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Review Article

A Review on the Coronary Artery Disease Landscape: Tissue and Market Analysis, Treatments, and Trials.

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Running Title: A Review on the Coronary Artery Disease Landscape: Tissue and Market Analysis, Treatments, and Trials.

Abstract

Coronary artery disease (CAD) remains the leading global cause of morbidity and mortality, driven by progressive atherosclerotic plaque accumulation within the coronary arteries. The pathogenesis involves complex structural, cellular, and molecular alterations, including endothelial dysfunction, smooth muscle cell phenotypic switching, extracellular matrix remodeling, vascular stiffening, and chronic inflammation. Current pharmacologic, surgical, and device-based interventions mitigate symptoms but do not reverse disease progression. As a result, the global CAD market continues to expand rapidly, with significant growth driven by an aging population, lifestyle risk factors, technological innovation, and increased awareness of cardiovascular health. This review provides a comprehensive overview of the biological mechanisms underlying healthy and diseased coronary tissue, analyzes market trends and drivers, and evaluates both established and emerging treatment modalities. Novel technologies in stent design, intravascular lithotripsy, orbital atherectomy, and RNA-based therapeutics are highlighted, alongside early-stage tissue engineering approaches under investigation. Together, these developments reflect the ongoing shift toward more targeted, durable, and patient-specific strategies in the management of CAD.

Keywords : coronary artery disease (CAD), atherosclerosis, stents, angioplasty, tissue engineering, drug-eluting stents, lipid-lowering therapy, intravascular lithotripsy, orbital atherectomy, regenerative medicine.

INTRODUCTION

Coronary artery disease (CAD) is the most common type of heart disease [1]. It is a condition characterized by the buildup of plaque within the coronary arteries, leading to reduced oxygen delivery to the heart tissue [2] This remains the leading cause of morbidity and mortality, and affects millions in developed and developing regions [2]. It predominantly impacts those in industrialized nations where sedentary lifestyles and poor diets are common [2]. The calcifications develop silently over the years and eventually manifest as chest pain, heart attacks, and cardiac death [3]. Modern medicine offers a range of treatment options, such as therapeutics, surgical interventions, and implanted devices, that primarily aim to manage risk factors and reduce the likelihood of acute events [1]. As the demand for improved CAD management grows, this paper will examine healthy and diseased tissue, current market trends, established treatment methods, and promising innovations in both pharmaceuticals and medical devices currently undergoing clinical investigation.

HEALTY TISSUE

CAD affects the coronary arteries, which supply the myocardium with oxygenated blood [64]. The heart is a muscle that requires a constant flow of oxygen-rich blood to work properly, therefore, these arteries are integral for sustaining life [65]. These vessels wrap around the outside of the heart and branch off from the aortic root [66]. There are two main coronary arteries, the right and left, with each having smaller branches that go deeper inside the heart muscles [65, 66]. The right coronary artery supplied blood to the right atrium and ventricle [65]. It also supplies the sinoatrial and atrioventricular nodes, which are important for sending electrical signals through the heart so it can contract [65]. It also supplies blood to one-third of the interventricular

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septum [65]. The left main coronary artery supplies blood to the left atrium and ventricle [65]. It also supplied blood to the other two-thirds of the interventricular septum [65].

The coronary arteries are composed of three major cell types: endothelial cells, smooth muscle cells, and adventitial fibroblasts [67]. Endothelial cells line the innermost layer of the artery (the intima), forming a barrier between the blood and the vessel wall [67]. They help to regulate vascular tone, mediate exchange of gases and nutrients, and play key roles in inflammation and thrombosis [67]. Smooth muscle cells, located in the middle layer (the media), are responsible for controlling blood vessel constriction and dilation, which helps maintain blood pressure and flow [67]. These cells also contribute to vascular remodeling and respond to injury or disease by proliferating or producing extracellular matrix [67] The outermost layer (the adventitia) constrains fibroblasts, which provide structural support through collagen production and are involved in tissue repair, immune cell recruitment, and vessel stabilization [67]. Together, these cell types form a dynamic and responsive system essential for coronary artery development, function, and regeneration [67].

These arteries are made of three distinct layers, the intima, media, and adventitia, as shown in Figure 1. The intima is the innermost layer, which interfaces with the blood [69,70]. This is a thin and delicate layer made from a single layer of endothelial cells [69,70]. These cells play an important role in maintaining vascular homeostasis by controlling vascular tone, inhibiting platelet aggregation, and controlling the passage of substances between the bloodstream and vessel wall [69,70]. In healthy vessels, there will be lipid accumulation or immune cell infiltration [69,70]. Additionally, the low permeability of the vessels helps protect them from harmful substances [69,70]. The next layer is the media, which is composed of vascular smooth muscle cells (VSMCs) in concentric or helical layers [69,70]. This also has collagen, elastin, and proteoglycans [69,70]. The media holds most of the mechanical properties of the artery and is responsible for the vessel's vascular contractility and tone regulation [69,70]. It also helps to maintain the extracellular matrix (ECM) and can adjust vessel diameter in response to central nervous system signals [69]. In their healthy state, the VSMCs of the media are in a contractile phenotype, meaning that they are non-proliferative and have low synthetic activity [69,70]. This entire layer is immunoprivileged and has little to no inflammatory cell presence [69,70]. The final, and outermost layer of the artery is the adventitia[70]. This is made from connective tissue, collagen and elastic fibers, fibroblasts, and lymphatics [69,70]. Its main function is to provide mechanical support and anchor the vessel to the tissue around it [69,70]. In its healthy state, it has infrequent immune cell presence, and fibroblasts help to maintain structural integrity, only responding to stress when needed [69]. All these layers work together to allow for the transport of blood, as the intima will regulate interactions with the blood, the media allows for mechanical and contractile support, and the adventitia maintains structural integrity and vascular health [69,70]. In healthy tissue, the balance of cellular and molecular activity protects the artery from inflammation, lipid infiltration, and structural integrity [69,70].

DISEASE TISSUE

The main indicator of CAD is the development of atherosclerotic plaque [72]. This plaque is a buildup and mixture of cholesterol, cellular waste products, fatty substances, calcium, and fibrin [73]. This plaque narrows the arterial lumen, making it very dangerous as it impedes blood flow [72]. This can become fatal in the coronary arteries, as this means that the heart isn't receiving adequate oxygen to continue pumping, therefore making some parts ischemic [72]. The first step of plaque development is the fatty streaks, which form because of the subendothelial deposition of lipid-forming macrophages [72]. When this occurs, the intima layer breaks, causing monocytes to enter the subendothelial space, where they turn into macrophages [72]. The macrophages will take up oxidized LDL particles, which eventually lead to foam cell formation [72]. The newly developed plaque, which forms, could either grow or stabilize over time [72].

The development of the plaque contributes a great amount to the structural changes of each layer of the arteries [74]. The intima becomes thicker due to smooth muscle cell (SMC) migration from the media and proliferation [74]. The intima is where the fatty streak comes from, and because of the macrophage presence, it also experiences chronic inflammation [74]. The SMCs of the media transition from contractile to synthetic phenotypes [74]. This means that it becomes proliferative, migratory, and produces matrix proteins and proteases [74]. Its integrity also becomes compromised as elastin fragments and collagen orientation become disorganized [74]. Lastly, the adventitia becomes more inflamed as well due to immune cells, neovessels, and activated fibroblasts increases [74, 75]. The ECM also remodels, and collagen production increases, essentially contributing to vessel stiffening [74].

