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Review Article

Implants For Cardiovascular Diseases

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ABSTRACT

Cardiovascular diseases (CVDs) remain a leading cause of morbidity and mortality globally, necessitating continuous advancements in medical interventions. Implantable devices have emerged as promising solutions for managing various aspects of cardiovascular pathologies. This comprehensive review explores the current landscape of innovative implants in the realm of cardiovascular diseases. The review begins by examining the pivotal role of implantable devices in addressing cardiac conditions, ranging from heart failure to arrhythmias. Focus is placed on cardiac rhythm management devices, including pacemakers, implantable cardioverter-defibrillators (ICDs), and cardiac resynchronization therapy devices, highlighting their evolving technologies and clinical applications. Furthermore, the review delves into advancements in the field of cardiovascular stents, discussing novel materials and designs aimed at optimizing vascular patency while minimizing complications. The integration of drug-eluting technologies and bioresorbable materials into stent development is explored, with emphasis on their impact on patient outcomes. The discussion extends to ventricular assist devices (VADs) and total artificial hearts, elucidating their role in providing temporary or long-term mechanical circulatory support. A critical evaluation of challenges and future prospects in enhancing the biocompatibility and durability of these devices is presented. In addition, the review encompasses the burgeoning field of bioelectronic implants, elucidating how neuromodulation devices and bioelectronic medicine are revolutionizing the management of hypertension and heart failure. The integration of smart sensors and closed-loop systems for real-time monitoring and adaptive interventions is discussed in the context of personalized cardiovascular care. Ultimately, this review aims to provide a comprehensive overview of the diverse landscape of cardiovascular implants, offering sights into their evolving technologies, clinical efficacy, and potential avenues for future research and development.

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The continuous innovation in implantable devices holds great promise for improving the prognosis and quality of life for individuals affected by cardiovascular diseases.

INTRODUCTION

Cardiovascular disease (CVD) refers to conditions affecting the heart and blood vessels, ranging from coronary artery disease to cardiomyopathies. These diseases are the leading causes of premature death globally and cause significant financial burdens. Current medical treatments are insufficient for critically ill patients, but advancements in blood clotting materials enable interventional surgery and implantable devices in clinics, potentially saving their lives. [1,2]

The World Health Organization reports that cardiovascular disease (CVD) claims 17.9 million lives annually globally, with coronary artery disease (CAD) being the most prevalent type. Preferred cardiovascular disease (PAD) is a secondary concern, with 22% of CAD patients also suffering from PAD. [3] The rapid economic development and Westernized lifestyle have led to an increase in cardiovascular diseases (CVDs) among Indians. Factors such as unhealthy diets, physical inactivity, harmful alcohol and tobacco use, elevated body mass index, waist-hip ratio, and metabolic risk factors like hyperglycaemia, hyperlipidaemia, and high blood pressure are known causes of CVDs. [4] Implantable Medical Devices (IMDs) are widely used in medicine for diagnostic and therapeutic purposes, covering various pathologies like diabetes monitoring, high blood pressure telemetry, cardiac reporters, and defibrillators. These devices interact with physiological processes like heartbeat, mediate sensing, local stimulation, data recording, and drug delivery. The latest IMDs can transmit vital measurements like blood pressure, glucose level, and electrocardiogram, aiding clinical decision-making and providing a personalised medical approach to diagnosis and therapy. [5]

IMDs fall into one of two categories: passive or active. A medical device that is completely turned off, such as a bare metal coronary artery stent, is known as a passive IMD. A medical device that is "fully or partially introduced, surgically or medically, into the human body and is equipped for its functioning with a source of electrical energy" is known as an active implantable medical device (IMD). Active IMDs are designed to transmit electric impulses to organs or tissues in order to monitor physiological or pathological signals and/or to produce therapeutic effects. [5]

Polymer implants in cardiovascular medicine have led to a need for future devices that directly contact blood flow, such as catheters, blood vessel grafts, vascular stents, artificial heart valves, occlude systems, and circulatory support devices. These implants can activate platelet activation, secretion, adherence, and aggregation, triggering plasmatic coagulation and immunological responses, depending on the material's hemocompatibility. [6]Controlled release implants can optimize treatment for cardiovascular diseases by avoiding adverse drug effects. These implants implant a drug delivery device at the site of a pathologic process, producing high regional concentrations but low net systemic doses. This approach optimizes therapy where needed and avoids high-level drug exposure, ensuring optimal treatment for various cardiovascular diseases. [7]

