Influence of thrombosis, stenosis and catheter on rheological characteristics of blood: A systematic review

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Abstract

Understanding potential disease causation due to stenosis and thrombosis and its treatment by utilising catheters and magnetic field has gained increasing attention from experts worldwide. Endothelial injury or plaque rupture can trigger thrombosis, which can cut off the supply of blood to the heart or brain, causing stroke or a myocardial infarction. In the regions of stenosis, narrowing of lumen of arteries and high shear rate generate conditions that increase platelet build-up and blockage. Treatment like catheters and magnetic field are famously being implemented in modern medicine as a way of removing blood clots inside a constricted artery in light to improve the blood circulation inside a human body. This article reviews the impact of the simultaneous presence of stenosis and thrombosis on blood flow characteristics and the effects of using catheter in clearing the obstructions in the lumen of blood vessels. We also introduce significant recent development on blood flow modelling relating to the subject matter. A sample mathematical model is considered from the literature to explain the influence of aforesaid arterial constrictions and clinical therapy for future directions in the medical field. Based on the collected literature, we note that the angioplasty catheter greatly increases blood flow as compared to infusion and guidewire catheters because it uses a balloon-tipped catheter to remove occlusions in the artery lumen. This comprehensive review and the proposed mathematical model together with the clinical data may offer directions for further studies, especially on one specific type of catheter for balloon angioplasty as the best treatment for clearing the occlusions in the diseased artery.

Keywords: Blood flow; Constrictions in arteries; Catheters; Thrombosis; Non-Newtonian fluids; Clinical applications.

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Abbreviations

CAD	Coronary Artery Diseases
LDL	Low-density Lipoproteins
SMCs	Smooth Muscle Cells
AP	Activated Platelets
AF	Atrial Fibrillation
TF	Tissue Factor
PLS	Plasminogens
RBCs	Red Blood Cells
WBCs	White Blood Cells
ADP	Adenine di-Phosphate
GpIb	Glycoprotein Ib
LMWH	Low Molecular Weight Heparin
VADs	Ventricular Assist Devices
DVT	Deep Venous Thrombosis
PE	Pulmonary Thromboembolism
ATIII	Antithrombin III
Rx	Rapid Exchange
OTW	Over-the-wire
POBA	Plain Old Balloon Angioplasty

1. Introduction

Blood flow under normal physiological and abnormal pathological conditions is a fascinating subject area to research, as when the artery is completely blocked, the restricted blood flow could potentially lead to chest discomfort or a heart attack. The majority of mortalities in affluent countries are caused by cardiovascular disorders, the majority of which are linked to irregular blood flow along arteries in some way. The human circulatory system delivers oxygen and vital nutrients to cells while also eradicating waste substances within the same cells. Blood is made up of blood cells that are suspended in plasma, an aqueous solution. Plasma, which makes up 55% of blood fluid and is 92% water in volume, comprises of dispersed proteins, carbohydrates, blood cells, mineral ions and hormones [1]. erythrocytes (well-known as red blood cells), leukocytes (well-known as white blood cells), thrombocytes (well-known as platelets), make up

the majority of blood cells. Red blood cells are tiny semi-solid elements that upsurge blood viscosity and influence the action of the fluid. Plasma has been noted to behave like a Newtonian fluid [2], whereas entire blood displays a non-Newtonian nature [3].

The pulsatile character of arterial blood flow is a substantial aspect. The heart's left ventricle chamber intermittently discharge blood to the entire arterial system of the body [4, 5]. Generally, the flow of blood is thought to be laminar. However, the evolution of stenosis, such as stiffness of the artery wall, triggers turbulence and diminishes the needed blood movement, occasioning in organ malfunction. Thus, a meticulous understanding of blood flow is a major perception in the diagnosis of vascular disorders [6, 7]. The pressure p and flow velocity u are the two most important key parameters of blood flow characteristics [8]. In the cases of stenosis and thrombosis occurring simultaneously, the catheter treatment is efficient in reducing the obstructions which are formed in the lumen of the blood vessel.

1.1 Coronary artery diseases

Atherosclerosis formed in the coronary arteries causes Coronary Artery Diseases (CAD), which might be asymptomatic [9, 10]. According to Udaya and Ramiah [11], coronary artery disease is the dominant agent contributing global fatality. When the endothelial function of the arterial wall is disturbed, atherosclerosis grows due to the accumulation of lipoprotein droplets in the coronary intima [12]. Water insoluble lipids spread in the bloodstream by binding to water soluble lipoproteins termed apolipoproteins. In high concentrations, low-density lipoproteins (LDL) have the potential to pervade the disturbed endothelium and encounter oxidation [13, 14]. This oxidized LDL draws in leukocytes to the coronary intima, where they might be collected by macrophages, yielding in the production of foamy cells. These cells with a foamy structure multiply and create lesions named as fatty streaks. This is the first kind of atherosclerotic lesions that can be seen. Fig. 1 displays the plaques formed in the lumen of coronary artery.

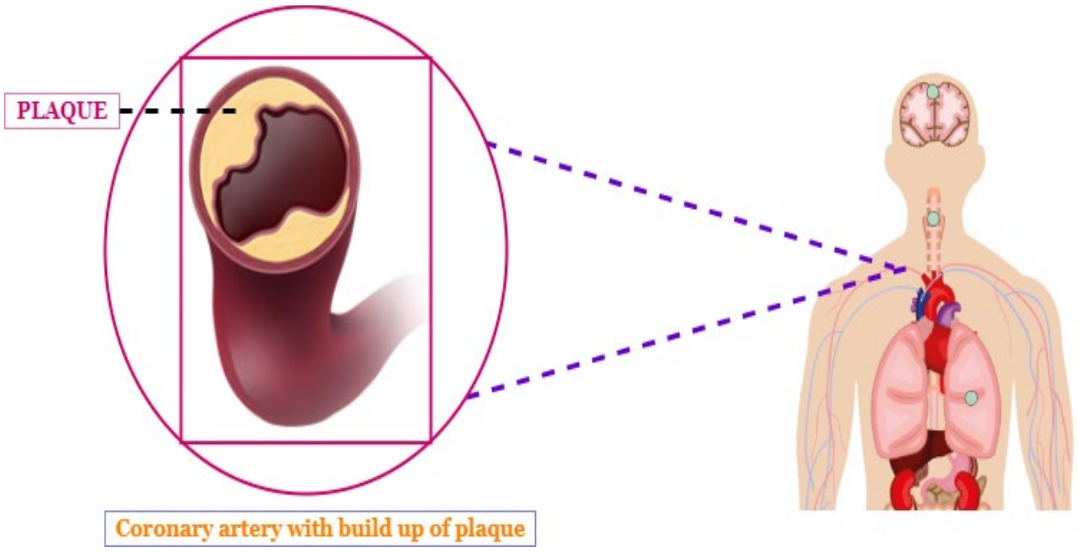


Fig. 1: Development of plaques in the lumen of coronary artery.

The creation of such lesions sends out signals that draw smooth muscle cells (SMCs) to the fatty streak's location. SMCs start to multiply and generate extracellular matrix, primarily proteoglycans and collagen. The atherosclerotic plaque begins to form and accumulates a substantial volume of extracellular matrix produced by SMCs, making the lesion to proceed to fibrous plaque. Small blood vessels grow as the fibrous plaque that obtrudes in the lumen of the coronary vessel, potentially calcifying the plaques. The ultimate lesion is complex and progressive which consists of a fibrous cap overlaying a lipid-rich core accommodating necrotic material and is potentially thrombogenic [15]. Inhibition of blood flow happens on account of the growth of atherosclerotic plaque in the coronary artery, leading to a mismatch between the demand and supply of myocardial oxygen [16]. The symptoms of CAD appear as heaviness, substernal discomfort, and a pressure-like consciousness that may extend to the back, jaw, arm, or shoulder.

1.2 Stenosis

Arterial stenosis is a condition in which fats and other substances accumulate in the arteries, a condition known as atherosclerosis (see Fig. 2). The first stage is the initial fatty deposits at the arterial wall. The second stage shows the narrowing of the artery due to the deposits and eventually in the third stage, there is an almost complete blockage of the artery. It may cause a heart attack because it restricts blood flow. The starting and progression of stenosis or vascular lesions, as well as the establishment of atherosclerotic plaques, in the human cardiovascular system's vessels, have

been studied from various perspectives. Few researchers have experimentally studied on blood flow patterns in relatively blocked pipes [17 – 19]. Several authors [20 - 22] proposed mathematical models for analyzing unsteady movement in a stenotic blood vessel. These analytical models deliver valuable insights into the impact of various parameters like, stenosis, blood viscosity, blood vessel elasticity, and blood vessel geometry on blood flow. Consequently, the investigation of blood motion via the stenosed artery is needed.

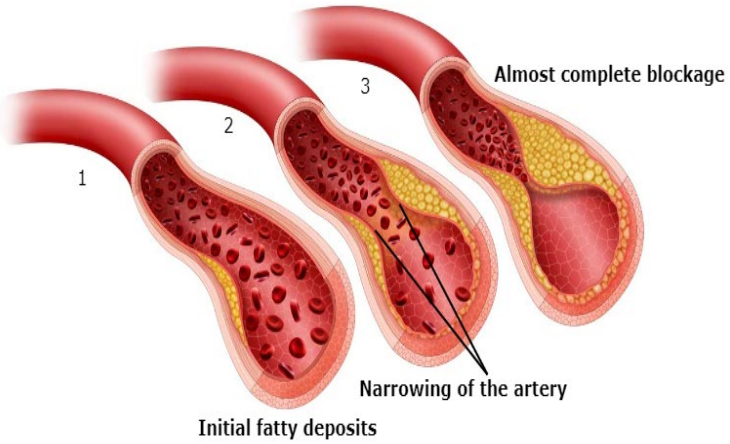


Fig. 2: Three stages of stenosis progression in blood vessels.

Few researchers considered blood as Newtonian fluid [23–27] when it flows at higher shear rate (>100/s) in larger diameter arteries. Newtonian actions not merely accounts blood flow in an artery of a large radius, but it also expresses gas transport in the atmosphere [28]. Non-Newtonian behavior, according to Ismail et al [29], is a significant factor. Their research demonstrates that blood turns into non-Newtonian when the radius of an artery is less than $300\mu m$. There are several non-Newtonian models that are commonly used to represent blood movement behaviour, for instance Herschel-Bulkley fluid, Casson fluid and Carreau fluid are some of them which are more frequently used [30–33].

Puskar et al. [34] investigated the dynamics of blood flow in cylindrical pipes system by assessing pressure drop contrary to the wall, pressure and shear stresses at the wall. Manisha et al. [35] investigated a non-Newtonian blood flow model with the influence of various geometry of stenosis on several flow quantities. The Power-law model is applied to investigate the non-Newtonian property of blood. Recent study of Sarwar and Hussain [36] incorporated the use of gold nanoparticles to improve the flow of blood via a constricted artery due to stenosis and they

have shown that they can refine the presentation of the flow of blood by managing the behaviour of nanoparticles.

