Brief overview about Interarm Systolic Blood Pressure Difference and Coronary Artery Disease

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Abstract

Background: Under normal physiological circumstances, the BP reading is often same for both the arms. However, a BP difference between both arms is frequently encountered in various general populations. Inter-arm blood pressure difference (IAD), also known as interarm systolic blood pressure difference (IASBPD), refers to the variation in systolic blood pressure measurements between the left and right arms. It is normal to have an IAD of <5 mmHg. An IAD is defined as a variance in systolic BP of >10 mmHg. It has emerged as a clinically significant parameter that can provide valuable insights into cardiovascular health and risk assessment. The measurement of blood pressure in both arms has gained attention as a simple, non-invasive method to identify potential underlying vascular abnormalities and to evaluate the risk of cardiovascular diseases. Understanding the clinical significance of IAD has prompted researchers and healthcare professionals to explore its potential as a risk marker and prognostic indicator. The evaluation of IAD can provide valuable information regarding underlying vascular pathology and may contribute to risk stratification and treatment decision-making. Additionally, IAD assessment can be easily incorporated into routine blood pressure measurements, making it a practical and cost-effective tool in clinical practice. Coronary artery disease (CAD) is a cardiovascular disease which has been found to be the leading cause of death in both developed and developing countries. CAD is an atherosclerotic disease which is inflammatory in nature, manifested by stable angina, unstable angina, myocardial infarction (MI), or sudden cardiac death. Risk factors for CAD include high blood pressure, high cholesterol, smoking, diabetes, and a family history of heart disease. CAD is often diagnosed through a combination of tests, including a physical exam, blood tests, and imaging studies such as an electrocardiogram (ECG), echocardiography and a coronary angiogram. Treatment options for CAD include lifestyle changes, medications, and procedures such as angioplasty or coronary artery bypass surgery.

Keywords: Interarm Systolic Blood Pressure Difference, Coronary Artery Disease

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Introduction

Under normal physiological circumstances, the BP reading is often same for both the arms. However, a BP difference between both arms is frequently encountered in various general populations. Inter-arm blood pressure difference (IAD), also known as interarm systolic blood pressure difference (IASBPD), refers to the variation in systolic blood pressure measurements between the left and right arms. It is normal to have an IAD of <5 mmHg. An IAD is defined as a variance in systolic BP of >10 mmHg. It has emerged as a clinically significant parameter that can provide valuable insights into cardiovascular health and risk assessment **(1)**.

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marker and prognostic indicator. The evaluation of IAD can provide valuable information regarding underlying vascular pathology and may contribute to risk stratification and treatment decision-making. Additionally, IAD assessment can be easily incorporated into routine blood pressure measurements, making it a practical and cost-effective tool in clinical practice **(2)**.

Etiology

The cause for IAD can be both physiological and pathological. In younger people, inter-arm BP difference can occur when a muscle compresses an artery supplying the arm or by a structural problem that prevents smooth blood flow through an artery. In older people, it is usually due to a blockage arising due to atherosclerosis. Other causes are subclavian artery stenosis, aortic aneurysm, aortic coarctation, vasculitis, fibromuscular hyperplasia, connective tissue disorders, and thoracic outlet compression. Hence, it is vital to detect an inter-arm BP difference for further vascular assessment and management of risk factors

Inter-arm blood pressure difference (IAD) can arise from a variety of physiological and pathological factors, contributing to variations in blood pressure readings between the right and left arms. This disparity in blood pressure can offer crucial insights into vascular health and potentially indicate underlying conditions that warrant further evaluation. The underlying mechanisms of IAD can differ based on age groups **(3)**.

Physiological Causes:

Inter-arm blood pressure differences can be attributed to various physiological factors. One common physiological cause is the compression of an artery supplying one arm by a muscle during blood pressure measurement. Additionally, structural anomalies within an artery can hinder smooth blood flow and result in varying pressure readings between arms. Higher pressures are more frequent in the right arm and range in most individuals from 10 to 20 mmHg or greater in systole, and to a similar extent but less often in diastole. A BP difference between the left and right arms—even when large—is statistically a normal variant and need not necessarily cause concern. When the disparity is persistent, however, the arm with the higher pressure should be used for all subsequent BP measurements **(4)**.

Pathological Causes:

Inter-arm blood pressure disparities often stem from underlying pathological conditions, notably atherosclerosis, wherein arteries narrow or block due to plaque buildup, causing reduced blood flow and noticeable pressure differences. Aortic dissection, involving a tear in the aorta's inner lining, can similarly provoke such discrepancies due to compromised blood flow. Additional potential contributors encompass subclavian artery stenosis, aortic aneurysm, aortic coarctation, vasculitis, fibromuscular hyperplasia, connective tissue disorders, and thoracic outlet compression—all capable of impacting blood vessel health and flow patterns across the arms **(3)**.

Indications for Measurement

Interarm Systolic Blood Pressure Difference (IAD) measurement is indicated in various clinical scenarios as follows:

1. Hypertension Assessment: IAD measurement is recommended as an adjunctive tool in the evaluation of hypertension. By measuring blood pressure in both arms, any significant interarm differences can be detected. An IAD ≥10 mmHg may indicate underlying vascular or arterial abnormalities that contribute to hypertension. Identifying such differences can guide treatment decisions and help tailor antihypertensive therapy for optimal blood pressure control **(2)**.
2. Peripheral Artery Disease (PAD): IAD measurement is particularly relevant in patients suspected or diagnosed with peripheral artery disease. Peripheral artery disease is characterized by the narrowing or blockage of arteries supplying the limbs. An elevated IAD may suggest the presence of subclavian or brachial artery stenosis, which is commonly associated with PAD. IAD measurement aids in the identification and evaluation of arterial abnormalities in patients with PAD, contributing to effective management strategies **(5).**.
3. Severe Chest Pain and Suspected Aortic Dissection: Acute aortic dissection (AAD) is a cardiovascular condition with high mortality. Inter-arm difference in blood pressure and pulse deficit are well-known characteristics of AAD. Inter-arm difference in blood pressure associated with aortic dissection is thought to be caused by decreased blood flow in the upper arm from an AD extending to the brachiocephalic artery (BCA) or left subclavian artery (LSCA) **(6)**.
4. Cardiovascular Risk Assessment: IAD measurement serves as an additional risk marker in cardiovascular risk assessment. Studies have shown that a higher IAD is associated with an increased risk of cardiovascular events, such as heart attacks and strokes. In individuals with low to medium cardiovascular risk scores, measuring IAD can help identify those who may benefit from intensified preventive measures and closer monitoring to reduce their cardiovascular risk **(3)**.
5. Diabetes and Hypertension: Patients with both diabetes and hypertension are at a higher risk of developing cardiovascular complications. IAD measurement provides valuable information in this population. Elevated IAD has been associated with increased left ventricular mass, arterial stiffness, and diabetic nephropathy.

Incorporating IAD measurement into the management of patients with diabetes and hypertension can aid in risk stratification and guide treatment decisions to prevent cardiovascular complications **(6)**.

