Coronary artery bypass grafting versus drug-eluting stents: has coronary bypass found its successor?

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Coronary Artery Bypass Grafting Versus Drug-Eluting Stents

Has Coronary Bypass Found Its Successor?

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Introduction

The human heart is an amazing organ. Three thousand gallons of blood flow throughout the body because of the heart pumping the blood out each day (Cleveland Clinic, 2009). The heart needs its own blood supply to operate and to deliver the oxygenated blood the rest of the body needs. The coronary arteries, which stem directly from the aorta, is how the heart receives its blood supply to function. Two main coronary arteries, the right and the left, provide the blood and oxygen the heart needs in order to pump out the blood and nutrients to the rest of the body. The right coronary artery (RCA) branches into the right marginal artery and the posterior descending artery (PDA). The main portion of the right coronary artery provides blood to the right side of the heart. The right side of the heart then pumps out the blood to the lungs to become oxygenated. The remaining portion of the right coronary artery and its main branch, the posterior descending artery, along with the branches of the circumflex artery, runs across the surface of the heart’s inferior side, supplying the inferior portion of the left ventricle and posterior of the septum (Cleveland Clinic, 2009). The left coronary artery (LCA) branches into the circumflex artery and the left anterior descending artery (LAD). The circumflex artery supplies blood to the left atrium and the lateral and posterior of the left ventricle. The left anterior descending artery supplies the inferior and anterior portions of the left ventricle and the anterior portion of the septum (Cleveland Clinic, 2009). With huge responsibility, the heart can still encounter problems that can endanger the heart itself and the rest of the body.
Heart disease is the leading cause of death in the United States. Coronary artery disease, the most common form of heart disease, affects 16.8 million Americans (Cleveland Clinic, 2009). In 2005, 444,687 people died from coronary artery disease (U.S. Centers for Disease Control and Prevention [CDC]). Two out of every three males over the age of forty years will have a cardiovascular event and over one out of every two females will experience one as well (National Heart Lung and Blood Institute, 2009). It is estimated that heart disease will cost the United States 304.6 billion dollars in 2009 (CDC, 2009). Coronary artery disease is a serious health issue that affects everyone, regardless of race, gender, or socioeconomic status.

Coronary artery disease is a condition where plaque builds up and become prevalent within the arteries. The plaques cause the arteries to narrow and the heart is unable to get the blood it needs to operate optimally. The plaques can be made up of many components such as: cholesterol, fat, calcium, and other substances within the blood. Plaque buildup is called atherosclerosis. As the plaque builds up, it decreases the amount of oxygen the heart is receiving, creating stress which can lead to angina, or a myocardial infarction. As a person continues to live with this condition, the heart can weaken tremendously and lead to heart failure and or arrhythmias (National Heart Lung and Blood Institute [NHLBI], 2009).

The pathophysiology of coronary artery disease is a slow process that can start before adolescence. The coronary arteries are shaped like hollow tubes so blood can easily flow freely. The walls are smooth and elastic, lined with a layer
called endothelial cells (Cleveland Clinic, 2009). This layer provides a barrier
between the blood stream and the coronary artery walls; at the same time,
controlling the function of the artery through chemical signals being released in
response to various stimuli. Coronary artery disease begins when the vessel wall
starts to show streaks of plaque. As the individual ages, the substances build up,
which cause slight injury to the vessel wall (Cleveland Clinic, 2009). Since the
vessel wall is now injured, the body initiates an inflammatory cascade causing
cells to be released to the injured vessel. This makes the vessel wall more
adherent than usual, causing other normally non-adherent substances traveling
through the blood stream to stick to the wall. This is how plaque buildup is
produced. The plaque can become different shapes and sizes over time. The
plaque is soft on the inside with a hard fibrous cap covering the outside.
Sometimes the hard lid can rupture or tear off, causing the soft plaque to be
exposed. Platelets come to the area and a blood clot forms around the plaque.
This process makes the arteries narrower; however, sometimes the clot breaks
and the blood supply is restored spontaneously. The worst scenario happens
when the clot totally blocks the blood supply to the heart. When this happens it
leads to acute coronary syndrome (Cleveland Clinic, 2009).

Acute coronary syndrome is defined as a blood clot that suddenly blocks
the blood supply causing one of three serious conditions. One condition is
unstable angina which is defined as chest pain or discomfort that happens when
not enough oxygenated blood is flowing to an area of the heart muscle (Institute).
Unstable angina can occur in a person who has never experienced this type of
pain before, or, it can occur in a person who has had angina before but is experiencing a new onset of angina presenting in a different way. The second condition is non-ST segment elevation myocardial infarction (NSTEMI). This type of heart attack, or MI, does not cause major changes on an electrocardiogram (ECG). However, chemical markers in the blood indicate that damage has occurred to the heart muscle (Cleveland Clinic, 2009). Heart muscle breaks down when the heart is damaged. The heart releases chemicals in the body that can be detected by a blood screen. These are referred to as cardiac enzyme markers known as myoglobin, troponin, and creatine phosphokinase (CPK). Findings of myoglobin and CPK in the blood are suggestive of a heart attack. Findings of troponin in the bloodstream are diagnostic of a MI. The third acute coronary syndrome is ST segment elevation myocardial infarction (STEMI). This is a type of heart attack that is caused by a prolonged period where the heart is not receiving blood due to a blockage in the artery. When the blockage affects a large area of the heart, it causes changes on the ECG as well as the chemical markers found in the blood (Cleveland Clinic, 2009).

Other problems that stem from long standing coronary artery disease include heart failure and arrhythmias. The heart has not failed completely; however, it is failing to pump enough blood to the rest of the body (Institute). When the heart is not pumping enough blood it causes the body to incur stress since the body is receiving less oxygenated blood as well. Individuals with long standing coronary artery disease can experience arrhythmias. These are defined by problems with the speed or rhythm of the heart beat (Institute).
With all of the problems that can arise from coronary artery disease, the heart can try and compensate through collateral circulation (Cleveland Clinic, 2009). If an artery starts to get narrow, the heart will create a vessel or use another vessel nearby to reroute the blood supply to the area of the heart that is not getting enough blood and nutrients. However, this can create too much stress on the vessel that is not used to the extra workload. It could also deprive a different area of the heart from receiving enough blood supply.

Coronary artery disease is extremely common and researchers have identified individual risk factors that predispose people to this problem. People are prone to one disease over another based on lifestyle, genetics and environment. Risk factors can play a tremendous role in how a person can progress to severe coronary artery disease. Risk factors can be broken down into modifiable and non-modifiable risk factors.

Non-modifiable risk factors include gender, advanced age, family history of heart disease, and race (Cleveland Clinic, 2009). Men have a higher risk of having a cardiovascular event than women do at a younger age. However, after the age of 70 years, men and women are at equal risk for coronary artery disease. As a person ages, the risk of coronary artery disease increases, especially after 65 years of age. This is due to the fact that coronary artery disease is an extremely slow process that starts in the adolescent and continues to build up as one ages. Family history of heart disease is important since it is shown that coronary artery disease runs in families. Furthermore, it is more significant and alarming if a first degree relative has a cardiovascular event prior
to age 50 years. When considering race, African Americans are the most susceptible to coronary artery disease because they have more severe high blood pressure than most other races (Cleveland Clinic, 2009).

Modifiable risk factors include smoking, high blood cholesterol and high triglycerides, high blood pressure, uncontrolled diabetes with insulin resistance, physical inactivity and obesity (NHLBI, 2009). Smoking damages the endothelium and constricts the blood vessels. Once damaged, the body reacts by bringing cells and other substances to help heal the area; however, the body does not realize that while healing the vessel, it is also causing more damage and further narrowing of the arteries leading to hypertension. In addition, the tightening of the vessels due to smoking causes less blood flow through those arteries which causes less nutrients to be supplied to that particular area. In addition to hypertension, smoking is known to increase cholesterol. High cholesterol is another component of coronary artery disease, especially high LDL and low HDL (Cleveland Clinic, 2009). Cholesterol, in general, has two components, LDL and HDL. LDL stands for low density lipoprotein. This is considered the bad cholesterol because it takes the cholesterol from the liver and deposits it anywhere in the body. One of the main components of plaques is cholesterol, so if a person has high LDL, there is a high chance of it getting deposited in the arteries. In contrast, HDL, high density lipoprotein, does the opposite of LDL. It takes the cholesterol from the liver and excretes it from the body. In general, LDL should not exceed 100 mg/dL and the HDL should be over 40 mg/dL (Cleveland Clinic, 2009). Furthermore, it is recommended that patients
with coronary artery disease should not exceed an LDL level of 70 mg/dL or a triglyceride level above 150 mg/dL. High blood pressure exceeding 140/90 is also a risk factor for coronary artery disease along with risk factors for MI and stroke. The arteries are constricted and cannot dilate. The constriction makes pressure within the arteries rise from all of the components in the blood stream. Along with the constriction, the blood is not able to spread throughout the body as easily due to the increased pressure. The heart must compensate with increased force, which eventually leads to heart failure if not controlled.

Uncontrolled diabetes is a slow and progressive vascular disease. It is another risk factor for coronary artery disease (Cleveland Clinic, 2009). Vascular disease occurs because the body’s blood sugar level are too high due to insufficient insulin, or the vessels being resistant to insulin (Institute). Insulin is a hormone that is excreted by the pancreas in response to normal body function when consuming energy. Insulin takes the sugar from the blood stream and transports it into the tissues and organs for energy. When the vessels are resistant to insulin, the sugar stays in the blood stream and it becomes trapped within the arteries. When arteries are damaged, they become “sticky.” This allows substances like sugar, plaque and other substances to build up in the arteries. Physical inactivity, being overweight and/or obesity also contribute to coronary artery disease due to a lower metabolism. Having a lower metabolism leads to prolonged absorbing of substances, therefore staying in the arteries longer.
There have been some emerging risk factors that affect coronary artery disease that are being researched currently. They include C-reactive protein, homocysteine, and fibrinogen (Mayo Clinic, 2009). C-reactive protein is produced by the liver in response to injury or infection. It is also produced by the muscles in the coronary arteries. This substance is used to let the body know that there is some kind of inflammation occurring. When the coronary arteries are injured, the inflammatory cascade is initiated and C-reactive protein enters the blood to help the body heal, but it can damage the arteries. C-reactive protein is non-specific risk for coronary artery disease. High amounts of C-reactive proteins do not always hurt patients, it only signals there is inflammation occurring in the body.

