


REVIEW

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Systematic review on the application of computational fluid dynamics as a tool for the design of coronary artery stents

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Abstract

Background Every year thousands of people die from atherosclerosis. This heart disease causes artery hardening, which impairs blood flow. For this type of disease, the primary treatment is the application of stents. Observing the importance of the application of stents in the treatment of atherosclerosis, the present work aimed to carry out a systematic review of the literature on the applicability of computational fluid dynamics in the design of stents for coronary arteries.

Main body of abstract To achieve the objective of this work, a review protocol was used. According to the method employed, we selected 16 articles to be read and analyzed in detail. Based on these studies, it was possible to verify that the works had two primary goals. The first was to model blood flow precisely to have CFD as a simulation and design tool. The second was to search for geometries of better performance, considering flow parameters that are believed to affect the stent lifespan—increasing time for stent replacement. Regarding the mathematical models for blood flow, it was verified that non-Newtonian models in transient regimes presented the best results. Regarding stent geometry, it was found that strut geometry and stent thickness can greatly influence wall shear stress parameters, which affect restenosis formation, and that the design of stents with innovative geometries has the potential to increase the lifespan of arterial stents.

Short conclusion After completing the work, a document that serves as a knowledge base for works that apply stents as a treatment and support material for further research was obtained.

Keywords Stent, Computational fluid dynamics, Atherosclerosis

1 Background

Cardiovascular diseases have always been a source of mortality among human beings, making it a challenge to solve them, both for medical and engineering professionals. Atherosclerosis is among the diseases that cause the most deaths [1].

Atherosclerosis is a disease caused by the hardening of the arteries due to the accumulation of fatty plaques inside them. This causes a change in blood flow, leading to severe consequences for the heart [2]. As a form of treatment, it is possible to use a device called a stent, which aims to restore blood flow in the region affected

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by the disease [3]. For example, in Fig. 1, one can see the application of a stent in an artery, where, through the introduction of a catheter inside the artery, the stent is inflated and positioned in such a way as to clear the passage of blood.

A recurrent inconvenience in this intervention is the need for new stent implantation. This is because, over time, new cells and layers of fat are deposited in the region of the stent, once again decreasing the diameter of the artery (this phenomenon is called restenosis) [3, 4]. One of the possible solutions employed is the change in the material of the stent, replacing the metallic stents with other so-called drug-eluting stents (they release a type of drug that reduces the chances of restenosis) and biodegradable [5]. However, although such a solution has good results, restenosis often occurs [3, 4].

To find new ways to minimize this problem, it is possible to use knowledge of computational fluid dynamics (CFD) applied to blood flow. One of the main advantages is that in the first stage of design and performance testing, the analyses are performed "in silico", i.e., virtually. As pointed out by Rocha et al. [6], currently, patient-specific CAD models allow for obtaining accurate results for the simulation of human hemodynamics. These models can be obtained from medical examination images of each patient. CAD modeling from medical imaging examinations is becoming more and more realistic, and the future points to increasing the accuracy of geometries and simulations and incorporating computational models to expand research and incorporate CFD simulation as a tool for clinical examinations, according to the authors. Based on this, the present work aims to carry

out a systematic review of the literature of works that use computational fluid dynamics to improve the performance of stents, proposing new forms of design, as well as more accurate mathematical models for blood flow.

2 Main text

2.1 Review protocol

A review protocol [7] was followed to verify the state of the art of CFD application for stent analysis, as detailed in Table 1.

We sought to structure the review by defining the conceptual framework and the central question of the research: "is it possible to improve coronary artery stent geometry based on CFD results?", i.e., we searched if CFD is a valuable tool for stent design. Based on this question, we sought to verify in the literature the state of the art in research aiming to improve stent design to reduce the restenosis process, using CFD. Thus, we sought to identify how fluid dynamic analysis can be effective for this type of research and innovation. Other tools, such as structural analysis (finite element method), which could be used, were not considered. This research was limited to investigating the use of CFD to analyze the stent performance and design.