BIOMATERIALS IN CARDIOVASCULAR IMPLANTS

Biomaterial-based implants are crucial in cardiovascular interventions and are expected to continue growing in relevance. Recent trends in biomaterial science could lead to improved therapies or new interventional procedures, emphasizing the importance of these advancements as an innovation pipeline for future cardiovascular devices. [8]

A biomaterial is a substance, either synthetic or natural, used for treating, augmenting, or replacing

body tissues, organs, or functions. It can be used for any duration and can be used as a whole or part of a system. The definition was simplified in 1986 at the European Society for Biomaterials Consensus Conference, defining biomaterial as a non-viable material used in medical devices intended to interact with biological systems. [9]

Biomaterials are a rapidly growing trend in materials science, used in implants, artificial organs, and medical instruments. The selection of biomaterials for implants depends on factors such as material selection, environmental impact, bioavailability assumptions, tissue reaction mechanisms, biophysical, biochemical, and biomechanical requirements, corrosion and abrasion, surface layering technology, and structural problems. These materials are expected to play more sophisticated, longer-term roles in tissues, customizing and optimizing the material-tissue interface to ensure optimal long-term clinical outcomes. [9] Biomaterials used on implants include bio ceramics, polymers, composite materials, and metals and alloys. Polymers, which consist of repetitions of constitutional units, are particularly useful as biomaterials due to their ability to be synthesized in various molecular architectures and their well-tuned properties, allowing them to meet specific requirements for biomedical or clinical applications. [8] Degradable polymers have been studied as biomaterials since 1988, with poly-l-lactic acid (PLLA), polyglycolic acid/polylactic acid, and polycaprolactone being proposed. These polymers decompose in the human body after 12-24 months for the lactic-acid family, and over 24 months for polycaprolactone. Metal research on degradable biomaterials is more recent, as corrosion resistance is a key requirement for metallic biomaterials. The idea of using degradable metals for temporary implant fabrication requires a break from this paradigm. [10] Magnesium (Mg) was the first metal used for biodegradable implants in 1938. However, due to its unknown degradation behavior and the rise of stainless steel, it was abandoned. As Mg technology advances, it has regained interest as a basic material for biodegradable implants. Currently, two classes of Mg- and Fe-based alloys are proposed.

STENT BASED DRUG DELIVERY SYSTEM

A stent is a hollow cylindrical device used to support and keep obstructed body conduits open, allowing fluid to flow through. Originating from the 19th-century English dentist Charles Thomas Stent, it is widely used in interventional therapy to treat occlusion or stricture of tubular body structures like blood vessels, oesophagus, biliary tract, pancreatic The duct, urethra, colon, trachea/bronchus, and nose are affected by its mechanical support and expansion. of the lumen

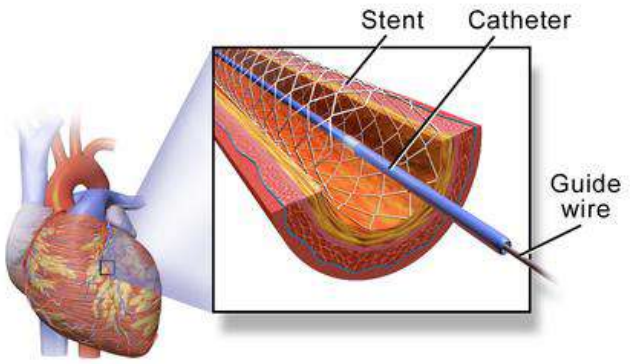


Fig 1 [stent placement in coronary artery]

Drug delivery stents consist of three components: the stent platform, delivery system, and therapeutic agent. They can be divided into metallic and polymeric stents. Metallic stents are made from various metals like 316L stainless steel, tantalum, cobalt-chromium, nickel-titanium, magnesium, and platinum-chromium alloys. Polymeric stents use biocompatible or bioinert polymers as the backbone. The Mg alloy stent can be absorbed in the form of inorganic salts. Biodegradable polyesters or polyanhydrides, such as polylactide, poly(lactide-coglycolide), poly(-caprolactone), and polysalicylate, are used as

