CARDIOVASCULAR BIOMATERIALS: THE EVOLUTION OF STENTS

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ABSTRACT

Cardiovascular diseases continue to impose a considerable health burden globally and stand as one of the leading causes of mortality in Brazil. Given the strong influence of lifestyle factors on their development, preventive and behavioral interventions are essential. In this context, recent progress in cardiovascular biomaterials, especially in stent technology, presents promising perspectives for improved patient care. This literature review examines the evolution of cardiovascular stents over the past two decades. Research drew on databases such as PubMed, Scopus, SciELO, Elsevier, Web of Science, and Google Scholar. Findings show stent technology advanced from basic bare-metal frames to sophisticated drug-eluting and bioabsorbable designs. These innovations have reduced the need for invasive procedures like Coronary Artery Bypass Grafting, curbing restenosis rates. Stents have thus become integral to coronary artery disease management, providing minimally invasive treatment pathways. Ongoing research and development remain vital to improving stent performance, enhancing patient outcomes, meeting evolving challenges in cardiovascular care.

KEYWORDS

Coronary Artery Disease, Stents, Biomaterials

1. INTRODUCTION

Cardiovascular Diseases (CVD) are characterized as a leading cause of mortality, both in Brazil and among developing nations worldwide. Coronary Heart Disease (CHD), also known as Coronary Artery Disease (CAD), has been historically identified as the primary cause of death in the Brazilian population, with the exception of 2020 when this position was overtaken by COVID-19, relegating CHD to second place. Furthermore, it is worth noting that in 2016, this disease was classified as the foremost contributor to years of life lost among Brazilians, highlighting the urgent need for research aimed at its resolution [1].

A large proportion of these diseases are preventable through educational and preventive measures that address modifiable behaviors, particularly inadequate diet, obesity, tobacco and alcohol use, and insufficient physical activity. Moreover, a notable association with other diseases, such as diabetes mellitus, systemic arterial hypertension, and dyslipidemia, is observed. Therefore, it can be concluded that lifestyle changes contribute to reducing the risk of developing CVD and, consequently, premature death [2].

CAD is characterized by the decreased blood flow to the cardiac muscle (myocardium), which occurs through the obstruction of the coronary arteries responsible for nourishing and oxygenating this organ. This condition is directly related to the degree of occurrence of this occlusion, caused by various factors, such as atherosclerosis, which leads to the stenosis (narrowing) of the arteries, reducing blood flow [3]. Additionally, it is known that the gradual progression of this process leads to various complications, such as pain, restriction of physical activity, and sudden death, as seen in extreme cases [4,5].

The treatment of CAD aims primarily at prevention, as well as the alleviation of anginal symptoms, improvement in the quality of life of individuals, and reduction of mortality. Thus, it is observed that the available treatment options nowadays include physical activity, drug therapy, dietary prescription, Percutaneous Coronary Intervention (PCI) or coronary angioplasty, and Coronary Artery Bypass Grafting (CABG) surgery [6].

PCI was developed in 1977, heralded as a non-surgical treatment for coronary artery obstructions, involving the insertion of a balloon catheter/stents to increase blood flow to the heart. However, stents emerged later, only in 1986, designed to reduce the constant rate of restenosis. Nevertheless, the prevalence of this phenomenon led to the introduction of drug-eluting stents in 1999 [7]. As expressed in the CENIC/SBHCI registry of 1999, stent implantation became the standard device used for this intervention [8].

Stents are biomaterials developed primarily to be implemented in processes related to the cardiovascular system. Thus, through technological and scientific developments, different types of stents have been generated, classified as bare metal (first generation), drug-eluting and polymer-coated (second generation), and bioabsorbable (third generation). It is also worth mentioning that this methodology is a less invasive alternative to open-heart surgery [9,10,11]. This literature review seeks to delve into the evolutionary trajectory of cardiovascular stents, accentuating their pivotal role in addressing coronary artery disease.

2. METHODOLOGY

The research was conducted using secondary databases in Portuguese, Spanish, and English over the past 20 years. The platforms used for the search included PubMed, Scopus, Scielo, Elsevier, Web of Science, and Google Scholar. The search terms employed were “stents,” “metallic stent,” “drug-eluting stent,” “polymeric stent,” “bioabsorbable stent,” “stent thrombosis,” “nickel-titanium stent,” and “nitinol stent.” Additionally, foundational articles with older references were also considered. Articles were included if they primarily addressed the three generations of stents and involved cardiac stents used in human subjects. Studies focusing on other biomaterials applied to the cardiovascular system or those conducted exclusively in animal models were excluded. The search covered the period between January 2005 and December 2025. A total of 378 articles were initially identified. After the removal of duplicates and screening of titles and abstracts, 142 studies were selected for full-text analysis. Following the application of inclusion and exclusion criteria, 46 articles were included in this review.