The context of the review is general, covering the period from 2008 to 2021. The search strategy is aggregative, as "the question is about a well-defined and homogeneous question" [7]. As inclusion criteria, it was established that the studies should propose improvements to stent geometry based only on fluid dynamic analysis. On the other hand, studies that dealt

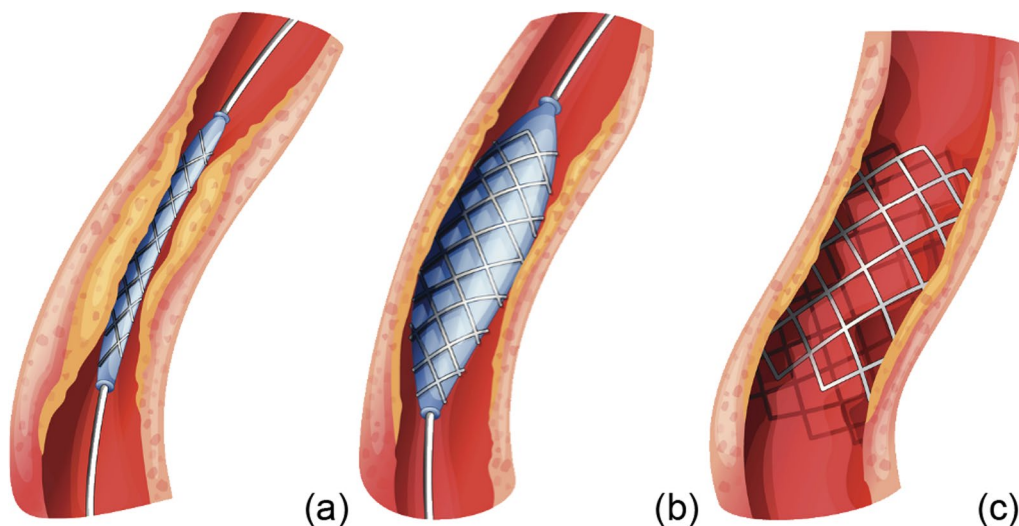


Fig. 1 Application of the stent inside a coronary artery: **a** introduction of the catheter; **b** stent inflation and positioning and **c** unobstructed artery. Source: Image by brgfx on Freepik.com

Table 1 Systematic review protocol

Systematic review protocol	
Conceptual framework	Improve stent geometry based on fluid dynamics
Context/horizon	General, 2008 a 2021
Theoretical currents	Computational fluid dynamics
Review strategy	Aggregative
Search criteria	Studies that treat and use fluid dynamic analysis in relation to coronary artery stents should be included and those that are not coronary artery stents (such as stents in the urethra for the treatment of strokes, etc.) and that did not use exclusively computational fluid dynamic analysis should be excluded (such as structural analysis)
Review question	Is it possible to improve coronary artery stent geometry based on CFD results?
Search terms/database	'STENT' AND 'GEOMETRY' AND 'CORONARY' (Scopus/Elsevier)

Table 2 Keywords employed in search

Keywords	Number of findings
'stent' AND 'cfid'	404
'stent geometry' AND 'cfid'	161
'stenosis' AND 'cfid'	594
'stent' AND 'coronary'	57,993
'stent' AND 'coronary' AND 'cfid'	113
'stent' AND 'flow'	15,918
'stenosis' AND 'flow'	36,166
'stent' AND 'fluid'	3703
'stent geometry' AND 'fluid'	363
'stent geometry' AND 'flow'	569
'stenosis' AND 'coronary'	503

with stents for other systems of the human body and others that presented different CFD methodologies were excluded.

Then, we tried to establish the keywords. Table 2 summarizes the attempts at combinations to delimit the research in the best possible way.