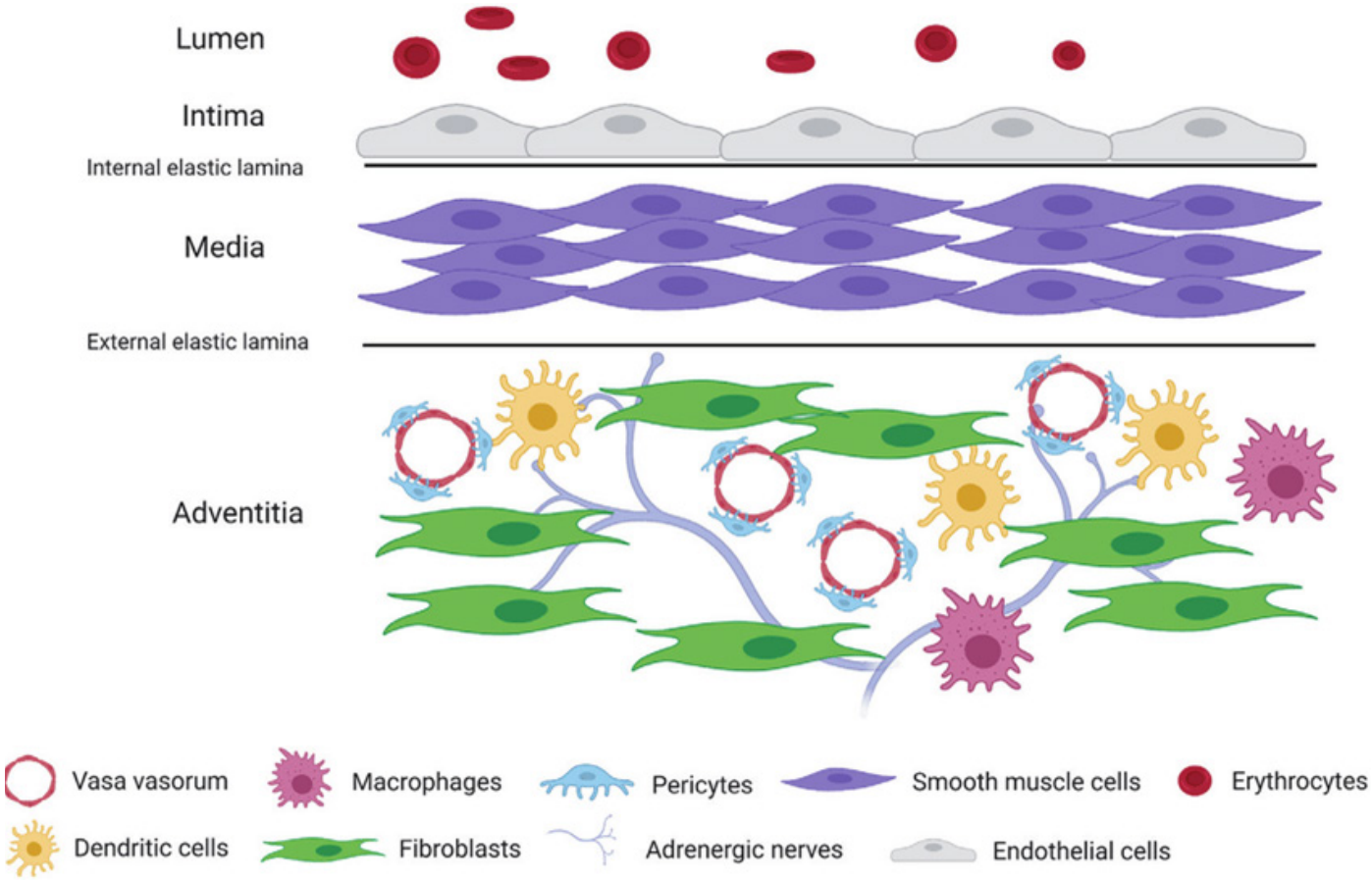
Due to these physical changes in the layers, there are also mechanical and cellular properties of the vessel wall which are altered [74]. The diseased arteries become stiffer and less compliant, as they have a 2.5 to 2.9 increase in elastic modulus, about 45% higher stress compared to healthy arteries, and a reduction in strain capacity by about 35% [74]. The distortion of the normal stress distribution across the cells often leads to plaque rupture [74]. At the cellular level, the endothelial cells become dysfunctional as they produce less nitric oxide and more adhesion molecules [75]. This overall increases the

recruitment of inflammatory cells like monocytes and T cells [75, 76]. On the other hand, the SMCs lose their contractility and take on a synthetic, pro-inflammatory role, eventually leading to enzymatic degradation of collagen and elastin, which destabilizes the plaque and increases the risk of rupture and thrombosis [76].

MARKET SIZE & TRENDS

CAD is the leading cause of mortality in the US and accounts for 610,000 deaths per year nationwide [4]. Globally, it is the third leading cause of death, and is associated with 17.8 million deaths annually [4]. Due to its worldwide prevalence, the CAD global market is valued at USD 22.07 million in 2024, and is expected to reach USD 46.23 billion by 2031, as seen in **Figure 1** [5]. This market is likely to grow at a CAGR of 8.86% [5,6]. This growth can be attributed to the rising prevalence of CAD in aging populations, advancements in medical technology, and increased awareness and education surrounding heart health [5].

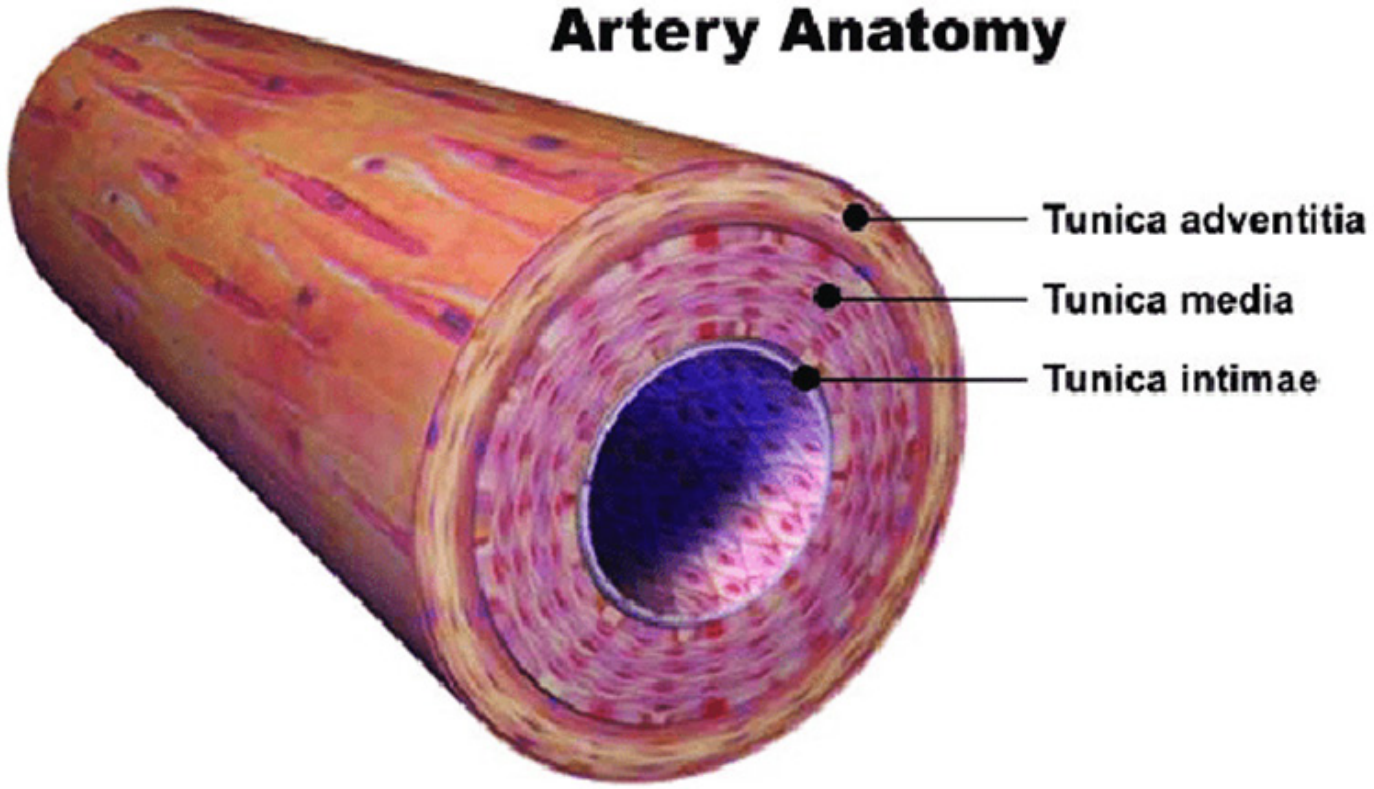
Figure 1. Schematic diagram of coronary artery structure [68]



