# BETWEEN A STENT AND A HARD PLACE:

# RESTENOSIS PREVENTION METHODS

By

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**ABSTRACT**

Coronary Artery Disease (CAD) is the most common cause of death in the United States. CAD, also known as atherosclerotic heart disease, occurs from the accumulation of cholesterol- related plaques within the coronary arteries. A common treatment modality is Percutaneous Coronary Intervention (PCI), including the use of heart stents. To gain a better understanding of this treatment, education regarding basic anatomy and physiology of the cardiovascular system is necessary. In addition, knowledge of the disease state with associated risk factors, diagnosis and treatment is also required. A common occurrence after the insertion of a coronary stent is the restenosis of the stent, requiring further therapy. Lifestyle modifications to reduce stent restenosis include: weight loss, heart healthy diet, exercise, and management of coexisting diabetes. This thesis serves to educate the reader about the underlying physiology of CAD with emphasis on PCI and the use of stents. Stent restenosis with modifiable risk factors to reduce its incidence will be presented.

## ANATOMY AND PHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM

### HEART

To gain understanding of the utility of heart stents in cardiac patients, a general overview of the cardiovascular system and coronary artery disease (CAD) is essential. There are not many organs in the human body that are as essential for survival as the heart. Death can occur within three short minutes in the absence of this beating organ. The cardiovascular system is comprised of the heart, the vascular system and blood, with the former being the driver of this vital organ system.

Weighing less than one pound, this muscle is about the size of a clenched fist. It is situated in the middle of the chest below the sternum, using the rib cage and vertebrae as sources of protection.[2] There is a popular misconception that the heart is located on the left side of the chest, for that is where one places his or her hand during the pledge of allegiance and national anthem. CPR, cardiopulmonary resuscitation, has now been replaced by compression only resuscitation as an effective means of revival due to the position of the heart. Quick, rapid compressions on the sternum can be life saving rather than needing to pause to include rescue breathing.[1]

The heart is divided into four chambers, separated into left and right components by the interventricular septum. As illustrated in figure one, the upper two chambers of the heart are labeled the atria, while the bottom two are the ventricles.[3]

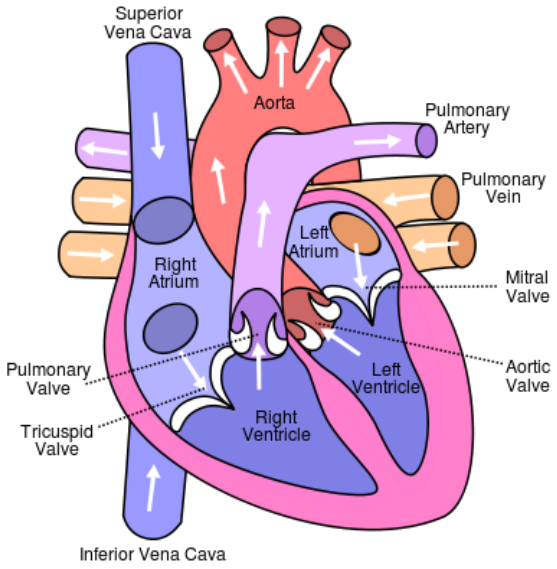


Figure 1 (Basic Anatomy of the Heart)

The heart is composed of cardiac muscle, enabling it to contract as well as maintain coordinated heartbeats. The heart muscle is composed of three layers: the outer pericardium, the muscular myocardium responsible for involuntary contraction, and the inner endocardium. Each layer possesses a unique, specialized structure with a

corresponding function. Together, the three layers of the heart ensure that blood is properly carried to all organs in the body.[5] Cardiac muscle cells, or cardiomyoctyes, are able to contract due to the fact that they work together as a functional syncytium. Intercalated discs serve to hold adjacent cardiomyocytes together and are composed of desmosomes and gap junctions. Desmosomes are the "molecular velcro" that attach intercalated discs, while gap junctions are channels that form when the opposing membranes of the intercalated discs approach each other in close proximity. Unlike skeletal muscle, either all of the cardiac muscle contracts or none of it does, based on the idea that the heart works as a functional syncytium. To better understand what a functional syncytium is, one can think of the individual heart cells as doing the wave in a crowded football stadium. Each cell works together with others to enhance the overall function, so that ultimately the heart can contract as one[1].

The heart is recognized as being the hardest working organ in the human body as it pumps blood to all body tissues. Five liters of blood travel through blood vessels that link cells of our organs and body parts every day. The sequence of blood flow through the heart is key to understanding how this organ functions. Impairments in blood flow or its efficiency can result in serious consequences including oxygen deprivation. When there is a lack of oxygen, other vital organs, such as the liver and kidneys, cannot function properly, potentially leading to grave illness or even death.

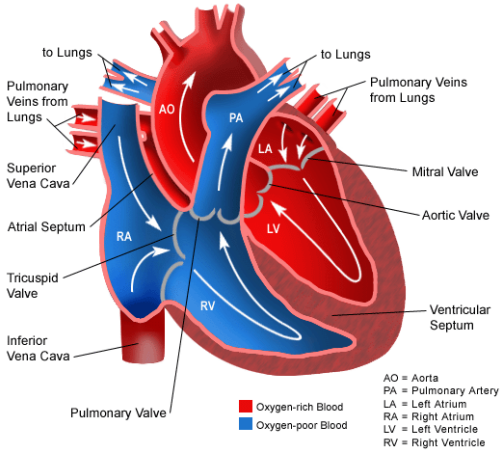


Figure 2 (Blood Flow Through the Heart)

Figure two depicts the sequential flow of blood through the heart.[4] Deoxygenated blood (venous blood) returns to the heart via the superior and inferior vena cava, which are major veins. Blood then enters the right atrium, flows down into the right ventricle via the tricuspid valve, and leaves the heart via the pulmonary artery. Four rings of dense fibrous connective tissue known as the heart valves ensure the unidirectionality flow of blood. These heart valves serve as an anchor for the attachments of the atrial and ventricular musculature. Next, the blood travels to the lungs via pulmonary circulation where it picks up oxygen and returns to the heart via the pulmonary veins. For basic clarification purposes, veins carry blood to the heart and arteries carry blood away from the heart (respectively colored blue and red in most diagrams). The oxygenated blood enters the left atrium, subsequently flows through the mitral (bicuspid valve) into the left ventricle, and leaves the heart through the main artery in the body, the aorta. In addition to the two atrioventricular valves, there is another pair of valves, which include the aortic and pulmonary valves, and are known as the semilunar valves.[1]

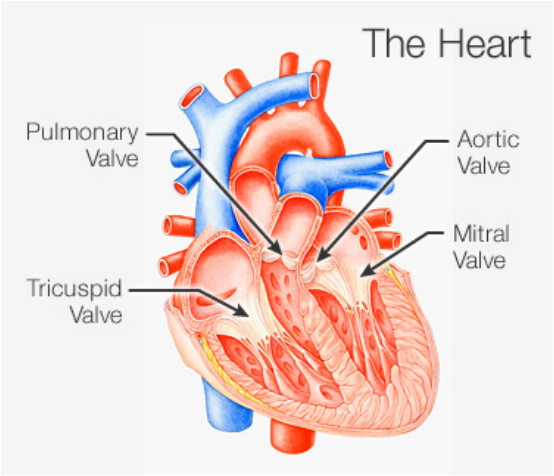


Figure 3 (Valves of the Heart)

As seen in figure three, these four heart vales control the flow of blood through the heart by opening and closing during the organ's contractions. They open or close in response to

pressure gradients or differences generated within the heart itself.[6] Blood then supplies all body organs with oxygen and other nutrients via systemic circulation and the process repeats itself indefinitely. After the oxygenated blood reaches the body tissues, it is returned to the heart for subsequent repeated cycles.

It is obvious that the heart must contract over and over again in order to sustain life. The heart maintains the pressure necessary for constant blood flow through its contraction mechanisms. In an average human lifespan, the heart contracts about three billion times and only rests for a fraction of a second between beats and this endurance is due in part to its microcellular basis.[1]

It is imperative that the structure of a sarcomere be briefly mentioned since a sarcomere is the basic contractile unit of a cardiac muscle cell. It comprises a set of filamentous proteins situated between two Z lines, which are made of the protein alpha-actinin. Actin and myosin are proteins that make up the majority of the length of the sarcomere, as figure four illustrates.