As can be seen, some combinations resulted in a very expressive number of academic works. Words such as 'STENOSIS' AND 'FLOW' AND 'STENT' AND 'FLOW' retrieved works that employed structural analyzes and bare-metal stents that meet the exclusion criteria established in Table 1. Thus, it was observed that the best combination of words corresponds to 'STENT' AND 'CORONARY' AND 'CFD' because, with these, it was possible to exclude works that did not comply with the protocol effectively. Then, the 113 texts found were analyzed. Among these, 30 were chosen to be read in full, while the others were disregarded based on the reading of the abstract and the criteria of inclusion/exclusion. Thus, 16 studies were selected to compose state of the art on the analyzed topic. Table 3 summarizes the texts chosen.

2.2 Analyzed articles

Sixteen articles concerning CFD analysis of blood flow through vessels with stents were fully read and analyzed. Most of the selected papers analyzed commercial stents and compared their geometry in terms of better system response in terms of fluid dynamic quantities. Other documents explored existing geometries and suggested their improvement based on simulation results. Finally, some papers evaluated the mathematical modeling for blood rheology (Newtonian or non-Newtonian fluid) and boundary conditions (steady or pulsating flow) to properly analyze the flow systems consisting of vessels and stents. The rheological modeling of blood as a single-phase fluid was one of the aspects approached by the analyzed works. Blood is a suspension of red blood cells in plasma. Therefore, blood may present non-Newtonian effects such as shear-thinning, viscoplasticity and viscoelasticity [22]. The degree to which these non-Newtonian effects affect the flow is a crucial aspect of the performance of simulation results. Because of this, the rheological modeling of blood was an item that was analyzed when reviewing the selected articles for the present work. In the following paragraphs, a summary of the contribution of each selected work to the state of the art is made.

Initially, Dehlaghi et al. [2] analyzed which stent design parameters were the ones that most influenced wall shear stress. The authors studied three-dimensional and two-dimensional stents, modeling blood as a Newtonian and incompressible fluid. As for the flow, a steady-state regime was adopted. As the main results, it was found that the number of struts (small cells that make up the stent), their profile, and the distance between them are the geometric parameters that most influence the flow.

Like the present work, Murphy et al. [5] reviewed how computational fluid mechanics had been used to predict and minimize the incidence of restenosis in arteries with stents. The authors divided the subject into two

Table 3 List of articles selected to compose the systematic review

Title	References	Blood fluid models	Flow modeling and assumptions	Main findings
Analysis of wall shear stress in stented coronary artery using 3D computational fluid dynamics modeling	[2]	Newtonian	Laminar, steady-state	Number of struts (small cells that make up the stent), the profile and the distance between them are the geometric parameters that most influence the flow
Predicting neointimal hyperplasia in stented arteries using time-dependent computational fluid dynamics: A review	[5]	Review of models employed up to 2010	Review of models employed up to 2010	It was possible to observe trends in research and the results of evaluations of which commercial models were the most efficient
The influence of strut-connectors in stented vessels: A comparison of pulsatile flow through five coronary stents	[8]	Non-Newtonian (Carreau model)	Laminar, pulsatile	The length of the struts and their alignment with the flow were the factors that most influenced hemodynamics
Three-dimensional numerical simulation of blood flow in two coronary stents	[9]	Newtonian	Laminar, steady-state and pulsatile	Closed-cell stent was more efficient than open-cell stent
Optimization of cardiovascular stent design using computational fluid dynamics	[10]	Newtonian	Laminar, pulsatile	From the application of an optimization algorithm for the geometry of the stents, it was possible to observe that the optimal angle between the struts was 40°
Hemodynamic simulation of intra-stent blood flow	[11]	Newtonian	Laminar, steady-state and pulsatile	As for the models used to characterize the blood, the Newtonian model proved to be quite efficient and the one that reduces the computational effort. As for the flow, the transient regime (pulsatile) was necessary to have more accurate results
Identification of hemodynamically optimal coronary stent designs based on vessel caliber	[12]	Newtonian	Laminar, pulsatile	For good hemodynamic conditions (high WSS) the larger the diameter of the vessel, the greater the number of struts was necessary
Cardiovascular stent design and wall shear stress distribution in coronary stented arteries	[13]	Non-Newtonian (Carreau model)	Laminar, steady-state	The thickness of the struts had the main effect on wall shear stress
A sensitivity analysis of stent design parameters using CFD	[14]	Non-Newtonian (Carreau model)	Laminar, steady-state	The most important parameter to be analyzed is the thickness of the stents' struts
Effects of cardiovascular stent design on wall shear stress distribution in straight and curved arteries	[15]	Non-Newtonian (Carreau model)	Laminar, steady-state	In the case of arteries without curvature, the geometric profile of the struts does not influence the shear stress. However, for arteries with curvature these values vary considerably
Effects of the inlet conditions and blood models on accurate prediction of hemodynamics in the stented coronary arteries	[16]	Newtonian and non-Newtonian	Laminar, steady-state and pulsatile	Modeling blood as a Newtonian fluid may overestimate the WSS result. Transient regime brings more accurate results
Comparison of stented bifurcation and straight vessel 3D-simulation with a prior simulated velocity profile inlet	[17]	Non-Newtonian (Carreau model)	Laminar, steady-state	The analysis of a bifurcated artery could be replaced by a simpler geometry (without bifurcation) with good results for the angle of branches of 70° and 90°