backbone materials. These materials degrade into small molecules that can be metabolized and eliminated by the human metabolic pathway. Bioabsorbable stents hold great promise for the next generation of drug delivery stents. [11] Polymers offer advantages for drug delivery from stents, including easy adjustment of drug loading, controlled drug delivery, drug protection, and well-established protocols for preparing drug-containing polymers. However, unexpected problems have arisen when using polymer-based drug-delivery carriers for stents. When stents are expanded at the implantation site, the shear force of balloon expansion causes mechanical defects in the polymer coating, leading to defects such as cracks, fissures, ridging, waving, peeling, and delamination. These defects are a major concern as polymer fragments detached from stents can cause adverse reactions. Despite these challenges, polymer-based drug-delivery carriers remain effective in controlling drug release. [12] A polymer-free drug delivery method for stents has been a dream for clinicians and engineers due to the limitations of polymer-based systems. One early approach involved dipping stainless-steel stents in paclitaxel ethanol solution, then evaporating the solvent to leave drug precipitate on the stent surfaces. [9]. However, most of the loaded drug was lost during the stent implantation procedure. Hence, the stent surfaces were modified either physically or chemically to carry the drug and to release it for a sustained period.

Implants for Heart Failure Heart failure affects over 5 million Americans, with acute decompensated heart failure (ADHF) being the leading cause of hospitalization among people over 65 years old. This public health concern is significant, with hospitalization expenses imposing a significant financial burden on the healthcare system. Readmission rates for ADHF can be as high as 50% at 6 months, and most patients admitted with ADHF have a history of heart failure. This presents an opportunity for upstream strategies to detect early HF destabilization and implement therapies to restabilize patients and avoid hospitalization. [13] Device-based monitoring and intervention in chronic heart failure (CHF) disease management presents a significant opportunity. Cardiac implantable electronic devices (CIEDs) are rapidly expanding their role in HF patients, offering a new paradigm for outpatient HF monitoring. Traditional CIEDs have primarily focused on electrophysiological applications like pacing and anti-tachycardia therapies. Emerging technologies that link biological sensors to CIEDs have opened up novel monitoring strategies that can take advantage of implantable devices. Sensors in HF disease management can take various forms, including the patient, healthcare provider, or the device itself. Implantable sensors offer advantages over self-monitoring systems, as they can detect subtle changes during early destabilization, overcoming factors like subjectivity and variable patient ability. [13] An implantable cardioverter-defibrillator (ICD) is a battery-powered device that detects and stops irregular heartbeats, also known as arrhythmias. It continuously checks the heartbeat and delivers electric shocks when needed to restore a regular heart rhythm. The ICD has sophisticated programming to distinguish between normal and dangerous rhythm disturbances, based on the heart rate. Above a certain threshold, the defibrillator can deliver an electrical pulse to restore normal rhythm. [14,15]

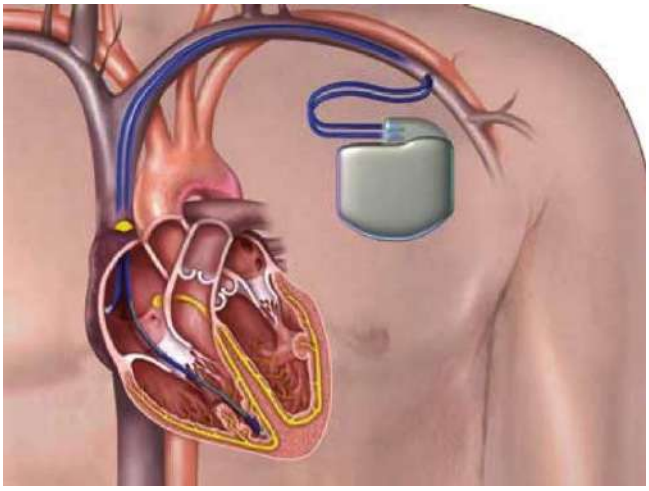


Fig 2 [placement of defibrillator for heart failure]

The use of an implantable cardioverter-defibrillator (ICD) has been proven beneficial in patients with symptomatic systolic heart failure due to coronary artery disease. The management of heart failure has improved since the ICD trials, and many patients now receive cardiac resynchronization therapy (CRT). In both European and U.S. guidelines, prophylactic ICD implantation is a class 1 recommendation for heart failure and reduced left ventricular systolic function. However, the evidence for the benefit is stronger for patients with ischemic heart disease..[16] A study by the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) found that patients with New York Heart Association class III or IV heart failure who received medical therapy, a cardiac resynchronization therapy (CRT) pacemaker, or a CRT defibrillator showed significantly lower all-cause mortality in association with a CRT defibrillator than with medical treatment alone. However, a CRT defibrillator was not proven to be superior to a CRT pacemaker.

