


Review

Computational Flow Dynamic Analysis in Left Atrial Appendage Thrombus Formation Risk: A Review

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Abstract: Atrial fibrillation (AF) is a common cardiac arrhythmia characterized by irregular and rapid electrical activity in the atria, leading to ineffective contraction and poor blood flow. More than 90% of the left atrial (LA) thrombi that cause thromboembolic events during atrial fibrillation (AF) develop in the left atrial appendage (LAA). AF modifies the hemodynamics of the left atrium, which can result in thrombosis of the LAA, systemic embolism, and stroke. The current options to reduce thromboembolic events are oral anticoagulation, surgical LAA exclusion, or percutaneous LAA occlusion. However, the mechanism underlying thrombus development in the LAA remains poorly understood. Computational fluid dynamics (CFD) analysis can be used to better understand the risk of thrombus formation and subsequent embolic events. CFD enables the simulation and visualization of blood flow patterns within the heart, including complex structures such as the LAA. Using CFD, researchers can analyze the hemodynamics of blood flow, identify areas of stagnation or turbulence, and predict the risk of thrombus formation. The correlation between blood flow dynamics, atrial fibrillation, and the risk of stroke has been highlighted by CFD studies investigating the underlying mechanism of thrombus formation in the LAA. This review study intends to provide a comprehensive overview of the factors involved in thrombus formation and their implications for clinical practice by synthesizing the insights acquired from these CFD studies.

Keywords: computational fluid dynamics; left atrial appendage; thrombus formation; hemodynamics; atrial fibrillation



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1. Introduction

The left atrial appendage (LAA), originating from the left atrium during fetal development, is described as a long, tubular, hooked structure with variations in size, shape, and volume [1]. The morphology of the LAA is highly diverse from patient to patient and is typically divided into four distinct types based on the structure it evokes: “Chicken wing” is the most frequent morphology (48%), followed by “Cactus” (30%), “Windsock” (19%), and “Cauliflower” (3%) [2]. Nevertheless, the classification is frequently open to misinterpretation and is reliant on the imaging plane. The volume size of LAA also varies significantly with the morphology [3]. Due to the LAA’s characteristics mentioned above, its effect on left atrial (LA) flow is difficult to evaluate.

Literature reveals that LAA is the most prevalent region for thrombus formation, increasing the risk of stroke in patients with atrial fibrillation (AF) [4–6]. AF is an electrophysiological pathology with irregular atrial beats, affecting between 1% and 2% of the general population, approximately 8% of people over 80 years old [7,8]. It has been identified as the principal cause of thromboembolic events, such as stroke and vascular dementia [9]. Consequently, there is an urgent need for more effective strategies for identifying and preventing thromboembolic events in AF patients [10]. AF can result in electrical,

structural, and contractile remodeling [11–13]. Atrial expansion, LA dysfunction, and inadequate atrial contraction result in thrombus development, especially in the LAA [11–13]. Furthermore, blood stagnation frequently occurs in the LAA since the blood flow velocity drops dramatically [1,6,13]. Consequently, LAA has received interest as a therapeutic target for preventing thrombosis, particularly in AF patients.

Several therapies are currently available to prevent thrombus formation: (i) oral anticoagulation (i.e., warfarin and direct oral anticoagulants) [14–16]; (ii) LAA surgical exclusion [17]; and (iii) LAA percutaneous occlusion [18,19]. However, all of these options have drawbacks that restrict their practice and effectiveness, such as the possibility of hemorrhagic consequences in the case of anticoagulation therapy [14–16] and the risks associated with invasive and transcatheter procedures (for example, vascular injury, air-embolic events, and peri-device leaks) [17] for surgical and percutaneous treatments, respectively [18,19]. Although numerous treatments have been proven to reduce the risk of thrombotic events, research has shown a significant residual risk [1,13,20,21]. Due to the diverse morphological factors, such as shape, size, and LAA volume, the reported approaches may fail. In addition, researchers have recognized hemodynamic parameters such as velocity, vorticity, and shear stress as thrombosis predictors [22,23].

Blood flow within the left atrium has currently been evaluated using several methodologies. Transesophageal echocardiography (TEE) can measure the speed at which the LAA empties. However, in clinical practice, TEE cannot accurately measure other hemodynamic parameters, especially in the thrombus regions, since it can either incorrectly label muscles as thrombi or misidentify thrombi hidden in one of the lobes [24,25]. Consequently, an improved strategy must be developed. In clinical research, 4D magnetic resonance imaging (MRI) is a cutting-edge technology that provides more information about 3D blood flow during the cardiac cycle. However, resolution limitations make it difficult to obtain blood flow parameters precisely. In addition, scan times are relatively long [26,27].

