Dissertation on

“LOW ANKLE BRACHIAL INDEX AS A PREDICTOR OF CORONARY ARTERY DISEASE-A HOSPITAL BASED STUDY ”

Submitted in partial fulfilment for the Degree of

M.D GENERAL MEDICINE

BRANCH – I

INSTITUTE OF INTERNAL MEDICINE
MADRAS MEDICAL COLLEGE
THE TAMIL NADU DR. MGR MEDICAL UNIVERSITY
CHENNAI – 600003
2016 - 2019
CERTIFICATE

This is to certify that the dissertation entitled. “LOW ANKLE BRACHIAL INDEX AS A PREDICTOR OF CORONARY ARTERY DISEASE-A HOSPITAL BASED STUDY”

is a bonafide original work done by Dr. IBENA JESNI.I in partial fulfilment of the requirements for M.D. GENERAL MEDICINE BRANCH – I examination of the Tamil Nadu Dr. M.G.R Medical University to be held in April 2019, under my guidance and supervision in 2018

Prof. Dr. S.TITO., M.D.,
Director I/C,
Professor of Medicine,
Institute of Internal medicine,
Madras Medical College & RGGGH,
Chennai 600003.

Prof. Dr. R. PENCHALAIAH., M.D.,
Guide and supervisor,
Institute of Internal Medicine,
Madras Medical College & RGGGH,
Chennai 600003.

Prof. Dr. R. JAYANTHI., M.D., FRCP (Glas)
DEAN
Madras Medical College &
Rajiv Gandhi Government General Hospital
Chennai - 600003
DECLARATION BY THE CANDIDATE

I hereby solemnly declare that the dissertation entitled “LOW ANKLE BRACHIAL INDEX AS A PREDICTOR OF CORONARY ARTERY DISEASE-A HOSPITAL BASED STUDY” is done by me at Institute of Internal Medicine, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai during 2017 under the guidance and supervision of DR. R. PENCHALAIHAH., M.D., This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, Chennai towards the partial fulfilment of requirement for the award of M.D. Degree in General Medicine (Branch I)

Dr. IBENA JESNI.I
Post Graduate Student,
M.D. General Medicine,
Place: Institute of Internal Medicine,
Madras Medical College &RGGGH
Date: Chennai 600003.
ACKNOWLEDGEMENT

I express my heartful gratitude to the Dean, Prof. **DR.R.JAYANTHI., M.D., FRCP(GLAS)** Madras Medical College & Rajiv Gandhi Government General Hospital Chennai-3 for permitting me to do this study.

I am very grateful to Prof. **Dr. R.PENCHALAIAH., M.D.,** Professor of Medicine, Institute of Internal Medicine, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai-3 who guided, trimmed my work throughout the period of my study and for his constant support.

I am very grateful to Prof. **Dr. SWAMINATHAN, M.D., DM.,** Director of Institute of Cardiology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai-3 who guided my work throughout the period of my study and for his constant support for my thesis.

I am very much thankful for the help rendered by my Assistant Professors **Dr. T. SIVAKUMAR M.D., Dr. D.DAMODHARAN., M.D.,** for their constant help and encouragement.

I am extremely thankful to all the Members of the **INSTITUTIONAL ETHICAL COMMITTEE** for giving approval for my study.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>Myocardial Infarction</td>
</tr>
<tr>
<td>CAD</td>
<td>Coronary Artery Disease</td>
</tr>
<tr>
<td>CAG</td>
<td>Coronary Angiogram</td>
</tr>
<tr>
<td>ABI</td>
<td>Ankle Brachial Index</td>
</tr>
<tr>
<td>PCI</td>
<td>Percutaneous Coronary Intervention</td>
</tr>
<tr>
<td>CABG</td>
<td>Coronary Artery Bypass Grafting</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>ECHO</td>
<td>Echocardiogram</td>
</tr>
<tr>
<td>STEMI</td>
<td>ST elevation MI</td>
</tr>
<tr>
<td>LMCA</td>
<td>Left main coronary artery</td>
</tr>
<tr>
<td>LAD</td>
<td>Left anterior descending artery</td>
</tr>
<tr>
<td>RCA</td>
<td>Right coronary artery</td>
</tr>
<tr>
<td>LCX</td>
<td>Left circumflex artery</td>
</tr>
<tr>
<td>OM</td>
<td>Obtuse marginal</td>
</tr>
<tr>
<td>D1, D2</td>
<td>Diagonals 1 and 2</td>
</tr>
<tr>
<td>SHT</td>
<td>Systemic Hypertension</td>
</tr>
<tr>
<td>PAD</td>
<td>Peripheral Arterial Disease</td>
</tr>
<tr>
<td>IFG</td>
<td>Impaired Fasting Glucose</td>
</tr>
<tr>
<td>IGT</td>
<td>Impaired Glucose Tolerance</td>
</tr>
</tbody>
</table>
# CONTENTS

<table>
<thead>
<tr>
<th>S.No.</th>
<th>TITLE</th>
<th>PAGE NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>2.</td>
<td>AIMS AND OBJECTIVES</td>
<td>2</td>
</tr>
<tr>
<td>3.</td>
<td>REVIEW OF LITERATURE</td>
<td>3</td>
</tr>
<tr>
<td>4.</td>
<td>MATERIALS AND METHODS</td>
<td>48</td>
</tr>
<tr>
<td>5.</td>
<td>OBSERVATION AND RESULTS</td>
<td>54</td>
</tr>
<tr>
<td>6.</td>
<td>CONCLUSION</td>
<td>74</td>
</tr>
<tr>
<td>7.</td>
<td>LIMITATIONS</td>
<td>75</td>
</tr>
<tr>
<td>8.</td>
<td>RECOMMENDATIONS</td>
<td>76</td>
</tr>
<tr>
<td>9.</td>
<td>SUMMARY</td>
<td>77</td>
</tr>
<tr>
<td>10.</td>
<td>BIBLIOGRAPHY</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>ANNEXURE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PROFORMA</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>INFORMATION SHEET</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>PATIENT CONSENT FORM</td>
<td>93</td>
</tr>
<tr>
<td></td>
<td>TAMIL CONSENT FORM</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td>TAMIL INFORMATION SHEET</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>INSTITUTIONAL ETHICAL COMMITTEE APPROVAL</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>PLAGIARISM REPORT</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>PLAGIARISM CERTIFICATE</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td>MASTER CHART</td>
<td>99</td>
</tr>
</tbody>
</table>
INTRODUCTION
INTRODUCTION

Atherosclerosis contributes to increasing mortality and morbidity.

A simple and a non invasive and bedside test –The ABI can be used to predict the atherosclerotic cardiovascular events even in primary care settings.

An ABI less than 0.9 is an indicator of atherosclerotic vascular diseases in different vascular territories.

It is sensitive and specific as angiography.

Both symptomatic and asymptomatic patients with atherosclerosis and peripheral vascular disease are at increased risk of adverse cardiovascular events.

Data from National health and Nutrition Examination Survey (NHANES) shows that the prevalence of Peripheral vascular disease among people aged over 70 years of age is three times more when compared to patients between 40 to 50 years of age.

70 percent of PAD patients have atherosclerotic sequelae in some other vascular bed.

Well controlled and repeated ABI measurements by practitioners are enough as clinical gatekeepers for decision making.

Considering all the above factors this study is being undertaken.
AIMS AND OBJECTIVES
AIMS AND OBJECTIVES

1. To determine the relationship between peripheral artery disease and coronary artery disease in high risk population using Ankle Brachial Index.

2. To study the relationship between various risk factors like blood pressure, diabetes and dyslipidemia and Ankle Brachial Index values.

3. To study the influence of aging process and the relation to ABI.
REVIEW OF LITERATURE
REVIEW OF LITERATURE

1. The correlation between peripheral arterial disease and coronary artery disease using ankle brachial index was done by Sarangi et al.

The study was conducted in inpatients older than 45 years who were randomly selected and had one or more risk factors for peripheral vascular disease.

Based on ABI value of <0.9, PAD was diagnosed in 32 out of the 182 patients studied that is, 18 percent of the study population. Coronary artery disease was present in 15 cases of peripheral arterial disease patients which is statistically significant number of patients.

2. The relation between ankle brachial index and coronary artery disease severity and risk factors—an angiographic study was conducted by Sadeghi et al.

This study is a cross sectional descriptive analytic research study on patients with suspected CAD. Characteristics of the study population were obtained using a standard questionnaire that included family history, past history, and the conventional atherosclerotic risk factors including diabetes, hypertension, hyperlipidemia and smoking. An ABI value of <0.9 was considered positive that is patient was diagnosed as peripheral arterial disease and an ABI value of >0.9 was considered as ABI negative that is normal. The study subjects were subjected to coronary angiography and the results of the questionnaire and the angiographic findings were compared between the two study groups. Out of the
125 patients studied low ABI was seen in 25 patients (20 percent). The prevalence of ABI positive among men were 25.9 percent and 7.5 percent respectively. The prevalence of risk factors for atherosclerosis were significantly higher among the ABI positive group and the ABI positive patients had a more severe stenosis. The mean value of occlusion of different coronary vessels was also significantly higher in the ABI positive group with the left main coronary, right coronary artery, left anterior descending artery, diagonal artery 1 and left circumflex artery involvements (p value <0.05)

3. IMPACT ABI trial (Impressive predictive value of ankle brachial index for long term outcomes in patients with cardiovascular disease)

This study was a retrospective cohort study done in a single center where 3131 patients were enrolled, who were hospitalized for cardiovascular disease. The age of the population studies 54 to 80 years. Patients were categorized into low (≤ 0.9), borderline (0.9-0.99) and normal ABI (>1). The primary endpoint was MACE (major acute cardiovascular event).

The study concluded that during a follow up period of 4.8 years incidence of MACE (low vs borderline vs normal): 32.9% vs 25% vs 14.6 % with a p value of <0.0001 the cardiovascular deaths also differed significantly across ABI (26.2% vs 18.7% vs 8.9 percent ) with a p value of <0.0001 %.

