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A scientometric survey of scaffold-based research in cardiovascular disease: Trends, influences, and future directions

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A B S T R A C T

This scientometric study gives a comprehensive survey of the highly influential scientific literature at the intersection of cardiovascular disease and scaffold technology. By testing a curated dataset of 200 highly cited articles, this review maps the intellectual landscape, determines key research fronts, and keeps tracking the evolution of this dynamic field. The analysis discloses a dominant concentration on tissue engineering applications, specifically for myocardial infarction repair, vascular graft development, and heart valve replacement. Key themes incorporate the exploration of novel biomaterials such as biodegradable polymers, decellularized matrices, hydrogels, and electrospun nanofibers, and the integration of advanced fabrication methods such as 3D bioprinting. The survey also determines seminal contributions from leading research groups and highlights the synergistic relationship between material science, cell biology, and clinical cardiology which drives innovation. In addition, the survey tracks the rising prominence of enabling technologies which include conductive scaffolds for cardiac patches and the application of stem cells. The study not only synthesizes the current state of knowledge but also determines emergent trends and potential future trajectories, underscoring the critical role of scaffold-based strategies in advancing cardiovascular regenerative medicine. The results consolidate a vast body of literature to inform researchers and funding agencies about the field's structure and its most essential avenues of investigation.

1. Introduction

Cardiovascular diseases (CVDs) is one of the causes of mortality for human life in the world, pushing a substantial impact on global healthcare systems (Yao et al., 2021). Conventional treatments, such as pharmacological management and surgical interventions, often do not succeed to fully recover lost tissue functionalities, pushing to a more interest in regenerative medicine methods. Within this theme, the implementation of scaffolds, temporary three-dimensional structures which support cell attachment, proliferation, and differentiation, has appeared as an important strategy. Scaffolds are built to mimic the native extracellular matrix (ECM), giving mechanical support and biochemical cues to help tissue regeneration following ischemic events, such as myocardial infarction (MI), or to replace damaged vasculature (Pashneh-Tala, MacNeil, & Claeyssens, 2016; Reis, Chiu, Feric, Fu, & Radišić, 2016).

The area of scaffold-based cardiovascular study is interdisciplinary science, drawing from materials science, bioengineering, cell biology, and clinical medicine. This convergence has created a significant and quickly expanding body of literature. Navigating this complex intellectual terrain needs analytical tools which can quantify and visualize survey trends, intellectual networks, and the effect of scientific outcome. By implementing scientometric rules, it is easy to move beyond a qualitative review to a data-driven assessment of the field's development.

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This present study offers a scientometric investigation of highly cited articles at the nexus of "cardiovascular disease" and "scaffold". The extracted dataset consists of 200 high-impact articles, which serve as a proxy for the most significant works in this domain. The aims of this survey are to determine the most prolific researchers and influential articles; to map the conceptual structure and some research themes; to trace the temporal evolution of key topics; and to highlight new frontiers. Unlike traditional narrative studies, this analysis will present a comprehensive survey on the intellectual pillars of the field, providing a macroscopic perspective on how knowledge has been constructed, disseminated, and implemented. Through this method, the study plans to provide a consolidated overview which could guide future research efforts, foster collaboration, and inform strategic decision-making in cardiovascular regenerative medicine.

2. Methodology

The data for this scientometric survey was extracted from the Scopus database and targeted search was built using the query string: "cardiovascular disease" AND "scaffold". This search returned a total of 1,411 papers. To concentrate the analysis on the most impactful studies, the outputs were sorted by "Cited by" count, and the top 200 most cited articles were chosen for in-depth analysis. This method helps us to locate the publications which have generated the most substantial scholarly dialogue and influence within the field.

The metadata for these 200 publications, including titles, authors, publication years, source titles, author keywords, abstracts, and citation counts, was exported for analysis. The analytical method was primarily descriptive and qualitative, concentrating on determining patterns and trends within the dataset. Key metrics studies included the annual distribution of papers, the most prolific and highly cited journals, the frequency and co-occurrence of author keywords, and the identification of seminal works through citation analysis.