Nowadays, computational modeling can provide a detailed knowledge of the mechanisms and effects of AF [28,29]. Personalized computer models can enable the modeling of fibrosis, atrial fiber orientation, and wall thickness heterogeneity's influences on AF within realistic geometry and tissue properties [30,31]. The computational modeling process is carried out with the assistance of numerical analytic techniques and computational fluid dynamics (CFD). It can provide more quantitative data regarding blood flow and evaluate thrombosis risk [32]. Additionally, it can assess blood flow in specific regions containing LAA lobes. CFD has proved to be a valuable complementary tool for recommending ideal device sizing and placement for LAA occlusion device implantation [32]. In addition, CFD can be applied to better comprehend blood flow patterns following the LAA occlusion procedure and to estimate the risk of device-related thrombosis (DRT) for a given patient and device configuration.

This study aims to review the CFD simulation studies that analyzed hemodynamic parameters and thrombus formation risk. To the authors' knowledge, there has been no published literature review on this subject to date.

2. CFD Simulation for Thrombus Formation Risk

2.1. Process Description: From Obtaining a CT Scan to CFD Simulation of Left Atrial Appendage

It is essential for diagnosis, treatment planning, and risk assessment to comprehend the hemodynamics of the left atrial appendage. Obtaining a CT scan and conducting a CFD simulation of the left atrial appendage is necessary to shed light on the methodology and considerations required for an accurate and meaningful analysis. The patient is placed on the examination table and positioned within the CT scanner. Multiple perspectives of the heart and left atrial appendage are captured. The resulting image data is saved for future examination. The CT images acquired are transferred to a computer and processed by specialized software. LA and LAA contours have been defined and segmented to produce a three-dimensional model of the structure. This model is the basis for subsequent CFD simulations. Mesh generation is the process of discretizing a 3D model into a computational mesh. In this

phase, the model is subdivided into smaller elements that depict the geometry of the left atrial appendage and its surrounding structures. The resolution of the geometry is crucial for accurate CFD simulations. The CFD simulation's conditions are specified. This includes identifying fluid properties such as viscosity and density, as well as the system's initial and boundary conditions, such as inlet and outlet velocities, pressures, and flow characteristics. After defining the boundary conditions and generating the geometry, specialized software performs the CFD simulation. Mathematical equations are solved numerically, allowing for the prediction of flow behavior. After the CFD simulation has been completed, the results are analyzed and interpreted. Figure 1 presents a scheme of the process.

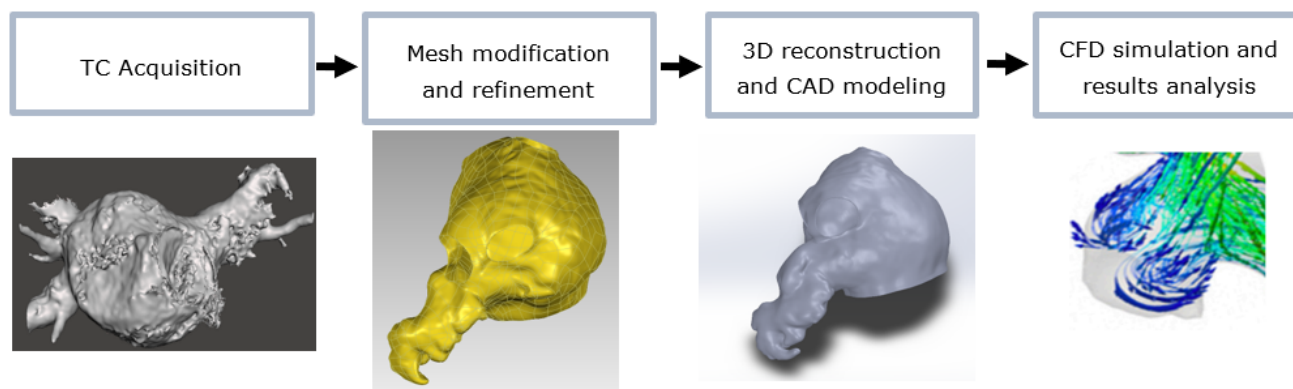


Figure 1. Scheme of the process: from CT to CFD results.