6. Screening for Subclavian Artery Stenosis: IAD measurement can serve as a screening tool for subclavian artery stenosis, a condition characterized by narrowing of the arteries supplying the arms. Patients with symptoms suggestive of subclavian artery stenosis, such as arm claudication (pain or fatigue with arm movement), can undergo IAD measurement to assess for significant differences between the arms. Detecting an elevated IAD may prompt further diagnostic evaluation and appropriate management **(7)**.
7. Follow-up after Cardiovascular Interventions: Monitoring IAD is essential in the post-interventional phase following procedures such as angioplasty or stent placement. IAD measurement helps assess the success of the procedure and detect any residual arterial abnormalities. Changes in IAD over time can provide valuable information about the patency and functional status of the treated arteries, guiding ongoing management and follow-up care **(8)**.

Measurement Technique

The measurement of Interarm Systolic Blood Pressure Difference (IAD) involves comparing systolic blood pressure readings between the left and right arms. It is a simple and non-invasive method that can provide valuable information about potential underlying vascular abnormalities and cardiovascular risk. To ensure accurate and reliable measurements, a standardized measurement technique is followed. The measurement begins by positioning the patient in a comfortable and relaxed position. It is recommended that the patient sits or lies down for at least five minutes before the measurement to allow for proper relaxation. The arms should be positioned at the same level as the heart to minimize any gravitational effects on blood pressure **(9)**.

A standard tourniquet is typically used during the measurement. The tourniquet has a width of 12-13 cm and a length of 35 cm, although larger or smaller sizes may be used if needed. The tourniquet is placed around the upper arm, approximately 2-3 cm above the antecubital fossa (the inner bend of the elbow). The tourniquet should be snug but not excessively tight to avoid discomfort or interference with blood flow. Blood pressure is measured simultaneously in both arms using a calibrated sphygmomanometer or an automated blood pressure device. The blood pressure cuff is wrapped around the upper arm just below the tourniquet. The cuff should cover at least 80% of the upper arm circumference. The device is then activated to inflate the cuff and measure the systolic blood pressure **(10)**.

Multiple measurements are typically taken in each arm to ensure accuracy and reliability. The measurements can be performed manually by a healthcare professional or by an automated device. The systolic blood pressure readings from both arms are recorded and compared to calculate the interarm systolic blood pressure difference (IAD). A difference of 10 mmHg or more between the arms is often considered significant. It is important to note that certain factors may influence IAD measurements. Factors such as arm position, cuff size, patient positioning, and the timing of the measurement can impact the results. Therefore, it is crucial to follow standardized guidelines and protocols to minimize potential sources of error and ensure consistency in measurement technique **(3)**.

Outcome

A difference in systolic blood pressures between arms, referred to as inter-arm difference (IAD), has also been shown to be associated with increased risk of cardiovascular morbidity and mortality, and is associated with increasing pulse pressure and arterial stiffness. An IAD ≥10 mmHg is found in 11% of people with hypertension and 7% of those with diabetes. The precise etiology of an IAD is incompletely established; however, arterial changes seem to be a common contributor. A body of evidence now exists to support recognition of IAD as an early marker for subsequent vascular disease, and to quantify that risk for cardiovascular events **(18)**.

Clinical significance of Interarm Systolic Blood Pressure Difference measurement in Coronary Artery Disease Patient

Interarm Systolic Blood Pressure Difference measurement in patients with coronary artery disease (CAD) carries evident clinical significance. Firstly, IAD measurement provides valuable information regarding the severity and extent of arterial stenosis in CAD patients. Patients with CAD and an IAD ≥10 mmHg tend to have a higher severity of coronary artery stenosis compared to those with an IAD <10 mmHg. This suggests that IAD measurement can serve as a predictive factor for the existence and severity of CAD, aiding in risk stratification and treatment planning . Secondly, IAD measurement can help identify individuals with CAD who are at a higher risk of future cardiovascular events. Patients with an IAD ≥10 mmHg have been shown to have a significantly higher probability of experiencing cardiovascular events, including myocardial infarction and stroke. This independent association between elevated IAD and adverse cardiovascular outcomes highlights the clinical significance of incorporating IAD measurement into the management of CAD patients. By identifying those at increased risk, appropriate interventions and preventive measures can be implemented to reduce the risk of future events. Therefore, IAD measurement can serve as a valuable prognostic marker, aiding in risk assessment and long-term management of CAD patients **(11)**.

In addition to its prognostic value, IAD measurement can help guide treatment decisions in CAD patients. By assessing the degree of interarm blood pressure differences, healthcare professionals can gain insights into the response to treatment and the effectiveness of interventions such as revascularization procedures. Monitoring changes in IAD over time can assist in evaluating the success of interventions and identifying residual arterial abnormalities that may require further management. Moreover, IAD measurement is a non-invasive, easily accessible, and cost-effective technique. It can be performed in a primary care or clinical setting, allowing for widespread application and incorporation into routine clinical practice. The simplicity and low cost of IAD measurement make it a practical tool for risk assessment and monitoring in CAD patients. Coronary artery disease (CAD) is a cardiovascular disease which has been found to be the leading cause of death in both developed and developing countries. CAD is an atherosclerotic disease which is inflammatory in nature, manifested by stable angina, unstable angina, myocardial infarction (MI), or sudden cardiac death. Risk factors for CAD include high blood pressure, high cholesterol, smoking, diabetes, and a family history of heart disease. CAD is often diagnosed through a combination of tests, including a physical exam, blood tests, and imaging studies such as an electrocardiogram (ECG), echocardiography and a coronary angiogram. Treatment options for CAD include lifestyle changes, medications, and procedures such as angioplasty or coronary artery bypass surgery **(12)**.

Anatomy of Coronary Arteries

In the normal heart, oxygenated blood is supplied by two coronary arteries that arise from ascending aorta. The RCA and LMCA extend from the aortic root to supply different regions of the heart. The RCA gives rise to the sinoatrial nodal branch of the right coronary artery, posterior descending artery branch of the RCA, and the marginal branch. The LMCA branches into the circumflex and LAD. The circumflex artery gives rise to the left marginal artery and posterior descending artery (in a left-dominant heart). The left anterior descending artery gives off the diagonal branches. The RCA supplies blood to the right side of the heart. The sinoatrial nodal branch of the RCA provides blood to the SA node, and the atrioventricular nodal artery delivers blood to the AV node. The marginal branch of the right coronary artery provides blood supply to the lateral portion of the right ventricle. The posterior descending artery branch supplies blood to the inferior aspect of the heart. The LMCA supplies blood to the left side of the heart. The LAD provides blood to the anterior ventricular septum and the greater portion of the anterior portion of the left ventricle. The LCx supplies blood to the lateral wall of the left ventricle and sometimes to the posterior inferior aspect of the heart when there is left heart dominance **(13)**..

