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A Review On: Left Main Coronary Artery Stenosis"

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ABSTRACT

Significant morbidity and mortality are linked to left main coronary artery stenosis (LMCAS), a high-risk subtype of coronary artery disease. As it supplies a significant amount of the left ventricle, it is mainly brought on by atherosclerosis and can result in severe myocardial ischemia. In order to diagnose LMCAS, coronary angiography is used, with supplementary imaging methods including intravascular ultrasound (IVUS) and multislice computed tomography (MSCT) for a more thorough evaluation. Although management techniques have changed considerably, coronary artery bypass grafting (CABG) remains the gold standard. Innovations in drug-eluting stents (DES) for percutaneous coronary intervention (PCI), however, have introduced alternative revascularization options, with ongoing debate regarding long-term clinical outcomes. This review comprehensively examines the pathophysiology, diagnostic approaches, and evolving treatment paradigms for LMCAS. In order to improve patient selection standards and revascularization outcomes, more research is required.

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INTRODUCTION: Among the most crucial indicators of high rates of morbidity and death is substantial left main coronary artery disease, a relatively high-risk subtype of coronary artery disease. Given its

phenotypic diversity, there are still concerns over the optimal treatment plan for patients despite its therapeutic significance. Concerns regarding clinical outcomes and long-term prognoses remain when comparing coronary artery bypass grafting versus percutaneous coronary intervention, despite the fact that current evidence-based guidelines offer information about revascularization choices. Its goal is to provide a thorough examination of current methods for the identification, evaluation, and management of left main coronary artery disease. [1]

When a patient was dying from shock following an acute myocardial infarction in 1912, James Herrick discovered left main coronary artery (LMCA) disease. Three to five percent of patients undergoing cardiac catheterization have this lesion, which frequently occurs as a result of one or more other epicardial arteries being involved together. Unusual clinical entities include LMCA's isolated, significant involvement when other epicardial coronary arteries do not have angiographically noticeable lesions. [2]

People with severe left main coronary artery (LMCA) stenosis have long been treated with heart bypass grafting (CABG). A paradigm shift in therapy for LMCA lesions is necessary, as evidenced by recent advancements in percutaneous coronary intervention (PCI) methods and the introduction of drug-eluting stents. [3]

A luminal diameter stenosis of 50% indicates that LMCA stenosis is angiographically substantial. Because halting the left main coronary artery without collateral flow or a patent bypass graft to the left anterior descending or circumflex arteries impacts flow to approximately 75% of the left ventricle, patients with substantial stenosis of the left main coronary artery are at high risk. In angiography, the terms "left main equivalent" and "protected" versus "unprotected" LMCA disease are synonymous. [2]

1.1 CORONARY ARTERY: The English term "belonging to a crown or wreath" (coronary) is derived from the Latin word "coronarius." Viewed from above, the coronary vessels encircle the root of the great vessels in cross-section like a tilted, inverted crown. [4]

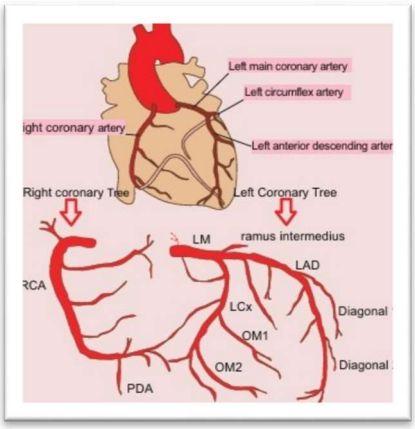

Fig.no.1- Coronary Artery Structure (5)

Usually originating from ostia in the left and right sinuses of Valsalva, the left and right coronary arteries comprise the epicardial coronary artery system. Approximately 50% of people have a "third coronary artery" (also known as the "conus artery") that starts from a different ostium in the right sinus. The right ventricle may have several branches that originate from additional, smaller ostia in the right sinus. (4)

Starting at the base of the ascending aorta are the coronary arteries. Remember that the sinuses of Valsalva, or three semilunar cusps, are found in the aortic valve. On the left and right, the equivalent coronary arteries originate from the semilunar cusps. The third sinus, also known as the non-coronary sinus, is the posterior semilunar cusp and is not connected to a coronary artery. (4)

A. LEFT CORONARY ARTERY

ANATOMY:

The central region of the left aortic tube gives birth to a small trunk that forms the left major coronary artery at its superior boundary. Before entering the left atrioventricular groove in the aortic wall, the artery travels left, superior, and anterior from its ostium. (6)

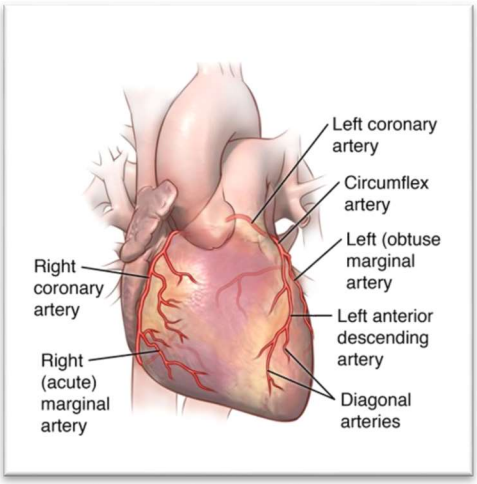

Fig.no.2. Right and left coronary artery [7]