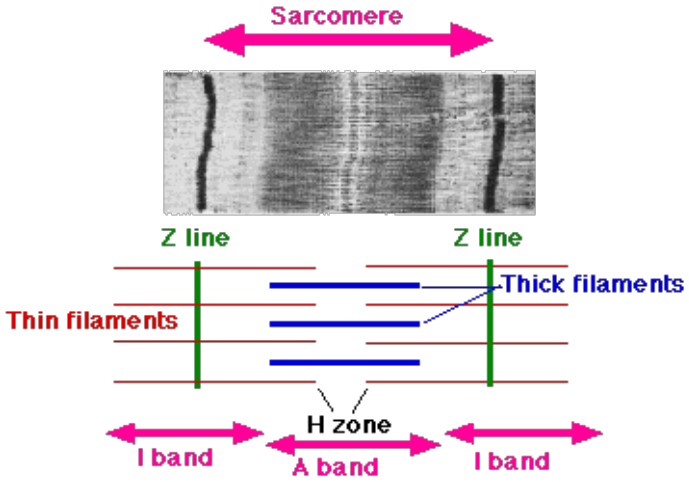


Figure 4 (Structure of a Sarcomere)

Actin monomers are assembled to form thin filaments, which cover a majority of the I band but also extend into the A band. The A band is where thick and thin filaments

overlap during contraction. Conversely, thick filaments are composed of myosin. Thick filaments are connected from the H zone, or middle of the sarcomere composed entirely of myosin, to the Z line by the protein titin. The proteins actin and myosin are responsible for muscle contraction. Before contraction can occur, an inward flux of calcium ions from the extra cellular fluid causes the depolarization of the cell. Calcium also allows for the attachment of the myosin head to the actin filament, commencing the start of contraction. The sliding filament model, a universally accepted concept, serves to explain how contraction in the heart occurs. Myosin filaments slide along actin to shorten the muscle fiber, made up of many sarcomeres. Muscle contracts as the sarcomeres shorten. Contraction is then terminated when the intracellular calcium is removed by the sarcoplasmic reticulum. This process repeats continuously.[7]

To ensure that this complex organ functions properly, four factors exist that directly affect cardiac performance. These are termed: preload, afterload, heart rate, and myocardial contractility. Preload is defined as the pressure generated in the left ventricle at the end of diastole, while afterload is the resistance to ejection of blood from the left ventricle. Heart rate is the amount of beats per minute, and the heart beats about seventy times per minute every day. Lastly, myocardial contractility refers to the ability of the heart to contract. These factors have a major impact on cardiac output and performance, for a defect in one can lead to serious cardiac disease.[1]

**BLOOD**

In addition to the heart, the cardiovascular system also includes the vascular system as well as the blood itself, functioning to transport blood and other nutrients throughout the body to supply the body's organs. In the averaged sized human being, the

heart pumps approximately 5 liters of blood daily through 60,000 miles of blood vessels. The components of blood and its proper circulation are vital in maintaining homeostasis, defined as the balance of internal functions throughout the body. The transport of blood supplies nutrients to all cells while simultaneously removing wastes. In total, blood accounts for about eight percent of total body weight.[8]

Hematology is defined as the study of blood and its corresponding components. Hematology is a separate medical discipline, but this paper will focus on the cardiovascular implications of hematology. Blood has both cellular and non-cellular parts. The cellular component of blood consists of red blood cells (erythrocytes), white blood cells (leukocytes), and platelets (thrombocytes). Erythrocytes are the most numerous of the blood cells, for one milliliter of blood contains approximately five billion red blood cells, and they control tissue oxygenation by carrying oxygen to the tissues via hemoglobin as well as carry carbon dioxide to the lungs for excretion. The main function of blood is to carry oxygen to various tissues, and this is executed efficiently due to the biconcave shape of erythrocytes, enabling them to be flexible enough to fit through blood vessels of the smallest caliber. The presence of hemoglobin, an oxygen-carrying molecule, also makes this possible. A disproportionate amount of hemoglobin can lead to illness, the most common of which is anemia, defined by abnormally low hemoglobin and/or erythrocyte concentration in the blood. Another example, although rare, is Methemoglobinemia where too much hemoglobin is present, and the person turns blue because oxygen cannot be properly released into the circulation.[9]

Leukocytes, the second cellular component of blood, function to defend against microorganisms and remove debris, thus playing an important role in immunology. White blood cells can either be classified as granulocytes or agranulocytes. Granulocytes consist of neutrophils, eosinophils, and basophils. Neutrophils, being phagocytic (cells that eat) specialists, are the most abundant white blood cells and are significant during inflammation. They are considered to be the first defenders when an infection arises, and are capable of cleaning up debris. Eosinophils are involved in parasitic infections as well as in allergic conditions such as asthma. Lastly, knowledge regarding basophils is minimal, although it is known that they are capable of storing and releasing histamine and heparin. Heparin is an anti-coagulant, while histamine deals with blood vessel leakiness and allergic response.

The agranulocytic portion of white blood cells is comprised of monocytes and lymphocytes. Monocytes circulate in the blood until they develop into macrophages, or "big eaters", in the body's tissue. Lymphocytes can be divided into two subcategories: B and T cells. B cells are activated in response to an infection and they secrete antibodies that attach to the surface of the infectious agent. The antibodies will then either kill the foreign agent or allow other white blood cells to attack, playing a key role in guarding the body against infection. On the other hand, T cells are essential for human immunity as they can directly destroy specific target cells or help other cells do so.[1]

The third vital component of the blood includes platelets. Platelets are derived from megakaryocytes in the bone marrow. Platelets circulate in the blood and bind together when they recognize damage in the vasculature. For example: when an individual accidently cuts herself with a knife, platelets bind to the site of the damaged

blood vessel, forming a blood clot to stop the bleeding. Thrombocytopenia, an abnormally low level of platelets in the blood, can lead to many bleeding disorders. As figure five illustrates, each of these three cellular components of blood has a unique shape, further enhancing their ability to perform their individual tasks.[10] For example: hemoglobin consists of a globin protein and an iron heme group, which gives the red blood cell its color and also helps form its specific shape.[11]

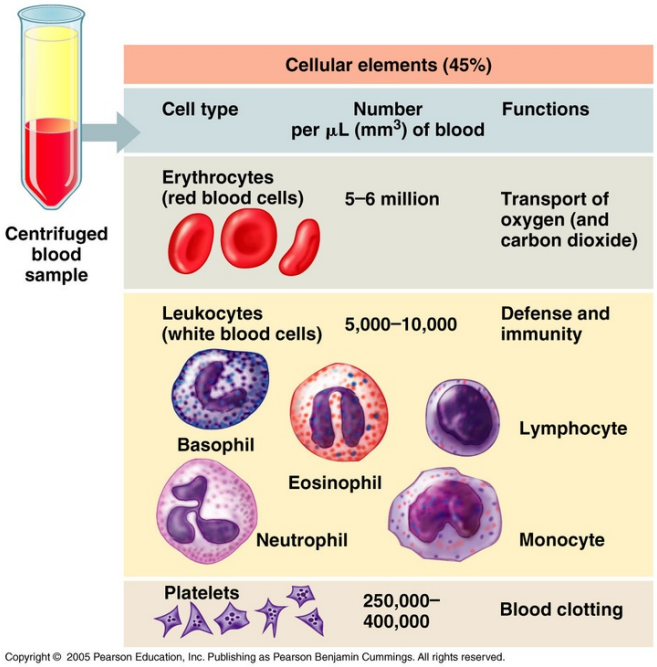


Figure 5
(Cellular Components of Blood)

In addition to the cellular components of blood just described, the non-cellular portion of the blood includes plasma and the proteins situated within it. Mostly composed of water, the main job of plasma is to transport blood along with nutrients, antibodies, chemical messengers, and waste products in order to maintain homeostasis. Plasma proteins such as albumin and globulin establish an osmotic gradient between the blood and interstitial fluid to sustain blood pressure. In addition, these plasma proteins are responsible for buffering changes in pH to further balance bodily functions.

As the heart contracts to deliver blood to the body tissues, the force exerted by the blood against the arteries can be measured. This is termed blood pressure, measured by a sphygmomanometer, a type of medical instrument. A normal blood pressure recording reads a systolic blood pressure of 120 with a diastolic blood pressure of 70 (120/70 mmHg). Systolic blood pressure is defined as the pressure inside the arteries when the heart muscle is contracting, while diastolic blood pressure is the pressure associated with heart relaxation. When the cardiovascular system is healthy, normal blood pressure is maintained as there is no impediment to blood flow within the vasculature.[1]

**VASCULATURE**

The third portion of the cardiovascular system consists of the vasculature, or blood vessels. This system of vessels functions to transport blood to all parts of the body, and serves to provide cells with nutrients while removing their wastes. Four main types of blood vessels exist: arteries, arterioles, capillaries, and veins. During circulation, blood leaving the heart flows in the direction of the vascular tree labeled below. Specific information regarding each of the main types of blood vessels will be discussed below.