The image shows the three major layers of the coronary artery: the intima, media, and adventitia, along with the structural organization and cell types present in healthy coronary arteries

This market is segmented into diagnosis, treatment, end-user, and distribution channel sub-segments [6]. The diagnostic market diverges into electrocardiograms, echocardiograms, nuclear stress tests, cardiac catheterization, and heart CT scans [6]. Within this sub-segment, CT scans make up the largest portion of the diagnostic market [6]. Next, the treatment segment is split into medication, surgery, and additional therapy [6]. These methods are used to treat the overall disease, manage high blood pressure and cholesterol (common risk factors for CAD), and lower the likelihood of heart-related incidents [6]. Within this category, medications account for a large portion of the treatment market, because they are used as a first-line therapy, as shown in **Figure 2** [6, 7]. The end user market is split into hospitals and specialty clinics, with a large portion lying in the hospitals, because they act as a source for acute care and surgical procedures (such as angioplasties and bypass) [6]. Similarly, the distribution channel market is split into hospital, retail, and online pharmacies, with hospital pharmacies leading the segment because patients are diagnosed and treated in hospitals, where medications are typically dispensed [5].

Figure 2. Schematic diagram of the layers of the artery [71].

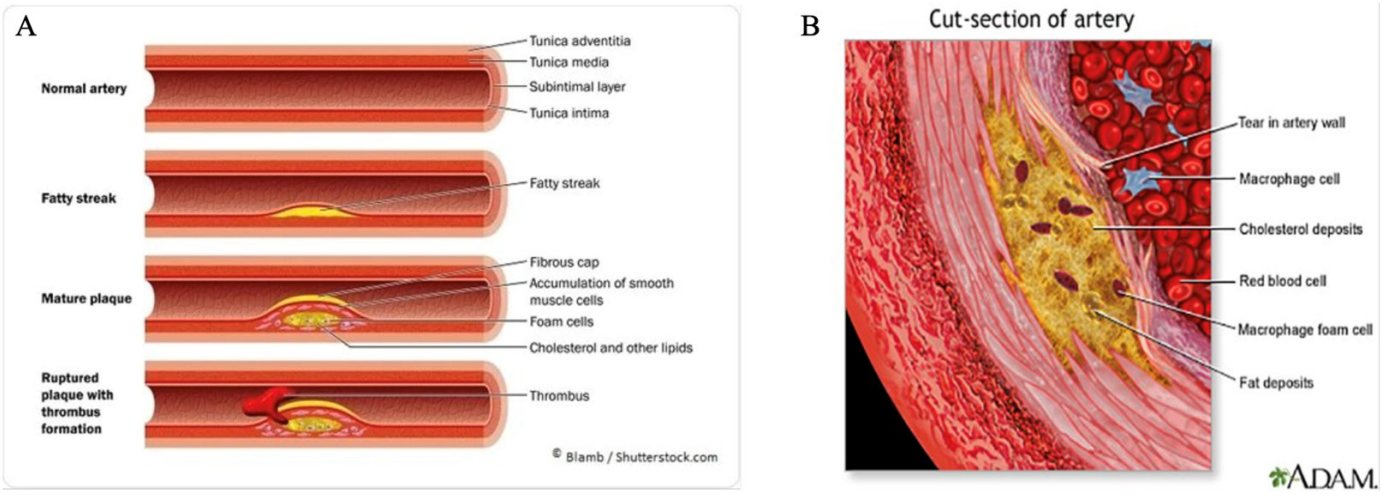


This image shows the major layers of the arteries, including the intima, media, and adventitia

A major driver for this market is the global increase in heart disease, as it causes about 18 million deaths annually [5]. The Centers for Disease Control and Prevention found that CAD was the leading type of heart disease in May of 2024 [8]. In this year, it was found that 5% of adults 20 and older have coronary artery disease, while 1 in 5 deaths occurred in adults younger than 65 years old [8]. When assessed on a regional basis, it is observed that CAD is mostly present in developed nations due to lifestyle factors, such as physical inactivity, smoking, and stress [5, 9]. Another major driver of the CAD market is the growing aging population, as this disease begins showing symptoms later in the lifetime [8]. Lastly, increased awareness of heart health is a driver, as it encourages individuals to seek medical attention for small but significant symptoms they may experience [5]. Greater awareness and education about the symptoms and warning signs of CAD have led to higher screening rates, resulting in more individuals being diagnosed with the disease [5]. A noticeable trend in the CAD market is the increased preference for minimally invasive procedures, such as angioplasties and stenting, as opposed to traditional surgeries [5]. This is primarily because these solutions require shorter hospital stays, lower risk of infections, faster recovery, and superior post-surgical outcomes [5].

When the CAD market is assessed from a global scope, North America has and will continue to have the largest share of the global CAD market [10]. This dominance is primarily attributed to the high prevalence of CAD in the region, driven by lifestyle-related risk factors [10]. The sedentary lifestyle habits, poor diet, and high stress levels increase the risk of developing coronary artery disease, as they contribute to hypertension, obesity, insulin resistance, and other key drivers of atherosclerosis [10]. Additionally, North America benefits from advanced medical technologies, including widespread use of diagnostic imaging, catheter-based interventions, and drug therapies, which allow for early detection and aggressive management of the disease [10]. The well-developed healthcare infrastructure allows for access to cardiovascular care, while early diagnosis capabilities promote life-saving interventions [10]. Together, these factors create a healthcare environment that detects and manages CAD at higher rates, therefore reinforcing North America's leading role in the global CAD market [10]. Furthermore, Asia is predicted to experience the fastest growth in this market due to demographic and socioeconomic changes. The rapidly aging population increases the number of age-related cardiovascular conditions, while urbanization and economic development lead to sedentary lifestyles and increased consumption of processed foods [10]. Additionally, as the healthcare system continues to improve and develop, access to diagnostic tools and treatment options is expanding [10]. This leads to higher detection rates and demand for therapeutic solutions [10]. These geographic profiles are illustrated in **Figure 3** [11].

Figure 3. Diagram of atherosclerotic plaque progression [77, 78].



(A) The image shows the stages of atherosclerosis: normal artery, fatty streak, mature plaque, and ruptured plaque with thrombus formation.
(B) The image shows a cross-section of an advanced plaque, highlighting lipid buildup, foam cells, red blood cells, and a disrupted arterial wall.

EXISTING PRODUCTS

Current products for the treatment of CAD split off into medications, surgical procedures, and medical devices [12]. These methods are widely used and proven to be effective in managing symptoms, preventing future events, and improving long-term survival [12].