Crucial details about the left major coronary artery	
Origin	Aortic sinus on the left side of the ascending aorta
Branches	arteries of the left anterior descent and circumflex
Supply	The anterior two thirds of the interventricular septum, the atrioventricular bundle, the left atrium, the left ventricle, a portion of the right ventricle, and the sinuatrial node (40%)

Table.no.1- Crucial details about the left major coronary artery [7]

The left coronary artery has two branches;

The apex of the heart is reached by the left anterior descending artery obliquely moving down the anterior interventricular groove. The inferior (posterior) interventricular groove is where it typically loops around the inferior border of the heart, and it forms anastomoses with the descending inferior (posterior) branch of the right coronary artery. Both of the heart's ventricles are supplied by the left anterior descending artery through its septal branches. The left anterior descending artery typically branches diagonally along its path, crossing the left ventricle's anterior surface.[7]

The smaller circumflex branch of the left coronary artery wraps around the left heart border and onto the inferior surface of the heart along the left part of the atrioventricular groove (coronary sulcus). Often, it ends inside the coronary sulcus before it reaches the inferior interventricular groove. At the border of the left heart, the left marginal artery, a large branch of the circumflex artery, typically emerges to supply the

left ventricle. Additionally, the circumflex artery produces smaller anterior and inferior branches to supply the left ventricle. [7]

The left major coronary artery is normally 10 mm (2–23 mm) long, with women's arteries measuring 3.9 ± 0.4 mm and men's 4.5 ± 0.5 mm. The ostium, shaft, and distal segment make up its three constituent parts. The histological characteristics of the ostium, which include the most elastic tissue of the coronary veins, a high density of smooth muscle cells, and the absence of an adventitia layer, may account for a specific response (such as greater elastic rebound) during PCI. [8]

During diastole, the left major coronary artery's blood flow reaches its maximum of 200 ml/min/100 g at a speed of 40–60 cm/s. [9]

Anatomical variation:

There are several anatomical variances in the heart arteries. In certain situations, the LCA may not exist at all, in which case its branches emerge straight from the ascending aorta. Other variants of the LCA include changes in length, origination and course, branching, and the angle of bifurcation. [7]

1.2 LEFT CORONARY ARTERY STENOSIS

LMCAS is serious but its severity and treatment needs vary from patient to patient. Left Main Coronary Artery Stenosis (LMCAS) is too broad a term to be clinically useful. To accurately assess the condition, consider these key factors:[2]

1. Narrowing severity
2. Location of narrowing
3. Presence of narrowing in other coronary arteries
4. Heart ventricle condition

Additionally, consider how the narrowing affects the patient's body, such as:

1. The amount of exercise needed to start symptoms
2. Blood pressure changes

A. ETIOLOGY

Blood flow to a significant area of the heart may be significantly impacted by left main coronary artery stenosis (LMCAS), which is a narrowing of the left major coronary artery. [2] Other than atherosclerosis,

or plaque accumulation, the precise cause of severe Left Main Coronary Artery (LMCA) disease is unknown. According to research, LMCA narrowing is primarily caused by atherosclerosis. [2] Additional uncommon reasons include :

1. Inflammatory diseases (e.g., syphilitic aortitis, giant cell arteritis, Takayasu disease, Kawasaki disease)
2. Valve calcification or replacement
3. Trauma from coronary angiography
4. Radiation therapy

Some cases show severe thickening of the artery wall due to fibrous tissue, without plaque buildup.

Increased aortic and left main ostium artery pressure can cause damage to the arterial lining, which can then cause fibromuscular proliferation and the development of atherosclerotic plaques. Because of the outward expansion of the arterial wall, the internal diameter of the artery may not vary much in the early phases of plaque development. Atherosclerotic lesions in this region, however, can cause the artery's lumen to constrict, which can lead to stenosis, because the smooth muscle lining of the ostium does not have this compensatory dilatation. [10]

1. Atherosclerosis:

The accumulation of cholesterol, fat, and other materials on the arterial walls, which results in plaques that restrict or obstruct blood flow, is the most frequent cause of atherosclerosis. Smoking, diabetes, high blood pressure, high cholesterol, and a sedentary lifestyle can all contribute to this. [11]

2. Inflammatory Diseases:

Inflammation and constriction of the coronary arteries, especially the left major coronary artery, can result from autoimmune conditions such as Takayasu arteritis and Kawasaki disease.