Homocysteine is an amino acid that helps build and maintain tissue. Excessive levels of homocysteine could possible increase a patient's risk of coronary artery disease (M. Clinic) because abnormal homocysteine levels may plays a role in atherosclerosis. Homocysteine a direct toxin that damages the arterial lining, interferes with clotting factors, and helps oxidize LDL (Barrett, 2003). These three factors are major reasons that atherosclerosis builds up and why it is possible that homocysteine can be a risk factor for coronary artery disease. The mechanism, however, is not completely understood. Fibrinogen is a protein that plays a major role in blood clotting. Too much fibrinogen in the blood can lead to excessive aggregation of platelets, which equals clotting (Mayo Clinic, 2009). Clotting in the coronary arteries can lead to occlusion of the vessels which can then cause angina or a myocardial infarction.
Sleep apnea, stress, and alcohol have been researched as possible risk factors for coronary artery disease (NHLBI, 2009). Untreated sleep apnea can increase blood pressure, increase blood sugar or insulin resistance and increase the risk of a MI or stroke. Stress is a common trigger of a MI during an emotionally upsetting event, usually involving anger. Heavy drinking damages the heart muscles by weakening the muscles, creating a dilated cardiomyopathy. This leads to heart failure. In addition, heavy drinking worsens the other risk factors associated with coronary artery disease (NHLBI, 2009).

There are several ways to decrease the chances of advancing coronary artery disease. Before using medication to help combat coronary artery disease, there are many lifestyle changes that can be made to help slow the progression of the disease. These include smoking cessation, eating healthy foods, exercising regularly, losing excess weight, and reducing stress (Mayo Clinic, 2009). Smoking cessation reduces blood pressure and stops damage to the blood vessels, which eliminates the inflammatory cascade damage to those vessels, which equals less plaque. Eating healthy, exercising regularly, and losing excess weight are all interrelated. These three things help reduce blood pressure and cholesterol which play a role in the plaque buildup in the arteries. High stress and narrowing of the coronary arteries will increase the likelihood of a cardiovascular event. Reducing stress will decrease the risk of acute coronary syndrome.

A doctor or physician assistant can also prescribe many drugs that may help coronary artery disease, along with the lifestyle changes. The major groups
include cholesterol-modifying medications, aspirin, beta blockers, nitroglycerin, angiotensin-converting enzyme (ACE) inhibitors, and calcium channel blockers (M. Clinic). The cholesterol-modifying medications have many drugs within this class, and with different mechanisms that accompany them. In general, these medications help to decrease the total amount of cholesterol in the body, by lowering the low density lipoprotein, LDL, and boosting the high density lipoprotein, HDL. The classes in this group are statins, niacin, fibrates and bile acid sequesterants (Mayo Clinic, 2009). Aspirin can also decrease coronary artery disease. Aspirin is an antiplatelet drug that can decrease CAD. Platelets play a key role in blood clotting, so lowering the platelets in the body lowers the chances of excess platelet activation which causes clots (Mayo Clinic, 2009). However, clotting is a normal part of healing when a vessel is injured. If a person is injured in an accident, antiplatelets prevent clotting which may intensify the bleeding, making it more difficult to control. Beta blockers are drugs that slow the heart rate and decrease blood pressure. This drug class works by decreasing the heart’s demand for oxygen. Nitroglycerin is a powerful vasodilator that can be given intravenously as well as administered by tablets, sprays, and patches. It helps control symptoms pertaining to chest pain by dilating the coronary arteries (Mayo Clinic). Angiotensin-converting enzyme (ACE) inhibitors help decrease blood pressure by blocking the conversion of angiotensin I by the kidney. This mechanism may help prevent the progression of coronary artery disease. Finally, calcium channel blockers help relax muscles that surround the coronary arteries.
These drugs help open up the arteries increasing the blood flow throughout the heart (Mayo Clinic, 2009).

With all of the available information regarding the pathophysiology of coronary artery disease, a doctor or physician assistant should correctly test for and diagnose coronary artery disease. There are several tests that can be used to help determine if a patient has coronary artery disease. Current testing uses the electrocardiogram (ECG), echocardiogram, stress test, coronary catheterization, CT scan, and magnetic resonance angiogram (MRA) (Mayo Clinic, 2009). An electrocardiogram (ECG) sends electrical signals through the heart and records these signals on a graph. The ECG is a non-specific test for coronary artery disease. It establishes a baseline reading of the heart to see if any past heart attacks can be documented. ECG can also be used while the patient is symptomatic to see if there are ECG changes consistent with an MI. Symptomatic patients may also wear a Holter monitor. This is an ECG machine that is portable and can be worn for 24 hours to visualize how the heart reacts to a normal day of activities. An echocardiogram uses sound waves to produce images of the heart (Mayo Clinic). The echocardiogram helps the doctor or physician assistant determine if all parts of the heart are working and pumping properly. If parts of the heart are moving weakly, the heart may have been damaged during a MI. It also could mean the heart is not receiving enough oxygen which can cause the heart to work slower than normal (Mayo Clinic, 2009). A stress test can be performed if the patient’s symptoms occur during physical activity. A stress test is done under supervision and the patient either
walks on a treadmill to induce heart stress from physical activity or stress can be
induced chemically if the patient is unable to walk on a treadmill or it is suspected
that the treadmill will cause symptoms to persist or cause a MI. Coronary
catheterization is a minimally invasive diagnostic procedure used to help
visualize the heart vessels and blood flow through the heart (Mayo Clinic, 2009).
The cardiologist injects a dye, contrast agent, into the arteries through a long,
thin tube threaded through an artery, usually the femoral artery in the leg. The
dye outlines the artery and helps identify narrow areas and blockages on the X-
ray images (Mayo Clinic, 2009). With the catheter already in place, the
cardiologist can perform a procedure known as a stent implantation if a blockage
is found during the cardiac catheterization. A computerized tomography scan (CT
Scan) can also be performed to visualize the coronary arteries (M. Clinic). In
addition, a magnetic resonance angiogram (MRA) can be performed by using
MRI technology. This checks for narrowing or blockages; however, the details of
the blockages are seen more clearly on a coronary catheterization (Mayo Clinic,
2009).

There are a few procedures that can restore the blood flow to the heart
with symptomatic or progressive disease. Transmyocardial laser
revascularization (TMR) is a form of treatment intended to improve blood flow to
areas of the heart. (Cleveland Clinic, 2009). A laser with carbon dioxide is used
to create small channels in the heart muscle, which improves blood flow to the
heart. This is a good adjunct to a bypass surgery. The main two procedures used
today are angioplasty with stent placement (percutaneous coronary
revascularization), and coronary artery bypass graft surgery. Percutaneous coronary revascularization is a procedure performed by inserting a long, thin catheter into the narrow artery, commonly the femoral artery. A wire is passed through the catheter into the narrowed coronary artery. The balloon is inflated, pushing the deposits against the artery walls allowing blood flow to be re-established. A stent is often left in the artery to keep the artery open so the plaque does not block the artery again. Coronary artery bypass surgery is an extremely invasive procedure where an artery or vein from another part of the body is used as a bypass to the blocked artery (Mayo Clinic, 2009). This allows blood to flow past the blocked artery.

Coronary artery bypass grafting, also known as CABG, has been used for nearly fifty years. In 1953, Dr. John Gibbon performed the first successful open heart operation using a cardiopulmonary bypass machine. Two years later, Sidney Smith harvested a saphenous vein from a leg and used it as a graft from the aorta to direct blood flow from the aorta into the myocardium past the blocked vessel (Medtronic, 2009). This procedure is reserved for severe cases of coronary artery disease in which lifestyle changes and medications are insufficient (NHLBI, 2009). If an individual is a candidate for CABG, the goals after the surgery are to decrease symptoms, to improve quality of life, resume an active lifestyle, improve the pumping action of the heart, decrease chances of a MI, and to increase the chance of survival (NHLBI, 2009).

There are two types of grafting that can be performed, artery and vein grafting. Arterial grafts have a better potency and are less likely to become
reoccluded than vein grafts. The left internal mammary artery is the most commonly used artery due to its close proximity to the LAD (NHLBI, 2009). Within the past few years, the use of radial arteries has been found to be far more superior to veins. They have been found to have greater patency than veins with greater longevity than veins. Bypass arteries have also been found to have less plaque buildup than veins.

There are two ways to prepare the mammary artery for grafting. The artery can be kept intact from its origin, due to the fact that it has a great oxygen-rich blood supply. It can then be attached to the coronary artery, distal to the site of blockage (Cleveland Clinic). The other method to prepare a mammary artery is to remove the artery completely from its origin, which is called a free mammary artery, and attach it between the LAD and the aorta. Within the last decade, over 90% of all patients received a minimum of one internal mammary artery graft (Cleveland Clinic, 2009). The radial artery is another commonly used artery in grafting. It can be used because most people receive blood supply from the ulnar artery and will not have any lack of perfusion if the radial artery is removed (Cleveland Clinic, 2009). If the radial artery is to be considered for use, careful preoperative testing needs to be performed to assess if the radial artery is used more in the blood supply of the arm and hand than previously suspected. Vein grafting is common as well; however, these grafts are more likely to develop plaque and become blocked over time. The greater saphenous vein, which runs along the medial leg, is the most commonly used vein for grafting (NHLBI, 2009).
The original vein harvesting method was to open the leg completely to expose to harvest the saphenous veins for harvesting. However, the bridge technique replaced the original technique. This technique invades making 1-2 inch incisions about every 7 inches in order to expose the vein and improve wound healing. Endoscopic vein harvesting or minimally invasive harvesting is now commonly used, but it has not replaced the traditional bridging technique.