Table 3 (continued)

Title	References	Blood fluid models	Flow modeling and assumptions	Main findings
Evaluation of coronary flow conditions in complex coronary artery bifurcations: stenting using computational fluid dynamics: Impact of final proximal optimization technique on different double-stent techniques	[18]	Non-Newtonian (Carreau model)	Laminar, steady-state	The authors tested different stent techniques for a bifurcated artery with a 50° angle (Nano-Crush, Modified T, DK-Crush and Cullote). The "Nano-Crush" and "Modified T" were the best techniques for this type of configuration
The conical stent: in coronary artery improves hemodynamics compared with the traditional cylindrical stent	[19]	Newtonian	Laminar, steady-state	When using the non-commercial conical profile for the stents, it was observed that it is more efficient than the cylindrical one, presenting regions with higher values of WSS
Valuation of implanted-stent impact on coronary artery trifurcation blood flow by using CFD	[20]	Newtonian	Laminar, steady-state	It was found that the position of the stent when placed in an artery with trifurcation influences hemodynamics. This can be observed by obtaining results with different shear stress distributions for different stent placements
Investigation of flow characteristics of coronary slot stents using computational fluid dynamics	[21]	Newtonian	Laminar, steady-state	As observed in previous works, the thickness of the struts has a considerable influence on the WSS values

main topics: model effects and stent design effects. In the first part, the article explained how different fluid models (Newtonian and non-Newtonian) and boundary conditions had performed in terms of accuracy and efficiency. In this first part, they concluded that modeling blood as a Newtonian fluid could negatively affect the quality of results. However, inaccurate or poorly modeled boundary conditions would be the most significant source of errors in CFD results. In the second part, considerations were made about stent design based on fluid dynamics. Thus, the authors reviewed studies that compared commercial types of stents to analyze which parameters are most relevant for design to minimize restenosis. They discovered that low WSS and high OSI could lead to restenosis and that these parameters needed to be analyzed together.

Differently from the previous papers, in the work of Pant et al. [8], the authors use the three-dimensional model to analyze five different types of commercial stents to verify how their design can influence hemodynamics. Considering the fluid as non-Newtonian and the pulsating flow at the inlet, the authors concluded that the length of the struts and their alignment with the flow are the factors that most influenced hemodynamics.

Further, in the analysis of stent geometry, in the article by Gori [9], two different types of three-dimensional stent models were compared. Their differences were the position of the struts: an open-cell stent and the other with a closed-cell stent. In addition, the blood was modeled as a Newtonian and incompressible fluid, while the leakage was analyzed for both the steady state and the transient case. The analysis of the shear stress distribution showed that the closed-cell stent was more efficient in avoiding restenosis.