As this is a narrative literature review, no formal tools for risk of bias or methodological quality assessment, such as CASP or JBI, were applied. The selection of studies was based on thematic relevance to the evolution of cardiovascular stents, clinical application in humans, and the presence of information regarding stent generations, materials, and clinical outcomes.Data from each selected study were manually extracted using a structured template that included variables such as stent generation, material composition, type of drug eluted when applicable, clinical outcomes including restenosis and thrombosis, and the context of use. The synthesis of the findings was carried out through thematic narrative analysis, structured around the technological and generational evolution of the stents. Two reviewers independently conducted the study selection and data extraction. Any discrepancies were resolved through discussion and consensus. This review follows a narrative format and aims to provide a critical overview of advances in cardiovascular stents, without attempting to perform a systematic synthesis of outcomes.

3. Results and Discussion

3.1. NiTi Cardiac Stents: Perspectives from Materials Science and Engineering

Stents are tubular prostheses used to provide mechanical support to stenosed arteries or other non-vascular conduits until the risk of complete closure is eliminated. There are different types of stents, including bare-metal, drug-eluting, bioabsorbable, and dual-therapy stents. Cardiovascular stents, expandable tubular structures, are used to treat narrowed arteries without the need for open-heart surgery [9-12]. Figure 1 below illustrates the progressive development of atheromatous plaque in the arterial wall.

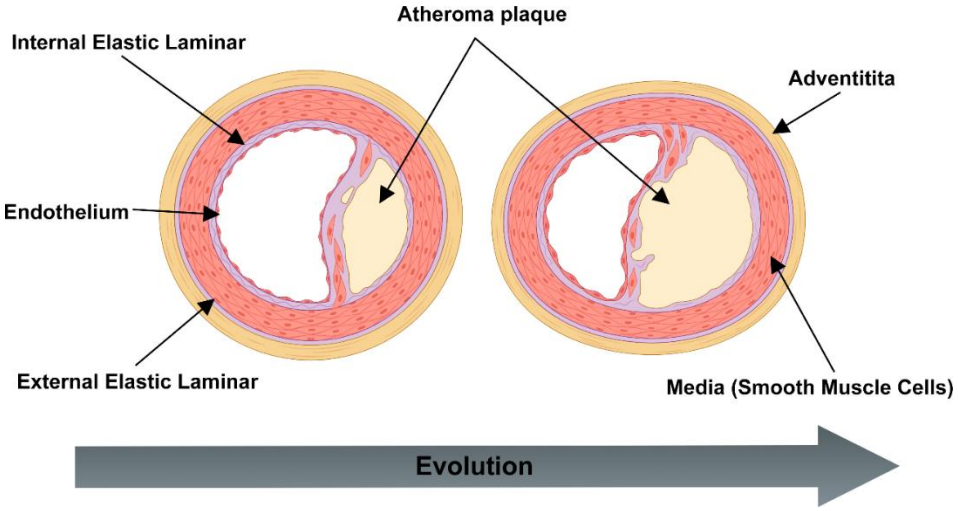

Figure 1. Progressive development of atheroma plaque in the arterial wall
Source: by the authors.

Classification is based on their expansion nature and design, which can be divided into two main groups: self-expanding and balloon-expandable stents. First-generation stents were predominantly metallic, known as bare-metal stents, mainly made from stainless steel, chromium-cobalt (CoCr) alloys for balloon-expandable stents, and nickel-titanium (nitinol) alloys for self-expanding ones. However, despite surgical advancements, these stents had disadvantages such as a higher risk of thrombosis and restenosis. During procedures, intravascular lesions were frequent, leading to In-Stent Restenosis (ISR) - the main cause of arterial blockage over time. ISR results from excessive smooth muscle cell proliferation inside the blood vessel, progressively blocking it [9,12,13].

The first clinical use of stents was introduced to reduce the risk associated with percutaneous transluminal coronary angioplasty, a procedure used to reopen narrowed arteries. This procedure uses a catheter with a folded balloon, inflated in the narrowed area of the artery to compress the obstructive plaque and widen the obstructed inner wall [14,15]. Nonetheless, the elevated mechanical stress exerted by the device can heighten the risk of thrombosis, as it may lead to vascular injury during catheter placement and balloon inflation [16].

The concept of the cardiovascular stent subsequently revolutionized the treatment of coronary artery-related diseases. Stents represent a prudent alternative to surgery, first introduced with balloon angioplasty in 1977 by Grüntzig (1978). This evolution continued with the first human prosthesis of a self-expanding stent in 1986 and subsequently in 1987 with the first human prosthesis of a balloon-expandable stent [17,18].