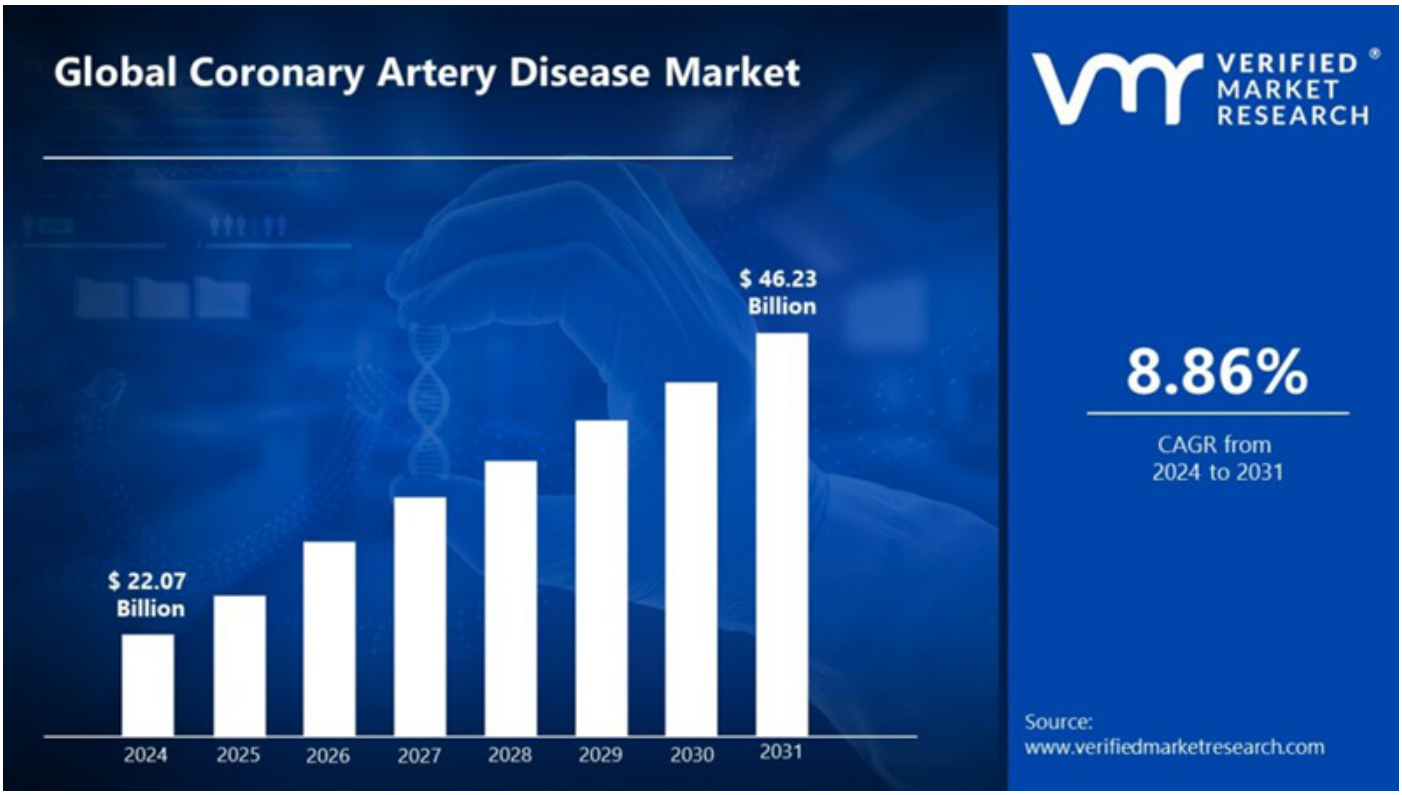
The most common medications for treating CAD and its symptoms are statins, ACE inhibitors, beta blockers, and antiplatelet medicines [12]. Statins inhibit the HMG-CoA reductase enzyme, which is required for the synthesis of cholesterol in the liver [13]. By blocking this enzyme, there is decreased cholesterol, which effectively reduces low-density lipoprotein (LDL) cholesterol levels in the blood [13]. This inevitably slows the buildup of plaque in the coronary arteries [13]. Additionally, statins help existing plaque, making it less likely to rupture and cause blockages, while also reducing inflammation [13]. ACE inhibitors and beta blockers are often prescribed together, as they work to decrease blood pressure and lower the workload of the heart [12]. ACE inhibitors will work to induce vasodilation by inhibiting the renin-angiotensin system, while beta blockers will decrease heart rate and contractility by blocking adrenergic receptors [14]. By conjunctively alleviating the heart's workload, it slows the progression and reduces the risk of CAD [14]. Lastly, antiplatelet medications are used as a secondary prevention for patients with existing CAD [15]. This drug works by preventing the formation of blood clots in narrowed and damaged coronary arteries, therefore preventing plaque rupture [15]. Other medications include calcium channel blockers, nitrates, and ranolazine [12]. Overall, although these medications do not fully eliminate CAD and plaque, they help to manage risk factors, which reduces the likelihood of heart attacks and disease progression [12]. **Table 1** summarizes common brand-name medications, their manufacturers, and their primary functions in the treatment of CAD.

Table 1. Common medication types, brands, and companies used to treat CAD [16, 24].

Drug Class	Common Drugs (Brands)	Company	Mechanism of Action	Special Characteristics
Statins	Atorvastatin (Lipitor), Rosuvastatin (Crestor)	Pfizer (Lipitor), AstraZeneca (Crestor)	Inhibit HMG-CoA reductase to lower LDL cholesterol	Reduce plaque buildup and inflammation; improve survival
ACE Inhibitors	Lisinopril (Prinivil, Zestril), Enalapril (Vasotec)	Merck, AstraZeneca, others	Block conversion of angiotensin I to angiotensin II	Lower BP, reduce afterload, protect against heart failure post-MI
Beta Blockers	Metoprolol (Lopressor, Toprol-XL), Atenolol (Tenormin)	Novartis, AstraZeneca, Teva	Block β1-adrenergic receptors to reduce heart rate and contractility	Lower myocardial oxygen demand; improve post-MI outcomes
Antiplatelets	Aspirin, Clopidogrel (Plavix), Ticagrelor (Brilinta)	Bayer (Aspirin), Sanofi/BMS (Plavix), AstraZeneca (Brilinta)	Inhibit platelet aggregation	Prevent clot formation in stents and narrowed arteries; reduce heart attack risk

When plaque buildup becomes advanced, medical procedures such as plaque removal or the implantation of devices are often necessary to restore blood flow and prevent complications [12]. Coronary artery bypass surgery (CABG) is one type of procedure performed to treat narrowing or blockages in one or more coronary arteries [25]. This procedure restores blood flow to the heart muscles by creating a new path for blood so it can move around the blocked artery [25]. During this procedure, a healthy blood vessel is removed from the lower leg or chest and will take on the role of the graft [26]. One end of the graft is connected to the area below the blocked artery, while the other is connected to the aorta or other part of the heart, effectively making a new path for blood to move around the blockage, as seen in **Figure 4A** [26, 27]. It is important to note that this procedure does not cure CAD, but rather reduces painful symptoms like chest pain [26].
Another commonly performed procedure for CAD is a balloon angioplasty [28]. As seen in **Figure 4b**, an inflatable balloon-tipped catheter is fed through either the radial artery (in the wrist) or the femoral artery (in the groin) [28, 29]. Once it reaches the blocked area of the vessel, the balloon is inflated to crush the occluding plaque and to restore the appropriate vessel diameter [28, 29].

Figure 4. Global Coronary Artery Disease Market Trend (2024–2031) [6]