The aim of the methodology involved a systematic content analysis of the papers. The process included categorizing the concentration of each paper (e.g., myocardial tissue engineering, vascular grafts, biomaterial development, drug delivery) and the kind of scaffold technology employed (e.g., electrospun nanofibers, hydrogels, decellularized matrices, 3D-printed constructs). The contributions of leading authors and institutions were explored to map the intellectual network. In addition, the evolution of study themes over time was traced by comparing the predominant key issues in earlier against more recent publications within the dataset. This multi-faceted method helps for a comprehensive synthesis of the knowledge structure, key advancements, and trajectory of scaffold-based cardiovascular study as reflected in its most cited literature.

3. Analysis of Publication Trends and Journal Influence

The analysis of publication years within the dataset of 200 highly cited papers discloses the dynamic and growing nature of scaffold-based cardiovascular studies. The earliest publication in this curated list goes back to 1986 (Smith, 1986), which investigated fibrinogen and fibrin in association with atherosclerosis, giving insight to the long-standing recognition of ECM components in cardiovascular pathology. However, most important works were published from the mid-2000s onwards, with a substantial concentration in the 2010s. This growth aligns with substantial advancements in biomaterial science and a paradigm shift towards regenerative medicine strategies. The years 2015, 2016, and 2017 are specifically well-represented, showing a period of intense research activity and high-impact discovery in this domain.

The journal pace for this field is quite diverse, encompassing high-impact periodicals from specialized domains in biomaterials, tissue engineering, and cardiovascular medicine. The most frequently happening journals in the dataset include *Biomaterials* and *Acta Biomaterialia*, underscoring the central role of material science in this interdisciplinary effort (See Fig. 3). These publications publish foundational studies on novel polymer synthesis, scaffold fabrication techniques, and material-biological interactions. Also prominently featured are *Circulation Research* and *Circulation*, which are premier journals in basic and clinical cardiovascular science. The presence of publications in these journals emphasize the clinical relevance and translational potential of scaffold-based methods, bridging the gap between engineering and medicine. Other substantial outlets include *Advanced Drug Delivery Reviews*, *Tissue Engineering* journals, and *Journal of the American College of Cardiology*, reflecting the multifaceted nature of the research, which spans drug delivery, regenerative biology, and clinical cardiology.

The effect of a journal is not completely a function of the number of papers it publishes in a field, but also the effect of those individual articles. In this dataset, various articles published in *Biomaterials* and *Circulation Research* have garnered exceptionally high citation counts, cementing their status as landmark publications. For example, the work of Hasan et al. (2014) on electrospun scaffolds for vascular tissue engineering, published in *Acta Biomaterialia*, were cited over 650 times, building it as a key reference in the field. Moreover, the comprehensive review by Pashneh-Tala et al. (2016) on tissue-engineered vascular grafts in *Tissue Engineering - Part B: Reviews* maintained over 650 citations, highlighting its relevance as a consolidating resource. The distribution of these highly cited papers across a range of prestigious journals shows that the field's knowledge base is being constructed and validated through a robust, multi-journal discourse which reaches a broad academic audience.