Three types of bypass surgery are currently available. The first is the traditional coronary artery bypass grafting. This is the most common type of CABG. This is typically used when at least one major artery needs to be bypassed (NHLBI, 2009). This procedure typically takes three to five hours to perform, depending on the extent of the blockage or blockages. An incision is made down the mediastinum between the supraclavicular notch and the xiphoid process. The sternum is then cut to allow exposure of the heart. Drugs are used to stop the heart from beating so the surgeon can graft the vessels quickly and with more accuracy than if the heart were beating. A heart-lung machine keeps oxygen-rich blood moving throughout the body (NHLBI, 2009). The machine acts as the heart, so the heart can remain still to correct the blockages, allowing the rest of the body to receive the blood supply it needs. The heart is taken off of bypass, once the grafts are in place and the heart is pumping again. The second type of bypass surgery is the off-pump coronary artery bypass grafting. This non-traditional method is similar to the traditional bypass. The main difference with this procedure is that the heart continues to beat while the bypass graft is placed. Since the heart is pumping, there is no need for a heart-lung machine to keep the
blood flowing. The main reason to use this procedure over the traditional bypass is that the off-pump bypass reduces the risk of complications that can occur with the heart-lung machine. This is true, particularly in people who have suffered a stroke in the past, who are over age 70 years and who have diabetes, lung disease, or kidney disease (NHLBI, 2009). Other advantages to this type of bypass are that it reduces bleeding during surgery and decreases the need of a blood transfusion, reduces the risk of infection, stroke, and kidney complications, along with lowering the chance of memory loss, and difficulty concentrating. In addition, patients have a faster recovery in comparison to the traditional bypass surgery. The third type of bypass is called the Minimally Invasive Direct Coronary Artery Bypass Grafting. There are many types of minimally invasive grafting procedures. This surgery only requires small incisions rather than opening the sternum to expose the heart (NHLBI, 2009). This minimally invasive procedure is known as the Davinci Robotic procedure. The Davinci Robotic procedure is commonly used with just one vessel disease in which you can robotically resects the left internal mammary artery for bypass.

There are still many aspects regarding patient care to consider once the bypass surgery is completed. The first day is spent in the intensive care unit where the patient’s heart rate and blood pressure are monitored extensively. Furthermore, medications are administered to help regulate blood circulation and blood pressure and the patient is extubated. In order to leave the ICU, the patient must be able to breathe without mechanical ventilation and have no obvious major complications from the surgery. Once the doctors and physician assistants
feel comfortable with the recovery progress, the patient is moved to the cardiac step-down care for three to five days (NHLBI, 2009).

Patient education is instrumental to the recovery phase as well. Patients must be instructed on what to expect at home and when they can expect the after-effects from surgery to be completed. Typically recovery lasts for four to six weeks (NHLBI, 2009). Symptoms during the recovery phase often include discomfort or itching from healing incisions, swelling of the area where an artery or vein was taken for grafting, muscle pain, fatigue, mood swings, depression, difficulty sleeping, loss of appetite, constipation, and chest pain around the site of sternum incision (NHLBI, 2009). With a traditional CABG surgery, a full recovery is expected to take four to six weeks, or longer. However, recovery time is generally reduced with non-traditional bypass. Many patients inquire when it is safe to resume sexual intercourse, drive a car, and return to work. These are important issues to discuss during patient education prior to discharge. Most people can resume sexual activity within about four weeks. They can typically start to drive again within eight weeks, and can return to work in about six weeks (NHLBI, 2009).

As with any procedure, risks and complications can arise at any moment. Even though complications are uncommon, they include wound infection, bleeding, anesthesia reactions, fever, pain, stroke, MI, and death (NHLBI, 2009). When fever associated with chest pain develops, it may be due to inflammation involving the lung or pericardium. This is seen within one to six weeks after surgery. The heart-lung machine can have its own complications and risks.
Memory loss and difficulty concentrating are more commonly seen in the elderly who have high blood pressure or lung disease, and who drink excessive amounts of alcohol (NHLBI, 2009). These side effects have been shown to dissipate several months after surgery. The heart-lung machine also increases the risk of blood clots which can travel to the brain and cause a stroke. Overall, the more urgent the patient’s condition, especially in emergent situations, the higher the risk that complications might arise due to the need of the bypass occurring without time to consider other risk factors. Saving the patient’s life becomes the primary concern in an emergent situation. The less urgent the patient’s condition, the more time the provider has to run tests and determine the safest procedure for the patient.

Open heart surgery is not a cure for CAD. The patient needs to be aware that the coronary artery disease has not resolved. Most people remain symptom free for as long has ten to fifteen years (Mayo Clinic, 2009). Sometimes the graft can become blocked and another bypass graft will need to be placed over the original bypass graft (NHLBI, 2009). Regular checkups with the cardiologist or cardiology physician assistant are still needed. Tests will occasionally be used to assess if the heart is operating properly. These tests may include an ECG, echocardiogram, cardiac catheterization or a stress test (NHLBI, 2009). All patients need to be on lifetime medication, and adhere to the major lifestyle changes that were discussed earlier.

The first successful coronary angioplasty was performed in 1977 in Zurich, Switzerland. The significance of this successful procedure demonstrated that
patients with coronary artery disease can be treated with minimally invasive surgery (Society for Cardiovascular Angiography and Interventions, 2009). There are two main problems associated with coronary angioplasty, elastic recoil and neointimal hyperplasia. Neointimal hyperplasia is described as the immune system’s reaction to the intrusion of angioplasty (Mark, 2009). The extracellular matrix can become exposed at the site of the balloon inflation causing damage to the endothelial surface leading to hyperproliferation of the smooth muscle cells below it. These cells move into the intima, where they form a lesion. Tissue in the area can become thick and form scars and the artery undergoes a subsequent remodeling of its structure. The end result is arterial blockage and obstructed flow (Mark, 2009). Elastic recoil is a rebound effect of the artery. Once the balloon is deflated, the artery can experience recoil and rebound back to form a narrow stenotic artery. This has a tendency to happen in 5-10% of patients within a few hours, or even minutes of the surgery (Mark, 2009). Approximately 30% of all patients experience re-narrowing after angioplasty (Society for Cardiovascular Angiography and Interventions, 2009).

To combat the problem of elastic recoil and neointimal hyperplasia, the first stent was placed in the human artery in 1986. This helped to eliminate the collapsed arteries following angioplasty (Society for Cardiovascular Angiography Interventions, 2009). The goal for these bare metal stents was to hold the inner wall in the newly compressed position, retaining the new, larger diameter (Mark, 2009). There are many sizes and different strengths of stents available to help maintain the newly opened artery. The medical field thought they had found their
answer to CAD, however, three to six months post-surgery, restenosis surfaced again. Although the stents were able to eliminate the elastic recoil, the body still leaned toward neointimal hyperplasia. To combat this problem, surgeons used a dose of radiation emitted from the catheter to inhibit cell division called brachytherapy (Mark, 2009). The coronary arteries were treated with radiation to stop the cell injury cycle that caused more blockages. This local, low-dose radiation procedure does not produce massive systemic side effects that are commonly associated with other radiation procedures.

Researches started to look into the pharmacology to see what could be done to improve the use of stents. The answer was in the pharmacology. Using the body’s circulatory system to introduce medicine to deliver therapy was the idea that researches thought could be most beneficial (Medtronic, 2009). Doctors and drug companies began to test drugs that were known to interrupt the biological processes that cause the restenosis (Medtronic, 2009). The stents were then coated with these drugs or the drug was imbedded in a thin polymer within the stent for timed release (Medtronic). The results were remarkable. Drug eluting stents reduced the restenosis rate from 30% to below 10% (Medtronic, 2009). Drug eluting stents replaced coronary bypass surgery in the early 2000s and have become the treatment of choice by the cardiologist.

Even with drug eluting stents surpassing coronary bypass surgery and the bare metal stents, there are some problematic issues beginning to surface now. Most of the major problems with the drug eluting stents are not apparent in the short term, but occur years after the stent is placed. One problem with stents,
whether it is the bare metal or the drug eluting type, is that they are permanently placed. They become incorporated into the vessel and cannot be removed. If restenosis occurs, a physician cannot place another stent in the same location. Furthermore, a cardiothoracic surgeon cannot bypass any area of that stent to restore blood flow. This can be a potentially fatal problem because if the artery becomes blocked again, surgeons cannot revascularize a stented area due to the anatomical changes that have occurred to the vessel. Another problem is the occurrence of late stent thrombosis and late sudden occlusion of the coronary artery. It is proposed that drug eluting stents inhibit the growth of normal tissue. The normal tissue inhibits blood clotting on the stent (Fogoros, 2009). The patient with drug eluting stents can be at a higher risk for sudden clotting. In November of 2009, researchers presenting at the World Congress of Cardiology, showed support that patients treated with drug eluting stents may have a higher long-term risk of poor outcomes due to restenosis or reocclusions, compared to patients treated with bare metal stents (Fogoros, 2009).

Coronary artery bypass surgery was previously considered the best way to revascularize the heart. Then bare metal stents were introduced with some success; however, the stents experienced restenosis of the blocked coronary artery 30% of the time. Finally, drug eluting stents entered the field virtually replacing the CABG procedure with hardly any complications in sight. However, eight years removed from the introduction of drug eluting stents, there are problems starting to arise. Has coronary artery bypass met its successor or will the CABG procedure become more prominent again? Which procedure will
become the gold standard? What other complications are yet to be discovered with the drug eluting stents?
Literature Review/Discussion

CABG versus PCI

Serruys, et. al., 2009 compared percutaneous coronary intervention (PCI) with coronary artery bypass surgery. The clinical trial, the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX), aimed to assess the most advantageous revascularization strategy for patients needing intervention. The trial was a prospective clinical trial, conducted in several sites in Europe and in the United States. Serruys et al. (2009) randomly assigned 1800 patients to undergo either CABG or PCI. A cardiologist determined the patients could receive either method of revascularization prior to randomized group assignment. The method of PCI involved Taxus Express paclitaxel-eluting stents, with aspirin prescribed for all patients in the PCI group. The technique for CABG was left to the discretion of the cardiothoracic surgeon. Patients’ vessels were targeted for revascularization if the vessel had less than 1.5 mm in diameter with stenosis of 50% or more. Combined major adverse cardiac and cerebrovascular events, death from any cause, stroke, myocardial infarction, or repeat revascularization within the 12-month period after randomization were the outcomes of the trial.