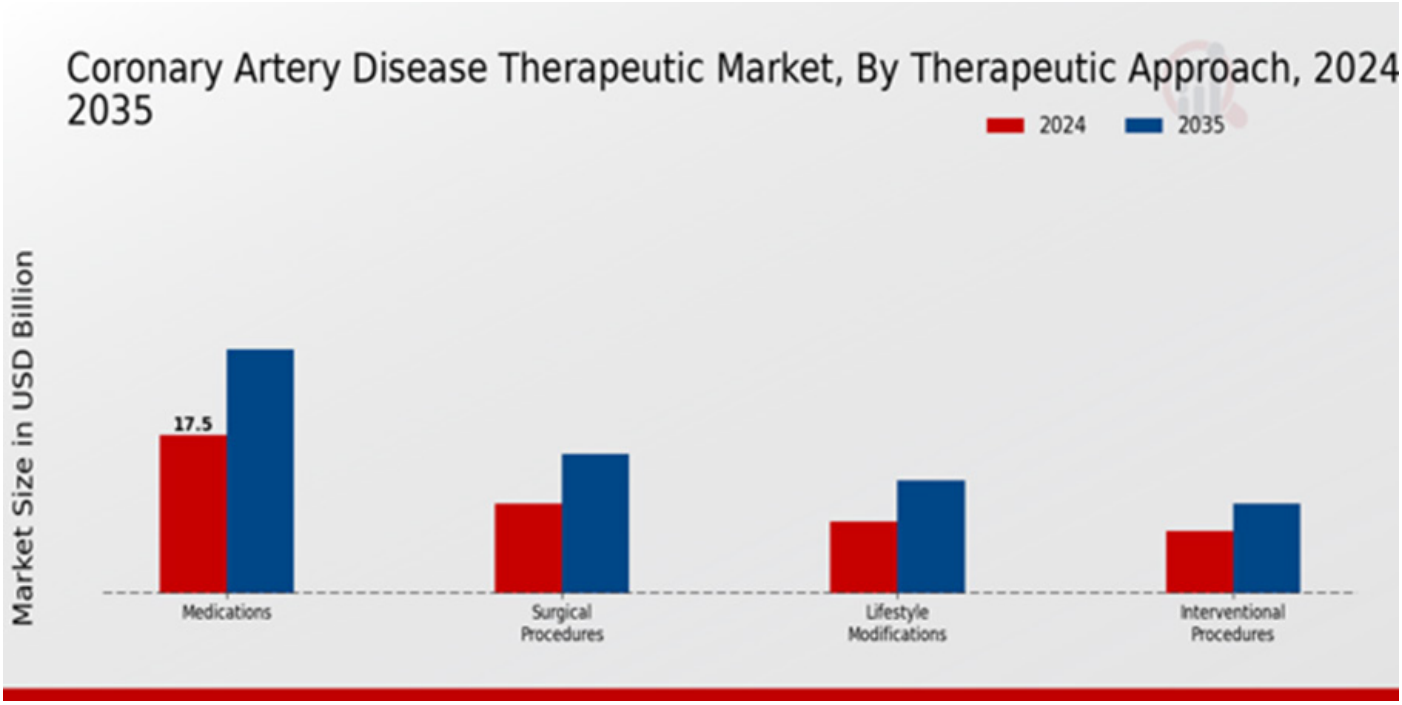


The image shows the projected growth of the global CAD market, increasing from $22.07 billion in 2024 to $46.23 billion in 2031, with a CAGR of 8.86%.

To help maintain the vessel at an appropriate diameter after the procedure, a stent will be placed [28]. A stent is a small, expandable metal mesh coil, which is placed to maintain the size of the blood vessel and prevent it from closing up again [30, 31]. Recently, cardiac stent use has increased due to the ease of insertion and effectiveness [32]. There are many types of stents, the most common being bare-metal stents and drug-eluting stents [32]. As the name suggests, bare-metal stents are made of stainless steel, cobalt chromium, or platinum chromium [33]. However, these have the issue of the vessel becoming restenosed, where the diameter of the lumen is reduced after the angioplasty [34]. This response is part of the body's natural wound healing process triggered by the angioplasty, which causes mechanical injury due to the force applied to the vessel walls [34]. As a result, inflammation and proliferation of smooth muscle cells lead to the formation of a thick tissue layer over the stent, effectively narrowing the vessel lumen once again [34]. A solution to this was the development of drug-eluting stents, which are the same as bare-metal but have a drug seeded on them to delay restenosis [35]. These are coated with antiproliferative drugs that will inhibit the growth of vascular smooth muscle cells, as shown in **Figure 5** [35, 36]. Common drugs seeded on drug-eluting stents are sirolimus, everolimus, zotarolimus, biolimus, as they will block the mTOR pathway [35]. This stops the cell cycle in the G1 phase and prevents extra tissue growth, which can occlude the diameter of the vessel [35]. A comparison of composition, performance, and indications for bare-metal and drug-eluting stents is outlined in **Table 2.**

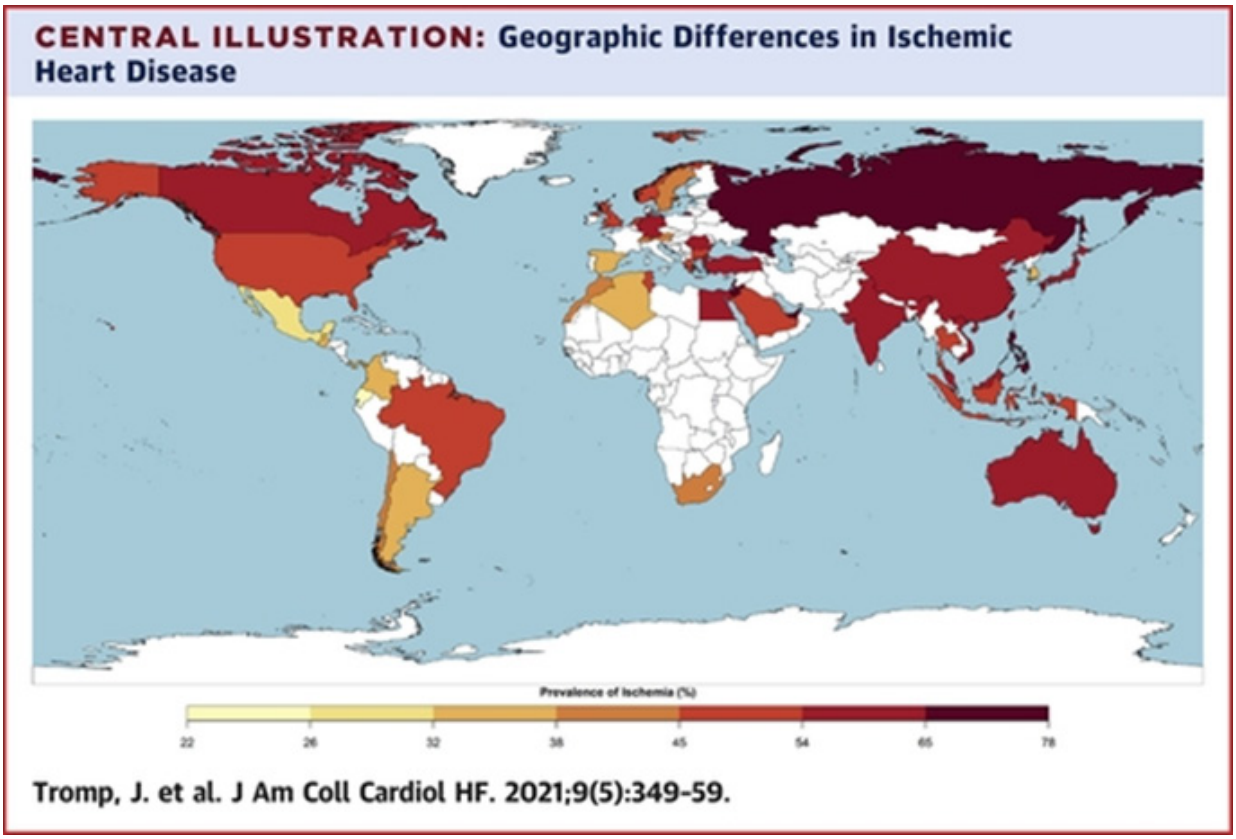
Table 3 and **Figure 6** present notable commercially available stents, organized by manufacturer, stent type, unique features, and FDA approval status.

Figure 5. CAD Therapeutic Market by Sub-Segment (2024–2035) [7]



The image shows projected market sizes for medications, surgical procedures, lifestyle modifications, and interventional procedures in 2024 and 2035.

Figure 6. Geographic Prevalence of Ischemic Heart Disease [11]



The image shows global variation in ischemic heart disease prevalence, highlighting regional disparities in coronary artery disease burden.