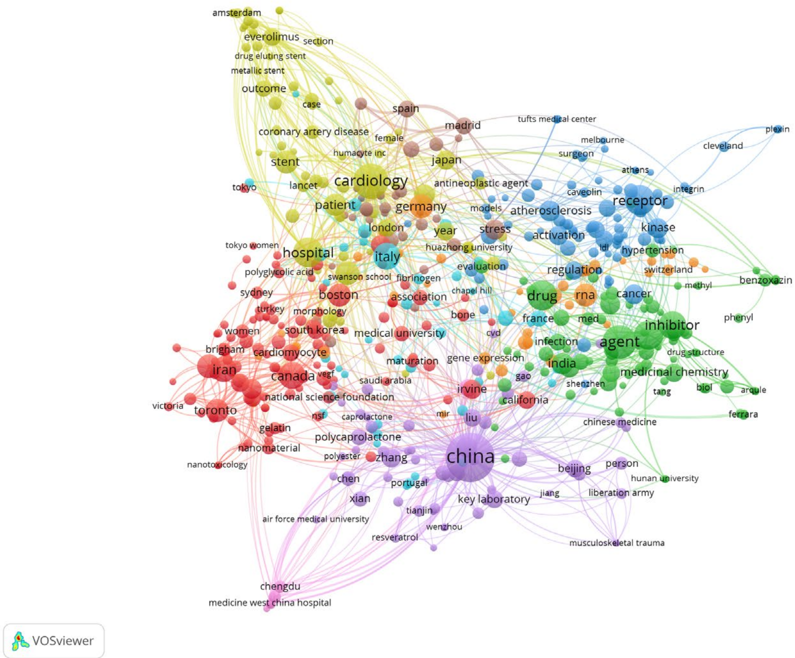


Fig. 1. Network Visualization

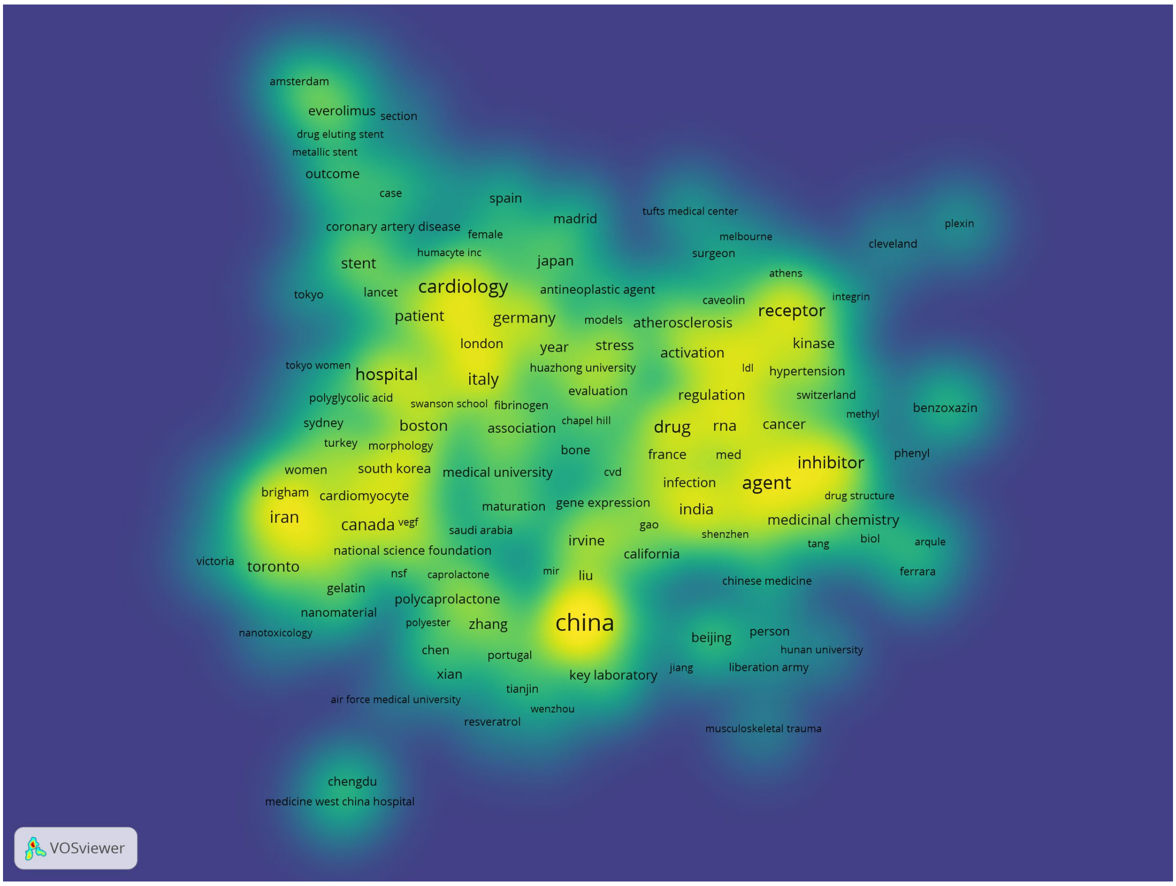
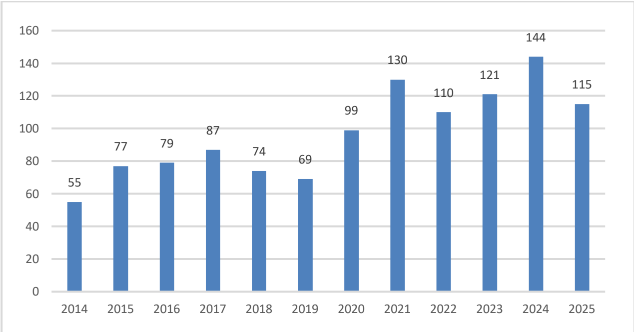