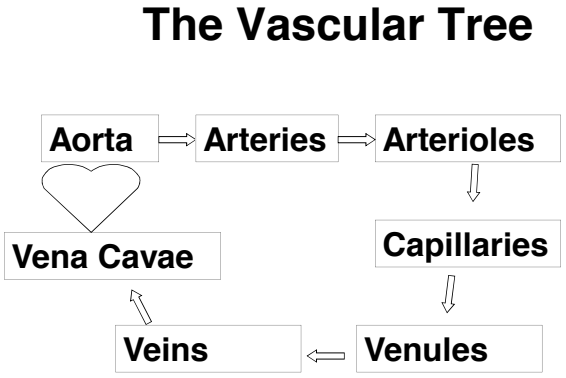


Figure 6
(Vascular Tree)

Before discussing the importance of each vessel, it is necessary to mention the relationship of blood flow to its corresponding pressure gradient and vascular resistance. The rate of blood flow through a vessel is directly proportional to the pressure gradient and inversely proportional to vascular resistance. The pressure in a vessel is considered to be the driving force for blood flow through it. On the other hand, resistance is dependent on two key factors: blood viscosity and vessel radius. Viscosity is defined as the friction developed between molecules of fluid as they slide over each other during the flow of blood. Thus, as viscosity increases, so does the resistance, thereby slowing the rate of blood flow. Since the resistance is inversely proportional to the fourth power of the radius, a slight change in vessel radius leads to a large change in flow.[1]

Arteries are considered specialized blood vessels, for they can act as both pressure reservoirs and rapid passageways. Arteries are thick-walled vessels containing some smooth muscle and a lot of elastin, which allows them to function in high-pressure environments. The arteries are the vessels involved in the measurement of blood pressure. As stated earlier, blood pressure is defined as the force exerted by the blood against a vessel wall. This occurs as a result of changes in arterial pressure. Blood pressure is dependent on the volume of blood contained in the vessel and the compliance of the vessel, or how easily it can stretch. As arteries leave the heart, they become smaller in size and eventually transform into arterioles.[12]

Arterioles are the main resistance vessels in the body due to their decreased radius. Just as in the arteries, arterioles function to carry blood away from the heart to the body's tissues. Unlike the arteries, however, arteriolar walls contain very little elastic connective tissue. Arterioles are surround by a thick layer of smooth muscle that is

innervated by sympathetic nerve fibers and is sensitive to several local hormones. Changes in smooth muscle radius can lead to subsequent contraction and relaxation, which can be seen in figure seven below. Vasoconstriction, or contraction of the smooth muscle, is characterized by an increase in resistance and its inverse decrease in blood flow through the vessel. This is due to the decrease in arteriolar radius. On the contrary, vasodilation is considered to be the relaxation of smooth muscle, resulting in increased blood flow through the vessel with a decreased resistance. Vasodilation leads to an increased arteriolar radius.

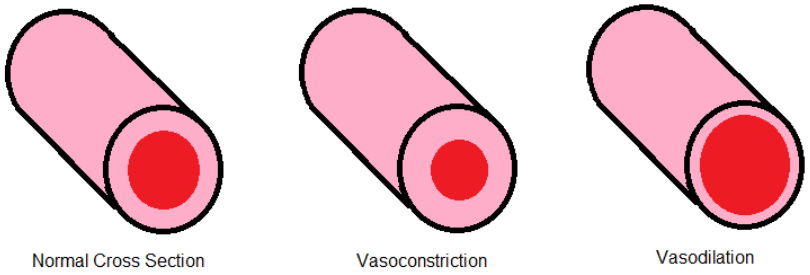


Figure 7
(Vasoconstriction versus vasodilation)

There are several substances that can lead to smooth muscle contraction and relaxation. For example: Endothelin causes arteriolar smooth muscle contraction, or vasoconstriction. On the other hand, Endothelial- derived relaxing factor (EDRF) causes local arteriolar vasodilation by inhibiting the entry of calcium into smooth muscle cells. Other metabolic changes that cause vasodilation include increased carbon dioxide and potassium concentrations, decreased oxygen levels, and prostaglandin and adenosine release. Vasodilation and vasoconstriction play a key role in the flow of blood through a vessel, and can impact downstream effects in the vasculature.[1]

After blood travels through the arteries and arterioles, it is brought to the capillaries where exchange of nutrients and gases occurs. In contrast to the arteries where blood moves relatively quickly, blood moves slowly through the capillaries due to the

large number of capillaries in the body (10-40 billion). In addition, capillaries are known to have a low resistance due to the vast number of them. The majority of capillaries are known as continuous capillaries, meaning there are no gaps between the endothelial cells. Continuous capillaries can be found in the skin as well as skeletal muscle.

Once the circulating blood leaves the capillaries, it moves to the veins. Veins serve as passageways back to the heart as well as blood reservoirs. Since veins have large radii and are thin walled, they experience little resistance to flow. Veins have less smooth muscle than arteries and experience little elasticity. An important aspect of the veins is known as venous return: the amount of blood that returns to each atrium per minute from the veins. Venous return can be enhanced by many factors. These include: cardiac contraction, skeletal muscle activity, respiratory activity, the presence of one way venous valves, and lastly sympathetically induced venous vasoconstriction. Together, these factors ensure that blood is properly returned to the heart.[1]

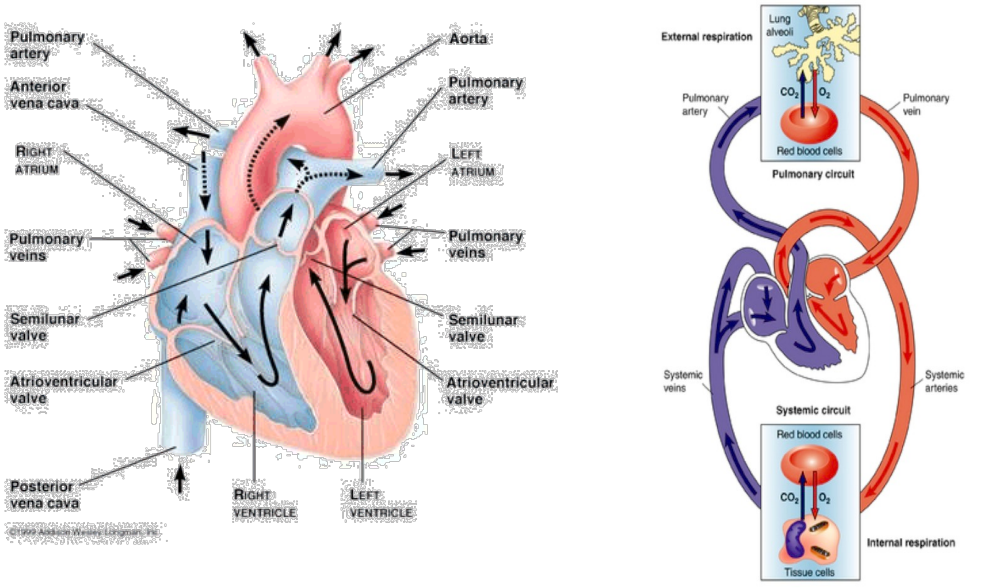


Figure 8
(Circulation of blood through the heart)

The proper circulation of blood with its integral components is the role of the cardiovascular system. On average, the heart muscle pumps 5 liters of blood every

minute through the vasculature of the entire body. There are two main circulatory loops associated with the cardiovascular system that help to transport blood: systemic and pulmonary. As shown in figure eight, the systemic circulation carries oxygenated blood from the left side of the heart via the aorta to the rest of the body tissues. Waste products are removed and deoxygenated blood can then be returned to the right side of the heart via the vena cavae. The pumping chambers of the heart that are associated with systemic circulation are the left ventricle and left atrium. On the contrary, pulmonary circulation is responsible for transporting deoxygenated blood from the right side of the heart to the lungs, where it picks up oxygen to then return to the left heart. As displayed in figure eight, pulmonary circulation is usually depicted in blue (deoxygenated blood) in diagrams while systemic circulation is in red (oxygenated blood).[13] Since this circulation loop is closed, any obstructions to blood flow due to blockage or stenosis can negatively alter the flow of blood. This causes a compensatory increase in the pressure needed to push blood through the narrowed vessels. This resistance to flow will also impair the heart's function and lead to multiple cardiovascular disorders.[1]

**CORONARY VESSELS**

As opposed to circulation through the majority of the body's organs, blood flow through the heart is not in a steady state. It is considered to be pulsatile, or displaying a rhythmic motion. During cardiac systole, or contraction, coronary blood flow decreases and conversely increases during cardiac diastole, or filling. Blood flow is reduced during systole for two reasons. First, the open aortic valve blocks the entrance to the coronary vessels.[14] Also, the contracting myocardium compresses the major branches of the coronary arteries. Therefore, most of the blood flow to the heart muscle occurs during a

period of cardiac diastole. The timing of coronary blood flow plays an important role in maintaining homeostasis. This is due to the fact that arterial pressure increases and venous pressure decreases during diastole. The opposite occurs in cardiac systole. In instances characterized by a rapid heart rate when the diastolic time is reduced, like in exercise for example, the limited time for blood flow through the heart is important. When one exercises, the rate of coronary blood flow can increase up to five times its resting rate. At rest, the heart extracts 65% of oxygen compared to other tissue beds. Even during strenuous exercise, the heart muscle receives adequate blood flow. The vasodilation of coronary arterioles is responsible for the increased delivery of blood to cardiac cells. Metabolites such as adenosine and nitric oxide influence the amount of vasodilation in the coronary vessels.