4. Sukhija R et al studied the correlation of ankle brachial index with the severity of coronary artery disease in 273 patients whose mean age was 17 years with peripheral arterial disease. These patients had obstructive coronary
artery lesions (>50% occlusion). Out of the 155 patients with an ABI of <0.40, 130 patients had 3 to 4 vessel disease which accounted for 84 percentage. 11% of them had double vessel disease and 5 percent had single vessel Coronary artery disease from which they concluded that as the ABI values are lower there occurred more prevalence of 3 or 4 vessel coronary artery disease than single vessel disease.

5. In the study done by Eduardo d et al prospective analysis of the data from 100 patients with coronary artery disease as confirmed using coronary angiogram and with more than 70 percent stenosis of at least one sub epicardial coronary artery with a cutoff value of less than 0.9 as abnormal.

The average age of the study population was 77.4 years and the most prevalent risk factor was hypertension. The median later follow up appointment was at 28.9 months. A low ABI was seen in multiarterial CAD than in uniarterial CAD.

5. Dinaldo et al did a prospective analytical cross sectional study over a period of one year that included 163 patients according to the inclusion and exclusion criteria. The Poisson regression method was used to assess whether ABI was an independent predictor of coronary stenosis more than 50 percent.

They concluded that the patient group with low ABI had higher prevalence of stenosis more than 50 percent in the left anterior descending artery and the left main coronary artery than those with normal ABI value.
6. Felipe and colleagues conducted a study on the relation of ABI and the complexity of coronary artery disease which analysed patients more than 65 years undergoing coronary angiogram for ischaemic heart disease and analysed the coronary artery anatomy using the SYNTAX score and the American Heart Association Criteria

In this study that recruited 204 patients with a median age of 72.5 years, stable angina was present in 51 percent of the study population. Although peripheral vascular disease was clinically present in only 1 percent of the study population it was found in 45 percent using ABI measurement. The number of lesions present per patient, the number of patients with complex coronary lesions and the SYNTAX scores were significantly higher in the abnormal ABI group. This study thus concluded that low ABI could discriminate a group of patients with greater occurrence of Type B 2 or type C lesions but with similar median SYNTAX score in patients more than 65 years.

7. Moatasem S Amer and colleagues conducted a case control study on the association between ABI and coronary artery disease severity among elderly Egyptians which included 200 patients aged more than 60 years who were divided into 100 cases and 100 controls according to ABI and then evaluated the severity of CAD using SYNTAX and Jeopardy scores and number of diseased vessels which were significantly high in patients with peripheral vascular disease. All of the 3 measures had negative correlation with ABI (p value ≤0.001 for Jeopardy; <0.001 for SYNTAX and 0.004 for number of diseased vessels).
8. The study done by Marlene Grenon which was a prospective cohort study in CAD patients symptomatic PAD patients had a higher risk of CV events of 70 percent (p value 0.04 ) and 80% higher risk of death (p value of 0.006).

9. In the study conducted by Rosamond, ABI was measured in 12186 patients in the atherosclerosis Risk in The community study, and fatal and nonfatal events were assessed through phone calls, discharge summaries and death certificates and in live patients through ecg taken regularly at 3 year intervals. Participants were followed for 13.1 years and Hazard ratios were calculated using the Cox regression methods. During the study period almost 964 events (fatal and nonfatal) occurred. The hazard ratios were 2.81 for men and for women it was 2.05. The risk of CHD increased exponentially with decreasing ABI and it continued to decrease in patients with ABI of >1 in all age and race and gender subgroups. Even lowering of ABI by 0.1 increased the hazard by 25% in white women and by 34% in African American men and 32 percent in African American females.
**PERIPHERAL VASCULAR DISEASE**

Peripheral vascular disease is the occlusion of arteries distal to the bifurcation of the aorta. It also refers to chronic arterial disease of the legs which is atherosclerotic in origin. The WHO defines this pathology as atherosclerosis obliterans. Some of the most important studies using ABI like the Framingham Heart Study, The San Diego Study, The Rotterdam Study have concluded that asymptomatic peripheral arterial disease is much common than the symptomatic disease.

**CLASSIFICATION OF LIMB ISCHAEMIA:**

Stage 1-no clinical symptoms

Stage 2-intermittent claudication

2a-well compensated disease where the patient can walk more than 200 metres

2b-poorly compensated- disease where the patient can walk only less than 200 metres

Stage 3-rest pain

Stage 4-gangrene and ischaemic ulcer

Limb ischaemia is also classified as

Functional limb ischaemia

Critical limb ischaemia
Functional limb ischaemia

Here flow of blood to the limbs is normal when limbs are at rest; but will not be increased during exercise.

It presents clinically as claudication.

Claudication is defined as muscle discomfort in the limb reproducibly produced by exercise and that will be relieved by rest within 10 minutes.

Critical limb ischaemia

It is persistently recurring ischaemic pain in the limbs for more than two weeks which requires regular analgesics for more than 2 weeks or is associated with ulceration or gangrene of the foot or toes with an ankle systolic pressure <50 mmHg or toe systolic pressure <30mmHg. In these cases the Ankle brachial pressure index will be less than 0.3.

Claudication is a specific but may not be a sensitive feature of peripheral arterial disease.

Around 90% patients with an ABI of less than 0.9 may not have claudication.(falsely negative)

An ABI of 0.9 to 0.99 is considered as borderline ABI value.

Such patients may be asymptomatic at rest but experience symptoms due to compromised vascular flow while walking or using the limbs
INTERPRETATION OF ABI RESULTS:

>0.90 is normal ABI

0.70-0.89 is mild disease

0.50-0.69 is moderate

<0.50 is severe

>1.3 is due to non compressible severely calcified vessel as is the case in old age

ANKLE BRACHIAL INDEX:

It is a very useful tool to indicate the presence of lower extremity peripheral arterial disease.

It is a very cost effective assessment especially in the primary care setting as well as to identify patients at increased risk of lower extremity injury after blunt or penetrating trauma to predict the prognosis of limb recovery post surgery.

An ABI value of less than 0.9 cutoff value has sensitivity of 90% and specificity of 98% for detecting a lower extremity stenosis of more than 50%.

Previous studies have showed an inverse relation between ABI and cardiovascular diseases and atherosclerotic diseases elsewhere.

It can detect and predict the existence of CAD in an otherwise asymptomatic patient.
The idea of Comparing peripheral versus central pressures was first found by Winsor18 using Rubber strain gauge and mercury method.

ABI can be compared to findings on peripheral angiography and by comparing with doppler ultrasound of the lower limb which is the gold standard.

SHORTCOMINGS OF ABI:

1. An incorrectly done test, probably due to wrong technique may yield false positive or false negative results that may lead to either delayed diagnosis of an existing disease or to unnecessary treatment for a non existing disease.

2. In patients with heavily calcified blood vessels which are non compressible as in the elderly patients and diabetic patients, as a result of arterial medial wall calcification the ABI measurements may not be precise and there may be false negative ABI.

3. About 10 percent of the population may lack the dorsalis pedis or the posterior tibial artery thus make it impossible to measure this non invasive test.

4. Certain medications like antihypertensives and antiplatelet drug treatments and statin therapy may influence the values of ankle brachial index. ABI is age and blood pressure dependent and these two factors themselves are linked to each other.

5. The accepted methodology of current techniques do not make necessary corrections for physiological variations over time in baseline blood pressure and for other confounding factors like respiratory variations of blood pressure,
thus requiring the need to use reference values as a range rather than point values

6. As ABI values are mostly from observational studies only, the value of 0.9 is possibly due to inherent limitation of the methods (noninvasive) used for BP measurement using an occlusive cuff without considering control for physiological beat to beat variation for example during breathing. Still beat to beat variations can be measured only if both upper and lower limb pressures are recorded synchronously which is technically cumbersome and hence not recommended by any studies.

7. Technical factors such as over and rapid deflation of the ankle cuff can yield falsely low systolic pressures at the ankle.

Contraindications for ABI measurement

ABI measurement is contraindicated in persons in whom the use of an occlusive sphygmomanometer cuff during measurement of blood pressure may worsen the lower extremity injury

**PREPARATION:**

Necessary equipments for measuring ABI include

Appropriate size cuff for upper and lower extremities with a properly working sphygmomanometer

Doppler device (Hand held 5 to 10 m Hz )
Ultrasound gel

Examination table

**PREPARATION OF THE PATIENT FOR THE PROCEDURE**

Patient must lie on the examination table in the supine position

No other specific preparation needed

**Technique**

The patient is made to lie supine with the arms and legs at the heart level for at least 10 minutes prior to blood pressure measurement.

Select an appropriate sized BP cuff (whose width would be at least 20% more than the diameter of the limb).

The cuff must completely encircle the lower/upper extremity.

The ankle cuff should be tied somewhere between the malleolus and the calf muscle.

Adequate room should be left below the cuffs to permit the placement of the ultrasound gel so that the Doppler device would adequately measure the brachial, dorsalis pedis and the posterior tibial pulses.

Obtain the systolic pressure of both the arms (brachial artery) and then select the higher value among the two as the brachial systolic pressure.

Note that the difference between them should be less than 10 mm Hg only.
The brachial pulse is best felt medial to the biceps tendon at the antecubital fossa.

Similarly obtain the anterior and posterior tibial systolic pressures of one side limb and then select the higher of the two values as the ankle pressure.

The posterior tibial arterial pulse is best appreciated just below and dorsal to the medial malleolus.

The dorsalis pedis pulse is best felt over the dorsum of the foot between the proximal part of the first and the second metacarpal boned just above the navicular bone and medial to the tendon of the extensor hallucis longus.

Obtain similar values from the opposite leg and consider the highest value as the ankle pressure.

Place the Doppler probe over the the arterial landmarks and identify the arteries.

On application of the arterial probe pulsations should be audible.

If the pulsations are not audible then reposition the probe till you can hear the pulsations.

Doppler probe must be placed at 45 to 60 degrees to the vessel and not at 90 degrees.

Inflate the cuff to around 20 mmHg above the expected systolic pressure.

The Doppler sounds now disappear.
Now slowly deflate the cuff at 1 mm/second.

Record the pressure point at which the Doppler sounds reappear which gives the systolic pressure measurement of that particular limb.

