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Comparison of properties of cardiac vascular stent materials

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Abstract. Cardiovascular disease (CVD) is a serious threat to human health and life, an important public safety issue, and one of the leading causes of death in the world. Typically, the treatment involves implanting stents in the patient's blood vessels to support the vessels and keep the blood flow open so that oxygen and nutrients can be delivered. This paper will discuss and compare the three main categories of vascular stent materials: 1) organic materials; 2) inorganic materials; and 3) composite materials. Existing bio-organic materials are mostly organic materials that exist in large quantities in the human body and are mostly used as bio-coatings applied to metal bodies, in addition to polyester cardiovascular scaffolds, which are a major category for future development. Inorganic materials are currently the main components of cardiovascular scaffolds, mainly metals, and bio-ceramics. Metals, as the earliest basic materials utilized by mankind, also play a major role in cardiovascular scaffolds. To enhance some specific properties of existing cardiovascular scaffolds, composite materials have been developed, and in the field of materials engineering composite materials are regarded as a major project for future development. This paper will discuss the advantages and disadvantages of each material in turn and explore the future direction of materials in this field. The development of cardiac vascular stent materials will make up for the deficiencies in clinical medicine that cannot be solved by drug-based therapies and is an indispensable part of the development of human science and technology.

Keywords: cardiovascular stents, material engineering, in-stent restenosis.

1. Introduction

Cardiovascular stents as life-saving medical devices are important for the development of medicine and material science. Since the 20th century, several medical doctors and scientists have invented and designed different cardiovascular stents. The introduction of cardiovascular stents has saved thousands of patients, greatly prolonged their lives, solved previously untreatable diseases through drugs and surgery, greatly improved the quality of life of patients, and is one of the indispensable medical devices in the field of contemporary medicine and material science. However, due to its tiny shape and structure and the need to be placed in the patient's body for a long period of time to achieve a high degree of biocompatibility, corrosion resistance, and structural stability, and the need for researchers and developers to have knowledge in the fields of medicine, materials engineering, microelectronics, and other areas, the research and development of cardiovascular scaffolds is still fraught with difficulties. At the same time, however, there is also lots of space for development and prospects, and future research and development will mainly focus on reducing the re-narrowing of cardiovascular stents after

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implantation, pre-treatment of inflammation and complications, and the role and influence of different coating materials [1].

The predecessor of the cardiac vascular stent was the balloon angioplasty, invented by Charles Dotter, a technique that dilates the aorta by inflating the aorta through the implantation of a balloon catheter to dilate arteries with atheromatous plaque [2]. However, this technique has not been widely used in clinical practice because it can lead to overdistension and rupture of the vessel. Julio Palmaz then proposed that a stent could be implanted in the patient by attaching it to the tail of the balloon and passing it through the subcutaneous vascular system. The cardiovascular stent will inflate the balloon after reaching the blockage position to deploy the support to support the inner wall of the blockage position. However, the first successful human implantation was not performed until 1986, because before then doctors needed to solve two major challenges that arose after vascular stent implantation [3]. According to the medical records at the time, the implantation was a milestone success, greatly reducing the patient's mortality and prolonging his survival. According to the patient's imaging follow-up, the implantation of the vascular stent greatly expanded the minimum lumen diameter changing from a mean [±SD] of 1.88±0.43 to 2.48±0.51 mm and from 37±12 to 21±10 percent, respectively; $P<0.0001$ [3].

However, due to the limited technology and lack of materials at the time, doctors used stainless steel and cobalt-chromium alloys. As a support material, since these two materials are not highly biocompatible, they produce a large amount of intimal hyperplasia in the patient's body, resulting in a much higher rate of restenosis of the vessel.

