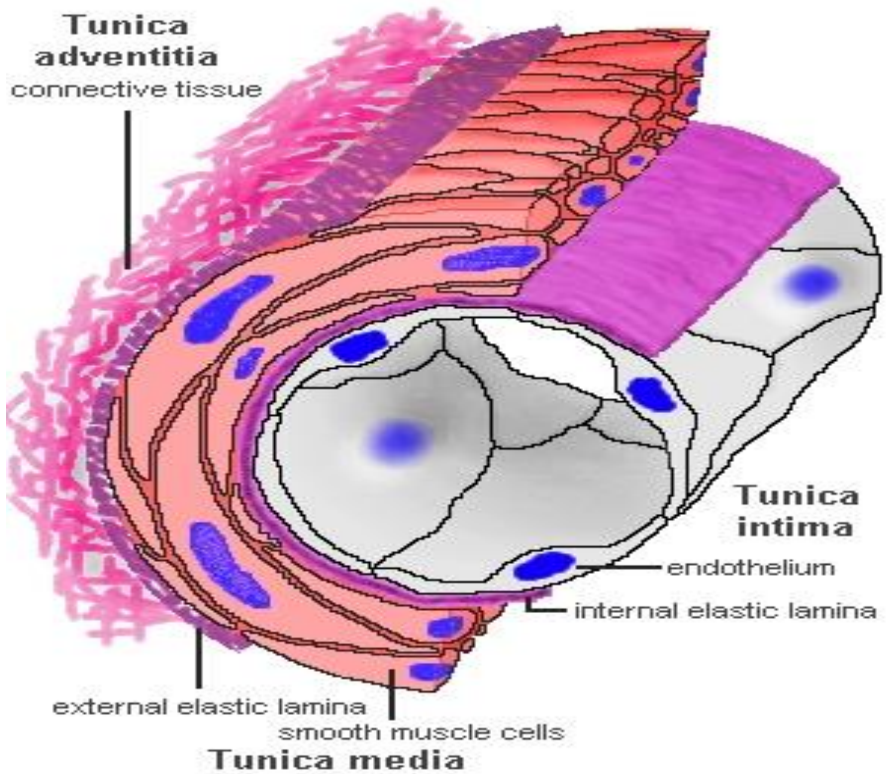


Fig 2.17 Histology of vessels

2.6.2 Intima-Media Thickness

Intima-media thickness (IMT), also called intimal medial thickness, is a measurement of the thickness of tunica intima and tunica media the innermost two layers of the arterial wall.

IMT is used to detect the presence of atherosclerotic disease in humans and more contentiously to track the progression of atherosclerosis. The use of IMT as a non-invasive tool to track changes in arterial walls has increased substantially since the mid-1990s. An increase in IMT is predictive of future cardiovascular disease. Variations in IMT between different locations, such as the inflow side of branches, the inner curvature at bends and opposite the flow divider at bifurcations may reflect differences in local hemodynamic forces. However, an IMT greater than 0.9-1mm is almost certainly are indicative of atherosclerosis and increased risk of cardiovascular disease (Mannami T et al 2004).

2.6.3 Large arteries:

The aorta and its branches (brachiocephalic, subclavian, pulmonary, beginning of common carotid and iliac) are distinguished by their great elasticity. This helps them smooth out the large fluctuations in blood pressure created by the heartbeat. During systole, their elastic laminae are stretched and reduce blood pressure. During diastole, the elastic rebound helps maintain arterial pressure.

- Tunica intima: Large arteries often have a large subendothelial layer, which grows with age or disease conditions (arteriosclerosis). Both connective tissue and smooth muscle are present in the intima. The border of the intima is delineated by the internal elastic membrane. The internal elastic membrane may not be conspicuous because of the abundance of elastic material in the tunica media.
- Tunica media: This is the thickest of the three layers. The smooth muscle cells are arranged in a spiral around the long axis of the vessel. They secrete elastin in the form of sheets, or lamellae, which are fenestrated to facilitate diffusion. The number of lamellae increase with age (few at birth, 40-70 in adult) and with hypertension. These lamellae, and the large size of the media, are the most striking histological feature of elastic arteries. In addition to elastin, the smooth muscle cells of the media secrete reticular and fine collagen fibers and proteoglycans (all not identifiable). No fibroblasts are present.
- Tunica adventitia: This is a relatively thin connective tissue layer. Fibroblasts arethe predominant cell type and many macrophages are also present. Collagen fibres predominate and elastic fibres (not lamellae) are also present. The collagen in the

adventitia prevents elastic arteries from stretching beyond their physiological limits during systole. Blood vessels supplying the adventitia and outer media are also present; these are called vasa vasorum ("vessels of the vessels"). (The inner part of the media is supplied from the lumen via pinocytic transport) (Mannami T et al 2004).

2.6.4 Medium Arteries

The majority of named arteries are medium (muscular or distributive) arteries. There is no sharp dividing line between elastic (large) and muscular (medium) arteries; in areas of transition, arteries may appear as intermediates between the two types. Medium arteries have less elastic tissue than large arteries, the predominant constituent of the tunica media is smooth muscle.

- Tunica intima: The tunica intima is thinner than in large arteries, there are fewer smooth muscle cells and less elastic tissue. The outermost part of the intima is defined by a very prominent internal elastic membrane (not obscured by elastic lamellae as in large arteries). The basement membrane of the endothelium may rest directly on the internal elastic membrane, or be separated by a subendothelial layer of CT. The tunica intima increases in thickness with age, and may also become expanded by lipid deposits.
- Tunica media: Smooth muscle cells predominate in the tunica media, and little elastic material is present. As in large arteries, no fibroblasts are present. Elastic fibres (few), collagen, and ground substance are produced by the smooth muscle cells. These are arranged in a spiral fashion and their contraction helps maintain blood pressure. In tissue preparation, the internal elastic membrane of the intima appears wavy due to the contraction of the smooth muscle of the media.
- Tunica adventitia: The main constituent of the adventitia is collagen fibres, secreted by fibroblasts. Elastic fibres are also present, a concentration of such fibres at the inner boundary of the adventitia is called the external elastic membrane. The external elastic membrane is not as prominent as the internal, and as arteries get smaller (see small arteries, below) disappears much earlier. The tunica adventita is relatively larger than in

elastic arteries, it can be up to the same size as the media. It will often blend in with the CT of surrounding structures. Adipose cells may be present.

2.7 Anatomy:

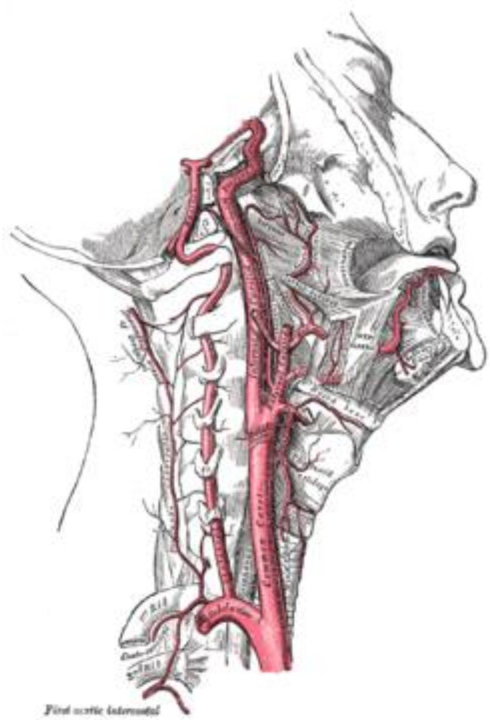


Fig. 2.18 Superficial dissection of the right side of the neck, showing the carotid and subclavian arteries.

The principal arteries of supply to the head and neck are the two common carotids; they ascend in the neck and each divides into two branches, (1) the external carotid, supplying the exterior of the head, the face, and the greater part of the neck; (2) the internal carotid, supplying to a great extent the parts within the cranial and orbital cavities. [3]

The Common Carotid Artery (A. Carotis Communis): the common carotid arteries differ in length and in their mode of origin. 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 to the innominate artery, and therefore consists of a thoracic and a cervical portion (Mannami T et al 2004).

Thoracic 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.

Relations: In front, it is separated from the manubrium sterni by the Sternohyoideus and Sternothyreoideus, the anterior portions of the left pleura and lung, the left innominate vein, and the remains of the thymus; behind, it lies on the trachea, esophagus, left recurrent nerve, and thoracic duct. To its right side below is the innominate artery, and above, the trachea, the inferior thyroid veins, and the 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.

2.8 Cervical Portion:

The cervical portions of the common carotids resemble each other so closely that one description will apply to both (Fig. 3). Each vessel passes obliquely upward, from behind the sternoclavicular articulation, 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 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 (Mannami T et al 2004).

Relations: 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 Sternocleidomastoideus, Sternohyoideus, Sternothyreoideus, 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 Stylohyoideus and posterior belly of the Digastricus, and below by the superior belly of the 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 vertebræ by the Longus colli 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 the 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 recurrent nerve crosses obliquely behind the artery; 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 bifurcation of the common carotid artery is a reddish-brown oval body, known as the glomus caroticum (carotid body). It is similar in structure to the glomus coccygeum (coccygeal body) which is situated on the middle sacral artery.

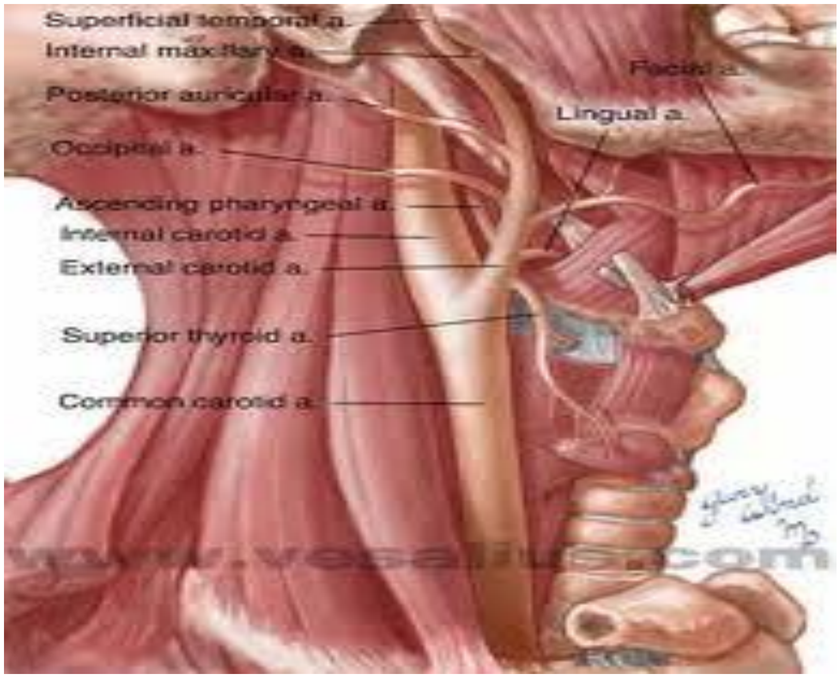


Fig 2.19 Showing the CCA and some of its branches

Peculiarities as to Origin**:** The right common carotid may arise above the level of the upper border of the sternoclavicular articulation; this variation occurs in about 12 per cent. 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 varies 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.

Peculiarities as to Point of Division**:** 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 cricoid cartilage; one case is related by Morgagni, where the artery was only 4 cm. in length and divided at the root of the neck. Very rarely, the common carotid ascends in the neck 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.

Occasional Branches: The common carotid usually gives off no branch previous to its bifurcation, 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.

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 descendens of the occipital; the vertebral takes the place of the internal carotid within the cranium (Mannami T et al 2004).

2.9 Physiology

2.9.1 Functional Morphology

Arteries Arterioles: The characteristics of the various types of blood vessels are listed in the walls of all arteries are made up of an outer layer of connective tissue, the adventitia; a middle layer of smooth muscle, the media; and an inner layer, the intima, made up of the endothelium and underlying connective tissue. The walls of the aorta and other arteries of large diameter contain a relatively large amount of elastic tissue, primarily located in the inner and external elastic laminas. They are stretched during systole and recoil on the blood during diastole. The walls of the arterioles contain less elastic tissue but much more smooth muscle. The muscle is innervated by noradrenergic nerve fibres, which are constrictor in function and in some instances by cholinergic fibers, which dilate the vessels. The arterioles are the major site of the resistance to blood flow, and small changes in their calibre cause large changes in the total peripheral resistance (Bowman TS et al 2005).

Table 2.6. Characteristics of various types of blood vessels in humans.

Vessel	Lumen Diameter	Wall Thickness	All Vessels of Each Type: Approximate Total Cross-Sectional Area (cm^2)	Percentage of Blood Volume Contained[1]
Aorta	2.5 cm	2 mm	4.5	2
Artery	0.4 cm	1 mm	20	8
Arteriole	30 µm	20 µm	400	1
Capillary	5 µm	1 µm	4500	5
Venule	20 µm	2 µm	4000	
Vein	0.5 cm	0.5 mm	40	54
Vena cava	3 cm	1.5 mm	18	

[1] In systemic vessels. There is an additional 12% in the heart and 18% in the pulmonary circulation.