Even with technological advances and the emergence of new generations of stents, the ISR rate remains an active issue. The ideal stent should exhibit characteristics such as low profile, appropriate expansion, adequate radial strength, minimal recoil, sufficient flexibility, radiopacity/magnetic resonance compatibility, thrombosis resistance, and drug-release capability to prevent restenosis [18].

Metals play a crucial role as stent materials, chosen for their mechanical properties and ability to be visualized in X-ray images. Metallic stents and stent grafts have assumed significant importance in non-invasive medical procedures. Thus, there is constant evolution in new techniques for treatments using metallic stents, and this evolution is expected to continue in the foreseeable future. Although innovative ideas for treatments are regularly presented, research and development of suitable materials for this device remain notable challenges in the perspective of materials science and engineering [12,16,19].

Material selection is a critical consideration, requiring various essential characteristics. These materials must exhibit sufficient mechanical strength and ductility while ensuring biocompatibility and antimicrobial properties [20,21]. The cardiovascular stent must have sufficient elasticity to be compressed for delivery and then expand in the lesion area, maintaining the necessary size when implanted. An ideal stent should possess properties as formulated by Mani *et al*. (2007):

(1) ability to be compressed on the balloon catheter;
(2) good expansibility rate;
(3) sufficient radial strength and negligible recoil;
(4) adequate flexibility;
(5) radiopacity/magnetic resonance imaging with appropriate compatibility;
(6) high thromboresistance;
(7) absence of restenosis after implantation;
(8) non-cytotoxicity;
(9) drug delivery capability.

However, conventional metallic materials demonstrate suitability for these properties when appropriate metal alloys are chosen. Moreover, it is important to note that other artificial organs and medical devices are not limited to metals alone, including ceramics, polymers and their combinations, as well as natural biomaterials. In the context of coronary applications, bare metal stents (uncoated) were the first to be used. These stents exhibit remarkable mechanical properties and enhanced corrosion resistance and are commonly made from materials such as stainless steel 316L (316L SS), platinum-iridium alloy (Pt-Ir), Co-Cr alloy, and NiTi [12,13,22].

Initial stents, and most current ones, are primarily made with stainless steel 316L due to its mechanical characteristics and corrosion resistance. However, these materials face limitations in terms of minimum radiopacity and nickel release. Attempts to improve radiopacity through coating stainless steel 316L stents with gold were not satisfactory [10,23]. In contrast, greater success was achieved in fluoroscopic visualization with NiTi ones with the addition of radiopaque markers fixed at the stent ends. To address the problems related to nickel release in stents made from stainless steel 316L and NiTi, researchers applied surface treatments, effectively reducing the nickel content on the surface and increasing corrosion resistance [4,24,25]. Stainless steel, despite its strength and hardness, presents limited biocompatibility, making it unfavorable for preventing thrombus formation. Although NiTi alloy has better short-term biocompatibility, it may over time result in nickel migration, causing immune response problems [23,26,27].

In the context of stents, notable examples using Ni-Ti alloy include the Smart stent and the Radius stent. However, it is important to note that this alloy may have problems such as cracking and pitting corrosion, with corrosion noted in aortic endoprostheses, evidencing pitting and craters in the alloy. The range of compositions exhibiting the desired properties in the Ni-Ti alloy is narrow, usually close to the atomic ratio of 1:1 between titanium and nickel. Additionally, the specific properties of Ni-Ti are influenced by transformation temperature, composition, presence of impurities, and thermal history [28,29].

In this sense, due to its shape memory effect, and thus its expansion with body temperature, NiTi stents ensure the return of fluid flow. Additionally, due to the symmetrical crystalline atomic arrangement of one nickel atom associated with four titanium atoms, this corresponds to a lower susceptibility of nickel to come into contact with the organism. Titanium alloys are more recommended than stainless steel due to their elastic properties [11].

NiTi is a highly elastic and fracture-resistant alloy; however, its nickel release can contribute to issues such as intimal hyperplasia. While titanium is inert, nickel, when released in high levels, can cause respiratory problems and allergic reactions. The titanium oxide layer present on nitinol stents stabilizes its surface, preventing harmful reactions with human tissues. The fracture of NiTi stents may be related to surface polishing and coating with amorphous oxides. Some research has identified that NiTi can induce an inflammatory response, promoting an increase in interleukin-1ß secretion by monocytes. These facts indicate the need to carefully consider the structural integrity and potential effects of NiTi in medical devices [30].

