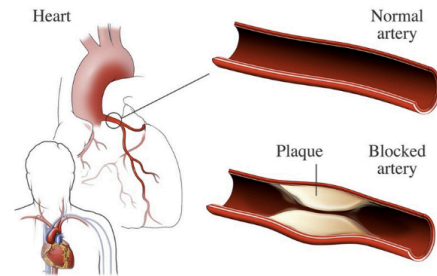


# Limiting the Side Effects of Coronary Artery Disease Treatments

Sofia Pyatalova

## Introduction

Coronary Artery Disease (CAD) is a heart disease, sometimes referred to as coronary heart disease or ischemic heart disease, which occurs when the heart receives an insufficient amount of oxygen-rich blood due to an accumulation of plaque in a coronary artery which narrows the artery (Fig. 1) (Encyclopedia Britannica, 2024). Plaque is the material which is formed by the accumulation of cholesterol or fat (Encyclopedia Britannica, 2024). The symptoms indicative of CAD include chest pain, dizziness, nausea, shortness of breath, and heart attacks (National Heart, Lung, and Blood Institute, 2023). This is the most common variant of heart disease, affecting around 5% of the American population aged 20 and older, as well as being one of the leading causes of death in the US and worldwide (Centers for Disease Control and Prevention, 2023). Such statistics indicate the diagnosis and treatment of this disease is crucial.



**Figure 1:** A normal artery compared to a blocked artery (National Heart, Lung, and Blood Institute, 2023).

The process of diagnosis starts with a risk assessment of the potential patient, which includes a review of the individual's and their family's medical history, measuring blood pressure, and running blood tests (National Health Service, 2024). If the results indicate that the individual may be at risk of CAD, they will be referred to diagnostic tests and procedures (National Health Service, 2024). Such tests include electrocardiograms, stress tests, coronary angiography, and cardiac MRI among other options (National Health Service, 2024). After diagnosis, there are multiple treatment options available to patients, the common ones being angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, nitrates, ranolazine, statins, coronary artery bypass graft (CABG), and coronary angioplasty (National Health Service, 2024; National Heart, Lung, and Blood Institute, 2023).

Each of the above treatment options is well researched, and there is an understanding of the mechanisms by which they act as well as the side effects. However, there is not enough wide ranging research into the ways that side effects could be mitigated. Over the course of data collection for this analysis, there was no single source that discussed the course of action for practitioners attempting to limit the side effects to CAD treatments that their patients may be experiencing. Making such research available would make it easier to address side effects which would make the recovery process of people who got treatment for CAD easier. A study by Mr. Hirani, Mr. Patterson, and Mr. Newman (2008) on patient thoughts on their treatment found that patients had concerns regarding the side effects of their respective treatments. Participants were asked to represent their stance on a statement related to their CAD treatments provided by the researchers with a rating of 1 through 5, 5 being 'strongly agree' (Hirani et al., 2008). There was a section on possible concerns that patients may have, mainly focusing on side effects with questions such as "I worry about the physical side-effects of the treatment" (Hirani et al., 2008). In response to the section, the ratings were between 3 and 2, indicating a mild level of disagreement with the statements, although not completely (Hirani et al., 2008). This indicates that although side effects were not a key

issue with the patients, the amount of concern was sufficient. In order to combat this fear, it is imperative that we not only support the patients through every step of their treatment, but also provide them with relief for their concern.

### **Methodology**

The purpose of this project is to research the side effects of common treatments of coronary artery disease and analyse the ways that they could be prevented. In order to do so, a large variety of sources were consulted, mainly hailing from peer reviewed scientific journals and official websites of health institutions. In filtering the sources, the relevance of the study to the topic of CAD and the credibility of the source in which it appeared were the main considerations.

At the start of this analysis, the most commonly prescribed treatments were compiled and researched. From that list of 7 possible treatments, 2 were selected for greater analysis. The selected treatments were nitrates and coronary artery bypass graft surgery. Nitrates were chosen for the expansive time frame over which they had been used while the surgery was selected as an alternative to medication.