Patients in each group had similar baseline characteristics. However, patients in the PCI group had significantly higher blood pressure of greater than 130/80 mm Hg than the CABG group. The CABG group had a higher prevalence of number of smokers, high triglyceride levels (≥150 mg per deciliter) and reduced high density lipoprotein (<40 mg per deciliter for men and <50mg per deciliter for women). Results from the trial showed that the PCI group had
significantly higher repeat revascularization rates than the CABG group (13.5%, 243 patients vs. 5.9%, 106 patients $P<0.001$). Furthermore, rates of major adverse cardiac and cerebrovascular events at 12 months were significantly higher in the PCI group versus the CABG group (17.8%, 320 patients vs. 12.4%, 223 patients; $P=0.002$). Rate of death and myocardial infarction were similar; however, stroke was significantly higher in the CABG group (2.2%, 39 patients vs. 0.6%, 10 patients $P=0.003$). These results clearly mark that CABG is superior to PCI in this trial. Stroke was the only outcome that was seen in the CABG group to be significantly higher than in the PCI group. The PCI group was given antiplatelet medication to reduce the risk for a stroke with stent implantation. Complication rates vary between the different CABG procedures. On-pump CABG is associated with a higher incidence of stroke. More on-pump procedures in this study may have led to this result. It was not determined if antiplatelet medication given prior to the CABG group would have lowered the risk of stroke.

There were several limitations for this trial. A 12-month follow-up period may not be completely reflective of long-term outcomes for comparing CABG and drug-eluting stents. Medications differed between groups in these trials, which show the variations in standard of care between the two groups, and may have affected outcomes. Also more patients withdrew after randomization to the CABG group than those in the PCI group. With randomization in a blinded manner, the performance of treatment could not be blinded because clinicians and participants could not possibly know future treatment assignments (Serruys, et al., 2009).
Multi-Vessel Disease

There have been several clinical trials and meta-analyses for multi-vessel coronary artery disease involving CABG versus PCI. Arterial Revascularization Therapies Study (ARTS), Argentine Randomized Trial of Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients With Multiple Vessel Disease (ERACI-II), Medicine, Angioplasty or Surgery Study for Multi-Vessel Coronary Artery Disease (MASS-II) and Surgery of Stents (SoS). These trials looked at long term outcomes of bypass surgery versus percutaneous coronary intervention. However, these studies were conducted in the time where drug eluting stents were not available.

There was a six year follow up analysis of the SoS trial. The analysis consisted of 988 randomized patients. The goal of this follow up study was to report long term survival and examine outcomes in various subgroups (Booth, et al., 2008). Both groups from the SoS trial, CABG or PCI with bare metal stents, had similar baseline characteristics with few major outliers. An interesting concept to point out is that in the PCI group, interventionists could select any commercial stent available. Each patient in this trial could have a completely different type of bare metal stent. Clinical outcomes at 2 years showed that patients had a significantly higher rates of repeat revascularization in the PCI group compared to those managed with CABG (20.7%, 204 patients versus 6.0%, 59 patients with a P<0.001). Still, the incidence of death and nonfatal Q-wave myocardial infarctions were similar and not significant between PCI and
CABG groups. At the six year follow up, mortality was significant in the PCI group (53 patients, 10.9%) versus 34 (6.8%) within the CABG group (p=0.022). However, there was little evidence to support that treatment affected mortality between the subgroups. The major difference can be seen with the patients who died of cancer between the PCI and CABG groups. Cancer was the reported predominant cause of noncardiovascular death. Twenty patients died of cancer in the PCI group compared to eight in the CABG group. One can conclude that the patient could have already had cancer and the interventionist thought it would have been too risky to perform a CABG so the patient was placed in the PCI group or, the cancer was terminal and the patients were placed in the PCI group for symptomatic relief since PCI is noninvasive and recovery is easier compared with bypass. Finally, the treatment to fight the cancer, chemotherapy and or radiation, was contraindicated for patients with a CABG and therefore they were unable to receive the CABG. Treatment of the cancer can also affect reliability and assessment of differences in cardiovascular and noncardiovascular events.

Overall, the SoS trial showed that CABG is managed better with a lower mortality rate at the six year follow up. There are theories as to why CABG is considered better than PCI. One is that a functioning bypass graft will continue to protect an indigenous coronary vessel, even if the graft is subject to disease progression or abrupt closure at any site proximal to the graft anastomosis. Second, CABG revascularization is associated with more complete revascularization. Finally, CABG can provide a more appropriate type of revascularization for patients with long-term diffuse disease.
In the same year of the analysis of the SoS six year follow up study, a meta-analysis with a five year level data from the ARTS, ERACI-II, MASS-II and SoS trials was finished. All of these randomized trials yielded no difference in death rates between the two revascularization strategies, with the exception of the SoS trial (Daemen, et al., 2008). The SoS trial showed a significantly lower survival rate in the PCI group than in the CABG group. This 5-year meta analysis study was a collection of patient information within each study to assess outcomes. The primary end point of this study was the composite of death, stroke, or myocardial infarction. The secondary endpoint was occurrence of major adverse cardiac and cerebrovascular accidents, death, stroke, myocardial infarction and repeat revascularization (Daemen, et al.).

In this meta-analysis 3051 patients were pooled and profiled between June 1995 and June 2000 from the different randomized trials. One thousand five hundred and thirty three patients were randomized in a CABG procedure and 1,518 patients were in the PCI group. There were significantly more patients with 3-vessel disease, with complete revascularization performed in the CABG group compared to PCI group (40.0%, 1220 patients vs. 36.1%, 1101 patients with a P<0.001). Five year follow up showed no significant difference in death, MI and stroke between the randomized PCI with bare metal stents and CABG groups (16.7%, 509 patients vs. 16.9%, 515 patients p=0.69) (Daemen, et al., 2008). However, repeat revascularization and major adverse cardiac and cerebrovascular events rates were significantly higher in the PCI group compared to CABG group (29.0%, 884 patients vs. 7.9%, 241 patients p<0.001
and 39.2%, 1195 patients vs. 23.0%, 701 patients p<0.001). This demonstrated that there were significantly lower overall major adverse cardiac and cerebrovascular events in the CABG group at five years.

The same meta-analysis was conducted by Mercado, et al. (2005) and yielded similar results of a one year mortality of multi-vessel disease. The study showed similar protection, with CABG or PCI, against death, MI or stroke at one year. Repeat revascularization in the PCI group was still significantly higher than the CABG group; however, it provided several insights to these meta-analyses. One insight was the substantial differences in the trial designs (Mercado et al., 2005). ARTS, SoS, and ERACI-2 were multinational studies, while MASS-2 was a single-center study. The patient population differed at each trial by comorbidity, coronary anatomy, and periprocedural risk. However, to compensate for these differences Mercado et al. (2005) used adjusted analysis after the original analysis to try and compensate for the differences in each trial. Adjusting the data allowed them to use only information that pertained to the current study. A positive aspect to this one year meta-analysis is that it conducted subgroup analyses on several groups including age, gender, diabetes mellitus, smoking, and number of diseased vessels. Mercado et al. concluded that there was no statistical significance with one year mortality when comparing PCI and CABG.

With the meta-analyses, it seems that prior to the innovation and clinical trials of drug eluting stents, the PCI group with bare metal stents have a higher repeat revascularization, therefore, higher adverse events. There are now several trials currently underway to compare PCI with DES and CABG. In one of
the first studies comparing PCI drug eluting stents with CABG, (Hannan, et al., 2008) identified 17,400 patients during October 2003 through December 2004 through the Percutaneous Coronary Intervention Reporting System (PCIRS) of the New York State Department of Health and the Cardiac Surgery Reporting System (CSRS). These registries contained information about demographics, coexisting conditions, and hemodynamic state. The data was adjusted for differences based on the risk factors among the patients. In this study, there were 9,963 subjects receiving DES and 7,437 subjects receiving CABG. Hannan et al. (2008) excluded patients based on previous revascularization, if the patient had left main coronary artery disease, and a new recent myocardial infarction, totaling of 11,695 patients (Hannan, et al., 2008). End points for this study were based on the death rate in the hospital after the procedure or within 30 days, and the death, MI, or repeat revascularization at 18 months follow up. The baseline characteristics of the CABG group and the PCI group were fairly similar with the exception of the CABG group being significantly older, more likely to be male, to be non-Hispanic, to be white, to have a lower ejection fraction, to have had previous MI, to have other coexisting conditions, and to have three vessel disease (Hannan, et al., 2008).

The results showed that within the 18 months follow up, patients who received the drug-eluting stents had a significantly higher revascularization rate. Of these patients who received the DES, 28.4% (1,620 patients) underwent repeat PCI and 2.2% (125 patients) underwent CABG (Hannan, et al., 2008). For the CABG group, only 5.1% (290 patients) and 0.1% (5 patients) going through
repeat revascularization. Both differences were statistically significant (p<0.001) in those undergoing repeat revascularization (Hannan et al., 2008). The CABG group with three-vessel was associated with a lower 18-month rate of death and MI than treatment with DES for patients with two and three-vessel disease. In addition, the adjusted survival rate for the CABG group was 94.0% (5,362 patients) versus 92.7% (5,288 patients) for the DES group (p=0.03). The adjusted rates of survival free from myocardial infarction was 92.1% (5,254 patients) for the CABG group versus 89.7% (5,117 patients) for the DES group (p<0.001). For patients with two-vessel disease in the CABG group, the adjusted survival rates compared to the PCI group at 96.0% (5,476 patients) versus 94.6% (5,396 patients) (p=0.003) and the adjusted rate of survival free from MI was 94.5% (5,391 patients) versus 92.5% (5,277 patients) (p<0.001) (Hannan et al., 2008). The trial showed that among patients with three-vessel disease, those who underwent CABG had significantly lower adjusted rates of death and death or MI compared with those that received drug eluting stents.

While the previous study showed CABG having significantly lower rates of death and death to an MI compared with DES, a clinical trial conducted by Yang, et al., (2007) found different outcomes when comparing DES and CABG. The study included 466 patients, with 235 patients by PCI, DES, and 231 patients by CABG. The revascularization strategy was determined on a bias basis and the patient’s preference. Bypass surgery was preferred for patients with left main disease, in-stent restenosis, and diffuse lesions. PCI was recommended for those with lesions suitable for the procedure and other complex characteristics.
Coronary artery bypass graft surgery was performed off-pump 97% of the time, and the PCI procedure was conducted with antiplatelet therapy with aspirin three days before the procedure. End points of the trial were the incidence of major adverse cardiovascular events within the first 30 days of procedure. Baseline characteristics remained similar; however, left main disease and three-vessel disease were seen more significantly in the CABG group due to the trial recommending surgery over PCI for these characteristics.