2.2. Works Selection

In order to be included in this analysis, the studies must be written in English, perform a CFD simulation, and evaluate the thrombus risk assessment in the LAA. Every LAA shape was considered. In terms of CFD software, there was no restriction. Abstracts from meetings and conference papers were excluded. The expected outcomes are the influence of hemodynamic parameters, LAA shape, and CFD characteristics in thrombus formation risk.

During the process of the literature search, eligibility criteria were formulated in order to facilitate the independent selection of titles, descriptors/abstracts found. The literature search identified 65 relevant abstracts of full-text articles. After eliminating duplicate results (n = 14), a total of 51 potentially eligible articles were selected. Conference papers (n = 9) and brief communications (n = 2) were excluded. In total, 16 papers were excluded for various reasons, including CFD blood simulations concerning the LAA or LA not being the main focus of the study (n = 15) and the production of personalized LAA occluders (n = 1). A flow diagram depicting this disposition of the studies was constructed (Figure 2). Characteristics of the included studies are shown in Table 1.

Table 1. Characteristics of the included studies.

Ref	Number of Participants/Cases	Population Characteristics	Summary	Outcomes Measured
[33]	2	AF	Investigation of the different hypotheses commonly assumed when performing atrial simulations for AF patients. It compares the rigid and flexible models and calculates two families of hemodynamic indices (wall shear-based and blood age distribution-based).	Range of indices that are usually applied to assess thrombus formation within the LAA
[34]	2	AF	The study discusses how computational fluid dynamics can be used to study the relationship between LA structural remodeling and intracardiac thrombosis. It describes how this approach was used to study two patients and found that it successfully captured characteristic features of LA blood flow.	<ul style="list-style-type: none"> • LA global flow characteristics • Vortex structure • Time course of LAA emptying

Table 1. Cont.

Ref	Number of Participants/Cases	Population Characteristics	Summary	Outcomes Measured
[35]	4	AF	A computational fluid dynamics approach is used to study the relationship between the shape of the LAA and the risk of thrombotic events. The “cauliflower” morphology is associated with a higher risk of thrombosis.	<ul style="list-style-type: none"> • Velocity • Shear strain rate • Virtual contrast residuals
[36]	4	Non-valvular AF	The correlation between LAA morphological features and computational fluid dynamics analysis for non-valvular AF patients is studied. It finds that there is a larger ostium, reduced motility for the cauliflower and cactus shapes, and lower velocity values from the CFD analysis.	<ul style="list-style-type: none"> • LAA fluid dynamics. • Morphological features of four different LAA shapes. • Geometrical parameters of LAA. • Velocity values from CFD analysis.
[37]	6	People with and without LAA thrombus or a history of transient ischemic attacks	Computational fluid dynamics is used to study how LA anatomy and function impact LA and LAA hemodynamics. It found that the blood inside the LAA of patients with a history of transient ischemic attacks had marked alterations in residence time and kinetic energy. The LA conduit, reservoir, and booster functions distinctly affect LA and LAA hemodynamics. Fixed-wall and moving-wall simulations produced different LA hemodynamic and residence time predictions for each patient, with fixed-wall simulations risk-stratifying the cohort worse than moving-wall simulations.	<ul style="list-style-type: none"> • Residence Time • Kinetic Energy • Velocity
[38]	---	Healthy and AF	Investigation of the effect of the changes in contractility and shape occurring in AF patients on the local hemodynamics that establishes into the LA appendage.	The essential role of the LAA wall contractility on the factors that may promote the formation of thrombus and consequent ischemic complications
[39]	20	AF patients with and without a history of stroke.	Differences in morphological and hemodynamic parameters between AF patients with and without a stroke history are analyzed. It finds that there are significant differences in both morphological and hemodynamic parameters between the two groups. The residual blood ratio in LAA was significantly smaller in the stroke group than in the non-stroke group. The residual particle ratio within LAA was considerably smaller in the stroke groups than in the non-stroke group. These parameters may be additional risk factors that can be used to better risk stratify AF patients.	<ul style="list-style-type: none"> • LAA actual depth. • Direct length. • Blood residual ratio. • Particle residual ratio
[3]	2	AF	CFD simulation framework for predicting treatment outcomes of LAA closure with atrial fibrillation is discussed. The CFD simulations with AF flow boundary conditions were performed to analyze flow characteristics within the LA before and after LAA closure. The framework utilizes automated LA/LAA image segmentation to reduce image processing. Results showed that the flow velocity magnitudes were significantly reduced by a maximum factor of 2.21, flow streamlines were considerably stabilized, and mitral regurgitation was reduced.	<ul style="list-style-type: none"> • Variabilities in LAA’s shape, size, and contractility which may result in the ineffectiveness of this procedure. • Flow characteristics (velocity, flow patterns, and vortices), • CFD was performed in LA with and without LAA, to mimic LAA closure procedure.
[40]	4	two patients with sinus rhythm and two with AF	The hemodynamics of the left atrium, highlighting differences between healthy individuals and patients affected by atrial fibrillation, were analyzed. It uses patient-specific geometries of the left atria to simulate blood flow dynamics and introduces a novel procedure to compute the boundary data for the 3D hemodynamic simulations. It evaluates several fluid dynamics indicators for atrial hemodynamics and investigates the impact of geometric and clinical characteristics on the risk of thrombosis.	<ul style="list-style-type: none"> • Thrombus formation • Atrial fibrillation • Age stasis
[41]	---	---	The LAA occluder configurations found after manipulation of device settings in the VIDAA platform were linked to a reduced risk of thrombus formation outside the implanted device, according to a qualitative analysis of blood flow streamlines and Endothelial Cell Activation Potential maps.	Different LAAO device settings can be tested to minimize the areas prone to thrombus formation after device implantation.
[42]	4	AF	The main goal of this work was to perform patient-specific hemodynamics simulations of the LA and LAA and jointly analyze the resulting blood flow parameters with morphological descriptors of these structures in relation to the risk of thrombus formation.	LAA morphological descriptors such as ostium characteristics and pulmonary configuration