Having narrowed the scope of the research down, the drug interactions with the body of the patient was researched in order to better understand how the side effects came to be. From there, the side effects and their causes were recorded to provide a pathway for combating them. Next, the ways that the side effects could be mitigated through either additional treatment or lifestyle changes. In the case of medication, the possible negative interactions with the initial treatment were considered and avoided. Finally, in the discussion and conclusion sections ideas for potential fields of studies for more refined treatments were presented.

### **Background Research**

There are several favoured treatments for CAD, some of which remedy the symptoms while others seek to cure the condition. Mitigating the symptoms usually involves loosening blood vessels in order to allow for an increased amount of blood flow; while curing the condition addresses the buildup of plaque causing it. Treatments can be separated into two main categories: medicines and surgeries/procedures. In the medicine section, there are angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, nitrates, ranolazine, and statins. Coronary artery bypass graft (CABG) and coronary angioplasty are surgeries and procedures, respectively, that are available to patients with CAD.

#### Medicines

Angiotensin-converting enzyme (ACE) inhibitors are a type of medicine which strive to treat high blood pressure (National Health Service, 2024). The mechanism that allows them to achieve the desired effects consists of preventing the hormone angiotensin-2, which narrows blood vessels, from operating (National Health Service, 2024). Since blood vessels relax, that allows an easier access to blood to the heart, easing it as well (National Health Service, 2024). This medicine is preferential for CAD treatments because the plaque in blood vessels that is the cause of CAD narrows them, causing blood pressure to increase while trying to continue its route. Easing the blood vessels widens them, which makes sure that the blockage does not affect the blood supply extensively. While taking ACE inhibitors, patients commonly experience dizziness and have a dry cough as side effects (National Health Service, 2024). Rare side effects which

affect less than 1% of the people taking this medicine are issues with the blood supply to their kidneys (National Health Service, 2024).

Another set of medicines that is accepted as a treatment for CAD are calcium channel blockers, which are sometimes referred to as calcium antagonists. They are employed to treat CAD, chest pain, arrhythmia, and other blood vessel conditions due to their characteristic of causing muscles to ease and opening blood vessels (Mayo Clinic, 2023). Calcium channel blockers operate through blocking heart and artery cells from receiving calcium, since calcium tightens blood vessels (Mayo Clinic, 2023). Preventing blood vessels from tightening further allows for a more or less adequate blood flow. Common side effects for this treatment include dizziness, increased heart rate, fatigue, headaches, nausea, and flushing in the face (Mayo Clinic, 2023).

A category of medicines called nitrates are available as a treatment for CAD. They have uses in quickly averting chest pain, as well as for relief of blockages in blood flow. Also, nitrates are used in order to lower blood pressure and alleviate heart pain (Abrams, 1995; National Health Service, 2024). In order to do so, they relax blood vessels and prevent reductions in blood flow to certain parts of the body (Abrams, 1995; American Heart Association, 2022). The reason that nitrates are used to treat CAD is because the relaxation of blood vessels widens them, and since most symptoms of CAD are caused by the narrowing of the blood vessels, it relieves the symptoms. Another problem arising from CAD is that some areas of the body do not have enough access to blood, and nitrates reduce that. However, the medicines do have some side effects, specifically headaches, flushed skin, and dizziness (National Health Service, 2024), as well as creating a tolerance to the treatment with continuous use (Münzel et al., 2011).

A different medicine that can be used to remedy CAD is ranolazine, which is given to patients experiencing chronic chest pains and limits disbalances in blood flow (Scirica, 2007). Ranolazine reduces and balances the amount of calcium and sodium in heart cells through hindering the sodium's current during the heart's electrical activity (Scirica, 2007). Through balancing the amount of calcium and sodium, they prevent the main symptom of CAD from affecting individuals extensively, since calcium and sodium contract the heart and blood vessels. Through preventing contraction, they allow the necessary amount of blood to be available to the body. People who take ranolazine may experience side effects that include nausea, dizziness, headaches, constipation, as well as rarer side effects of irregular heartbeat, difficulty breathing, and even fainting (MedlinePlus, 2016).