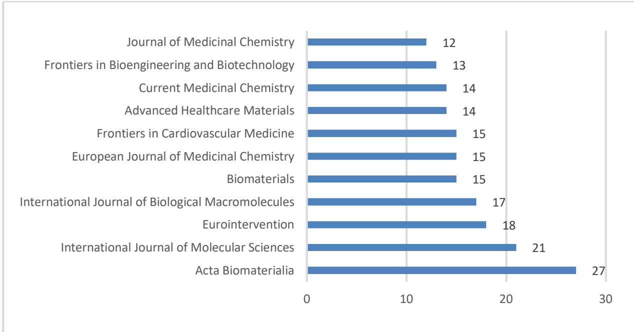
Fig. 2. Density Visualization

The scientometric analysis built through VOSviewer gives two complementary perspectives on the research landscape. Fig. 1 (Network Visualization) shows the co-occurrence of keywords and institutional affiliations, highlighting the structural relationships within the field. An important linkage is observed between China and Chengdu Medicine West China Hospital, implying the central role of this institution in collaborative cardiology research. Surrounding these nodes are clusters of terms such as cardiology, disease, artery, outcome, and stent, which collectively reflect the thematic concentration on cardiovascular interventions and clinical outcomes. The dense interconnections among these terms show a well-established study network where clinical practice and academic inquiry converge, reinforcing the hospital's influence in shaping discourse on cardiovascular medicine.

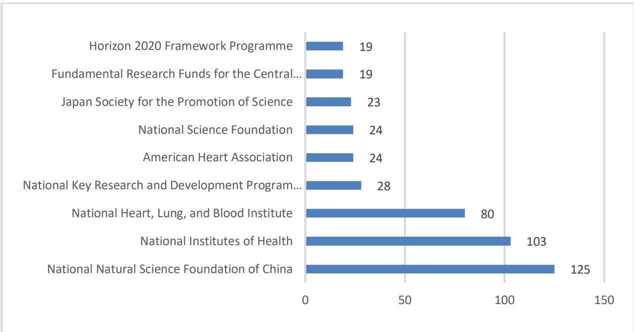
Fig. 2 (Density Visualization) shifts the emphasis from structural connections to intensity of research activity. Countries such as China, Iran, Italy, and India tend to be high-density regions, underscoring their substantial contributions to the global cardiology literature. The visualization also highlights pharmacological and molecular themes, with terms like drug, agent, inhibitor, receptor, and cardiology emerging as hotspots. This density pattern implies a dual emphasis: on one hand, clinical cardiology and interventional procedures; on the other, pharmacological innovation and receptor-targeted therapies. The overlap of geographic and thematic density points to the growing internationalization of cardiovascular research, where Asian and European countries are particularly active. Fig. 3 provides more basic scientometrics data.



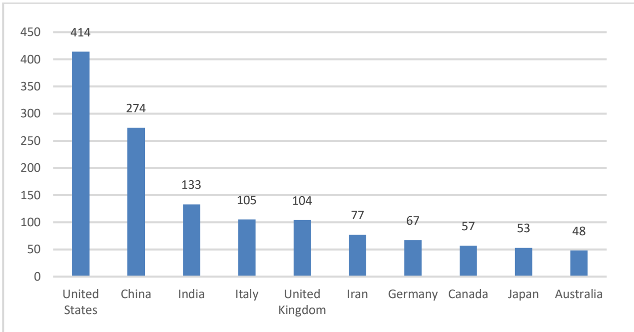
(a)The number of publications per year



(b)Diversity of the publications and journals



(c)Funding agencies



(d)Documents per country

Fig. 3. Some basic scientometric information

4. Major Research Themes and Focal Points

The content analysis of the 200 papers discloses various dominant and interconnected study themes. These themes are the primary fronts where substantial scientific effort and innovation have been concentrated, as evidenced by the high citation counts of the associated publications.