This laid the foundation for the subsequent demand for multi-material coated stents and composites. The coating materials commonly used in modern medicine include inorganic coatings, polymeric coatings, radioactive coatings, and drug coatings. Each type of coating material has its own corresponding large number of advantages and disadvantages. For example, inorganic material coatings have higher potentials that may lead to the movement of proteins in the plasma, and the brittle nature of inorganic coatings makes them prone to rupture and scratch the blood vessels. Polymer coating materials, on the other hand, are more pliable than inorganic coatings, meaning that they are more easily deformed in the patient, but are more biocompatible. These coatings are usually complexes of choline phosphate and metals. There are two main types of drug coatings, one of which is a sponge-like structure in which the drug is coated on a sponge structure that continues to release and degrade for six months to a year after implantation. The other form breaks down the drug chemically and physiologically. The advantage of this type of coating is that the drug is released continuously after implantation. However, to achieve the purpose of slow drug release, the stent itself is highly susceptible to metabolism and degradation in the body, and the stent's sustainable time is greatly reduced [4]. The following section describes the properties of different types of cardiac vascular stents according to the broad categories of materials used to classify them.

2. Organic materials

Most organic stents on the market today refer to organic coatings applied to the surface of inorganic metal stents for the purpose of releasing drugs and reducing the likelihood of thrombosis, with fewer single organic stent materials. Organic coatings include drug coatings, polymer coatings, and so on. For example, the now technologically mature chitosan-silica xerogel hybrid coating is a novel material that can be used to improve the corrosion and wetting resistance of the main part of the alloy and effectively carry sirolimus for more than three weeks, and this coating can significantly reduce in-stent restenosis and minimize the risk of blood clots [5].

2.1. Polyester

Polyester-based cardiac stents have been shown to produce more inflammation and some degree of intradermal damage than similar polytetrafluoroethylene (PTFE) materials, and this inflammatory response leads to elevated serum levels of IL-8 and the development of malignant tumors. However, due to the lack of data at this time, researchers are unable to definitively state whether the reclusions of blood

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vessels caused by this material are due to the material itself or to the effects of the structural design and the endothelium of the bone [6].

Polyester implantable materials first appeared to solve the high toxicity, low biocompatibility, and non-degradability of metal and alloy materials. Non-degradable metal materials mean that a second invasive surgery is needed to remove the implanted material, while polyester can be metabolized and degraded within a certain period in the body to solve the defects of the metal material to a large extent. Polyester has been proven to be the only polymer material that can be hydrolyzed, and the metabolites will eventually produce water and carbon dioxide, making it one of the least toxic stent materials available. Polyester has been widely used in other implantable materials in vivo, such as bio sutures, scaffolds for fracture fixation, or cellular transplants, but has not been used extensively in the cardiac scaffold segment due to its strength and stiffness. Moreover, since polyester-based materials can be easily synthesized, they can be used for large-area production with lower cost and higher production efficiency and have great potential for development [7].

2.2. Collagen

Collagen, as one of the natural polymers contained in the human body itself, undoubtedly receives the least physiological rejection, is non-toxic, and has the highest biocompatibility. However, the low hardness and rigidity of collagen as a single material also prevent it from being used as the main material for cardiac vascular scaffolds. It can be used as a coating material, but there is not a large amount of research and data on the use of collagen as a cardiac vascular scaffold coating since it could promote cellular regeneration in the human body, which is highly susceptible to causing blood clots. However, materials scientists have attempted to develop synthetic collagen to reduce the likelihood of collagen thrombosis in the body.

2.3. Hyaluronic acid (HA)

HA is an organic substance found in large quantities in the human body. Researchers have likewise considered hyaluronic acid as an organic coating on metallic cardiac vascular stents. Hyaluronic acid reduces the likelihood of thrombosis compared to natural collagen. Li Yang et al. in 2021 prepared a metal-based cardiac vascular scaffold coated alternately with recombinant human collagen type III (hCOLIII) and hyaluronic acid and demonstrated that this coating can reduce thrombosis due to the coagulation properties associated with collagen. This alternate coating on cardiac vascular scaffolds creates a biomimetic endothelium that reduces inflammation, minimizes the likelihood of intravascular thrombosis, and supports endothelial cell proliferation. The coating has a high probability of reducing restenosis within the cardiac vascular stent and providing protection to the endothelium compared to a single natural collagen or artificially prepared collagen. This technology compensates for the shortcomings of the collagen coatings mentioned above by reducing the likelihood of thrombosis due to collagen's tendency to cause coagulation but is currently not widely available for clinical use due to the high cost of preparation [8].