Statins are a group of medicines which are prescribed to manage cholesterol in blood (National Heart, Lung, and Blood Institute, 2023). They operate through expanding the amount of low-density lipoprotein (LDL) receptors in the liver, and thus prevent the excessive production of cholesterol (National Health Service, 2024). Since cholesterol is the cause of plaque buildup in blood vessels, which is CAD, limiting the amount of cholesterol available to the bloodstream mitigates CAD. Side effects of statins that are experienced frequently include muscle pain, digestion problems, dizziness, headaches, sickness, low blood platelet count, trouble sleeping, and feeling weak (National Health Service<sub>1</sub>, 2022).

### Surgeries/Procedures

An alternative to those medications is a treatment called coronary angioplasty, sometimes called percutaneous coronary intervention (PCI) (National Health Service<sub>2</sub>, 2022). During the procedure a tiny

balloon is inserted into the blocked artery to push the plaque outwards, thus allowing blood to flow more efficiently (National Health Service<sub>2</sub>, 2022). After, a tube is inserted into the artery to ensure it does not get blocked again by plaque (National Health Service<sub>2</sub>, 2022). Through unblocking blood vessels, it ensures that CAD is treated expeditiously, especially with more serious blockages. Patients who receive coronary angioplasty often experience bruising and bleeding in the area in which the artery was opened. The procedure can result in side effects such as damage to the artery, allergic reactions, excessive bleeding, and even heart attacks, although those are rare (National Health Service<sub>2</sub>, 2022).

A surgery that is available to treat CAD is the coronary artery bypass graft (CABG), which seeks to relieve the harm caused by the built up plaque (National Health Service<sub>3</sub>, 2021). In the surgery, a healthy artery from another part of the body is taken and attached to the blocked coronary artery on both sides of the blocked area, which allows blood to flow without impediment (National Health Service<sub>3</sub>, 2021). Through changing the course of blood flow, blocked arteries are avoided, making sure that the body gets the necessary amount of blood and individuals do not experience excessive symptoms of CAD. Side effects to this surgery take the form of chest pain around the areas of the surgical cuts, discomfort from the healing cuts, muscle pain and tightness, swelling in areas where the arteries were removed, problems sleeping and fatigue, constipation, loss of appetite, and mood swings (National Heart, Lung, and Blood Institute<sub>1</sub>, 2022).

## Data and Analysis

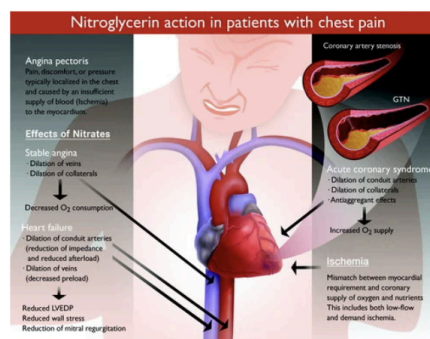
As demonstrated above, there are numerous ways to address CAD. From the 7 mentioned earlier, the 2 that this project focuses on are nitrates and coronary artery bypass graft (CABG) surgery. Nitrates were selected due to the immense amount of studies available due to the longevity of their use. CABG surgery is studied as the alternative to nitrate treatment, since it is an example of mechanical intervention in the individual's body, rather than being a medication.

### Nitrates

At a molecular level, nitrates have an extensive mechanism which ultimately relaxes blood vessels and helps relieve chest pain and prevents platelets from clumping. Nitrates are made up of organic nitrate esters, which are metabolised with the help of the enzymes glutathione S-transferase, cytochrome P-450, and conceivably esterases (Torfgård, 1994). This process creates nitric oxide, which evokes soluble guanylate cyclase (Torfgård, 1994). In turn, the enzyme codes for the production of cyclic GMP that triggers the cGMP-dependent protein kinase (Torfgård, 1994).

However, this system has some side effects, notably: headaches, flushed skin, dizziness, and tolerance towards the medication (Münzel et al., 2011; National Health Service, 2024). Each of these occur due to a step of the process by which the medication works, however they can be mitigated.