2.9.2Biophysical Considerations

Blood always flows, of course, from areas of high pressure to areas of low pressure, except in certain situations when momentum transiently sustains flow. The relationship between mean flow, mean pressure, and resistance in the blood vessels is analogous in a general way to the relationship between the current, electromotive force, and resistance in an electrical circuit expressed in Ohm's law:

Current (I)= Electromotive Force (E)/Resistance (R)

Flow (F)= Pressure (P)/Resistance (R)Flow in any portion of the vascular system is equal to the **effective perfusion pressure** in that portion divided by the **resistance.** The effective perfusion pressure is the mean intraluminal pressure at the arterial end minus the mean pressure at the venous end. The units of resistance (pressure divided by flow) are dyne·s/cm^5. To avoid dealing with such complex units, resistance in the cardiovascular system is sometimes expressed in **R units,** which are obtained by dividing pressure in mm Hg by flow in mL/s (see also Table 1). Thus, for example, when the mean aortic pressure is 90 mm Hg and the left ventricular output is 90 mL/s, the total peripheral resistance is 90mm Hg/90 mL/^{3}= 1R unit. [4]

Methods for Measuring Blood Flow Blood flow can be measured by cannulating a blood vessel, but this has obvious limitations. Various devices have been developed to measure flow in a blood vessel without opening it. **Electromagnetic flow meters** depend on the principle that a voltage is generated in a conductor moving through a magnetic field and that the magnitude of the voltage is proportionate to the speed of movement. Since blood is a conductor, a magnet is placed around the vessel, and the voltage, which is proportionate to the volume flow, is measured with an appropriately placed electrode on the surface of the vessel. Blood flow velocity can be measured with **Doppler flow meters.** Ultrasonic waves are sent into a vessel diagonally from one crystal, and the waves reflected from the red and white blood cells are picked up by a second, downstream crystal. The frequency of the reflected waves is higher by an amount that is proportionate to the rate of flow toward the second crystal because of the Doppler Effect.

Indirect methods for measuring the blood flow of various organs in humans include adaptations of the Fick and indicator dilution techniques. One example is the use of the Kety N_2O method for measuring cerebral blood flow. Another is determination of the renal blood flow by measuring the clearance of para-aminohippuric acid. A considerable amount of data on blood flow in the extremities has been obtained by plethysmography. The forearm, for example, is sealed in a watertight chamber (plethysmograph). Changes in the volume of the forearm, reflecting changes in the amount of blood and interstitial fluid it contains, displace the water, and this displacement is measured with a volume recorder. When the venous drainage of the forearm is occluded, the rate of increase in the volume of the forearm is a function of the arterial blood flow (venous occlusion plethysmography).

Applicability of Physical Principles to Flow in Blood Vessels

Physical principles and equations that are applicable to the description of the behaviour of perfect fluids in rigid tubes have often been used indiscriminately to explain the behaviour of blood in blood vessels. Blood vessels are not rigid tubes, and the blood is not a perfect fluid but a two-phase system of liquid and cells. Therefore, the behaviour of the circulation deviates, sometimes markedly, from that predicted by these principles. However, the physical principles are of value when used as an aid to understanding what goes on in the body rather than as an end in themselves or as a test of the memorizing ability of students (Bowman TS et al 2005).

2.9.3Laminar Flow

The flow of blood in straight blood vessels, like the flow of liquids in narrow rigid tubes, is normally laminar (streamline). Within the blood vessels, an infinitely thin layer of blood in contact with the wall of the vessel does not move. The next layer within the vessel has a low velocity, the next a higher velocity, and so forth, velocity being greatest in the center of the stream. Laminar flow occurs at velocities up to a certain critical velocity. At or above this velocity, flow is turbulent. Streamline flow is silent, but turbulent flow creates sounds. The probability of turbulence is also related to the diameter of the vessel and the viscosity of the blood. This probability can be expressed by the ratio of inertial to viscous forces as follows:

$$Re = \rho DV/\eta$$

Where Re is the Reynolds number, named for the man who described the relationship; ρ is the density of the fluid; D is the diameter of the tube under consideration; V is the velocity of the flow; and η is the viscosity of the fluid. The higher the value of Re, the greater the probability of turbulence. When D is in cm, ρ is in cm/s^{-1}, and η is in poises, flow is usually not turbulent if Re is less than 2000. When Re is more than 3000, turbulence is almost always present. Laminar flow is disturbed at branching of arteries, but normally not to the point that turbulence is produced. Constriction of an artery increases the velocity of blood flow through the constriction, producing turbulence, and consequently sound, beyond the constriction. Examples are bruits heard over arteries constricted by atherosclerotic plaques and the sounds of Korotkoff heard when measuring blood pressure (see below).

In humans, the critical velocity is sometimes exceeded in the ascending aorta at the peak of systolic ejection, but it is usually exceeded only when an artery is constricted. Turbulence occurs more frequently in anemia because the viscosity of the blood is lower. This may be the explanation of the systolic murmurs that are common in anemia.

Shear Stress & Gene Activation

Flowing blood creates a force on the endothelium that is parallel to the long axis of the vessel. This **shear stress** (γ) is proportionate to viscosity (η) times the shear rate (dy/dr), which is the rate at which the axial velocity increases from the vessel wall toward the lumen.

$$\gamma = \eta(dy/dr)$$

Change in shear stress and other physical variables such as cyclic strain and stretch produce marked changes in the expression of genes in the endothelial cells that are related to cardiovascular function. The receptors are probably integrins attached to the cytoskeleton of the cells. The second messengers are IP_3, DAG, and components of the MAP kinase pathways and the genes that are activated are those that produce growth factors, integrins, and related molecules (Table 2). Over 15 endothelial cell genes have been shown to be activated by various physical forces (Bowman TS et al 2005).

Table 2.8. **Genes in human, bovine, and rabbit endothelial cells that are affected by shear stress, and transcription factors involved.**

Gene	**Transcription Factors**
Endothelin-1	AP-1
VCAM-1	AP-1, NF-$_{K}$B
ACE	SSRE, AP-1, Egr-1
Tissue factor	SP1
Tissue factor	Egr-1
TM	AP-1
PDGF-α	SSRE, Egr-1

PDGF-β	SSRE
ICAM-1	SSRE, AP-1, AP-1, NF-$_{K}$B
TGF-β	SSRE, AP-1, AP-1, NF-$_{K}$B
Egr-1	SREs
c-fos	SSRE
c-jun	SSRE, AP-1
NOS 3	SSRE, AP-1, NF-$_{K}$B
MCP-1	SSRE, AP-1, NF-$_{K}$B
[1] **Modified from Braddock M et al: Fluid shear stress modulation of gene expression in endothelial cells. News Physiol Sci 1998; 13:241.**	

2.9.4Average velocity

When considering flow in a system of tubes, it is important to distinguish between velocity, which is displacement per unit time (eg, cm/s), and flow, which is volume per unit time (eg, cm^3/s). Velocity (V) is proportionate to flow (Q) divided by the area of the conduit (A):

$$V=Q/A$$

Therefore, Q = A×Q, and if flow stays constant, velocity increases in direct proportion to any decrease in A.

The average velocity of fluid movement at any point in a system of tubes in parallel is inversely proportionate to the *total* cross-sectional area at that point. Therefore, the average velocity of the blood is high in the aorta, declines steadily in the smaller vessels, and is lowest in the capillaries, which have 1000 times the *total* cross-sectional area of the aorta. The average velocity of blood flow increases again as the blood enters the veins and is relatively high in the vena cava, although not so high as in the aorta. Clinically, the velocity of the circulation can be measured by injecting a bile salt preparation into an arm vein and timing the first appearance of the bitter taste it produces. The average normal arm-to-tongue circulation time is 15 seconds.

Poiseuille-Hagen Formula

The relation between the flow in a long narrow tube, the viscosity of the fluid, and the radius of the tube is expressed mathematically in the Poiseuille-Hagen formula:

$$F= (P_A-P_B)\times(\pi/8)\times(1/\eta)\times(r^4/L)$$

where;

F= Flow

P_A-P_B= Pressure difference between the two ends of the tube

H- viscosity

R= radius of the tube

L= length of the tube

Since flow is equal to pressure difference divided by resistance (R),

$$R= 8\eta L/\pi r^4$$

Since flow varies directly and resistance inversely with the fourth power of the radius, blood flow and resistance in vivo are markedly affected by small changes in the calibre of the vessels. Thus, for example, flow through a vessel is doubled by an increase of only 19% in its radius; and when the radius is doubled, resistance is reduced to 6% of its previous value. This is why organ blood flow is so effectively regulated by small changes in the calibre of the arterioles and why variations in arteriolar diameter have such a pronounced effect on systemic arterial pressure.

Viscosity & Resistance

The resistance to blood flow is determined not only by the radius of the blood vessels (vascular hindrance) but also by the viscosity of the blood. Plasma is about 1.8 times as viscous as water, whereas whole blood is 3-4 times as viscous as water. Thus viscosity depends for the most part on the hematocrit, i.e., the percentage of the volume of blood occupied by red blood cells. The effect of viscosity in vivo deviates from that predicted by the Poiseuille-Hagen formula. In large vessels, increases in hematocrit cause appreciable increases in viscosity. However, in vessels smaller than 100 um in diameter, i.e., in arterioles, capillaries, and venules, the viscosity change per unit change in hematocrit is much less than it is in large-bore vessels. This is due to a difference in the nature of flow through the small vessels. Therefore, the net change in viscosity per unit change in hematocrit is considerably smaller in the body than it is in vitro. This is why hematocrit changes have relatively little effect on the peripheral resistance except when the changes are large. In severe polycythemia, the increase in resistance does increase the work of the heart. Conversely, in anemia, peripheral resistance is decreased, in part because of the decline in viscosity. Of course, the decrease in hemoglobin decreases the O_2-carrying ability of the blood, but the improved blood flow due to the decrease in viscosity partially compensates for this. Viscosity is also affected by the composition of the plasma and the resistance of the cells to deformation. Clinically significant increases in viscosity are seen in diseases in which plasma proteins such as the immunoglobulins are markedly elevated and in diseases such as hereditary spherocytosis, in which the red blood cells are abnormally rigid. [4]

Velocity & Flow of Blood

Although the mean velocity of the blood in the proximal portion of the aorta is 40 cm/s, the flow is phasic, and velocity ranges from 120 cm/s during systole to a negative value at the time of the transient backflow before the aortic valve closes in diastole. In the distal portions of the aorta and in the large arteries, velocity is also greater in systole than it is in diastole. However, the vessels are elastic, and forward flow is continuous because of the recoil during diastole of the vessel walls that have been stretched during systole. This recoil effect is sometimes called the Windkessel effect, and the vessels are called Windkessel vessels; Windkessel is the German word for an elastic reservoir. Pulsatile flow appears, in some poorly understood way, to maintain optimal function of the tissues. If an organ is perfused with a pump that delivers a nonpulsatile flow, there is a gradual rise in vascular resistance, and tissue perfusion fails (Bowman TS et al 2005).

2.10 Pathology

Although carotid intima-media thickness is strongly associated with atherosclerosis, thickening of the intima-media may not be due to atherosclerosis. Intimal thickening is a complex process, depending on a variety of factors, including blood pressure, local hemodynamics and shear stress (Mannami T 2004).

2.10.1 Atherosclerosis

Atherosclerosis may manifest as coronary heart disease (e.g. angina, myocardial infarction, sudden death), cerebrovascular disease (e.g. stroke and transient ischaemic attack) or peripheral vascular disease (e.g. claudication and critical limb ischaemia). These entities often coexist and the pathogenesis of the disease is similar. Occult coronary artery disease is common in those who present with other forms of atherosclerotic vascular disease, such as intermittent claudication or stroke, and is an important cause of subsequent morbidity and mortality in these patients (Mannami T 2004).

2.10.2 Pathophysiology

Atherosclerosis is a progressive inflammatory disorder of the arterial wall that is characterised by focal lipid-rich deposits of atheroma that remain clinically silent until they become large enough to impair arterial perfusion or until ulceration or disruption of the lesion results in thrombotic occlusion or embolisation of the affected vessel. These mechanisms are common to the entire vascular tree, and the clinical manifestations of atherosclerosis depend upon the site of the lesion and the vulnerability of the organ supplied (Mannami T 2004).

Atherosclerosis is a disorder that begins early in life; abnormalities of arterial endothelial function have been detected among high-risk children and adolescents (e.g. cigarette smokers and those with familial hyperlipidaemia or hypertension), and early atherosclerotic lesions have been found in the arteries of victims of accidental death in the second and third decades of life. Nevertheless, clinical manifestations often do not appear until the sixth, seventh or eighth decade.