**ANKLE BRACHIAL INDEX CALCULATION:**

\[
\text{ABI} = \frac{\text{Ankle systolic pressure}}{\text{brachial systolic pressure}}
\]

Calculated by taking the systolic pressure the ankle pressure divided by the brachial systolic pressure. Calculated ABI must be recorded to two decimal points.
MEASUREMENT OF ANKLE BRACHIAL INDEX
Atherosclerosis | Stages of development

Fatty streak development
- Endothelial dysfunction
  - 24h shear stress
  - ↑ LDL concentration
  - Smoking
  - Diabetes
- Lipoprotein entry and modification
  - Intimal accumulation of LDL proteins
  - Oxidation and glycation of lipoprotein

This inflammatory response takes decades and is reversible
- Foam cell formation
  - Monocytes engulf the oxidized LDL and become foam cells
- Leukocyte recruitment
  - Endothelial cells and SMCs induce expression of adhesion molecules and release chemotactants
  - ↑ monocytes, ↑ T-cell recruitment

Plaque progression
- Intima continues to thicken due to
  - ↑ SMC proliferation
  - ↑ leukocyte recruitment
- Evolution of the fatty streak and calcification
- Luminal narrowing
  - Plaque growth into the lumen causes flow limitation

  1. Claudication
     if limited flow in peripheral vessels
  2. Angina
     if flow limitation in the coronary circulation
- Fibrous capsule
  - SMC apoptosis
  - Lipid rich core surrounded by fibrous capsule

Plaque disruption
- Plaque size vs. stability
  - Thickens fibrous capsules cause more narrowing but are more stable
  - Thinner fibrous capsules are less stable despite causing less narrowing
- ACS
ATHEROSCLEROSIS

PATHOGENESIS:

It is a chronic complex inflammatory condition of the elastic and muscular arteries involving as systemic and segmental disease process. It begins in childhood itself as fatty streaks. It is one of the major causes of death and disability in the developing countries. Current predictions estimate that by the year 2020, Cardiovascular diseases especially atherosclerosis will become the leading cause of global total disease burden. Atherosclerosis affects different regions of the circulation preferably and has distinct manifestations depending on the circulatory bed affected. Atherosclerosis of the coronary arteries cause coronary artery disease and angina pectoris. Atherosclerosis affecting the central nervous system causes stroke and transient ischaemic attacks. Splanchnic circulation involvement can cause bowel ischaemia. The kidneys can be affected either directly as renal artery stenosis or as a common site for atheroembolic disease. Even within a particular arterial bed stenosis due to atherosclerosis tends to occur focally especially in certain predisposed regions. In the coronary circulation the proximal Left anterior descending artery is more frequently blocked due to atherosclerosis. Similarly atherosclerosis has a predilection for the proximal part of the renal arteries and in the extra cranial circulation to the brain, the carotid bifurcation. Atherosclerotic lesions form at the branching points of the vessels where there would be turbulent flow. Ectasia and aneurysmal disease frequently occur in the aorta. In addition to focal, flow limiting stenosis, nonocclusive intimal thrombosis also occurs.
diffusely with high frequency in affected arteries as evidenced by intravascular ultrasound and postmortem studies. Atherosclerosis in humans occurs over many years usually decades. Growth of atherosclerotic plaques does not occur in a smooth linear fashion but rather discontinuously with periods of relative quiescence punctuated by periods of rapid evolution.

After a generally prolonged silent period, atherosclerosis clinically manifests. The clinical expressions may be chronic for example the development of stable effort induced angina pectoris or as intermittent claudication which is predictable and reproducible. Alternatively in some instances, a dramatic acute clinical event like stroke or MI or sudden cardiac death may be the first manifestation of the presence of atherosclerosis. Other individuals may never experience clinical manifestations of the disease despite the presence of extensive atherosclerotic disease in postmortem studies.

INITIATION OF ATHEROSCLEROSIS

Fatty streak represents the initial lesion of atherosclerosis. These very early lesions arise from the focal increases in the lipoprotein content within the intima. This accumulation of lipoproteins is due to increased permeability or leakiness of the vascular endothelium. The lipoproteins also bind to the extracellular matrix of the intima thus increasing the residence time of the lipid particles, where they bind with the glycosaminoglycans of the arterial extracellular matrix which slows the egress of these lipid rich particles from the intima. These bound lipoproteins then undergo oxidized modification. Forming
hydroperoxides, oxysterols, lysophospholipids and aldehyde breakdown products of fatty acids and phospholipids. Modification of the apoprotein moieties may occur including the peptide backbone breaks and the derivatization of certain amino acid residues.

The inflammatory molecules within the plaque contain the enzyme myeloperoxidase which cause production of hypochlorous acid HOCL that yields chlorinated species like chloro tyrosyl moieties. HDL molecules which are thus chlorinated act as poor acceptors of cholesterol a finding that suggests impaired reverse cholesterol transport (which is the anti atherogenic mechanism of HDL) due to oxidative stress. Lipoprotein associated phospholipase A2 which is a member of the phospholipase family can generate pro inflammatory lipids including lysophosphatidyl choline bearing oxidized lipid moieties from oxidized LDL.

**LEUCOCYTE RECRUITMENT**

Accumulation of leucocytes characterize the early atherosclerotic lesions. The inflammatory cells found in an atheromatous plaque include monocyte derived macrophage sand lymphocytes. Various adhesion molecules and receptors for leucocytes found on the endothelial surface recruit leucocytes on the surface of the atheroma which is augmented by the oxidatively modified LDL. Laminar shear forces in normal arteries suppress the expression of adhesion molecules. Ordered pulsatile laminar flow causes production of nitric oxide which acts a s vasodilator and also acts a local anti-inflammatory
autocoid. Also laminar shear stress increases the production of superoxide dismutase and inhibits the thioredoxin reducing protein which inhibits the activity of the endogenous anti-inflammatory protein thioredoxin. Chemoattractant like monocyte chemoattractant proteins direct the migration of leucocytes to the vessel wall.

**FOAM CELL FORMATION**

Once resident within the intima the monocytes transform into macrophages and lipid laden foam cells. By receptor mediated endocytosis. Lipid accumulation and thus the propensity for atheroma formation ensues if the amount of lipid entering the artery wall exceeds that removed by mononuclear phagocytes. Lipid overload in the lesion is prevented by export by the phagocytes and also by the reverse cholesterol transport by HDL. Thus transfer is mediate through specialized cell surface proteins called as ABCA1.

Some foam cells may die due to apoptosis which results in the formation of lipid rich centre called as the necrotic core. In advanced disease there is build up of fibrous tissue by the extracellular matrix. Cytokines present in the plaque like TNF and IL1 induce the production of growth factors like PDGF and FGF which cause plaque evolution. PDGF causes migration of smooth muscle cells from the vascular media to the intima. TGF beta stimulates interstitial collagen production by the smooth muscle cells. These mediators not only arise from the neighboring cells (paracrine) but also arise from the cell itself (autocrine pathway). Products of blood coagulation and thrombosis contribute to atheroma
evolution. This justifies the use of the term athero thrombosis. Fatty streak forms behind a morphologically normal endothelium. Micro thrombi form at the sites of endothelial denudation. Activated platelets release numerous factors that can promote the fibrotic response. Thrombin stimulates protease activated receptors that can signal smooth muscle proliferation, migration, and extracellular matrix production.

**MICROVESSELS**

Neovascularization occurs in connection with the artery’s vasa vasorum. These act as the portal for entry and exit of leucocytes from the atheroma. Atherosclerotic plaques often contain fibrin and hemosiderin and later accumulate calcium.

**PLAQUE INSTABILITY AND RUPTURE**

A superficial erosion or a frank plaque rupture causes thrombus that precedes the unstable angina or the persistent thrombus causes acute MI. Rupture of the fibrous cap causes contact between the coagulation factors and the highly thrombogenic tissue factor. The healing process involves the laying down of extracellular matrix and fibrosis. Those plaques with thin fibrous cap, large lipid core and high content of macrophages are more likely to rupture. In contrast those with dense extracellular matrix and a thick fibrous cap without substantial tissue factor rich lipid cores are less vulnerable to plaque disruption.
Ulcerated plaque is highly thrombogenic causing thrombosis and further critical block of the vessel leading to tissue ischemia and infarction distally. Plaques are dynamic in nature with progression and regression phases. Plaque progression has a unique property of adaptation so that as the plaque progresses lumen caliber is tried to be preserved till critical stenosis occurs. Stenosis beyond 40 percent is said to be critical. Beyond this compensatory mechanism fails causing rapid progression and further stenosis of lumina. Stenosis more than 40 percent causes atrophy of the tunica media and makes the vessel wall unstable leading to dilatation and aneurysm.

Atherosclerosis is common after 50 years but can occur at an earlier age group also. It occurs in males and females as well. Family history is common. Veins are not diseased. Arterial wall is thickened on palpation. Features of ischemia may be seen in the affected limb. Absent or feeble pulses including the main arteries of the limb may occur. Abdomen should be examined for aortic aneurysm.

**THE CONCEPT OF ATHEROSCLEROTIC RISK FACTORS:**

The Framingham Heart Study which was a prospective community based study provided immense support to the risk factors contributing to atherosclerosis.

Risk factors can be classified as those modifiable by lifestyle and pharmacotherapy and those that are immutable or are genetically determines and thus re non modifiable.
The major risk factors (those that are recognized by the Current National Cholesterol Education Project Adult Treatment Panel ATP III) exclusive of LDL cholesterol that modify LDL goals

Smoking

Hypertension (BP of 140/90 mmHg or on antihypertensive medication)

Low HDL levels (less than 40 mg/dl)

Diabetes mellitus

Family history of coronary artery disease

  CHD in male first degree relative <55 years or

  CHD in female first degree relative less than 65 years

  Age (≥45 years in females and ≥55 years in males)

Lifestyle risk factors

  Obesity (BMI >30 kg/ sq.m)

  Physical inactivity

  Atherogenic diet

Emerging risk factors (Non traditional risk factors)

  Lipoprotein (a)

  Homocysteine
Prothrombotic factors

Impaired fasting glucose

Pro inflammatory markers (C reactive protein)

Subclinical atherosclerosis

**LIPID DISORDERS:**

Abnormalities in the lipoproteins and lipid metabolism are among the most firmly established factors for atherosclerosis. Lipid profile must be done in all adults more than 20 years of age. The screen should include fasting lipid profile (Total cholesterol, triglycerides, LDL and HDL) and must be repeated every 5 years.