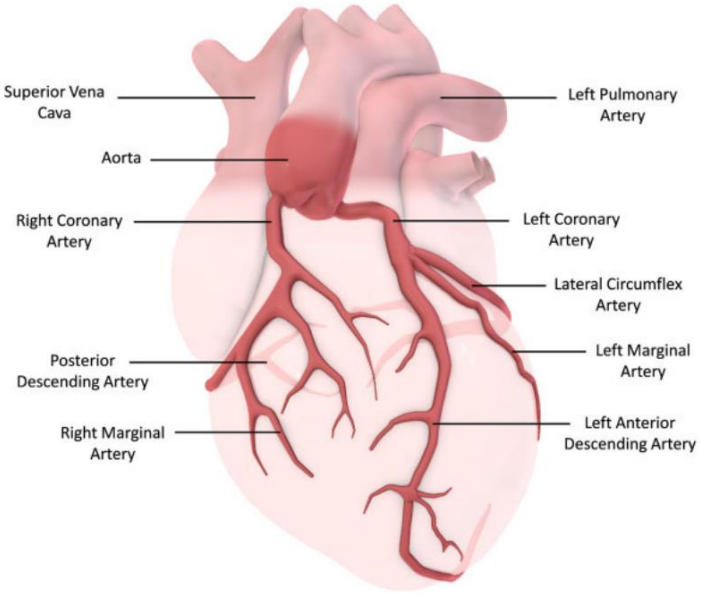

Fig. (1): Anatomy of the coronary arteries **(14)**.

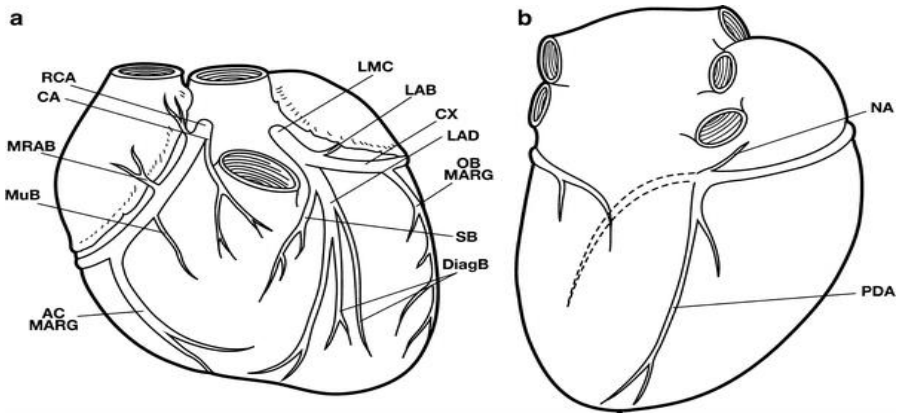

Fig. (2): Diagrams of the main coronary arteries and their branches as seen from the anterior (**a**) and posterior (**b**) aspects of the heart. This illustration shows the common phenomenon in which the right posterior descending artery (RPDA) arises from the terminal branch of the right coronary artery (RCA) **(14)**.

Epidemiology

Coronary artery disease is common in both developed and developing countries. In one study, it was estimated that CAD represented 2.2% of the overall global burden of diseases and 32.7% of cardiovascular diseases. It costs over 200 billion dollars annually to the health care system in the United States. **(12)**.

In Egypt, the National Hypertension Project (NHP) found an adjusted overall prevalence of CAD is 8.3%. Increasing prevalence in developing countries, high expenses of surgical and other treatment modalities, side effects, and the resultant inability make CAD one of the most important medical and health issues **(15)**.

Risk factors for coronary artery disease

The risk factors of coronary artery disease have been divided into non-modifiable and modifiable. The non-modifiable risk factors include: age, male sex, and family history which cannot be altered. According to the American Heart Association [AHA], the modifiable risk factors which can be altered by medical and lifestyle interventions are: hypertension, hypercholesterolemia, physical inactivity, diabetes, overweight, obesity and tobacco smoking **(16)**.

Non-traditional contributors to CAD encompass various factors. Chronic inflammation, marked by elevated markers like CRP, promotes atherosclerosis and arterial plaque formation. Elevated homocysteine levels damage arteries and increase clotting likelihood. Higher levels of lipoprotein(a) [Lp(a)] heighten atherosclerosis and clotting risk. Metabolic syndrome, with obesity, high blood pressure, and lipid issues, elevates CAD and diabetes risks. Psychosocial factors, like stress and depression, impact CAD risk via behavior and physiology. Hormonal changes, post-menopausal estrogen decline, also influence CAD risk. Emerging research indicates air pollution, particularly PM2.5 fine particles, plays a role in CAD development. Sleep apnea raises hypertension, diabetes, and CAD risks. Chronic kidney disease, impacting blood pressure and more, intensifies CAD risk **(17)**.

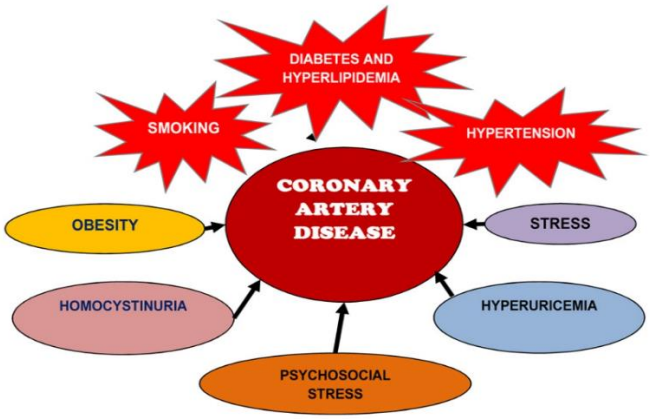

Fig. (3): Various risk factors associated with coronary artery disease **(16)**.

Pathophysiology of coronary artery disease

CAD mainly occurs due to atherosclerosis and its progression is associated with environmental and genetic factors. Atherosclerosis is a chronic process, characterized by progressive accumulation of lipids, fibrous elements, and inflammatory molecules in the walls of the large arteries. Atherosclerosis starts with the efflux of low-density lipoprotein (LDL) cholesterol to the sub-endothelial space, which can be changed and oxidized by various agents. Oxidized/modified LDL particles are powerful chemotactic molecules that prompt expression of vascular cell adhesion molecules and intercellular adhesion molecules at the surface of endothelium, and stimulate monocyte adhesion and migration to the sub endothelial space. Monocytes transform into macrophages in the intima media **(18)**.

Macrophages enchain oxidized LDL through scavenger receptors to become foam cells and release pro inflammatory cytokines including interleukins and tumor necrosis factor. The development of fatty streak in which foam cells appear in the sub-endothelial space it is the final result of this process. Moreover, in the sub-endothelial space accumulate other forms of leukocytes, including lymphocytes and mast cells accumulate. The interaction between monocytes, macrophages, foam cells and T-cells induce a cellular and humoral immune response (inflammatory cascade) with the production of several pro inflammatory molecules such as interleukin-6 (IL-6) and tumor necrosis factor (TNF-α). The process continues with the migration of smooth muscle cells from the medial layer of the artery into the intima, following of fatty streak to a more complex lesion. As soon as smooth muscle cells are in the intima media, they produce extracellular matrix molecules that are developing a fibrous cap which is covering the initial fatty streak. Inside the fibrous cap the foam cells die, therefore release lipids that collect in the extracellular space, forming a lipid-rich pool (necrotic core). This process results in the formation of the second atherosclerotic lesion, the fibrous plaque **(19)**.