3. Inorganic materials

The inorganic materials used for vascular stents mainly include metals and ceramics, except for hydroxyapatite (HAP), which is also used in some stent structures. The predominant inorganic materials on the market today are still metals and alloys, but due to the limitations of a single material, attempts have been made to apply different coatings to metals to address restenosis and biological rejection. The earliest vascular stents were composed of stainless steel and cobalt-chromium, but due to lower biocompatibility prone to in-stent in occlusion, so there were later magnesium and zinc alloy materials.

3.1. Metal

Metal, as the most basic material, has a high degree of hardness and stability and was the initial material used when attempting to design cardiac stents. However, most metallic materials do not meet the characteristics of non-toxicity, biocompatibility, and corrosion resistance, and because the stent needs

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to be placed in a narrowed blood vessel, there is a high demand for its hardness and flexibility. Since most metallic materials have high hardness and are prone to wear and fatigue-induced fracture after cycling in the body, the hardness of the material should also be considered when designing the stent structure [9]. In some cases, the use of two or more cardiac stents with overlapping supports is common, and metal cardiac stents are prone to crevice corrosion as well as wear and tear that reduces corrosion resistance, which is one of the major drawbacks of using metal cardiac stents. This is a major disadvantage of using metal cardiac stents. Moreover, metal and alloy cardiac stents are susceptible to fatigue cracking and fracture under high curvature. In addition, magnesium, as the fourth most abundant cation in the human body, is a cation that can be metabolized by the human body and has a certain degree of corrosiveness in the human body's circulatory system, which means that magnesium alloy cardiac vascular scaffolds can be degraded within a certain period of time, making it one of the implantable cardiac vascular materials with a great deal of potential for development.

3.2. Hydroxyapatite (HAP)

HAP has been used extensively as a replacement material for bone stents, but hydroxyapatite cardiac vascular stents are currently used in a narrower range of applications. Helena M Beusekom van et al. demonstrated in 2007 that hydroxyapatite can be used as an inert material to replace polymers to minimize the interference of drug release with vascular healing [10]. They also prepared Cypher and compared the effect of hydroxyapatite in porcine coronary arteries and found that both had the same effect on delayed vessel healing. Hydroxyapatite as an inorganic coating material is not as promising as some of its orthopedic replaceable implant materials.

3.3. Ceramic

Ceramics, as new implantable biomaterials, have different material properties from metals and polymers, and their inactive chemical properties make them stable in vivo over time. Ceramics have low toxicity, high biocompatibility, and antimicrobial properties, and therefore can be used as coating materials for cardiac vascular stents. Implantable bioceramic-based materials are categorized into three main groups: resorbable ceramics, bioactive ceramics, and bioinert ceramics. However, ceramics are not recommended as a major part of cardiac vascular scaffolds due to their high brittleness and low flexibility, which prevents them from adapting to narrow intracardiac vessels with flexural activity. Metal cardiac vascular scaffolds were chosen to be coated with bioactive ceramic materials. Bioinert ceramics can form fibrous tissue and produce an inflammatory response after implantation. Cardiac vascular scaffolds coated with bioceramic materials will greatly reduce toxicity and potential alternation between electrons and organisms, reducing toxic reactions caused by potential differences [11].