3.2. First, Second, and Third Generation Coronary Stents

Coronary stents were introduced in the 1980s, and over the years, improvements and techniques have been developed to prevent complications and possible issues. In this regard, since the inception of stent use for CAD, they have been associated with Dual Antiplatelet Therapy (DAPT) to prevent thrombosis. However, this type of therapy has a disadvantage of increasing the risk of bleeding. Therefore, acetylsalicylic acid (ASA) and a P2Y12 inhibitor (such as clopidogrel, ticagrelor, or prasugrel) are typically used. For patients with drug-eluting stents, it is common to recommend DAPT for a longer period, usually at least 12 months after stent placement, to prevent thrombotic events [11,31,32]. Table 1 and Figure 2 below present the main characteristics and comparative schematic of first, second and third-generation stents.

Table 1. Main characteristics of stents in relation to generation

Generation	Stent type	Material	Pharmacological Coating	Primary Purpose
1ª	Bare Metal Stents	Stainless steel or metal alloys	Absent	Mechanical support, vessel closure prevention
2ª	Drug-Eluting Stents	Stainless steel or metal alloys	Present	Drug release to reduce restenosis
3ª	Bioabsorbable Stents	Bioabsorbable materials (e.g., biodegradable polymers)	Some with pharmacological coating	Not only provide temporary support but also are absorbed by the body eventually
3ª	Biologic-Coated Stents	Various materials	Some with biological coating	Provide structural support and promote integration with vascular tissues
3ª	Drug-Eluting Stents with Sustained Release	Stainless steel or metal alloys coated with polymers that release drugs over time	Present	Sustained drug release

Adapted from Prado (2021); Oliveira (2021); Araujo (2023).

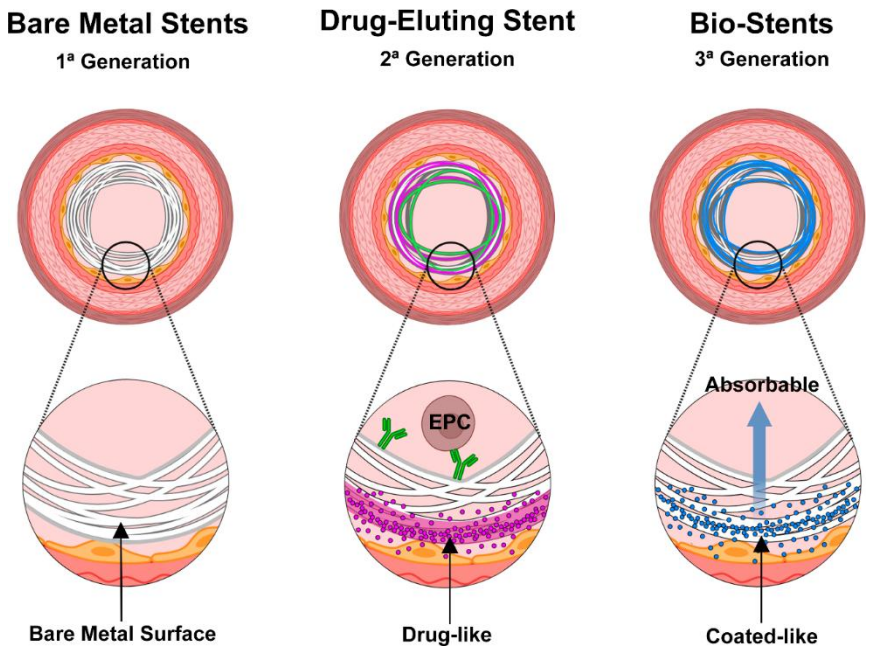

Figure 2. Comparative schematic of first, second, and third-generation stents
Source: by the authors.

In this scenario, non-pharmacological metallic stents (first generation) have an advantage because one month after implantation, thanks to the rapid proliferation of fibro-intimal tissue, the risk of bleeding is lower in the short term. However, pharmacological stents are still more recommended due to the lower risk of restenosis. There are various types of pharmacological stents (second generation), such as sirolimus-eluting, paclitaxel-eluting, cobalt-chromium everolimus-eluting, platinum-chromium everolimus-eluting, zotarolimus-eluting Endeavor, and zotarolimus-eluting Resolute stents; among these, there are first, second, and third-generation stents, with the latter two having thinner struts that cause fewer risks of vascular injury, inflammation, and thrombus formation compared to thicker struts. Although they have a higher risk of deformation, second and third-generation stents have a difference in the platform of stainless, steel chrome alloys - from 130-149 to 81-91 μm) - which reduces target vessel myocardial infarction during the procedure and late [32-34].

Second-generation pharmacological stents with durable polymer coatings have the ability to reduce lumen loss in the blood vessel, decreasing target lesion and revascularization rates compared to first-generation stents. The polymer's function is to control the drug release directly into the vessel lesion to avoid adverse effects. However, in high-risk patients, an increased risk of late stent thrombosis has been reported due to polymer hypersensitivity reactions. Biodegradable polymeric drug-eluting stents have polymer coatings that degrade over a period ranging from 2 to 9 months. The aim of this design was long-term safety, having the same safety as metallic stents and the same effectiveness as durable polymer pharmacological stents, which remain adhered to the stent after drug elution but may cause local hypersensitivity reactions with eosinophilic infiltration increasing thrombotic potential [35-37].