Table 1. Cont.

Ref	Number of Participants/Cases	Population Characteristics	Summary	Outcomes Measured
[43]	1	Patients with left ventricular assist devices	Using patient-specific simulations, the study investigated the effect of left atrial appendage occlusion (LAAO) on thrombosis-related parameters. It found that LAAO significantly decreases the atrial stagnation volume and the time blood remains in the LAA.	<ul style="list-style-type: none"> Atrial velocity Atrial stagnation volume Blood residence time in the LAA
[44]	2	Patients with different shapes and volumes of LAA	CFD simulations are used to study the blood flow in the LAA. The study found that the morphology of the appendage can affect the risk of thrombosis formation.	<ul style="list-style-type: none"> Velocity Vorticity Blood flow rate
[45]	2	AF patients who underwent catheter ablation	A novel model was presented to elucidate relations between catheter temperature, patient-specific atrial anatomy, and blood velocity and predict how they change from SR to AF. The models can quantify blood flow in critical regions, including residence times and temperature distribution for different catheter positions, providing a basis for quantifying stroke risks.	<ul style="list-style-type: none"> Average blood velocity The percentage of blood remaining in the LA for longer than one cycle The maximum temperatures
[46]	---	AF	A mathematical model to quantify the LAA dead volume is discussed. A novel methodology was presented to study blood stasis risk within the left atrium appendage in the absence of atrial contraction due to fibrillation.	<ul style="list-style-type: none"> The proposed index is an effective way of quantifying the LAA dead volume. Stagnation can be detected in the LAA dead volume. Fluid dynamic behavior in the LAA dead volume is independent of the rest of the LAA.
[47]	6	Six people with a wide range of conditions, including normal LA function and a variety of LA dysfunctions, as well as subjects in sinus rhythm and with AF	The impact of non-Newtonian blood rheology on LA stasis in patient-specific simulations is investigated. The study found that slow flow in the LAA increases blood viscosity, altering secondary swirling flows and intensifying blood stasis.	<ul style="list-style-type: none"> Effects of hematocrit and rouleaux formation kinetics on blood viscosity, altering secondary swirling flows and intensifying blood stasis
[22]	3	One healthy patient and two patients with AF	The effects of AF on blood flow and hemodynamic parameters are investigated. The study uses MRI to construct models of a healthy left atrium and two atria with fibrillation. The results show that each characteristic phenomenon of AF influences hemodynamics and that high-frequency fibrillation has a significant impact on the stagnation of blood flow.	Effects of atrial fibrillation on blood flow and hemodynamic parameters
[48]	1	AF patients	The effect of AF on thrombosis in the left atrium is explored. The study uses a patient-specific anatomical shape of the left atrium and considers the non-Newtonian property of the blood. The results indicate that AF can aggravate thrombosis, which mainly occurs in the LAA.	Thrombosis risk in the left atrium under atrial fibrillation
[49]	6	LAA Chicken wing	To investigate the risk of thrombosis in the LA and LAA of AF patients, CT imaging and CFD analysis were utilized. The results revealed that the LAA exhibited lower blood flow velocity and time average wall shear stress values (TAWSS), indicating an increased propensity for thrombus formation. Moreover, AF patients exhibited elevated relative residence time (RRT) values in the LAA, highlighting the elevated risk of thrombosis in this population.	<ul style="list-style-type: none"> Shear Rate Thrombus Prediction Model Time Average Wall Shear Stress (TAWSS) Oscillatory Shear Index (OSI) Relative Residence Time (RRT)
[50]	36	AF patients and synthetic ellipsoidal left atria models	A sensitivity analysis is performed to identify the most relevant LA and LAA morphological parameters in atrial blood flow dynamics. Simulations were run on synthetic ellipsoidal left atria models where different parameters were individually studied. Additionally, the authors observed that pulmonary vein configuration critically influenced LAA blood flow patterns.	<ul style="list-style-type: none"> LAA shape LA volume Pulmonary vein configuration
[51]	6	Non-valvular AF	Simulations of fluid dynamics after LAA occlusion were performed in order to predict thrombus formation after LAA occlusion. The results of the simulation showed that thrombus formation was sensitive to changes in the parameters of the simulation. The authors concluded that the simulation could be used to predict thrombus formation in clinical settings.	Sensitivity analysis of different boundary conditions scenarios available in the literature to identify the optimal modeling choices for predicting DRT.