Cardiac Tissue Engineering and Myocardial Repair. A significant portion of the literature is devoted to repairing damaged myocardium, specifically following myocardial infarction. The central challenge is to develop scaffolds which may give mechanical support to the infarcted wall, prevent adverse remodeling, and encourage the regeneration of functional cardiac tissue. Seminal work in this area has explored a variety of biomaterials. For instance, injectable hydrogels based on chitosan, alginate, or decellularized ECM have been widely studied for their capability to be delivered minimally invasively and to build a favorable microenvironment for cell retention and repair (Singelyn & Christman, 2010; Ke et al., 2020). In addition, the development of advanced cardiac patches has been a primary attention. These include patches composed of natural polymers like collagen and chitosan (Tamimi, Rajabi, & Pezeshki-Modaress, 2020), synthetic elastomers, and composite materials. The integration of conductive components, such as carbon nanotubes or gold nanoparticles, into these patches is a substantial advancement, as it tries to improve electrical signal propagation between engineered and host cardiomyocytes (Jalilinejad et al., 2023; Ashtari et al., 2019). The review by Reis et al. (2016) gives a comprehensive overview of the different biomaterial strategies employed in myocardial tissue engineering, categorizing them into injectable hydrogels and pre-formed scaffolds.

Vascular Graft Development and In-Situ Regeneration. The creation of bioengineered blood vessels, especially small-diameter grafts (<6 mm) for coronary and peripheral bypass surgery, is another major theme. The limitations of existing autografts and synthetic grafts have driven the study for tissue-engineered alternatives. This study stream is divided into two overarching strategies. The first involves the in-vitro fabrication of a mature vessel based on scaffolds seeded with cells, such as endothelial cells and smooth muscle cells, often cultured in bioreactors to reach mechanical strength (Pashneh-Tala et al., 2016). The second, more recent strategy concentrates on in-situ regeneration, where an acellular, bioresorbable scaffold is implanted and is used as a template for the body's own cells to infiltrate and regenerate a functional neovessel (Dahl et al., 2011; Wang et al., 2020). Materials research for vascular grafts is extensive, encompassing synthetic biodegradable polymers like poly(ε-caprolactone) (PCL) and poly(glycerol sebacate) (PGS), as well as natural materials like decellularized matrices and collagen (Gong et al., 2016; Khosravi et al., 2016). The optimization of scaffold properties, including compliance, suture retention strength, and burst pressure, to match native vessels is considered as a critical area of investigation (Hasan et al., 2014).

Biomaterial Innovation and Scaffold Fabrication Technologies. Underpinning the application-specific themes is a continuous drive for biomaterial innovation. A primary trend is the shift from passive, structural scaffolds to bioactive, instructive matrices. This is the incorporation of specific peptide sequences (e.g., RGD for cell adhesion), growth factors, and microRNAs to actively direct cellular processes such as angiogenesis, differentiation, and matrix deposition (Webber et al., 2010; Zhou et al., 2016). The choice of material is important, with studies covering natural polymers (collagen, chitosan, alginate, hyaluronan), synthetic polymers (PCL, PLA, PLGA), and hybrids. Fabrication technology is also essential. Electrospinning has appeared as a dominant technique for building nanofibrous scaffolds that closely mimic the topography of the native ECM, leading to a plethora of studies on electrospun vascular grafts and cardiac patches (Zhao, Zhang, Lu, & Xu, 2015; Braghirolli, Steffens, & Pranke, 2014). 3D printing and bioprinting have also received traction, permitting for the exact spatial patterning of cells and biomaterials to create complex, multi-layered tissue constructs, such as vascularized heart patches (Maiullari et al., 2018; Mosadegh, Xiong, Dunham, & Min, 2015).

Bioresorbable Stents and Device Scaffolding. While the term "scaffold" in this context often goes back to tissue engineering matrices, a substantial structure of influential literature pertains to coronary stents, which are intravascular scaffolds. The evolution from bare-metal stents to drug-eluting stents (DES) is a major leap forward in combating in-stent restenosis. The current frontier, heavily featured in the dataset, is the development of fully bioresorbable vascular scaffolds (BVS). These devices, normally made of polymers like poly(L-lactide), give temporary mechanical support and drug delivery before being fully absorbed by the body, thereby restoring vasomotion and eliminating a permanent implant (Zong et al., 2022; Capodanno et al., 2015). The clinical outcomes and optimization of implantation techniques for BVS, such as the "PSP" (Predilation, Sizing, Post-dilation) protocol, have been the subject of extensive and highly cited clinical research (Ortega-Paz et al., 2017).

5. Key Authors and Collaborative Networks

The study of authorship within the dataset discloses various key individuals and study groups which have consistently produced highly influential work, shaping the direction of scaffold-based cardiovascular research. These leaders often head interdisciplinary teams, giving the collaborative nature of the field.