4. Composites

Medical polymers have excellent characteristics such as high hydrophilicity, corrosion resistance, and drug coating, but low biocompatibility, low mechanical properties, and low degradability limit the use of single polymers in bioimplantable materials. Therefore, the disadvantages of single polymers have been minimized by combining multiple polymers or combining polymers with metals. Composites, however, can reduce the toxicity associated with single polymer materials, increase biocompatibility, and make the structure more stable. Cardiac scaffolds made from a combination of two materials are more blood compatible, stronger, and less likely to scratch blood vessels with their adjustable stiffness, which is currently a large area of development for cardiac scaffold materials. Composites can combine the advantages of each of the two materials, e.g., the metal material is much stronger and more wear-resistant, while the polymer is much sparser and more porous to be coated with drugs.

4.1. Polymer and metal

Polymers used in implantable cardiac stents are usually classified into two main groups, natural polymers, and synthetic polymers. The natural polymers include gelatin, chitin, collagen, etc., while the synthetic polymers include poly (l-lactic acid) (PLLA), polytetrafluoroethylene (PTFE), poly (vinyl chloride) (PVC), etc. The combination with polymers solves the problem of ion poisoning due to the high potential of most metals, and the susceptibility of metals to corrosion. Most existing polymer-to-metal cardiac scaffolds are made of metal or alloy as the main part, and the upper surface in direct contact with blood tissue is covered by polymer(s). Such structures can simultaneously utilize the high strength of metals with the biocompatibility and low toxicity of polymers [12].

4.2. Polymer and polymer

Based on the above exploration of different materials, it is easy to see that thrombosis and restenosis after cardiac vascular stent implantation are a problem that cannot be solved by most materials. While the toxicity and structural rigidity of the material can be studied and tested before implantation, the physiologic response to the material varies from patient to patient, as does the location and curvature of the blood vessel, which also affects restenosis and thrombus generation [13]. Blockages formed after implantation of cardiac vascular stents are mainly produced by anticoagulant cells and collagen factors, so the biochemical degradability of polymers can solve this kind of problem. However, a single polymer material may not have the characteristics of low toxicity, high biocompatibility, high strength, etc. Therefore, the researchers can produce the compound material of two and more polymer materials by 3D printing and waving. The polymer located in the upper layer needs to have anticoagulant properties and rapid endothelialisation to reduce the possibility of thrombosis. Examples from current experiments are the coating of 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) as well as hyaluronic acid on plasma polypropylene amine (PPAm) scaffolds and it has been demonstrated that such coatings have strong antiplatelet properties.

5. Conclusion

This paper describes the advantages as well as disadvantages of a variety of cardiac stent materials, and by analyzing the different materials, the most suitable cardiac stent materials are currently found to be the major types of metals. However, through the improvement of different technologies at this stage, multiple material coatings have brought new developments for cardiac stents. Cardiac vascular stents from the initial metal stents mainly consisted of stainless steel, nickel-titanium alloy, or cobalt-chromium alloy, but due to the implantation of these types of stents can produce in-stent restenosis and other problems, drug-coated cardiac vascular stents have been developed. Drug-coated cardiac vascular stents are mostly used for diabetic patients who have a strong rejection of metal stents. In addition to drug-coated cardiac vascular stents, biodegradable stents have been developed today, which further solve the problem of needing to open the wound twice to remove the implanted stent after implantation. In addition to this, work is still underway to develop polymer cardiovascular stents, radioactive cardiovascular stents, and various organically coated stents for use in patients with different conditions. Current cardiac vascular stent materials are still mostly metal and alloy stents, which still dominate the cardiac vascular stent materials due to their lower production cost and high stability. As a human implantable material, cardiac vascular stents require a high level of material development, including high biocompatibility, moderate hardness and stiffness, and non-toxicity, as well as a high level of knowledge on the part of the material developer. This is a field that needs to be vigorously researched and developed by human beings in the future, but it is also a field in which the relevant researchers will encounter a variety of practical problems. The researchers hope that people can develop a new type of material that can solve all the problems of the existing materials at the same time at an early date. They also hope that the material will be able to meet the characteristics of large-scale production and reduce the cost of production and preparation, so that most patients can use this life-saving implantable scaffold without financial burden, which will become the welfare of all mankind.

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