Comparing next-generation durable polymer stents with everolimus and cobalt-chromium to metallic stents, there is a reduction in thrombosis risk. The EXAMINATION study showed that over a two-year follow-up, these third-generation stents were associated with a lower risk of thrombosis. In this context, the current gold standard is pharmacological coronary stents of metallic alloys with bioabsorbable polymer [32,34,38].

Although the second-generation pharmacological stents were developed to improve effectiveness in preventing vessel restenosis after coronary interventions, comparative studies have not shown significant differences with conventional stents (FERREIRA, 2020). A study comparing two main types of second-generation stents: one made of cobalt-chromium with everolimus elution, known for its low durable polymer load, and another made of stainless steel with biolimus A9 elution, characterized by a bioabsorbable polymer. In this randomized comparison, both stents were effective in suppressing neointimal response in the medium term and showed no indirect signs of local toxicity and late thrombosis by intracoronary ultrasound results. Overall, for most patients undergoing percutaneous coronary interventions, pharmacological stents are often considered a preferred option compared to metallic stents. This is due to the ability of pharmacological stents to reduce restenosis rates, thereby reducing the need for additional procedures to treat recurrent artery narrowing [11,35].

Pharmacological stents have a similar basic structure to metallic stents but are coated with a polymer that releases anti-proliferative medications over a long period, reducing the restenosis rate compared to non-pharmacological metallic stents. However, the choice of the most suitable stent type depends on various factors, including the patient's coronary anatomy, bleeding risk, patient adherence to antiplatelet therapy, and other specific clinical conditions [29,36,27].

The ESC/EACTS Guidelines on Myocardial Revascularization of 2018 address the use of metallic stents in certain contexts. These guidelines indicate that metallic stents are a suitable option in

certain situations, especially in patients with a low risk of bleeding, difficulty adhering to antiplatelet therapy, or a need for treatment with a limited dual antiplatelet therapy time [29].

However, it is important to note that, compared to pharmacological stents, metallic stents are associated with higher rates of restenosis, leading to the need for possible additional interventions at the treated site. Therefore, the use of pharmacological stents is still more appropriate in certain specific clinical scenarios, and the risk of restenosis versus bleeding risk and the patient's ability to follow recommended antiplatelet therapy should be taken into consideration [11].

The main challenges of coronary stents are possible inflammations and thromboses that may occur over time. Among the possible major isolated or combined cardiovascular and cerebrovascular events for the analysis of a cardiac stent, there are a new myocardial infarction, stent thrombosis, target vessel revascularization, stroke, and death [32].

The three main components of the stent are the metal platform/stem, the drug (with those from the limus family having a much higher safety profile), and the polymer that is the drug carrier to be released into the vessel wall. The evolution of stents, considering the polymers, progressed through various stages Durable polymer stents initially demonstrated efficacy in reducing late lumen loss in blood vessels but were also associated with an increased risk of late stent thrombosis in some situations, especially in high-risk patients. Next, bioabsorbable polymer stents emerged, designed to degrade over time, thus reducing complications associated with durable polymers [11].

The next evolutionary phase was the introduction of non-polymeric stents, which sought to minimize or completely eliminate the use of polymers as part of the stent, aiming to reduce adverse reactions related to polymers. Finally, advancements culminated in bioabsorbable stents, which besides not relying on polymers, are designed to completely dissolve after a certain period in the body, offering a safer long-term alternative for the treatment of heart diseases. The greatest challenge in stent manufacturing is polymers, the development of less thrombogenic and more biocompatible polymers. Among the problems related to first-generation polymers, there is a possible not so uniform distribution, the entrapment of stems preventing good stent expansion, and delamination. In this context, when durable, polymers can be a continuous source of inflammation, increase thrombosis risk, and cause delayed endothelialization. Finally, advancements culminated in bioabsorbable stents, which besides not relying on polymers, are designed to completely dissolve after a certain period in the body, offering a safer long-term alternative for the treatment of heart diseases [33,34].

An ideal intravascular stent should have opacity to facilitate visualization during insertion, radial strength to resist elastic remodeling, and post-implantation precision. A simple implantation system, with flexibility to pass through tortuous vessels, radial elasticity to resist external compression, and a small profile with great expansion capacity are essential. Furthermore, it is important that the stent presents minimal shortening after release, allowing easy rescue in case of deployment failures [35,36].