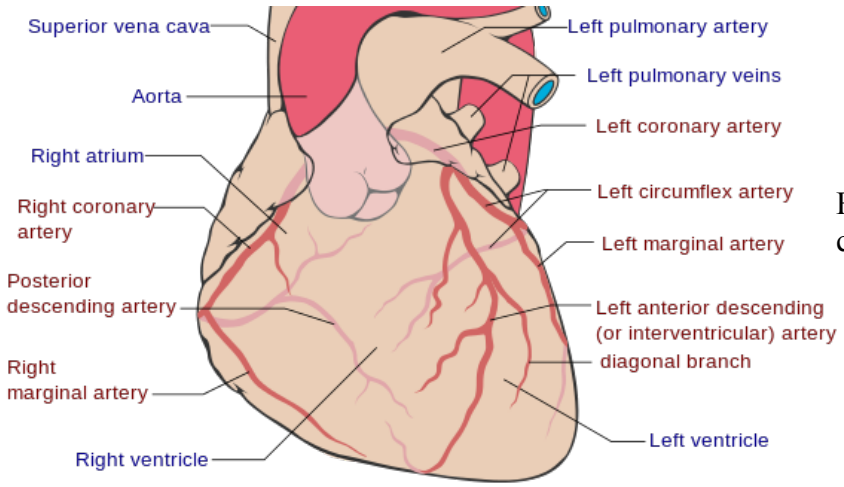


Figure 9 (coronary circulation)

Coronary circulation is simply defined as the branch of systemic circulation that supplies the heart. As shown in figure nine, coronary circulation is composed of: coronary arteries which receive blood through coronary ostia (openings associated with coronary vessels), coronary capillaries and coronary veins, the latter that empty into the right atrium through the coronary sinus. A sinus is defined as a large opening. There are

two major coronary arteries termed the right and left coronary arteries, where the left coronary artery is also referred to as the left main artery. These arteries transverse the epicardium and branch several times. The right coronary artery originates from the ostium (opening) behind the right aortic cusp. It then travels behind the pulmonary artery and extends around the right heart to the posterior surface, where it branches to the atrium and ventricle. There are three significant branches to the right coronary artery, which is shown in figure ten. Firstly, the conus supplies blood to the right ventricle. In addition, the right marginal branch is responsible for supplying blood to both the right and left ventricles, and lastly the posterior descending branch supplies blood to both ventricles as well. The latter artery moves to the posterior side of the heart and follows the posterior interventricular sulcus down between the right and left ventricle to perfuse the septum. The septum separates the right and left portions of the heart.[1]

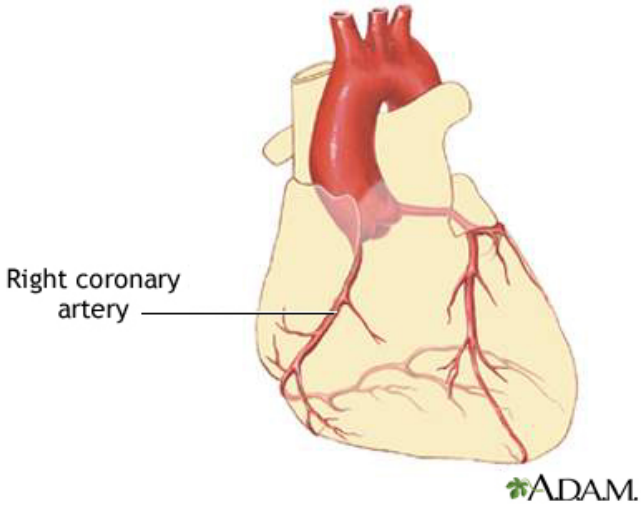


Figure 10 (right coronary artery)

The left coronary artery arises from an ostium located behind the left cusp of the aortic semilunar valve and branches into two smaller, important arteries. The left anterior descending artery (LAD) delivers blood to portions of the left and right ventricles as well as much of the interventricular septum. This artery travels down the anterior surface of

the septum toward the apex, or bottom, of the heart. On the other hand, the circumflex artery supplies blood to the left atrium and the lateral wall of the left ventricle. It travels down in the coronary sulcus, which functions to separate the left atrium from the left ventricle, to the left border of the heart. Also, the circumflex artery often can branch to the posterior surfaces of both the left ventricle and left atrium because it travels within the sulcus. Figure eleven portrays both the right and left coronary arteries, explicitly showing the branching of the left main.

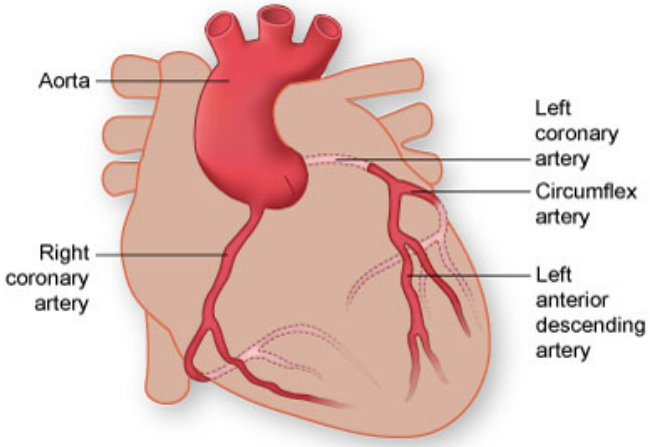


Figure 11 (right and left coronary arteries)

In addition to the two main coronary arteries, collateral arteries exist as a means of natural bypass. They provide a source of protection to the coronary vessels by connecting one branch of a coronary artery to another, thereby bypassing an obstruction. These specific arteries are bidirectional in terms of blood flow and are completely closed until needed, which makes it difficult to test for their presence. Collateral arteries open in response to an increased pressure caused by a constriction or obstruction of part of the coronary artery. The importance of these protective arteries can be seen in several various instances. First, collateral circulation serves to reduce the incidence of aneurysm formation (a weakened wall in the ventricle of the heart) after a myocardial infarction or heart attack. In addition, collateral arteries reduce the risk of severe consequences that

may follow a dysrhythmia resulting from a heart attack. A cardiac dysrhythmia reflects an irregular electrical activity of the heart, or an irregular heart beat. Finally, the presence of collaterals may also extend the window of time, allowing for reperfusion therapy following an infarction. Reperfusion occurs when blood flow is stopped and then re-introduced. One way to increase collateral growth is aerobic exercise. When heart rate increases, the rate of blood flow subsequently increases, which aids in the growth of collateral circulation.[1]

In addition to the presence of major arteries, coronary circulation also includes the extensive coronary capillary network. The heart has about 3,300 capillaries per square millimeter, which equals about one capillary per muscle cell. Therefore, changes in cardiac muscle can have a dramatic effect on blood flow in the capillary network as well as oxygen extraction. In ventricular hypertrophy or thickening of the ventricular walls, for example, the capillaries do not expand along with muscle fibers. Thus, the capillaries fail to diffuse oxygen to the larger area. Like capillaries located in other organs, the coronary capillaries allow for the exchange of blood gasses within the cells of the heart. After leaving the capillaries, blood, which originated in the coronary arteries, drains into the cardiac veins. These veins travel alongside the arteries and function to return blood to either the right atrium or right ventricle.

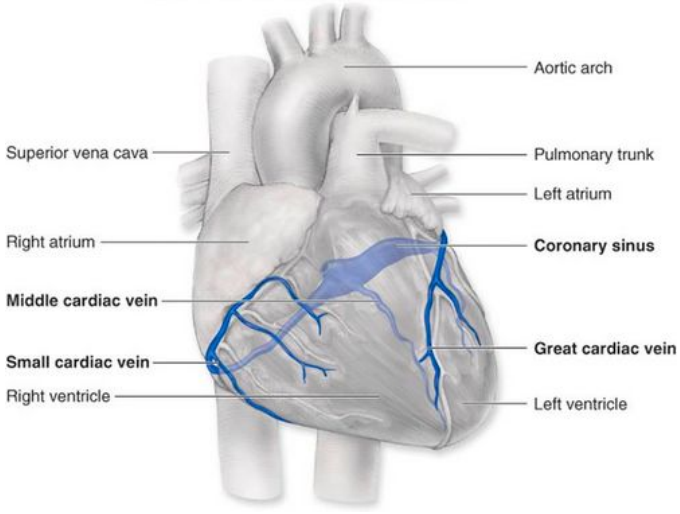


Figure 12 (cardiac veins)

As seen in figure twelve, the significant cardiac veins include the great cardiac vein, small cardiac vein, and middle cardiac vein. The coronary vessels are vital to the healthy function of the heart. When there is obstruction to blood flow or other coronary dysfunction, CAD will ensue.[1]

## CORONARY ARTERY DISEASE

### OVERVIEW AND DIAGNOSIS

Coronary artery disease (CAD) is the most common cause of mortality for both American males and females. Every thirty-three seconds, someone in the United States dies from an event associated with CAD and it is usually a myocardial infarction, or heart attack. CAD can also be classified as atherosclerotic heart disease or ischemic heart disease, but the latter is the more descriptive term.[1] There are many risk factors for this serious illness, which are categorized into two subgroups. The first one is risk factors that are either non-modifiable or modifiable by the individual, and the second group includes either conventional (major) or non-traditional (novel) risk factors.

The conventional, non-modifiable risk factors are ones that the patient has no control of. These include: advanced age, male gender, and family history (genetics). The risk for CAD increases with age and is more likely to be seen in men over forty-five and women over fifty-five. Risk factors that are considered conventional and modifiable include: dyslipidemia, cigarette smoking, hypertension, diabetes or insulin resistance, obesity, living a sedentary lifestyle, and eating an atherogenic diet (high in saturated fat and cholesterol). Many of these factors can be changed by the patient through changes in exercise, diet, and the use of medications. 80% to 90% of CAD patients will have

diabetes, dyslipidemia, hypertension, or are cigarette smokers. Lifestyle modifications can ameliorate risk factors to only a limited extent such as a borderline cholesterol level or a mildly obese individual, while pharmaceutical intervention is necessary to treat significant laboratory abnormalities.

One modifiable major risk factor for CAD is dyslipidemia, defined as an abnormal level of lipids in the bloodstream. There is a strong link between CAD and elevated plasma lipoproteins. Lipoproteins are lipids, phospholipids, cholesterol, and triglycerides that are bound to carrier proteins. If lipids get stored in the liver, adipose tissue, or arterial walls, plaque can form and cause many problems within the arterial system. Lipid metabolism refers to the degradation of lipids. Dietary fat is packaged into chylomicrons, small particles located in the small intestine. These particles then function in the absorption of fat as they transport the exogenous lipid from the intestine to the liver and periphery. Figure thirteen illustrates the cycle of lipid metabolism in a concise manner.