Table 2. Bare-metal vs drug-eluting stents [37-39]

Stent Type	Composition	Advantages	Limitations	Indications
Bare-Metal	• Metal stents made from stainless steel or cobalt-chromium	• Allow shorter duration of dual antiplatelet therapy (only 1 month) • Low cost	• High resotensis rate • More frequent need for repeat revascularization	• Patients with high bleeding risk • Poor DAPT adherence • Need for urgent surgery after stenting
Drug-Eluting	• Metal stent frame • Coated with anti-proliferative drug	• Low risk of restenosis • Fewer repeat procedures • Improve long-term outcomes	• Require longer dual antiplatelet therapy (6-12 months) • Hig cost • Risk of late stent thrombosis	• Patients at high risk of restenosis • Complex lesions • Diabetics • Long or small-vessel lesions

Table 3. Popular commercially available stent models and companies [40-44]

Product	Company	Stent Type	Composition	Special Characteristics	Premarket Approval
Xience Sierra	Abbott	Drug-Eluting	Cobalt-chromium wit everolimus drug + fluoropolymer coating	Excellent flexibility for complex anatomies Low restenosis and thrombosis rates	2018
Resolute Onyx	Medtronic	Drug-Eluting	Cobalt alloy with zotarolimus drug + durable polymer	Thin struts, high radial strength Approved for short DAPT in high-bleeding-risk patients	2017
Synergy XD	Boston Scientific	Drug-Eluting	Platinum-chromium with everolimus drug + bioabsorbable polymer	Ultra-thin struts Polymer dissolves over time to improve vessel healing	2020
Promus Elite	Boston Scientific	Drug-Eluting	Platinum-chromium with everolimus + durable polymer coating	Enhanced trackability and deliverability in complex lesions	2015
Mutli-Link Vision	Abbott	Bare-Metal	Stainless Steel	Good radial strength Faster endothelialization Short DAPT (1 month)	2003

PRODUCTS IN PRECLINICAL & CLINICAL TRIALS

As the number of individuals with CAD continues to grow, there is a need for improved therapies and devices that go beyond the current standard of care [45]. Researchers are actively exploring innovative products in both clinical and preclinical development stages [45].

Procedures and Devices

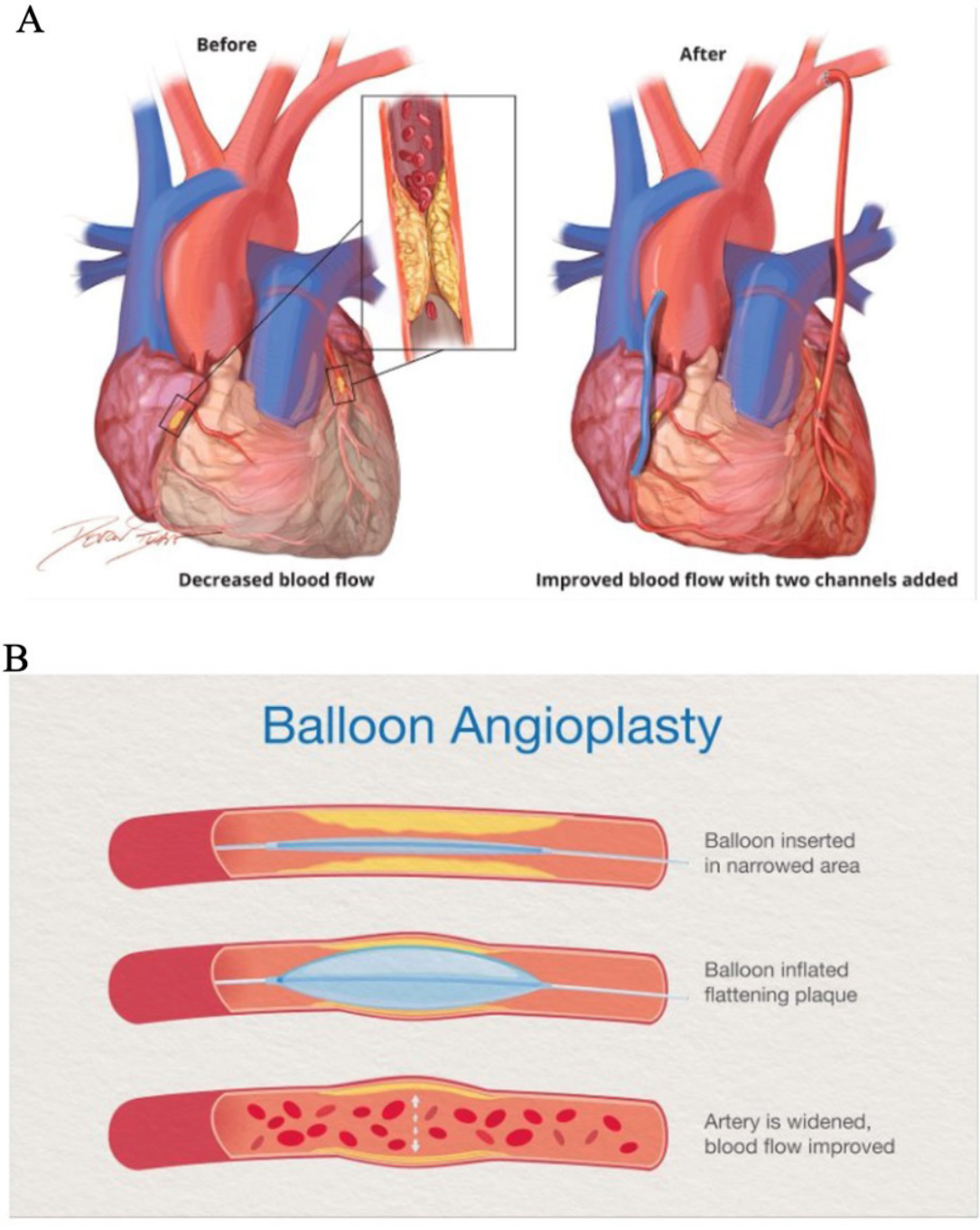
In the scope of procedures, Abbott is currently developing a Coronary Intravascular Lithotripsy (IVL) System, which uses a special device to prepare the blood vessels before stent insertion [45]. It is similar to a balloon angioplasty, where a balloon on a catheter is fed through the vessel and then expanded in the narrowed portion of the vessel [45]. However, this product differs in that the IVL system emits sound waves to fracture hardened plaque while minimizing damage to the surrounding soft tissue of the arterial lumen [45]. This vastly differs from the current balloon angioplasty, where mechanical force from balloon inflation is the main source of plaque destruction [34]. This product is currently in the pivotal study phase, where tests are being done to ensure that it is safe and effective in animals, and will subsequently be approved by the FDA [46].

Another novel procedure being pioneered by Abbott is the use of an orbital atherectomy to remove plaque and essentially replace balloon angioplasties [47]. This clinical trial is called the ECLIPSE trial, and is designed to assess the effectiveness of this procedure compared to the currently used balloon angioplasty [48, 49]. The main population for this procedure is individuals

with severely calcified coronary artery lesions [48]. This product works by having a catheter with a diamond-coated spinning crown [48, 49]. This crown will rotate and sand down the calcified plaque, allowing for minimal compression to occur and leading to adequate stent expansion [47, 48]. **Figure 7a** illustrates how the orbital atherectomy will work for removing plaque in the vessels [50].

Another key focus of innovation in CAD device development is the advancement of stent technologies. Shanghai MicroPort Medical (Group) Co., Ltd., has designed the Firehawk® rapamycin-eluting stent and is currently running a clinical trial to compare it against currently approved 2nd-generation drug-eluting stents [51, 52]. This stent differs from current devices as it applies rapamycin (the anti-proliferative drug) in an abluminal pattern by using a biodegradable polymer that fully resorbs over time [53]. This pattern minimizes vessel wall inflammation, promotes faster healing, and reduces the risk of late stent thrombosis [53]. **Figure 7b** illustrates the design of the Firehawk stent.