Accessibility to side branches is crucial, while minimal induction of problems such as intimal hyperplasia, thrombosis, and corrosion, along with durability and affordable price, are highly desirable characteristics. The second generation of drug-eluting stents was developed to maintain effectiveness in preventing restenosis of previous stents, reducing target vessel revascularization rates after PCI, and enhancing their safety. These new stents incorporated more biocompatible and bioabsorbable polymers to control drug release, and derivatives of sirolimus (everolimus and zotarolimus) to improve lipophilicity and cellular uptake. Among the representatives of this generation, the cobalt-chromium stent (605L) using everolimus with a durable polymer from Xience V® (Abbott Vascular, Santa Clara, United States), and the stainless-steel stent (316L)

releasing biolimus A9 with a bioabsorbable polymer derived from polylactic acid (PLA) from BioMatrix® (Biosensors International, Singapore) stand out [36-38].

Regarding non-polymeric stents, the Biolimus A9-coated BioFreedom stent is a stainless-steel stent with roughness, coated with medicine that comes into contact with the vessel wall, which demonstrated low median late loss of 0.17 mm at 12 months of follow-up in a 2012 study. The STEALTH I study demonstrated the efficacy and safety of Biolimus A9-eluting stents (BA9) in reducing angiographic late loss and presenting a low incidence of major cardiac events; they were highly effective in inhibiting intra-stent neointimal proliferation when compared to control stents, showing a minimum percentage of intra-stent obstruction at 6 months of follow-up [38].

In an animal model, 98% of the drug was found to have penetrated the vessel wall after one month. This suggests that the device could present a potential safety benefit and a reduced need for prolonged dual antiplatelet therapy (DAPT) compared to polymer-coated drug-eluting stents. The study also contributed to a better understanding of an underrepresented group of patients undergoing percutaneous coronary intervention, allowing for a clearer quantification of both thrombotic and hemorrhagic risks. Additionally, it may reduce the requirement for target lesion revascularization in patients who cannot tolerate extended DAPT and supports assessment of a shorter therapy duration already applied with active stents [33-36].

A recent meta-analysis evaluated the mixed treatment of 258,544 patients from 126 randomized trials comparing durable or biodegradable polymer drug-eluting stents, approved by the Food and Drug Administration, among themselves and with conventional metal stents. This study concluded that biodegradable polymer drug-eluting stents are superior to first-generation durable polymer drug-eluting stents but not to new-generation durable polymer stents in reducing target vessel revascularization. Last-generation durable polymer stents, especially everolimus and chromium-cobalt-eluting stents, present the best combination of efficacy and safety. The study also concluded that further research should be conducted to prove the usefulness of biodegradable polymer stents in the context of clinical outcomes with new-generation durable polymer stents [34].

Araujo *et al*. (2023) conducted a study in southern Brazil, comparing an ultra-thin-strut sirolimus-eluting stent (Inspiron®) with other third-generation drug-eluting stent platforms in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI). In this study, 706 patients were analyzed comparing the two stents, and both groups had similar favorable outcomes after a 17-month follow-up, supporting that Inspiron® is safe and effective in patients with STEMI [32].

A recent study compared the clinical performance of two biodegradable polymer drug-eluting stents after five years from the initial procedure. One hundred seventy patients (194 lesions) were randomized in a 2:1 ratio for treatment with the sirolimus-eluting Inspiron™ stent (SES) or the biolimus-eluting Biomatrix™ Flex stent (BES) latest generation, respectively, with the primary endpoint being the five-year rate of combined major adverse cardiac events defined as cardiac death, myocardial infarction, or target lesion revascularization. At five years, the primary endpoint occurred in 12.5% and 17.9% for the SES and BES groups, respectively (p=0.4). The main finding was that patients treated with the sirolimus-eluting Inspiron™ stent had good outcomes at five years, comparable to the control stent with biolimus elution Biomatrix™ Flex latest generation, and no cases of thrombosis were reported in the first year of follow-up [31].

An advantage of third-generation stents with bioabsorbable polymer is that it allows controlled drug release and slow dissolution of the polymeric material, avoiding stimuli for chronic inflammation and thrombosis risk caused by residual polymer post-elution. Researchers at the University of Campinas have been studying absorbable coronary stents that release nitric oxide to

promote vasodilation. The photocurable polymeric material was made by 3D printing. Nitric oxide release occurs for an extended period, and the material is slowly dissolved by the body, providing a technological advantage for the implant [11,37].

3.3. Technologies and Production Methods and Concerns

Additive manufacturing, unlike conventional manufacturing methods for stents, results in personalized stents for each patient, offering design flexibility, cost-efficient production, and less material waste. An additive manufacturing technique called Laser Powder Bed Fusion (LPBF) has been studied for stent manufacturing, by a high-energy fiber laser that melts the metallic powder. Thus, stents are built part by part from a digitally designed project [39].