1.21 Different shapes of stenosis

a) Axially symmetric stenosis

The mathematical representation of the axially symmetric can be described as

$$\bar{R}(\bar{z}) = \begin{cases} \bar{R}_0\left[1-\bar{s}\left\{\bar{L}_0^{n-1}\left(\bar{z}-\bar{d}\right)-\left(\bar{z}-\bar{d}\right)^n\right\}\right], & \bar{d}\le\bar{z}<\bar{d}+\bar{L}_0 \\ \bar{R}_0, & otherwise \end{cases}, \quad (1)$$

where $\bar{R}_0$ is the radius of unrestricted artery, $\bar{L}_0$ is the distance of the stenosis, $\bar{d}$ is the initial position of the stenosis, and $\bar{s} = \dfrac{\bar{\delta}_D}{\bar{R}_0\bar{L}_0^n}\left(\dfrac{n^{\frac{n}{(n-1)}}}{n-1}\right)$ where $\bar{\delta}_D$ is the stenotic depth at the outermost layer which is placed at $\bar{z} = \bar{d} + \dfrac{\bar{L}_0}{n^{\frac{1}{(n-1)}}}$ such that $\dfrac{\bar{\delta}_D}{\bar{R}_0} << 1$. The pictorial representation of the above stenosis is depicted below.

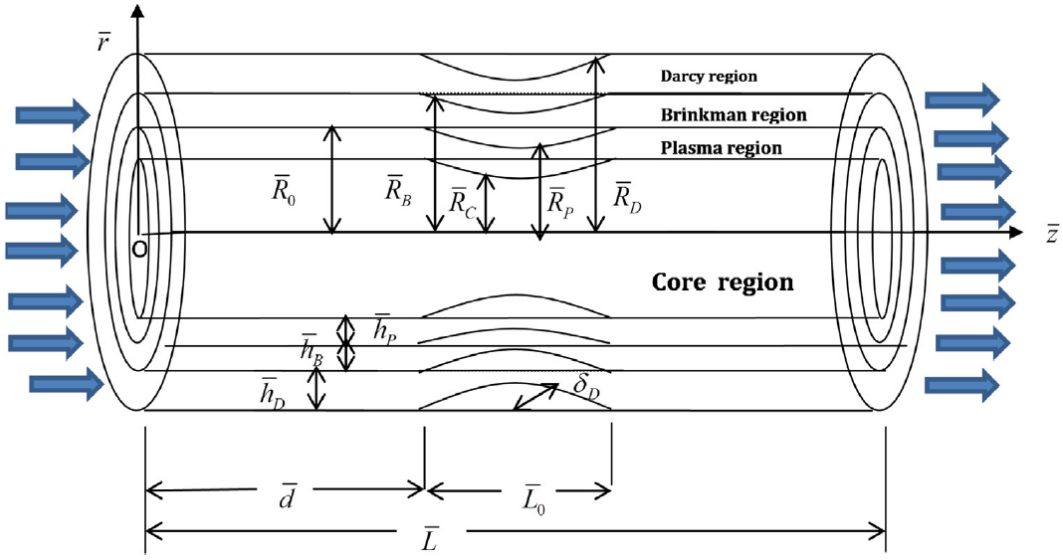


Fig. 3: Schematic diagram of axially symmetric stenosis. Retrieved from [30].

b) Asymmetric stenosis

The mathematical and pictorial representation of asymmetric stenosis is given below:

$$\bar{R}(\bar{z})/\bar{R}_0 = \begin{cases} 1-\bar{G}\left[\left(\bar{z}-\bar{d}\right)\bar{L}_0^{m-1}-\left(\bar{z}-\bar{d}\right)^m\right] & \text{if } \bar{z}\in\left(\bar{d},\,\bar{d}+\bar{L}_0\right) \\ 1 & \text{otherwise} \end{cases}, \quad (2)$$

where $\bar{G}=\left(\bar{\delta}_P/\bar{R}_0\bar{L}_0\right)m^{m/(m-1)}$, $\bar{R}(\bar{z})$ is the radius of the artery in the stenotic region, $\bar{\delta}_P$ is the maximum depth of stenosis at $\bar{z}=\bar{L}_0/m^{m/(m-1)}+\bar{d}$ such that $\bar{\delta}_P/\bar{R}_0 << 1$. The radius of the normal artery and the initial point of stenosis is denoted by $\bar{R}_0$ and $\bar{d}$, respectively. The indication of stenosis shape parameter is denoted by m.

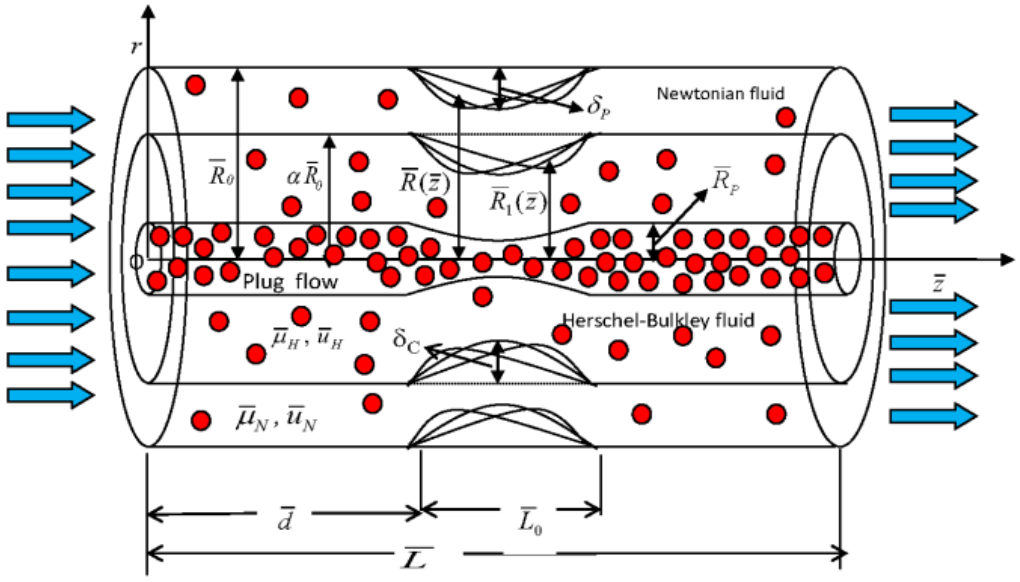


Fig. 4: Geometry of asymmetric stenosis. Retrieved from [31].

c) Overlapping stenosis

The geometry of overlapping stenosis is mathematically represented below.

$$\bar{R}(\bar{z},\bar{t}\,)=\begin{cases}\left[\left(\xi\bar{z}+\bar{r}_0\right)-\bar{\delta}\left(\dfrac{\cos\psi}{\bar{L}_0}\right)\left(\bar{z}-\bar{d}\right)\bar{g}\left(\bar{z}\right)\right]\bar{a}\left(\bar{t}\right) & \text{if } \bar{d}\le\bar{z}<\bar{d}+\left(\dfrac{3\bar{L}_0}{2}\right), \\ \left(\xi\bar{z}+\bar{r}_0\right)\bar{a}\left(\bar{t}\right) & \text{otherwise}\end{cases} \quad (3)$$

where

$$\bar{g}\left(\bar{z}\right)=\left\{11-\left(94/3\bar{L}_0\right)\left(\bar{z}-\bar{d}\right)+\left(32/\bar{L}_0^2\right)\left(\bar{z}-\bar{d}\right)^2-\left(32/3\bar{L}_0^3\right)\left(\bar{z}-\bar{d}\right)^3\right\}, \tag{4}$$

$$\bar{a}\left(\bar{t}\right)=1+b\left(1-cos\,\bar{\omega}\bar{t}\right)e^{-b\bar{\omega}\bar{t}}, \tag{5}$$

where $\bar{R}\left(\bar{z},\bar{t}\right)$ is the radius of the tapered stenotic arterial segment, $\bar{r}_0$ is the radius of the normal artery, ψ and $\xi(=tan\psi)$ are the tapering angle and slope of the tapering blood vessel, respectively, and the location of the stenosis is denoted by $\bar{d}$. $3\bar{L}_0/2$ is the stenosis length, $\bar{\delta}$ is the utmost depth of the overlapping stenosis, $\bar{a}\left(\bar{t}\right)$ is the parameter of the time-variant, b is an arbitrary constant and the angular frequency is denoted by $\bar{\omega}\left(=2\pi\bar{f}p\right)$ with $\bar{f}_p$ as the pulse frequency.

The pictorial description of the overlapping stenosis is shown in Fig. 5.

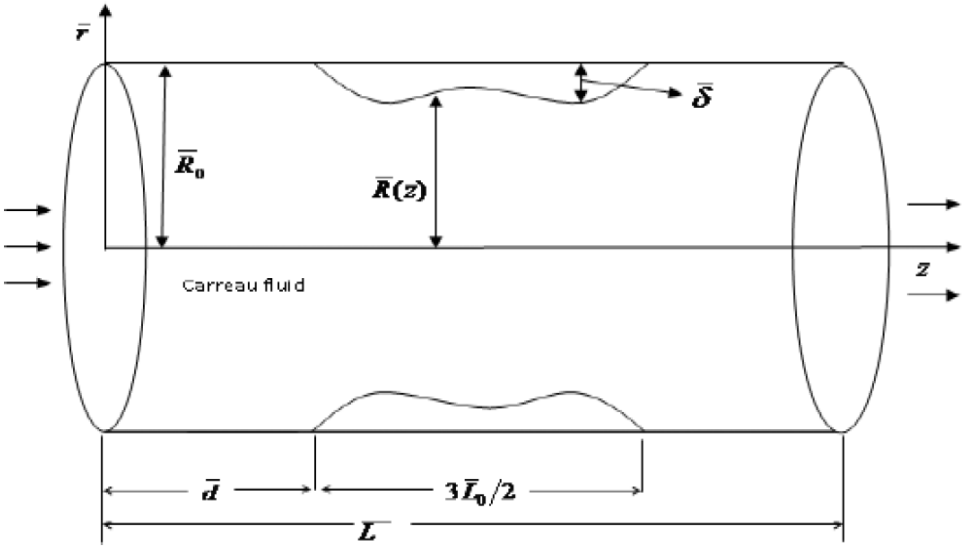
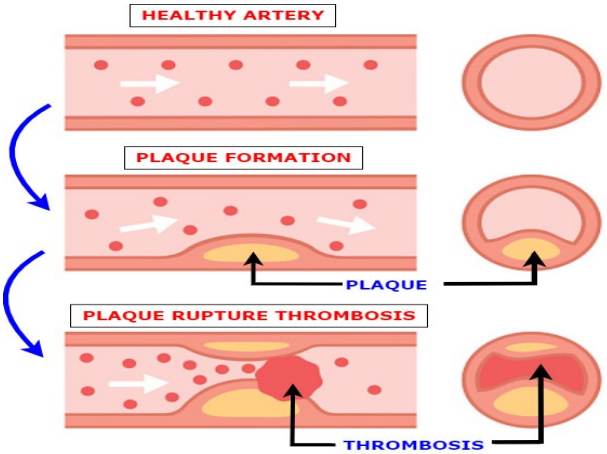


Fig. 5: Schematic diagram of the overlapping stenosis. Adapted from [37].