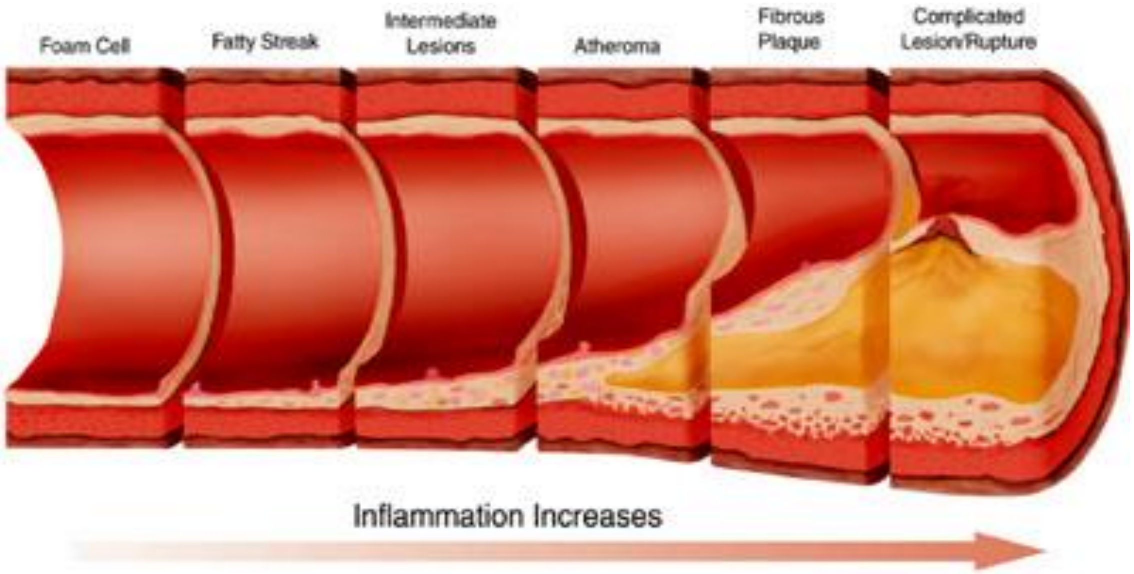


Fig 2.20 Showing the patho-physiology of arteriosclerosis

- Early atherosclerosis

  Fatty streaks tend to occur at sites of altered arterial shear stress, such as bifurcations, and are associated with abnormal endothelial function. They develop when inflammatory cells, predominantly monocytes, bind to receptors expressed by endothelial cells, migrate into the intima, take up oxidised low-density lipoprotein (LDL) from the plasma and become lipid-laden foam cells or macrophages. Extracellular lipid pools appear in the intimal space when these foam cells die and release their contents. In response to cytokines and growth factors produced by the activated macrophages, smooth muscle cells migrate from the media of the arterial wall into the intima, and change from a contractile to a repair phenotype in an attempt to stabilise the atherosclerotic lesion. If they are successful, the lipid core will be covered by smooth muscle cells and matrix, producing a stable atherosclerotic plaque that will remain asymptomatic until it becomes large enough to obstruct arterial flow (Mannami T 2004).

- Advanced Atherosclerosis

  In an established atherosclerotic plaque, macrophages mediate inflammation and smooth muscle cells promote repair; if inflammation predominates, the plaque becomes active or unstable and may be complicated by ulceration and superadded thrombosis.

Cytokines such as interleukin-1, tumour necrosis factor-alpha, interferon-gamma, platelet-derived growth factors and matrix metalloproteinases are released by activated macrophages and may cause the intimal smooth muscle cells overlying the plaque to become senescent, resulting in thinning of the protective fibrous cap; they may also digest collagen cross-struts within the plaque. These changes make the lesion vulnerable to the effects of mechanical stress and may lead to erosion, fissuring or rupture of the plaque surface. Any breach in the integrity of the plaque will expose its contents to circulating blood and may trigger platelet aggregation and thrombosis that extends into the atheromatous plaque and the arterial lumen. This type of plaque event may cause partial or complete obstruction at the site of the lesion and/or distal embolisation resulting in infarction or ischaemia of the affected organ. It is the common mechanism that underlies many of the acute manifestations of atherosclerotic vascular disease (e.g. acute lower limb ischaemia, myocardial infarction and stroke).

The number and complexity of arterial plaques increase with age and with systemic risk factors (see below) but the rate of progression of individual plaques is variable. There is a complex and dynamic interaction between mechanical wall stress and atherosclerotic lesions. 'Vulnerable plaques' are characterised by a lipid-rich core, a thin fibrocellular cap, an increase in inflammatory cells, and the release of specific enzymes that degrade matrix proteins. In contrast, stable plaques are typified by a small lipid pool, a thick fibrous cap, calcification and plentiful collagenous cross-struts. Lipid-lowering therapy may help to stabilise vulnerable plaques. Fissuring or rupture tends to occur at sites of maximal mechanical stress, particularly the margins of an eccentric plaque, and may be triggered by a surge in blood pressure (e.g. during exercise or emotional upset). Surprisingly, plaque events are often subclinical and may heal spontaneously; however, this may allow thrombus to be incorporated into the lesion, producing plaque growth and further obstruction to flow in the arterial lumen.

Atherosclerosis may also induce complex changes in the media that lead to arterial remodelling; thus, some arterial segments may slowly constrict (negative remodelling) whilst others may gradually enlarge (positive remodelling). These changes are poorly understood but are important because they may amplify or minimise the degree to which atheroma encroaches into the arterial lumen (Firas et al 2011).

2.10.3 Risk Factors

The role and relative importance of many risk factors for the development of coronary, peripheral and cerebrovascular disease have been defined in experimental animal studies, epidemiological studies and clinical interventional trials. Some key factors have emerged but do not explain all the risk; thus, unknown or as yet unconfirmed factors may account for up to 40% of the variation in risk of atheromatous vascular disease from one person to the next.

The impact of genetic risk is illustrated by twin studies; for example, a monozygotic twin of an affected individual has an eightfold increased risk, and a dizygotic twin a fourfold increased risk of dying from coronary heart disease compared to the general population.

The effect of risk factors is multiplicative rather than additive. People with a combination of risk factors (e.g. smoking, hypertension and diabetes) are at greatest risk and assessment should therefore be based on a holistic approach that takes account of all identifiable risk factors. It is also important to distinguish between relative risk (the proportional increase in risk) and absolute risk (the actual chance of an event). Thus, a man of 35 with a plasma cholesterol of 7 mmol/l (~170 mg/dl) who smokes 40 cigarettes a day is relatively much more likely to die from coronary disease within the next decade than a non-smoking woman of the same age with a normal cholesterol, but the absolute likelihood of his dying during this time is still small (high relative risk, low absolute risk).

- Age and sex. Age is the most powerful independent risk factor for atherosclerosis. Pre-menopausal women have much lower rates of disease than age- and risk-matched males; however, the gender difference disappears rapidly after the menopause. Randomised controlled trials have demonstrated that hormone replacement therapy has no role in the primary or secondary prevention of coronary heart disease. Indeed, isolated oestrogen therapy appears potentially to cause an increased cardiovascular event rate.

- Family history. Atherosclerotic vascular disease often runs in families. This may be due to a combination of shared genetic, environmental and lifestyle (e.g. smoking, exercise and diet) factors. The most common inherited risk characteristics (hypertension, hyperlipidaemia, diabetes) are polygenic. A 'positive' family history is present when clinical problems in first-degree relatives occur at relatively young age, such as < 50 years for men and < 55 years for women.
- Smoking. Smoking is probably the most important avoidable cause of atherosclerotic vascular disease; there is a strong, consistent and dose-linked relationship between cigarette smoking and ischaemic heart disease.
- Hypertension (see below). The incidence of atherosclerosis increases as blood pressure rises and this excess risk is related to both systolic and diastolic blood pressure as well as pulse pressure. Antihypertensive therapy has been shown to reduce coronary mortality, stroke and heart failure.
- Hypercholesterolaemia. Robust epidemiological data demonstrate that the risk of coronary heart disease and other forms of atherosclerotic vascular disease rises with plasma cholesterol concentration, and in particular the ratio of total cholesterol to high-density lipoprotein (HDL) cholesterol. A much weaker correlation also exists with plasma triglyceride concentration. Extensive large-scale randomised trials have shown that lowering total LDL and cholesterol concentrations reduces the risk of cardiovascular events including death, myocardial infarction and stroke, and also reduces the need for revascularisation.
- Diabetes mellitus. This is a potent risk factor for all forms of atherosclerosis and is often associated with diffuse disease that is difficult to treat. Insulin resistance (normal glucose homeostasis with high levels of insulin) is associated with obesity and physical inactivity, and is also a potent risk factor for coronary heart disease. Glucose intolerance accounts for a major part of the high incidence of ischaemic heart disease in certain ethnic groups, e.g. South Asians.

- Haemostatic factors. Platelet activation and high levels of fibrinogen are associated with an increased risk of coronary thrombosis. Anti-phospholipid antibodies are associated with recurrent arterial thromboses.
- Physical activity. Physical inactivity roughly doubles the risk of coronary heart disease and is a major risk factor for stroke. Regular exercise (brisk walking, cycling or swimming for 20 minutes two or three times a week) appears to have a protective effect which may be related to increased HDL cholesterol, lower blood pressure, reduced blood clotting, and collateral vessel development.
- Obesity. Obesity, particularly if central or truncal, is an independent risk factor, although it is often associated with other adverse factors such as hypertension, diabetes and physical inactivity.
- Alcohol. A moderate intake of alcohol (2-4 units a day) appears to offer some protection from coronary disease; however, heavy drinking is associated with hypertension and excess cardiac events.
- Other dietary factors. Diets deficient in fresh fruit, vegetables and polyunsaturated fatty acids are associated with an increased risk of vascular disease. Low levels of vitamin C, vitamin E and other antioxidants may enhance the production of oxidised LDL. Hyperhomocysteinaemia is associated with accelerated atherosclerosis including stroke and peripheral vascular disease. Low dietary folate, vitamin B_{12} and vitamin B_6 can elevate homocysteine concentrations.
- Personality. Certain personality traits are associated with an increased risk of coronary disease. Nevertheless, there is little or no evidence to support the popular belief that stress is a major cause of coronary artery disease (Bluth et al 2004).

2.10.3 Hypertension

Aetiology: In about 5% of unselected cases, hypertension can be shown to be a consequence of a specific disease or abnormality leading to sodium retention and/or peripheral vasoconstriction. In more than 95% of cases, a specific underlying cause of hypertension cannot be found. Such patients are said to have essential hypertension.

Pathogenesis: The pathogenesis of essential hypertension is not clearly understood. Different investigators have proposed the kidney, the peripheral resistance vessels and the sympathetic nervous system as the seat of the primary abnormality. In reality the problem is probably multifactorial. Hypertension is more common in some ethnic groups, particularly Black Americans and Japanese, and approximately 40-60% is explained by genetic factors. Important environmental factors include a high salt intake, heavy consumption of alcohol, obesity, lack of exercise and impaired intrauterine growth. There is very little evidence that 'stress' causes hypertension**(Bluth et al 2004).**

Definition of Hypertension

Table 2.8 Showing the types of HTN

Category	**Diastolic blood pressure (mmHg)**
Optimal	< 80
Normal	< 85
High normal	85-89
Grade 1 (mild)	90-99
Grade 2 (moderate)	100-109
Grade 3 (severe)	≥110
Grade 1	< 90
Grade 2	< 90

Exercise, anxiety, discomfort and unfamiliar surroundings can all lead to a transient rise in BP. Sphygmomanometry, particularly when performed by a doctor, can cause an unrepresentative surge in BP which has been termed 'white coat' hypertension, and as many as

20% of patients with apparent hypertension in the clinic may have a 'normal BP' when it is recorded by automated devices used in their own home. The risk of cardiovascular disease in these patients is less than that observed in patients with sustained hypertension but greater than that seen in normotensive subjects.

Adverse Effects: The adverse effects of hypertension principally involve the blood vessels, central nervous system, retina, heart and kidneys, and caDn often be detected clinically.

In larger arteries (over 1 mm in diameter) the internal elastic lamina is thickened, smooth muscle is hypertrophied and fibrous tissue is deposited. The vessels dilate and become tortuous and their walls become less compliant. In smaller arteries (under 1 mm) hyaline arteriosclerosis occurs in the wall, the lumen narrows and aneurysms may develop. Widespread atheroma develops and may lead to coronary and/or cerebrovascular disease, particularly if other risk factors (e.g. smoking, hyperlipidaemia, diabetes) are present.

These structural changes in the vasculature often perpetuate and aggravate hypertension by increasing peripheral vascular resistance and reducing renal function.

Hypertension is also implicated in the pathogenesis of aortic aneurysm and aortic dissection (Bluth et al 2004).

2.11 Previous Study:

Javad Alizargar et l 2018 Background and objectives: Hypertension (HTN) is an important risk factor for cardiovascular diseases. High blood pressure is a major cause of atherosclerosis which leads to myocardial infarction and stroke. Insulin resistance (IR) is correlated with HTN and atherosclerosis. To determine differences between the effects of HTN on the intima media thicknesses (IMTs) of the internal (ICA), external (ECA), and common carotid arteries (CCA), and evaluate the carotid plaque presence between hypertensive and normotensive individuals, a case-control study was designed among community-dwelling individuals. The relationship between the triglyceride glucose (TyG) index and atherosclerosis was also investigated in this study. Materials and Methods: Data from 77 hypertensive and 199 normotensive individuals were analyzed in this study. Results: The IMTs of the CCA, ICA, and ECA, and the TyG index were all higher in hypertensive individuals compared to the control group (all $p < 0.05$). After controlling for age, sex, the body-mass index, and TyG index, HTN was an independent predictor of a high CCA IMT (odds ratio (OR) = 2.48; 95% confidence interval (CI) = 1.24–4.93) and presence of plaque (OR = 2.36; CI = 1.15–4.85) in the carotid artery. Conclusions: HTN was an independent risk of carotid IMT thickening and atherosclerosis. TyG index could only predict the CCA IMT independent of other risk factors (OR = 2.09; CI = 1.07–4.09).

Xianglin Chi et al 2017 Objectives: This study aimed to investigate the relationship between the presence of carotid arteriosclerosis (CAS) and blood pressure variability (BPV) in patients with essential hypertension. Methods: One hundred and forty-four essential hypertension patients underwent ambulatory BP monitoring for 24 h after hospitalization. Common BPV metrics were calculated. General clinical parameters, including age, gender, height, weight, history of coronary heart disease, stroke, diabetes, hypertension, smoking and drink, were recorded. Biochemical indices were obtained from a blood test. Carotid intima-media

thickness (IMT) and carotid plaques were assessed to separate patients into a non-CAS group (IMT=0.9 mm; n=82) and a CAS group (IMT > 0.9 mm; n=62). BPV metrics and clinical parameters were analyzed and compared between the two groups. Multivariate logistic regression analysis was performed to determine the associated risk factors of CAS.
Results: Multivariate logistic regression analysis revealed that two BPV metrics, the standard deviation of daytime systolic blood pressure (SSD) (OR: 1.587, 95%CI: 1.242–2.028), the difference between average daytime SBP and nighttime SBP (OR: 0.914, 95%CI: 0.855–0.977), as well as three clinical parameters (age, OR: 1.098, 95%CI: 1.034–1.167; smoking, OR: 4.072, 95%CI: 1.466–11.310, and fasting blood glucose, OR: 2.029, 95%CI: 1.407–2.928), were significant factors of CAS in essential hypertension patients. Conclusion: SSD, in combination with the ageing, smoking and FBG, has been identified as risk factors for CAS in patients with essential hypertension.