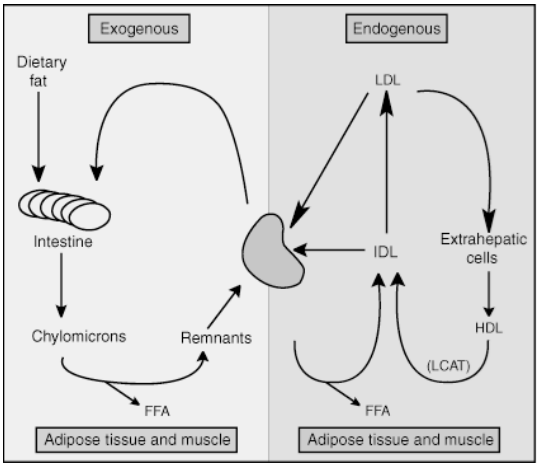


Figure 13 (Lipid Metabolism)

Total cholesterol is the combination of HDL and LDL. A desirable value is less than 200 mg/dL, borderline is 200-239 mg/dL, and high blood cholesterol refers to values over 240 mg/dL. The risk of developing CAD increases two-fold from low to high.

High-density lipoproteins (HDL) are known to be good cholesterol and high values of HDL are beneficial. An HDL value less than 40 mg/dL for men and 50 mg/dL for women is a major risk factor for heart disease. However, a value over 60 mg/dL for both genders is protective against heart disease. HDL functions to return excess cholesterol from the tissue back to the liver for metabolism, a process known as "reverse cholesterol transport". Fish oil consumption, weight loss, moderate alcohol use, and exercise can result in slightly increased HDL levels.

On the other hand, low- density lipoproteins (LDL) can be harmful. Normal levels are 100-129 mg/dL, borderline is 130-159 mg/dL, and high levels of LDL are 160 mg/dL and above. A strong indicator of coronary risk is an increased serum concentration of LDL. These harmful proteins work to deliver cholesterol to the tissues. As well as existing as a risk for CAD, LDL plays a role in inflammation, endothelial injury, and immune response. Aggressive reduction of LDL with diet and cholesterol lowering drugs can decrease the risk of heart disease. Two examples include statins, which lower cholesterol, and ezetimibe, which decreases fat absorption.[1]

Another modifiable and major risk factor for CAD is hypertension, or high blood pressure. Pre-hypertensive states (systolic blood pressure between 120-139 mmHg/ diastolic blood pressure between 80-89 mmHg) and mild hypertension can be reversed with lifestyle modifications such as exercise, diet, weight loss, and stress reduction. Prescription medications are required for more significant levels of hypertension, including beta-blockers and calcium channel blockers.

Cigarette smoking is another risk factor in this category and 21% of the annual mortality from CAD is attributed to this. The risk for heart disease increases with

smoking, but can conversely decrease with smoking cessation. One year after quitting smoking, an individual's risk of dying from sudden CAD decreases by 50%. After three years of cessation, the risk of CAD returns to that of a non-smoker. One mechanism of smoking leading to increased CAD is that nicotine causes an increase in heart rate, which leads to arteriolar vasoconstriction and an increase in heart work. The mean arterial pressure also rises, which subsequently causes an increase in afterload and blood pressure. These effects contribute to CAD separate from any lipid related risk. Cigarette smoking also increases levels of LDL in the blood.

In addition to the previously mentioned risk factors, diabetes is a serious pandemic in our society. It is the seventh leading cause of death in the US, affecting almost twenty million citizens. Diabetes is a chronic metabolic disorder with hyperglycemia, high blood sugar. Juvenile diabetes (or type one diabetes) is caused by a lack of insulin production and is considered an autoimmune disease. Adult onset diabetes (type two) results when the body does not properly utilize insulin, and it can be caused by environmental (obesity and diet) and/or genetic factors. Diabetes can lead to severe complications such as retinopathy, neuropathy, renal disease, and cardiovascular disease. The risk of mortality from CAD is greater in diabetics, and they are more likely to develop ischemic heart disease, resulting in heart attacks, than non-diabetics with other CAD risk factors.

Another major, modifiable risk factor for CAD is obesity. Two thirds of the American adult population is considered overweight or obese, resulting in an increased risk for CAD and even cerebrovascular disease (stroke).

More recently developed, non-traditional (novel) risk factors for CAD include surrogate markers for inflammation and thrombosis. Some of these include: C reactive protein, homocysteine, and fibrinogen. When these are elevated, there is an increased risk for systemic inflammation and thrombosis, not necessarily specific to CAD.[1]

When an individual possesses some or many of these risk factors, he or she will have a propensity to develop CAD with its continuum into myocardial ischemia and myocardial infarction. In a healthy patient, the coronary arteries supply adequate blood flow to meet the demands of the myocardium, and myocardial ischemia results when the demands for oxygen and nutrients are not met. This causes impairment in cellular metabolism. The most common cause of the decreased blood flow is the presence of plaque in the coronary circulation. Small, stable plaques do not lead to immediate coronary events, but when they enlarge, and cause a major narrowing of a coronary artery or become unstable, problems can occur. Unstable plaques are prone to rupture or ulceration, causing the underlying tissues in the vessel wall to be exposed, thus leading to platelet adhesion and clot formation, resulting in myocardial ischemia.[15]

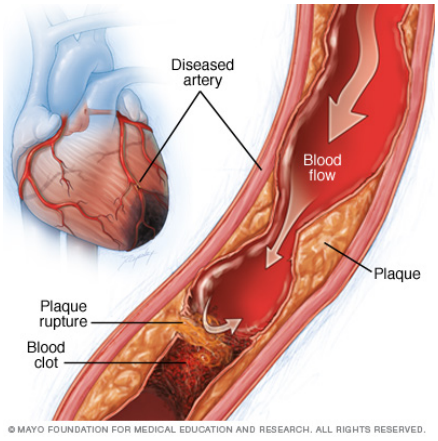


Figure 14 (Myocardial Ischemia)

If myocardial ischemia is not abruptly reversed, a heart attack, or myocardial infarction (MI) defined as the death of cardiac muscle, will ensue. Heart attacks are the leading

cause of death in the United States. The initial event in a MI is a sudden change in the morphology, or appearance, of a plaque. The plaque can then be exposed to collagen and necrotic plaque contents, which can then cause vasospasm due to platelet aggregation. The extrinsic pathway of coagulation can be activated, forming a clot, which thus blocks the coronary artery. This resulting loss of critical blood supply to the myocardium leads to an infarction.

The extent of damage caused by the MI depends on the location and extent of necrosis. Dysrhythmias, septal rupture, sudden death, and aneurysms can develop as a result of myocardial infarction.

Patients experiencing ischemic heart disease (IHD) can show a variety of clinical symptoms. Ischemic heart disease is a condition of recurring chest pain or discomfort due to a lack of oxygen. The most common form of chest pain in IHD is stable angina, which results in predictable pain caused by chronic coronary obstruction. The discomfort is transient, and no permanent damage occurs if blood flow is later restored. The pain can be described as if a clenching fist is squeezing the heart. Stable angina is most seen when people do work/exercise and symptoms include increased pallor, abnormal breathing, and excessive sweating. A different form of chest pain, which is unpredictable and can occur at rest, is called Prinzmetal angina. This is caused by coronary artery vasospasm, and not by atherosclerosis. Finally, an individual with CAD may have silent ischemia, where no detectable symptoms are present. In this scenario there is no chest pain and it is therefore difficult to detect, and so it becomes a significant cause of death.

In addition to a patient's complaints, physical examination plays a role in the diagnosis of CAD. Firstly, hypertension is the most obvious finding. Extra and rapid heart sounds may be detected (left ventricular gallop or S3), revealing an impaired LV function during the ischemic attack. Bruits can be heard through a stethoscope, which may help diagnose CAD. Small fat deposits, or xanthelasmas, may develop around the eyelids. In addition, arcus senilis may exist, where a yellow lipid ring surrounds the cornea. The latter suggests dyslipidemia and atherosclerosis.

Testing through electrocardiography, or ECG, is important in the diagnosis of myocardial ischemia. ST elevation can be seen in patients with silent ischemia and is indicative of transmural ischemia. Figure fifteen displays the various ECG variations associated with myocardial ischemia.