A uncommon chronic inflammatory disease, Takayasu disease (also known as Takayasu arteritis) mainly affects large arteries, particularly the aorta and its major branches, such as the coronary arteries. [12]

Inflammation in the coronary arteries brought on by Kawasaki illness can result in scarring and left coronary artery constriction (stenosis).[13]

3. Radiation Therapy:

A long-term consequence of radiation therapy to the chest for diseases such as breast cancer or lymphoma is coronary artery stenosis, which includes LMCAS. [14]

4. Trauma:

Trauma to the chest (e.g., during an accident) can damage the coronary arteries and result in stenosis over time. [15]

5. Valve Calcification and Valve Replacement:

Valve Calcification: [16]

1. Aortic valve calcification can lead to:
   - Aortic stenosis (narrowing)
   - Increased pressure on left coronary artery
   - Accelerated atherosclerosis (plaque buildup)
2. Mitral valve calcification can lead to:
   - Mitral stenosis (narrowing)
   - Increased pressure on left ventricle
   - Decreased blood flow to left coronary artery

Valve Replacement: [17]

1. Aortic valve replacement (AVR) can:
   - Improve blood flow to left coronary artery
   - Reduce pressure on left ventricle
   - Possibly require coronary artery bypass grafting (CABG)
2. Mitral valve replacement (MVR) can:
   - Improve blood flow to left ventricle
   - Reduce pressure on left atrium
   - Possibly require CABG

B. PATHOPHYSIOLOGY OF LEFT MAIN CORONARY ARTERY STENOSIS:

The main cause of left main coronary artery (LMCA) stenosis is atherosclerosis, which is the accumulation of cholesterol, fatty deposits, and other materials (plaque) in the arterial walls. This

process causes the artery to narrow, which lowers the heart's blood supply. In LMCA stenosis, the artery that provides a significant amount of blood to the left side of the heart narrows. (11)

Key steps involved in the pathophysiology include:

1. Endothelial Dysfunction

- **Initiation**: Damage to the endothelial cells lining the artery's inner surface is the first step in atherosclerosis. Risk factors include high blood pressure, smoking, diabetes, hyperlipidemia (high levels of LDL cholesterol), and mechanical stress from turbulent blood flow can all cause this dysfunction.
- **Mechanism**: Under normal conditions, the endothelium regulates vascular tone and prevents the adhesion of inflammatory cells. Dysfunctional endothelium, however, becomes more permeable and loses its ability to produce protective substances like nitric oxide (NO). This impairs vasodilation and creates a pro-inflammatory, pro-thrombotic environment.
- **Consequences**: As a result, plaque can form because low-density lipoproteins (LDL) can pierce the artery wall. (18)

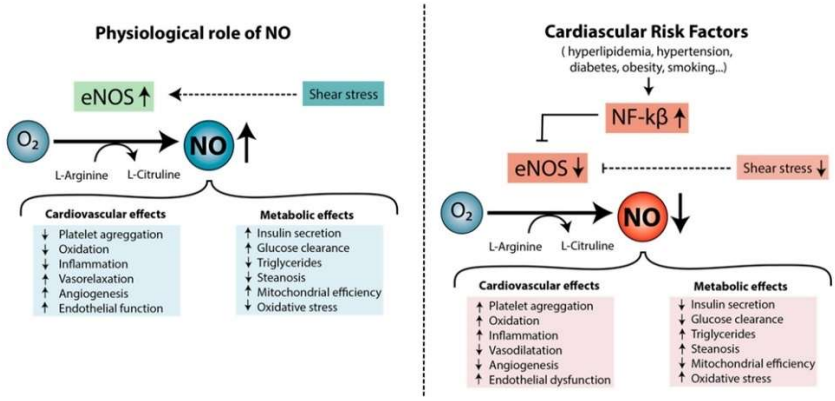

Fig.no.3 Role of Nitrogen Oxide (11)

2. Lipid Infiltration

- **LDL Accumulation**: Once the endothelium is compromised, LDL particles accumulate in the subendothelial space (the intima layer). Over time, these LDLs undergo modifications, particularly oxidation, forming oxidized LDL.

- **Endothelial Activation**: The release chemicals that endothelial cells use to adhere in response to oxidized LDL draws circulating monocytes, a subset of white blood cells. Additionally, oxidized LDL stimulates endothelial cells, which starts the inflammatory response and draws in more immune cells.
- **Inflammation**: Monocytes adhere to the endothelium and migrate into the intima, where they differentiate into macrophages, engulfing the oxidized LDL particles. [19]

3. Fatty Streak Formation

- **Foam Cell Formation**: When macrophages consume oxLDL inside the intima, they change into lipid-rich cells called foam cells. Fatty streaks, the first obvious lesions that appear in the development of atherosclerosis, are created when these foam cells build up.
- **Role of Smooth Muscle Cells**: By consuming oxidized lipids, vascular smooth muscle cells (VSMCs) may also aid in the production of foam cells in addition to macrophages, therefore encouraging the accumulation of fatty material in the arterial walls.
- **Inflammatory Response**: The presence of foam cells perpetuates inflammation. The inflammatory cytokines released attract more immune cells to the site, accelerating the progression of the fatty streak into more advanced plaque. [20]

4. Movement and Multiplication of Smooth Muscle Cells

VSMC Activation: VSMCs in the tunica media (middle layer of the artery) are activated by cytokines and growth factors, such as platelet-derived growth factor (PDGF), released by macrophages, foam cells, and damaged endothelial cells. They are encouraged to step into the intimacy as a result.