The overall mortality was significantly higher in the CABG group than in the PCI (3.9%, 18 patients) versus 0.8% (3 patients, p=0.03) in the 30 day outcome. This may be accounted for by most of the patients with advanced disease were in the CABG group and that CABG is a more invasive procedure. The composite major adverse cardiovascular events were similar among CABG and PCI (3.8%, 17 patients) versus 6.1%, 28 patients, p=0.29). The late clinical follow up mean of 25 months showed no differences in cumulative incidence of death, MI or stroke (6.3%, 29 patients) in the CABG group versus 5.6% (26 patients) in the DES group (p=0.84) (Yang, et al., 2007). In addition, revascularization was significantly higher in the PCI group versus the CABG group (10.4%, 48 patients) versus 2.8%, 13 patients, p=0.001). This included statistically significant higher rates of major adverse cardiovascular events, such as MI, in the PCI group (14.5%, 67 patients) in the PCI group versus 7.9% (36 patients) in the CABG group p=0.03) (Yang, et al., 2007). Yang et al. (2007) concluded that multiple stenting has an innate limitation compared with CABG. PCI usually treats only focal areas of most significant occlusion while CABG may
bypass the susceptible plaques that could potentially develop into problem lesions over time. The choice of CABG is compelling for patients with left main disease and diffuse coronary disease, whereas PCI is ideal for patients with less diffuse disease and focal lesions.

A trial to find long-term mortality with drug-eluting stents versus CABG was performed in Korea. Between January 2003 and December 2005, a total of 3,042 patients completed this study with 1,547 in the DES group and 1,495 in the CABG group. All-cause mortality was the primary end point. Repeat revascularization and composite of death, Q-wave MI, and cerebrovascular events were the secondary end points (Park, et al., 2008). The CABG group was more likely to be male and have significantly higher prevalence of smoking and high cholesterol, history of MI, chronic lung disease, peripheral vascular disease, stroke or renal failure. The DES group had a higher prevalence of diabetes, hypertension, prior coronary angioplasty, and presented more commonly with unstable angina.

The unadjusted in-hospital mortality was significantly higher in the CABG group than in the DES group 45 patients, 1.5% versus 18 patients, 0.6% (p=0.01) (Park, et al., 2008). In the unadjusted analysis, long term outcomes favored DES; however, after adjustment DES and CABG were similar. In the secondary endpoints, there were significantly more patients needing repeat revascularization in the DES group over the CABG group (11.8% (358 patients) versus 4.6% (139 patients) p<0.001) with more of a significant difference in the
diabetic group (Park, et al., 2008). There were also significantly more patients with overall major cardiovascular and cerebrovascular events in the DES group.

A similar trial performed by Yang et al. (2008) was conducted in Seoul, Korea with a total number of 831 patients, 441 patients in the DES group and 390 in the CABG group. The trial showed no statistically significant differences in the rates of composite death, CVA, or AMI at 12 months between the DES group and the CABG group. However, there was crossover evidence in the mortality and composite end point. This suggests that the outcomes of the CABG group will be better in the long-term over the DES group. In addition, patients treated with DES were significantly more likely to require repeat revascularization as well as higher rates of major adverse cardiovascular and cerebrovascular events than in the CABG group.

A center in Shanghai, China conducted a nonrandomized, observational study to compare the clinical outcomes of drug eluting stents versus coronary artery bypass grafting for the treatment of multivessel disease. The study end point was major adverse cardiovascular events within the first 30 days of revascularization (Yang, et al., 2007). Baseline characteristics of the study included 466 patients in which 235 patients were in the DES group and 231 were in the CABG group. The outliers in this study were left main artery disease (2.6% vs. 24.7%, p<0.001) and three vessel disease (54% vs. 65%, p=0.02) being more significantly prevalent in the CABG group (Yang, et al., 2007).

The 30-day outcomes showed that the DES group experienced two patient deaths and nine deaths in the CABG group. Overall, mortality was
significantly higher in CABG group than in DES group (3.9% vs. 0.8%, P=0.03), however, the composite major adverse cardiovascular event rates were similar in the two groups (3.8% vs. 6.1% p=0.29) (Yang, et al., 2007). Late clinical outcomes showed two additional deaths in the DES group and five deaths in the CABG group. Overall, there was no statistical significance in cumulative incidence of death, MI, and stroke (6.3% for the CABG group versus 5.6% for the DES group p=0.84). However, the study found there was a significant difference in the repeat revascularization rate in the PCI group (10.4% vs. 2.8% p=0.001). Since there is a higher repeat revascularization rate, there is a significant chance of higher major adverse reactions in PCI group over the CABG group (14.5% versus 7.9% p=0.03) (Yang, et al., 2007). There were significantly increased length of hospital stay and morbidity associated with CABG surgery (3.9% versus 0.8% p=0.03). In addition, no significant difference was found in composite incidence of death, MI and CVA. However, major adverse cardiovascular events in long term outcomes were significantly higher in the PCI group (14.5% versus 7.9% p=0.03) with the main reason due to need for repeat revascularization (Yang, et al., 2007).

In conclusion, the study determined that PCI with multiple stents has limitations compared with CABG and PCI is an appropriate treatment for focal areas. Generally, CABG is a procedure for patients with left main coronary artery disease and diffuse lesions.
Diabetes poses greater difficulty when determining what type of revascularization procedure a patient needs. In the SoS six-year study with follow-up study, Booth et al. (2008) examined the diabetic patient population. There were more insulin-dependent patients in the CABG group (19 versus 9), while 49 patients in the PCI group versus 65 patients in the CABG group had their diabetes controlled with oral hypoglycemic drugs or diet alone. There were no other differences in baseline characteristics between the PCI and CABG groups.

The two-year follow up results showed there was little evidence with the impact of treatment strategy on outcomes between diabetics and nondiabetics (Booth, et al., 2008). The six-year mortality follow up among the diabetic population showed 17.6% (12/68) in the PCI group died and 5.4% (4/74) in the CABG group died. Among nondiabetic patients, 9.8% (41/420) died in the PCI group versus 7.0% (30/426) in the CABG group (Booth, et al., 2008). Statistical analyses confirmed that there was no significance between types of treatment and outcome with diabetic patients versus nondiabetic patients. In addition, mortality with CABG alone was 5.4% in the diabetic population compared to 7.0% in the nondiabetic patient, showing that mortality is higher in the PCI group for both the diabetic and nondiabetic patient population (Booth, et al., 2008).

In conclusion, at four-years patients that were managed with CABG had a lower mortality rate than those randomized to the PCI, bare metal stent group. Furthermore, the five-year survival rate was higher in CABG but only by 0.2%. The sample sizes could have affected the results of the trial. It is difficult to come
to a conclusion based on this trial alone with diabetic patients consisting of fewer than 200 patients in the study and over 800 patients represented in the nondiabetic group (Booth, et al., 2008).

The meta-analysis conducted by Daemen et al. (2008) also compared a subgroup population of diabetics and showed similar results. In patients with diabetes, the cumulative incidence of death was 12.4% (34 patients) with PCI bare metal stents compared to 7.9% (21 patients) in the CABG group, showing no statistical significance (p=0.09). In nondiabetic patients, the cumulative incidence of death was 7.7% in PCI group and 8.3% in the CABG group (p=0.55). However, repeat revascularization in the diabetic population was significantly higher in the PCI group with bare metal stents than in the CABG group (29.7% versus 9.2%, p<0.001) (Daemen, et al., 2008). Similarly to the SoS trial, this meta-analysis cannot come to any conclusions due to its small sample size of diabetic patients compared to the population as a whole.

A trial with a high prevalence of diabetic patients was needed. With more than 35% of the patients with diabetes in both the PCI with drug eluting stents and the CABG cohorts, Javaid, et al. (2007) evaluated 1,680 patients with multivessel disease undergoing either CABG or PCI with DES revascularization over an 18-month period. All patients had either two-vessel or three-vessel disease. Two-vessel disease was defined by both vessels undergoing revascularization during the same hospitalization and three-vessel disease was revascularization within a six-week index. The method of revascularization was at the physician's discretion and included a consultation with a cardiothoracic
surgeon. Major end points of this study integrated cumulative rates of death, Q-wave MI, cerebrovascular events, target revascularization failure (TVF), and composition of major adverse cardiovascular and cerebrovascular events (MACCE). Composition of major adverse cardiovascular and cerebrovascular events is defined by the total of events that occurred whether it was caused by the procedure or not.

The study used 1,680 patients with 1,080 being treated for 2-vessel disease, (196 CABG and 884 DES). Of those, 189 patients in the CABG group (96.4%) and 593 in the PCI group (67.1%) underwent revascularization of the left anterior descending artery (p<0.001). Six hundred patients were treated for three-vessel disease, with 505 patients in the CABG group and 95 patients in the PCI group. Of the 600 the patients, the incidence of chronic renal disease and previous CABG were significantly lower in the DES group than the CABG group (Javaid, et al., 2007). Baseline characteristics for patients undergoing two-vessel disease CABG had lower prevalence of dyslipidemia, chronic renal failure, and peripheral vascular disease than the PCI DES group, all being statistically significant (Javaid, et al., 2007).

Significantly higher mortality at one year occurred in patients with two-vessel disease in the PCI group compared to the CABG group (2.6% (28 patients) versus 8.1% (87 patients) (p=0.006). CABG patients experienced significantly lower TVF and major adverse cardiovascular and cerebrovascular events compared to PCI patients (5.6% (60 patients) versus 13.3% (143 patients) p=0.001 and 9.7% (104 patients) versus 21.2% (228 patients) p<0.001).
However, CABG and PCI experienced similar rates of Q-wave MI, while CABG patients had a significantly higher likelihood of a cerebrovascular event (2.0%, 21 patients versus 0.1%, 1 patient $p<0.005$) (Javaid, et al., 2007). Three-vessel disease outcomes at one-year showed similarity between the CABG and PCI groups with Q-wave MI and cerebrovascular events, (CVE); however, the PCI group experienced significantly higher TVF and mortality compared to the CABG group (18.8%, 112 patients versus 5.7%, 34 patients, $p<0.001$ and 10.9%, 65 patients versus 3.1%, 18 patients, $p=0.006$). The CABG group experienced significantly lower overall major adverse cardiovascular and cerebrovascular events (10.8%, 64 patients versus 28.4%, 170 patients, $p<0.001$).