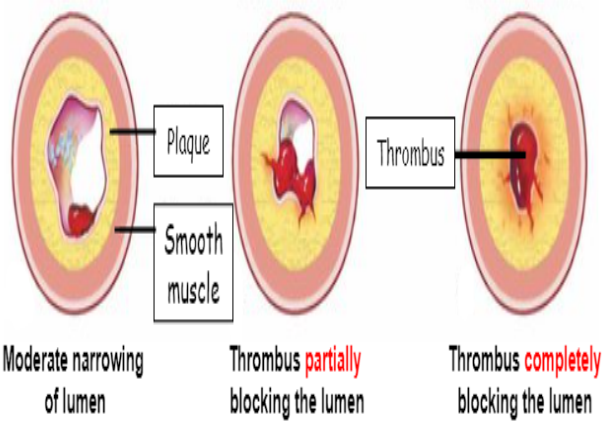
1.3 Thrombosis

Figs. 6(a) and 6(b) show the difference between a healthy artery and constricted arteries (in the presence of a plaque) which led to the growth of a blood clot. To keep blood in a delicate equilibrium state, a variety of systems have been functioning. Clot formation and maintenance are influenced by a various factors and processes. Blood, a fluid tissue, coagulates under standard conditions because of an inequality in favour of prothrombotic factors [34, 35]. Subsequently, this stimulates several processes such as, abnormal high shear stresses, vessel wall injury, endothelial

dysfunction, flow recirculation, and stasis influence clot maintenance. Under normal flow conditions, clot development (or haemostasis) has progressed to enclose abnormalities in the circulatory scheme and stem haemorrhage as a segment of a physiological feedback that led to the recovery of normal flow. Virchow [40] propounded that the vast stimuli during thrombus evolution exhibits the symptoms such as (i) local flow stasis or inactivity, (ii) artery damage, and (iii) an increased natural inclination for blood to clot.



Blood clot normally forms only when the haemostatic stimulus approaches a definite threshold. This threshold is regulated by both biochemical and hemodynamic factors such as local flow situations, the possibility of membrane uniting spots for catalysis, the concentration of multivalent ions such as calcium, and, lastly, the concentration of reagents contained in blood clot establishment, i.e., aspects of platelets coagulation. It is common to contemplate the haemostatic system as 'system idling' as a result of subthreshold stimuli, ready to react swiftly for a minute, until the threshold is attained. Throughout haemostasis, the system acknowledges in a way that ultimately restores it to a condition of idling while also redressing the original stimulus.



(a) Geometry of plaque and thrombosis formation.

(b) The cross-sectional view of the hardening of the arteries.

Fig. 6: Schematic illustration of thrombosis progression.

Pathological conditions can arise as a result of either hypo or hyperfunction of any or all of the haemostatic. Contrarily, hypofunction of these components leads to clot dysfunction or maintenance, resulting in bleeding disorders. system's components. Hyperfunction of these functions, on the other hand, appears to result in unseemly clot maintenance or formation, i.e., thrombotic or thromboembolic afflictions. The endothelium is critical in keeping blood fluidity by stabilising an ordinary inclination to blood clot in isolation with a set of offsetting means (for example, thrombomodulin excretion, nitric oxide, and so on).

When the endothelium of blood vessels is damaged, blood interacts with proteins in the sub-endothelial layers, which causes a clot to form [41]. Platelet aggregation occurs in conjunction with activation of platelets and subsequent adherence to the surface of the subendothelial layer. Simultaneously, the extrinsic coagulation path, which is especially vigorous in the presence of tissue casualty, results in the development of thrombin and thus the splitting of fibrinogen produces fibrin monomers, which polymerize to establish fibrin strands. Fibrinolysis, the procedure that leads to the deterioration of fibrin molecules that occurs concurrently with the establishment of clot and thus it results in clot disintegration. This process contains various interacting mechanisms that work together to cure vascular damage and stem blood shortfall while causing only momentary or no tissue ischemia. Furthermore, the rheological components have an important role in modifying the response at each stage [42].

Mathematical modelling has unfolded as a valuable technique for complementing experimental data and as a result, it establishes a clear understanding on the haemostatic system. Engineers explore various possibilities to lessen such a circumstance within a cardiovascular method which would benefit greatly from a model that could forecast areas prone to clot development as well as record the extent of clotting once launched. Models which assist us in understanding the interaction of chemical and rheological components under the various flow circumstances encountered in the human vasculature system, are much needed. Models of this kind are now in their infancy, incline to emphasis on particular facets of this multidimensional topic. In this article, we provide a mathematical model that takes blood rheology into account with the simultaneous presence of stenosis and thrombosis.

1.3.1 Formation of blood clots

When there is a disproportion in the volume of flowing blood (that favours prothrombotic factors), rheologically significant interactive processes are initiated such as, the activation of platelet accompanied by their adhesion, aggregation, and coagulation [39, 40]. This happens as a result of a difference of stimuli, such as a destruction to the vessel wall, contact with a foreign surface exogenously, for instance glass, or pro- and anti-thrombotic factor imbalances within the complete endothelium itself [45], or abnormal flow circumstances, such as stagnation and recirculation zones. Incessant exposure to high shear stresses can also cause stimulation of platelets. [46]. These stimulated platelets (AP) can then aggregate by attaching to one another and to fibrin. The extraneous coagulation pathway is believed to initiate the development of the TF-VIIa molecular complex on the damaged vessel surface, which is launched by the vulnerability of the cell membrane to protein tissue factor (TF).

Coagulation entailed a sequence of enzymatic reactions encompassing plasma zymogens, anionic phospholipids on calcium ions and AP membranes, which results in the establishment of thrombin from prothrombin [47]. Thrombin breaks down the peptide bonds in fibrinogen and thus forming fibrin, a stringy polymeric molecule. Accumulation of platelets and fibrin mesh develop the blood clot, and their creation is part of haemostasis, the regular feedback to vessel disturbance. Fibrin, together with other coagulation pathway intermediates and endothelial cell enzymes, catalyse and partake in a series of reactions that result in the change of plasminogen (PLS) to plasmin, thereby activating clot dissolving [44]. Dissolving of clot may also happen as a result of increased shear stresses.

1.3.1.1 Components of blood and its rheological behaviour

Blood is made up of gel-like 'cell' substance suspended in aqueous solution, called plasma. Red blood cells (RBCs)(erythrocytes), white blood cells (WBCs) (leukocytes), and platelets (thrombocytes) make up roughly 98 percent of the cell matter (which forms about 46 percent of the volume in human blood). Haematocrit is the ratio of the volume occupied by RBCs in the volume of whole blood. Plasma is mostly made up of water (92–93%), in which numerous substances are dissolved together with diverse ions. Plasma performs as a viscous Newtonian liquid with a viscosity of 1.2 cP. [48]. RBCs are flexible biconcave discs without nuclei. The

membrane of RBC is made up of proteins (spectrin) and lipids and accounts for 3% of the total weight of the RBC. The RBC cytoplasm is a 32 g/100 ml solution of haemoglobin in water.

Micropipette aspiration tests by Evans and Hochmuth [49] revealed that RBCs have viscoelastic behaviour. They further propounded that the RBC's viscoelastic character is solely owing to the RBC membrane's viscoelastic qualities. Granulocytes, monocytes, and lymphocytes are types of leukocytes that make up less than 1% of blood volume. Except in relatively small channels like capillaries, their impact on blood rheology is not thought to be significant. In micropipette aspiration tests, granulocytes show viscoelastic qualities [50]. As a result, the different components of blood have varying rheological qualities.

Whole blood is well recognized for its shear-thinning capabilities and stress-relaxation behaviour [51]. Blood's shear-thinning qualities have been linked to the disassemble of RBC-rouleau aggregates that arise at low shear rates [52], while its stress-relaxation characteristics have been linked to the RBC membrane's viscoelastic character [53]. Blood's viscoelastic nature is barely noticeable at greater shear rates [54]. We simulate entire blood as a non-Newtonian fluid which has stress dependent relaxation time [55].

1.3.1.2 Platelets Activation, Adhesion and Aggregation

Platelets make up a modest percentage of the particulate suspension in blood plasma (by volume, around 3 percent). They are extremely vulnerable to all the blood constituents as well as to physical and chemical agents [56]. Megakaryocytes produce platelets, which are tiny discoid cell fragments with a volume of about 6 μm^3 . Activation of platelet is a procedure through which an idle discoid platelet undertakes a sequence of morphological and chemical variations that cause the organelles (within the platelet) to cluster, glycoproteins (on the platelet membrane) to alter conformation, and long pseudopods to extend, resulting in a sticky spiny sphere. One of the essential aspects of platelet activation is a brief raise in cytoplasmic calcium ion (Ca_2) levels, which leads to the creation of an actino–myosin complex that aids platelet to contract. The platelet contains many chemicals in three kinds of organelles (granules, dense bodies, and lysosomal granules), and some of them, such as thromboxane and ADP, are discharged in the course of activation and aid in the activation of additional platelets.

Platelets are stimulated first and then work together with plasma proteins and fibrin to bond with sub-endothelial tissue, where they build platelet collections and eventually develop a clot. GpIb and GpIIb-IIIa, membrane-bound complexes, play a key part in this process [57]. By rising the likelihood of collisions with other platelets and enhancing fluidity of the membrane, the expansion of lengthy pseudopods, usually with a time lag, favours aggregation [58]. The shape shift, followed by macromolecule binding, results in increased 'stickiness', which promotes clot formation.

Platelets that have been activated also serve to the assembly of complex enzymes which are required for clotting. Several authors [53, 56, 57] provided more information on platelet activation, adhesion and aggregation. Macroscopic analyses of deposition, platelet adhesion, and growth of thrombus in annular flow through chambers. Baumgartner [61], Affeld et al. [62] and Tschopp et al. [63] reported that flow behaviour (shear rates) affect the rate and degree of platelet deposition, union, and formation of mural thrombus [63].

Platelet activation and lysis are inarguable to happen in reaction to extended exposure to high shear pressures [64]. Aggregation of platelet are prone to breaking up when subjected to strong shear forces [65]. Shear pressures can contribute to the platelet activation by causing erythrocytes to rupture and discharge haemoglobin. The natural platelet (activation) inhibition mechanisms are known to be hampered by haemoglobin. The magnitude of the forces needed to harm red blood cells are far greater than to those needed to harm platelets, thus haemoglobin's role in platelet activation is likely minor.

1.3.1.3 Types of Clots and their Rheological Behaviour

A clot is made up of a fibrin matrix including aggregation of platelet, WBCs, RBCs, as well as plasma. Fibrin fibres normally make up below 1% of the total volume of the blood structure. There are three types of blood clots: plasma clots, fibrin-rich clots, and entire blood clots. The polymerization of fibrinogen by thrombin and the maintenance of fibrin by XIIIa are the reactions that lead to their creation; immobilization of other elements follows. Ligated clots are those in which the fibrin fibres have been interlinked (by adding XIIIa), while unligated clots are those in which the fibrin assembly has not been crosslinked. Well fibrin clots are set up at a high pH (about 8.0 and higher), while the abrasive fibrin clots are set up at a lesser pH (about 7.4–7.5, or close to physiological circumstances).

Treatment of fibrinogen solutions with thrombin produces fibrin-rich clots. Whole blood clots are generated by adding calcium chloride to (typically citrated) blood, whereas plasma clots are generated by using plasma with thrombin and calcium chloride (added up to increase platelet stimulation). There is evidence to suggest that the blood clot, or as a minimum the fibrin matrix, has viscoelastic behaviour, which changes considerably depending on the fibrin architecture [66]. The ionic power (concentration of phosphates and NaCl) of the solution, the concentration of fibrinogen in the solution, and the amounts of Calcium ion (Ca_2) in the solution are the characteristics which affect blood clot characteristics [67]. The rheological behaviour of the clot is also influenced by the flow circumstances (shear rate, etc.) amid the clot's foundation [68] and age.