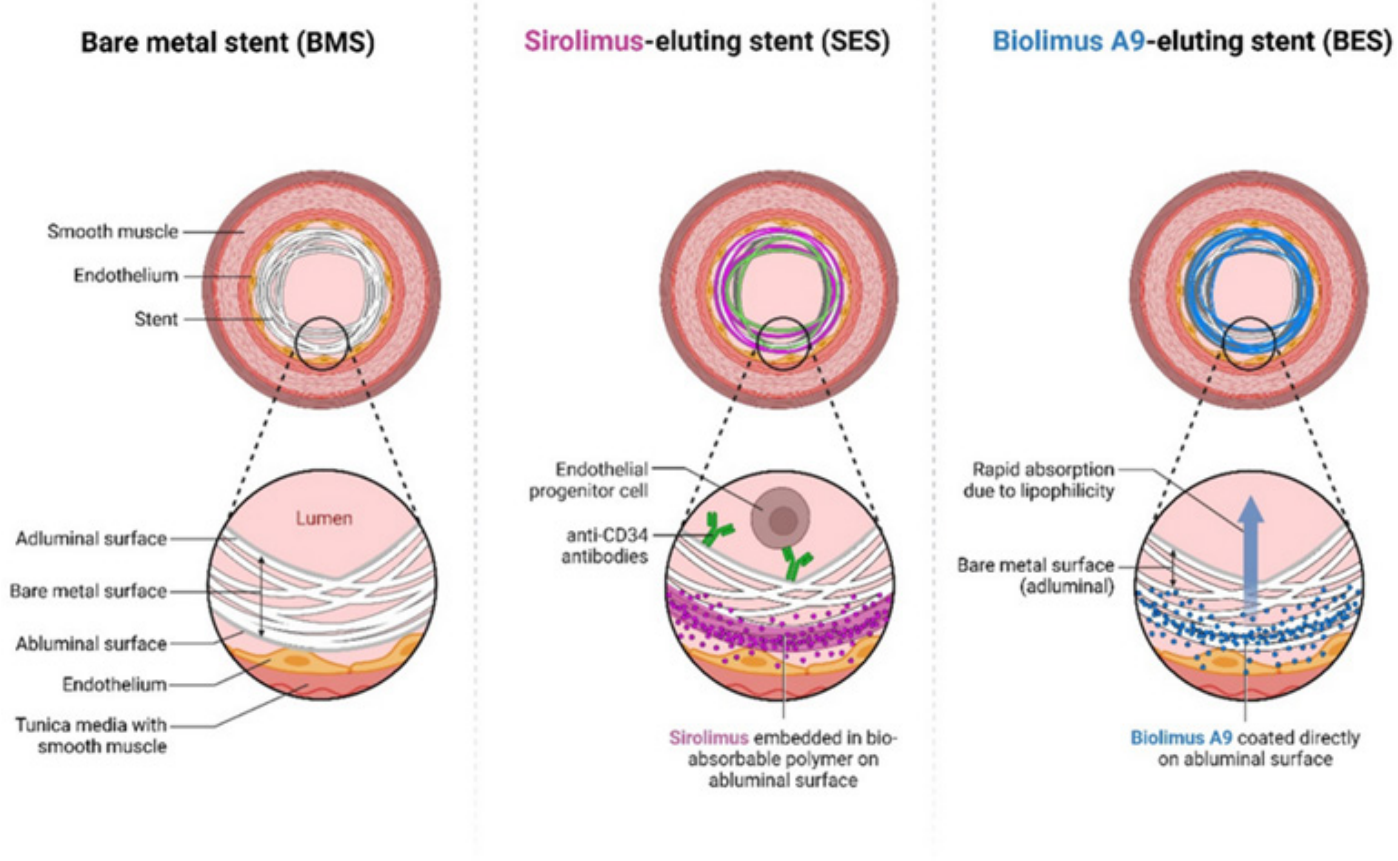
Figure 7. Coronary Artery Bypass Graft and Balloon Angioplasty Procedures [27, 29]



(A) The image shows before and after views of the CABG procedure, with grafts creating new paths for blood to bypass a blocked artery.

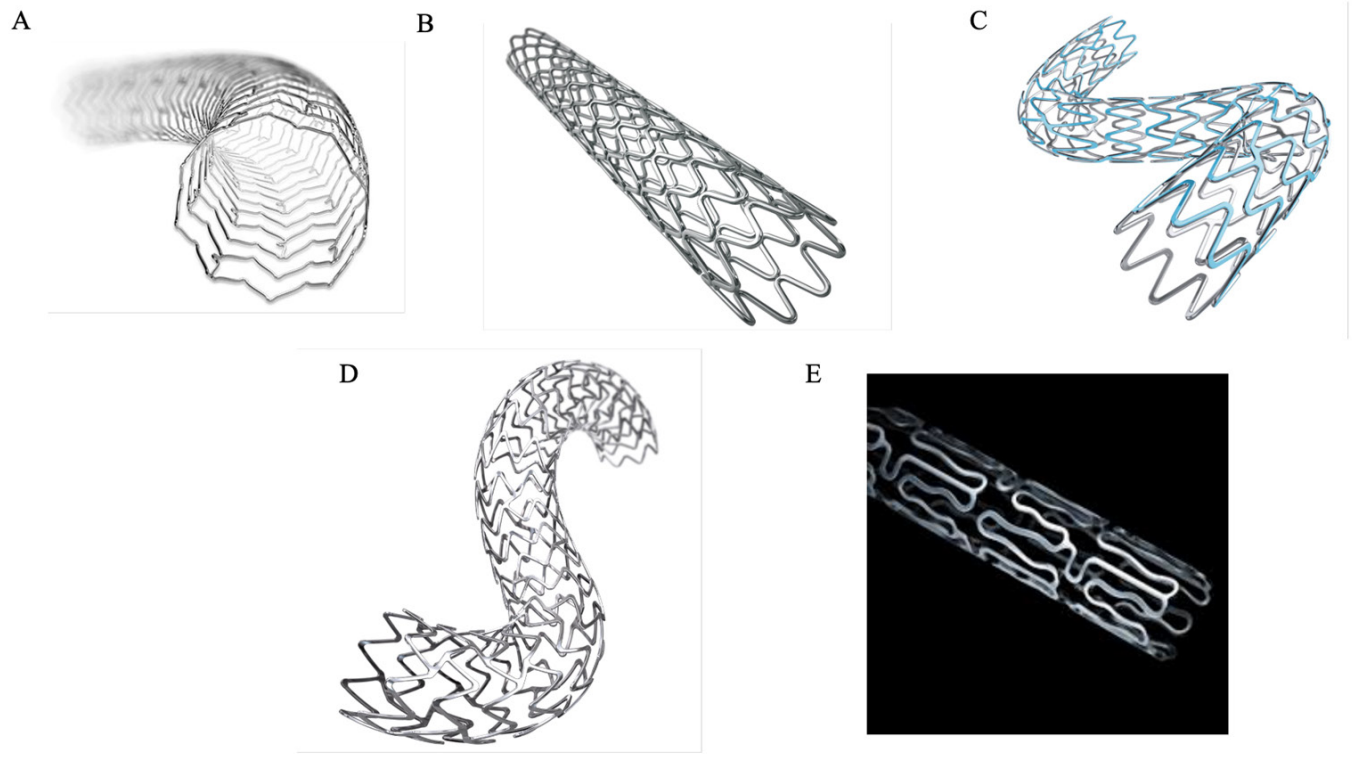
(B) The image shows a schematic of balloon angioplasty, where an inflated balloon compresses plaque to widen the artery and restore blood flow.