Merwyn Fernandes et al 2016 Aims and Objectives: Cerebral ischemic stroke is life-threatening and debilitating neurological disease, it is the third leading cause of death in the world. Studies have shown that there is a close relationship between carotid artery stenosis and ischemic cerebral vascular disease. This study is done to assess the carotid arteries with the help of color Doppler sonography and to correlate cerebrovascular accidents. Materials and Methods: The prospective study was carried out on 50 patients using purposive sampling technique. Risk factors such as hypertension, diabetes mellitus, smoking, and family history were documented. The data gathered from color Doppler examination consisted of peak systolic velocity of common carotid artery (CCA) and internal carotid artery (ICA), velocity ratios between CCA and ICA and plaque characteristics as seen on real-time image. Statistical Analysis Used: The collected data were analyzed and presented in the form of tables, figures, graphs, and diagrams wherever necessary. As this study deals with the only frequency distribution of various factors, so no tests of significance were applied. Results: The highest incidence of stroke was found in the male population in the age group of 60–69 years. Various risk factors included hypertension, diabetes mellitus, smoking, and family history. Of 50 patients, 12 patients showed significant stenosis (>60%). Atherosclerotic plaques were seen in 39 patients (78%). Conclusion: Color Doppler examination is an economic, safe, reproducible, and less time-consuming method of demonstrating the cause of cerebrovascular insufficiency in extracranial carotid artery system and will guide in instituting treatment modalities.

Shao-Yuan Chuang et al 2016 *Background and Purpose*—High blood pressure is a major cause of cardiovascular events, and carotid flow pulsatility may be associated with cardiovascular events. However, the combined effect of blood pressure and flow pulsatility on the development of stroke remains unclear. Therefore, we investigated the combined influence of central blood pressure and pulsatility index (PI) on the incidence of stroke.

Methods—Baseline data from 2033 adults (=30 years) without stroke history in the Cardiovascular Disease Risk Factor Two-Township Study were linked to incident stroke. Common carotid flow PI was calculated by peak systolic velocity, end-diastolic velocity, and mean vessel velocity, which were measured in the common carotid artery. Hazard ratios for the risk of total stroke resulting from high central systolic blood pressure (CSBP) and high PI were calculated with Cox proportional hazard models.

Results Over a median follow-up of 9.81 years, 132 people incurred stroke events. The incidence rates of stroke were 1.3, 6.4, and 13.2 per 1000 person-years for tertile groups of CSBP (*P* for trend<0.05) and 4.3, 7.0, and 9.4 per 1000 personyears for tertile groups of PI (*P* for trend<0.05). Compared with the first tertile of CSBP, hazard ratios were 4.88 (95% confidence interval, 2.29–10.43) for the second tertile and 10.42 (5.05–21.53) for the third tertile. Hazard ratios of PI Were 2.18 (1.39–3.42; third tertile) and 1.64 (1.02–2.63; second tertile) compared with the first tertile. The individuals with a high CSBP and high PI had a 13-fold higher stroke risk compared with those with low CSBP and low PI (13.2;1.75–99.71) after adjusting for age, sex, and traditional cardiovascular risk. *Conclusions*—CSBP and common carotid PI jointly and independently predicted future stroke. Carotid flow pulsatility may play an important role in the development of stroke.

Basil N. Okeahialam et al 2011 As part of a larger study of cardiovascular risk factors in nonhypertensive type 2 diabetes patients, we subjected a cohort of diabetics to B mode ultrasonography of the carotid artery to measure the intima media thickness (IMT) and compared it with values in hypertensives and apparently normal controls matched reasonably for gender and age. All groups were comparable in terms of age and gender representation. The mean (SD) of carotid IMT right and left was 0.94 mm (0.12), 0.94 mm (0.16); 0.93 mm (0.21), 0.93 mm (0.15); 0.91 mm (0.17), 0.91 mm (0.13) for diabetic, hypertensive, and normal groups, respectively. There was a nonsignificant tendency to raised IMT for the disease groups from the normal ones. Diabetic and hypertensive Nigerians are equally burdened by cardiovascular disease risk factors. Apparently normal subjects have a reasonable degree of burden suggesting the need to evaluate them for other traditional and emerging risk factors.

David H. Evans et al 2011 Ultrasonic colour Doppler is an imaging technique that combines anatomical information derived using ultrasonic pulse-echo techniques with velocity information derived using ultrasonic Doppler techniques to generate colour-coded maps of tissue velocity superimposed on grey-scale images of tissue anatomy. The most common use of the technique is to image the movement of blood through the heart, arteries and veins, but it may also be used to image the motion of solid tissues such as the heart walls. Colour Doppler imaging is now provided on almost all commercial ultrasound machines, and has been found to be of great value in assessing blood flow in many clinical conditions. Although the method for obtaining the velocity information is in many ways similar to the method for obtaining the anatomical information, it is technically more demanding for a number of reasons. It also has a number of weaknesses, perhaps the greatest being that in conventional systems, the velocities measured and thus displayed are the components of the flow velocity directly towards or away from the transducer, while ideally the method would give information about the magnitude and direction of the three-dimensional flow vectors. This review briefly introduces the principles behind colour Doppler imaging and describes some clinical applications. It then describes the basic components of conventional colour Doppler systems and the methods used to derive velocity information from the ultrasound signal. Next, a number of new techniques that seek to overcome the vector problem mentioned above are described. Finally, some examples of vector velocity images are presented.

Hamid R. Tahmasebpour, et al 2005 Ultrasonography (US) of the carotid arteries is a common imaging study performed for diagnosis of carotid artery disease. In the United States, carotid US may be the only diagnostic imaging modality performed before carotid endarterectomy. Therefore, the information obtained with carotid US must be reliable and reproducible. Technical parameters that can affect the accuracy of carotid US results include the Doppler angle, sample volume box, color Doppler sampling window, color velocity scale, and color gain. Important factors in diagnosis of atherosclerotic disease of the extracranial carotid arteries are the intima-media thickness, plaque morphology, criteria for grading stenosis, limiting factors such as the presence of dissection or cardiac abnormalities, distinction between near occlusion and total occlusion, and the presence of a subclavian steal. Challenges to the consistency of carotid US results may include lack of a standard protocol, poor Doppler technique, inexperience in interpretation of hemodynamic changes reflected in the Doppler waveform, artifacts, and physical challenges. Hindrances in the classification of problematic carotid artery stenoses may be overcome by following a standard protocol and optimizing scanning techniques and Doppler settings.

Ta-Chen Su, et al 2001 Background and Purpose—Extracranial carotid artery (ECCA) atherosclerosis has been associated with hypertensionrelated stroke. The present study was aimed at investigating the determinants of ECCA atherosclerosis in patients with hypertension in Taiwan. Methods: The extent and severity of ECCA atherosclerosis were measured by high-resolution B-mode ultrasonography and expressed as maximal intima-media thickness (IMT) of the common carotid artery, ECCA plaque score, and carotid stenosis $50%. From July through December 1996, 263 hypertensive patients (146 with hypertension and 117 with borderline hypertension) and 270 normotensive adults from the Chin-Shan Community Cardiovascular Cohort participated in this study. Risk factors and ECCA atherosclerosis were stratified by the blood pressure status.

Results—A significant dose-response relationship was found between the status of hypertension and the severity of carotid atherosclerosis. Multivariate logistic regression models revealed that hypertension (including borderline), male gender, smoking, and age $65 years significantly increased the risk of thicker IMT. The risk of ECCA plaque score .6 increased significantly in conjunction with hypertension, age $65 years, left ventricular hypertrophy on ECG, and smoking. However, hypertension and smoking were the 2 evident determinants of carotid stenosis $50% after adjustment for other covariates. Compared with the normotensive subjects, the ORs (and 95% CIs) for the hypertensive patients to develop carotid atherosclerosis were 5.0 (3.0 to 8.4) indexed by maximal common carotid artery IMT $75th percentile, 3.7 (1.8 to 7.9) by ECCA score .6, and 4.8 (1.4 to 16.5) by carotid stenosis $50%. Conclusions—Hypertension strongly influence carotid atherosclerosis. Our findings reinforce the hypothesis that hypertension has a major role in the pathogenesis of atherosclerosis.

Rajesh Sharma et al 2001 The current observational study was conducted to evaluate the morphology of extracranial parts of carotid arteries by colour doppler in patients of stroke and to assess the peak systolic velocity ratio of internal carotid artery/common carotid artery and its utility in diagnosis of the carotid arterial disease. Duplex ultrasound is an inexpensive, non-invasive method that can provide functional and anatomical information about vessel stenosis and plaque morphology. It is a sensitive method for detection of atherosclerotic plaque and provides considerable information about the extent and severityof plaque as well as the resulting diminution of arterial lumen.The study of Colour Doppler of carotid arteries was carried on 35 patients presenting with stroke. The data gathered included grey scale and Doppler findings of common carotid, internal carotid and external carotid arteries. In this study, the commonest lesion found was the atherosclerotic plaque. Most common risk factor for increased intima -media thickness of carotid vessel is found in patients with history of smoking > 10 years. Atheromatous plaque was most commonly found in the left carotid and bilateral system

Luigi Lusiani et al 1989 We noninvaslvely evaluated the prevalence and severity of atherosclerotic lesions of the internal carotid artery in 146 nonobese, nondiabetic hypertensive patients who were free of cardiovascular symptoms. We found internal carotid artery disease in 63 patients (43%), 26 (18%) with unilateral disease and the other 37 (25%) with bilateral disease. Disease severity was correlated with age but not duration of hypertension, cholesterol level, or current smoking habit We also followed disease progression and clinical outcome with respect to cardiovascular events for 3 years in a subgroup of 95 unselected patients. In 20 of the 93 survivors (21.5%) we noted progression of the atherosclerotic lesions that was predicted by neither risk factors nor initial status of the internal carotid artery. New neurologic symptoms developed in four survivors (4%) and symptoms of cardiac ischemia in six (6%). No survivor who developed new cerebrovascular symptoms showed progression of carotid disease. These data provide useful elements for a rational approach to prevention of the atherosclerotic complications of hypertension.

Chapter Three

Material and Methods

3.1 Material:

Equipment (General Electric- LOGIQ Bool XP ultrasound machine& convex (1-5 MHZ) ultrasound probes- pulsed Doppler transducer 2MHZ).

TCD machine: Color Transcranial Doppler system.

3.2 Study Design:

It was prospective study where the patient selected conventionally done to determine the potential patient for hypertensive for adult patients.

3.3 Study area:

This study would be conducted in Libya

3.4 Study population:

This study consisted of 368 patients; 130 of them were normal (71 male and 59 female) and 238 hypertensive patients (143 male and 95 female)

3.5 Study variables:

11 variables were used to collect the data for each of them they include; Systolic blood pressure, Diastolic blood pressure, Body Mass Index, Heart Rate, Plasma Total Cholesterol, Plasma Total Glyceride, Right Intima Media Thickness, Left Intima Media Thickness, Right Resistive Index and Left Resistive Index

3.6 Sampling:

Patients with carotid artery in hypertensive patients using color doppler, were the data of this study consisted of 368 patients; 130 of them were normal (71 male and 59 female) and 238 hypertensive patient (143 male and 95 female),11 variable were used to collect the data for each of them they include; Systolic blood pressure, Diastolic blood pressure, Body Mass Index, Heart Rate, Plasma Total Cholesterol, Plasma Total Glyceride, Right Intima Media Thickness, Left Intima Media Thickness, Right Resistive Index and Left Resistive Index.

3.7 Study criteria:

3.7.1 Inclusion criteria: Age, from 19 to 90 years.

3.7.2 Exclusion criteria: Children patients.

3.8 Data collection:

3.8.1 Technique: After taking permission, the patient is positioned lying face-up on the examination table. A clear water-based gel is applied to the lateral aspect of the neck, the transducer is firmly held against the skin with mild to moderate pressure. After completion of the examination the gel is rubbed off using a tissue (Fine), and the patient is asked to wait while the ultrasound images are reviewed.

3.9 Data Analysis:

The analysis was done use the Statistical Package for Social Sciences (SPSS) version 20 (SPSS Inc., Chicago, IL, USA) frequency distribution of all variables were produce, using suitable table and graph.

3.10 Ethical consideration

Research purpose and objectives will be explained to participant clear simple words.

Participant has right to voluntary informed consent. Participant has right to withdraw at any time without any deprivation. Participant has right to no harm (privacy and confidentiality by using coded questionnaire). Participant has right to benefit from the researcher knowledge and skills.