1.3.1.4 Impacts of Clot Formation

The mortality and morbidity of ailments caused entirely or partially by thrombus development or destruction are critical and important to analyse [69]. Most major cardiovascular diseases have negative repercussions due to coagulation disorders, as outlined below. These illnesses are the biggest source of fatality in the advanced world as a whole. This section is divided into two: (i) formation and development of pathologic thrombus and its subsequent physiological disorders and (ii) illnesses developed by defective thrombus creation and pathetic conditions arsing as its consequence.

The first subsection presents the anatomy of blood clot by the locations of pathologic thrombus or thrombo-embolus. This is accomplished due to the location of the thrombus/thrombo-embolus which determines the clinical manifestation of these disorders and, in many cases, the required therapy. The second section, alternatively, presents the malfunctioning of haemostatic system component(s). This is because, while the etiology and pathogenesis of various diseases differ, they all exhibit the symptom of bleeding disorders. Moreover, treatment usually consists of simple component replacement or, in rare situations, pharmaceutical augmentation of haemostatic system function.

1.3.1.5 Thrombus formation and associated disorders

(a) Atrial Thrombosis

Atrial dysrhythmias, for instance atrial fibrillation and atrial flutter, are the most common causes of intra-atrial thrombus development. Ineffective or non-existent atrial contraction is a hallmark of these dysrhythmias. Diastolic blood rheology through ventricles is lesser as well as gentler than systolic blood flow from the ventricles to greater arteries at rest. Defective atrial contraction aggravates this, satiating the situation of regional flow inaction required for thrombus growth. Pathologic effects of intra-atrial thrombi are usually caused by downstream embolization instead of in situ impacts.

In the acute setting, treatment of these dysrhythmia conditions focuses on rate regulator and alteration of dysrhythmic to cardioversion through pharmacological or electrical therapy procedure. Even though pharmacologic or surgical therapy [70] for instance, the Maze procedure established by Cox [68, 69] may cure the dysrhythmia in the chronic setting, atrial thrombus development and embolization which is frequently a deep apprehension [73]. Anticoagulants (protein inhibitors) such as intravenous heparin, low molecular weight heparin (LMWH) subcutaneous infusions, or warfarin, an oral vitamin K competitive antagonist, are used to treat this ill condition.

Unusual anticoagulation methods, such an instance straight thrombin antagonist infusions (for example, bivalirudin, argatroban, lepirudin), may be employed in selective cases [74]. While anti-platelet therapy has modest advantages in terms of outcomes for individuals with atrial fibrillation [75], it is far inferior to anti-coagulation therapy [76].

(b) Ventricular Thrombosis

For obvious hemodynamic reasons, intraventricular cavitary thrombus should be significantly less prone to develop than intra-atrial thrombosis [74, 75]. The ventricles (usually the left) naturally produce intracavitary thrombus in two situations. First, although rare (4–15 percent), significant systolic ventricular dysfunction (either major or due to 'afterload mismatch') can bring about cavitary thrombus [79]. Slow and low systolic ventricular discharge depletion in the presence of sufficient to excessive ventricular preload, i.e., slow and low flow with universal or local ventricular hypokinesis, is suggested to be the cause.

The occurrence of cavitary thrombus is lower in patients with mitral regurgitation whose left ventricle is "auto" afterload-reduced by a parallel low afterload discharge path, which supports

this concept [80]. Second, ventricular aneurysm (normally in the left, and due to previous myocardial infarction) defined by local ventricular wall dilatation and diminishing with paradoxical growth all through ventricular systole (dyskinesis) is related with an elevated degree of intracavitary thrombus establishment [81]. Various of the negative outcomes of ventricular thrombi, like those of atrial thrombi, directly affect ventricular systolic (and diastolic) function [82].

Unalike chronic atrial fibrillation, when anticoagulation is more important (or more significant) than treating the underlying dysrhythmia, ventricular thrombus treatment focuses on treating the underlying disease. This is due to two factors: (i) the underlying illness responds better to treatment than AF, and (ii) there is slight indication, and no forthcoming randomized data, that anti-platelet therapy or anticoagulation is beneficial. Healing of severe systolic dysfunction/heart failure with pharmacologic (inotropic assistance and afterload lessening; diuretic agents) agents which diminishes the hazard of thrombus growth by increasing cardiac output, though anticoagulation is still commonly used in spite of the lack of evidence to concur its usefulness.

Furthermore, surgical 'reverse ventricular remodelling' techniques are being used as heart failure treatments, especially for patients with left ventricular aneurysms/severe regional dysfunction that is commonly ischemic/infarctional in basis. The physics underpinning these treatments' favourable benefits are assumed to revolve around ventricular size reduction and refurbishment of standard ventricular geometry, eventuating in improved pumping action (lessened wall stress/raised pressure head) [83].

Another therapeutic option for heart failure is artificial device technology by means of ventricular assist devices (VADs). However, VADs have the same limits as any non-endothelialized foreign substance in terms of lasting therapy for heart failure: (i) infection, and (ii) thromboembolic and bleeding problems [84]. To avoid thrombus development inside the device components, all currently commercially accessible VADs need either anti-platelet (Heartmate) or anti-coagulant (Abiomed; Thoratec) medication.

(c) Valvular Thrombosis

Development of thrombus on cardiac valves is more common when artificial mechanical valves are used. Since mechanical valve prostheses [85] have a thrombogenic and non-endo-

thelialized surface, they need anticoagulation with heparin or warfarin. Anti-platelet treatment is ineffective as it reduces only thrombus development and thromboembolism. Furthermore, as atrioventricular valves have lower and slower flow than aortic and pulmonic valves, it is a standard preparation to anti-coagulate mechanical mitral and tricuspid valves to a larger extent than aortic and pulmonic valves. Butchart et al. and Ezekowitz [73, 83] provided an appropriate evidence to demonstrate the effectiveness of this technique. The mechanical valve prostheses have principal disadvantage, as they are stronger than xenograft prostheses or allograft. The most common thrombus-related complications are embolic [87]. In situ, thrombus development can cause valve stenosis or constriction, leading to heart failure [88].

(d) Arterial Thrombosis

Arterial inadequacy, or poor local arterial blood circulation (ischemia) and oxygen distribution characterize many of the illnesses mentioned in this section. Atherosclerotic insufficiency can be acute or prolonged. The cause of acute inefficiency is either embolic or in situ. In situ inefficiency is an acute condition caused by thrombus growth on the surface of an atherosclerotic plaque; it is crucial to record that the pre-existing plaque isn't always significantly stenotic, although it can be. A large stable plaque instigating arterial stenosis may clear in the acute situation as well as in very rare circumstances. Nevertheless, these abrasions usually apparent episodically (occasionally) over a long duration of time, infrequently triggering severe or irretrievable ischemia/infarction (i.e., constant plaque appearances are chronic).

As previously stated, depending on plaque instability or stability, distinct arterial plaques can cause acute or chronic in situ arterial inefficiency. However, embolic processes can potentially produce acute insufficiency. The majority of these embolic procedures are either athero-embolic or thrombo-embolic in nature [89]. As a result, treatment techniques for these diverse forms of arterial insufficiency differ based on different pathophysiologic causes. The two regular and relevant instances of pathologic thrombosis/thromboembolism are the acute coronary syndromes and arterial inadequacy in the extremities.

(e) Capillary Thrombosis

Microvascular thrombosis is a poorly known condition with unknown clinical implications. Sepsis related intravascular coagulation is the most clinically important case. Many vasculitides

are among the other examples. Thrombus formation is caused by endothelial impairment in the context of inflammation and bacterial surface moieties. This could lead to pivotal (small vessel) ischemia and infarction. According to research, stimulated protein C, an anticoagulant, enhances results in sepsis patients [90]. The mechanisms underlying these amended consequences are unknown, but they could be the result of the reduced microvascular thrombosis and increased tissue perfusion, or to anti-inflammatory or other impacts of stimulated protein C.

(f) Pulmonary Thromboembolism and Venous Thrombosis

Deep venous thrombosis (DVT), including or excluding pulmonary thromboembolism (PE), is a main source of mortality and morbidity, and is one of the top roots of mortality in hospitalised patients [91]. The standard triad of Virchow caters an outline for the insight of the pathogenesis of DVT/PE [92]. A variety of hypercoagulable conditions raise the hazard of DVT growth. These are usually genetic ailments in which coagulation aspects are produced in excess or in mutant hyper functional forms, or anti-coagulant or fibrinolytic factors are made in insufficient quantities or in mutant dysfunctional systems [93].

Factor V Leiden (the most ordinary genetic hypercoagulable state) [94], mutant prothrombin, protein C deficit [95], protein S deficit [96], and ATIII deficit are all common disorders [97]. DVT formation is also governed by hemodynamics [98]. The hypercoagulable states mentioned above are more prone to cause venous thrombi instead of arterial thrombi. This is believed to be due to the fact that movement of blood in the venous system is of low-pressure and often slower; further, venous valves are the locations of flow separation that are inclined to the growth of thrombus.

Some of the factors that aggravate venous stasis are the extreme blood immobility, venous valvular inadequacy, aligning underneath the level of the right atrium and increase the hazard of development of DVT. This is especially important in postsurgical patients, who are transiently hypercoagulable and frequently ambulant. Ultimately, injury or endothelial dysfunction increases the risk of DVT development. Damages to the venous endothelium, whether caused by indwelling venous tools or subordinate to instrumentation also increases the risk of developing DVT.

As with arterial thrombi, the pathologic outcomes of DVT are either local or distal (due to embolization) [99]. Extremity edema may result from impaired extremity venous drainage. In

dreadful instances, with deep venous obstruction and insufficient superficial venous system, collateral venous return, trans-extremity blood movement (i.e., deep venous constriction lowers extremity of arterial movement of blood) [100]. This is aggravated by interstitial edema and subsequent capillary collapse in the affected limb.

Despite these local effects, pulmonary embolism from DVT is the chief source of mortality and morbidity [101]. DVT with pulmonary arterial embolization has serious cardiac and pulmonary consequences. Patients with lack of anticoagulation along with those for whom anticoagulation is contraindicated, have a vena caval filter implanted. This avoids DVT embolization.

1.4 Catheter

An arterial catheter is a narrow void tube injected into an artery (typically in the groin or wrist) to monitor blood pressure more precisely than a blood pressure cuff [102]. The catheter is also used to test the level of oxygen and carbon dioxide in the bloodstream on a regular basis. Catheters are also used in balloon angioplasty [103]. The following are the most likely reasons for using catheters and their benefits:

- **Hypotension (Low blood pressure)**
  When a patient is taking powerful drugs that stimulate the heart in order to keep higher blood pressure, it is especially important to check blood pressures in larger diameter blood vessels. The arterial catheter guides to measure the blood pressure more accurately as well as to record the second-to-second blood pressure level.

- **Hypertension (High blood pressure)**
  In some cases, blood pressure can rise to life-threatening levels. Such high blood pressure must be gradually reducing in stages, and arterial catheter readings aid in guiding the treatments.

- **Severe lung problems**
  When a patient has a critical lung condition that needs more regular inspections (more than four times per day) of oxygen or carbon dioxide levels in the blood which can be done with

the use of catheters. The arterial catheter is also used to take out blood sample without the need for numerous needle sticks.

