

Review article

Adaptive Mechanism of Laminar Flow to Anatomical Changes in Coronary Arteries: A Clinical and Fluid Mechanic Hypothesis Generating Exercise with ChatGPT

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ABSTRACT

Coronary artery disease (CAD) is a common cardiac problem associated with multiple co-morbidities and high mortality. Despite tremendous efforts in research, scientists are still unable to identify and explain the mechanisms leading to atherosclerosis and its progression or regression. In an effort to disrupt the current passive concepts on atherosclerosis, the authors challenged the artificial intelligence (AI)-based language model ChatGPT with provocative questions in a hypothesis-generating exercise. In the study of flow in pipes or biomedical systems, laminar flow is the standard that is most efficient without damaging the wall and components of the system. However, not all pipes or arteries, or veins are straight. The fluid or blood needs to navigate mild or acute curves, cross smooth or rough surfaces of the inner lumen, or flow in the same direction or against the main flow. As fluid courses through these dynamic systems, the laminar flow accommodates and changes its flow patterns for the successful transportation of fluid and materials. This review emphasizes the metamorphosis of laminar flow in various environments of pipes (or vessels in the biomedical system) to promote energy conservation and efficient transport.

KEYWORDS Dynamic Coronary Angiography, Laminar flow, Turbulent flow, Antegrade coronary flow, Retrograde coronary flow.

INTRODUCTION

Coronary artery disease (CAD) management includes percutaneous coronary intervention (PCI) or coronary bypass surgery (CABG), which are effective but costly and associated with multiple co-morbidities or loss of income. Prevention of CAD through the correction of risk factors, such as hypertension (HTN), hyperlipidemia (HLP), and no smoking, is the best strategy [1]. Many patients improve clinically, and their lesions shrink with better control of HTN and HLP. However, some patients do not improve and even progress to an acute coronary syndrome, including ST segment elevation myocardial infarction [2]. Despite tremendous efforts, scientists are still unable to identify and explain the mechanisms leading to atherosclerosis and its progression or regression. As a result, current preventive measures for CAD are merely generic blanket treatments without a personalized medical approach that is suboptimal to the expectations of patients and society in the 21st century.

Previous research on the mechanism of CAD has been limited to longitudinal observational trials or bench studies using small laboratory animals. The Framingham study identified and confirmed the risk factors for CAD, including HTN, HLP, smoking, type A personality, and strong family history [3]. Elevated levels of LDL cholesterol were shown to have a mechanistic pathology through histological samples of arteries from rabbits fed with a high cholesterol diet [4]. However, despite these findings, the initial or subsequent natural injuries that trigger the attachment of LDL cholesterol molecules to the receptor-ligand on the surface of the endothelial cell were never identified nor confirmed by any current hemodynamic or imaging modality.

Over the past five years, the present team of researchers has utilized the investigative methodology and operating techniques of hydraulics engineers to study the coronary, iliac, and common femoral circulation. The hypothesis was to investigate whether abnormal flows, such as turbulent flows, damage the intima of arteries and initiate the formation of atherosclerotic plaques, whereas laminar flow may help prevent the development of new stenosis or the build-up of existing lesions. The goals of this review were (1) to identify laminar flow and its changes when passing through different structural formations of a pipe or anatomical configurations of an artery, (2) to analyze these arterial metamorphoses from a hydraulic perspective, and (3) to assess their clinical implications.

In an effort to disrupt the current passive concepts on atherosclerosis (which are at a dead end, without new direction nor startling discovery in recent years), the authors challenged the artificial intelligence (AI)-based language model ChatGPT with provocative questions in a hypothesis-generating exercise. The authors' intention is to enlist the assistance of ChatGPT in an effort to provoke radical changes for disruptive innovation from AI. Quotes from hydraulic engineering sources will be included in the usual format, whereas the replies from OpenAI (San Francisco, USA) will be quoted in toto and formatted in italics.

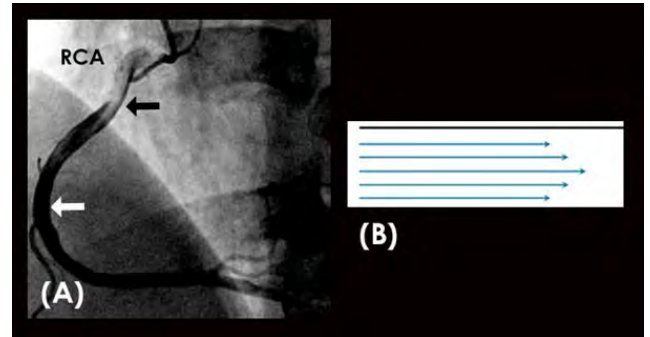


FIGURE 1. The laminar flow is characterized with orderly flowing pattern with a pointed tip (black arrow).