Chapter four
Results

4.1 Results

Table 4-1the mean and standard deviation of the study variables for normal and hypertensive patients

Group Statistics			
Status		Mean	Std. Deviation
Age	Normal	58.4783	4.46063
	Hypertension	60.1087	4.83611
SBP	Normal	120.0087	6.25663
	Hypertension	150.9674	4.61322
DBP	Normal	79.7739	3.64408
	Hypertension	96.3370	3.97969
HR	Normal	79.1391	2.47051
	Hypertension	76.7326	3.40340
BMI	Normal	28.6870	3.58815
	Hypertension	26.9543	3.70811
PTC	Normal	151.7391	21.41346
	Hypertension	173.1326	4.01741
PTG	Normal	117.3304	3.55917
	Hypertension	168.2043	5.94194
Rt IMT	Normal	0.6474	0.02942
	Hypertension	0.8998	0.05795
Lt IMT	Normal	0.6109	0.02214
	Hypertension	0.8907	0.03912
Rt RI	Normal	0.6461	0.03461
	Hypertension	0.7465	0.03825
Lt RI	Normal	0.6109	0.13941
	Hypertension	0.7528	0.03569

Table 4-2 significance difference between normal and hypertensive patients for the study variables using t-test

	t-test for Equality of Means	
	t	Sig. (2-tailed)
Age	-7.63	.056
SBP	-80.52	.000
DBP	-57.50	.000
HR	9.78	.000
BMI	1.84	.069
PTC	-53.77	.000
PTG	-136.90	.000
RIMT	-73.65	.000
LIMT	-114.32	.000
RRI	-34.68	.000
LRI	-27.06	.000

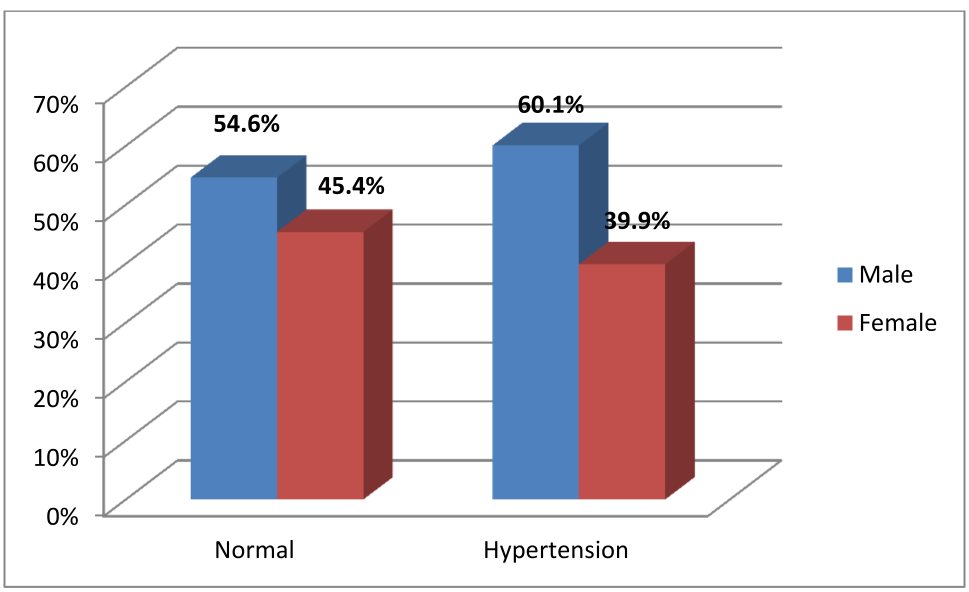


Figure 4-1 bar graph of gender percentage in each class as normal and hypertensive

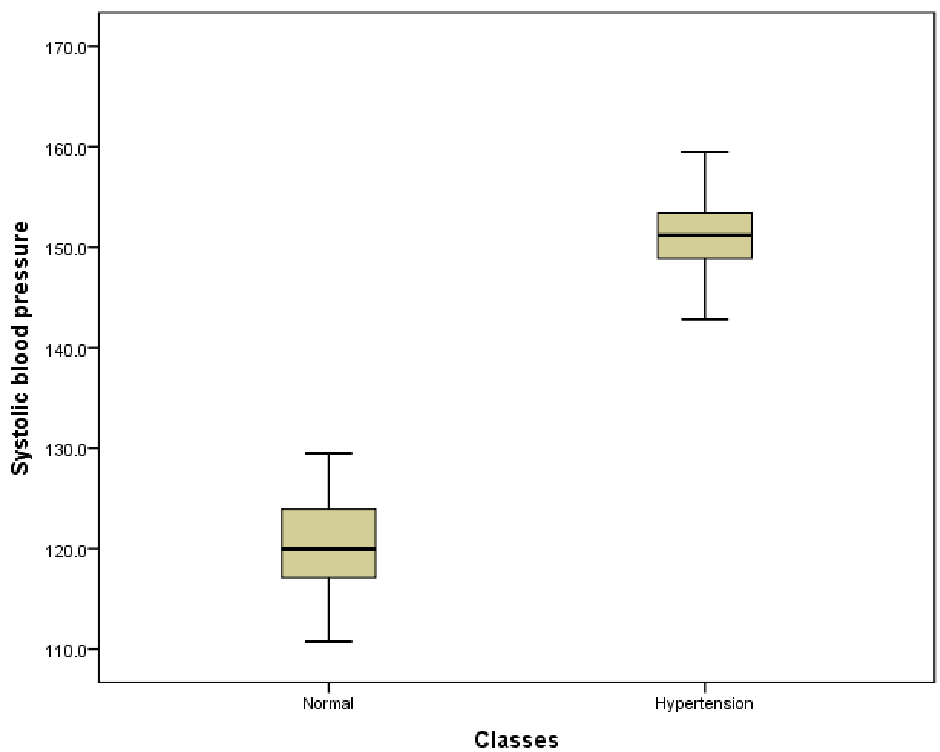
Table 4-3 the mean and standard deviation of the study variables for normal respondents in respect to gender and the significance difference using t-test

Group Statistics control					t-test value	p-value
Gender		N	Mean	STD		
Age	Male	71	58.00	3.014	.287	.775
	Female	59	57.85	3.028		
SBP	Male	71	120.406	4.2487	.429	.668
	Female	59	120.080	4.3843		
DBP	Male	71	79.970	2.3140	-1.984	.049
	Female	59	80.769	2.2521		
HR	Male	71	79.449	1.8194	-.947	.345
	Female	59	79.717	1.2979		
BMI	Male	71	29.438	2.3287	1.378	.171
	Female	59	28.868	2.3738		
PTC	Male	71	147.523	6.1998	.098	.922
	Female	59	147.412	6.6817		
PTG	Male	71	117.590	2.4196	-.592	.555
	Female	59	117.836	2.2724		
RIMT	Male	71	.6497	.01859	.854	.395
	Female	59	.6468	.02063		
LIMT	Male	71	.6125	.01306	-.541	.589
	Female	59	.6139	.01565		
RRI	Male	71	.6508	.02328	-.412	.681
	Female	59	.6525	.02346		
LRI	Male	71	.6165	.06172	-1.265	.208
	Female	59	.6310	.06927		

Table 4-4 the mean and standard deviation of the study variables for hypertensive patient in respect to gender and the significance difference using t-test

Group Statistics Hypertensive					*t*-test value	*p*-value
Sex		N	Mean	STD		
Age	Male	143	60.47	3.20	-.240	.811
	Female	95	60.57	3.06		
SBP	Male	143	151.09	3.049	-1.023	.307
	Female	95	151.49	3.001		
DBP	Male	143	96.67	2.758	1.170	.243

	Female	95	96.25	2.641		
HR	Male	143	77.21	2.428	-.517	.606
	Female	95	77.37	2.348		
BMI	Male	143	27.00	2.521	-.508	.612
	Female	95	27.16	2.216		
PTC	Male	143	173.42	2.924	-.296	.767
	Female	95	173.53	2.722		
PTG	Male	143	168.21	3.834	-.583	.560
	Female	95	168.50	3.865		
RIMT	Male	143	.9010	.0383	-.458	.648
	Female	95	.9033	.0335		
LIMT	Male	143	.888	.0265	-.591	.555
	Female	95	.890	.0237		
RRI	Male	143	.744	.0263	-1.292	.198
	Female	95	.748	.0248		
LRI	Male	143	.752	.0215	1.283	.201
	Female	95	.748	.0257		



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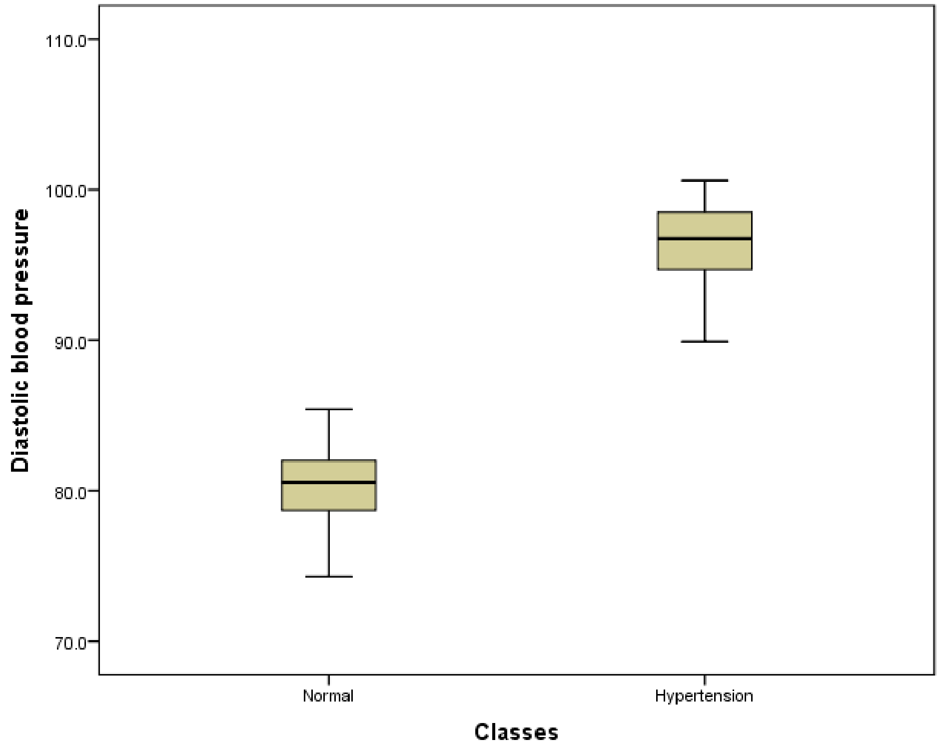
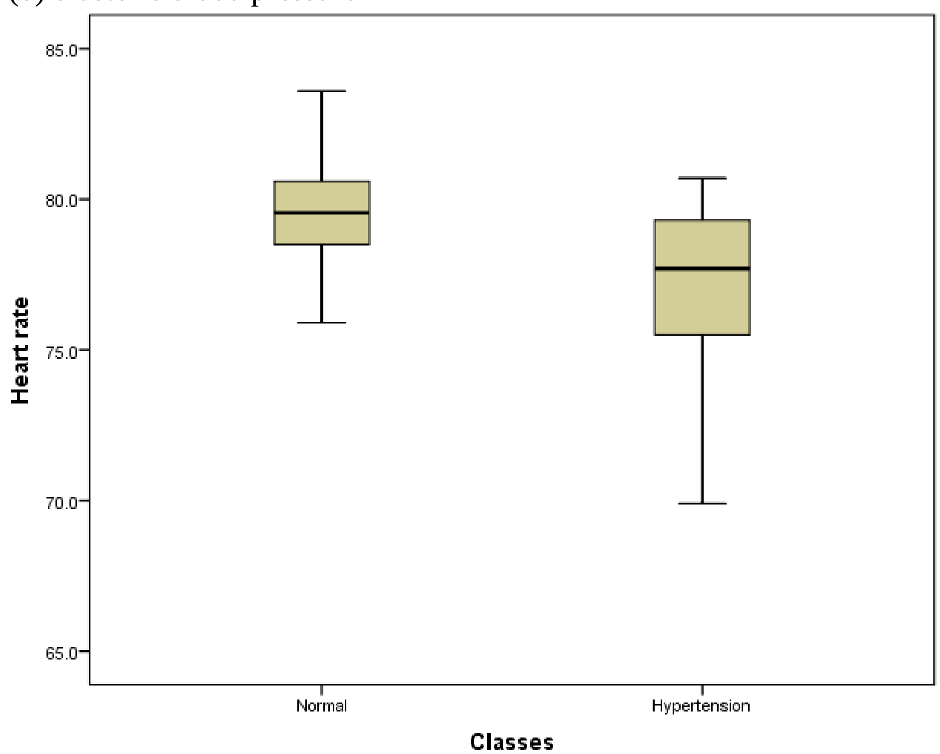


(b)

Figure 4-2 box plot show the mean and the variation between normal and hypertensive patients for (a) systolic blood pressure and (b) diastolic blood pressure