The current available vascular stents are manufactured from cobalt-chromium alloys, nitinol, and stainless steels, mainly using conventional methods such as laser cutting of microtubes and photochemistry. The use of LPBF techniques for stent manufacturing offers advantages over conventional methods, including waste reduction in production (compared to laser micromachining) and improvement in geometric flexibility of stent production, besides the great potential for customization and specific treatment for each patient - recently, several studies have focused on studying and evaluating the use of this technique for stent geometry production viability [39,40].

Nitinol is currently being used as self-expanding stents for treating occluded vessels. However, some mechanical failures have been observed, which can lead to stent support loss, thrombus formation, and restenosis. Partial or complete stent fractures have been reported in aortic, renal, and pulmonary implants, as well as in arteries of the lower limbs, such as the superficial femoral and popliteal arteries. Consequently, the long-term structural stability of a stent model must be considered a key parameter in its design. In light of this, it becomes essential to refine the stent structure through a detailed engineering assessment capable of analyzing the connection between its geometry and mechanical performance. This process should aim to improve fatigue resistance without compromising other essential biomechanical criteria [39].

Overall, the protective film of NiTi is stable; however, in contact with physiological fluids, such as in medical application, it may undergo electrochemical reactions due to the aggressive environment of the human body, aggravated by mechanical forces and wear. The presence of chlorine ions from plasma can dissolve areas where the protective film is not fully formed, creating a metal/chlorine interface. Surface characteristics, composition, and structure influence these reactions. These sites with inadequate passivation promote pitting corrosion, a form of localized corrosion that causes the formation of small holes in the metal, similar to pits. In addition to not being able to come into contact with the exposed environment to avoid allergy and rejection, it is necessary for the stents' surface to present roughness, allowing good cellular activity. Therefore, corrosion, wettability, and fatigue tests should be carried out to verify resistance, hydrophilicity, and service life, respectively [11].

Although NiTi self-expanding stents have superelastic and shape memory properties, one of the main issues with them is fatigue fracture, as they are subjected to a long-term pulsatile cyclic load by heartbeats (typically 4×107 cycles/year). A study proposed a structural optimization approach of the stent scaffold, using finite element analysis and multi-objective genetic algorithms to reduce the maximum deformation of the scaffold, increasing the stent's lifespan. Another study focused on an optimization-based simulation methodology to enhance the fatigue strength of NiTi stents, using Response Surface Methodology (RSM), Kriging interpolation, and Sequential Quadratic Programming (SQP) algorithm, and reduced the deformation amplitude generated by cyclic pulsatile load, which was able to improve fatigue resistance, prolonging the stent's lifespan [39].

In a study, percutaneous embolization of acquired arteriovenous fistulas (AVFs) was successfully performed using a self-expanding nitinol vascular plug in two cases, demonstrating its efficacy even when dual antiplatelet therapy was in use. This device consisted of a cylindrical prosthesis made of an uncovered nitinol mesh, featuring a reduced profile, eliminating the need for a sheath and allowing repositioning and removal when necessary. Additionally, the plug was compatible with 5 to 7 F guiding catheters, varying depending on the chosen model, and it was recommended that its size be 30 to 50% larger than the target vessel diameter to minimize the risk of distal embolization. Thus, in both cases of iatrogenic aorto-coronary fistulas undergoing percutaneous occlusion with a self-expanding NiTi device (vascular plug), success was achieved [40,41].

Two studies reported severe corrosion in first-generation nitinol endovascular grafts in just 5 months after implantation. Another study found corrosion in explanted cardiovascular stents made of nitinol, stainless steel, and cobalt-based alloys. However, these studies predominantly identified corrosion qualitatively through microscopy and did not have corresponding controls to definitively distinguish in vivo corrosion from pre-existing characteristics in the manufacturing process. It was found that nitinol stent groups with rupture potentials less than 200 mV showed evidence of in vivo corrosion after 6 months of implantation. On the other hand, nitinol stents with potentials starting at values above about 600 mV did not show signs of in vivo corrosion after the same 6-month period of implantation. In a study, the placement of nitinol stents coated with Dacron® in dogs' aorta was evaluated, concluding that, despite the coated stents inducing greater intimal hyperplasia, the luminal area was not altered [30].

Significant corrosion of stent materials can impair the structure or function of the device and trigger a biological response. In cardiovascular stents, corrosion by-products can provoke an inflammatory response in cells, increasing neointima growth in the vessel, leading to restenosis; metal ions can be transported systemically by blood flow or remain in vascular tissues. This is especially relevant for NiTi implants, as about half of its composition is nickel, a substance associated with allergic reactions, nephrotoxicity, and carcinogenicity at various doses. Although adverse events related to hypersensitivity (e.g., contact dermatitis) have been reported in cardiovascular implants, a direct causal link between corrosion and these adverse events has not yet been established. Research studies capable of more directly identifying the ramifications of corrosion in medical implant biomaterials, especially those containing nickel, would be critical to fill this critical knowledge gap [42].