- **Fibrous Cap Formation**: When VSMCs reside inside the intima, they proliferate and create extracellular matrix components like collagen and elastin. These fibers contribute to the protective fibrous cap that covers the fatty stripe.
- **Stabilizing the Plaque**: The fibrous cap is intended to contain the lipid core and prevent the exposure of the thrombogenic (clot-forming) components of the plaque to the bloodstream. At this stage, the lesion is called a fibrous plaque. [21]

5. Plaque Development

- **Plaque Growth**: As the plaque grows, it undergoes further changes. The lipid core expands, mainly due to the accumulation of more foam cells, lipid deposits, and dead cells. Meanwhile, the fibrous cap thickens as more VSMCs and extracellular matrix proteins are deposited.
- **Necrotic Core**: As foam cells die (a process called apoptosis), they release their lipid content, contributing to the formation of a necrotic core—a lipid-rich, cell-free zone within the plaque. The plaque can enlarge over time, further narrowing the artery (stenosis), reducing blood flow.
- **Inflammation Continues**: The extracellular matrix is broken down by the enzymes secreted by inflammatory cells, such as matrix metalloproteinases (MMPs), which weaken the fibrous cap and increase the plaque's susceptibility to rupture. [11]

6. Plaque Rupture and Thrombosis

- **Fibrous Cap Rupture**: In advanced atherosclerosis, the fibrous cap may become thin due to the continuous breakdown of collagen by inflammatory enzymes. A thin fibrous cap is prone to rupture, especially in areas of high mechanical stress.
- **Exposure of Lipid Core**: Tissue factor, a protein that causes clotting, and other highly thrombogenic substances in the necrotic core are exposed to the bloodstream when the fibrous cap bursts.
- **Thrombus Formation**: A blood clot (thrombus) forms at the site of the rupture as a result of platelets in the blood adhering to the exposed area. In order to stabilize the clot, fibrin is deposited and the coagulation cascade is triggered.
- **Acute Ischemic Events**: Unstable angina, myocardial infarction (heart attack), or sudden death are examples of acute coronary syndrome that can result from a thrombus that becomes large enough to totally block the artery. [11]