Later in seeking better stent design concerning hemodynamic performance, Gundert et al. [10] presented a new idea: instead of comparing some commercial designs; the authors employed an optimization algorithm to achieve the optimal angle between the struts. Modeling blood as a Newtonian, incompressible fluid and adopting boundary conditions that characterize the transient regime, this work concluded that the optimal angle would be 40°.

With the advancement of research, it was questioned how the stent design could affect its effectiveness and whether the models used in the simulations were the most appropriate. Given this, Hsiao et al. [11] focused their analysis on the modeling done for the flow and the boundary conditions applied to find the most accurate possible. The authors compared Newtonian and non-Newtonian models, pulsating and steady-state flow regimes. It was observed that the modeling as a Newtonian fluid presents little difference from the non-Newtonian one. Therefore, it is more interesting to model

for the simplest case (Newtonian) to reduce the computational effort. As for the flow, it was observed that the blood flow is better characterized using transient flow inlet conditions.

At the same period, the work of Gundert et al. [12] sought to analyze the relationship between the number of struts and the diameter of the artery using an optimization algorithm. Thus, using the exact modeling as in Gundert et al. [10], the authors concluded that for good hemodynamic conditions (high WSS), the larger the diameter, the greater the number of struts. As the artery with stenosis already has a reduced diameter, stents with fewer struts would be more effective in practice.

Also, using optimization algorithms, Hsiao et al. [13] sought to modify some geometric parameters in the stents to analyze which has the most significant effect on the shear stress values. The model used considered blood as a non-Newtonian fluid in a steady state. Of the parameters analyzed, it was observed that the thickness of the struts is what most influences the wall shear stress values.

Similarly, Stiehm et al. [14] also analyzed the influence of stent design parameters and their influence on WSS. The authors used the exact modeling (non-Newtonian fluid with Carreau's model) and boundary condition (flow in steady state). They concluded that the most critical parameter to be analyzed is the stent thickness. The main difference between these two works was the software used for numerical simulations. Stiehm et al. [14] used OpenFOAM and Hsiao et al. [11, 13] used ANSYS FLUENT.

Then, the following papers started to analyze how the curvature of the arteries could influence hemodynamics. First, Hsiao et al. [15] modeled blood using the Carreau model and steady-state flow. In the case of arteries without curvature, it was observed that the profile of the struts did not significantly influence the WSS. For arteries with curvature, however, the values varied considerably and tended to have smaller measurements when compared to arteries without curvature. They concluded that inserting a stent in a curved region increases the area of low shear stress.

In the work of Jiang et al. [16], the authors analyzed how inlet boundary conditions and blood rheology modeling affected the results and analysis performed in the arteries with stents. The authors concluded that when considering the fluid as Newtonian, although the computational time is reduced, there is a risk of overestimating the results, especially the WSS. Because of this, it is more accurate to model blood as non-Newtonian for arteries with stents. In addition, the authors also conclude that the boundary conditions with pulsating profile at the inlet are more accurate.

In a different approach, Wüstenhagen et al. [17] compared blood flow in an artery with a bifurcation and another without (equivalent to a straight tube). This analysis considered blood as an incompressible and non-Newtonian fluid (Carreau model). The steady flow was applied as a boundary condition to a bifurcated artery with a stent. Three situations were considered (each one varying the angle between the branches with values of 70°, 90° and 110°), and the velocity profile at the exit was obtained after the simulation. Based on this, new analyzes were performed considering the artery as a tube, with an inlet velocity profile equal to that obtained for the bifurcated artery. The objective was to verify if the results, mainly of wall shear stress, were similar and if the numerical analysis of the bifurcated artery could be replaced by a “straight line” (reducing the computational effort). It was possible to conclude that this substitution could be made, but for the 110° angle, the results tended to be more imprecise.

Advancing further in analyzing bifurcated geometries, Rigatelli et al. [18] used fluid CFD to compare four techniques for placing stents in arteries with a 50° bifurcation, namely, Nano-Crush, Modified T, DK-Crush, and Cullote. Blood was modeled as an incompressible and non-Newtonian fluid under a laminar flow and steady-state regime. As a result of the analyzed parameters (especially the shear stress distribution), it was observed that the “Nano-Crush” and “Modified T” techniques were the most efficient since they generated a blood flow profile and WSS distribution more physiological.