ATP III guidelines try to match the intensity of treatment to an individual’s risk. Patients are divided into three treatment strata. The number of risk factors for each person is counted. Individuals with less than 2 risk factors are classified a slow treatment intensity arm with an LDL goal of less than 160mg/dl. Those with more than 2 risk factors are evaluated for 10 year risk of ASCVD events. Those with risk score of ≤ 20 % are classified as intermediate risk and are treated with a n LDL goal of 130 mg/dl and those with score more than 20 percent or any evidence of atherosclerosis or a known diabetic (which is now considered as a CHD risk equivalent) fall under the most intensive treatment group with an LDL goal of <100 mg/dl. Those with LDL levels exceeding their target by at least 30 mg/dl need therapy. Secondary goals
include non HDL cholesterol lowering. Cut off points for non HDL cholesterol is 30 mg/dl more than that of LDL cholesterol.

**INSULIN RESISTANCE AND THE METABOLIC SYNDROME**

Aging and obesity underlie the current epidemic of diabetes. The abnormal lipid profile seen in diabetics is called as the diabetic dyslipidemia. Although the LDL levels are found to be near average in most of the diabetics the LDL particles are small and dense and more atherogenic. Other features of diabetic dyslipidemia are low HDL and increased triglycerides. Statins should be considered for diabetics more than 40 years of age with total cholesterol ≥135mg/dl.
### ATP III GUIDELINES TO INITIATE HYPOLIPIDEMIC DRUGS

**NCEP ATP III Clinical Trial Update**

<table>
<thead>
<tr>
<th>High Risk</th>
<th>Moderately High Risk</th>
<th>Moderate Risk</th>
<th>Lower Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD or CHD risk equivalents</td>
<td>≥ 2 risk factors (10-y risk 10%-20%)</td>
<td>≥ 2 risk factors (10-y risk 0%)</td>
<td>0-1 risk factors</td>
</tr>
<tr>
<td>LDL-C Goal &lt; 100 mg/dL</td>
<td>LDL-C Goal &lt; 130 mg/dL</td>
<td>LDL-C Goal &lt; 130 mg/dL</td>
<td>LDL-C Goal &lt; 160 mg/dL</td>
</tr>
<tr>
<td>Initiate TLC ≥ 100 mg/dL</td>
<td>Initiate TLC ≥ 130 mg/dL</td>
<td>Initiate TLC ≥ 130 mg/dL</td>
<td>Initiate TLC ≥ 160 mg/dL</td>
</tr>
<tr>
<td>Consider Drug Therapy ≥ 100 mg/dL</td>
<td>Consider Drug Therapy ≥ 130 mg/dL</td>
<td>Consider Drug Therapy ≥ 160 mg/dL</td>
<td>Consider Drug Therapy ≥ 190 mg/dL</td>
</tr>
<tr>
<td>(&lt; 100 mg/dL: consider drug options)</td>
<td>(&lt;100-129 mg/dL: consider drug options)</td>
<td>(160-189 mg/dL: LDL-C-lowering drug optional)</td>
<td></td>
</tr>
</tbody>
</table>

CLINICAL IDENTIFICATION OF THE METABOLIC SYNDROME
(any three)

Abdominal obesity (Waist circumference)

Men->102 cm

Women->88 cm

Triglycerides>150 mg/dl

Blood pressure≥135/≥85 mmHg

Fasting glucose >110 mg/dl

HDL cholesterol

Men <40 mg/dl

Women <50 mg/dl.

MALE SEX/POSTMENOPAUSAL STATE

After menopause coronary disease accelerates in women. HDL levels fall post menopausally. Multiple observational and experimental trials have shown that oestrogen therapy in females lowers the coronary risk. In the Heart and Estrogen/Progesterone Replacement Study postmenopausal survivors of acute MI were randomized to estrogen/progesterone combination or a placebo. This study failed to show recurrence of CAD in patients in the therapeutic wing. The JUPITER trial randomized more than 6000 women over the age of 65 years without any CVS disease and with an LDL of <130 mg/dl but with hS-CRP
>2mg/L to statin versus placebo and found positive outcomes in the statin treated arm.

**DIABETES MELLITUS:**

Glucose tolerance is divided into 3 categories-

1. Normal glucose homeostasis,

2. Diabetes mellitus and

3. Impaired homeostasis. A fasting glucose of <100 mg/dl, blood glucose level of <140 after a glucose challenge and a HbA1C of <5.6% are considered as normal glucose tolerance.

**CRITERIA TO DEFINE DIABETES MELLITUS**

Symptoms of diabetes (polyuria, polydipsia, polyphagia) plus

1. Fasting blood glucose of >126 mg/dl or
2. Blood glucose of >200 mg/dl after a 2 hour oral glucose challenge, or
3. a HbA1c of >6.5% is considered as diabetes

**RISK FACTORS FOR DEVELOPING DIABETES**

Family history of diabetes mellitus(parent or a sibling with Type 2 diabetes)

Physical inactivity

Obesity

Race/ethnicity
Previously diagnosed IGT or IFG or AIC>5.7 to 6.4%

History of gestational diabetes or a history of delivery of a baby weighing >4 kg

Hypertension

HDL <35 mg/dl or triglycerides >250 mg/dl

Polycystic ovarian disease

Metabolic syndrome

Acanthosis nigricans

History of cardiovascular disease

The ADA recommends screening of all the persons more than 45 years of age every 3 years. Earlier screening is recommended if they are overweight (BMI>25 kg/sq.m) or there is an additional risk factor for diabetes. In contrast to long latency period before diagnosis in type 2 diabetes there is no such lag period in case of type 2 diabetes.

Insulin resistance is central to the development of diabetes.

Diabetes (DM) has reached epidemic proportions worldwide, and its prevalence is on the rise. The implications of a diagnosis of diabetes are as severe as a diagnosing a coronary artery disease (CAD). Cardiovascular mortality increase in all age groups and for both sexes rises equivalently with Diabetes or a history of MI and the two are synergistic (Figure 1). In addition, DM (especially type 2), is associated with risk factors for cardiovascular disease (CVD). Amongst adults with DM there is 75% to 85% prevalence of hypertension, 70% to 80% for increased LDL, and 60% to 70% association
with obesity. CAD is the main cause of death in both type 1 and type 2 diabetes and Diabetes is associated with a 2 to 4-fold increased mortality due to heart disease. Over 70% of people more than 65 years of age with Diabetes will die from heart disease or stroke. Further, in patients with Diabetes, there is an increased mortality after Myocardial infarction, and worse long-term prognosis.

![Figure 1](image_url)

**Figure 1**
Event rates for endpoint of nonfatal MI, nonfatal stroke, and CV death in males (A) and females (B) stratified by age in relation to diabetes and a prior Myocardial infarction.

In the western world, one third of all percutaneous PCI procedures are done on patients with Diabetes and ~25% of patients undergoing CABG surgery have DM; the outcomes of these major procedures is less effective than in those patients without DM. DM modifies the body’s response to arterial injury, in the form of profound consequences in terms of risk for restenosis and stent
thrombosis. Although considerable improvement has been there in the management of patients with CAD, the coronary event rates still remain high among patients with DM. Thus, optimal medical therapy and prompt selection of revascularization technique is critical for patients with DM.

The following literatures summarise the current evidence regarding the effectiveness of multiple and revascularization procedures in patients with diabetes.

Glycemic control and CV outcomes

DM, while it has been known since the antiquity, this disease can only be dated to the era after wide-spread insulin usage. Prior to insulin replacement, DM was a universally fatal disease primarily in children. The Diabetes mellitus of today, with its chronic manifestations, is due to the lifesaving and the life-prolonging insulin effects and thus naturally many people have wondered how the“tight” control of blood sugar with precise insulin doses would affect CV risk. In general, tight glycemic control is associated with an higher risk for episodes of hypoglycemia but minimal or no mortality benefits. The ACCORD trial was designated to test if the treatment targeting normal glycemic status reduces the risk of CV events in type 2 Diabetes. More than 10,000 patients enrolled were randomized into either a standard treatment protocol that aimed at a target HbA1c levels of 7% and 8% or an intensive strategy arm that aimed to attain an A1c value of less than 6.0%. The median HbA1c values with the standard strategy was found to be 7.5%; and the intensive strategy attained a
median A1c value of 6.4%. Still, the intensive strategy was associated with almost 22% increase in the all-cause mortality and morbidity and the study was terminated after a median follow-up of around 3.4 years.

The ADVANCE trial randomized 11,140 patients to a strategy of intensive glucose control (with primary therapy with the sulfonylurea drug gliclazide and also additional drugs as needed to attain a target A1c of <6.5%) versus a standard therapy, with the glycemic target goal set as per the “local guidelines”. The median A1c levels attained in the intensive versus standard arms were 6.3% and 7.0 percent, respectively. The Intensive treatment caused a relative decrease of 10% in the primary outcome of major macrovascular disease events; P=0.01, mainly due to reduction in nephropathy which is a microvascular sequelae

The **metabolic environment of diabetes mellitus may further impact negatively on the islet cell function for example in case of chronic hyperglycemia**

impairs islet function by a mechanism called as glucotoxicity and leads to further worsening of the glycemic status. Improvement in glycemic status causes improvement in islet function also.

Elevation of free fatty acid levels may also worsen islet cell function (lipotoxicity)
HYPERTENSIVE VASCULAR DISEASE

Hypertension doubles the risk of cardiovascular diseases. Blood pressure increases steadily in the first two decades of one’s lifetime. Blood pressure tracks over time in children and between adolescent and young adult. Among individuals more than 60 years women have higher BP than men. Among adults diastolic BP also increases till 55 years after which it tends to decrease. As a consequence the pulse pressure widens beyond 60 years of age. Thus the probability that an adult will develop hypertension during his lifetime is almost 90%. Acculturation is an important contributor. 60% of the hypertensives are >20% overweight.