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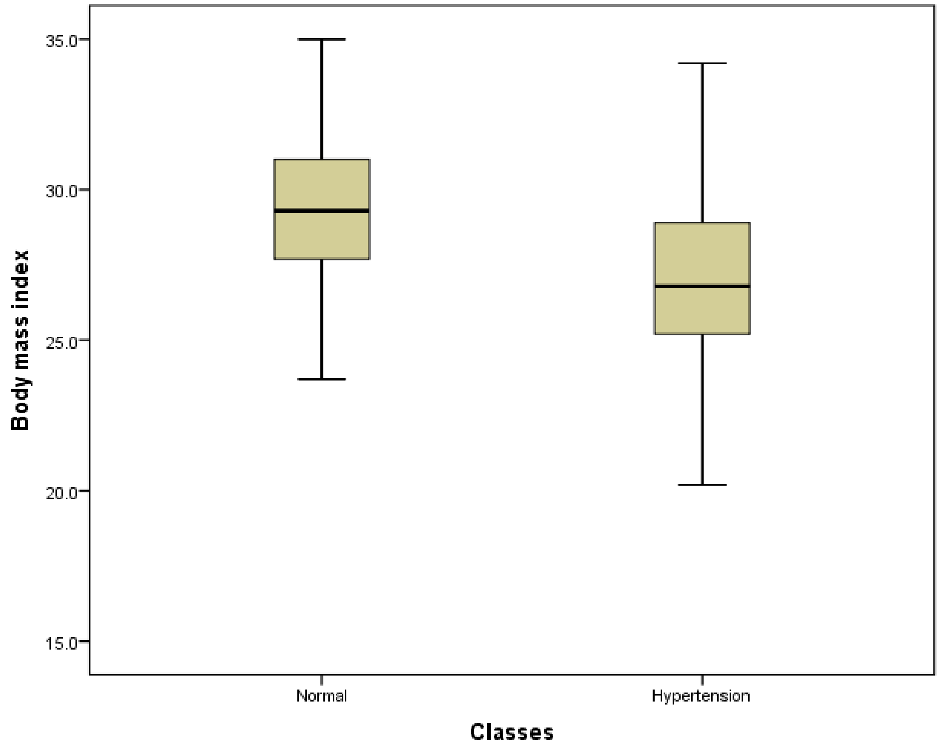
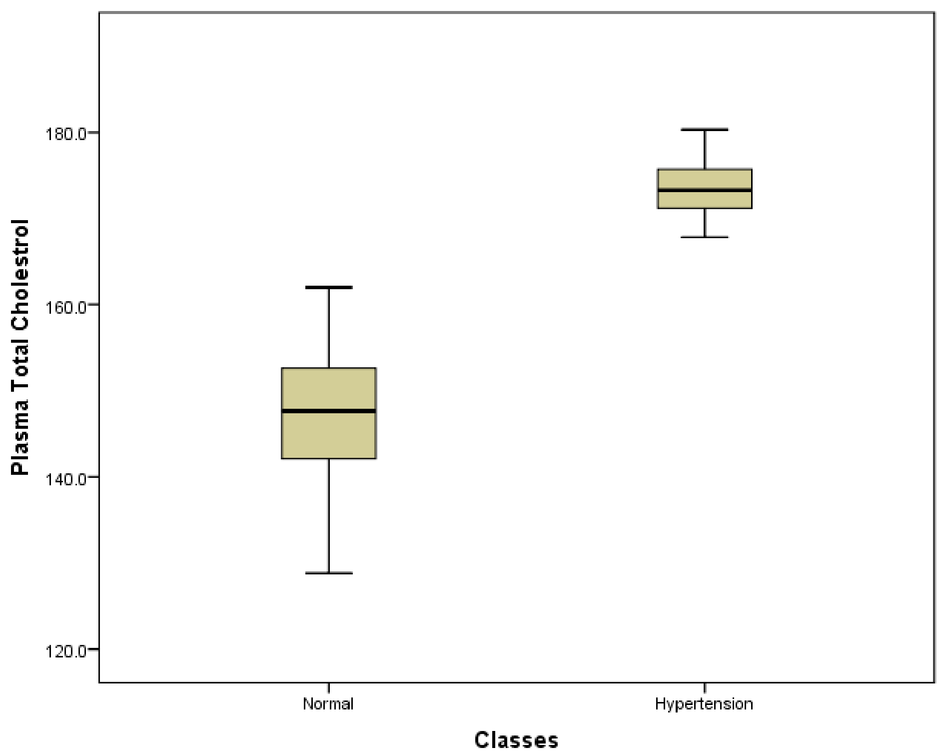


(b)

Figure 4-3 box plot show the mean and the variation between normal and hypertensive patients for (a) heart rate and (b) BMI



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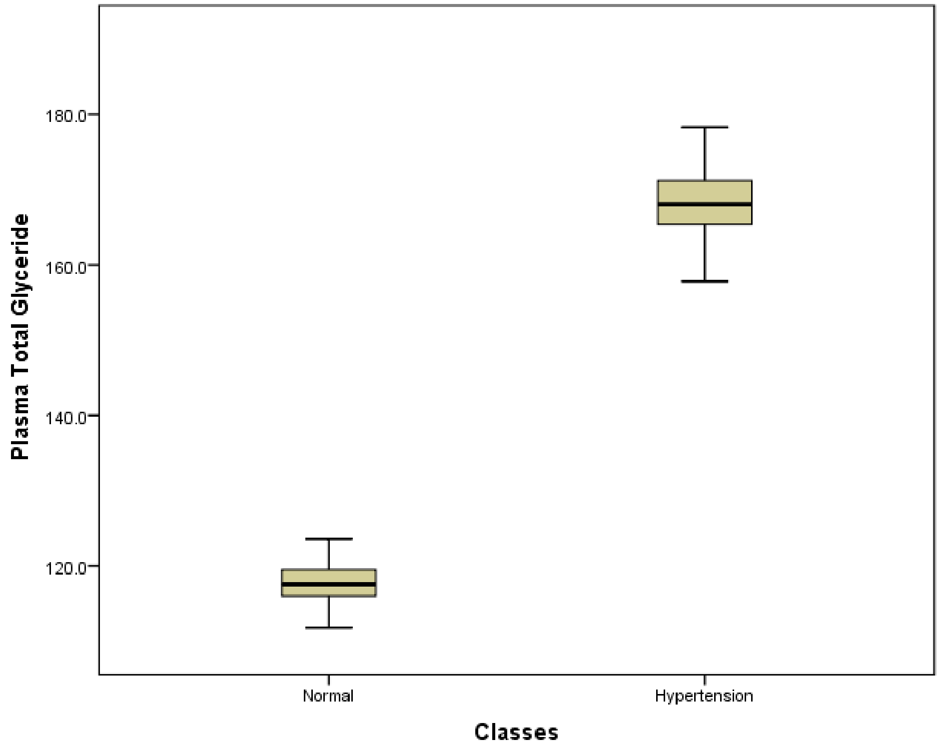
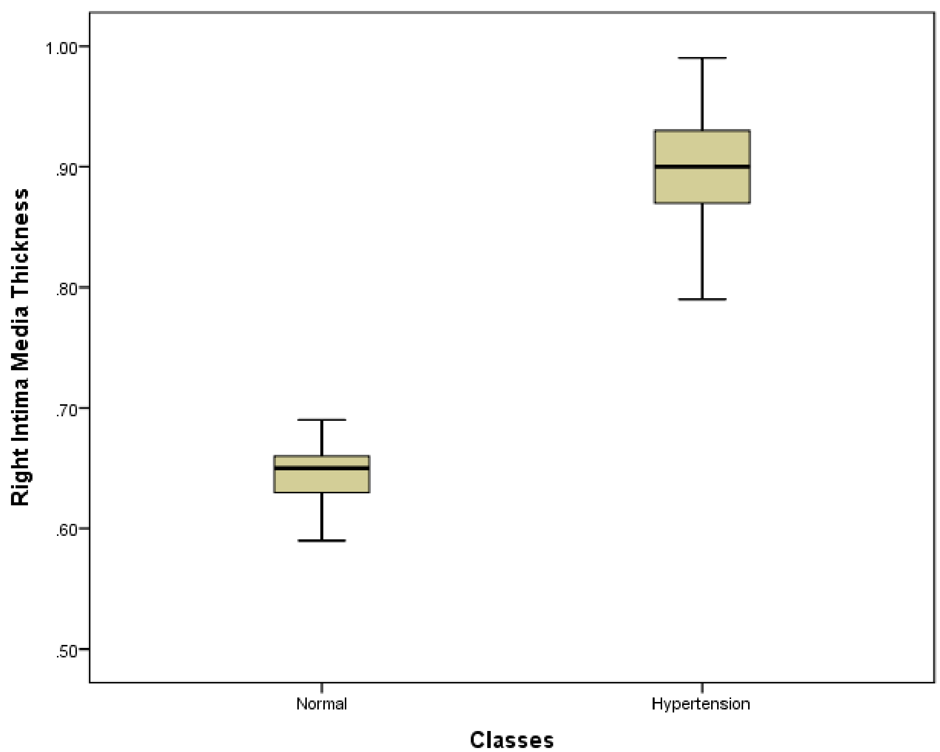


(b)

Figure 4-4 box plot show the mean and the variation between normal and hypertensive patients for (a) PTC and (b) PTG



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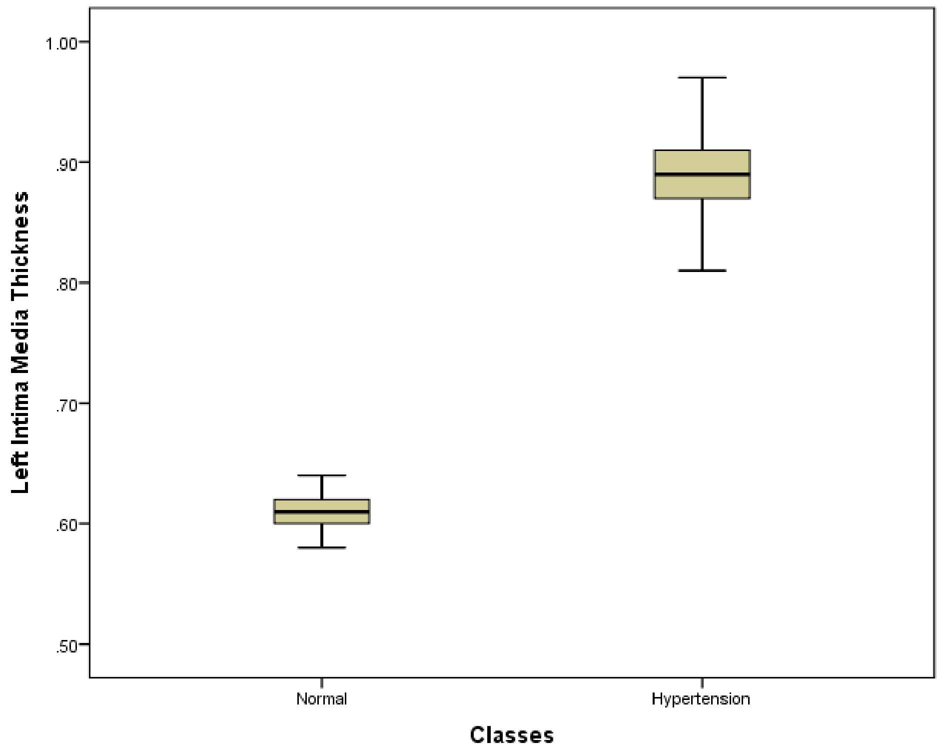
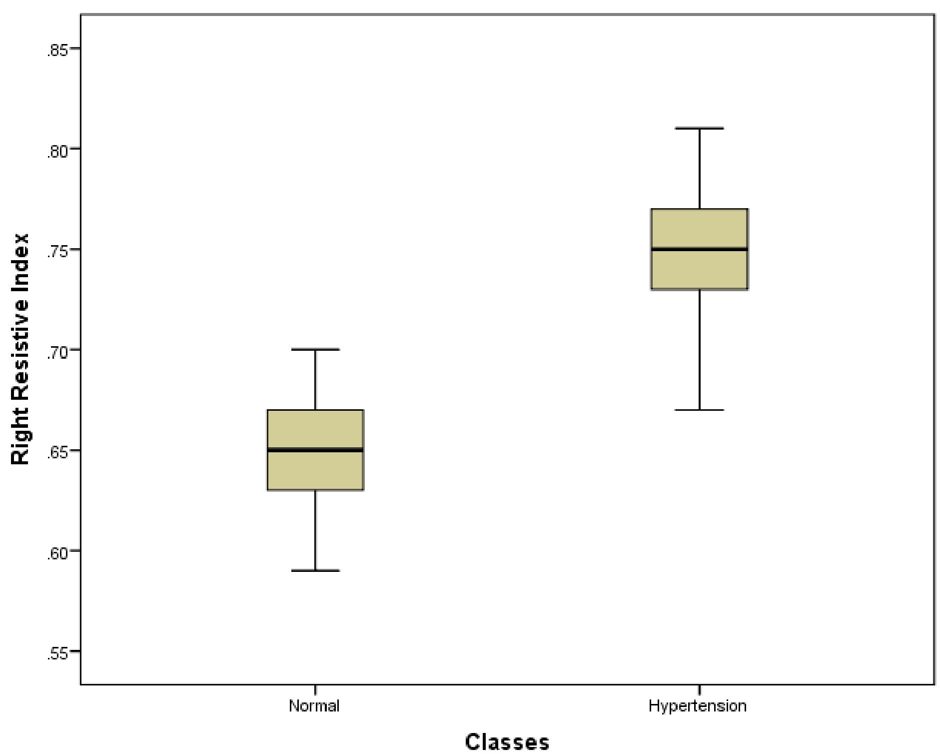


(b)

Figure 4-5 box plot show the mean and the variation between normal and hypertensive patients for (a) Rt IMT and (b) Lt IMT