LAMINAR FLOW

Angiographic Description. Laminar flow is defined as a smooth, orderly movement of fluid, with each layer flowing in parallel to one another and the streamlines in parallel to the axis of the artery. There is no mixing or diffusion between layers, and the flow remains stable and predictable. Due to friction with the wall, the speed of the flow is highest at the center and lower near the peripheries. Laminar flow is identifiable by its typical pointed tip, as shown in Figure 1.

Hydraulic Perspective. The operating mechanism of blood flow is determined by the Hagan-Poiseuille's law, which integrates the velocity profile over the cross-sectional area to yield the volumetric flow rate Q :

$$Q = \frac{\pi R^4 \Delta p}{8 \mu L}$$

Where Δp is the pressure drop across a pipe length of L and radius R , the flow of fluid, whether it be water or blood, is determined by gradients [5]. These gradients are typically highest closer to the source of the fluid, whether it be a pipe or a river, etc., and decrease in magnitude as the fluid moves towards the distal end or the delta [6].

Clinical Implications. According to the Hagan-Poiseuille's law, blood flow in the coronary or aortic arteries is influenced by gradients, and the speed of the flow is highest at the origin and lowest near the end. As a result, the proximal segment of the coronary artery is more prone to erosion injuries, while lesion secondary to accumulation from deposition is more common in the distal segment with lower gradients [6]. This hydraulic mechanism may also explain the presence of bulky and rapidly-growing lesions in the proximal coronary segment and the slow-growth lesions at the distal end [7].

Because of the smooth and orderly movement of laminar flow, there is no mechanical injury to the intima, and there is minimal contact or diffusion of suspended materials or solutes from the blood into the arterial wall. Consequently, based on the new imaging technique, the presence of laminar flow could predict no future lesions and no plaque rupture in the observed coronary segments [8] (Figure 2).



FIGURE 2. Schema of an entrance flow with change to laminar flow

TABLE 1. Classification of Flows in Mechanical and Biomedical Systems

Laminar Flow
Entrance Flow
Helical Flow
Boundary layer
Recirculating Flow
Reverse Flow
Vortex Formation
Turbulent Flow
Water Hammer Event (or Shock)

ChatGPT Perspective. *The development of laminar flow in a pipe can be explained by the balance between inertial forces and viscous forces. When the fluid flows through a pipe, it experiences resistance from the walls of the pipe. This resistance creates a shear stress at the boundary layer, near the wall of the pipe where the fluid velocity is zero. If the velocity of the fluid is low, the viscous forces dominate and the flow remains laminar [9].*

METAMORPHOSIS OF FLOWS IN MECHANICAL AND BIOMEDICAL SYSTEMS

In the operation and maintenance of pipes, pumps, tubes, or channels (or in the physiology and pathophysiology study for flows in arteries and veins), laminar flow is the standard for normal operation with optimal volume flow rate, while not damaging the lining of the tubes or components of the pumps (nor injuring the tunica intima of the arteries). As the fluid (or blood) flows through an elbow (or a curve), divides at a fork (or a bifurcation), turns at a tee (or a bend), etc., the patterns of flow do not always remain laminar. Specifically, when turning around a soft curve, the blood may flow on a helical fashion. At the entry of a bifurcation, the flow divides into separation flow with recirculating layers (organized vortex formation). As the tube becomes larger (or the arteries grow larger with age), the vortices become disorganized, and turbulent flow may develop. When the arterial wall becomes calcified and rigid, the blood flow may form a boundary layer of slow speed due to high friction upon the wall. Depending on the alteration of the structural design of pipes or arterial anatomy, along with other complex factors, the laminar flow could transform or degenerate into various flow patterns listed in Table 1.

HELICAL FLOW

Angiographic Description. In long, straight pipes or coronary segments, laminar flow is considered ideal. However, when the coronary arteries become tortuous and the