Figure 8. Bare-Metal and Drug-Eluting Stent Designs [36]



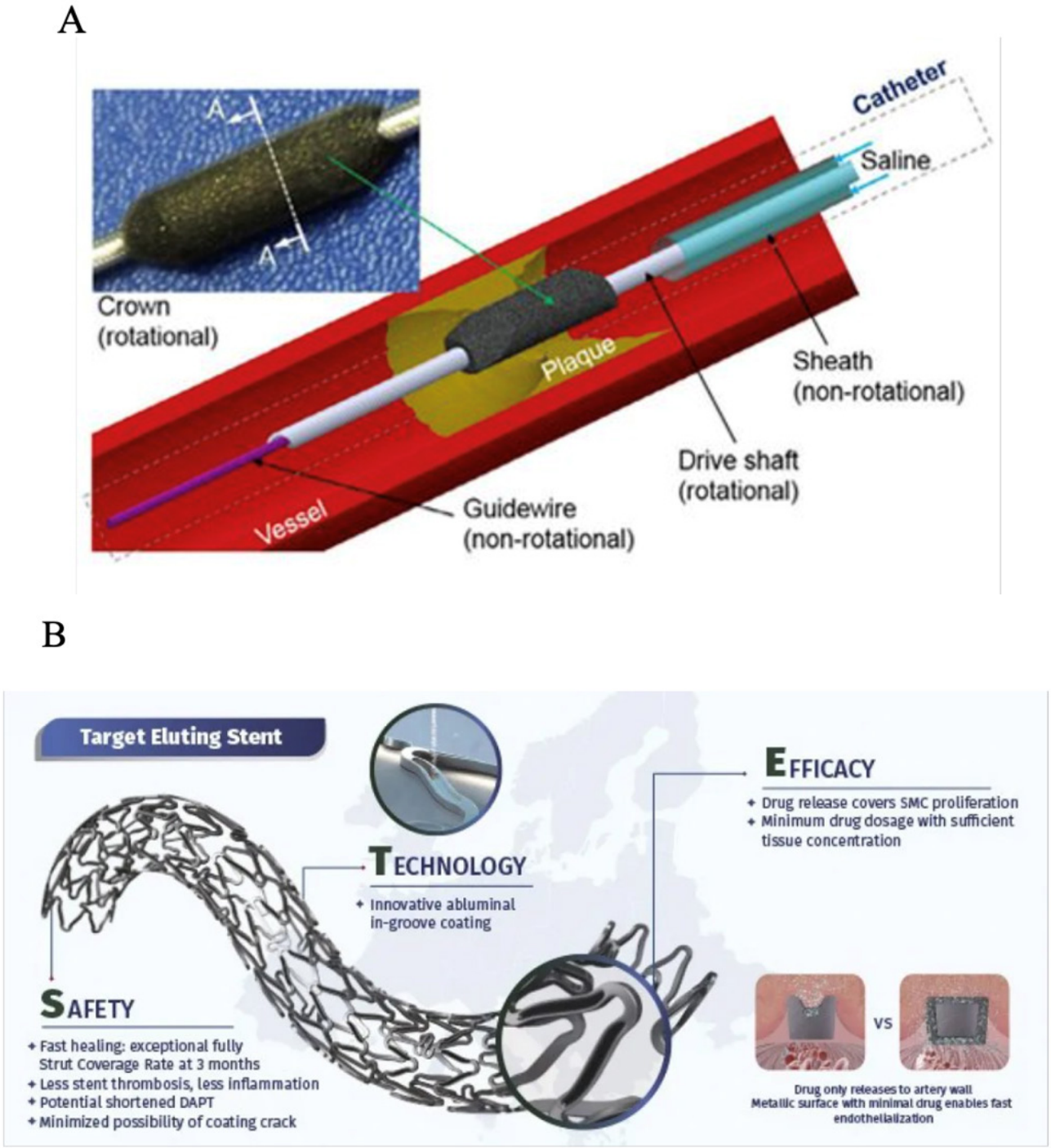
The image shows structural differences between bare-metal stents and two drug-eluting stents: sirolimus-eluting (SES) and biolimus A9-eluting (BES), highlighting drug placement and absorption mechanisms.

Figure 9. Commercially Available Coronary Stents [40-44]



The image shows five FDA-approved stents: (A) Xience Sierra (Abbott), (B) Resolute Onyx (Medtronic), (C) Synergy XD (Boston Scientific), (D) Promus Elite (Boston Scientific), and (E) Multi-Link Vision (Abbott).

Figure 10. Orbital Atherectomy and Firehawk® Stent Design [50-54].



(A) The image shows a schematic of orbital atherectomy using a rotating crown to remove calcified plaque.

(B) The image shows the Firehawk® stent with abluminal groove coating for targeted rapamycin release and minimized inflammation.

Therapeutics and Medications

A growing number of innovative therapeutics are being investigated in trials as well. Currently, in Phase IIIb, there is a drug called Inclisiran [55, 56]. This is a lipid-lowering therapy for individuals with non-obstructive coronary artery disease, and is to be used in conjunction with statins [55, 56]. This works by using a small interfering RNA (siRNA) to block the production of PCSK9 in the liver, therefore enhancing the clearance of LDL-C from the bloodstream [55, 56]. This treatment differs from current medications because it only needs to be administered twice a year, making it more convenient [55, 56]. During the current clinical trials, it is being tested to see if it can reduce the total volume of plaque in the coronary arteries [55, 56]. Additionally, a company named Eli Lilly is developing Lepodisiran, a novel siRNA therapy that targets lipoprotein [57]. This is a genetically determined cardiovascular risk factor that is untreated by current medications [57]. This new therapeutic works by silencing the

messenger RNA responsible for apolipoprotein(a) production, thereby reducing the levels of circulating lipoprotein(a) [Lp(a)] in the blood [57]. The ACCLAIM-Lp(a) trial is currently in Phase 3 and is evaluating the efficacy of Lepodisiran in reducing cardiovascular risk in participants with high lipoproteins [57].

Tissue Engineering Solutions

While no tissue engineering solutions for CAD are currently available on the market, several approaches are actively being explored and developed in research and early clinical settings [58].

A company named Humacyte is developing the Human Acellular Vessel (HAV), which is a vascular graft designed to be an alternative to autologous vessels used in procedures like CABG [58, 59]. This product is seeded with human vascular smooth muscle cells on a biodegradable polymer scaffold [58, 59]. Over time, the cells lay down a natural extracellular matrix that matches the tube-like structure of the blood vessels [58, 59]. The cells are then removed, leaving a non-immunogenic acellular scaffold that mimics the natural blood vessels [58, 59]. After implantation, the patient's cells will repopulate the graft and promote integration and patency [58, 59]. This solution helps avoid complications associated with vein harvesting, demonstrates a lower risk of rejection and infection, and provides an alternative for patients who lack suitable autologous vessels [58, 59]. Although this product is currently in Phase 3 for dialysis access, CAD applications are being explored [58-60].

Another potential tissue engineering product is the aXess graft by Xeltis [61, 62]. This is a novel tissue-engineered vascular device designed to allow natural vessel regeneration through endogenous tissue restoration [61,62]. This is made from a biodegradable supramolecular polymer and provides an initial mechanical scaffold to support blood flow while it is being remodeled by the patient's cells in vivo [61-63]. Eventually, the polymer fully resorbs, leaving behind a living, fully biological vessel composed of the patient's native tissue [61, 62]. Some advantages of this product are that it improves long-term patency, minimizes the risk of immune rejection, and reduces the likelihood of restenosis [61-63]. This was mostly developed for dialysis access, however, it is being explored for potential applications in CABG [61-63]. It is currently undergoing clinical trials in Europe and has promising potential to transform graft-based interventions for CAD [61-63].

CONCLUSION

Coronary artery disease (CAD) remains one of the most pressing global health challenges, responsible for high rates of morbidity and mortality [2] Although there are effective treatments such as medication, surgical procedures, and devices, there is still no cure, and many patients continue to face serious complications [12]. As the global burden grows in rapidly developing regions, there is an increasing demand for more effective, durable, and accessible treatment solutions [45]. Recent advancements in stent design, surgical technologies, and pharmaceutical therapies reflect a strong push toward more targeted and innovative approaches to care [45]. With ongoing research and development, the future of CAD treatment is working to find ways to manage symptoms and address the underlying progression of the disease, intending to improve long-term outcomes for patients worldwide [58]

Abbreviations

coronary artery disease (CAD), extracellular matrix (ECM), vascular smooth muscle cell (VSMC), human acellular vessel (HAV), intravascular lithotripsy (IVL), computed tomography (CT), coronary artery bypass grafting (CABG), dual antiplatelet therapy (DAPT), magnetic resonance imaging (MRI), Food and Drug Administration (FDA), small interfering ribonucleic acid (siRNA), proprotein convertase subtilisin/kexin type 9 (PCSK9), lipoprotein(a) [Lp(a)], computer-aided manufacturing (CAM), computer-aided diagnosis (CADx), ST-elevation myocardial infarction (STEMI), drug-eluting stent (DES), bare-metal stent (BMS).

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Conflict Of Interest

Authors declare that there is no conflict of interest.

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