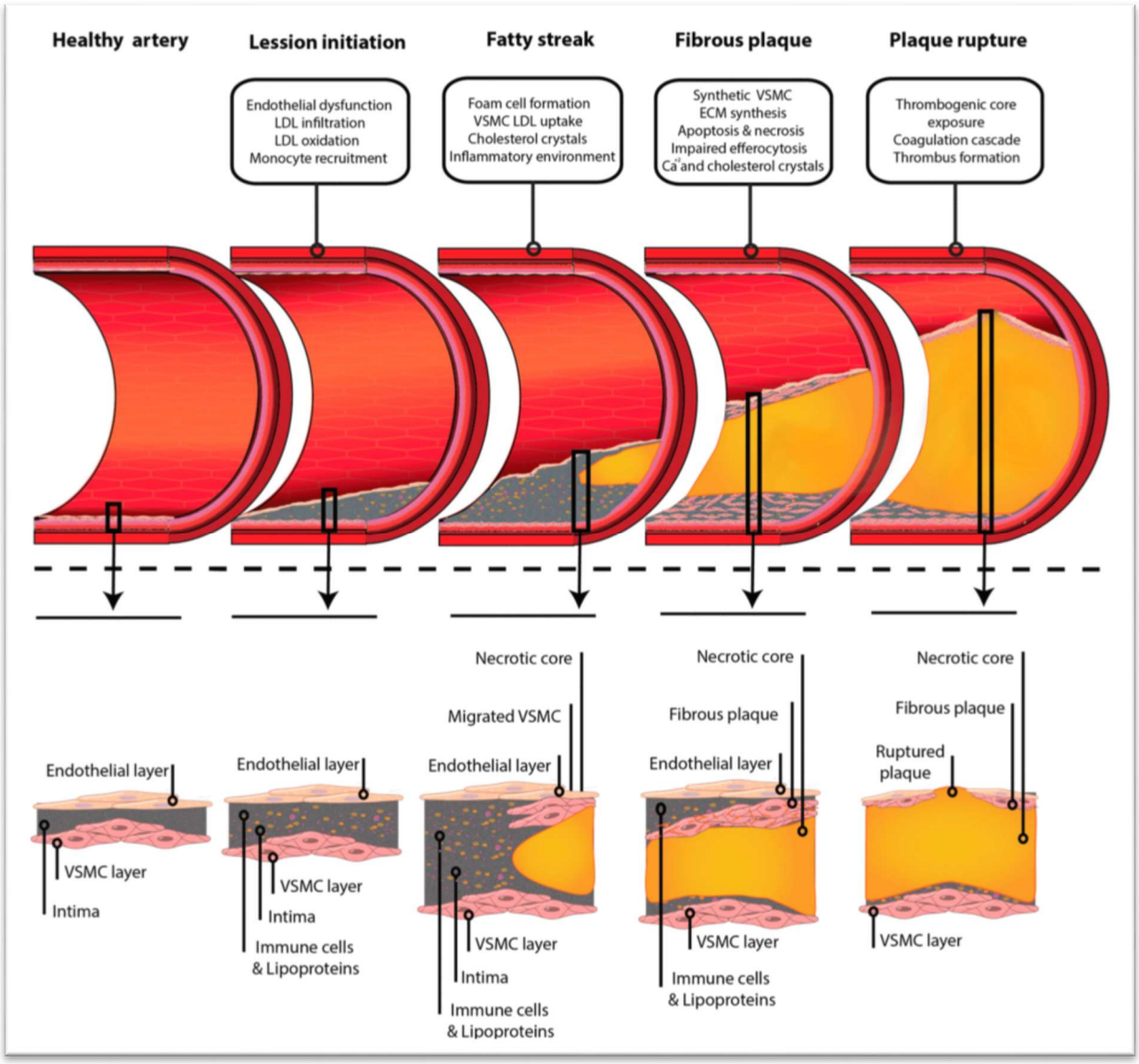

Fig.no. 4. Diagram showing the progression of plaque from a healthy artery to its rupture [11]

C. DIAGNOSTIC TEST:

Even though they are well known, the clinical signs of LMCA stenosis are not useful for diagnosis because of their inadequate predictive value and sensitivity. Typically, angiography is used to diagnose left main or left main similar disease. ECG findings during activity testing or in people who have experienced myocardial infarction (MI) may, however, suggest left main or three-vessel disease.

(1)

SR.NO.	DIAGNOSTIC TEST
1.	Chest X-Ray and Cardiac Fluoroscopy
2.	Electrocardiogram
3.	Exercise Stress Test
4.	Coronary Angiography
5.	Intracoronary Ultrasound Imaging (IVUS)
6.	Multislice Computed Tomography (MSCT)

TABLE.NO.2. DIAGNOSTIC TEST [1]

1) CHEST X-RAY AND CARDIAC FLUOROSCOPY [6]

Chest X-rays and cardiac fluoroscopy can detect calcium buildup in the Left Main Coronary Artery (LMCA) region.

Limitation:

1. Can't predict severity of blockage
2. Can't pinpoint exact location of blockage

2) ELECTROCARDIOGRAM [1]

One useful diagnostic method for determining whether left coronary artery stenosis is present is an echocardiography. It can give details regarding the structure, blood flow, and function of the heart.

1. **Left Ventricular Function**: Echocardiography can evaluate left ventricular size and function. In cases of significant stenosis, you might see changes in wall motion, such as hypokinesis or akinesis in areas supplied by the affected artery.
2. **Doppler Imaging**: Color Doppler can assess blood flow across the mitral valve and pulmonary veins, helping to identify diastolic dysfunction that can occur with ischemic heart disease.
3. **Stress Echocardiography**: This can be particularly useful. By inducing stress (exercise or pharmacological), you can observe changes in wall motion that may indicate ischemia due to stenosis.

4. **Signs of Ischemia**: You may see indirect signs of coronary artery disease, such as left atrial enlargement, which can result from chronic pressure overload.

5. **Comparison with Other Tests**: While echocardiograms provide important functional information, they may be supplemented with other tests like coronary angiography for a direct assessment of stenosis severity.

3) EXCERSISE TEST [2]

When evaluating left coronary artery stenosis, an exercise stress test is a helpful diagnostic tool, particularly for patients who may have coronary artery disease (CAD).

Procedure

1. **Preparation:** Patients are typically advised to avoid heavy meals, caffeine, and certain medications before the test.

2. **Baseline Measurements:** Initial measurements of heart rate, blood pressure, and electrocardiogram (ECG) readings are taken at rest.

3. **Exercise Phase:** Patients are instructed to progressively increase the intensity of their activity, typically on a stationary bike or treadmill. A pharmacologic drug may be used to mimic the effects of exercise for people who are unable to do so.

4. **Monitoring:** Throughout the test, heart rate, blood pressure, and ECG are continuously monitored to observe for any signs of ischemia, such as ST-segment changes.

5. **Post-Test Assessment:** After exercising, recovery heart rate and any symptoms experienced during the test are evaluated.

4) CORONARY ANGIOGRAPHY [1]

One important diagnostic technique for assessing left coronary artery stenosis is coronary angiography. Direct viewing of the coronary arteries is made possible by coronary angiography, which aids in the detection of blockages or narrowing (stenosis) in the left coronary artery, which provides blood to a sizable section of the heart muscle.

Procedure

1. **Preparation**: Patients may be asked to fast and discontinue certain medications.

2. **Access**: The femoral or radial arteries are typically used to implant a catheter.
3. **Contrast Injection**: In order to highlight the coronary arteries on X-ray pictures, a contrast dye is administered through the catheter.
4. **Imaging**: Real-time X-ray images (fluoroscopy) are taken to visualize blood flow and identify areas of stenosis.

5) INTRACORONARY ULTRASOUND IMAGING (IVUS) [1]

To evaluate left coronary artery stenosis, a sophisticated diagnostic method called intracoronary ultrasound imaging (IVUS) is utilized. High-resolution pictures of the coronary arteries taken from inside the vessel are provided by IVUS, enabling a thorough assessment of the degree of stenosis, artery diameters, and plaque features.