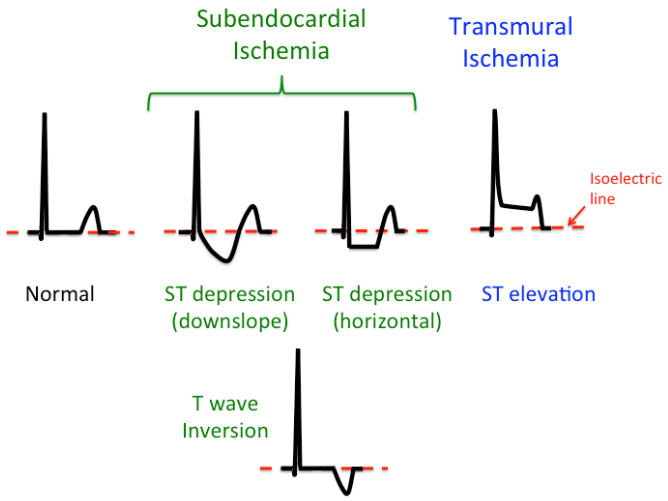


Figure 15 (ECG variations in both subendocardial and transmural ischemia)

Transient ST depression and T wave inversion are associated with subendocardial ischemia. Transmural and subendocardial ischemia differ in the amount of ventricle wall affected. In transmural ischemia, the more common of the two, the full thickness of the ventricle is affect. Subendocardial ischemia is limited to the inner one third to one half of the ventricular wall. Laboratory studies including a lipid panel and some of the

previously mentioned surrogate markers can also be ordered. There are more provocative tests, such as stress echocardiography and treadmill studies, that can also be ordered.[1]

## MANAGEMENT OF CAD

Once ischemia is diagnosed, there are many ways to treat it. As a brief introduction to treatment, therapeutic modalities include medication, procedural intervention, and finally surgery. Commonly used medications include beta- blockers, calcium channel blockers, platelet aggregation inhibitors, and other pharmaceutical intervention to treat CAD risk factors such as dyslipidemia and diabetes. Beta- blockers increase the supply of oxygen and reduce myocardial demand. Calcium channel blockers obstruct the influx of calcium into smooth muscle and myocardial cells, thus slowing the heart rate to allow extra filling time in the coronary vessels. Percutaneous coronary intervention (PCI) is a general term where procedures are performed to either stent the narrowed vessels or move the obstructing plaque to the sides of the coronary artery, known as balloon angioplasty. More detailed descriptions of PCI will be covered in the next section of this paper. Lastly, coronary artery bypass graft surgery, where another native vessel is used to bypass the blockage, is used as last resort.

The initial management of CAD mainly focuses on establishing and eliminating the modifiable risk factors. In addition, if there are comorbid conditions such as hypertension, diabetes, and anemia, these need to be addressed and promptly controlled. If these two early interventions are unsuccessful as in the case with more advanced disease, then specific pharmacologic therapy and/or PCI are necessary. Examples of reversible, non-pharmacologic measures include: moderate and regular exercise, heart healthy diet, smoking cessation, and stress and weight reduction.[1]

As mentioned above, commonly used medications to control heart disease include nitrates such as Nitroglycerin, which assist in dilating blood vessels, enhancing blood flow through otherwise narrowed and restricted vessels, which may relieve angina, a common symptom of CAD. Drugs that suppress platelet activity such as Aspirin and Clopidogrel (Plavix) lower the risk of heart attack by reducing clot formation within arteries. In addition, cholesterol reducing agents, predominantly statins, function to increase HDL and lower LDL and other "bad cholesterols", which ultimately will lower the total plaque load within the vessels. Beta- blockers increase the supply of oxygen and reduce myocardial demand by blocking beta-adrenergic receptors. In addition, these drugs cause contraction of the smooth muscle of the peripheral arteries, thereby reducing blood flow to body tissues.[16] ACE inhibitors are medications that slow the activity of the enzyme ACE, which functions by lowering the production of angiotensinogen II. This then causes blood vessels to dilate, blood pressure to fall, and ultimately makes it easier for the heart to function.[17] When medications alone fail to control the symptoms and progression of heart disease, procedural interventions and surgery are the only remaining options to combat this fatal disease.

Percutaneous coronary intervention (PCI) is a general term where procedures are performed to either stent the narrowed vessels or move the obstructing plaque to the sides of the coronary artery, known as balloon angioplasty. More detailed descriptions of PCI will be covered in the next section of this paper.

If lifestyle modification, pharmacologic therapy, and PCI have not sufficiently managed the patient's CAD, cardiac surgery is the next option. A coronary artery bypass graft (CABG), performed by a cardiothoracic surgeon, comprises the use of a lower

extremity vein, the saphenous vein, or the mammary artery, to function to bypass the obstructed coronary artery with the assistance of a cardiopulmonary bypass machine.

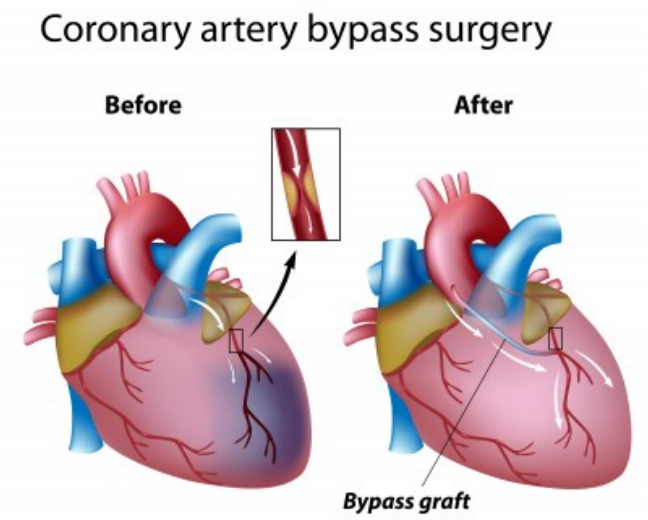


Figure 16
(CABG Surgery)

According to the American Heart Association, CABG surgeries are among the most commonly performed major surgeries. As seen in figure 16, this restores blood flow to the heart, but is an invasive procedure with increased morbidity and mortality.[18] Overall mortality associated with CABG surgery is 3-4%. After surgery, heart attacks occur in 5-10% of patients and are the main cause of death while stroke occurs in only 1-2% of patients. Complications increase with several factors including diabetes, age, chronic lung disease, poor heart muscle function, and chronic kidney failure.[19]

**PCI IN DETAIL**

The technological advances in PCI have led to a significant reduction in the need for major CABG surgery, especially due to the development and utilization of stents. Stents are required when there is up to 70% blockage in the coronary artery. This can be clinically demonstrated and confirmed by coronary angiography, which uses contrast dye

to visualize the blockage. In the past, coronary angioplasty was the predominant method to relieve obstructed coronary arteries and is still widely used today.

In cases where both lifestyle and pharmacologic measures fail to treat the patient's heart condition, the next step in management is percutaneous coronary intervention (PCI). This is minimally invasive compared to open-heart surgery, but still is not without risks. PCI is defined as a procedure that widens narrowed or unblocks obstructed coronary arteries. The coronary artery is considered severely compromised when the blockage is 70% or greater. The procedure is performed under conscious sedation where the patient receives an intravenous sedative, but breathes on his or her own. The patient also receives a local numbing medicine at the site of the incision, commonly the groin region so the cardiologist can access the femoral artery.[1]

Before the PCI is actually begun, cardiac catheterization is done as the diagnostic procedure to identify the location and extent of the coronary vessel blockage. A small tube, or catheter, is inserted into the femoral artery and is then guided up to the chest and into the heart using an x-ray imager. A contras agent is injected through the catheter to visualize the flow through the coronary arteries while the heart is pumping. This is known as coronary angiography. At this point, the cardiologist can decide whether or not PCI is necessary or the correct procedure. Although cardiac catheterization with or without PCI is an invasive procedure, most people have reported little pain associated with the exam.[20]

The most common PCI modalities include balloon angioplasty and stent placement. During balloon angioplasty, as shown in figure 17, the cardiologist inserts a cardiac catheter surrounded by a small balloon into a coronary artery. Then the balloon is

expanded to push the obstructing plaque to the sides of the vessel wall. The balloon is then removed and a stent may or may not be used to keep the vessel open. Either one or both of these PCI treatments will allow more blood flow through the coronary vessels, thus supplying adequate oxygen to the heart muscle. This results in the relief of associated chest pain and can both thwart an active heart attack and prevent any future ones.[21]

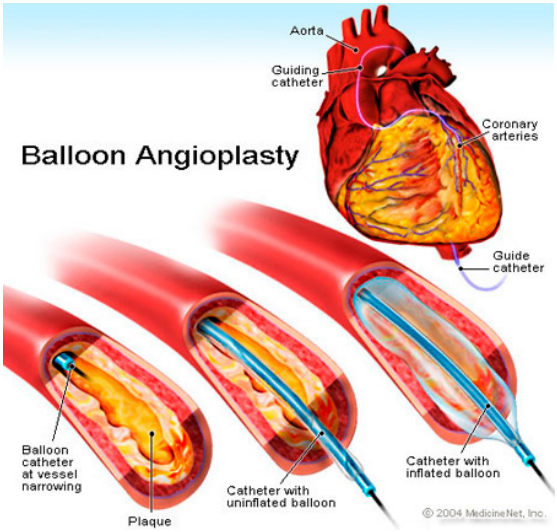


Figure 17
(Balloon angioplasty)

In addition to balloon angioplasty, stenting is another technique used in PCI. As mentioned previously, stenting may be done immediately following an angioplasty, but also may be a stand- alone procedure. A stent is a small, expandable mesh- like tube that can be inserted into a coronary artery to allow for proper blood flow through the vessel. The stent is usually made of metal and has a scaffold- like appearance. In cases where larger arteries are occluded, fabric stents, also called stent grafts, may be utilized. A stent can prevent constriction of the vessel by keeping the underlying plaque away from the vessel's lumen. Stents are usually permanent devices, but re-occlusion of the coronary arteries can occur, requiring further angioplasty or re-stenting. Stenting has reduced the rate of re-occlusion by about 40%. Compared with no stents, six-month re-obstruction

rates were cut in half. However, compared to coronary bypass surgery (a much more invasive measure), the rate of success of stents is low because they do not protect against future heart attacks or prolong life. These operations have over a 95% success rate.[22] Stents have evolved from a simple mechanical tube into drug eluting stents, which are most commonly currently deployed. These stents are coated with medication that is continuously released into the vessel wall to prevent tissue proliferation, such as scar tissue, from causing re-stenosis. Drug-eluting stents are made of metal with a polymer coating and a drug, either Sirolimus or Paclitaxel, mixed into the polymer. Sirolimus is an antibiotic known to be a potent inhibitor of smooth muscle cell proliferation. Paclitaxel interferes with the normal breakdown of microtubules during cell division. In drug-eluting stents, the rate of recurrence of blockage within the first year is less than with metal ones. Also, bare metal stents have proven to display higher rates of blockage recurrence. Although today metal stents are the most common, the development of bio-absorbable stents is a topic of interest in the medical field. These new models are made of either polymer or metal that is dissoluble, and several types of these stents have already been tested. However, their larger and bulkier construction is the reason why bio-absorbable stents are not yet commercially available.[23] In addition, MRI- guided coronary stents and stents that are more flexible are some examples of the advancements in this developing medical field.[24] Images of stents can be seen in figures 18 and 19.