The age related increase in BP is augmented by high NaCl intake. Low intake of calcium and potassium may be also contribute. The urine sodium potassium ratio correlates strongly with BP than either alone. Alcohol intake, stress and low physical activity also contribute. Hypertension is a polygenic disease acting in concert with environmental factors. Genetic factors may also contribute to hypertensive nephropathy.

Mechanisms of hypertension

Arterial pressure is determined by cardiac output and the total peripheral resistance. Cardiac output is the function of stroke volume and heart rate. Peripheral resistance is determined by the changes in the small arteries and arterioles (functional and anatomic changes).
Hypertensives have stiffer arterioles. A number of devices like ultrasound and MRI are used to evaluate the arterial stiffness. Vascular endothelium also modulates vascular tone by producing vasodilators like nitric oxide which is a potent vasodilator. This endothelium dependent vasodilation is impaired in hypertensives. This is assessed by using high resolution ultrasound before and after the hyperemic phase of reperfusion after 5 minutes of forearm ischemia.

Endothelium dependent vasodilation is also assessed by i.v infusion of endothelium dependent vasodilators like acetyl choline. Endothelin is a vasoconstrictor peptide produced by the endothelium. Hypertensive heart disease is a consequence of the structural changes leading to LVH and CCF. Aggressive control of hypertension reverses the LVH. Several studies suggest that an ABI of <0.8 is associated with elevated BP especially systolic.

Home blood pressure and ambulatory blood pressure are generally lower than the office BP. BP is higher in the morning hours, thus MI and stroke are common in the early morning hours. Night time blood pressure is 10% to 20% less than daytime BP and an attenuated nocturnal dip is associated with increased CV risk. White coat hypertension is associated with increased CV risk. 80-95% patients are diagnosed as essential hypertension. Essential hypertension tends to be familial.

Measurement of blood pressure

Before the measurements are taken, individual should be seated quietly in a chair for 5 min, in a quiet room. At least 2 measurements should be made. The
centre of the cuff should be at the heart level and the width of the bladder cuff should be at least 40% of arm circumference. Cuff should be deflated at 2mmHg/sec. SBP is the first koratkoff sound and the diastolic BP is the last koratkoff sound heard. Ambulatory measurements use the oscillometric method and typically take readings every 15 to 30 minutes. Blood pressure should be measured in both the upper limbs and in the supine, sitting and standing position.

LAB INVESTIGATIONS IN A HYPERTENSIVE PATIENT:

Renal:

Urinalysis, albumin excretion, serum BUN / creatinine

Endocrine

Serum sodium, potassium, calcium, TSH

Metabolic

Fasting blood sugar, lipid profile

Others:

ECG

Hematocrit
DYSREGULATED COAGULATION OR FIBRINOLYSIS

The stability of the plaque depends on the balance between fibrinolytic system like plasmin and the antifibrinolytic system like plasminogen activator inhibitor. Patients with diabetes have elevated levels of PAI. Prophylactic Aspirin is beneficial in women with 10 year ASCVD risk of ≥20% and in men with 10 year ASCCD risk of ≥10% without CHD and for treatment of patients with established CHD.

HOMOCYSTEINE:

Homocysteine has been implicated to be associated with CAD. But homocysteine levels should be measured only in young patients with CAD in those with atherosclerosis out of proportion to the risk factors.

INFLAMMATION

Inflammation also contributes to coronary risk. Patients with elevated hs-CRP levels have high cardiovascular risk. CRP serves as validated biomarker for risk but not as a direct contributor to the pathogenesis. CRP levels rise with body mass (obesity) and lower with weight reduction. Evidence suggests that lipid lowering therapy also acts by suppressing the inflammation

LIFESTYLE MODIFICATION

Physicians should advise the patient on smoking cessation and about healthy dietary practices to maintain ideal body weight and to optimize the risk factors
long before the atherosclerotic disease manifests. Physical activity of at least 30 minutes per day is needed.

**ISCHAEMIC HEART DISEASE**

**CORONARY ATHEROSCLEROSIS**

Epicardial coronaries are the major site of atherosclerosis. When the stenosis is >50% there is a limitation of the ability to increase the flow on demand. When the diameter is reduced by >80 % there is diminished flow even at rest. Critical occlusions of the Left main and the Left anterior descending artery are particularly hazardous. Chronic narrowing causes development of collaterals which may be sufficient to maintain myocardial viability but not during increased demand.

The normal myocardium converts fatty acids and glucose into CO2 and water. In severe oxygen deprivation fatty acids cannot be used up and the glucose is converted to lactic acid. The duration of the injury determines if the myocardial injury is reversible (<20 min in the absence of collaterals) or irreversible (>20 minutes). Ischemia also causes ECG changes like T wave inversion (non-transmural intra myocardial ischemia), transient ST depression reflecting patchy sub endocardial ischemia and ST elevation reflecting severe transmural ischemia. Exercise tests in asymptomatic patients may reveal evidence of silent myocardial ischemia. Coronary angiogram findings reveal plaques in these patients. In contrast to the asymptomatic phase of the disease
the symptomatic phase is characterized by chest discomfort either due to angina or due to Myocardial infarct.

**INVESTIGATIONS**

- Fasting lipid profile
- Urine routine-to rule out microalbuminuria in diabetics
- Blood sugar and HbA1c
- Hematocrit and complete blood count
- Creatinine
- Thyroid function tests
- Hs-CRP
- Chest x-ray (to detect cardiomegaly, LV aneurysm)
- Electrocardiogram

The 12 lead ECG in a patient with angina may be normal at rest or there may be features of old MI. Although repolarization abnormalities example ST-T changes, left ventricular hypertrophy and intraventricular conduction changes may also be present they are non-specific. Dynamic ST-T changes that occur during anginal episodes and disappear thereafter are considered more specific.
STRESS TESTING

It involves a standardized increment in work load while the symptoms, ECG and BP are monitored. Exercise duration is limited by symptoms and is stopped when there is severe chest discomfort or shortness of breath or dizziness or severe fatigue or when there is an ST depression of more than 2mm.

Fall in BP of more than 10mmHg or the development of ventricular arrhythmias. The ischemic ST segment response is defined as horizontal or down sloping depression of >1 mm and lasting longer than 0.08 seconds. T wave abnormalities, conduction disturbances and ventricular arrhythmias during the tests are non-diagnostic. Negative stress tests in which the target heart rate (85% of predicted heart rate during exercise) is not achieved is also non diagnostic. False positive and false negatives occur in one third cases. The overall sensitivity is only 75%. It cannot detect lesion of left circumflex since it is not represented on the surface ECG.

False positive tests seen in those with preexisting ST-T changes, digitalis and antiarrhythmic therapy, abnormal potassium levels and intra ventricular conduction abnormalities. Measure the total duration of exercise, the external work performed9the stage of exercise) and the internal cardiac work (product of heart rate and BP). Modified heart rate limited rather than symptom limited tests can be done in patients as early as 6 days after MI. Contraindications to stress testing include rest angina within 48 hours, unstable rhythm, severe aortic stenosis, acute myocarditis, CCF, pulmonary hypertension and infective
endocarditis. The development of angina or severe ST depression before stage II of Bruce protocol indicates severe IHD.

**CORONARY VASCULAR ANATOMY**
CORONARY ARTERIOGRAPHY:

It outlines the lumina of the coronary arteries and can be used to exclude significant coronary occlusion. But it does not provide information about the vessel wall and so severe form of atherosclerosis that does not encroach upon the lumina may not be diagnosed. Atherosclerosis initially causes bulging of the artery without encroaching on the lumen, a process called as remodeling. Later in the course of the disease it would cause luminal compromise.

INDICATIONS FOR CAG

1. CAG is considered for chronic stable angina patients who are severely symptomatic despite medical management and are being considered for revascularization.

2. Patient with troublesome symptoms to confirm the diagnosis of IHD.

3. Patients with known angina who have survived cardiac arrest.

4. Patients with ischemia on laboratory testing with clinical or lab evidence of LV dysfunction

5. Patients at high risk of sustaining coronary events based on signs of severe ischemia on non-invasive methods

6. Negative or non-diagnostic stress test for confirming the diagnosis

7. Patients with history of repeated admissions for suspected ACS but in whom the diagnosis is not confirmed
8. Patients whose career involves the safety of other people (pilots, firefighters, police) in whom there is a suspicious or proven CAD by non-invasive tests.

9. Patients with Aortic stenosis and hypertrophic cardiomyopathy in whom chest pain due to CAD cannot be excluded.

10. Males >45 years and females > 55 years who undergo open cardiac procedures like valve replacement or repair in whom here may be a preexisting asymptomatic CAD

11. Patients after MI especially those at high risk for recurrence of angina or the presence of heart failure, frequent VPCs, or signs of ischemia on the stress tests

12. Patients with angina pectoris regardless of severity in whom non-invasive tests indicate poor exercise performance or severe ischemia.

13. Patients in whom Coronary artery spasm or other non-atherosclerotic causes of MI are suspected, for example, Coronary artery anomaly, Kawasaki disease.

Obstructive lesions of the left main coronary or the left anterior descending artery proximal to septal branch are associated with poor prognosis because of the greater area of myocardium at risk. Greater the number of risk factors, greater is the severity of coronary artery disease.
Non-invasive alternatives to CAG are CT angiography and cardiac MR angiography. (limitations include higher radiation exposure with CT angiography compared with conventional angiography, motion artefacts associated with cardiac cycle during MR angiography).

**CORONARY ARTERY DISEASE AND PERIPHERAL ARTERIAL DISEASE ASSOCIATION**

It is a well known fact that peripheral arterial disease is associated with other arterial diseases also especially coronary artery disease and cerebrovascular disease.

Peripheral arterial disease affects approximately 16 percent of the population over the age of 55 years.

The association of CAD and PAD increases the risk of all cause mortality than while CAD and PAD exist alone as single entities.

Atherosclerosis is a systemic or a generalized disease process, hence may affect any artery in the body from the head to foot.

But the most common clinical events rise from atheromatous process affecting the coronary arteries, the carotid arteries, the aorta, the arteries of the lower limbs.

Data from patients with suspected coronary disease who were subjected to coronary angiogram shows that the actual prevalence of Coronary artery disease is high when evaluated by using ABI.
Longevity itself is a risk factor associated with development of both Coronary as well as peripheral vascular disease.