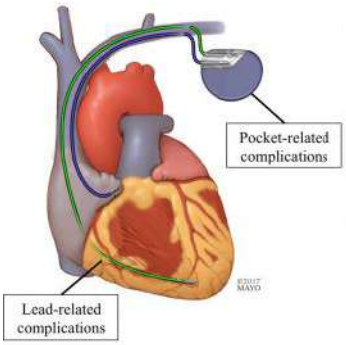
Advancements for Cardiovascular Implants

Conventionally, cardiovascular stents are fabricated using chromium-platinum compounds and nickel-titanium alloys (nitinol). A smart stent would require a wireless sensor node consisting of a transducer, associated readout electronics and communication infrastructure. Transducers can be used to detect various signals within the stent; ranging from blood pressure, volume flow or cell growth. Photolithography is a mainstay of microfabrication sensor techniques which allows the light patterned creation of 2D features on a microscopic scale. Traditional photolithography is a subtractive process using light patterns through an optical mask to pattern a photoresist which can then be used as a physical mask in an etching process to produce suitable high-resolution sensors that can be encapsulated and mounted on suitable IMDs. In contrast, stereolithography 3D printers provide an additive process that in the future can be used to make the IMDs as they use photopolymerization of a photo-sensitive liquid placed in a reservoir by a computer-aided positionally programmed laser beam or a digital light projector with computer-aided platform.[17] Self-reporting vascular devices will have universal medical appeal as stents are placed throughout the body. For example, stents are frequently used in the heart, brain, kidney renal and carotid arteries as well as ureters and oesophagus to name but a few. Synthetic grafts are used as native vessel replacements are clinically ubiquitous and used for peripheral access such as for blood exchange in haemodialysis patients. Being relatively large bore vessels and surface mounted may make these the most suitable targets for the next generation of SMART devices. The endovascular Via Bahn Graft and Hero graft have been designed for haemodialysis patients who suffer from venous stenosis.

Leadless pacemaker

conventional pacemakers still have the same structure since its early introduction in the 1960s, which consist of an extravascular pulse generator containing the power source and the electronic circuitry connected to the cardiac myocardium

using transvenous leads. This system is associated with up to 9.5% rate of complications, which includes device-related complications such as hematoma or pocket infection, as well as lead placement-related complications, such as pneumothorax, cardiac perforation, and lead dislodgement.[18]



Transvenous pacemaker complications	Rate (%)
Immediate complications	
Pneumothorax	0.6-0.9 [3, 24]
Cardiac perforation	0.1 - 0.3 [3, 27]
Hematoma	0.2 – 0.7 [3, 26]
Intermediate complications	
Lead dislodgement	0.4 – 1.7 [3, 25]
Pocket revision because of pain	0.4 [3]
Late complications	
Lead-related re-intervention • Conductor fracture • Insulation break	1.7 - 2.4 [3, 25]
Pacemaker infections	1.8-1.9 per 1000 pacemaker years [4, 5]

Fig 3 [complications of conventional pacemaker]

The ideal leadless pacemaker should be compact, lightweight, small enough to permit placement of multiple devices in the future if or when it is needed, and easily implanted and extracted. The device should not be associated with significant thromboembolic events or cause mechanical ectopy. The delivery system should not cause any associated damage to the valvular or sub-valvular apparatus. The incidence of myocardial perforation should be similar to or lower than transvenous leads.[18] The first leadless pacemaker available for commercial use was the Nano stim (Abbott), which was subsequently recalled in 2016 following concerns of premature battery failure and docking button detachment. Currently, there are two available leadless pacemakers: the Micra VR and the Micra AV (Medtronic). The two Micra devices are identical in design, both occupying 0.8 cc and weighing. [19]

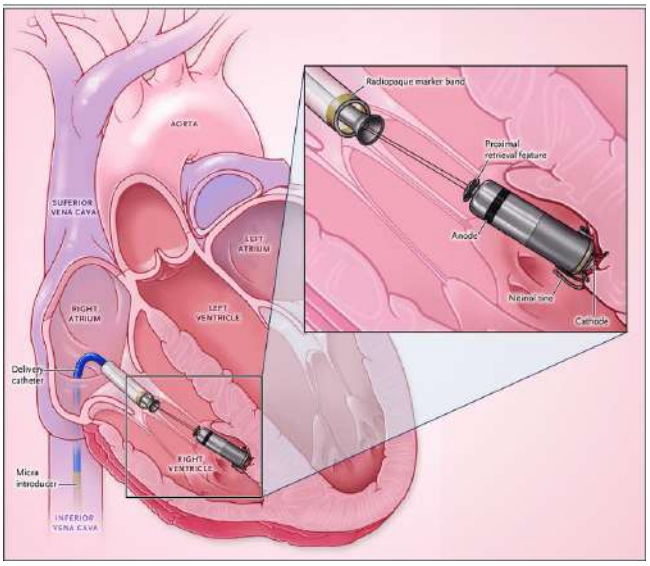


fig 4 [showing micra VR pacemaker placed in heart]