Contrary to what was being analyzed so far, Yu et al. [19] innovated by analyzing the hemodynamics of a stent with a conical profile, i.e., a varying diameter stent. The idea was to promote the increase in shear stress by narrowing the cross-sectional flow area. Although the built geometry was a simplified model, it was possible to observe that the shear stress values for the conical stents are higher, when compared to the cylindrical profile, resulting in a better performance. As for modeling, the authors modeled blood as a Newtonian fluid with steady-state inlet condition.

Aiming to model situations with more complex geometries, Fujimoto et al. [20] analyzed a trifurcated artery to see if stent placement affects blood flow and the possibility of restenosis. When modeling blood as a Newtonian fluid, laminar flow and steady-state regime, different positions were tested between the stent and the trifurcation, and it was found that they influenced the values of shear stress. This type of influence is limited to the area around the branch. They concluded that the stent should be placed in a position that did not overlap with the peaks of inlet velocity. Thus, it would be necessary to analyze the region of the trifurcation in which the highest

velocity values would occur to avoid placing the stent in this area.

Finally, Wang et al. [21] analyzed a specific type of commercial stent. They made several modifications in the geometry to reach an optimal pattern and verify which parameters most influence the WSS values. Blood is modeled as a Newtonian fluid at a steady state. With the main result, and corroborating with others previously found, it was observed that the thickness of the struts significantly influences the WSS.

Considering the works that appeared in the literature citing those analyzed here (e.g., [23, 24]), it was noticed that the trend that followed was the modeling of fluid–structure interaction. In this case, the coupling between the structural simulation of the vessel walls and the stent and the simulation of blood flow has the potential to bring more realistic results. Therefore, it is possible to envision the application of simulation methods in engineering to optimize medical device designs, especially stents, in the near future.

3 Conclusions

Based on the systematic review, it was possible to analyze a set of 16 works to verify how state of the art is in the research of fluid dynamic analysis of the design of coronary artery stents in a time range between 2010 and 2020. Furthermore, it was possible to verify the broad applicability of computational fluid mechanics in this area based on research that sought to describe the best design and blood flow model to minimize restenosis.

In general, it was possible to observe that Newtonian and non-Newtonian models are employed for blood flow. However, when explicitly comparing Newtonian and non-Newtonian models, non-Newtonian models were more accurate in predicting the risk of restenosis. Also, the transient pulsatile fluid model has been widely used in recent research. In addition, it is worth noting that CFD results may be helpful in the design of new stent geometries. Such an approach can reduce the restenosis rate and prolong the time the stent remains in the patient. It is expected that in the coming years, more research can advance in this direction to verify in vivo if suggested changes in geometry are indeed effective.

With the analysis of the set of papers selected in the present review and their indication of future trends, we may conclude that coupling CFD modeling with structural modeling and simulation, that is, the modeling of fluid–structure interaction (FSI), can bring more realistic results and make stent design optimization a standard process shortly.

Abbreviations

CFD Computational fluid dynamics

FSI	Fluid structure interaction
OSI	Oscillatory shear index
WSS	Wall shear stress
TAWSS	Time-averaged wall shear stress

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The source for Fig. 1 was the Freepik site: https://www.freepik.com/free-vector/diagram-showing-stent-with-balloon-angioplasty-human_8145405.htm#query=stent&position=0&from_view=search.

Author contributions

MXGV contributed to conception of the work, acquisition, analysis, interpretation of data, and draft of the work. FSFZ contributed to conception of the work, interpretation of data, and draft and reviewed of the work. CEEdF contributed to interpretation of data and review of the work. DPW contributed to conception of the work, interpretation of data, and review of the work. All authors read and approved the final manuscript.

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Availability of data and materials

As this is a review work, no data is available.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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