Table 1. Cont.

Ref	Number of Participants/Cases	Population Characteristics	Summary	Outcomes Measured
[52]	---	AF	A discussion regarding how the LAA is a frequent location of thrombus formation in patients with AF is reported. It reviews how recent studies have suggested that it is crucial to incorporate LAA geometrical and hemodynamic features to evaluate the risk of thrombus formation in LAA.	<ul style="list-style-type: none"> LAA-related factors associated with thrombus formation and cardioembolic events
[53]	---	AF	The researchers selected a LA chamber model and created a framework to connect the different LAAs from the other four patients to this model. These new anatomical models formed the computational domain for the CFD study. CFD simulations were conducted to evaluate the relation between LAA shape and blood flow characteristics in atrial fibrillation (AF) conditions.	<ul style="list-style-type: none"> Velocity Vorticity LAA Orifice Velocity Residence Time

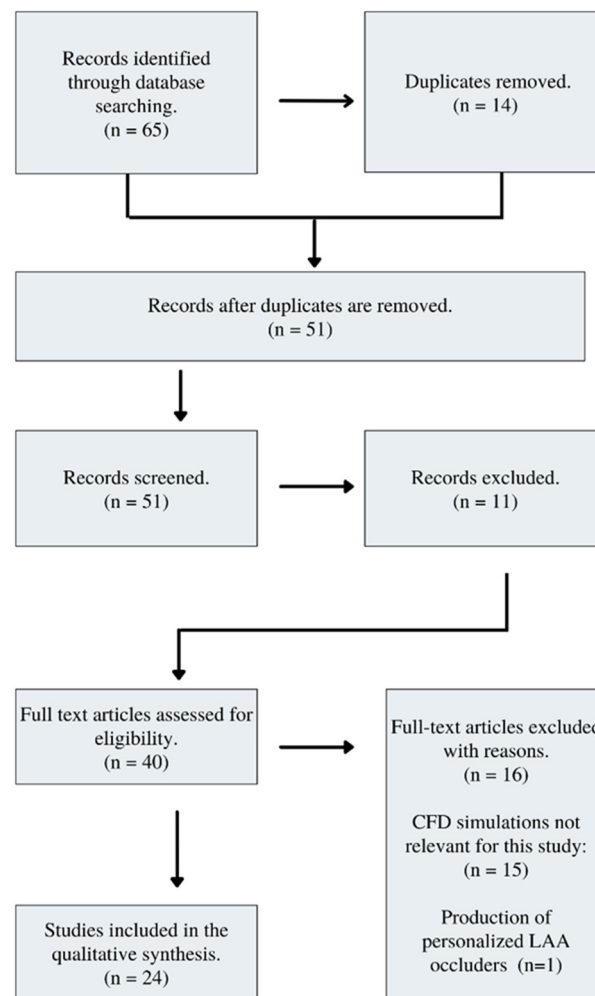


Figure 2. Flow diagram of study selection.