One of the most prominent names is Ali Khademhosseini, whose group has made significant contributions at the intersection of biomaterials, microengineering, and regenerative medicine. His studies, often in collaboration with others like Samad Ahadian and Akbari Mohsen, spans the development of electrically conductive scaffolds for cardiac tissue engineering (Ashtari et al., 2019), gelatin-based hydrogels, and innovative fabrication methods. Similarly, the group of Milica Radišić has been instrumental in advancing cardiac tissue engineering, particularly through the implementation of perfusion bioreactors (Brown, Iyer, & Radišić, 2008) and the development of elastomeric scaffolds like poly(glycerol sebacate) (PGS).

In the domain of vascular tissue engineering, the works of Laura E. Niklason and Christopher K. Breuer have been seminal. Niklason's first work on bioreactor-based cultivation of tissue-engineered blood vessels (Dahl et al., 2011; Naito et al., 2011) and Breuer's research on translating these technologies, including the implementation of bone marrow-derived cells, are landmark achievements. Their collaborations with clinical researchers highlight the translational pathway from bench to bedside.

The field of bioresorbable stents is heavily impacted by clinical researchers like Patrick W. Serruys and Yoshinobu Onuma, who have led major clinical trials evaluating devices like the Absorb BVS (Onuma et al., 2016). Their study gives the critical clinical evidence which helps the adoption and refinement of these technologies. From a biomaterials perspective, scientists like David J. Mooney and Steven G. Wise have made important impacts. Mooney's group has explored the implementation of injectable alginate hydrogels (Bidarra, Barrias, & Granja, 2014) and sophisticated drug delivery systems for cardiovascular applications, while Wise's work on tropoelastin and its non-thrombogenic properties (Waterhouse, Wise, Ng, & Weiss, 2011) has advanced the field of biomimetic material design.

This leading information is often interconnected through co-authorship, forming a dense collaborative network. For instance, the work of Khademhosseini frequently has collaborators from different institutions worldwide, showing the globalized effort in this study area. The presence of such networks accelerates innovation by combining expertise in material synthesis, cell biology, biomechanics, and clinical medicine, ensuring that scaffold development is informed by a deep understanding of cardiovascular pathophysiology.

6. Evolution of Keywords and Conceptual Shifts

The analysis of author-provided keywords gives a valuable window into the conceptual concentration and its evolution over time within the dataset. The most frequent keywords act as a high-level summary of the field's core concerns. Unsurprisingly, “Tissue Engineering” is one of the most dominant terms, showing in a vast number of articles, confirming it as the overarching paradigm. “Biomaterials” is equally prevalent, highlighting the foundational role of material science. Application-specific terms like “Cardiac Tissue Engineering”, “Vascular Tissue Engineering”, “Myocardial Infarction”, and “Vascular Grafts” are consistently common, reflecting the primary therapeutic targets.

A closer examination discloses a better temporal shift in keyword emphasis, marking the evolution of the field. In earlier highly cited papers (pre-2010), the concentration was on establishing fundamental principles. Keywords such as “Biocompatibility”, “Extracellular Matrix”, “Collagen”, and “Polymer” were prominent, indicating a primary concern with identifying appropriate materials and showing their basic safety and functionality in a biological context. The keyword “Electrospinning” began to rise in frequency during this period, signaling its adoption as a key fabrication technology.

From around 2010 onwards, the keyword landscape has been more sophisticated and application-driven. The rise of “Hydrogels”, specifically “Injectable Hydrogels”, points to the growing interest in minimally invasive delivery strategies for myocardial repair. The appearance of “3D Printing” and “Bioprinting” in more recent, highly cited published papers marks the advent of additive manufacturing as a transformative tool for creating complex, patient-specific constructs. Moreover, the keyword “Bioresorbable Stents” or “Bioresorbable Vascular Scaffolds” appears as a distinct and highly cited cluster, correlating with the clinical development and trialing of these devices.

Another substantial trend is the integration of biological and material concepts. Keywords like “Stem Cells”, “Mesenchymal Stem Cells”, and “iPSC” (induced pluripotent stem cells) are frequently coupled with scaffold terms, underscoring the strategy of combining cells with biomaterial carriers. The keyword “Angiogenesis” is persistently important, reflecting the critical requirement for vascularization in any engineered tissue. More recently, the inclusion of “Conductive Scaffolds” and specific materials like “Graphene” or “Carbon Nanotubes” in keywords denotes a frontier focused on enhancing the electrophysiological integration of engineered cardiac tissues. This evolution from basic material exploration to the sophisticated integration of advanced fabrication, biological cues, and electroactive properties illustrates the field's maturation and its continuous push towards more biomimetic and functional solutions.