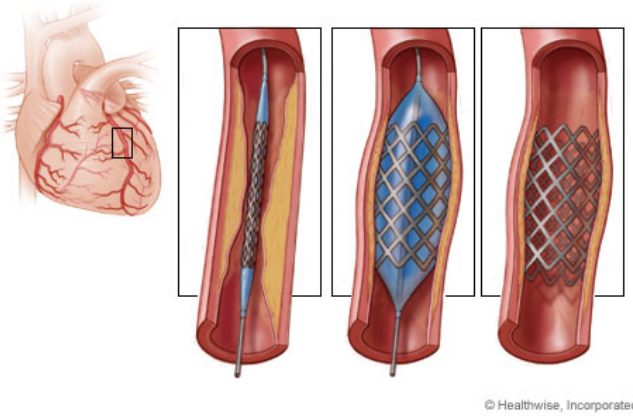


Figure 18 (stent placement procedure)

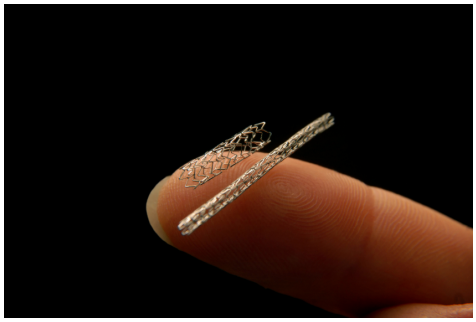

Figure 19 (stent)

There are two main types of stents that are used in the common practice of PCI: bare metal stents (BMS) and drug- eluting stents (DES). In addition to the metal scaffolding of a stent, DES contain an anti-proliferative drug whose function is to inhibit neointimal growth. As mentioned earlier in this paper, drug- eluting stents contain a polymer coating and a drug, either sirolimus or paclitaxel, mixed into the polymer. Neointima refers to scar tissue that forms within blood vessels, and it is also the main cause of vessel restenosis. Because these stents lack this drug, 10-20% of patients with BMS experience re-narrowing at the one-year mark. Clinical studies have shown that DES reduce restenosis by 50-70% compared to metal only ones, thus making DES the predominantly utilized stent in current practice. Although the creation of DES has proven beneficial in lowering the rate of restenosis, it does have an important limitation...there is an increased risk for long- term stent thrombosis compared to BMS.[25] Stent thrombosis occurs when a previously placed coronary stent becomes blocked by a blood clot, and it can result in myocardial infarction or possibly death. For this reason, the overwhelming majority of patients with DES require a dual anti-platelet therapy consisting of aspirin and a platelet receptor blocker such as platelet P2Y receptor blocker. The cardiologist must weigh the benefits of DES with its anti-platelet therapy with the risks they pose due to bleeding complications.[26]

**RESTENOSIS**

Although stents are now widely used in PCI and serve as an excellent alternative to major bypass surgery, they are not without limitations. One of the major drawbacks of stents is their inability to maintain vessel patency for long periods of time in some instances. If this occurs, restenosis, or the gradual re-narrowing of the stented coronary vessel, has now once again caused a restriction in blood flow through the coronary vessels. When a stent is initially placed into a vessel, new tissue consisting of healthy endothelial cells is able to grow, allowing blood to flow unobstructed through the coronary artery without clotting, thus relieving the patient's angina (chest pain caused by a reduction in blood flow to the heart). If stent restenosis occurs, the most common time interval is between 3-12 months after the original stent was inserted. Stent restenosis becomes a less likely occurrence after the initial 12 months of insertion. Figure 20 shows intracoronary vessel restenosis.[27]

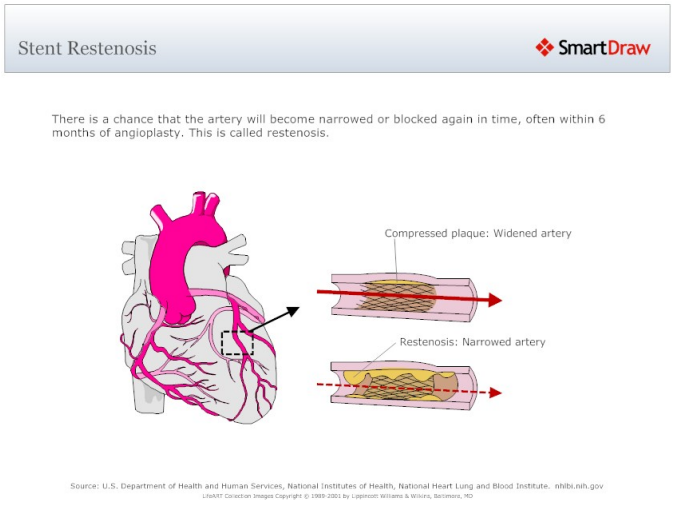


Figure 20
(Vessel restenosis following PCI)

Another challenge faced by the cardiologist is his or her ability to limit or reduce risk factors once a stent has been inserted. In a review of patients six months after angiography with PCI and BMS placement, the rate of restenosis was 16% without any

major risk factors. These risk factors include: diabetes, having had multiple stents previously implanted, weight and body mass index, hypertension, nickel allergies, chronic kidney disease, and the shape of the coronary vessel lesion. In the presence of any of these risk factors, however, the incidence of restenosis was as high as 59%. In addition, the diameter of the vessel lumen has shown to be a significant predictor of the risk of restenosis both in patients with BMS and DES. Although the rate of restenosis is much less in the presence of DES (5-15% depending on the duration and complexity of the lesion), it still exists. Several predictors for restenosis in DES include: diabetes and an increased stented length as well as other factors. The patient who develops stent restenosis will present with cardiac symptoms such as recurrent chest pain, and many cardiologists utilize an intravascular ultrasound device to evaluate the restenotic stent.

To treat restenosis properly, many different steps can be taken by the physician. Initially, balloon angioplasty is commonly employed to expand the stent further and remove unnecessary tissue from the area. The interventional cardiologist may then decide to insert a new drug-eluting stent within the original stent, especially if it was metal only. Further treatment measures can include intracoronary radiotherapy, but re-stenting with DES has proven to be more beneficial both short term and in the long run. When evaluation has revealed that further stenting will not be successful and the patient is thus not a PCI candidate any longer, CABG surgery may be necessary. Although much more invasive with much more morbidity than PCI, CABG surgery has the advantage of a much lower rate of coronary artery restenosis compared to stents, especially BMS.[28]

**LIFESTYLE MODIFICATIONS**

Although stent restenosis can be evaluated and successfully treated even if needing to resort to CABG surgery, prevention of restenosis is the optimal goal. In addition to medical therapy prescribed by a cardiologist to prevent restenosis, the patient needs to be empowered to reduce the modifiable risk factors. Hopefully, the patient has received a wake up call from his or her incident of the life- threatening chest pain or heart attack. Obesity, poor diet, lack of exercise, hypertension, diabetes, and smoking are just several examples of risk factors that can cause detrimental problems in the cardiovascular system and lead to restenosis.