- **Arterial stenosis**

  When there is stenosis in the arteries, catheter treatment is used to dissolve or remove it. One such example is the use of a catheter with a balloon to treat arterial stenosis which is known as balloon angioplasty.

Some of the complications of arterial catheterization are listed as below [101, 102]:

- **Experiencing discomfort during the procedure**

  The needle poking and catheter positioning at the time of introducing into an artery may cause discomfort. To alleviate the pain, doctors administer local numbing medication. The pain is usually minor and it goes away once the catheter is in place.

- **Infections**

  When catheters injected into the body, they can travel from the skin into the bloodstream. The longer the catheter is in the artery, the more likely it is to become contaminated. To reduce the possibility of contamination, special care should be taken when bandaging the skin at the location of the catheter and replacing the tubing.

- **Blood clots**

  Clots that form on the tips of arterial catheters can obstruct flow of blood. A hand or limb may be amputated if another blood channel cannot transport blood to the area beyond the blockage. Such a tragedy is extremely rare. When the catheter is inside the artery, the intensive care unit (ICU) staff monitors blood flow in the hand or leg on a regular basis to reduce the possibility of these complications.

- **Bleeding**

  During the catheter insertion procedure, bleeding may occur. If no remedy is done, the bleeding may stop automatically after few seconds with loss of blood. ICU personnel may need to remove the catheter and apply pressure to the site on occasion to reduce the blood loss.

Cardiac catheterisation is a minimally invasive treatment utilised to diagnose and treat heart problems [106]. Catheterisation is the process of inserting tiny tubes (catheters) into the cardiovascular system under x-ray control to collect useful data on blood circulation and pressure inside the heart, as well as determining any blockages in the veins which supplies blood to the coronary arteries (heart muscle). Plaques build-up in arteries develop arterial constriction, which can cause a variety of symptoms like chest discomfort and shortness of breath when it becomes severe (developed significantly to obstruct more than 50% of the flow region).

If the symptoms are stable, a catheterisation may be recommended as an elective procedure, or as an emergency procedure. When the symptoms are sudden and the treating physician is observed that they may indicate a current or imminent heart attack. Based on the location and number of blockages, the treatment strategy will include the use of specialist drugs and possibly the implantation of a stent or referral for bypass surgery to upsurge blood flow to the heart muscle and reduce symptoms.

For cardiac catheterization, catheters can be inserted into the groin or wrist arteries. The femoral artery is a larger blood vessel which is connected to the heart directly. Because of these advantages, the femoral artery has become the preferred entry point for catheterisation procedures. Nonetheless, the radial artery is increasingly being used for cardiac catheterization procedures.

1.4.1 Balloon Angioplasty

A catheter balloon is a type of "soft" catheter with a stretchable "balloon" at its end that is used during a catheterisation procedure to expand a small hole or channel inside the blood vessel. As shown in Fig. 7, the flattened balloon catheter is inserted first to the constricted site of an artery and then it is inflated there to perform the appropriate operation of widening the flow region and thereafter it will be deflated for withdrawing from the site [107]. Rapid Exchange (Rx) or Over-the-wire (OTW) angioplasty balloon catheters are also available for reducing the severity of the obstruction in the lumen of blood vessels. When a balloon angioplasty is used to condense the plaque developed inside a congested coronary artery, a Plain Old Balloon Angioplasty (POBA) procedure is administrated.

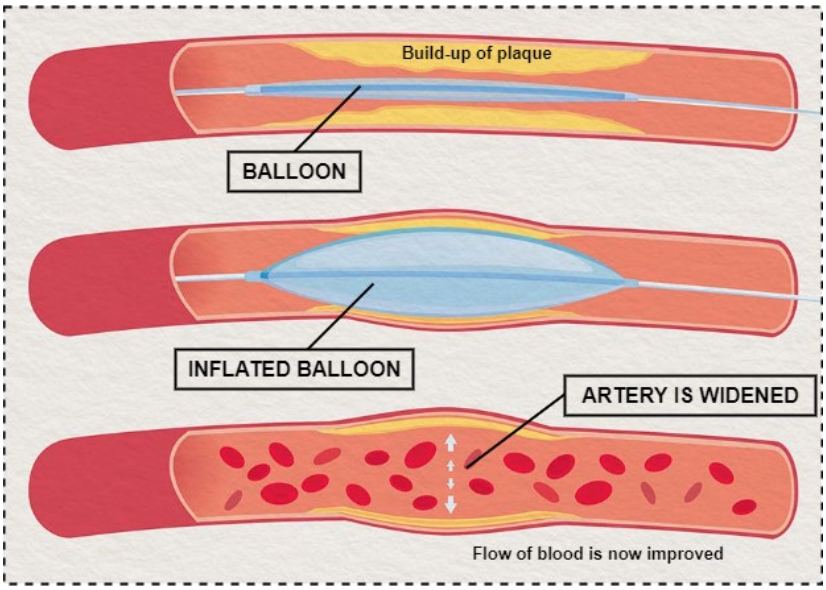


Fig. 7: Exhibition of balloon angioplasty procedure. The balloon is injected inside the tapered artery and it is then it is inflated to widen the flow region of the artery which will eventually enhances the blood to flow in the neighbourhood of the constricted artery.

During angioplasty, stents are deployed using balloon catheters (see Fig. 8) [108]. Balloon catheters with stents attached are delivered to the constricted site of the artery. When the cardiologist inflates the balloon gradually, the stent expands to the maximum of cross-sectional area to compress the plaques towards the arterial wall and when the balloon deflated, the stent stays with the compressed plaques/arterial wall and the balloon catheter is separated from the stent. Balloon expandable stents are stents that work in tandem with a balloon catheter [109].

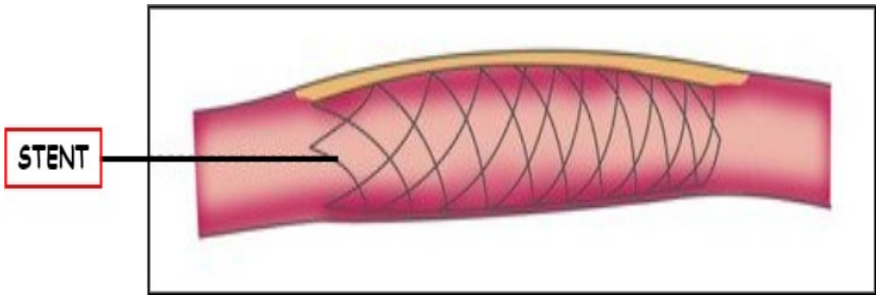


Fig. 8: A stent. It is a small, mesh wire tube which is often placed during the procedure of Balloon Angioplasty, to keep the artery open after the balloon is deflated and removed.

Catheters are remarkably crucial in present medicine and have become a standard diagnostic and therapeutic tool [110]. A catheter's frictional resistance to flow or increased impedance in a stenotic artery changes the velocity distribution. Each experimentation requires a catheter of a proper size to limit the inaccuracy caused by wave reflection at the catheter tip [111].

1.5 Nanofluids

Nanofluids are minute elements suspended in base liquid with at least one primary dimension under 100 *nm*. It has become the focus matter of widespread research and biomedical application. Previous research indicates that nanofluids have strengthened the thermal properties of base fluids, like viscosity, thermal conductivity, thermal diffusivity and convective heat transfer coefficients [112]. Furthermore, nanoparticles with biomedical characteristics are widely used in several medical treatment procedures [113].

Nanofluids have the potential to be a better choice among the heat transfer fluids in a diversity of heat transfer usages. Owing to the general existence of suspended nanoparticles with high thermal conductivity, they are anticipated to offer improved thermal operation than conventional fluids. Numerous studies have recently disclosed the enrichment of thermal conductivity and elevated heat transfer amount of nanofluids. Several researchers reported that the substantial surge in heat transfer rate with the practise of numerous nanofluids when associated to conventional fluids. Understanding the characters of nanofluids, for instance, thermal conductivity, viscosity, and specific heat, is critical for their use in a variety of applications. Further research into the fundamentals of heat transfer and friction aspects in the circumstance of nanofluids is thought to be essential to broaden the implementations of nanofluids.

2. Literature survey on catheterized stenosed arteries with thrombosis

This section reviews the literature on the effects of the presence of stenosis, thrombosis, and catheter in blood rheology through constricted arteries. A clot in a blood vessel, particularly a stenotic artery, may restrict the blood velocity and flow rate of blood flow. Attributable to the insertion of catheter in the lumen of the artery, an annular area around the centre of artery is developed in the blood vessel amid the presence of blood clot and the stenosis in the arterial wall. Only a few analyses on the formation of clots in blood vessels have been included.

Authors	Year	Method(s)	Findings
Mekheimer, K.S., and Elmaboud, Y.A. [114]	2008	• Analytical methods • Numerical computations by using MATHEMATICA software	• The pressure rise increases with the increase in the height of the clot. • Without the presence of clot, the results are in a good agreement with those obtained by Srinivasacharya et al. [115]
Ellahi, R., Rahman, S.U., Nadeem, S., and Akbar, N.S. [116]	2014	Homotopy perturbation method	• As the stenotic height grows, the height of the impedance profile rises. • As the slip parameter increases, the velocity distribution also increases.
Ahmed, A., and Nadeem, S. [117]	2016	Euler-Cauchy method	The presence of aluminium content in the blood consisting of both copper and titanium nanoparticles resulted in increased skin friction.
Sankar, D.S., and Lee, U. [118]	2008	• Regula-Falsi method • Trapezoidal rule	As yield stress or catheter radius ratio rises, the flow rate and velocity reduce.
Sankar, D.S. [119]	2009	Perturbation method	The velocity distribution and flow rate decrease as the yield stress increase but skin friction, width of the plug flow zone, and longitudinal impedance surges.
Srivastava, V.P., and Srivastava, R. [120]	2009	• Continuum approach • Integration method	• Effective viscosity and frictional resistance increase with increasing haematocrit. • The flow characteristics of catheterized arteries are smaller than those of non-catheterized arteries for any given set of parameters.

Srivastava, V.P., Vishnoi, R., Mishra, S., and Sinha, P. [121]	2010	Numerical integration	• The flow impedance increases with catheter size and is significantly dependent on stenotic height. • Shear stress reaches its maximum value at the critical axial distance in the stenotic area.
Srivastava, V.P., and Rastogi, R. [122]	2010	Integration method	Even a minor increase in catheter size can result in a significant increase in impedance amplitude and skin friction.
Mekheimer, K.S., Salama, F., and Elkot, M. [123]	2015	Perturbation method	The transportation of the axial velocity curves via a Newtonian fluid is significantly lower than that of a Carreau fluid near the balloon's wall, but the opposite behaviour was observed in the zone between the stenosis and the balloon.
Elnaqeeb, T., Mekheimer, K.S., and Alghamdi, F. [124]	2016	• Numerical integration • MATHEMATICA	There is a definitive link between nanofluid volume fraction and velocity, indicating that the presence of nanofluid increases velocity in comparison to base fluid.
Elkot, M.A., and Abbas, W. [125]	2017	Crank-Nicolson implicit finite difference scheme	The impact of a moving magnetic field increases the blood's speed.
Zidan, A.M., McCash, L.B., Akhtar, S., Saleem A., Issakhov, A., and Nadeem, S. [126]	2021	MATHEMATICA	The velocity decreases in the middle as the channel constricts with increasing stenotic height, but it drops towards the numerous stenosis wall.