7. Discussion and Future Perspectives

The scientometric analysis of 200 highly cited articles has given us a robust overview of the past achievements and current state of scaffold-based cardiovascular study. The field has matured from foundational investigations on biomaterial compatibility to the development of complex, bioactive, and patient-specific constructs. The dominance of cardiac and vascular tissue engineering themes confirms the pressing clinical need for solutions that go beyond palliation to true regeneration. The successful translation of some technologies, such as bioresorbable stents and decellularized matrices, from laboratory concepts to clinical products gives more evidence about the entire study enterprise and provides a roadmap for other technologies in the pipeline.

Various future directions, already hinted at in the most recent influential articles, are likely to define the next decade of research. First, the pursuit of **personalized medicine** will intensify. The combination of 3D bioprinting with patient-specific imaging data and the implementation of autologous iPSC-derived cells will enable the fabrication of custom-tailored grafts and patches that minimize immunogenic responses and improve functional outcomes (Maiullari et al., 2018; Kucukgul et al., 2015). Second, the development of **“smart” or responsive scaffolds** is an emerging frontier. These next-generation biomaterials would be designed to sense and respond to their local microenvironment, for instance, by releasing therapeutic agents (e.g., anti-inflammatory drugs, miRNAs) on demand in response to specific pathological signals like elevated reactive oxygen species or protease activity.

Third, the challenge of **vascularization** is an important hurdle for thick tissue constructs. Future research will likely concentrate on more specialized strategies to build pre-vascularized networks within scaffolds, maybe by combining 3D printing of vascular channels with the promotion of angiogenesis through controlled release of multiple growth factors with distinct temporal profiles (Brudno, Ennett-Shepard, Chen, Aizenberg, & Mooney, 2013). Fourth, the integration of **immunomodulatory strategies** will become increasingly essential. Rather than being viewed as inert, scaffolds are now understood to actively interact with the host immune system. Designing biomaterials which could modulate the immune response towards a pro-regenerative, anti-fibrotic phenotype represents a paradigm shift with immense therapeutic potential (Li et al., 2019).

Lastly, the convergence of **electronics and biomaterials** will continue to advance. Beyond conductive scaffolds for cardiac patches, the integration of flexible, biodegradable sensors within scaffolds could help real-time monitoring of tissue regeneration, hemodynamic parameters, or scaffold degradation, providing valuable data for post-implantation management and personalized therapy adjustments (Hong et al., 2019). In summary, the field of scaffold-based cardiovascular research, as mapped by its most influential literature, is a vibrant and rapidly evolving discipline. Its continued progress will depend on sustained interdisciplinary collaboration, a focus on clinical translation, and the embrace of emerging technologies that make scaffolds not just structural templates, but active partners in the complex process of cardiovascular regeneration.

8. Conclusion

This scientometric survey has analyzed the intellectual landscape of highly influential studies concerning scaffolds for cardiovascular disease. By investigating a curated dataset of 200 highly cited published papers, the study has delineated the major publication trends, determined the core journals and leading authors, and mapped the dominant research themes of cardiac repair, vascular graft development, and biomaterial innovation. The analysis has disclosed a field that is deeply interdisciplinary, firmly grounded in biomaterial science, yet decisively oriented towards addressing pressing clinical challenges in cardiology.

The evolution of keywords and research concentration has shown a transparent trajectory from basic material characterization to the development of sophisticated, bioactive, and patient-specific constructs. The rise of technologies like electrospinning, 3D bioprinting, and the clinical introduction of bioresorbable stents mark substantial milestones in this journey. The collaborative networks uniting material scientists, bioengineers, cell biologists, and clinicians have been instrumental in driving this progress, ensuring that engineering solutions are biologically informed and clinically relevant.

As the field looks forward, the integration of smart materials, advanced manufacturing, immunomodulation, and electronic monitoring systems promises to usher in a new era of regenerative cardiovascular medicine. The foundational knowledge captured in these 200 highly cited papers gives the springboard for these future innovations. This consolidated overview serves not only as a testament to the achievements of the past but also as a guidepost for scientists, clinicians, and policymakers, highlighting the most promising pathways toward creating transformative scaffold-based therapies for the millions of patients affected by cardiovascular disease worldwide.

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