Javaid et al. (2007) then compared the diabetic population. In two-vessel disease, 70 patients underwent CABG while 305 underwent PCI DES. In three-vessel disease 187 patients underwent CABG and 39 patients underwent PCI DES. Post-procedure two-vessel disease Q-wave MI rates were similar among both cohorts. Cerebrovascular events occurred at significantly higher rates in the CABG group (4.3% (3 patients) versus 0.3% (1 patient) $p=0.02$). However, diabetic patients undergoing CABG showed significantly reduced mortality compared with the PCI group (1.4% (1 patient) versus 12.8% (39 patients) $p=0.005$), reduced TVF (2.9% (2 patients) versus 14.3% (44 patients) $p=0.008$), and reduced major adverse cardiovascular and cerebrovascular events (8.6% (6 patients) versus 26.6% (81 patients) $p=0.001$). One-year outcomes for three-vessel disease showed significantly reduced mortality and TVF in the CABG group (3.2% (6 patients) versus 18.4% (7 patients) $p=0.002$ and 4.8% (9
patients) versus 25% (10 patients) p<0.001). Q-wave MI and cerebrovascular event rates were similar among both cohorts; however, overall combined major adverse cardiovascular and cerebrovascular events were significantly lower in the CABG group (10.7% (20 patients) versus 41.0% (16 patients) p<0.001).

In the nondiabetic population with two-vessel disease, there were 126 patients in the CABG group and 579 in the PCI DES group. The three-vessel disease groups included 318 patients who underwent CABG and 56 patients who underwent PCI DES. The unadjusted outcomes for two-vessel disease showed no difference in mortality between CABG and PCI groups; however, the CABG group showed significantly lower TVF and MACCE (6.3% (8 patients) versus 12.9% (75 patients) p=0.04 and 10.3% (13 patients) versus 18.5%(107 patients)). Three-vessel disease results at one-year demonstrated a significant reduction of TVF and a trend of lower MACCE in the CABG cohort (6.2% (20 patients) versus 15.4% (9 patients) p=0.04 and 10.9% (35 patients) versus 20% (11 patients) p=0.06) (Javaid, et al., 2007).

With the outcomes adjusted for significant differences in baseline characteristics, the diabetic population still showed significantly higher outcomes for combined major cardiovascular and cerebrovascular events and mortality with both 2 and 3-vessel disease. However, the nondiabetic population which showed significantly higher occurrences without adjustment showed no statistical significance with adjustment. Javaid et al. (2007) concluded the high population of diabetics in the study most likely pushed the results towards significance.
The study shows that patients with diabetes are at a higher risk of major adverse cardiovascular and cerebrovascular events and mortality. Without any adjustment, the CABG cohort would have lower rates due to more comorbidities and severe illness seen in the PCI with DES group. However, Javaid et al. (2007) decided to adjust the results to compensate for the baseline characteristics. Once the results were adjusted, it was clear that CABG is more beneficial over PCI in the presence of diabetes. In conclusion, this study shows that CABG is preferable over PCI with drug-eluting stents in the diabetic population. Even with drug-eluting stents reducing restenosis and target revascularization failure in comparison to bare metal stents, outcomes with these stents in high-risk patients, like diabetics, are still substandard to CABG.

A study conducted in Italy aimed to compare one-year outcomes after PCI with DES implantation to off-pump bypass grafting with patients experiencing multivessel disease and left anterior descending coronary artery disease with underlying diabetes (Briguori, et al., 2007). The 149 patients in the CABG group were generally older with higher rates of 3-vessel disease than those in the PCI group which had sixty nine patients. Two major endpoints in the study were identified with management and follow up. One endpoint was the composite major cardiac and cerebrovascular events at 12 months, while the second endpoint was the composite of death of any cause, nonfatal MI, or cerebrovascular events at 12 months.

With adjustment, DES had a significantly increased risk for major cardiac and cerebrovascular events during the cumulative post-procedure 12-month
period (p=0.020) (Briguori, et al., 2007). The rate of revascularization was also significantly higher in the PCI with DES group than the CABG group (p=0.001). This was due to higher rates of target lesion revascularization and disease progression with the drug-eluting stent group. In addition, with more repeat revascularization, the higher the chance is of major cardiovascular and cerebrovascular events.

Finally, patients with diabetic retinopathy was a subgroup identified in the study that shows poorer outcomes after PCI with DES implantation and off pump bypass surgery (Briguori, et al., 2007). There were 21 patients with diabetic retinopathy in the DES group and 36 patients in the CABG group. The retinopathy in diabetic patients having poor outcomes can be due to retinopathy being a sign of uncontrolled or late stage of diabetes.

The SYNTAX and TAXUS studies randomly assigned 1,899 patients (452 with medically treated diabetes) to receive a drug eluting stent or coronary artery bypass grafting surgery. This study was performed to determine the one-year overall outcome between the two different types of revascularization when left main disease and/or three vessel coronary artery disease is present. Of the 1,800 patients, 452 had medically treated diabetes (221 in the CABG group and 231 in the DES group). Of the diabetic patients, 182 (40.3%) used insulin to control their diabetes while 270 patients (59.7%) treated their diabetes with hypoglycemic agents. One-year major cardiovascular and cerebrovascular events were evaluated in 94.6% of the CABG patients (849) and 98.7% of the DES patients (891) (Banning, et al., 2010).
Comorbid risk factors were overall significantly higher in the diabetic population versus the non-diabetic population. These patients had higher BMI, HTN and hyperlipidemia. An interesting finding in this study was that, post-procedure medications were not the same for the CABG and DES groups. For example, at discharge, the CABG group had a significantly lower chance of being discharged home with a statin versus the DES group (73.8% versus 83.0%, p <0.001) for reasons not explained in the research (Banning, et al., 2010).

The one-year clinical results in non-diabetics versus the diabetic patients showed there was significantly higher major cardiovascular and cerebrovascular events after DES treatment compared to CABG treatment in the diabetic patient population (26.0% versus 14.2%, p=0.003). There was, however, no statistical significance between end point of death, CVA and MI between diabetic and non-diabetic patients. Mortality was significantly higher in diabetic patients versus non-diabetic patients in both the CABG and DES groups (p=0.01 and p<0.001). Repeat revascularization was significantly higher in the DES group compared to the CABG group in both diabetic and non-diabetic patients which further increased the major adverse cardiovascular and cerebrovascular events in the DES group (diabetic patients 20.3 versus 6.4 p<0.001, non-diabetic patients 11.1 versus 5.7 p<0.001). An interesting finding was in the diabetic population had significantly higher repeat revascularization compared to the non-diabetic population when using DES (p<0.001). However, there was no significance found in repeat revascularization between diabetic and non-diabetic patients in the CABG group (p=0.74) (Banning, et al., 2010).
At the end of this one-year observational study, an important finding was that patients with left main artery disease or multi-vessel disease had major adverse cardiovascular and cerebrovascular events at a significantly higher rate in the diabetic patients. However, they were not significant in the non-diabetic population but tended to trend higher. Another important point found was that there was no significance in composite death, CVA, or MI regardless of their diabetic status. Repeat revascularization rate was significantly higher in the DES group compared to the CABG group regardless of diabetic status. In addition, patients with diabetes had a statistically significant increased risk of repeat revascularization rate compared to non-diabetic patients when treated with DES (Banning, et al., 2010).

The conclusion of this study showed how the presence of diabetes should dictate what type of revascularization procedure is performed on a patient. In a patient with multi-vessel disease with diabetes present, CABG offers the best one-year outcome when accompanied with major adverse reactions.

There are two main types of drug eluting stents, paclitaxel and sirolimus. Two studies demonstrated how effective the two types of drug eluting stents are compared to bare metal stents in diabetics, while a separate article compared paclitaxel versus sirolimus drug eluting stents in diabetic patients. In the paclitaxel-eluting (TAXUS) stent trial, 1,314 patients were randomized to either a drug eluting stent group or the bare metal stent group. Three hundred and eighteen patients in the trial (24.2%) had diabetes, with 213 of the 318 receiving
oral glycemic medication and 105 receiving insulin. Baseline characteristics were similar among the subgroups without any outliers (Hermiller, et al., 2005).

The results showed a reduced late lumen loss and late loss index in the paclitaxel stent group compared to the bare metal stent group. Late lumen loss is defined as the difference of the diameter of the stented segment post-procedure compared to follow up angiograms. The results showed a greater late minimal lumen diameter, meaning the diameter post-procedure had minimal changes in diameter at follow-up visits, and lower diameter stenosis, meaning when stenosis occurred, it was occurring at a slower rate. The paclitaxel stent also reduced the frequency of diffuse in-stent restenosis in patients with diabetes (Hermiller, et al., 2005). When restenosis did occur, the lesions were significantly smaller. The paclitaxel-eluting stent lowered the one-year rates of major cardiovascular events, target revascularization failure, target lesion revascularization (TLR), and TVR, to a comparable degree in diabetics on oral medications and those requiring insulin and to people without diabetes. The trial concluded that the paclitaxel eluting stent significantly reduced late lumen loss, late loss index, and restenosis compared with the bare metal stents. However, in terms of efficacy with patients taking oral agents versus insulin, the trial found no significant difference (Hermiller, et al., 2005).

The sirolimus-eluting stent trial pooled 100 diabetic patients with multivessel disease for PCI with sirolimus-eluting stent (SES) placement and 122 diabetic patients for bare metal stent implantation (Hermiller, et al., 2005). The endpoint of the trial was the frequency of major cardiac events at 12-months. The
incidence of major adverse cardiac events was 25 per 100 patients in the PCI with SES group compared to 54 per 122 in the bare metal stent group (p=0.03). There was no significant difference found in those requiring insulin and those using oral medication (Briguori, et al., 2005). Repeat revascularization was statistically lower in the SES group than in the bare metal stent group. Revascularization was necessary in 17 per 100 patients in the SES group and 50 per 122 in the bare metal stent group (p<0.001). Most of the 25 patients who experienced major adverse cardiovascular events in the SES group were insulin dependent and had chronic renal insufficiency. Variables were analyzed to understand the reason behind the results. The variables included clopidogrel treatment discontinuation, chronic renal insufficiency, insulin treatment, and complete revascularization. The independent predictors of major cardiovascular events during the follow up period were premature clopidogrel treatment discontinuation (p=0.020) and chronic renal insufficiency (p=0.0004) (Briguori, et al., 2005). They determined that SES is superior in diabetic patients in comparison to bare metal stents.