3. Model development

The mathematical formulation of blood motion in an artery with stenosis, thrombosis and catheter makes use of the following assumptions:

- We treat blood as viscous incompressible fluid.
- We assume the steady flow of copper nanoparticles suspended blood through narrow artery.
- The artery is presumed to be composed of two coaxial tubes such as (i) the inner tube in which thrombosis is developed and (ii) the outer tube in which an axisymmetric mild stenosis is formed.
- The catheter is coaxially introduced.
- Blood is considered as non-Newtonian Carreau fluid.
- Geometry is also expressed mathematically through equations.
- Since the blood flow is considered as axi-symmetric, the flow quantities of blood flow are independent of the variable of azimuthal angle.

The geometry of the arterial segment in the presence of the mild asymmetric stenosis, thrombosis and catheter is depicted in depicted in Fig. 9. The MATLAB and MATHEMATICA softwares were widely used to obtain the analytical solution/numerical of pressure gradient, temperature, velocity distribution, resistance to flow, and skin friction as well as to produce data for graphical and tabular form of results and to generate data for our study's clinical applications.

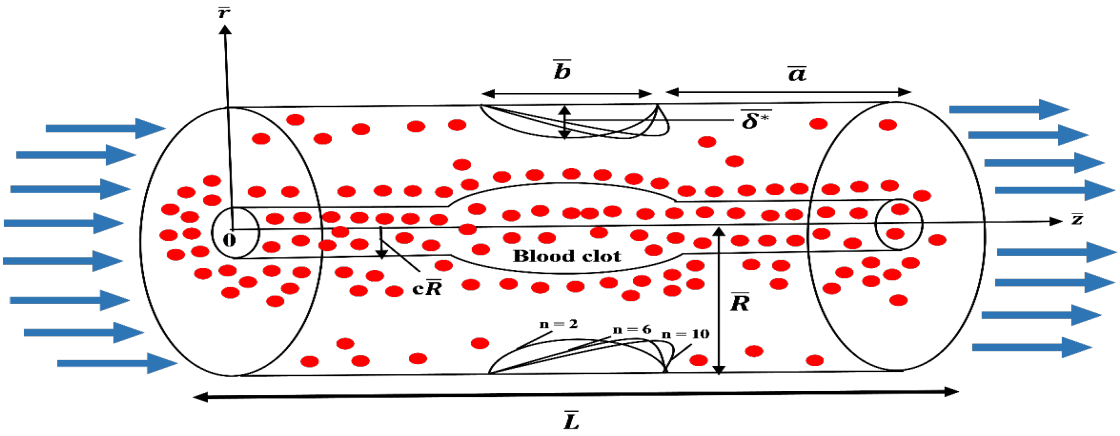


Fig. 9: Geometry of a moderately stenosed catheterised artery with thrombus.

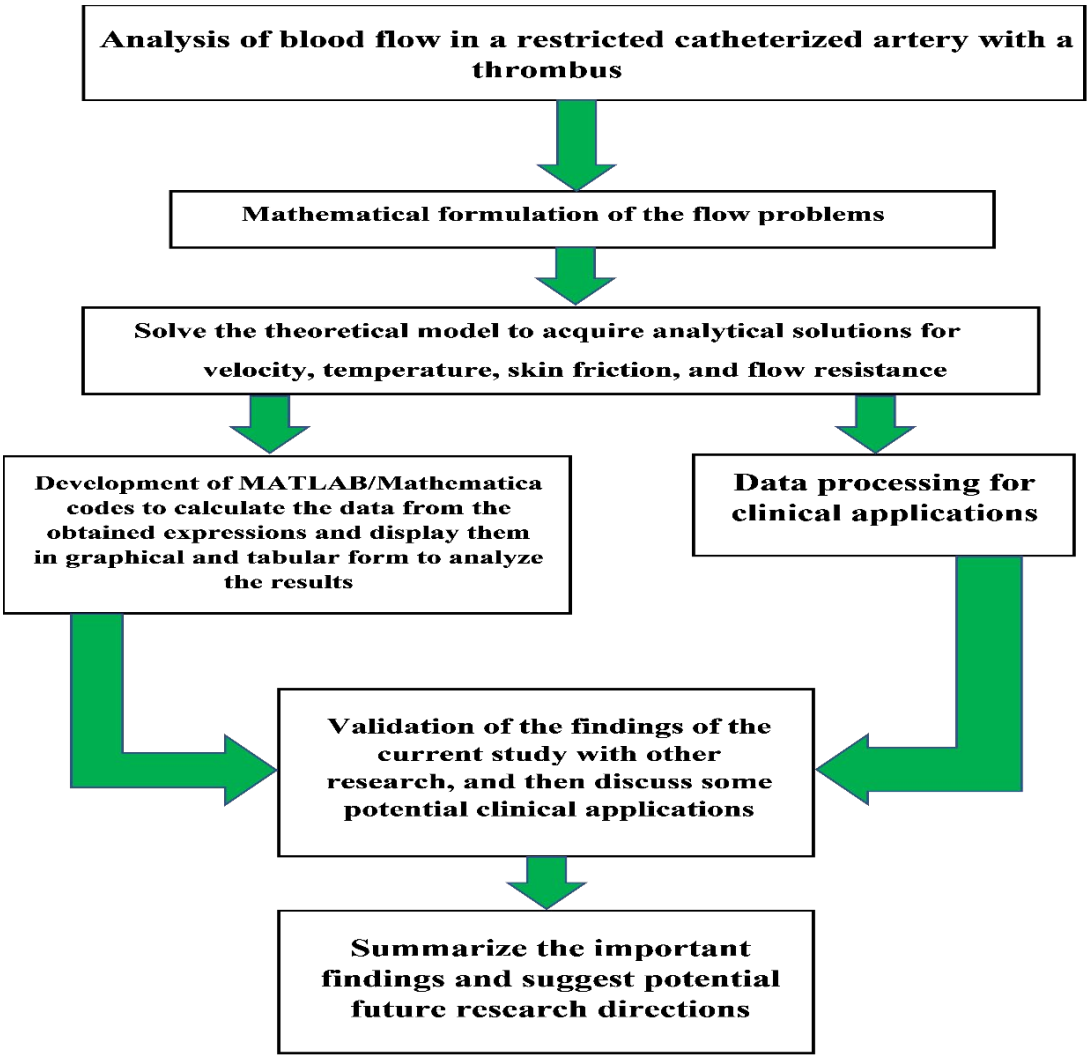


Fig. 10: Schematic diagram of the flow problem.

The governing equations of motion (momentum and thermodynamical equations of motion) in their dimensionless form are given below:

$$\frac{\partial p}{\partial r} = 0, \tag{6}$$

$$-4\frac{\partial p}{\partial z} - \frac{1}{r}\frac{\partial}{\partial r}\left[r\left\{ \left(\frac{\partial w}{\partial r} \right) + We^2 \left(\frac{m-1}{2} \right) \left(\frac{\partial w}{\partial r} \right)^3 \right\} \right] + \frac{Gr\theta}{(\rho\gamma)_f} = 0, \tag{7}$$

$$\frac{\partial^2\theta}{\partial r^2}+\frac{1}{r}\frac{\partial\theta}{\partial r}+\beta\frac{K_f}{K_{nf}}=0\,, \tag{8}$$

where β is the non-dimensional parameter of heat source or sink of the fluid, θ is the temperature, Q is the rate of flow of the fluid, Gr is the Grashof number and We is the Weissenberg number.

The nanofluid's thermo physical properties are delineated by the equations below [127]:

$$\alpha_{nf}=\frac{K_{nf}}{\left(\rho c_p\right)_{nf}}, \tag{9a}$$

$$\rho_{nf}=\left(1-\phi\right)\rho_f+\phi\rho_s, \tag{9b}$$

$$\left(\rho c_p\right)_{nf}=\left(1-\phi\right)\left(\rho c_p\right)_f+\phi\left(\rho c_p\right)_s, \tag{9c}$$

$$\left(\rho\gamma\right)_{nf}=\left(1-\phi\right)\left(\rho\gamma\right)_f+\phi\left(\rho\gamma\right)_s, \tag{9d}$$

$$\mu_{nf}=\frac{\mu_f}{\left(1-\phi\right)^{2.5}}, \tag{9e}$$

$$\frac{K_{nf}}{K_f}=\frac{\left(K_s+2K_f\right)-2\phi\left(K_f-K_s\right)}{\left(K_s+2K_f\right)+\phi\left(K_f-K_s\right)}, \tag{9f}$$

where $K_f,\rho_f,\left(\rho c_p\right)_f,\mu_f$ and γ_f are thermal conductivity, density, heat capacitance, viscosity and the base fluid's thermal expansion coefficient respectively, while $K_s,\rho_s,\left(\rho c_p\right)_s,\mu_s$ and γ_s are thermal conductivity, density, heat capacitance, viscosity and thermal expansion coefficient of the metallic nanoparticles respectively and ϕ is volume fraction of the nanofluid.

Non-dimensional form of the corresponding boundary conditions are given below:

$$\begin{array}{lllll}\theta=0 & at & r=\eta\left(z\right) & and & \theta=1 \quad at \quad r=\varepsilon\left(z\right)\\ w=0 & at & r=\eta\left(z\right) & and & w=0 \quad at \quad r=\varepsilon\left(z\right)\end{array}\,, \tag{10}$$

where $\varepsilon(z)$ and $\eta(z)$ in the non-dimensionals form turn out to be

$$\begin{aligned} \varepsilon(z) &= c + \zeta e^{-\pi^2 b^2 \left(z - \frac{z_d + 0.5}{b}\right)^2} && h \le z \le h+1, \\ &= c && otherwise \end{aligned}, \tag{11}$$

$$\begin{aligned} \eta(z) &= 1 - \kappa^* \left[b^{n-1}(z-a) - (z-a)^n \right] && h \le z \le h+1, \\ &= 1 && otherwise \end{aligned}, \tag{12}$$

and where $h = \frac{a}{b}, \kappa^* = \delta \frac{n^{\frac{n}{n-1}}}{n-1}$ and $\delta = \frac{\delta^*}{R}$.

4. Results and Discussions

Some significant results of the above mathematical model are highlighted here. The factors that influence the growth of stenosis and thrombosis in the lumen of arteries are investigated and the effects of several flow parameters that are used in the graphical representation of the results are discussed in brief [128]. The developed model can be employed to collect information on a wide range of applications related to biomedical engineering and clinical practice. Some of the most important findings are given below, and for additional information on the solutions, one can refer the study by Afiqah et al. [128].

The variance of temperature distribution for several values of greatest blood clot depth, ζ is plotted in Fig. 11. As a result of the limited availability of oxygen in the bloodstream, the temperature upsurges when the depth of the blood clot rises. As an example, pulmonary embolism can damage lungs and prevent other organs from getting sufficient oxygen. It is also apparent that the temperature levels are always higher when a catheter is present. Fig. 12 shows the velocity distribution for distinct values of Weissenberg number, We. With a progress in Weissenberg number, the magnitude of the velocity decreases, since the rising values of We increase the fluid particle's relaxation time and thus it intensifies the viscosity especially, causing resistance to blood's motion due to the drop in fluid velocity.