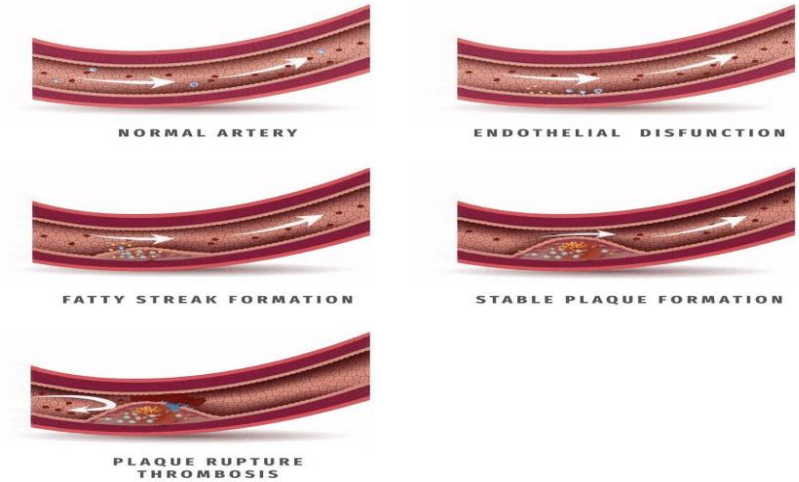

Fig. (4): The process of atherosclerosis and formation of the CAD **(19)**.

The thickness of the fibrous cap is important for the integration of the atherosclerotic plaque. The extrusion of this type of plaque into the lumen of the artery generates a limitation of flow, well known as stenosis, which is causing ischemia to the tissue and is expressed clinically as stable angina. Moreover, vulnerable plaques composed of a thin fibrous cap made mostly of type I collagen along with no or few smooth muscle cells, but abundant macrophages and pro inflammatory and pro thrombotic molecules leading to atheroma. Two types of plaque can be defined: stable and unstable or vulnerable, based on the balance between formation and degradation of fibrous cap. Stable plaques have an intact, thickset fibrous cap synthesized of smooth muscle cells in a matrix rich in type I and III collagen. Vulnerable plaques are likely to break, revealing the core of the plaque to circulating coagulation proteins, causing thrombosis, sudden artery lumen occlusion and therefore an acute coronary syndrome. Moreover, intraplaque hemorrhage is also a potential factor for the progression of atherosclerosis, which occur when the vasa vasorum invades the intima from the adventitia **(18)**.

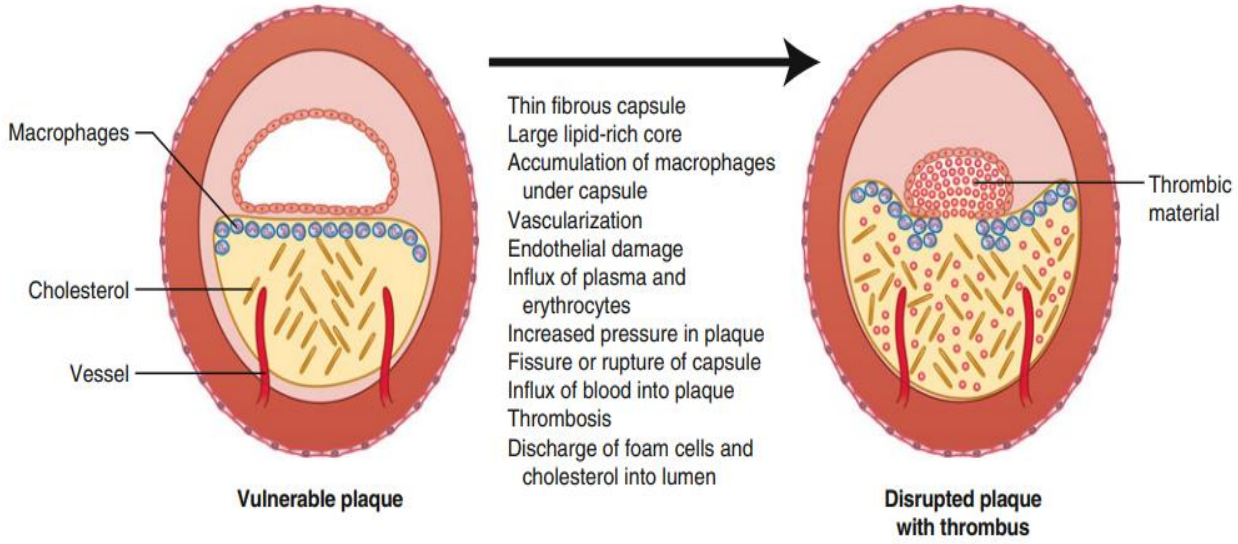

Fig. (5): Characteristics of the vulnerable plaque and mechanisms contributing to disruption of the plaque capsule and thrombosis **(20)**.

Evaluation

There are several modalities to evaluate for coronary artery disease including blood work, CXR, ECG, Echo, Stress test and cardiac catheterization to name the main ones. These tests are done depending on the context in which patients are presenting. The following are details on different diagnostic modalities we have available for the evaluation of coronary artery disease: **(21)**.

- **Blood investigations**

Cardiac biomarkers are blood tests that measure specific proteins that are released into the bloodstream when the heart is damaged or under stress. These biomarkers include Troponin, Myoglobin, CK-MB, and BNP. These biomarkers can help to confirm the diagnosis of CAD and determine the extent of the disease. Elevated levels of these biomarkers can also be used to monitor the patient's response to treatment and detect any changes in the patient's condition over time. In acute settings, cardiac enzymes and B-type natriuretic peptides are often done along with complete blood counts and metabolic panels. BNP provides information about volume overload of cardiogenic origin however it has its limitations. It can be falsely elevated in kidney diseases and falsely low in obesity. Cardiac enzymes like CK and troponin provide information about an acute ischemic event. In chronic settings, lipid panel provides important prognostic information. **(22)**.

Fasting plasma glucose and glycated haemoglobin (HbA1c) should be measured in every patient with suspected CAD. If both are inconclusive, an additional oral glucose tolerance test is recommended. Patients with diabetes should be managed according to specific Guidelines. A lipid profile, including total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides, should also be evaluated in any patient with suspected CAD to establish the patient's risk profile and ascertain the need for treatment. **(22)**.

- **Chest X-ray**

Chest X-ray is an important component of the initial evaluation of cardiac disease. The standard imaging films include standing posteroanterior (PA) and left lateral decubitus. Sometimes, anteroposterior (AP) projection is obtained especially in inpatient settings with the patient lying down, however, this interpretation of AP films is significantly limited. Proper analysis of PA and AP views provides useful and cost-effective information about the heart, lungs, and vasculature. Interpretation should be done in a stepwise pattern so that important information is not overlooked **(21)**.

- **Electrocardiogram (ECG)**

ECG is a very basic yet enormously helpful test in the evaluation of coronary artery disease. Important information to notice on an ECG is a heart's rate, rhythm, and axis. After that, information regarding acute and chronic pathologic processes can be obtained. In acute coronary syndrome, one can see ST-segment

changes and T wave changes. If an ACS has degenerated into arrhythmias, that can also be seen. In chronic settings, ECG can show information like axis deviation, bundle branch blocks, and ventricular hypertrophy. ECG is also a cost-effective and readily available testing modality that is not user-dependent. Acute myocardial ischemia may affect all components of the electrical activation of the heart, including the P wave, the PR interval, the QRS complex, the ST segment, and the T and U waves. The most dramatic ECG manifestation of acute transmural myocardial ischemia is ST-segment elevation (STE) in the leads facing the ischemic zone and ST-segment depression (STD) in the leads facing the anatomically opposite myocardial segments **(23)**.