3. Discussion

Abnormal electrical impulses in the roots of the pulmonary vein primarily cause AF. These impulses induce an uneven and inefficient contraction of the LA. This atypical contraction pattern promotes thrombus development in the LAA and is five times more prevalent in people with AF than in healthy patients [46,54]. Although several clinical investigations have analyzed the correlation between LAA morphology and stroke risk in individuals with AF, the underlying mechanisms are still unclear. Current risk categorization approaches for patients are obtained from major clinical trials based on demographic and clinical characteristics such as age, sex, hypertension, and a history of thromboembolic

disease [14]. Since they are all non-patient-specific, their predictive value for a particular patient could be enhanced by incorporating mechanical or local patient-specific indicators, such as cardiac morphology or blood flow.

Developments in medical imaging, including TEE, MRI, and 3D computed tomography (CT), have opened up the possibility of applying computational fluid dynamic (CFD) tools for the analysis of intracardiac flow. Early research on LA CFD was performed using complete left-heart simulations; hence, CFD analyses focusing on LAA are comparatively recent [55]. Few publications provide numerical analyses of flow patterns in the LA, with some including the LAA model.

According to the literature, the chicken wing morphology is the least critical when compared to the other geometries, which reveals a link between the LAA morphology and the risk of clot formation [33,35,36,46]. However, varied quantifications of the risks can be found in the literature depending on the population that was analyzed; thus, it is difficult to generalize the significance of this association [5,49]. Notably, the Cauliflower shape appears to be related to an increased risk of thrombus formation [4,35,36].

Several clinical investigations suggested that the risk of stroke could be reduced by utilizing hemodynamic data on the LA and mainly on the LAA [22,26,36,38,46,53,56]. Using a CFD approach, it is possible to access various biophysical indicators in a complex fluid dynamics system, such as velocity and pressure fields, cardiac blood flow rates, vorticity and turbulent kinetic energy, as well as specific metrics such as Wall Shear Stress (WSS), Time-Averaged Wall Shear Stress (TAWSS), Oscillatory Shear Index (OSI), Residence Time (RT), and Endothelial Cell Activation Potential (ECAP) [3,33–36,39,40,42–45,47,50,53].

The evaluation of velocity and pressure fields revealed insightful information regarding regions of disturbed flow, recirculation, and stagnation, which are known to contribute to thrombotic events [57,58]. These results confirm previous research that linked abnormal blood flow patterns to an increased risk of thrombus formation. The estimation of cardiac blood flow rates enabled a comprehensive evaluation of blood volume passing through various vasculature regions. Both low and high abnormal flow rates have been linked to an increased risk of thrombosis. The computation of vorticity and turbulent kinetic energy distributions yielded important information regarding the presence and magnitude of turbulent flow patterns. Vorticity denotes the local rotation of blood flow, whereas turbulent kinetic energy denotes the presence of turbulent flow patterns [53]. There is evidence that turbulent flow promotes endothelial dysfunction and thrombus formation. Both variables can affect the likelihood of thrombus formation. CFD permits the computation of vorticity and turbulent kinetic energy distributions, which aids in the identification of thrombosis-prone regions. WSS emerged as an important indicator of thrombus formation among the specific metrics investigated [59]. High WSS values were associated with endothelial cell damage, whereas low WSS values were associated with stagnant blood flow. It quantifies the frictional force imparted by the blood against the vessel wall as it flows. Measuring WSS helps identify regions of blood vessels where thrombosis risk may be elevated. In addition, the TAWSS evaluation presented a more comprehensive understanding of the shear stress experienced by endothelial cells throughout a cardiac cycle [60]. It is the average WSS value over a complete cardiac cycle. TAWSS assists in the identification of regions of the vasculature in which sustained low or oscillatory shear stress may contribute to endothelial dysfunction and consequent thrombus formation. OSI analysis permitted quantification of the magnitude and directionality of shear stress changes throughout a cardiac cycle [60]. High OSI values are associated with an increased risk of endothelial dysfunction and thrombus formation in regions with disturbed blood flow and a change in flow directionality. Analysis of Residence Time (RT) revealed the average time blood particles spend in specific regions of the vasculature [61]. Extended residence time caused by flow recirculation or stagnation can contribute to the formation of a thrombus. The identification of regions with extended residence time facilitates the identification of regions with an increased risk of thrombotic events. ECAP is a metric used to estimate the risk of endothelial cell activation, which contributes to thrombus formation [62]. It evaluates the