Headaches are caused due to the dilation of blood vessels caused by nitrates, which increases the blood flow to the brain (Erkan et al., 2015). There are a number of options available to treat headaches, such as



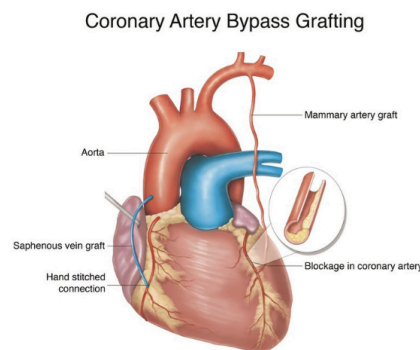
**Figure 2:** Effects of nitrates on the body (Münzel et al., 2011).

vitamins and supplements, herbal preparations, and behavioural treatments (Sun-Edelstein & Mauskop, 2011). For example, taking riboflavin may help due to it having the characteristic of helping with energy production as well as with the stability of cell membranes (Sun-Edelstein & Mauskop, 2011). Riboflavin should not have negative interactions with nitrates, allowing for use together (Mayo Clinic<sub>1</sub>, 2024). The symptoms of flushed skin occur for a similar reason, since the flow of blood increases to the skin, causing it (Better Health Channel, 2023). Nitrates cause blood vessels to dilate, bringing more blood to the area. Since blood is red, when more of it comes to an area of skin, the more colour begins to show through. If flushed skin is problematic, there are several ways to reduce it. For example, brimonidine gel and oxymetazoline hydrochloride cream are available to help treat redness in the skin, and work through contracting blood vessels in the face (Mayo Clinic<sub>2</sub>, 2024; Mayo Clinic<sub>3</sub>, 2024). These medicines have no known interactions with nitrates, making it possible to be used in conjunction with them (Mayo Clinic<sub>2</sub>, 2024; Mayo Clinic<sub>3</sub>, 2024). Dizziness is caused by low blood pressure. As mentioned before, nitrates relax blood vessels which allows more blood to flow through, lowering the pressure (Gupta, n.d.). This causes dizziness because low blood pressure results in not enough oxygenated blood reaching the brain (Better Health Channel, 2011). To reduce the effects of dizziness, it is recommended that patients take care to slowly transition from sitting to standing positions and vice versa, eating small meals often as opposed to 3 large meals, and increasing the amount of water they drink (National Health Service<sub>4</sub>, 2023). Another option available is wearing compression stockings since they put pressure on veins, improving circulation (National Health Service<sub>4</sub>, 2023). However, if the dizziness is severe, individuals have access to medication such as fludrocortisone, which raises the volume of blood accessible, and thus mitigates the cause of the side effect, which is a lack of oxygenated blood (Mayo Clinic<sub>4</sub>, 2022). Such medicine has no interactions with nitrates, making it possible to use together (Merative & Micromedex, 2024). The final common side effect of nitrates is tolerance which occurs with the continuous use for nitrates (Münzel et al., 2011). Due to tolerance, the treatment loses its effectiveness since the patient's body builds up a tolerance to the original dose of nitrates, meaning for the treatment to continue there needs to be an increase in dosage (Fung & Bauer, 1994). This is due to nitrates causing changes in the distribution of fluids and in hormone secretion which in turn limits their ability to relax blood vessels (Fung & Bauer, 1994). In order to counter nitrate tolerance, it is suggested that they should be used in combination with other medicines such as ACE inhibitors (Fung & Bauer, 1994). This is so since tolerance becomes an issue with continuous use, but when other medication is used in conjunction, it is avoided.

### Coronary Artery Bypass Graft Surgery

As covered earlier, the concept of CABG consists in providing blood flow with a 'detour' around the obstructed artery. This is done through grafting a healthy artery into the blocked artery, changing the course that blood takes (National Health Service<sub>3</sub>, 2021).

Of course, this treatment is not without side effects, and they consist of chest pain around the areas of the surgical cuts, discomfort from the healing cuts, muscle pain and tightness, swelling in areas where the arteries were removed, problems sleeping and fatigue, constipation, loss of appetite, and mood swings (National Heart, Lung, and Blood Institute<sub>1</sub>, 2022). The