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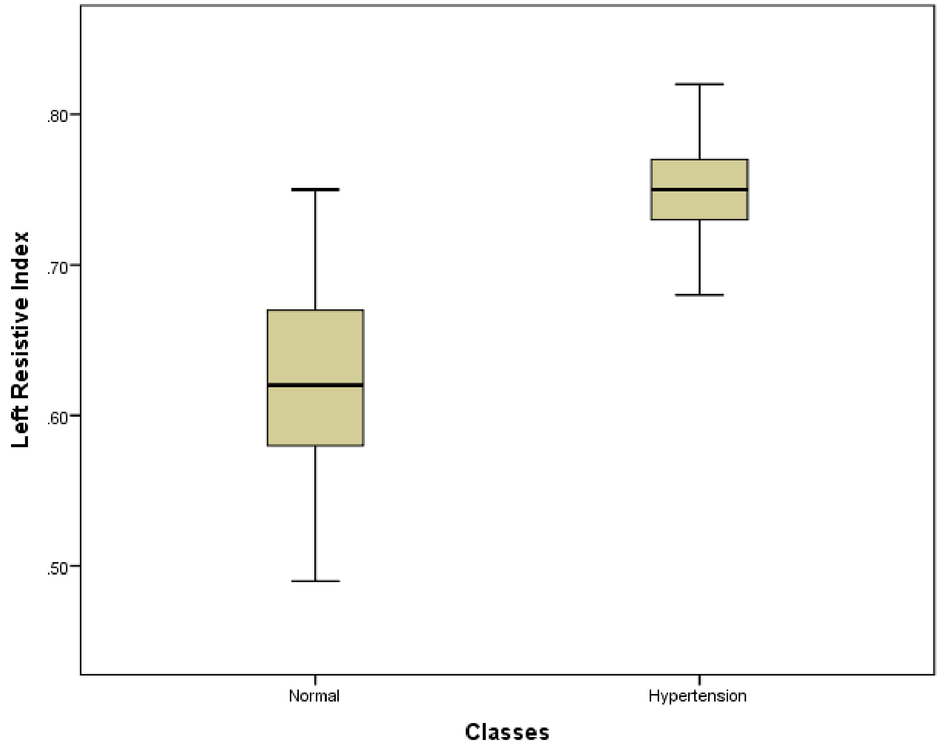

(b)

Figure 4-6 box plot show the mean and the variation between normal and hypertensive patients for (a) Rt carotid RI and (b) Lt carotid RI

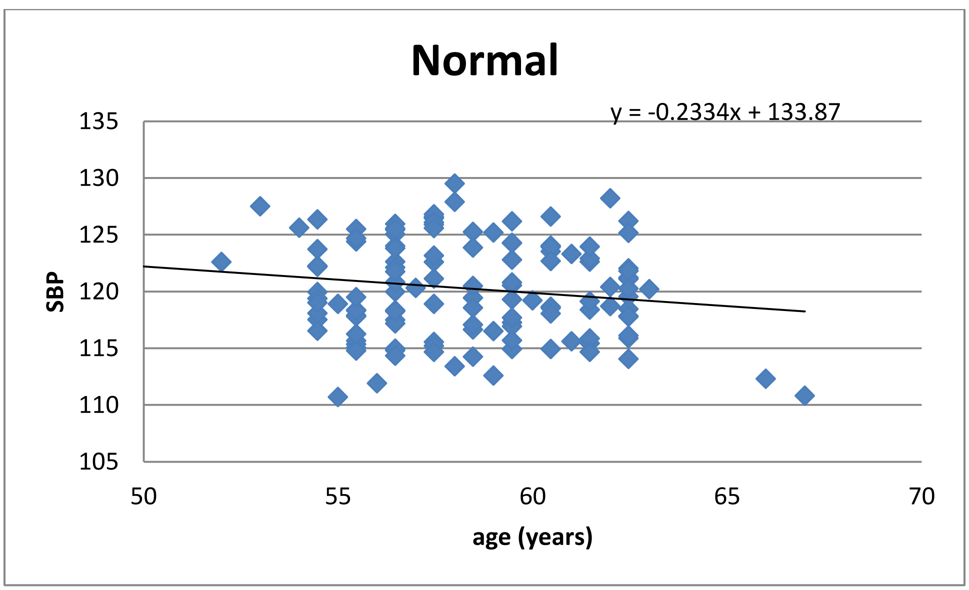

Figure 4-7 scatter plot show an inverse linear relationship between age and systolic blood pressure (SBP); with SBP decreases by 0.23 mmHg/year for normal starting at 134mmHg

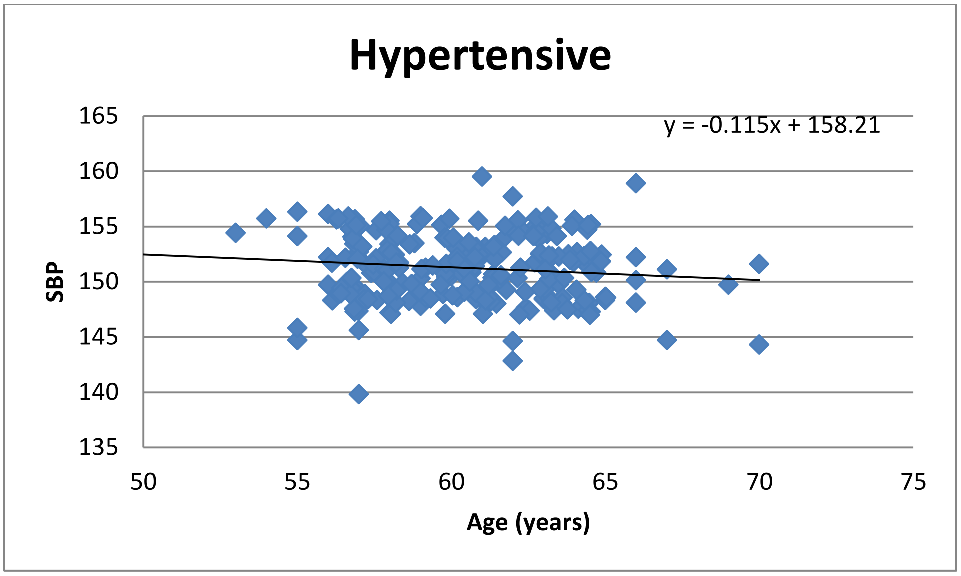

Figure 4-8 scatter plot show an inverse linear relationship between age and systolic blood pressure (SBP); with SBP decreases by 0.12 mmHg/year for hypertensive patients starting at 158mmHg

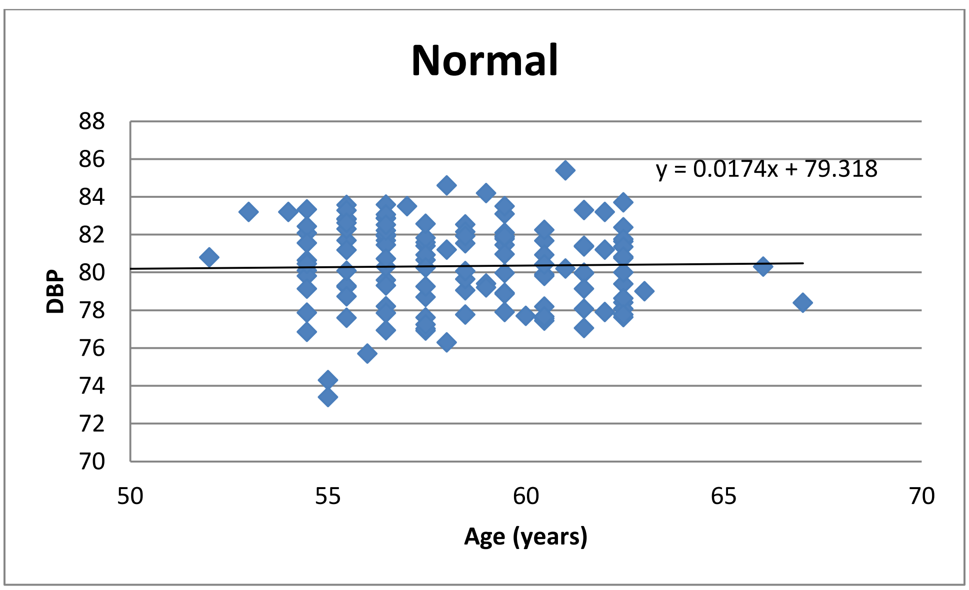

Figure 4-8 scatter plot show a direct linear relationship between age and diastolic blood pressure (DBP); with DBP increase by 0.02 mmHg/year for normal starting at 79 mmHg

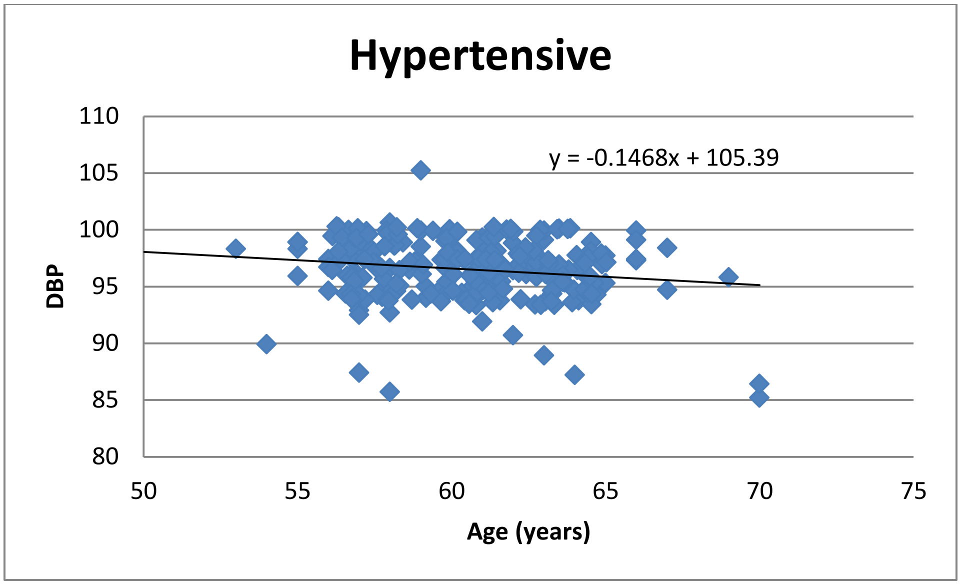

Figure 4-9 scatter plot show an inverse linear relationship between age and diastolic blood pressure (DBP); with DBP decreases by 0.15 mmHg/year for hypertensive starting at 105 mmHg

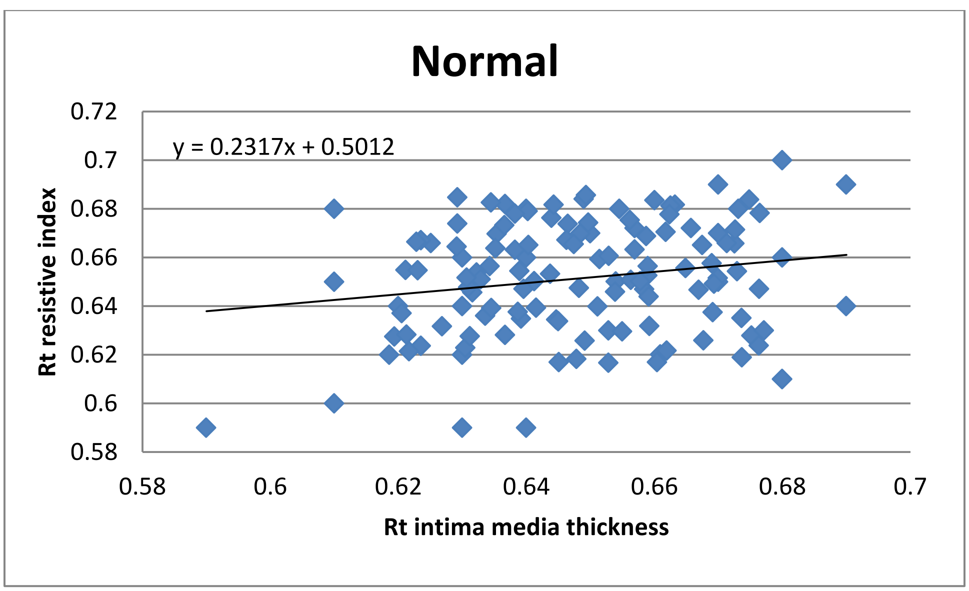

Figure 4-10 scatter plot show a direct linear relationship between Rt IMT and Rt carotid artery RI; with RI increase by 0.23 unit/cm of Rt IMT for normal starting at 0.5 mmHg

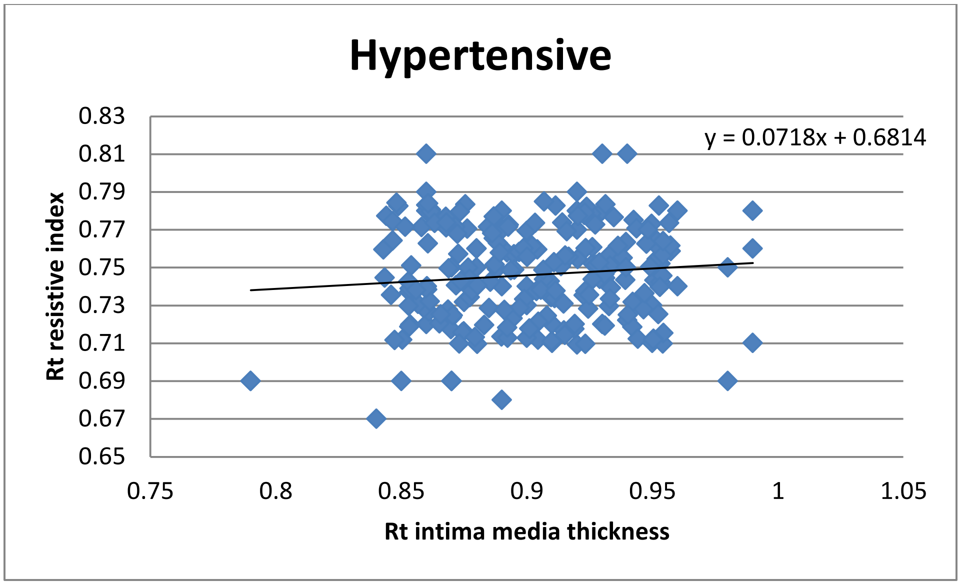

Figure 4-11 scatter plot show a direct linear relationship between Rt IMT and Rt carotid artery RI; with RI increase by 0.07 unit/cm of Rt IMT for hypertensive starting at 0.68 mmHg