In Fig. 13, the comparison of skin friction in Carreau fluid and Newtonian fluid flow are portrayed for various values of z_d. On account of the occurrence of constrictions (stenosis and

thrombosis) inside the artery at the same time and when the blood clot extends axially from 0 to 0.2, the skin friction decreases significantly, and when it flows axially from z = 0.2 to z = 0.3, the skin friction decreases further. It is also worth stating that the plot of skin friction produced from the Newtonian fluid model (where We = 0) agrees well with the complimentary figure in Fig. 13a of Elnaqeeb et al. [129] which authenticates the studies of Afiqah et al. [124].

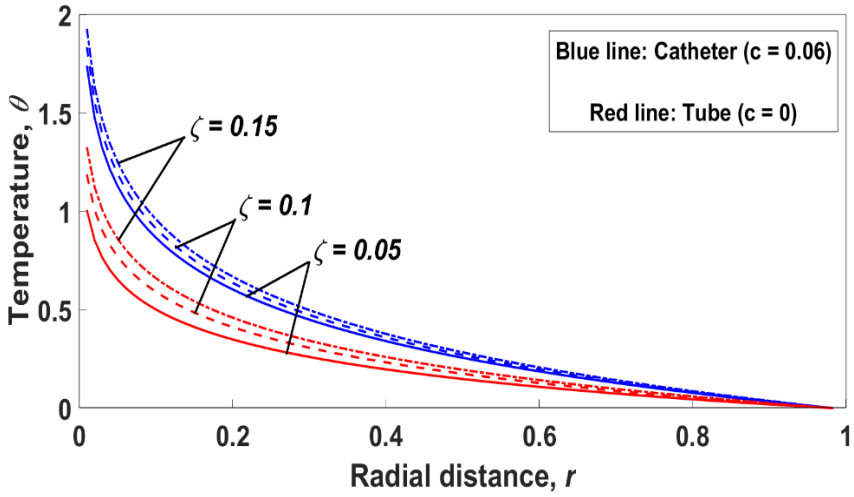


Fig. 11: Temperature with radial distance for different ζ values with $z = 0.9, b = 1, R = 1, a = 0, \beta = 0.2$ and $z_d = 0$. The blue curves signify the variation in the temperature of flowing blood in the presence of a catheter, while the red curves depict the temperature variation in the flowing blood in the absence of a catheter. This figure is adapted from Ref. [128].

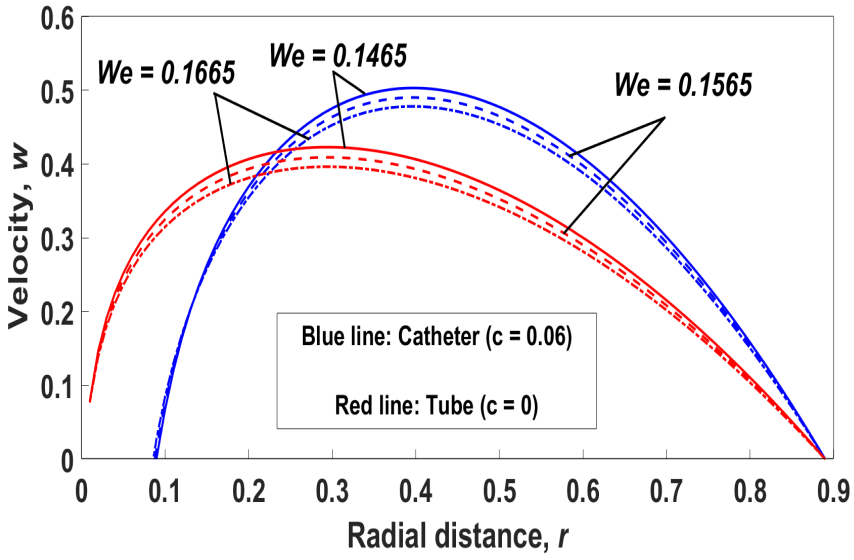


Fig. 12: Variation in velocity distribution for different values of We with $R=1, b=1, a=0, m=2$ and $Gr=5$. Velocity in the presence of catheter seems to be higher in magnitude compared to the velocity in the absence of catheter. Adapted from [128].

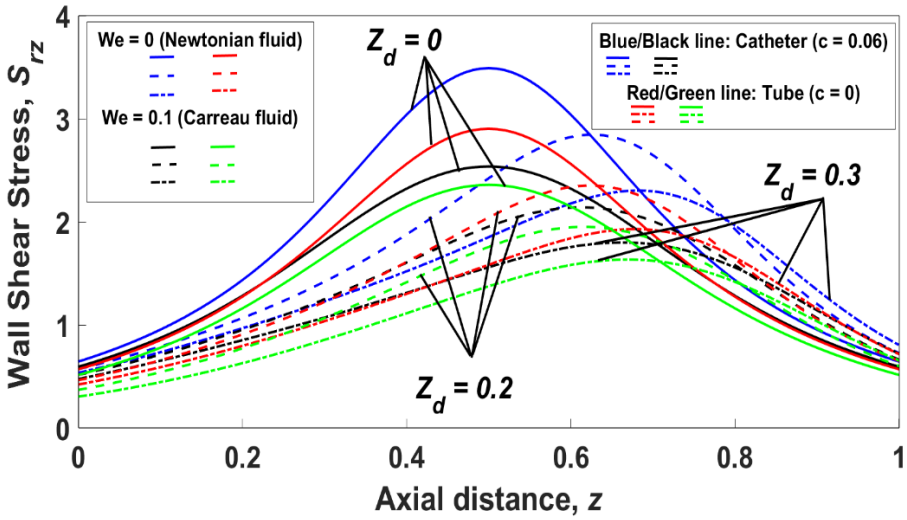


Fig. 13: Variation of wall shear stress with axial distance for several z_d values with $R=1, b=1, a=0, m=2, \beta=0.5$ and $Gr=5$. The blue and red curves denote the wall shear stress of Newtonian fluid and the black and green curves represent the wall shear stress of Carreau fluid. Adapted from Ref. [128].

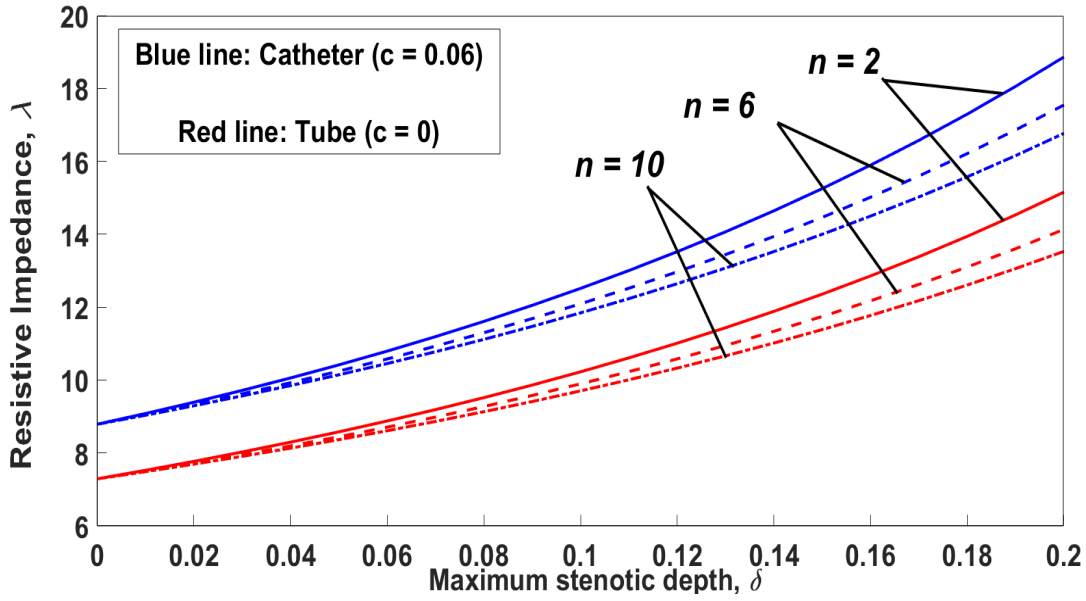


Fig. 14: Variation of resistive impedance to flow with maximum stenotic depth for several n values with $R=1, b=1, a=0, m=2, \beta=0.5$ and $Gr=2$. The rise in stenosis shape parameter results in a decrease of the resistance to flow. Adapted from [128].

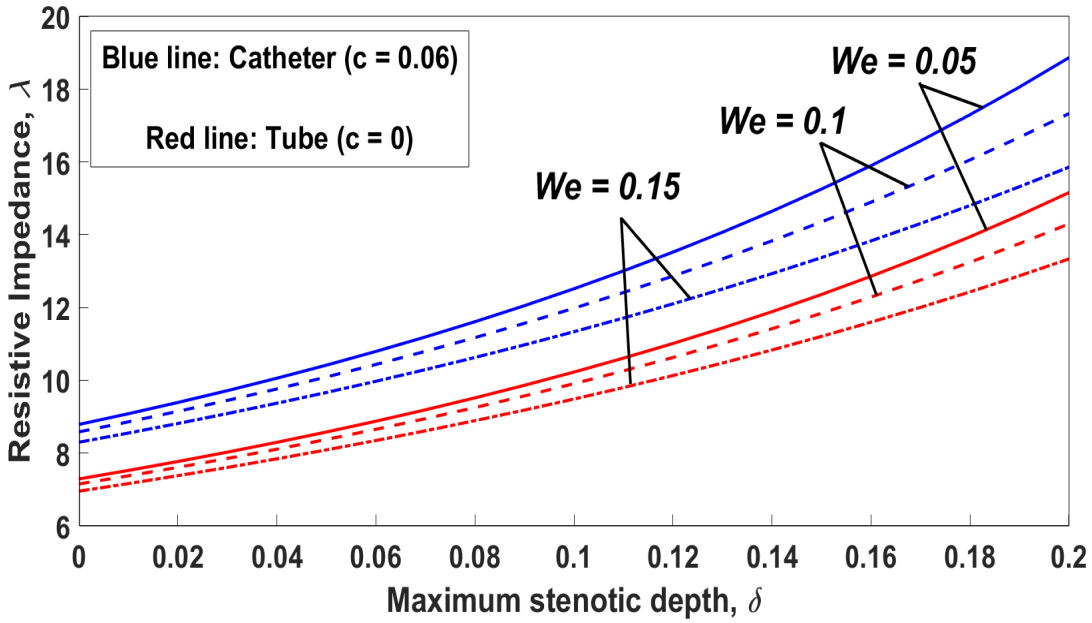


Fig. 15: Variation of resistive impedance to flow with maximum stenotic depth for several We values with $R=1, b=1, a=0, m=2, \beta=0.5$ and $Gr=2$. The resistance to flow is seen to increase as the Weissenberg number lessens. Adapted from [128].

Fig. 14 portrays the graph of resistance to flow with maximum stenotic depth for various parameter values of the stenosis shape, n. Resistive impedance appears to decrease insignificantly as n increases for both tube and catheter. The same pattern can be seen in Fig. 15 when it varies with Weissenberg number. It has been discovered that as the Weissenberg number rises, the resistance to flow lowers significantly due to an increase in relaxation time, which allows blood in the artery to move more readily.