When evaluating an electrocardiogram (ECG) to ascertain the responsible culprit vessel for a cardiac event, several vital anatomical elements should be considered this include:

1. **ST-Segment Elevation:** The presence and precise localization of ST-segment elevation serve as pivotal indicators for discerning the myocardial ischemic or infarcted area. Elevated ST segments signify myocardial injury. The afflicted leads demonstrating ST elevation serve to refine the identification of the potential culprit vessel.
2. **Reciprocal Changes:** The manifestation of reciprocal ST-segment depressions in leads opposing those with ST elevation provides supplementary insight. These alterations delineate areas of the cardiac muscle that are not directly impacted but react to the ischemic changes.
3. **ECG Manifestations in Diverse Vessels:**
    - LAD Involvement: Marked ST elevation in leads V1-V4, coupled with reciprocal changes observed in lead III.
    - LCx Involvement: Prominent ST elevation is apparent in leads I, aVL, V5, and V6, accompanied by reciprocal changes in inferior leads.
    - RCA Involvement: Evident ST elevation in leads II, III, and aVF, coupled with reciprocal changes manifesting in lateral leads.
4. **Supplementary Leads:** In scenarios suggesting posterior myocardial involvement, the inclusion of additional posterior leads (V7-V9) can proffer insights into potential posterior infarctions.
5. **Bundle Branch Blocks:** In the presence of bundle branch blocks, the assessment of discordant ST changes proves advantageous in the diagnosis of acute myocardial infarction.

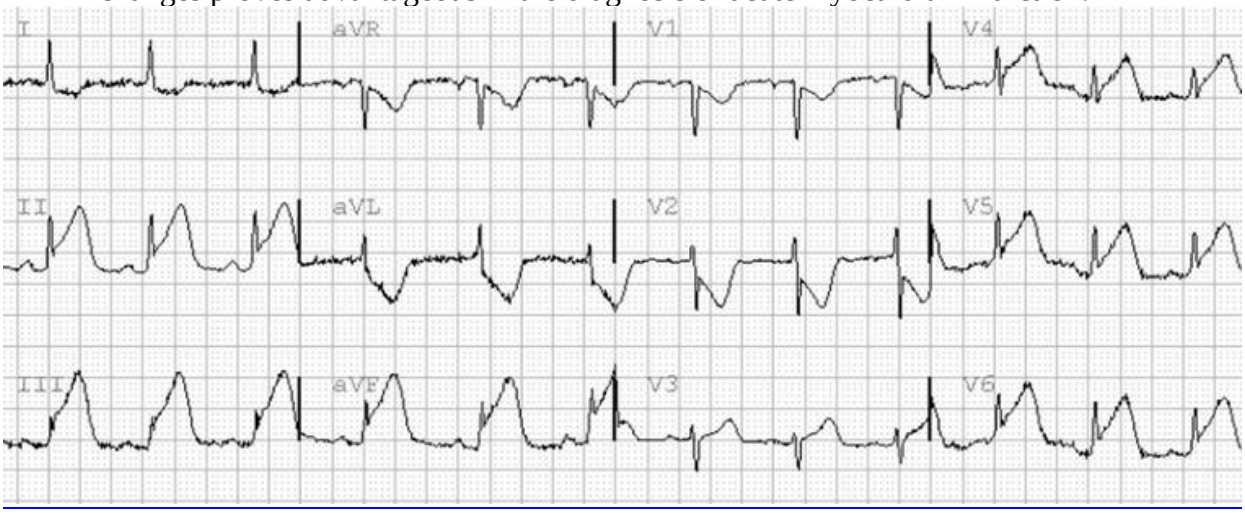

Fig. (6): Inferior and lateral STE-ACS. There is ST elevation in the leads II, III, aVF, and V_4–V_6. Leads I and aVL show reciprocal ST depression. ST elevation in leads V_1–V_2 represents lateral "mirror-image" ST deviation. There is Sclarovsky–Birnbaum grade III of ischemia in leads III, aVF, and V_6 **(23)**.

- **Echocardiography**

Echocardiography and magnetic resonance imaging at rest An echocardiographic study will provide important information about cardiac function and anatomy. LV ejection fraction (LVEF) is often normal in patients with CCS. A decreased LV function and/or regional wall motion abnormalities may increase the

suspicion of ischaemic myocardial damage, and a pattern of LV dysfunction following the theoretical distribution territory of the coronary arteries is typical in patients who have already had an MI. The detection of regional wall motion abnormalities can challenging by visual assessment, and detection of early systolic lengthening, decreased systolic shortening, or post-systolic shortening by strain imaging techniques might be helpful in patients with apparently normal LV function but with clinical suspicion of CCS **(24)**.

Decreased diastolic LV function has been reported to be an early sign of ischaemic myocardial dysfunction and could also be indicative of microvascular dysfunction. Echocardiography is an important clinical tool for the exclusion of alternative causes of chest pain and also aids in diagnosing concurrent cardiac diseases, such as valvular heart diseases, HF, and most cardiomyopathies, but it is important to remember that these diseases often coexist with obstructive CAD. The use of an echocardiographic contrast agent can be useful in patients with poor acoustic windows **(24)**.

- **Stress Test**

The stress test is a relatively non-invasive test to evaluate for coronary artery disease. It is used in the setting of suspected angina or angina equivalent and is helpful in ruling in or out coronary pathology when interpreted in an appropriate setting. During the test, the heart is artificially exposed to stress and if the patient gets certain abnormal ECG changes in ST segments or gets symptoms of angina, the test is aborted at that point and coronary artery disease is diagnosed. ECGs are obtained before, during, and after the procedure, and the patient is continuously monitored for any symptoms. There are mainly two types of stress tests; exercise stress test and pharmacologic stress test. In exercise stress tests, the patient has to run on a treadmill until he achieves 85% of the age-predicted maximal heart rate. If a patient develops exertional hypotension, hypertension (>200/110 mmHg), ST-segment elevations or depression, or ventricular or supraventricular arrhythmias **(25)**.

- Pharmacologic stress test is indicated in patients who cannot exercise. Dobutamine is used for assessing regional wall motion abnormalities. A graded dobutamine infusion starting at 5 mcg/kg/min and increasing at three-minute intervals to 10, 20, 30, and 40 ug/kg/min is the standard for dobutamine stress testing. During dobutamine echocardiography, images are obtained before the start of the infusion, at the end of each stage, and during the recovery. The importance of low dose stages plays a role in recognition of viability and ischemia in segments with abnormal function at rest, even if viability assessment is not the main objective of the test. Endpoints are the achievement of target heart rate (defined as 85% of the age-predicted maximum heart rate), new or worsening wall motion abnormalities of moderate degree, significant arrhythmias, and intolerable symptoms. To achieve the target heart rate, Atropine can be used in divided doses of 0.25 mg to 0.5 mg to a total of 2 mg. Atropine increases the sensitivity of dobutamine echocardiography in patients receiving beta-blockers and in those with single-vessel disease **(26)**.