A recent study explored the potential of additive manufacturing in producing personalized nitinol stents for treating complex peripheral arterial stenoses in lower limbs. Using the LPBF method, two stent models were investigated to analyze how process parameters impact their geometry, size, structural integrity, and phase transformations. The results showed that nitinol stents were successfully manufactured by LPBF, with strut diameters ranging from 250 µm to ≈ 560 µm. The stents' modulus of elasticity ranged from 56 to 73 GPa, aligning with conventional austenitic NiTi. This concludes that this approach could replace the conventional laser cutting process of metal tubes in manufacturing these medical devices. The application of LPBF showed potential to minimize material waste and allow the production of customized stents for patients by adjusting the geometry according to individual needs. These stents did not exhibit significant porosity and displayed modulus of elasticity comparable to commercial NiTi alloys. The importance of controlling the laser energy input was highlighted, which, when lower, resulted in less Ni evaporation, ensuring proper stent construction [40].

In summary, the development of coronary stents has been the focus of many medical and technological investigations, aiming to improve the safety and efficacy of these devices. One of the main challenges faced is the possibility of inflammation and thrombosis over time, events that can have serious consequences for patients. Innovative strategies, such as third-generation stents

with bioabsorbable polymers, have shown advantages by allowing gradual drug release and slow dissolution of the polymeric material, reducing stimuli for chronic inflammation and minimizing thrombosis risks [42,43].

Despite the promising advances in additive manufacturing and the application of NiTi alloys in cardiovascular stents, there are still important gaps regarding long-term in vivo validation and regulatory approval. While some studies have demonstrated the mechanical viability of 3D-printed stents and identified corrosion behaviors of NiTi under physiological conditions [11,30,39,42], the absence of extended clinical follow-up data limits definitive conclusions about their long-term safety and durability. Furthermore, the integration of these technologies into clinical practice faces regulatory challenges, as devices must undergo rigorous biocompatibility, fatigue resistance, and corrosion testing before approval by health authorities. In this context, studies have emphasized the importance of optimizing stent geometry and surface characteristics to mitigate risks such as fracture, ion release, and late complications [11,30,40]. Therefore, advancing from experimental to clinical stages will require not only technological refinement but also compliance with strict regulatory standards to ensure both efficacy and patient safety.

Additionally, studies are being conducted with coronary stents that release nitric oxide to promote vasodilation in cases of stenosis, using a photocurable polymeric material made by additive manufacturing. Meanwhile, NiTi, used in self-expanding stents, has faced mechanical challenges, such as partial or total fractures, compromising stent support and potentially resulting in complications such as thrombus formation and restenosis [11,30].

The ideal characteristics of a stent for carotid arteries involve a careful balance between high flexibility and conformability, allowing adaptation to cases with tortuous anatomy and broad plaque coverage to avoid late embolization of debris. Stents have annular rings arranged sequentially through bridges, with variations between open, closed, or hybrid cell designs, depending on the density of bridges between the rings. Open-cell stents have segments with space between adjacent rings, allowing better adaptation to vessel anatomy, but the plaque has less extensive coverage leading to a risk of tissue prolapse. Closed-cell stent plaques have greater coverage, but compliance is limited by having a higher density of bridge interconnections. Despite this difference, recent studies show that there is no significant difference in treatment efficacy and safety [44,45,46].

The search for enhancements in these devices involves studies that analyze the relationship between stent design and its structural strength, aiming to prolong the lifespan and ensure its integrity over time. However, NiTi corrosion, although rare, is a problem deserving attention, especially when in contact with physiological fluids. Elucidating the relationship between in vivo corrosion and pre-clinical characterization may be crucial to more accurately predict the safety and performance of NiTi devices, highlighting the importance of developing engineering techniques for optimizing the design of these stents [30,43].

4. CONCLUSION

The development of cardiovascular stents marks a significant advancement in the treatment of heart conditions like CAD. By restoring blood flow to the heart muscle, stents offer a less invasive alternative to traditional surgeries. Their evolution from bare metal to bioabsorbable designs demonstrates continuous innovation aimed at improving patient outcomes. Stents play a fundamental role in symptoms relief, enhancing quality of life, and reducing mortality rates associated with CAD. Ongoing advancements in stent technology highlight the need for long-term clinical trials comparing new-generation stents in diverse populations. Further exploration of bioabsorbable and polymer-free stents, additive manufacturing techniques for customized devices,

and corrosion resistance studies in NiTi alloys are recommended. These paths may offer safer and more effective solutions in cardiovascular interventions.

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