For the clinical applications, some relevant physiological data have also been included in tabular form. Table 1 computes the estimates of pressure gradient at distinct sites in the axial direction and for several catheters' types and for various z_d values with a fixed set of parameters. The pressure gradient is observed to decrease with increasing z_d for all three types of catheters. The capacity of catheters to relieve blood flow in a constricted arterial segments is demonstrated

by the decrease in pressure gradient. The estimates of flow resistance at various places in the axial direction, several kinds of catheters (Infusion, Angioplasty and Guidewire Catheter), and different Weissenberg number values are computed in Table 2. In view of the symmetric structure of the stenosis in this scenario, the flow resistance is computed only up to the axial position of $z = 0.5$. Although an increase in z induces an elevation in resistive impedance to blood flow, a surge in Weissenberg number leads to a lessening in resistive impedance to flow for all the three kinds of catheter. The enhancement of blood flow occures when the relaxation period parameter raises and the resistive impedancein to flow is reduced by introducing the catheter to the obtructiom site of the artieal segment to expedite the blood movement.

Table 3 illustrates the rates of increase in wall shear stress for various catheter radius ratios, *c*, and at various blood clot locations, z_d. These estimates certainly exhibits on how catheterization affects the fluid flow's shear stresses at the wall. When the radius of the catheter increases, we noticed the shear forces at the wall for the current Carreau fluid model increase significantly. Thus, it is necessary to use a catheter that is the right size to minimize inaccuracy brought on by wave reflection at the catheter tip. Another key point to remember is that when the blood clot advances further in the axial direction, the amplitude of wall shear stress decreases slightly.

Table 1: Estimates of pressure gradient at various sites in the axial direction and for several kinds of catheters and for distinct z_d values with $\beta = 0.5, \zeta = 0.1, \delta = 0.1$ $R = 1, b = 1, a = 0, n = 2, m = 2, We = 0.5, Gr = 5,$ and $Q = 0.985$. This table is adapted from [128].

Types of catheter	Range of catheter size	z	$z_d = 0.2$	$z_d = 0.4$	$z_d = 0.6$
Guidewire	0.08 - 0.18	0.2	1.08 - 1.28	1.05 - 1.27	1.05 - 1.27
		0.4	1.26 - 1.42	1.17 - 1.39	1.14 - 1.37
		0.6	1.36 - 1.47	1.26 - 1.42	1.17 - 1.39
		0.8	1.26 - 1.36	1.26 - 1.36	1.17 - 1.32
Infusion	0.14 - 0.33	0.2	1.05 - 1.27	1.21 - 1.40	1.21 - 1.40
		0.4	1.17 - 1.39	1.32 - 1.52	1.31 - 1.51
		0.6	1.26 - 1.42	1.37 - 1.55	1.32 - 1.52
		0.8	1.26 - 1.36	1.32 - 1.47	1.27 - 1.43
Angioplasty Catheter	0.3 - 0.6	0.2	1.38 - 1.84	1.38 - 1.84	1.05 - 1.27
		0.4	1.52 - 2.78	1.50 - 2.26	1.49 - 2.18
		0.6	1.57 - 4.86	1.52 - 2.78	1.50 - 2.26
		0.8	1.44 - 3.02	1.44 - 3.02	1.41 - 2.13

Table 2: The estimates of resistive impedance to flow at various sites in the axial directions and for several kinds of catheters for distinct We values with $R = 1, b = 1, a = 0, z_d = 0, m = 2,\ n = 2,\ Gr = 2,\ \beta = 0.5, \zeta = 0.15, \delta = 0.05$ and $Q = 0.05$. This table is adapted from [128].

Types of catheter	Range of catheter size	z	$We = 0.3$	$We = 0.5$	$We = 0.7$
Guidewire	0.08 - 0.18	0.1	6.60 - 8.36	5.54 - 6.84	4.80 - 5.85
		0.3	8.84 - 10.78	7.23 - 8.51	6.18 - 7.15
		0.5	10.05 - 12.01	8.09 - 9.32	6.86 - 7.76
Infusion	0.14 - 0.33	0.1	7.67 - 10.86	6.37 - 8.38	5.48 - 6.96
		0.3	10.02 - 13.58	8.04 - 10.19	6.80 - 8.36
		0.5	11.25 - 15.00	8.86 - 11.13	7.43 - 9.07
Angioplasty Catheter	0.3 - 0.6	0.1	10.36 - 16.83	8.08 - 12.19	6.75 - 9.83
		0.3	13.00 - 24.20	9.84 - 17.38	8.10 - 13.95
		0.5	14.35 - 35.75	10.73 - 25.61	8.78 - 20.54

Table 3: The estimates of increase in wall shear stress for various catheter radius ratio c and for different values of axial location of blood clot, z_d with $R = 1, b = 1, a = 0, m = 2, z = 0$, $We = 0.5$, $Gr = 2, \beta = 0.5, \zeta = 0.1, \delta = 0.1$ and $Q = 0.22$. This table is adapted from [128].

Ratio of increase in the skin friction for different catheter radius				
c	$z_d = 0.025$	$z_d = 0.05$	$z_d = 0.075$	$z_d = 0.1$
0.04	2.91	2.65	2.32	1.91
0.06	3.2	3.08	2.91	2.69
0.08	3.95	3.92	3.86	3.77
0.1	3.98	4.95	4.97	4.97

Table 4: The estimates of pressure gradient at different locations in the axial direction for various types of catheters for distinct values of n with $R=1, b=1, a=0, m=2, z_d=0$, $We=0.5$, $Gr=5, \beta=0.5, \zeta=0.1, \delta=0.1$ and $Q=0.985$. This table is adapted from [128].

Types of catheter	Range of catheter size	z	n = 2	n = 6	n = 10
Guidewire	0.08 - 0.18	0.2	1.17 - 1.32	1.08 - 1.23	1.07 - 1.21
		0.4	1.36 - 1.47	1.27 - 1.37	1.24 - 1.34
		0.6	1.36 - 1.47	1.36 - 1.46	1.32 - 1.43
		0.8	1.17 - 1.32	1.25 - 1.41	1.27 - 1.43
Infusion	0.14 - 0.33	0.2	1.27 - 1.43	1.18 - 1.33	1.17 - 1.31
		0.4	1.43 - 1.60	1.34 - 1.49	1.30 - 1.45
		0.6	1.43 - 1.60	1.43 - 1.59	1.39 - 1.55
		0.8	1.27 - 1.43	1.36 - 1.53	1.39 - 1.56
Angioplasty Catheter	0.3 - 0.6	0.2	1.41 - 2.13	1.31 - 1.79	1.29 - 1.75
		0.4	1.57 - 4.86	1.46 - 3.18	1.42 - 2.80
		0.6	1.57 - 4.86	1.56 - 4.78	1.52 - 4.06
		0.8	1.41 - 2.13	1.51 - 2.68	1.53 - 2.88

Table 5: The estimates of resistance to flow at different locations in the axial direction for various types of catheters for distinct values of ζ with $R=1, b=1, a=0, m=2, z_d=0, n=2$, $We=0.5$, $Gr=2, \beta=0.5, \delta=0.05$ and $Q=0.05$. This table is adapted from [128].

Types of catheter	Range of catheter size	z	$\zeta=0.05$	$\zeta=0.1$	$\zeta=0.15$
Guidewire	0.08 - 0.18	0.1	5.08 - 6.36	5.23 - 6.47	5.38 - 6.58
		0.3	5.85 - 7.12	6.32 - 7.48	6.74 - 7.83
		0.5	6.24 - 7.48	6.90 - 8.01	7.48 - 8.52
Infusion	0.14 - 0.33	0.1	5.89 - 7.86	6.02 - 7.96	6.14 - 8.05
		0.3	6.65 - 8.66	7.05 - 9.01	7.42 - 9.37
		0.5	7.02 - 9.03	7.59 - 9.58	8.11 - 10.19
Angioplasty Catheter	0.3 - 0.6	0.1	7.57 - 11.23	7.67 - 11.44	7.77 - 11.68
		0.3	8.36 - 12.83	8.70 - 14.01	9.05 - 15.77
		0.5	8.72 - 13.81	9.25 - 16.45	9.82 - 24.39

Table 4 depicts the variation of the pressure gradient in axial direction with different catheter types and stenosis shape parameter (n) values whereas Table 5 exhibits the estimates of the resistance to flow at different directions of z for varying values of ζ. The pressure gradient appears to decrease with rising stenosis shape parameter for all three types of catheters which

implies that catheters are capable of improving blood flow in the restricted artery. The formation of a clot in mildly stenotic artery causes an increase in flow resistance as depicted in Table 5. It is feasible to notice that the use of a catheter results in a significant increase in the magnitude of the resisitve impedance, in addition of the simultaneous presence of both stenosis and thrombosis in the artery.

Since the Angioplasty catheter uses a balloon-tipped catheter to clear occlusions in the lumen of the arteries, it may be inferred that it considerably improves blood flow when compared to Infusion and Guidewire catheters. It hastens clot disintegration and thrombolysis, which may lead to a quicker return of venous flow and a reduced requirement for prolonged chemical thrombolytic infusions. As the catheter's radius rises, the pressure distribution and resistive impedance increase as the artery's annular region shrinks. Additionally, it is vital to perceive that an upsurge in relaxation time (We), which accelerates blood flow and catheterization in a stenotic artery with thrombosis, increases its frictional resistance. The offered estimates may be valuable to clinicians in selecting their next course of action due to the increased use of catheters in clinical practice.

5. Conclusions

The influence of stenosis depth, blood clots thickness and insertion of catheter on blood flow characteristics are reviewed in this study. High turbulence, head loss, abnormal blood pressure and a congested flow state in ducts with the potential to collapse are some of the symptoms of diseased state of arteries. Some of the intriguing findings from this systematic review are collated below:

- Blood flow resistance decreases in intensity as flow rate and the stenosis shape parameter increase.
- With the rising of height of blood clot in a constricted artery, the blood pressure increases.
- As the stenosis shape and depth parameters grow, the blood's temperature decreases, which reduces blood flow through the artery.
- When compared to infusion and guidewire catheters, the angioplasty catheter treatment procedure significantly improves blood flow since it uses a balloon-tipped catheter to eliminate occlusions in the lumen of the arteries.

- Understanding the risk factors, adopting healthy lifestyles and preventative techniques, as well as early detection, will be useful in the management or eradication of such cardiovascular diseases.

Several relevant statistical measures have been computed and data analysis also has been performed to describe the current state of cardiovascular disease prevalence. It is more adverse and difficult to make deep understanding of blood flow measures when there is a gap in understanding of certain aspects of blood rheology in abnormal flow states such as, the presence of stenosis, blood clots and catheter in the lumen of blood vessels. Thus, it is envisaged that the sample mathematical model presented in Section 3 and the exciting theoretical results with the provided clinical applications in Section 4 could be useful in estimating the important rheological measures as well as to forecast the consequence of abnormalities in blood flow attributable to the occurrence of stenosis and thrombosis in a catheterised artery. The outcomes of this review can be utilised for imminent research especially in the context of the simultaneous presence of stenosis, thrombosis, and catheter as well as in helping the medical practitioners to make better diagnosis for patients diagnosed with cardiovascular diseases.

Statement of Competing Interest

The authors declare that the authors have no competing interest in the submitted research work for publication.

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Conflict of Interest Statement

The authors declare that they do not have any conflict of interest.

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