ABI deterioration is associated with clear increase in mortality and morbidity in CAD patients.

Excess risk is found in those with positive inflammatory biomarkers. The increased vulnerability to CAD is because of shared risk factors for the two diseases and by the presence of inflammation.

The predictive value of ABI in Cardiovascular mortality is comparable to that in Framingham Heart Study.

Combining ABI with traditional risk factors listed in Framingham Study of risk assessment would reclassify around 19 percent males and approximately 36 percent females into the appropriate treatment categories.

An ABI of more than 1.4 is also a risk for all cause mortality and cardiovascular morbidity even if the observations were not diagnostic because of the vessel incompressibility.

MODIFICATIONS OF THE ABI TECHNIQUE

Post exercise ABI measurements. Exercise unmasks patients with milder peripheral vascular disease.

But exercise ABI is not an option at all in patients with comorbidities due to respiratory or cardiac disease.
Around 15% patients are not candidates for exercise ABI or for hyperemia induction (which mimics exercising with an occlusive cuff)
MATERIALS AND METHODS
MATERIALS AND METHODS

STUDY CENTRE:

Madras Medical College and Rajiv Gandhi Government General Hospital

STUDY DESIGN:

Single centre observational study

VENUE:

Rajiv Gandhi Government General Hospital, Chennai

COLLABORATING DEPARTMENTS:

Institute of Internal Medicine and

Institute of Cardiology, Madras Medical College, Chennai

SAMPLE SIZE is calculated using the formula $4*\frac{p}{q}/d$ where $p$ denotes the prevalence of the disease, $q=1-p$ and the error range is denoted by $d$. Using the above formula the sample size was calculated to be 100.

METHODOLOGY

A complete history was obtained from our patients who were admitted as inpatients in the medical and cardiology wards including the past history and the history of risk factors like diabetes, systemic hypertension, smoking and hyperlipidemia.
A complete physical examination including the vitals was done. Detailed cardiovascular examination was done and the findings were confirmed using an electrocardiogram. All the patients who were admitted with CAD (ST elevation MI and non ST elevation MI and unstable angina were subjected to coronary angiogram. The Ankle brachial index was measured in the study population and the results were compared. Treatment was given for the CAD and the risk factors as well.

INCLUSION CRITERIA

1. Age >45 years

2. DIABETES:

   Symptoms of diabetes plus random blood glucose levels $\geq 200$ mg/dl or

   Fasting glucose $\geq 126$ mg/dl or 2 hour blood glucose $\geq 200$ mg/dl or

   The use of glucose lowering medication

3. HYPERTENSION:

   Systolic blood pressure of $\geq 140$ mmHg or diastolic BP of $\geq 90$ mmHg or

   If the patient is taking antihypertensive treatment

4. SMOKING:

   Regular use of tobacco for smoking one or more times per day or

   Patient has smoked in the past 30 days prior to hospital admission
5. DYSLIPIDEMIA:

Total cholesterol ≥ 200 mg/dl or

LDL ≥ 130 mg/dl or

HDL levels ≤ 40 mg/dl in men and ≤ 50 mg/dl in women or

Triglycerides level ≥ 200 mg/dl or

History of treatment with lipid lowering drugs

6. CORONARY ARTERY ANGIOGRAM

EXCLUSION CRITERIA

1. Patients with lower limb gangrene

2. Patients with ABI > 1.4

3. Patients with deformity of upper or lower limbs

4. Unclear results of ABI or coronary angiography

5. Patients who did not give consent for the procedure
STATISTICAL ANALYSIS PLAN

DATA ANALYSIS

Descriptive statistics was done for all data and were reported in terms of mean values and percentages.

Suitable statistical tests of comparison were done. Continuous variables were analysed with the unpaired t test.

Categorical variables were analysed with the Chi-Square Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$.

The data was analysed using SPSS version 16 and Microsoft Excel 2007.
SAMPLE SIZE ESTIMATION

Sample size was determined based on

**Study**

Correlation between peripheral arterial disease and coronary artery disease using ankle brachial index—a study in Indian population

**Authored by**

Sharmistha Sarangi et al

**Published in**

Indian Heart Journal 6401 (2012) 2–6

In this study, 45 patients (24.73%) in the study population had CAD. The occurrence of CAD in PAD-positive cases was 46.88% while in PAD-negative cases it was 20% (P = 0.001; statistically significant). (57% increased difference)

**Description:**

- The confidence level is estimated at 95%
- with a z value of 1.96
- the confidence interval or margin of error is estimated at +/-10
- Assuming p% =57 and q%=43
- Power of study at 80%
\[ n = p\% \times q\% \times \left[\frac{z}{\epsilon}\right]^2 \]

\[ n = 57 \times 43 \times \left[\frac{1.96}{10}\right]^2 \]

\[ n = 95 \]

Therefore 95 is the minimum sample size required for the study.

In my study I plan to recruit a minimum of 100 subjects

**STUDY PERIOD:** 1 year (August 2017 to July 2018)

**CONSENT**

All participants gave written/informed consent for the procedure

**ETHICAL COMMITTEE APPROVAL**

Institutional Ethical Committee of Madras Medical College approved the study

**METHODS:**

After measuring ABI patients were categorized into two groups that is ABI +ve group (an ABI of \(\leq 0.9\)) and ABI-ve group those with an ABI of \(< 0.9\)). All the patients who met the diagnostic criteria underwent diagnostic coronary angiography via the trans-femoral route with a 5F or 6F catheter. The dye used was Omnipaque300 (iohexol 647 mg, trometamol 1.2 mg). Based on the findings the coronary lesions were classified as CAD group if the stenosis was \(>50\%\) in the major epicardial coronary arteries.

These were further classified as
non-significant (<75% occlusion),

significant (≥75-99% occlusion) and

cut off (100% occlusion) respectively. The various vessel involvement (left main coronary artery, Left anterior descending, left circumflex, right coronary, obtuse marginal 1 and 2) in different patients were recorded.
OBSERVATION AND RESULTS
1. In this study, an analytical approach was adopted to determine the relationship between peripheral arterial disease and coronary artery disease in high risk population using ankle brachial index.

2. Data collected from 100 selected subjects were internally compared, tabulated, analysed and interpreted by using descriptive and inferential statistics based on the formulated objectives of the study.

Among the population studied 28 percent were ABI+VE and 72 percent were ABI–VE.

<table>
<thead>
<tr>
<th>Study Groups</th>
<th>ABI +ve Group</th>
<th>ABI -ve Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>28</td>
<td>72</td>
<td>100</td>
</tr>
<tr>
<td>Percentage</td>
<td>28.00</td>
<td>72.00</td>
<td>100.00</td>
</tr>
</tbody>
</table>
### AGE DISTRIBUTION

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>41-50</td>
<td>28</td>
<td>28.00%</td>
</tr>
<tr>
<td>51-60</td>
<td>72</td>
<td>72.00%</td>
</tr>
<tr>
<td>61-70</td>
<td>24</td>
<td>24.00%</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.00%</td>
</tr>
<tr>
<td>Age Groups</td>
<td>ABI +ve Group</td>
<td>%</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------</td>
<td>----</td>
</tr>
<tr>
<td>41-50 years</td>
<td>7</td>
<td>25.00</td>
</tr>
<tr>
<td>51-60 years</td>
<td>16</td>
<td>57.14</td>
</tr>
<tr>
<td>61-70 years</td>
<td>5</td>
<td>17.86</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>100.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age Distribution</th>
<th>ABI +ve Group</th>
<th>ABI -ve Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>56.00</td>
<td>55.61</td>
<td>55.72</td>
</tr>
<tr>
<td>SD</td>
<td>6.78</td>
<td>5.96</td>
<td>6.17</td>
</tr>
<tr>
<td>P value Unpaired t Test</td>
<td>0.779</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
It is evident from the age distribution table that most of the ABI+ve group subjects were in 51-60 years age group (57.14%) with a mean age of 56.00 years. In ABI-ve group majority too were in 51-60 years age group (54.17%) with a mean age of 55.61 years. (p= G0.779). The data subjected to unpaired t test reveals the existence of statistically non-significant association between age distribution and ABI study groups (p > 0.05)
It is evident from the gender status table that most of the ABI+ve group subjects were males (60.71%) and ABI-ve group subjects too were mostly males (75.00%) (p= 0.157). The data subjected to chi squared test reveals the existence of statistically non-significant association between gender status and ABI study groups (p > 0.05)
**Diabetes Mellitus Status**

<table>
<thead>
<tr>
<th>Diabetes Mellitus Status</th>
<th>ABI +ve Group</th>
<th>ABI -ve Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>18</td>
<td>26</td>
</tr>
<tr>
<td>Absent</td>
<td>10</td>
<td>46</td>
</tr>
</tbody>
</table>

**Diabetes Mellitus Status - Total**

- Present: 56, 56%
- Absent: 44, 44%
<table>
<thead>
<tr>
<th>Diabetes Mellitus Status</th>
<th>ABI +ve Group</th>
<th>%</th>
<th>ABI -ve Group</th>
<th>%</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>18</td>
<td>64.29</td>
<td>26</td>
<td>36.11</td>
<td>44</td>
<td>44.00</td>
</tr>
<tr>
<td>Absent</td>
<td>10</td>
<td>35.71</td>
<td>46</td>
<td>63.89</td>
<td>56</td>
<td>56.00</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>100.00</td>
<td>72</td>
<td>100.00</td>
<td>100</td>
<td>100.00</td>
</tr>
</tbody>
</table>

**P value**

Chi Squared Test 0.011

It is evident from the diabetes mellitus status table that most of the ABI+ve group subjects were diabetics (64.29%) and ABI-ve group subjects were mostly non diabetics (63.89%) (p= 0.011). The data subjected to chi squared test reveals the existence of statistically significant association between diabetes mellitus status and ABI study groups (p < 0.05)

**Discussion**

In our study the diabetes mellitus status between the ABI+ve group and ABI-ve group was meaningfully significant. This is evident by the increased incidence of diabetes in ABI+ve group compared to ABI-ve group (mean increased difference of 28.17 percentage points, 44% higher).
HYPERTENSION STATUS