Maintaining a healthy body weight is crucial in the prevention of cardiovascular related illness. Overweight people are more likely to acquire CAD because obesity increases blood pressure and most obese people are likely to eat a high- fat, high-cholesterol, and high-carbohydrate diet. In addition, obesity alone raises LDL serum levels. This leads to an increased triglyceride level and LDL cholesterol level while lowering HDL cholesterol, which is the good cholesterol. A high level of LDL cholesterol in the blood is a trigger for plaque buildup in the arterial walls. As the vessels narrow, blood flow is reduced and the heart cannot receive adequate oxygen and nutrients. Heart healthy diets can help to lower blood pressure and serum cholesterol levels. As recommended by the American Heart Association, this diet includes consumption of fruits and vegetables, grains, poultry and fish, nuts, and non-fat or low fat dairy products. At the same time, one must limit red meat, fried and greasy foods, and sugary foods and beverages.[29]

In addition to a healthy diet with monitoring of caloric intake, physical activity is also necessary to keep the heart healthy. According to the AHA, approximately 250,000 deaths annually in the US are attributed to a lack of exercise. Exercise lowers LDL cholesterol while raising HDL by stimulating enzymes that carry fat deposits out of the arteries and into the liver, thus preventing fatty plaques from getting stuck in the vessel wall. The flexibility of blood vessels increases with exercise, thus permitting enhanced blood flow through the coronary vessels, better perfusing the heart muscle so the heart can overall be more efficient. According to a study by the University of Maryland, exercise has been shown to lower blood pressure by stimulating nitric oxide, which keeps the blood vessels dilated. Sedentary individuals have a 35% higher risk of hypertension compared to those who exercise regularly. The AHA recommends at least 30 minutes of moderate exercise per day at least five days a week, and optimally every day. One may have to start slowly and build up in ten-minute increments. Any exercise will be beneficial including walking, biking, climbing stairs, sports, or working out at the gym.[30]

If a patient does not reduce the aforementioned modifiable risk factors, there will not only be a higher risk of restenosis, but also of the development and or progression of diabetes. Diabetes mellitus, a chronic condition defined by abnormally high levels of sugar (glucose) in the blood, affects a significant proportion of individuals in the United States. According to the CDC, the prevalence of diabetes was almost 21 million in the US in the year 2011. Figure 21 shows the increase in the number of diabetic patients in America over the years, a worrisome trend no doubt.[31]

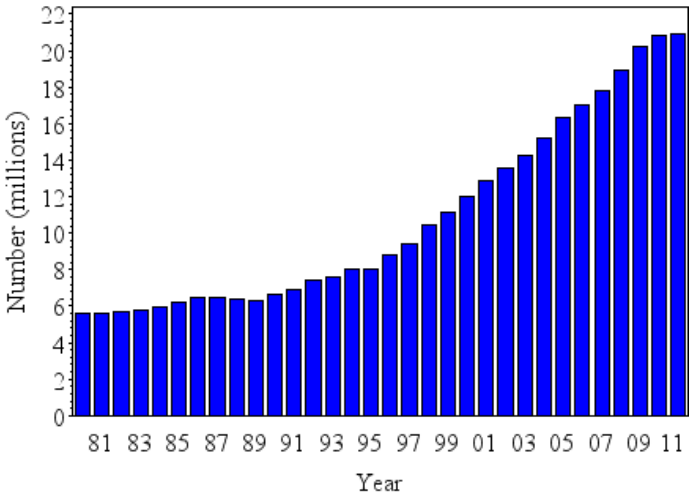


Figure 21 (Number of patients affected by diabetes over the years according to the CDC)

Cardiovascular complications of diabetes are the leading cause of morbidity and mortality in these patients, with CAD killing approximately 60% of these patients. Obesity, advancing age, genetics, and insufficient physical activity are all factors leading to diabetes, and therefore cardiovascular issues as well. Treating diabetic patients for coronary artery disease (CAD) can be challenging due to their elevated blood sugar levels and smaller coronary artery size. Several studies have been done to test the risk factor of diabetes in the rate of intracoronary stent restenosis. It has been shown that diabetes remains a major risk factor for restenosis regardless of the type of stent used: bare metal or drug- eluting. Restenosis as well as late stent thrombosis occurs much more frequently in diabetic patients, and because of this, open heart CABG surgery is often recommended to these patients.[32] However, in 2012 the FDA approved a Zotarolimus- eluting coronary stent to be specifically used for diabetic patients. Having the same design as any other drug- eluting stent, this stent has a different polymer and different delivery system than most others to specifically target diabetics.[33] There are many things diabetic patients can do to prevent the progression of their disease...strictly comply with a diabetic diet, take the prescribed medications whether oral agents or subcutaneous insulin, exercise regularly, and manage stress.[34]

Whether the cardiac patient is diabetic or not, cigarette smoking is an independent risk factor for CAD. Nicotine constricts blood vessels and carbon monoxide has been shown to damage the inner lining of these vessels, which makes them more prone to atherosclerosis. The risk of having a myocardial infarction in women who smoke 20 cigarettes or more a day is six times greater than that of non-smokers. The main difference between smokers and non-smokers in CAD is the baseline characteristics: smokers require PCI at an earlier age; they are more likely to have had a previous MI, etc. However, interestingly enough, previous studies have shown that cigarette smoking not does have a deleterious effect on intracoronary restenosis; in fact in a 2004 study from Vienna, smoking caused less restenosis. These results could be due to the smoker's increased amount of carbon monoxide in the blood. Carbon monoxide is an anti-inflammatory agent that dilates the vessels. In addition, carbon monoxide inhibits smooth muscle growth within the arterial wall, which is the cause of restenosis. Regardless of the possible but yet unproven, beneficial effect of smoking on restenosis, smoking in general still leads to progression of CAD and increased rates of heart attack.

**CONCLUSION**

In order to understand the role of PCI in the treatment of CAD, the use of stents with their inclination to restenosis and lifestyle modifications to limit the progression of both CAD and stent restenosis, the reader must first grasp basic anatomy and physiology of the cardiovascular system. It is also requisite to attain background knowledge of CAD, as it is the number one killer in the United States. Every 33 seconds, an American male or female will suffer a myocardial infarction (heart attack). PCI has become the most

common treatment for CAD, employing the use of stents. Lifestyle modifications to reduce risk factors, both for CAD and for stent restenosis, have been recommended to keep the patient heart healthy. Thomas Edison, one of the most famous inventors of our time, indeed had foresight but perhaps also some wishful thinking when he said, "The doctor of the future will give no medicine, but will educate his patients in the care of the human frame, in diet, and in the cause and prevention of disease."[35]

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# Between a Stent and a Hard Place: Restenosis Prevention methods

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## Abstract

Coronary Artery Disease (CAD) is the number one killer in the United States. Every 33 seconds, an American male or female will suffer a myocardial infarction (heart attack). A common treatment modality currently employed is Percutaneous Coronary intervention (PCI). One of the mainstays of PCI is the insertion of a coronary artery stent, a mesh-like metal tube that may elute specific anti-clotting drugs that functions to keep the coronary artery open. Frequently, there may be a narrowing or restenosis of the stent, requiring further therapy. Lifestyle modifications to reduce stent restenosis include: weight loss, heart healthy diet, exercise, and management of coexisting diabetes.

## Cardiovascular System

The Cardiovascular System is comprised of three main components: the heart, blood vessels, and blood. The heart contracts in coordinated heartbeats. It contains four chambers, two atria and two ventricles. The presence of valves prevents backflow and ensures the unidirectional flow of blood.

The blood vessels function to transport blood to all parts of the body. Four main types of blood vessels exist: arteries, arterioles, capillaries, and veins.

The coronary arteries supply blood to the heart muscle. Myocardial ischemia results when the demands for oxygen and nutrients are not met.

Blood has both cellular and non-cellular parts. The cellular component of blood consists of red blood cells (erythrocytes), white blood cells (leukocytes), and platelets (thrombocytes). The non-cellular portion of the blood includes plasma and the proteins situated within it.

## Risk Factors

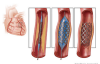
| | Conventional | Non-traditional |
|---|---|---|
| **Modifiable** | • Hypertension<br>• Cigarette smoking<br>• Diabetes<br>• Dyslipidemia<br>• Obesity<br>• Atherogenic diet<br>• Sedentary lifestyle | |
| **Non-Modifiable** | • Advanced age<br>• Male gender<br>• Family history | • Surrogate markers:<br>○ C reactive protein<br>○ Fibrinogen<br>○ Homocysteine |

## Cardiovascular Disease

CAD can also be classified as atherosclerotic heart disease or ischemic heart disease, but the latter is the more descriptive term. CAD occurs when plaque buildup in the coronary vessel walls (atherosclerosis) causes the coronary arteries to become narrowed or obstructed. This will lead to a decrease or cessation of blood flow to the myocardium, resulting in myocardial ischemia. If myocardial ischemia is not abruptly reversed, a heart attack, or myocardial infarction (MI) defined as the death of cardiac muscle, will ensue. Heart attacks are the leading cause of death in the United States.

## Treatments and **Issues**

- Eliminating modifiable risk factors
- Medications: beta- blockers, calcium channel blockers, platelet aggregation inhibitors, and other pharmaceutical intervention.
- PCI: balloon angioplasty and/or stent placement
- A coronary artery bypass graft (CABG), performed by a cardiothoracic surgeon usually as a last resort or in severe cases.



## Lifestyle Modification

| Risk Factor: | Lifestyle Modification: |
|---|---|
| Obesity | Weight loss<br>○ Medically supervised weight loss program for at least 6 months.<br>○ Eating fewer calories.<br>○ Burning more calories. |
| Poor diet | Heart healthy diet<br>○ Fruits and vegetables, grains, poultry and fish, nuts, and non-fat or low fat dairy products.<br>○ Limit red meat, fried and greasy foods, and sugary foods and beverages. |
| Sedentary Lifestyle | Exercise<br>○ 30 minutes moderate exercise per day |
| Diabetes | Strict adherence to diabetic therapy<br>○ Diabetic diet.<br>○ Prescribed medications whether oral agents or subcutaneous insulin.<br>○ Exercise regularly.<br>○ Manage stress. |
| Smoking | Cessation<br>○ May not contribute to a higher rate of restenosis. |

## Conclusion

PCI has become the most common treatment for CAD, employing the use of drug-eluting stents. Lifestyle modifications to reduce risk factors, both for CAD and for stent restenosis, have been recommended to keep the patient heart healthy.

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Appendix I (Poster Template)