The Micra VR was the first leadless pacemaker to gain FDA approval in 2016 and provides ventricular demand (VVI) pacing with accelerometer-based rate response. Although effective, the Micra VR does not provide atrioventricular (AV) synchrony.

Nanotechnology in cardiac implant

Nanotechnology is a promising and emerging field that uses nanoparticles to facilitate the treatment and/or diagnosis of various diseases such as cancer, diabetes, osteoarthritis, brain and retinal diseases, cardiovascular diseases and bacterial infections. Nanoparticles are defined as colloidal particulate dispersions or particles ranging from 10 to 1000 nm in size. Different types of nanostructure systems are designed for drug delivery and the manipulation and the fabrication of biomedical implantable devices have been extensively investigated over the past decades. For this reason, the utilization of nanoparticulate drug delivery systems in the field of biomedical is predicted to spread rapidly in recent years. [20]

Biomedical implants obviously provide a wide range of medical cures for many of the disorders, such as cardiovascular diseases. Vascular grafts, defibrillators, heart valves, pacemakers and stents are the most common cardiovascular implantable

devices used in the medical field. However, the present implant technology is facing a major difficulty of being perceived by the human body as foreign substances. Nanotechnology provides a medical solution to revolutionize biomedical implant technology by modifying and designing their structures thereby overcoming these problems. [20]

Implantable hemodynamic monitor

current approaches to monitoring patients with heart failure have generally focused on insensitive non-invasive markers of heart failure clinical status and failed to improve quality of life or to reduce hospitalization rates. Worsening heart failure symptoms, changes in vital signs, and weight gain are late and unreliable markers of worsening heart failure. Implantable hemodynamic monitors, which remotely provide direct measurement of intracardiac and pulmonary artery pressures (PAP) in ambulatory patients with heart failure, enable a proactive approach that shifts the focus from crisis management to stability management in patients with heart failure. [21]

CONCLUSION

In conclusion, the field of cardiovascular implantable devices has witnessed remarkable advancements, playing a pivotal role in the management of cardiovascular diseases. The diverse range of implants, from cardiac rhythm management devices to stents, ventricular assist devices, and bioelectronic implants, reflects the multifaceted approach taken to address the complexities of cardiovascular pathologies. The evolution of cardiac rhythm management devices has significantly improved patient outcomes, providing effective solutions for arrhythmias and heart failure. Continuous innovation in pacing technology, coupled with the development of sophisticated algorithms, has enhanced device performance and patient quality of life. However, challenges such as battery life and device infections remain areas of ongoing research and improvement. The progress in stent technology has revolutionized interventional cardiology, with an emphasis on improving vascular patency while minimizing complications. The integration of drug-eluting technologies and bioresorbable materials represents a paradigm shift in the design of these implants, aiming for more patient-friendly and effective solutions. Ventricular assist devices and total artificial hearts have emerged as crucial options for individuals with advanced heart failure, providing mechanical circulatory support as a bridge to transplantation or destination therapy. The ongoing refinement of device design, biocompatibility, and durability is essential for expanding their utility and improving patient outcomes. The integration of bioelectronic implants and neuromodulation devices marks a transformative approach to cardiovascular care. These technologies hold great promise in managing conditions such as hypertension and heart failure through personalized, adaptive interventions. The incorporation of smart sensors and closed-loop systems represents a significant step towards real-time monitoring and tailored therapeutic strategies. Looking ahead, the future of cardiovascular implantable devices lies in addressing current challenges and exploring novel frontiers. Continued research into materials, biocompatibility, and energy sources is crucial for enhancing the longevity and safety of implants. Moreover, the integration of artificial intelligence and data analytics may further optimize device performance and contribute to personalized treatment strategies. In summary, the ongoing evolution of cardiovascular implants underscores their significance in the ever-advancing landscape of cardiovascular medicine. As technology continues to progress, these implants have the potential to further transform patient care, offering more effective, personalized, and minimally invasive solutions for individuals grappling with cardiovascular diseases.

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