potential for endothelial cell activation by combining multiple hemodynamic parameters, including WSS, pressure, and strain. ECAP assists in identifying regions where endothelial dysfunction increases the risk of thrombosis. These statistical metrics provide valuable insights into the risk of thrombus formation.

Among the reported studies, one of the main discussed topics is the interaction between LAA hemodynamic parameters, morphological type, and further obtained results' comparison with the data collected by Di Biase et al. [4]. It is important to highlight that blood flow is critical in determining the possibility of thrombosis formation, particularly under AF conditions [44]. The flow patterns in the LA have been numerically analyzed in CFD studies [3,34,37], with some explicitly focusing on the LAA stasis in AF situations [33,35,50]. Some LAA morphological descriptors, such as ostium characteristics and pulmonary configuration, influenced LAA blood flow patterns [42]. As a result, these investigations were able to provide further knowledge on the AF phenomena and calculate inaccessible blood stasis-related parameters, such as residence time, vorticity, and shear stress. High volume, low blood flow velocity, and two-lobe-appendage are more likely to have blood stasis [42]. Furthermore, the distal part of LAA is reported as the most common region for blood stasis because of the lowest velocity magnitude [44]. Slow flow in the LAA increases blood viscosity, altering secondary swirling flows and intensifying blood stasis [47]. Non-Newtonian effects of blood rheology, neglected in several previous CFD studies, aggravate blood stasis and increase the likelihood of LAA thrombosis, a recognized risk factor in ischemic stroke. Non-Newtonian effects can be subtle when examined using instantaneous metrics but are manifested in the blood residence time [48]. Patient-specific CFD analyses of LA hemodynamics suggest that the thixotropic, shear-thinning rheology of blood can significantly affect flow patterns inside the atrial appendage in a hematocrit-dependent manner [47,48].

CFD simulations have some issues in assessing and quantifying the stasis risk for a particular patient since blood flow washing the LAA is a complex, multi-factorial process. There are primarily two ways to simulate CFD: fixed-wall simulations [3,34–36] and moving-wall simulations [34,37]. The first one does not account for the movement of the atrial wall; therefore, it may not accurately represent the atrial flow in all circumstances, especially in sinus rhythm. The other is based on reproducing the patient-specific heart action using medical imaging data. Thus, with this last approach, CFD simulations can properly replicate the hemodynamic state of the patient's atrium when medical imaging is performed. This presents a challenge for forecasting medium- and long-term stasis in patients with paroxysmal atrial fibrillation. The comparison of the outcomes of fixed-wall and moving-wall simulations has revealed that flow patterns and residence time are remarkably comparable in the case of a compromised function, particularly when both the reservoir and booster functions of the appendage are diminished [33,37]. By employing the rigid-wall concept, it becomes feasible to faithfully reproduce the important conditions corresponding to a specific atrial morphology, irrespective of the atrial function during the period of data acquisition. Consequently, this approach mitigates the potential for inaccurately prognosticating the long-term stability in paroxysmal atrial fibrillation (AF) patients, thereby addressing a significant apprehension associated with the moving-wall simulation method.

The presence of closure devices is also analyzed in the literature [3,41,43,51]. A comparison between the results indicated that LAA closure significantly impacted blood flow velocity and paths. LAA closure successfully reduced LA vortices in strength and duration, indicating that percutaneous LAA occlusion can effectively reduce flow patterns associated with thrombus formation.

4. Conclusions

CFD has made incredible progress in recent years, emerging as an effective tool for analyzing the patterns of blood flow and their impact on various cardiovascular diseases. Among these medical conditions, the formation of LAA thrombus poses a substantial risk

to atrial fibrillation patients. In the context of atrial fibrillation, these developments in CFD are increasingly acknowledged as a valuable resource for understanding the flow patterns within the LA and LAA and assessing the likelihood of blood stagnation in individual patients. This could enable the development of tools for identifying patient segments, selecting the optimal therapy, and supporting them during percutaneous intervention.