**Figure 3:** CABG surgery model  
(Liverpool Heart and Chest Hospital, n.d.).

physical side effects of the surgery consist of the discomfort around surgical cuts. When the body suffers a cut, platelets in the area gather to clot the cut, and the same thing occurs with surgical cuts. After the cut clots and excessive bleeding is prevented, new skin tissue starts building up (MedlinePlus<sub>1</sub>, 2022). During this process, pain, discomfort, tightness, and swelling are common, especially when the cuts are extensive, like surgical cuts are (MedlinePlus<sub>1</sub>, 2022). To counter such feelings, especially when they are a serious issue to the patient, a treatment can be simple pain medication, like paracetamol (Better Health Channel<sub>2</sub>, 2014). It eases pain and addresses the muscle strains around the cuts (Healthdirect, 2023). In turn, fatigue is induced after surgery due to the patient's body having an endocrine-metabolic response to it, as well as having a limited amount of nutrients available, as well as the patient being restricted in movement (Christensen & Kehlet, 1993). In order to combat fatigue after the surgery, a number of therapeutic steps can be taken in order to reduce the body's response to the surgery, mitigate pain caused by movement, as well as increasing the amount of nutrients available through exercise (Christensen & Kehlet, 1993). Loss of appetite is a common response to surgery. This is so because surgery results in a reduced volume of the digestive system and of ghrelin, and due to the reason that the hormones responsible for fullness are increased (Wagner et al., 2022). To reduce the loss of appetite that patients experience after surgery, they have several possible routes. Such options include eating small but regular meals during the day, as well as taking medications such as corticosteroids and dronabinol to stimulate appetite (Cleveland Clinic, 2022). Another option is for the patient to chew gum on the first feeling of hunger in order to stimulate appetite (Wagner et al., 2022). Lastly, mood swings after surgery occur most commonly due to side effects from anaesthesia (Pike, 2017). It shuts down the body and it takes time for it to regenerate again, causing swings in mood (Pike, 2017). Another factor that affects mood is the condition that patients don't immediately return to the *status quo*, causing them to be more likely to experience mood swings (New York Spine Institute, n.d.). To limit mood swings, patients are recommended to get rest, eat healthily, set targets to motivate themselves, go outdoors, and get support from trusted individuals (New York Spine Institute, n.d.). Apart from that, medications that help manage such issues exist, one of them being mood stabilisers (Cleveland Clinic<sub>1</sub>, 2022).

### Analysis

Ultimately, it is imperative that during treatment for CAD, individuals' lives are not needlessly affected by side effects of the treatment. In the above sections, the ways of limiting the common side effects of two treatments were discussed and have demonstrated the way which patients may be benefited. In the sections exploring nitrates and CABG, the most frequently experienced side effects were all studied for their causes and with that in mind, the ways to address them were suggested. Although information for limiting specific side effects is available, there is no in-depth compilation of how each treatment's side effects are recommended to be dealt with as of March 2024. Such a condition makes research in the topic more difficult due to the need to list through countless sources to find the necessary information. This is something this project aims to combat.

However, this project has its limitations. It covers only 2 of the 7 common treatments, making it specific only to cases in which they are used. Also, the information is generalised, as opposed to the unique condition that each patient possesses. No patient is a mere textbook example since they each have their own preceding conditions, body systems, and such. However, in the future to counter those limits, building off this research will provide the possibility to include all the common treatments as well as

explore the suggested courses of action more in depth. A future step for this specific research is to conduct a meta analysis to determine the merit of these suggestions, assuming such data is available. The field of CAD treatment side effects is not one that is commonly explored, so there is a need for more statistical data.

### **Conclusion**

Coronary artery disease is a condition that affects individuals daily, and one in which treatment is necessary due to its serious symptoms and effects on life. It results from cholesterol building up in arteries, limiting the amount of blood supply that can be delivered through it. There are seven common treatments for it: angiotensin-converting enzyme inhibitors, calcium channel blockers, nitrates, ranolazine, statins, coronary artery bypass graft surgery, and coronary angioplasty. Each of these treatments, although beneficial in their own right, come with side effects that affect the quality of life of the patients. This project focused on nitrates and coronary bypass graft surgery, and advised on how to mitigate the harmful side effects to improve their quality of life.

This project is unique in the fact that it compiled information on all the side effects of the discussed treatments and suggested ways of dealing with them, which does not have a published analog. It provides a base for future research that has the potential to improve the lives of the thousands of people undergoing treatment. Fundamentally, what this project aims to do is to provide medical practitioners with the tools to make the healing process of their patients with coronary artery disease less stressful and to allow them to live a relatively standard life.

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