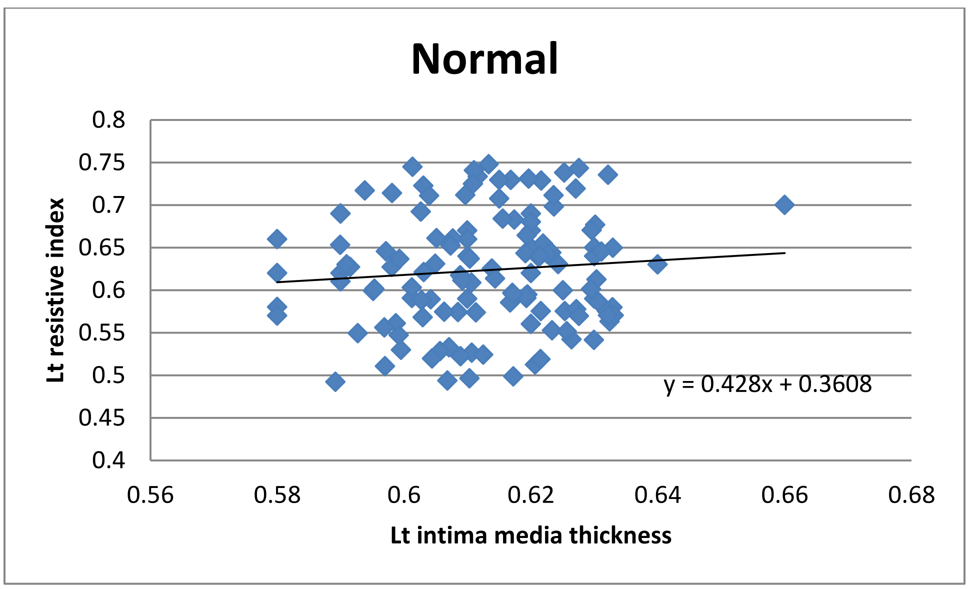

Figure 4-12 scatter plot show a direct linear relationship between Lt IMT and Lt carotid artery RI; with RI increase by 0.43 unit/cm of Lt IMT for normal starting at 0.36 mmHg

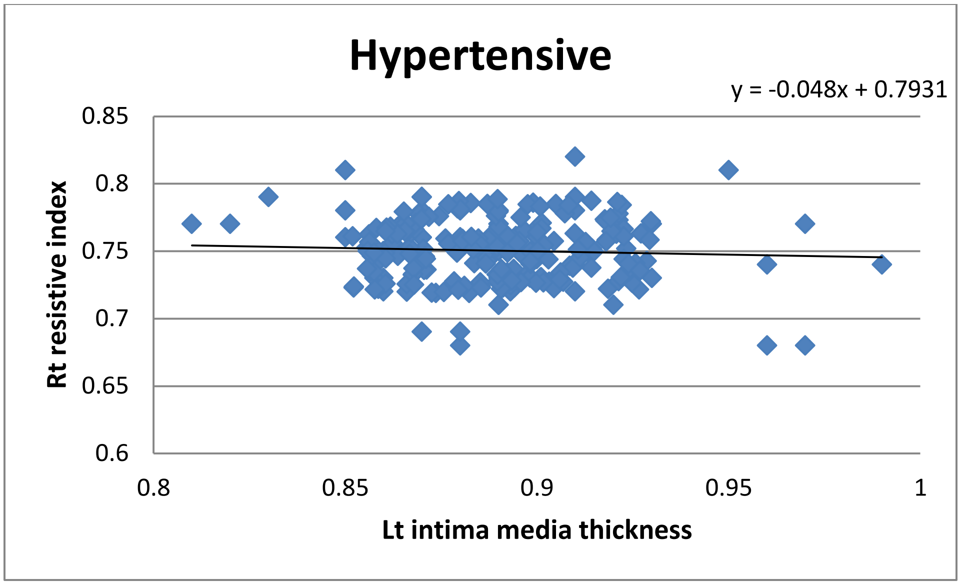

Figure 4-13 scatter plot show a direct linear relationship between Lt IMT and Lt carotid artery RI; with RI increase by 0.05 unit/cm of Lt IMT for hypertensive patients starting at 0.79 mmHg

Table 4-5 confusion matrix show the classification accuracy between normal and hypertensive patient using linear discriminant analysis and study variables (lab and ultrasound) as input

Classification Results

Classes			Predicted Group Membership: Normal	Predicted Group Membership: Hypertension	Total
Original	Count	Normal	130	0	130
		Hypertension	0	238	238
	%	Normal	100.0	0.0	100.0
		Hypertension	0.0	100.0	100.0

100.0% of original grouped cases correctly classified.

Table 4-6 the generated model coefficient by linear discriminant analysis for classification of unseen data

Fisher's linear discriminant functions

Classification Function Coefficients

	Status: Normal	Status: Hypertension
SBP	7.670	9.763
DBP	10.700	12.446
PTC	7.176	8.515
PTG	8.784	12.782
RIMT	476.709	673.203
RRI	898.761	991.124

(Constant)	-2385.101	-3827.210
Fisher's linear discriminant functions		

Table 4-7 A model of multiple regression equation for estimation of Rt RI using Rt IMT, PTG and PTC as input

Coefficients			
Model	Unstandardized Coefficients	t	Sig.
	B		
(Constant)	.371	14.490	.000
PTG	.001	9.880	.000
PTC	.001	2.714	.007
a. Dependent Variable: Rt RI			

Table 4-8 A model of multiple regression equation for estimation of Rt IMT using PTG and DBP as input

Coefficient			
Model	Unstandardized Coefficients	T	Sig.
	B		
(Constant)	-.020	-4.681	.0497
PTG	.004	20.272	.000
DBP	.002	3.244	.001
a. Dependent Variable: Rt IMT			

Chapter five

Discussion, Conclusion and Recommendation

The data of this study consisted of 368 patients; 130 of them were normal (71 male and 59 female) and 238 hypertensive patient (143 male and 95 female) where 11 variable were used to collect the data for each of them they include; Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Body Mass Index (BMI), Heart Rate (HR), Plasma Total Cholesterol (PTC), Plasma Total Glyceride (PTG), Right Intima Media Thickness (Rt IMT), Left Intima Media Thickness (Lt IMT), Right Resistive Index (Rt RI) and Left Resistive Index (Lt RI)

5-1 Discussion

The result of this study reveals that there is a significance differences between normal and hypertensive using t-test at $p = 0.05$ for SBP, DBP, HR, PTC, PTG, Rt IMT, Lt IMT, Rt RI and Lt RI and inconclusive for age and BMI (Table 4-1 and 4-2) this result dictate that, there is a real differences between the normal and hypertensive patient concerning the above mentioned factors while the age and BMI was not an influential factors they showed inconclusive differences.

Hypertensive condition in this sample seem to affect male more than female 60.1% (Figure 4-1), but concerning the 11 factors mentioned earlier there is no significance differences between male and female in case of normal or hypertensive groups separately; which means gender can't be consider as factor or grouping variables (Table 4-3 and 4-4).

Systolic and diastolic blood pressure concerning the normal and hypertensive patients showed remarkable differences between the two group where the values for hypertensive patient in average was apparently exceed that of the normal with a minimum variation that keep the differences between the two groups (Figure 4-2). The heart rate in average showed a considerable significance differences between the normal and hypertensive patient with some overlaps but usually the normal respondent showed normal higher values than hypertensive patient which tend to have low heart rate than the normal one might be to balance the pressure. While BMI for both groups showed minor differences in average and that difference was not significance using t-test at p = 0.05 hence BMI is not consider as causative factor leading to hypertensive (Figure 4-3).

The plasma total cholesterol (PTC) was higher as usual in hypertensive patient than normal and there is a significance differences between the two groups with minim variation for hypertensive group and higher relatively in the normal one but with clear boundaries between the two groups, which go with the usual assumption that hypertension associate with PTC status. Similarly plasma total glyceride (PTG) gives same result PTC but with minim variation between in the normal group and clear cut between the two groups (Figure 4-4).

The intima media thickness for the Rt and Lt carotid artery showed that, hypertensive patient associate with a thicker intima than the normal respondent with considerable variation attributed to hypertensive in respect to the stage of their condition and there is significance differences between the two groups using t-test at $p = 0.05$. while the blood flow concerning resistive index (RI) for Rt and Lt carotid artery reveals higher values for hypertensive patient as usual result attributed to thicker intima and high PTC and PTG. This differences between normal and hypertensive patient was significance at p = 0.05 using t-test; although the variation of RI in the normal group was considerable but mainly left side affected by the strong pressure released directly from the heart and accommodated by the elasticity of the normal intima media (Figure 4-6).

Systolic blood pressure in respect to age for normal group affected linearly by patient age, where the SBP decreases by 0.23mmHg/year starting at 134mmHg (Figure 4-7), for hypertensive patient it follows the same essence i.e. it decrease linearly by 0.12mmHg/year starting at 158mmHg. The decreases conceptually was higher in the normal respondent as a value of decrease and the starting point while for hypertensive it is already start as high value with minimal decrease in respect to age. In the same fashion diastolic blood pressure (DBP) decrease as a result of age increase, for normal by 0.02mmHg/year start at 79 (Figure 4-8), and for hypertensive it decreased by 0.15mmHg/year start at 105 (Figure 4-9).

This study also showed that there is a direct linear relationship between the intima media thickness and the blood flow resistive index. For the Rt carotid artery concerning the normal group the RI increases by 0.23unit/cm of intima media thickness starting at 0.5 (Figure 4-10), while for hypertensive group it increases by 0.1unit/cm starting 0.68 (Figure 4-11), which means that, RI increases to a critical level in case of hypertensive patients because the threshold level is higher than the normal although the increase in the normal is higher a little bit than that of the hypertensive but threshold compensate the result and make it normal for normal respondent.

The Lt carotid as mentioned earlier it receives outstanding pressure from the heart and that usually affected the intima media as well as the RI values which hindered the correlation between the two factors in both groups as well as with the other 11 factors that mentioned earlier. For normal group the RI index increases linearly by 0.4 unit /cm of intima media thickness starting at 0.36 (Figure 4-12); while for hypertensive patient RI decreases by 0.04 unit/cm of intima media thickness starting at 0.79 (Figure 4-13); this result dictate that the decreases of the RI is just abstractly because the decrease relative to the threshold consider negligible, while the increase in the normal group level the RI in the normal range.

Using stepwise linear discriminant analysis to classify the data into normal and hypertensive patients, 8 variables were chosen by the program as the most discriminant factors they include: SBP, DBP, BMI, PTC, PTG, Rt IMT, Lt IMT and Rt RI the classification accuracy was 100% as well as the sensitivity and specificity (Table 4-5) and the generated model that can be used to classify other groups (Table 4-6).

The also showed that the Rt RI index can be estimated using multiple regression equation that include PTG and PTC as input variable (Table 4-7). As well Rt IMT can be estimated using PTG and DBP as input variable (Table 4-8). For the Lt carotid artery the RI and the IMT they don’t show any correlation with the other explanatory variables due to the inconsistently of the values (RI and IMT) in the left carotid artery which affected by high pressure from the heart.

5-2 Conclusion

The main objective of this study was to study the carotid artery in hypertensive patients using color Doppler in order to find quantitative relation between the blood flow indices and the laboratory tests values.

This study was carried out in Libyan nationality during the period from 2015 to 2018 in 368 patients (130 normal and 238 hypertensive) using ultrasound grey scale and color Doppler to find the RI of Rt and Lt carotid artery and intima media thickness, as well as other parameters associated with hypertension.

The results of this study showed gender and age were not an associate factor for hypertension and somehow BMI in this study. Also the lab result well correlated with ultrasound result concerning classification of patients as normal or hypertension using linear discriminant equation below where the vote will be for the higher value come out of the equation:

$$\textbf{Normal} = [(SBP\times7.67) + (DBP\times10.70) + (PTC\times7.18) + (PTG\times8.78) + (RIMT\times476.71) + (LRI\times898.78)] - 2385.1$$

$$\textbf{Hypertensive} = [(SBP\times9.76) + (DBP\times12.45) + (PTC\times8.52) + (PTG\times12.78) + (RIMT\times673.20) + (LRI\times991.21)] - 3827.21$$

Resistive index and the intima media thickness for the Rt carotid can be estimated from PTG and PTC for RI and PTG and DBP for IMT using multiple linear regression equation as follows:

$$\textbf{Rt RI} = (PTG \times 0.001) + (PTC \times 0.001) + 0.371$$

&

$$\textbf{Rt IMT} = (PTG \times 0.004) + (DBP \times 0.002) - 0.02$$

5-3 Recommendation

- Sinologist should not use the blood flow indices and intima media thickness of the Lt Carotid artery to comment on the patient condition concerning hypertension.
- Laboratory test concerning PTC and PTG as well as blood pressure should be correlated with ultrasound results for confirmation
- Same study can be done in Sudanese at different latitude
- Other parameters of blood flow indices and ultrasound features can be included to expand the study.
- The generated equations can be used to have a quantitative results and confirmation of the decision

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Appendix (1)

Master data sheet

Gender	**Age**	**SBP**	**DBP**	**HR**	**BMI**	**PTC**	**PTG**	**RIMT**	**LIMT**	**RRI**	**LRI**	**Classes**
1	56											1
2	66											1
2	67											1
1	60											1
1	59											1
1	58											1
2	62											1
1	63											1
1	55											1
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2	54											1
1	53											1
1	58											1
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Gender: 1= Male, 2 = Female

Classes: 1= normal, 2 = Hypertensive