- **Coronary CTA**

Anatomical non-invasive evaluation, by visualizing the coronary artery lumen and wall using an intravenous contrast agent, can be performed with coronary CTA, which provides high accuracy for the detection of obstructive coronary stenoses defined by ICA, because both tests are based on anatomy. However, stenoses estimated to be 50-90% by visual inspection are not necessarily functionally significant, i.e. they do not always induce myocardial ischemia. Therefore, either non-invasive or invasive functional testing is recommended for further evaluation of angiographic stenosis detected by coronary CTA or invasive angiography, unless a very high-grade (>90% diameter stenosis) stenosis is detected via invasive angiography. The presence or absence of non-obstructive coronary atherosclerosis on coronary CTA provides prognosis **(27)**.

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- **Cardiac magnetic resonance**

Cardiac magnetic resonance (CMR) may be considered in patients with suspected CAD when the echocardiogram (having used contrast) is inconclusive. CMR will provide useful information on cardiac anatomy and systolic cardiac function, similar to that from an echocardiogram, in patients with no contraindications for CMR. CMR can assess global and regional function, and the use of late gadolinium enhancement CMR can reveal a typical pattern of scarred myocardium in patients who have already experienced an MI. Assessment of LV function is important in all patients for risk stratification and should therefore be performed in all symptomatic patients with suspected CAD. Management of patients with either angina or HF symptoms, with reduced LVEF <40% or a mid-range reduced LVEF of 40-49%, is described in section 4 of the Guidelines.Table (2): Resting echocardiography and cardiac magnetic resonance in the initial diagnostic management of patients with suspected coronary artery disease **(27)**.

Recommendations	Class	Level
Resting transthoracic echocardiogram is recommended for: (1) Exclusion of alternative causes of angina; (2) Identification of regional wall motion abnormalities suggestive of CAD; (3) Measurement of LVEF for risk stratification; (4) Evaluation of diastolic function.	IB	
Ultrasound of the carotid arteries should be considered, performed by trained clinicians, to detect plaque in patients with suspected CCS without known atherosclerotic disease.	IIa	C
CMR may be considered in patients with an inconclusive echocardiographic test.	IIb	C

- **Cardiac Catheterization**

Cardiac catheterization is the gold standard and most accurate modality to evaluate ischemic coronary heart disease. It is however an invasive procedure with associated complications. Not everyone is a candidate for the procedure. In non-ACS settings, patients with high pretest probability for CAD are usually the right candidates for it. In the ACS setting, all STEMI patients and selected NSTEMI patients get an emergent cardiac catheterization. This procedure is done in a cardiac catheterization lab, is expertise dependent, and is done under moderate sedation **(28)**.

Selecting appropriate testing

In patients in whom revascularization is futile due to comorbidities and overall quality of life, the diagnosis of CAD can be made clinically and only medical therapy is required. If the diagnosis of CAD is uncertain, establishing a diagnosis using non-invasive functional imaging for myocardial ischaemia before treatment is reasonable. In a patient with a high clinical likelihood of CAD, symptoms unresponsive to medical therapy or typical angina at a low level of exercise, and an initial clinical evaluation (including echocardiogram and, in selected patients, exercise ECG) that indicates a high event risk, proceeding directly to invasive coronary angiography (ICA) without further diagnostic testing is a reasonable option. Under such circumstances, the indication for revascularization should be based on appropriate invasive confirmation of the haemodynamic significance of a stenosis. In other patients in whom CAD cannot be excluded by clinical assessment alone, non-invasive diagnostic tests are recommended to establish the diagnosis and assess the event risk. The current Guidelines recommend the use of either noninvasive functional imaging of ischaemia or anatomical imaging using coronary CT angiography (CTA) as the initial test for diagnosing CAD **(27)**.

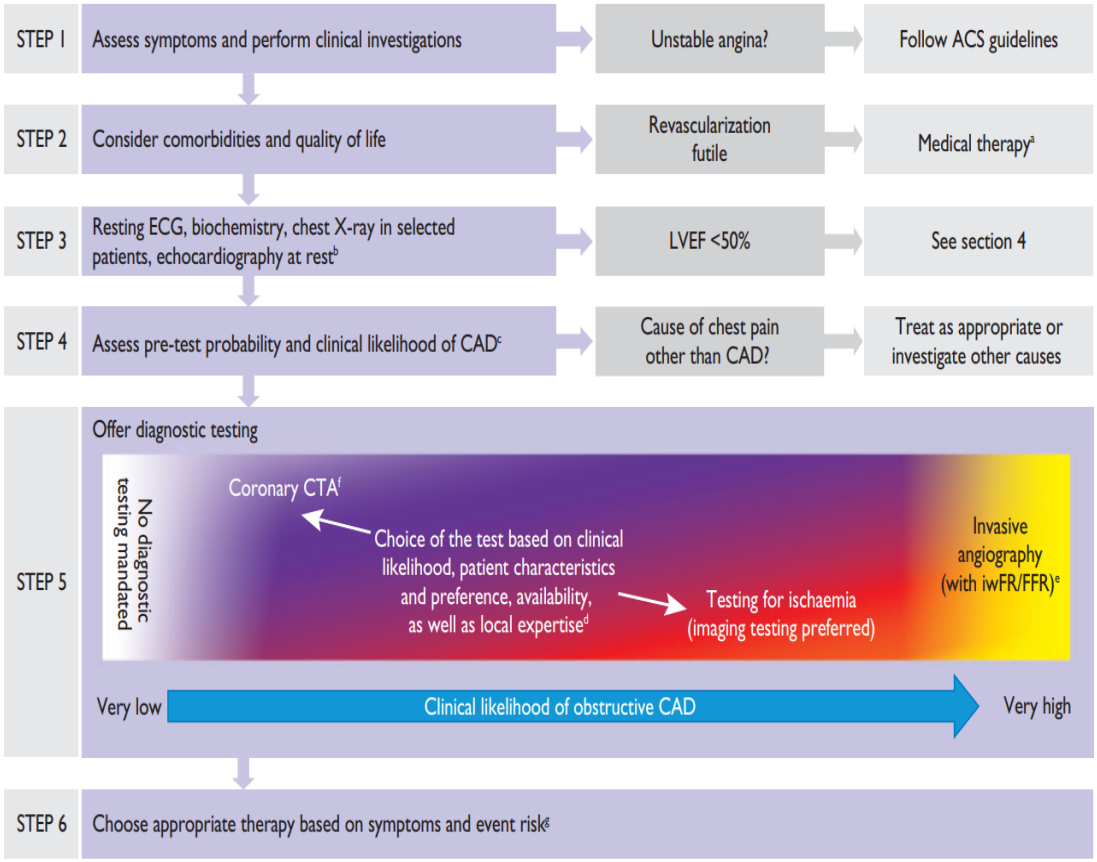

Fig (7): Approach for the initial diagnostic management of patients with angina and suspected coronary artery disease according to ESC Guidelines **(27)**.
ACS = acute coronary syndrome; BP = blood pressure; CAD = coronary artery disease; CTA = computed tomography angiography; ECG = electrocardiogram; FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio; LVEF = left ventricular ejection fraction. a If the diagnosis of CAD is uncertain, establishing a diagnosis using non-invasive functional imaging for myocardial ischaemia before treatment may be reasonable. b May be omitted in very young and healthy patients with a high suspicion of an extracardiac cause of chest pain, and in multimorbid patients in whom the echocardiography result has no consequence for further patient management. c Consider exercise ECG to assess symptoms, arrhythmias, exercise tolerance, BP response, and event risk in selected patients. d Ability to exercise, individual test-related risks, and likelihood of obtaining diagnostic test result. e High clinical likelihood and symptoms inadequately responding to medical treatment, high event risk based on clinical evaluation (such as ST-segment depression, combined with symptoms at a low workload or systolic dysfunction indicating CAD), or uncertain diagnosis on non-invasive testing. f Functional imaging for myocardial ischaemia if coronary CTA has shown CAD of uncertain grade or is non-diagnostic. g Consider also angina without obstructive disease in the epicardial coronary arteries.