Procedure

1. **Preparation**: Similar to coronary angiography, patients may need to fast and adjust medications.
2. **Access**: A catheter is inserted, usually via the femoral or radial artery.
3. **IVUS Catheter**: A specialized ultrasound catheter is advanced into the coronary artery.
4. **Ultrasound Imaging**: High-frequency sound waves create images of the arterial walls and any plaques present.
5. **Data Analysis**: The images are analysed to assess plaque morphology, the degree of stenosis, and overall artery health.

6) Multislice computed tomography (MSCT) [1]

A non-invasive imaging technique called multislice computed tomography (MSCT), often known as coronary computed tomography angiography (CTA), is used to assess left coronary artery stenosis.

Procedure

1. **Preparation**: Patients may need to refrain from eating or drinking before the scan and may be given beta-blockers to reduce heart rate.
2. **CT Scanner**: The patient lies on a table that moves through a ring-shaped CT scanner.
3. **Contrast Injection**: To improve coronary artery visualization, an intravenous injection of a contrast dye is administered
4. **Imaging**: Rapid scans are performed, capturing images of the heart during different phases of the cardiac cycle, often synchronized with the heart's rhythm.

D. EPIDERMIOLOGY:

Heart events have become far more common over the world, especially in many countries , but this varies by location. Coronary artery disease (CAD) was expected to cause 19 million fatalities by 2010 in developing nations like China, India, Latin America, Sub-Saharan Africa, and the Far East, up from 9 million in 1990. Common risk variables are associated with high CAD rates in China, however they do not adequately account for India's high prevalence. CAD is responsible for 43% of cardiovascular disease (CVD) deaths, which is consistent with Global Burden of Disease (GBD) estimates from 2001. Furthermore, the patterns and rates of CAD deaths differ greatly across high-income and low- or middle-income nations. (22)

LMCA illness is most commonly caused by atherosclerosis. In one study, substantial LMCA atherosclerotic disease was found during angiography in 11% of males over 65 who presented with NYHA class II angina, 13% with NYHA class III angina, and 9% with NYHA class IV angina. The comparable percentages were 0–7 and 12 for females. (22)

Certain cardiac procedures may result in iatrogenic lesions in the coronary arteries and left main coronary artery (LMCA)." Radiation therapy, for instance, has been connected to coronary artery disease; in a review of 68 instances, 11 of them involved stenosis, or narrowing, of the coronary artery openings (ostia). About 1% of instances result in surgical damage to the LMCA following cardiac surgery, such as from intubation during cardioplegia, but the risk of damage from percutaneous intubation varies between 0.2% and 1.7%. Up to 17% of patients who already have LMCA constriction prior to angioplasty will likely see worsening of the problem within six months. Furthermore, an improperly positioned aortic valve prosthesis may obstruct the coronary artery openings, leading to additional issues. These dangers emphasize how crucial cautious procedures and careful observation are, particularly for individuals who already have coronary heart problems. (22)

CORONARY ARTERY BYPASS GRAFTING AND DRUG ELUTING STENT IMPLANTATION ARE THE TWO TREATMENTS MOST OFTEN USED IN LEFT CORONARY ARTERY STENOSIS.

1.3. INTRODUCTION OF CORONARY ARTERY BYPASS SURGERY:

In coronary artery bypass grafting (CABG), the most common major surgical procedure, atheromatous blockages in a patient's coronary arteries are circumvented by harvested venous or arterial conduits. This

restores blood flow to the ischemic myocardium, restoring function, viability, and reducing anginal symptoms. [23]

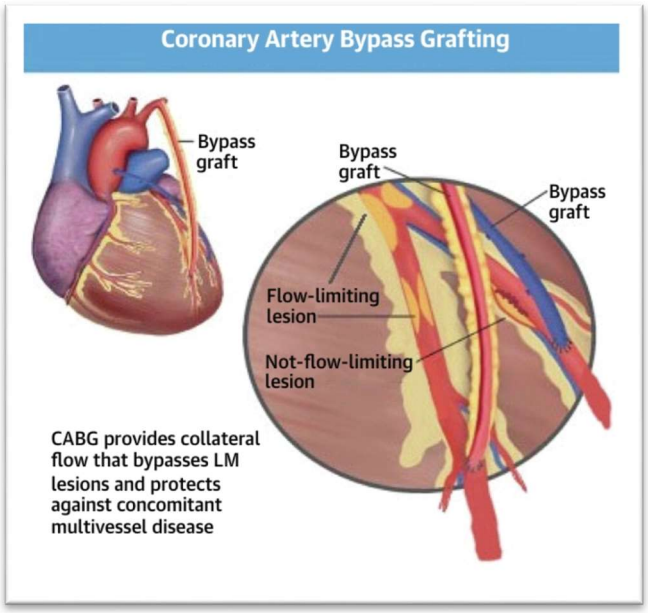

FIG.No.5. Coronary Artery Bypass Grafting [24]

Over past century, coronary artery disease (CAD) has the most common disorder to afflict cardiologists and cardiac surgeons. It was Turkey's biggest cause of death in 2013 (38.8%). In 2012, World Health Organization reported that the biggest cause of mortality globally was ischemic heart disease. Coronary artery disease is caused by an atherosclerotic plaque that narrows the coronary artery's inner lumen. Chest pain, syncope, dyspnea, and occasionally pulmonary edema are signs of this lesion. Moreover, it decreases coronary artery blood flow and oxygen supply to the heart [25]