Two German centers participated in a trial with 250 patients enrolled to determine prevention of restenosis in diabetic patients with either Paclitaxel eluting or Sirolimus eluting stents. All patients received a loading dose of clopidogrel before the stent implantation and were then randomly assigned to either the paclitaxel or sirolimus group during the angioplasty. (Dibra, et al., 2005). Complete follow up included angiography at 12-months for all patients. Several variables measured in this trial include the minimal diameter of the lumen
defined as the point where the vessel is experiencing the most stenosis, extent of stenosis which tells medical professionals the percentage at which the vessel is blocked, late luminal loss and net luminal gain which is how much length the vessel has gained since the procedure. The primary end point was in-segment late luminal loss on follow up with secondary end points including restenosis and the need for revascularization during the nine month follow up (Dibra, et al., 2005).

Follow up angiography was performed in 103 patients in the paclitaxel group (82.4%) and 102 patients in the sirolimus stent group (81.6%). Of all the patients that did not go through complete follow up, there was no statistically significant difference from those who did based on the baseline characteristics (Dibra, et al., 2005). The mean in-segment late luminal loss difference between paclitaxel and sirolimus was 0.24 millimeter, failing to show any weakness of the paclitaxel stent, instead showing the superiority of the sirolimus stent (p=0.002). This remained significant after adjustment for baseline characteristics (p=0.001).

Among patients requiring insulin, in-segment late luminal loss averaged 0.72 +/- 0.66 millimeter in the paclitaxel group and 0.41 +/- 0.42 millimeter in the sirolimus stent group (p=0.02). In non insulin dependent diabetics, in-segment late luminal loss averaged 0.65 +/- 0.60 millimeter in the paclitaxel group and 0.44 +/- 0.46 millimeter in the sirolimus stent group (p=0.03); all showing statistical significance. In-segment restenosis on follow up also showed statistical significance in favor of the sirolimus stent group with 7 of the 102 patients
experiencing restenosis in-segment compared to 17 of the 103 in the paclitaxel group (p=0.03).

Diabetic patients have a progressive form of atherosclerosis that increases the reactivity of the vascular wall to injury produced by the procedure at the stent margins. Since this was a diabetic study, the study experienced higher rate of late lumen loss than compared to other studies (Dibra, et al., 2005).

With the mechanisms being unclear, pharmacologic differences exist between sirolimus and paclitaxel stents. Patients experience different reactions with different drugs, even if both drugs accomplish the same outcome. Two drugs that accomplish a specific outcome does not mean they took the same direction to get to the desired outcome. They could have gotten there by two completely different ways. In addition, dose response differences of diabetic patients can play a role in these results. Diabetes does not take the same disease path from person to person. Therefore, each patient will need their own specific dose to combat coronary artery disease with diabetes. Finally, the delivery of each drug in the stent could account for these different results.
Unprotected Left Main Coronary Artery Disease

Left main coronary artery disease presents a debate on whether to perform coronary artery bypass surgery versus percutaneous coronary intervention with drug eluting stents. A trial conducted in Korea evaluated 1,102 patients with unprotected left main coronary artery disease who underwent stent implantation and 1,138 patients who underwent coronary artery bypass grafting surgery between January 2000 and June 2006 (Tomoda, 2008). Determining which procedure to use, PCI or CABG, was based on either the patient’s or the physician’s preference or patients were placed in the PCI group due to the high risk associated with CABG. From January 2000 through May 2006 bare metal stents were implanted. Drug-eluting stents were used from May 2003 through June 2006. All patients in the PCI groups were prescribed aspirin plus clopidogrel before or during coronary intervention (Tomoda, 2008). Patients treated with bare metal stents were prescribed the drugs for one month while patients treated with drug-eluting stents were prescribed the medications for at least 6 months.

Clinical follow-up with PCI and CABG was recommended at one-month, six-months and one-year. Mean follow up was 1,017 days in the PCI group and 1,152 days in the CABG group. End points in this study were death, the composition of death, Q-wave myocardial infarction, stroke, and target-vessel revascularization.

In this study, 318 patients in the PCI group received bare-metal stents (28.9%) and 784 (71.1%) received drug eluting stents. Within the drug-eluting stent groups, 607 received sirolimus stents (77.4%) and 177 (22.6%) received
paclitaxel-eluting stents. The study had 478 patients (42.0%) in the CABG group who underwent off-pump surgery (Tomoda, 2008). Baseline characteristics showed that there were significantly older patients that had a higher prevalence of diabetes, hyperlipidemia, smoking, and history of myocardial infarction in the CABG group than those receiving stents. In the combined PCI group, more patients had undergone previous coronary angioplasty and had restenotic left main coronary lesions (Tomoda, 2008).

During the three-year follow up period, there was no significant difference between the PCI group and the CABG group in death rates, including major adverse cardiovascular events. There was, however, a nonsignificant trend toward higher risk of major adverse events with drug-eluting stents (Tomoda, 2008). The trend could have showed statistical significance if the study used drug eluting stents for every patient undergoing PCI. Furthermore, the rate of target vessel revascularization was significantly higher in the PCI group than in the CABG group. Even though there are lower rates of repeat revascularization with drug-eluting stents compared to the bare metal stents, CABG was more effective than drug-eluting stents in reducing revascularization. However, this can be due to significantly higher rate of follow up angiography in the PCI group than in the CABG group (73.0% versus 14.6% P<0.001). Asymptomatic graft stenosis can be underestimated in the CABG group relative to the PCI group (Tomoda, 2008). Patients usually do not have follow up angiography post-CABG unless they experience symptoms. Therefore, estimation is the only way to calculate asymptomatic graft stenosis.
A single center trial involving left main artery stenosis treated with PCI, drug-eluting stents or CABG occurred between March 2002 and July 2004. End points of this study were composite occurrence of death or MI, stroke, repeat revascularization, and major adverse cardiac and cerebrovascular events during hospitalization and at one year (Chieffo, et al., 2006). Two hundred forty-nine patients were treated, 142 patients with CABG and 107 patients with drug eluting stent implantation. Paclitaxel eluting stents were used for 52 patients and 55 patients received sirolimus stents. Patients in the PCI group were significantly younger and had hypertension and renal failure less frequently than the CABG group. Diabetes and right coronary artery disease were more common in the CABG group; however, it was not statistically significant (Chieffo, et al., 2006).

During hospitalization, MI occurred in 10 patients after PCI (9.3%) versus 37 patients in the CABG group (26.05%). This was a significant finding (p=0.0009). Three patients died after CABG (2.1%) compared to no deaths after PCI. Two patients had cerebrovascular events after CABG while no patients in the PCI group experienced a CVA (Chieffo, et al., 2006). At one-year, there was a lower rate of target vessel revascularization in the CABG group compared to the drug eluting stent group (3.6% versus 19.6%, p=0.0001) as well as target lesion revascularization (3.6% versus 15.8%, p=0.001) (Chieffo, et al., 2006). At one-year, there was no statistical significance in death rates between the two treatment groups. However, PCI was associated with a lower occurrence of composite end points of death and MI with an unadjusted p=0.0002 and the adjusted p value still significant at 0.0005. The patients in the PCI group also had
significantly lower death, MI, and cerebrovascular events after adjustment (p=0.01). CABG was associated with a lower occurrence of target vessel revascularization before and after adjustment (p=0.0046).

An interesting aspect to this study compared complications of on-pump versus off-pump surgery. Eighty-eight patients (60.5%) had on-pump and fifty-six patients had off-pump surgery. Patients who did not require revascularization but had major cardiovascular and cerebrovascular events were significant with 21.4% versus 39.5% (p= 0.02) (Chieffo, et al., 2006). Hospital major adverse cardiovascular and cerebrovascular events were lower in the off-pump surgery group (19.6% versus 36.0%, p=0.04). The advantage of off-pump surgery was maintained but not significant at one-year with major cardiovascular and cerebrovascular events at 30.3% versus 43.0% with (p=0.15).

This study showed no difference in the degree of protection against death, stroke, MI, and revascularization at one-year with CABG and PCI drug-eluting stents. In addition, this study was adjusted to take into account the differences in baseline characteristics. With the sixteen patients who had restenosis after PCI, only five of these patients needed a subsequent CABG procedure. Of the three patients in the PCI group who died, only one death was due to the presence of a stent in the left main because of early discontinuation of antiplatelet therapy (Chieffo, et al., 2006). This shows that selecting patients who will be able to continue anticoagulant therapy is necessary in order to have successful long-term drug eluting stent placement. Without the correct patient population, there could be an increase in death due to drug eluting stents.
A limitation of this study is the timetable. The trial was only conducted for one-year. There was no statistical significance with death and major adverse events at one-year; however, this study did not evaluate long-term follow-up. In addition, the CABG group could have been penalized by this brief study because of the higher periprocedural major adverse cardiovascular and cerebrovascular events associated with this type of surgery (Chieffo, et al., 2006).

Another study similar to Chieffo et al. (2006) compared the same parameters with the exception of the PCI drug-eluting stents group had higher risk patients. The PCI group had significantly less men, more chronic renal insufficiency and more patients with unstable angina as a presenting symptom (Lee, et al., 2006). One hundred and seventy-three patients entered the study with fifty patients undergoing PCI and the remaining undergoing CABG. To undergo PCI, patients had one of several characteristics: high risk for CABG, limited life expectancy, patient refusal to undergo CABG, or patient deemed unsuitable for CABG. The primary clinical end points of this study were freedom from major adverse cardiovascular and cerebrovascular events at thirty days and intermediate term follow up.