Treatment / Management

Coronary artery disease could present either as stable ischemic heart disease (SIHD) or acute coronary syndrome (ACS). The former present in a chronic setting while the latter presents more in an acute setting. The management depends on the particular disease type. We will discuss the management of each subtype separately: **(16)**.

A. Stable Ischemic Heart Disease

Stable ischemic heart disease presents as stable angina. Stable angina typically presents as substernal chest pain or pressure that worsens with exertion or emotional stress and gets relieved with rest or nitroglycerin and is of 2 months duration. Stable Ischemic Heart Disease management includes the following: **(28)**.

- The first step in managing SIHD is lifestyle changes. This includes quitting smoking, eating a healthy diet low in saturated fat and cholesterol, and engaging in regular physical activity. These changes can help to reduce the risk of further progression of the disease and improve overall cardiovascular health **(29)**.
- Every patient should get guideline-directed medical therapy (GDMT) which includes low dose aspirin, beta-blocker, as-needed nitroglycerin, and moderate to high-intensity statin. If symptoms are not controlled with this, beta-blocker therapy should be titrated up to heart rates 55-60, and the addition of calcium channel blocker and long-acting nitrates should be considered. Ranolazine could also be added to relieve refractory anginal symptoms.
- If guideline-directed medical therapy has failed to relive angina, cardiac catheterization should be done to visualize the coronary anatomy and a decision should be made for percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) based on the patient profile.

Revascularization

Advance in techniques, equipment, stent and adjuvant therapy have established PCI as a routine and safe procedure in patients with SCAD and suitable coronary anatomy. The decision to revascularize a patient should be based on the presence of significant obstructive coronary artery stenosis, the amount of related ischemia, and the expected benefit on prognosis and/ or symptom. Revascularization can also be considered as first-line treatment in the following situation: post-myocardial infarction angina/ischaemia, left ventricular dysfunction, multivessel disease and/or large ischaemic territory, left main stenosis. The indications for PCI and CABG in CAD patients have clearly been defined by the recent recommendations on myocardial revascularization **(30)**.

After PCI for stable angina, 6 months of DAPT achieves the optimum balance of efficacy and safety in most patients. Premature discontinuation of a P2Y12 inhibitor is associated with an increased risk of stent thrombosis and is discouraged.284 However, a shorter duration of DAPT may be considered in those at high risk of life-threatening bleeding in view of the very low risk of stent thrombosis after 1-3 months. On the basis of phase III trials, 12 months is the recommended default duration of DAPT after ACS, but shorter duration may again be considered in those at high bleeding risk **(30)**.

B. Acute Coronary Syndrome

The acute coronary syndrome presents as sudden onset substernal chest pain or pressure typically radiating to the neck and left arm and may be accompanied by dyspnea, palpitations, dizziness, syncope, cardiac arrest, or new-onset congestive heart failure. Acute Coronary Syndrome (ACS) encompasses various cardiovascular conditions resulting from sudden reduced blood flow to the heart muscle, often due to plaque rupture in a coronary artery. The conditions include unstable angina, causing chest pain even at rest; Non-ST Segment Elevation Myocardial Infarction (NSTEMI), with partial artery blockage and heart muscle damage; and the severe ST Segment Elevation Myocardial Infarction (STEMI), involving complete artery blockage, demanding immediate intervention like angioplasty to restore blood flow and limit muscle damage. Prompt ECG is necessary for all patients with ACS to assess for STEMI and typically is done pre-hospital by an emergency medical services crew. STEMI is recognized by the presence of ST elevation in contiguous leads of 1 mm in limb leads or precordial leads excepting V2 and V3. In V2 and V3, men need to have 2 mm elevations and women 1.5 mm to qualify for STEMI diagnosis. New-onset left bundle branch block (LBBB) is also considered a STEMI equivalent. If STEMI is present, emergency PCI is warranted in a PCI capable facility or if a PCI facility is available within 2 hours distance. If the PCI capable facility is more than 2 hours away, intravenous thrombolytic therapy is indicated after making sure there are no contraindications to it **(31)**.

It is important to differentiate a true STEMI from other conditions that mimic STEMI on ECG like acute pericarditis, Brugada syndrome, early repolarization changes, and LVH associated changes. All patients should get a full dose of aspirin (324 mg) upon presentation. Nitrates should be given for pain relief after making sure there are no contraindications to nitrates like hypotension, RV failure, and consumption of phosphodiesterase inhibitors in the past 24-48 hours. High-dose statin therapy and beta-blockers should also be initiated early. P2Y12 inhibitors (prasugrel, ticagrelor) should be started based on the patient profile.

Patients who have NSTE ACS should get anticoagulation, typically heparin or enoxaparin are used. For NSTEMI, early invasive therapy within 24 hours is advised for patients with intermediate to high risk **(32)**