Angina pectoris is caused when the increased demand for an oxygenated blood supply is not met by the decreased blood flow via the coronary artery region. Although there are a number of methods, such as computed tomography, myocardial perfusion scintigraphy, and exercise testing, biplane coronary angiography is the most precise method for diagnosing the problem. [25]

The pathogenesis of CAD has been better understood, which has hastened efforts to improve the myocardial blood supply. In accordance with the findings of angiography, patients should receive either medical attention or invasive therapy. Because it improves quality of life, lowers angina, and promotes

survival, percutaneous coronary intervention and coronary artery bypass surgery (CABG) may be the sole available therapy choices for myocardial revascularization. [25]

Indications [23]

When high-grade blockages in either of the major coronary arteries cannot be cleared by percutaneous coronary intervention (PCI), CABG is typically recommended.

• Over half of the patients have a major illness.
• Two-vessel disease: one main artery + LAD

• Over 70% of people have three-vessel coronary artery disease, whether or not the proximal LAD is involved.

• One vascular condition with ischemia-related ventricular tachycardia in a person who survived sudden cardiac death that was more than 70%

• One or more large stenoses that are more than 70% in a patient who has significant anginal symptoms in spite of receiving the most medication possible.

A dedicated team of cardiovascular surgeons with substantial training and expertise in treating these complicated patients performs the procedure. The team includes anesthesiologists, nurses, surgical technicians, perfusionists, and the cardiothoracic surgeon and their helpers.

1.4. INTRODUCTION TO DRUG ELUTING STENT:

One kind of coronary stent that releases medication to stop the artery from restenosing (re-narrowing) is called a Drug-Eluting Stent (DES). Interventional cardiologists utilize vascular prostheses called drug-eluting stents (DES) to keep coronary arteries that have constricted due to arteriosclerosis open. [26]

A stent, a drug delivery system, and an anti-restenotic medication or therapeutic substance are the three main parts of DESs. [26]

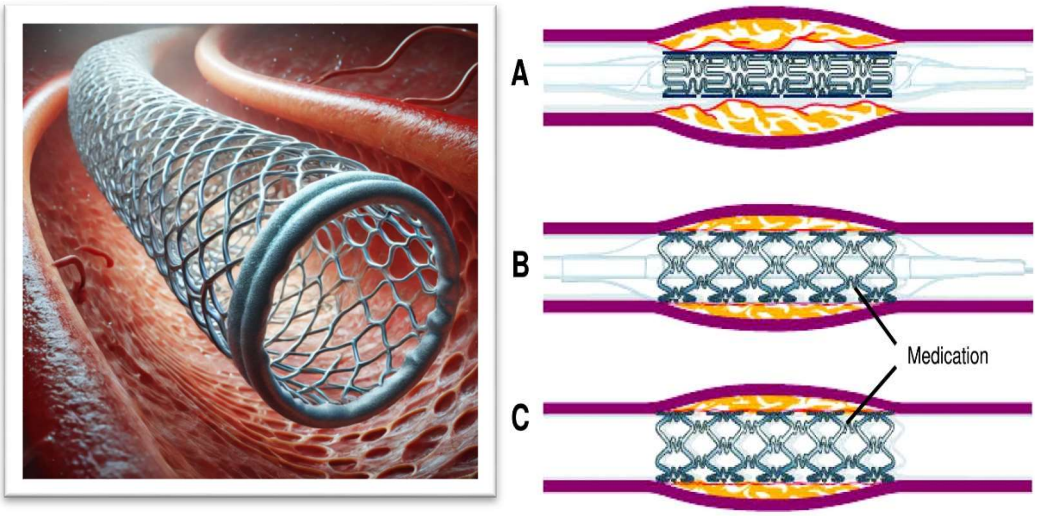

Fig.no.6. Drug Eluting stent [27]

A Stent

Nowadays, the majority of stents used in DESs are inserted by balloon dilatation and are constructed in modular or slotted-tube designs. The low profile stent is compressed with a balloon-tipped catheter and injected into the cardiovascular system via the radial or femoral arteries. As a result, the stent needs to be low crimped and incredibly flexible to pass through the intricate circulatory system. Stents should shorten as little as possible during expansion and when deployed, they should fit the vessel's shape without making it abnormally straight.

To achieve minimum radial recoil and a final diameter similar to the host vessel's during unloading, the stent must have strong radial strength and optimal vascular coverage. Also, because the stent serves as a conduit for the delivery of drugs, its geometrical design must promote uniform drug distribution across the channel.