Recent CFD research has enabled a better understanding of AF principles and the calculation of otherwise inaccessible parameters relating to blood stasis and atrial flow patterns. However, these studies have some limitations. The considerable sensitivity of CFD to numerical assumptions, such as boundary conditions and material properties, which are used to decrease computational costs and simplify the modeling process, represents the significant limitations of the technique.

The accuracy of CFD model results is dependent on a number of variables, including the resolution of medical images, the quality of the discrete grid, the choice of boundary conditions and turbulent model, and the computational parameter settings. These factors collectively affect the simulation's accuracy and its correspondence with real-world conditions. Regarding patient-specific boundary conditions, such as the flow profile in the mitral valve, obtaining precise and individualized data is a difficult undertaking. This aspect is essential for the future development and clinical deployment of patient-specific models. To improve the accuracy of CFD simulations, it is necessary to emphasize the need for additional research and technological advancements in the acquisition of precision patient-specific boundary conditions. This review also emphasizes the significant impact of simulation conditions on the flow field, specifically the selection between moving-wall and fixed-wall simulations, as well as the nature of velocity/pressure profiles. The analysis demonstrates distinct flow patterns that emerge from these variations, highlighting the importance of precisely defining boundary conditions and taking temporal changes in velocity and pressure profiles into account. This emphasizes the significance of selecting appropriate simulation parameters to enhance flow prediction capabilities in cardiology. By meticulously considering the effect of simulation conditions, it is possible to ensure more accurate representations of real-world scenarios and enhance the design and optimization of pertinent systems.

Insufficient appropriate reference solutions or experimental data for model validation and verification may potentially affect the CFD model development process.

5. Future Directions

CFD has played a pivotal role in elucidating the hemodynamic factors underlying LAA thrombus formation, thereby providing valuable insights into its mechanisms. In terms of expanding the understanding of LAA thrombus formation and its clinical significance, the future holds promising prospects for harnessing CFD's potential.

CFD's ability to generate patient-specific simulations is a significant technological advancement. By incorporating advanced imaging modalities, such as magnetic resonance imaging (MRI) and computed tomography (CT), it has become possible to generate patient-specific models of the LAA. These customized simulations take into account unique anatomical variations, including shape, size, and spatial orientation. In the future, it will be crucial for researchers to focus on refining and validating these patient-specific models. These efforts will increase the precision of CFD simulations, allowing for a more thorough understanding of LAA thrombus formation in individual patients.

Blood is a dynamic fluid composed of red blood cells, platelets, and plasma, all of which play a significant role in the process of blood clot formation. Future directions for CFD research include incorporating more complex models of blood constituents into simulations. By considering the behavior of these constituents and their interactions with the wall of the LAA and other blood components, it is possible to obtain a more comprehensive understanding of how blood clots form. These models have the potential to identify new hemodynamic markers that indicate blood clot formation and provide clinicians with valuable guidance for making informed decisions regarding anticoagulation therapy.

The formation of LAA thrombus involves intricate interactions between macroscopic and microscopic fluid dynamics. Although current CFD simulations provide useful insights into macroscopic flow patterns, they frequently struggle to accurately represent micro-scale phenomena. Future developments in CFD research look to develop multi-scale modeling techniques that bridge the gap between macroscopic and microscopic scales in order to overcome this limitation. These multi-scale models will allow for the investigation of phenomena of coagulation within the context of LAA thrombus formation, leading to a more comprehensive understanding of the underlying processes involved.

Combining artificial intelligence (AI) and machine learning (ML) techniques with CFD offers a fascinating chance to improve the understanding of LAA thrombus formation. AI/ML algorithms are capable of analyzing vast quantities of CFD simulation data and detecting intricate patterns that may not be immediately discernible to human observers. These algorithms have the potential to aid in the prediction of patient-specific thrombosis formation risks, the optimization of treatment strategies, and the improvement of patient outcomes. Utilizing the assets of CFD simulations and AI/ML capabilities, researchers can uncover new insights and create more accurate predictive models.

By analyzing future directions in CFD research, such as enhanced patient-specific simulations, incorporation of blood constituent models, multi-scale modeling, and integration with AI/ML techniques, it is possible to further improve our understanding of this complex phenomenon. These developments have the potential to influence the future of cardiovascular research and clinical decision-making, resulting in enhanced patient care and outcomes in the management of LAA thrombus formation.

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