Hypertension Status

<table>
<thead>
<tr>
<th>Hypertension Status</th>
<th>ABI +ve Group</th>
<th>ABI -ve Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Absent</td>
<td>8</td>
<td>42</td>
</tr>
</tbody>
</table>

Hypertension Status - Total

50, 50%

50, 50%
<table>
<thead>
<tr>
<th>Hypertension Status</th>
<th>ABI +ve Group</th>
<th>%</th>
<th>ABI -ve Group</th>
<th>%</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>20</td>
<td>71.43</td>
<td>30</td>
<td>41.67</td>
<td>50</td>
<td>50.00</td>
</tr>
<tr>
<td>Absent</td>
<td>8</td>
<td>28.57</td>
<td>42</td>
<td>58.33</td>
<td>50</td>
<td>50.00</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>100.00</td>
<td>72</td>
<td>100.00</td>
<td>100</td>
<td>100.00</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.008</td>
</tr>
<tr>
<td>Chi Squared Test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

It is evident from the hypertension status table that most of the ABI+ve group subjects were hypertensive (71.43%) and ABI-ve group subjects were mostly non hypertensive (58.33%) (p = 0.008). The data subjected to chi squared test reveals the existence of statistically significant association between hypertension status and ABI study groups (p < 0.05)

**DISCUSSION**

In our study the hypertension status between the ABI+ve group and ABI-ve group was meaningfully significant. This is evident by the increased incidence of hypertension in ABI+ve group compared to ABI-ve group (mean increased difference of 29.76 percentage points, 42% higher).
### Dyslipidemia Status

#### ABI +ve Group
- Present: 16
- Absent: 23

#### ABI -ve Group
- Present: 49
- Absent: 12

### Dyslipidemia Status - Total

- Present: 39, 39%
- Absent: 61, 61%
<table>
<thead>
<tr>
<th>Dyslipidemia Status</th>
<th>ABI +ve Group</th>
<th>%</th>
<th>ABI -ve Group</th>
<th>%</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>16</td>
<td>57.14</td>
<td>23</td>
<td>31.94</td>
<td>39</td>
<td>39.00</td>
</tr>
<tr>
<td>Absent</td>
<td>12</td>
<td>42.86</td>
<td>49</td>
<td>68.06</td>
<td>61</td>
<td>61.00</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>100.00</td>
<td>72</td>
<td>100.00</td>
<td>100</td>
<td>100.00</td>
</tr>
</tbody>
</table>

P value
Chi Squared Test 0.020

It is evident from the dyslipidemia status table that most of the ABI+ve group subjects had dyslipidaemia (57.14%) and ABI-ve group subjects mostly had no dyslipidemia (68.06%) (p= 0.020). The data subjected to chi squared test reveals the existence of statistically significant association between dyslipidemia status and ABI study groups (p < 0.05)

**DISCUSSION**

In our study the dyslipidemia status between the ABI+ve group and ABI-ve group was meaningfully significant. This is evident by the increased incidence of dyslipidemia in ABI+ve group compared to ABI-ve group (mean increased difference of 25.20 percentage points, 44% higher).
SMOKING STATUS

![Smoking Status Chart]

- **Present:**
  - ABI +ve Group: 16
  - ABI -ve Group: 31
  - Total: 47

- **Absent:**
  - ABI +ve Group: 12
  - ABI -ve Group: 41
  - Total: 53
It is evident from the smoking status table that most of the ABI+ve group subjects were smokers (57.14%) and ABI-ve group subjects were mostly non-smokers (56.94%) (p= 0.205). The data subjected to chi squared test reveals the existence of statistically non-significant association between smoking status and ABI study groups (p > 0.05)
CORONARY ARTERY DISEASE STATUS

Coronary Artery Disease Status

![Bar chart showing the number of patients with coronary artery disease status.](chart.png)

- **Present**: ABI +ve Group: 11, ABI -ve Group: 9
- **Absent**: ABI +ve Group: 25, ABI -ve Group: 55

Coronary Artery Disease Status - Total

![Pie chart showing the total number of patients with coronary artery disease status.](chart.png)

- **Present**: 20, 20%
- **Absent**: 80, 80%
It is evident from the CAD status table that most of the ABI+ve group subjects had no CAD (96.43%) and ABI-ve group subjects too mostly had no CAD (76.39%) (p= 0.048). The data subjected to chi squared test reveals the existence of statistically significant association between CAD status and ABI study groups (p < 0.05)

**DISCUSSION**

In our study the CAD status between the ABI+ve group and ABI-ve group was meaningfully significant. This is evident by the increased incidence of CAD in ABI+ve group (39.29%) compared to ABI-ve group (12.50%) (mean increased difference of 26.79 percentage points, 68% higher).
<table>
<thead>
<tr>
<th>Vessel Involved</th>
<th>ABI +ve Group</th>
<th>%</th>
<th>ABI -ve Group</th>
<th>%</th>
<th>Total</th>
<th>%</th>
<th>P value Chi Squared Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>LMCA</td>
<td>6</td>
<td>21.43</td>
<td>10</td>
<td>13.89</td>
<td>16</td>
<td>16.00</td>
<td>0.356</td>
</tr>
<tr>
<td>RCA</td>
<td>14</td>
<td>50.00</td>
<td>36</td>
<td>50.00</td>
<td>50</td>
<td>50.00</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>LAD</td>
<td>22</td>
<td>78.57</td>
<td>48</td>
<td>66.67</td>
<td>70</td>
<td>70.00</td>
<td>0.243</td>
</tr>
<tr>
<td>D1</td>
<td>8</td>
<td>28.57</td>
<td>8</td>
<td>11.11</td>
<td>16</td>
<td>16.00</td>
<td>0.032</td>
</tr>
<tr>
<td>D2</td>
<td>4</td>
<td>14.29</td>
<td>6</td>
<td>8.33</td>
<td>10</td>
<td>10.00</td>
<td>0.373</td>
</tr>
<tr>
<td>OM</td>
<td>10</td>
<td>35.71</td>
<td>14</td>
<td>19.44</td>
<td>24</td>
<td>24.00</td>
<td>0.001</td>
</tr>
<tr>
<td>LCX</td>
<td>14</td>
<td>50.00</td>
<td>26</td>
<td>36.11</td>
<td>40</td>
<td>40.00</td>
<td>0.203</td>
</tr>
</tbody>
</table>
It is evident from the vessel involved status table that most of the ABI+ve group subjects had LAD as vessel involved (78.57%) and ABI-ve group subjects too mostly had lad as vessel involved (66.67%) (p= 0.020). The data subjected to chi squared test reveals the existence of statistically significant association between vessel involved status (D1 and OM) and ABI study groups (p < 0.05)

**DISCUSSION**

In our study the vessel involved status between the ABI+ve group and ABI-ve group was meaningfully significant. This is evident by the

- Increased incidence of D1 involvement in ABI+ve group compared to ABI-ve group (mean increased difference of 17.46 percentage points, 61% higher).

- Increased incidence of OM involvement in ABI+ve group compared to ABI-ve group (mean increased difference of 16.27 percentage points, 46% higher)
CONCLUSION
CONCLUSIONS

We can conclude that:

Among our study population, Age, gender and smoking status had no statistically significant role to play in determination of the relationship between peripheral arterial disease and coronary artery disease in high risk population using ankle brachial index

This might be explained by the fact that older age is associated with stiff vessels and thus higher ABI values.

On internal comparison the following conclusions were observed

- ABI+ve patients associated with higher incidence of diabetes mellitus
- ABI+ve patients associated with higher incidence of hypertension
- ABI+ve patients associated with higher incidence of dyslipidemia
- ABI+ve patients associated with higher incidence of CAD
- The risk of coronary stenosis was significantly higher in ABI+ve patients with increased incidence of diagonal artery 1 (D1) and obtuse marginal artery (OM) involvements
- An abnormal ABI was an independent predictor of CAD, lesions in coronary arteries and atherosclerotic risk factors

This study is a hypothesis proving study.

Hence results have high clinical significance.
LIMITATIONS OF THE STUDY

1. This study involves 100 patient samples only. Larger study groups are needed to establish the exact relationship between the various CAD risk factors and Ankle Brachial Index.

2. This study does not demonstrate the association between advancing age and ABI values.

3. Although Low ABI is associated with increased risk of CAD this study does not elicit any difference in the percentage of involved vessels among the ABI positive or negative groups.

4. There is also no statistically significant relationship between ABI and sex groups. This is probably due to similar risk of CAD and other atherosclerotic risk in postmenopausal women as compared to males.

5. There is also no statistically significant difference among smokers and non-smokers probably due to lack of adequate control group.
RECOMMENDATIONS

1. Larger patient population sample and longer follow up period is required for more elaborate statistical analysis.

2. These findings suggest clinical importance of ABI and its relationship to peripheral arterial disease and coronary artery disease in high risk population.

3. Larger study population is probably needed to further investigate the effects of age, gender and smoking status on ABI and CAD risk.