Typically, physiologically inert materials like stainless steel are used to make stents. However, new correlations between strut thickness and ISR rates have made metallic alloys like cobalt-chromium the favored material for stent design, overtaking steel in recent years. Due to the development of metallic alloys with higher levels of strength and X-ray attenuation than stainless steel, it is now possible to construct stents with considerably smaller struts without sacrificing the device's strength, corrosion resistance, or radiopacity. Modern stent design is primarily focused on strengthening complicated metals, metallic alloys, and bioabsorbable materials. [26]

Drug-delivery mechanism:

Actual medication or therapeutic substance release via a desist mechanism is as important. It has been discovered that permanent synthetic polymer coating materials, such as polyethylene-co-vinyl acetate (PEVA) are the most efficient means of enhancing drug adherence and distribution from a stent. It is possible to produce a drug-polymer matrix that can be applied to the surface of the stent plate by carefully combining these materials with anti-restenotic drugs. While drug delivery is influenced by the kind, makeup, and amount of polymers used in the drug–polymer matrix, drug dispersion following deployment is driven by diffusion from the matrix.

In recent years, these permanent polymers have been replaced by more advanced biocompatible ones, like phosphorylcholine (PC) and the co-polymer polyvinyl difluoride-co-hexafluoropropylene (PVDF-HFP). These new polymers resemble the phospholipids on the surface of red blood cells, offering a stent platform that, when implanted, has no clinical impact on late arterial wall healing and minimal thrombus formation. Future studies in this area will mostly concentrate on creating novel drug-release systems and assessing polymer coating materials that are both biocompatible and bioabsorbable. [26]

Anti-restenotic drug

The arterial wall immediately initiates a healing response in the event that the vessel sustains mechanical damage during DES deployment. The first feature of this healing response is platelet activation in the intima, which leads to the recruitment of lymphocytes, neutrophils, and blood-borne monocytes as well as the creation of thrombus.

The uncontrolled proliferation and migration of smooth muscle cells (SMCs) toward the intimal layer, which is prompted by the mitogenic and chemotactic chemicals these cells release, results in neointimal enlargement and ISR. In order to maintain vascular healing, the optimal anti-restenotic drug should possess strong anti-proliferative qualities. Although several immunosuppressive and anti-proliferative medications have been studied for the prevention of ISR, only a tiny portion of them have demonstrated true efficacy in clinical trials to yet. [26]

GENERATION	STENT
First-Generation DES	I. Sirolimus-eluting stent (SES) II. Paclitaxel-eluting stent (PES)

Second-Generation DES	I. Everolimus-eluting stent (EES) II. Zotarolimus-eluting stent (ZES) III. Biolimus-eluting stent (BES)
Third-Generation DES	I. Novolimus-eluting stent (NES) II. Tacrolimus-eluting stent (TES) III. Sirolimus-analog eluting stent
Bioabsorbable DES	

TABLE.NO.3 DIFFERENT TYPES OF DES [28]

- **First-Generation DES:**

  (Sirolimus-eluting stent)

  Drug: Sirolimus (an immunosuppressant)

  Features: First-ever DES, approved by the FDA in 2003. Sirolimus helps prevent scar tissue formation. [28]

  (Paclitaxel-eluting stent):

  Drug: Paclitaxel (an anti-cancer drug)

  Features: The drug inhibits cell proliferation that could cause restenosis. FDA-approved in 2004.

- **Second-Generation DES:**

  (Everolimus-eluting stent)

  Drug: Everolimus (an immunosuppressant)

  Features: Improved polymer and drug delivery technology. Offers better safety and efficacy.

  (Zotarolimius-eluting stent)

  Drug: Zotarolimus (an immunosuppressant)

  Features: helps prevent scar tissue formation.

  (Biolimus-eluting stent)

  Drug: Biolimius (an immunosuppressant)

  Features: Inhibits the growth of scar tissue in artery after the stent implanted. [28]

- **Third-Generation DES:**

  (Novolimus-eluting stent (NES)

  Drug: Novolimus (an immunosuppressant)
  Features: Prevent the formation Restenosis

  (Tacrolimus-eluting stent (TES)

  Drug: Tacrolimus (an immunosuppressant)
  Features: Inhibit T- lymphocytes activation

  Sirolimus-analog eluting stent
  Drug: Rapamycin (an immunosuppressant)
  Features: Inhibit cell proliferation to prevent restenosis [28]

- **Bioabsorbable DES:**

  A bioabsorbable drug-eluting stent (DES), also known as a bioresorbable stent or biodegradable stent, is a type of stent used in coronary artery disease treatment that gradually dissolves after it has fulfilled its purpose of keeping an artery open. Unlike traditional metallic stents that remain permanently in the artery, bioabsorbable stents break down over time, typically within 2-3 years, leaving behind a healed vessel that can function naturally.

  These stents are coated with antiproliferative drugs like sirolimus analog (e.g., Everolimus or Biolimus) to prevent restenosis. The material used for the stent structure is typically a biodegradable polymer such as polylactic acid (PLA) or magnesium alloy, which the body metabolizes over time. [28]

Conclusion:

The condition known as left main coronary artery stenosis (LMCAS) is dangerous has a significant risk of consequences. Improvements in diagnostic technologies such as coronary angiography, IVUS, and MSCT have improved early assessment and detection. Although the long-term efficacy of DES is still up for question, its debut has offered alternatives to CABG, which has been the primary treatment. Achieving the best results requires selecting the appropriate treatment strategy. Future research should concentrate on creating better stent technologies, optimizing medicines, and improving patient selection in order to improve patient prognosis and treatment success.

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