References

1. Elmaghrabi, M. H., Hassanein, M. T., El-dosouky, I. I., & Sedik, E. H. (2023). The Effect of Inter-Arm Blood Pressure Difference on Left Ventricular Function. The Egyptian Journal of Hospital Medicine, 90(2), 3598-3602.
2. Heshmat-Ghahdarijani, K., Dabaghi, G. G., Rad, M. R., & Najafi, M. B. (2022). The Relation between inter arm blood pressure difference and presence of cardiovascular disease: a review of current findings. Current Problems in Cardiology, 47(11), 101087
3. Gopalakrishnan, S., Savitha, A., & Rama, R. (2018). Evaluation of inter-arm difference in blood pressure as predictor of vascular diseases among urban adults in Kancheepuram District of Tamil Nadu. Journal of Family Medicine and Primary Care, 7(1), 142.
4. Fred, H. L. (2013). Accurate blood pressure measurements and the other arm: the doctor is ultimately responsible. Tex Heart Inst J, 40(3), 217-219.
5. Mehlsen, J., & Wiinberg, N. (2014). Interarm difference in blood pressure: reproducibility and association with peripheral vascular disease. International journal of vascular medicine, 2014.
6. Sasamoto, N., Akutsu, K., Yamamoto, T., Otsuka, T., Sangen, H., Hayashi, H., Murata, H., Miyachi, H., Hosokawa, Y., & Tara, S. (2021). Characteristics of Inter-Arm Difference in Blood Pressure in Acute Aortic Dissection. Journal of Nippon Medical School, 88(5), 467-474.
7. Deşer, S. B., Yucel, S. M., Demirag, M. K., Kolbakir, F., & Keceligil, H. T. (2019). Relationship of inter-arm systolic blood pressure difference with subclavian artery stenosis and vertebral artery stenosis in patients undergoing carotid endarterectomy. Brazilian Journal of Cardiovascular Surgery, 34, 136-141.
8. Clark, C., Boddy, K., Warren, F., Mcdonagh, S., Taylor, R., Aboyans, V., Cloutier, L., McManus, R., Shore, A., & Campbell, J. (2018). Inter-arm differences in blood pressure and mortality: individual patient data meta-analysis and development of a prognostic algorithm (INTERPRESS-IPD COLLABORATION). Journal of Hypertension, 36, e105.
9. Gbaguidi, G. N., Kaboure, A., Houehanou, Y. C., Amidou, S. A., Houinato, D. S., Aboyans, V., & Lacroix, P. (2022). Inter-arm difference in systolic blood pressure: Prevalence and associated factors in an African population. PLoS One, 17(8), e0272619.
10. Verberk, W. J., Kessels, A. G., & Thien, T. (2011). Blood pressure measurement method and inter-arm differences: a meta-analysis. Am J Hypertens, 24(11), 1201-1208.
11. Das, S., Iktidar, M. A., Das, J., Chowdhury, F., & Roy, S. (2022). Inter-arm blood pressure difference as a tool for predicting coronary artery disease severity. Open Heart, 9(2), e002063.
12. Bauersachs, R., Zeymer, U., Brière, J.-B., Marre, C., Bowrin, K., & Huelsebeck, M. (2019). Burden of coronary artery disease and peripheral artery disease: a literature review. Cardiovascular therapeutics, 2019.
13. Saxton, A., Chaudhry, R., & Manna, B. (2019). Anatomy, Thorax, Heart Right Coronary Arteries.
14. Ramai, D., Lai, J., Monzidelis, C., & Reddy, S. (2018). Coronary artery development: origin, malformations, and translational vascular reparative therapy. Journal of cardiovascular pharmacology and therapeutics, 23(4), 292-300.
15. El-Moselhy, E., Mohammed, A., Abd El-Aziz, A., Sadek, I., Hagrass, S., & Farag, G. (2018). Coronary artery disease among elderly Egyptian patients: I. socio-demographic, lifestyle, psychosocial, medical, and biochemical risk factors. Am J Gerentol Geriatr, 1(2), 1006.
16. Malakar, A. K., Choudhury, D., Halder, B., Paul, P., Uddin, A., & Chakraborty, S. (2019). A review on coronary artery disease, its risk factors, and therapeutics. Journal of cellular physiology, 234(10), 16812-16823.
17. Lechner, K., von Schacky, C., McKenzie, A. L., Worm, N., Nixdorff, U., Lechner, B., Kränkel, N., Halle, M., Krauss, R. M., & Scherr, J. (2020). Lifestyle factors and high-risk atherosclerosis: Pathways and mechanisms beyond traditional risk factors. European journal of preventive cardiology, 27(4), 394-406.
18. Alfarisi, H. A. H., Mohamed, Z. B. H., & Ibrahim, M. B. (2020). Basic pathogenic mechanisms of atherosclerosis. Egyptian Journal of Basic and Applied Sciences, 7(1), 116-125.
19. Mageed, L. (2018). Coronary Artery Disease: Pathogenesis, Progression of Atherosclerosis and Risk Factors. Open Journal of Cardiology & Heart Diseases, 2(4), 1-7.
20. Buja, L. M. (2015). Coronary artery disease: pathological anatomy and pathogenesis. In Coronary artery disease (pp. 1-20). Springer.

21. Shahjehan, R. D., & Bhutta, B. S. (2021). Coronary artery disease. In StatPearls [Internet]. StatPearls Publishing.
22. Moldoveanu, S., Hunea, I., Damian, S. I., Knieling, A., & Iliescu, D. B. Postmortem Specificity of Troponin for Acute Myocardial Infarction Diagnosis Through Qualitative Dosing from Pericardial Fluid. Euro-Asian Journal of Surgery and Medicine, 13.
23. Birnbaum, Y., Wilson, J. M., Fiol, M., de Luna, A. B., Eskola, M., & Nikus, K. (2014). ECG diagnosis and classification of acute coronary syndromes. Annals of Noninvasive Electrocardiology, 19(1), 4-14.
24. Eek, C., Grenne, B. r., Brunvand, H., Aakhus, S., Endresen, K., Hol, P. K., Smith, H.-J. r., Smiseth, O. A., Edvardsen, T., & Skulstad, H. (2010). Strain echocardiography and wall motion score index predicts final infarct size in patients with non–ST-segment–elevation myocardial infarction. Circulation: Cardiovascular Imaging, 3(2), 187-194.
25. Pontone, G., Guaricci, A. I., Palmer, S. C., Andreini, D., Verdecchia, M., Fusini, L., Lorenzoni, V., Guglielmo, M., Muscogiuri, G., & Baggiano, A. (2020). Diagnostic performance of non-invasive imaging for stable coronary artery disease: A meta-analysis. International Journal of Cardiology, 300, 276-281.
26. Kossaify, A., Bassil, E., & Kossaify, M. (2020). Stress Echocardiography: Concept and Criteria, Structure and Steps, Obstacles and Outcomes, Focused Update and Review. Cardiol Res, 11(2), 89-96.
27. Knuuti, J., Wijns, W., Saraste, A., Capodanno, D., Barbato, E., Funck-Brentano, C., Prescott, E., Storey, R. F., Deaton, C., & Cuisset, T. (2020). 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: the Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC). European heart journal, 41(3), 407-477.
28. F Ibrahim, H., Farouk, H., & Helmy, I. (2022). Diagnostic aspects of multidetector CT in detection of coronary artery diseases versus interventional coronary Angiography. Benha Journal of Applied Sciences, 7(7), 57-63.
29. Mancini, G. J., Maron, D. J., Hartigan, P. M., Spertus, J. A., Kostuk, W. J., Berman, D. S., Teo, K. K., Weintraub, W. S., Boden, W. E., & Group, C. T. R. (2019). Lifestyle, glycosylated hemoglobin A1c, and survival among patients with stable ischemic heart disease and diabetes. Journal of the American College of Cardiology, 73(16), 2049-2058.
30. Voudris, K. V., & Kavinsky, C. J. (2019). Advances in management of stable coronary artery disease: the role of revascularization? Current treatment options in cardiovascular medicine, 21(3), 1-12.
31. Bhatt, D. L., Lopes, R. D., & Harrington, R. A. (2022). Diagnosis and treatment of acute coronary syndromes: a review. JAMA, 327(7), 662-675.
32. Kimura, K., Kimura, T., Ishihara, M., Nakagawa, Y., Nakao, K., Miyauchi, K., Sakamoto, T., Tsujita, K., Hagiwara, N., & Miyazaki, S. (2019). JCS 2018 guideline on diagnosis and treatment of acute coronary syndrome. Circulation Journal, 83(5), 1085-1196.