Lee et al. (2006) yielded similar results as Chieffo et al. (2006). In the thirty day outcome, the cerebrovascular event rate was statistically higher in the CABG group (8% versus 0%, p=0.03); however, there was no significant difference no in mortality. The overall major adverse cardiovascular and cerebrovascular events were significantly higher in the CABG group (17% vs. 2%, p<0.01). In addition, there were also significantly higher post-operative
complications in the CABG group, eight patients needed repeat operation for bleeding, six needed a permanent pacemaker, eight developed pleural effusions and two developed renal failure (Lee, et al., 2006). The estimated major adverse cardiovascular and cerebrovascular event free survival at six months and one year were 83% and 75% in the CABG group compared to 89% and 83% in the PCI group (p=0.20). There were seven deaths in the CABG group and two deaths in the PCI group.

Lee et al. (2006) showed that the treatment with drug eluting stents was equivalent to that of CABG. In addition, drug eluting stents provided comparable or lower rates of death, MI, and cerebrovascular events compared to CABG when patients were assigned groups based on medical advice and not patient preference. Overall, they demonstrated that drug eluting stents are a viable option for treatment of coronary disease.

White et al. (2008) compared outcomes of drug-eluting stents and coronary artery bypass graft surgery in patients with unprotected left main coronary artery stenosis. The CABG group included 223 patients while 120 patients were in the drug eluting stent group. The primary end points of this study were the rate of death and the rate of major cardiovascular and cerebrovascular events. Assessing the surgical risk was accomplished using two models, Parsonnet and Ellis, which divide patients into high and low surgical risk candidates. The Parsonnet score is a fifteen variable point system model while the Ellis score is a cardiac model point system to determine low and high surgical risk (Lee, et al., 2006). When referencing the Parsonnet score, the higher the
score, the higher the chances that a patient will experience mortality during or after the cardiac procedure.

Patient’s baseline characteristics in the study included more statistically significant patients over the age of 75 (49% vs. 33%, p=0.005) in the coronary artery bypass graft surgery group. Patients treated with drug eluting stents were less likely to present with stable angina (27% vs. 45%, p<0.001) and had a significantly higher Parsonnet score (17.3 vs. 13, p<0.001) than those treated with CABG. Survival was no different between the drug eluting stent group and the coronary artery bypass graft group among individuals with a Parsonnet score under 15. However, there was a non statistical trend toward higher mortality in the PCI group over the CABG group (Lee, et al., 2006). Patients with a Parsonnet score of over 15 were significantly more likely to experience a major adverse cardiovascular or cerebrovascular event. In addition, free survival, defined by survival without any cardiovascular and cerebrovascular events, was statistically lower in the drug eluting stent group (p=0.04) (Lee, et al., 2006).

White et al. (2008) found no significant difference between drug eluting stents and coronary artery bypass graft surgery. However, for patients who are at high risk in both the CABG group and the DES group, the mortality in the DES group was significantly higher than in the CABG group. The clinical cardiology community accepts higher rates of revascularization with drug eluting stents since the overall death rate is fairly similar to CABG (Lee, et al., 2006).

A comparison study of long-term (4 year) outcomes with patients with unprotected left main artery disease was conducted by Wu et al. (2010). This
was a single center observational study with a limited sample size performed in Beijing, China. The main findings in this study were similar to the composite major adverse cardiovascular and cerebrovascular events between DES and CABG in other studies. In addition, drug eluting stents were associated with significant higher rates of TVR compared to bypass grafting surgery.

The study received 438 patients between 2003 and 2006 with greater than 50% of unprotected left main coronary artery stenosis for which they underwent either DES or CABG. Overall, 331 patients were eligible for either CABG or DES. Eighty percent of the study sample were men, 28% had diabetes mellitus and 70% of the patients had acute coronary artery syndrome. In the four-year follow up period, 7.7% died (29 patients). Eighteen patients died from cardiovascular causes, twenty patients (5.3%) had MI, 12 (3.3%) had strokes and TVR was needed in 13% (47 patients). Most deaths happened within the first two-years in the DES group, 83% of patients; however, after two years, the mortality stabilized. In the CABG cohort, 17.4% died during hospitalization (Wu, et al., 2010). Angiographic follow up was performed more in the DES group versus the CABG group, (57% versus 16%, p<0.001), showing statistical significance. This was due to the standard protocol with DES placement versus the CABG protocol. Target vessel revascularization was significantly higher in the DES group versus the CABG group (p=0.02) (Wu, et al., 2010).

Overall, the composite end point of myocardial infarction, death, and stroke occurred in 15% of the CABG cohort and 8% in the DES cohort (p=0.10), showing no statistical significance. In addition, there was no statistical
significance in the major cardiovascular and cerebrovascular event rate after adjustment (p=0.42) (Wu, et al., 2010). This study showed that in a four year long-term outcome that there is no statistical significance between CABG and DES placement. However, there is a significant difference with target vessel revascularization. One can conclude that both procedures are sufficient with unprotected left main coronary artery disease; however, since the left coronary artery is extremely important for supply blood to the majority of the heart it might be plausible to perform a CABG so there is a lower chance of TVR.

Another long-term safety and efficacy study showed similar results. The study evaluated 2,240 patients with unprotected left main coronary artery disease who received PCI, bare metal or drug eluting stents, versus CABG. The MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization) Registry was designed to evaluate outcomes of PCI versus CABG for unprotected left main coronary artery disease in multiple centers in Korea (Park, et al., 2010). The 5-year risk of death, Q-wave MI, and stroke showed no statistical significance (p=0.59). However, the risk of TVR was significantly higher in the PCI group versus the CABG group (p<0.001) (Park, et al., 2010). However, since there is a significantly higher repeat revascularization rate in the DES cohort, CABG can be still classified superior to DES.
Prasugrel vs. Clopidogrel

Overall, clopidogrel (Plavix) has been used for post stenting to help reduce restenosis secondary to the implanted foreign body. However, prasugrel (Effient), a thienopyridine, is a prodrug that is rapidly metabolized to its active agent. This drug rapidly delivers high levels of platelet inhibition. The reason this drug is superior to Plavix is that Plavix goes through two CYP oxidation steps to get to its active metabolite where prasugrel only goes through one oxidation step. Recent studies have shown prasugrel to significantly reduce cardiovascular thrombotic events compared to Plavix. In addition, it has also been shown to have statistically significant reduction in stent thrombosis. There has been little research to date comparing Plavix to prasugrel when using drug eluting stents.
Conclusion

Coronary artery disease is the leading cause of death in the United States. Arterial walls are elastic and smooth which makes passage easier for substances in the bloodstream. However, when plaque builds up, it can create damage to the coronary arteries. While the damage occurs, the inflammatory cascade continues to make the coronary artery walls more susceptible for substances to attach. This is how plaques continue to build in the arteries, until the vessels cannot properly perfuse blood. This results in an acute coronary episode. These episodes can include, NSTEMI, STEMI, and unstable angina. There are two procedures to help treat plaque buildup in coronary vessels. Coronary artery bypass grafting surgery and percutaneous coronary intervention with drug eluting stents. There has been intense discussion as to which one is superior and which one should be the gold standard in coronary artery disease.

There were three subgroups that were identified in this literature research, patients with multi-vessel disease, diabetic patients and unprotected left main coronary artery disease. Studies regarding the superiority of CABG versus DES placement in patients with multi-vessel disease were inconclusive. One large study found outcomes for CABG superior to DES placement for all patients with multi-vessel disease. Another study found the same results; however, once they removed the diabetic population from the study of multi-vessel disease the results were not significant. It was found that diabetic patients with multi-vessel disease who underwent bare metal stents had significantly higher repeat revascularization rates, which then created significantly higher adverse events.
Drug eluting stents began to show more promise than the bare metal stents. Drug eluting stents still showed significantly higher revascularization rates, however, at a significantly lower rate than bare metal stents. Furthermore, most patients who needed repeat revascularization usually went back to percutaneous coronary intervention instead of coronary artery bypass surgery.

Left main artery disease created a more complex problem. The left main artery branches off into the LAD and left circumflex arteries supplying around 80 percent of the heart’s oxygen. All major studies pertaining to left main coronary artery disease show no statistical significance between CABG and DES procedures. However, a main issue found is the lack of long term studies. Most studies only completed a one-year follow up study. This can be attributed to most patients that have left main disease usually undergo CABG and long term follow up studies are not performed.

Drug eluting stents are an acceptable minimally invasive procedure for appropriate candidates with focal lesions. Surgeons continue to clinically treat left main artery disease with surgery due to the degree of blood supply the left main artery provides to the heart. These findings define the current standard of clinical care. Even though there is no statistically significant evidence based results when comparing DES with left main coronary artery disease, traditional bypass surgery should be recommended due to the amount of blood this vessel supplies.

When comparing DES to CABG in the subgroup of diabetic patients, CABG was found to be more beneficial over PCI in the presence of diabetes. Although the CABG on-pump procedure is associated with more cerebrovascular
events, overall CABG outcomes are superior to DES outcomes showing lower repeat revascularization rates, lower combined cardiovascular and cerebrovascular events, and lower overall mortality rates.

Overall, there are multiple factors that go into play when deciding whether a patient needs to undergo coronary artery bypass grafting surgery or percutaneous intervention, drug eluting stents. Drug eluting stents are a vast improvement compared to bare metal stents. There is however no superior method when comparing drug eluting stents to coronary artery bypass grafting surgery. There are instances where coronary artery bypass is superior to drug eluting stents; however, there have not been any instances where drug eluting stents are superior to coronary artery bypass grafting surgery. Drug eluting stents are new to the medical field and researchers are still working to improve them. Possibly one day in the near future, drug eluting stents may become superior to coronary artery bypass grafting surgery.
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Abstract

**Objective:** The purpose of this literature review was to exam the role of Coronary Artery Bypass Grafting Surgery and Percutaneous Coronary Intervention with Drug Eluting Stents in patients with coronary artery disease.

**Methods:** Articles were located by PubMed, Medtronic, Center of Disease Control, Mayo Clinic, and Cleveland Clinic.

**Results:** There were three subgroups defined in this literature research, multi-vessel disease, diabetic population, and left main artery disease.

**Conclusion:** Short term outcomes show that DES placement is comparable to CABG in left main artery disease. Long term outcomes are unknown for left main artery disease. CABG remains superior to drug eluting stents for diabetic patients and patients with multi-vessel disease.