4. This warrants further investigation of risk factors and early interventions to improve outcomes among these patients.

5. To raise awareness among practitioners that ABI is a very simple way of assessing MACE events in the future and thus make use of ABI in routine clinical examination and screening.
SUMMARY
SUMMARY

This study shows that there is positive association between various risk factors like diabetes, hypertension, dyslipidemia and low ankle brachial index (which is an indicator of generalized atherosclerosis) and CAD thus supporting the fact that **LOW ANKLE BRACHIAL INDEX IS A PREDICTOR OF CORONARY ARTERY DISEASE**, hence necessitating screening of at risk individuals at an earlier stage using ABI.
BIBLIOGRAPHY
REFERENCES


81


ANNEXURES
PROFORMA

Name

Age

Sex

Occupation

Address

Contact number

Symptoms

1. Chest pain
2. Dyspnea
3. Intermittent claudication

Patient characteristics

1. Smoker (duration, number of cigarettes per day)
2. Alcoholic
3. Diabetic (duration, if on treatment)
4. Hypertensive (duration and if on treatment)
5. Coronary artery disease
6. Peripheral vascular disease
Examination

Systolic Blood pressure

Right upper limb
Right lower limb
Left upper limb
Left lower limb

Pulse rate

Ankle brachial index

ECG

Coronary angiogram findings

PREVALENCE OF ATHEROSCLEROTIC RISK FACTORS IN ABI=VE AND ABI-VE PATIENTS

<table>
<thead>
<tr>
<th>Atherosclerotic risk factor</th>
<th>ABI+VE</th>
<th>ABI-VE</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
NON SIGNIFICANT AND SIGNIFICANT CUTOFF OCCLUSION OF DIFFERENT VESSELS ACCORDING TO ANGIOGRAPHIC FINDINGS IN ABI+VE AND ABI-VE PATIENTS

<table>
<thead>
<tr>
<th></th>
<th>ABI+VE</th>
<th>ABI-VE</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>LMA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCX</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
MEAN SD OF OCCLUSION OF DIFFERENT VESSELS ACCORDING TO THE ANGIOGRAPHIC FINDINGS IN ABI+VE AND ABI-VE PATIENTS

<table>
<thead>
<tr>
<th></th>
<th>ABI+VE</th>
<th>ABI-VE</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LMCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCX</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
INFORMATION SHEET

We are conducting a study on “LOW ANKLE BRACHIAL INDEX AS A PREDICTOR OF CORONARY ARTERY DISEASE-A HOSPITAL BASED STUDY”, among patients attending Rajiv Gandhi Government General Hospital, Chennai and for that your data will be valuable to us.

The purpose of the study is early diagnosis of CAD in patients with low ABI which is a marker of atherosclerosis that may aid in early treatment.

We are selecting certain cases and if you are found eligible, we may use your clinical and lab parameters for our study.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personal information will be shared.

Taking part in the study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time. Your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of this special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management and treatment.

Signature of the investigator                                     Signature of the participant
Date
Place
PATIENT CONSENT FORM

Study Detail : “LOW ANKLE BRACHIAL INDEX AS A PREDICTOR OF CORONARY ARTERY DISEASE-A HOSPITAL BASED STUDY”

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient’s Name :

Patient’s Age :

Identification Number :

Patient may check (√) these boxes

a) I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.

b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

c) I understand that sponsor of the clinical study, others working on the sponsor’s behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

d) I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.

e) I hereby consent to participate in this study.

f) I hereby give permission to undergo detailed clinical examination and blood investigations as required.

Signature of the investigatorStudy investigator’s name

Signature/thumb impressionPatient’s name and address
அனுமானங்கள்

அனுமானப்படி:

தான் அடி ஆண்டுகள் கொண்டு யாரமாகக் கொண்டளடக்கும் மோதுபவனுடன் மேல்புறம் செய்யாமல் குறைத்து வேறுபாடுவை அடிகமாக்குவதற்கு போது நிறைவு செய்யப்பட்டது.

இன்று ஆண்டுகளுக்கு வருந்து, அடி ஆண்டுகள் விளையாடும் சமயத்தில் எதையும் வேறுபாடு கொண்டு வைத்து பார்வை எடுத்துக்கொண்டது. இது அனுமானக் காண்பிக்கப்பட்டன, இந்த வேறுபாடு அவ்விரும் அடி ஆண்டுகளுக்கு பொறியல் அறிக்கையளிப்பு போலவே வைக்கப்பட்டது. இதன் மூலம் வெளிப்படுத்தப்பட்ட நிலைகள் வேறுபாடுகளை குறிக்கவும் மூலமாக வைக்கப்பட்டது.

அகழ்பாய்கள் போன்ற வருந்து செய்யல்லாமல் பற்றிய அறிஞப் பொருளைக் குறிப்பிட்டுப் பொருளைக் குறிப்பிட்டு வைத்து வைக்கப்பட்டது.

பலமென்று பதிவுபட்டாய் அனுமானம்

பலமென்று பதிவு

இன்று:

சூறு:
ஆசுரங்கள் வல்லன்

ஆசுரங்களுடன் இணைந்து வித்யா நிறுவனத்தில் உள்ள கல்வித்துறை மற்றும் விளையாட்டு முறைப்பட்டதாக நவீனிகம் செய்யப்பட்டதை அறிவத்தக்கது.

ஆசுரங்கள் வல்லன்:

செயல்: தொன்மை விளையாட்டு

ஆசுரங்கள் வல்லன்:

செயல்: புராண விளையாட்டு

செயல்:

இந்த ஆசுரங்கள் வல்லன் உள்ளது கல்வித்துறை மற்றும் விளையாட்டு முறைப்பட்டதாக நவீனிகம் செய்யப்பட்டதை அறிவத்தக்கது.

இந்த ஆசுரங்கள் வல்லன் உள்ளது கல்வித்துறை மற்றும் விளையாட்டு முறைப்பட்டதாக நவீனிகம் செய்யப்பட்டதை அறிவத்தக்கது.

இந்த ஆசுரங்கள் வல்லன் உள்ளது கல்வித்துறை மற்றும் விளையாட்டு முறைப்பட்டதாக நவீனிகம் செய்யப்பட்டதை அறிவத்தக்கது.
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.I.Bena Jesni
Post Graduate in M.D. General Medicine
Institute of Internal Medicine
Madras Medical College
Chennai 600 003

Dear Dr.I.Bena Jesni,

The Institutional Ethics Committee has considered your request and approved your study titled "LOW ANKLE BRACHIAL INDEX AS A PREDICTOR OF CORONARY ARTERY DISEASE- A HOSPITAL BASED STUDY" - NO.09082017

The following members of Ethics Committee were present in the meeting held on 01.08.2017 conducted at Madras Medical College, Chennai 3

1. Prof.Dr.C.Rajendran, MD., Chairperson
2. Prof.R.Narayana Babu, MD., DCH., Dean, MMC, Ch-3 : Deputy Chairperson
3. Prof.Sudha Seshayyan, MD., Vice Principal, MMC, Ch-3: Member Secretary
4. Prof.N.Gopalakrishnan, MD, Director, Inst. of Nephrology, MMC, Ch: Member
5. Prof.S.Mayilvahanan, MD, Director, Inst. of Int.Med, MMC, Ch-3 : Member
6. Prof.Rema Chandramohan, Prof. of Paediatrics, ICH, Chennai: Member
7. Prof. Susila, Director, Inst. of Pharmacology, MMC, Ch-3: Member
8. Prof.K.Ramadevi, MD., Director, Inst. of Bio-Chemistry, MMC, Ch-3: Member
9. Thiru S.Govindasamy, BA., BL, High Court, Chennai : Lawyer
10. Tmt. Arnold Saulina, MA., MSW., Social Scientist
11. Tmt. J.Rajakahmi, JAO, MMC, Ch-3 : Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003
Urkund Analysis Result

Analysed Document: ibena plagiarism.docx (D4245)
Submitted: 10/12/2018 3:42:00 AM
Submitted By: ibenajesni@gmail.com
Significance: 7%

Sources included in the report:

My preview thesis.docx (D42407138)
Nandhu thesis.Intro-limitation.docx (D42435367)
Final Thesis for plagiarism check.docx (D30571896)
DISSERTATION 1.docx (D31274930)
DISSERTATION 1.docx (D31303717)
http://stanfordmedicine25.stanford.edu/the25/ankle.html
http://citeseerx.ist.psu.edu/viewdoc/summary?doi=10.1.1.2;
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3347847/

Instances where selected sources appear:

25
PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled “LOW ANKLE BRACHIAL INDEX AS A PREDICTOR OF CORONARY ARTERY DISEASE-A HOSPITAL BASED STUDY” of the candidate Dr. IBENA JESNI.I., with registration Number 201611008 for the award of M.D in the branch of GENERAL MEDICINE. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 7 percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.
<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>diabetes</th>
<th>HTN</th>
<th>Smoking</th>
<th>ABI</th>
</tr>
</thead>
<tbody>
<tr>
<td>48</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.16</td>
</tr>
<tr>
<td>45</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.4</td>
</tr>
<tr>
<td>60</td>
<td>F</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>0.76</td>
</tr>
<tr>
<td>53</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.11</td>
</tr>
<tr>
<td>50</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.06</td>
</tr>
<tr>
<td>58</td>
<td>F</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>0.78</td>
</tr>
<tr>
<td>60</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.09</td>
</tr>
<tr>
<td>53</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.09</td>
</tr>
<tr>
<td>50</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>0.9</td>
</tr>
<tr>
<td>53</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.11</td>
</tr>
<tr>
<td>54</td>
<td>F</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>0.9</td>
</tr>
<tr>
<td>67</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>50</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>50</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>48</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>53</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>57</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>63</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>65</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>56</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>53</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>55</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>52</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>55</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td>55</td>
<td>M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>1.18</td>
</tr>
<tr>
<td></td>
<td>68 M</td>
<td>52 M</td>
<td>55 M</td>
<td>60 F</td>
<td>61 F</td>
</tr>
<tr>
<td>-------</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>Gender</td>
<td>M</td>
<td>M</td>
<td>F</td>
<td>F</td>
<td>F</td>
</tr>
<tr>
<td>Age</td>
<td>68</td>
<td>52</td>
<td>55</td>
<td>60</td>
<td>61</td>
</tr>
<tr>
<td>Yes/No</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Age</td>
<td>Gender</td>
<td>Age</td>
<td>Gender</td>
<td>Age</td>
<td>Gender</td>
</tr>
<tr>
<td>-----</td>
<td>--------</td>
<td>-----</td>
<td>--------</td>
<td>-----</td>
<td>--------</td>
</tr>
<tr>
<td>63</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>F</td>
<td>yes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>56</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>53</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>66</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>68</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>52</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>52</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>61</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>53</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>56</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>53</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Name</td>
<td>Gender</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
</tr>
<tr>
<td>------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
</tr>
<tr>
<td>53 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>56 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>67 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>50 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>45 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>48 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>66 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>53 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>55 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>53 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>48 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>55 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>48 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>53 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>55 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>53 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>53 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>52 M</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Vessel</td>
<td>ABI+</td>
<td>ABI-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------</td>
<td>------</td>
<td>------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LMCA</td>
<td>6</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>14</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>22</td>
<td>48</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D1</td>
<td>8</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D2</td>
<td>4</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OM</td>
<td>10</td>
<td>14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCX</td>
<td>14</td>
<td>26</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>