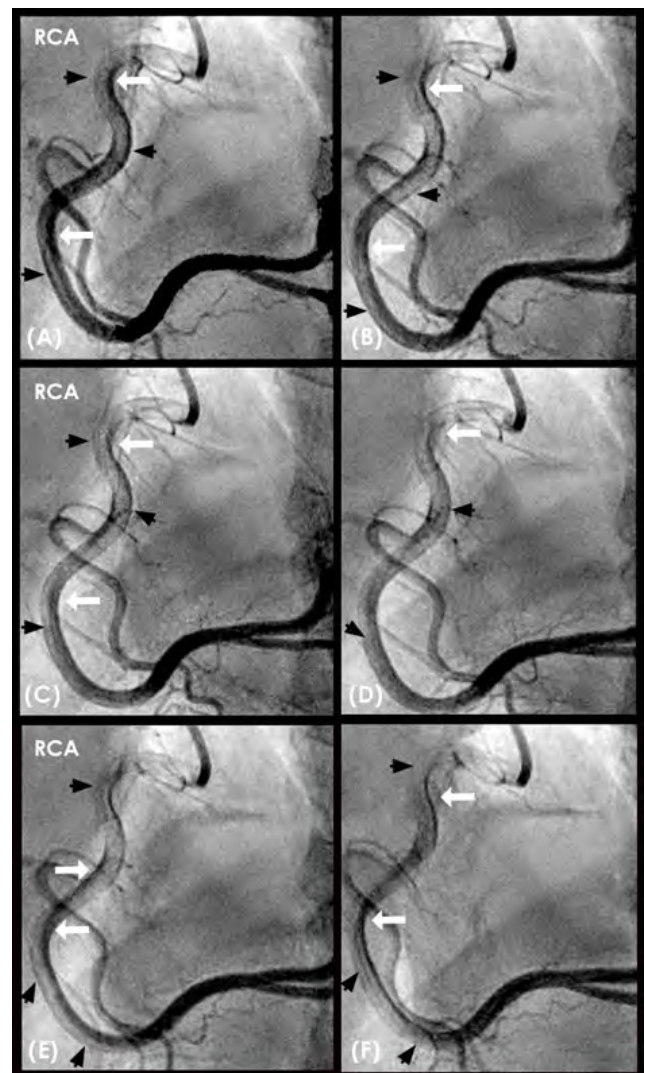


FIGURE 3. Helical Flow. (A-D) The blood (in white color) is observed moving along the apices of the curves (black arrowheads). The contrast (in black) with high viscosity occupies the inner curve (white arrows). (E-F) The contrast in black moves from one inner curve (first white arrow) to another inner curve (second white arrow).

blood flow encounters curves, the fluid layers near the outside curve or apex experience higher velocity, while those near the inner curve slow down. As a result, the blood moves from one apex to the next, this is called the helical flow (Figure 3).

ChatGPT Perspective. *In a helical flow pattern, the fluid moves faster on the outer edges of the pipe due to the effect of the centrifugal force. The faster-moving fluid at the outer edges of the pipe experiences less resistance from the pipe walls, resulting in a lower pressure drop (higher gradient to propel the flow) and a higher flow rate. The fluid layers closer to the center of the pipe move more slowly due to the effect of fluid viscosity and the resistance from the pipe walls (lower gradient so the flow is slower).*

To understand how the centrifugal force arises, consider a fluid element flowing through a curved pipe. As the fluid element moves along the curved path, it experiences a radial

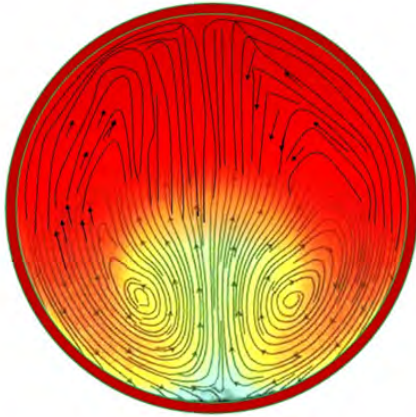


FIGURE 4. This is the image of “Dean vortices” in a cross-section of fluid flowing through a curved tube. The highest-velocity fluid is near the outer curvature, and the lowest-velocity fluid is near the inner curvature (adapted from reference [11]).

acceleration due to the curvature of the pipe. This acceleration creates a centrifugal force that pushes the fluid element away from the center of the curve [9].

Clinical Implications. Laminar flow refers to the smooth, unidirectional movement of blood, without turbulence or mixing of different layers. This type of flow minimizes energy losses and maximizes the amount of blood delivered to the tissues. When the laminar flow follows a soft, smooth curve, it needs to move in a helical pattern to maintain its organized, energy-saving mode [10].

ROTATIONAL FLOW

Angiographic Description. In rotational flow, the fluid particles rotate around the axis of the pipe while moving downstream. This rotational motion can be caused by various factors, such as the shape of the pipe, the velocity of the fluid, and the presence of obstacles or irregularities in the flow (Figure 4).

ChatGPT Perspective. In a curved pipe, the centrifugal force caused by the curvature of the pipe can induce a secondary flow perpendicular to the main flow. This secondary flow results in the formation of a series of vortices that are oriented in a helical pattern along the length of the pipe. This is called Dean’s flow. The direction of rotation of the vortices depends on the direction of the primary flow and the curvature of the pipe. The formation of vortices in curved pipes can enhance the mixing and heat transfer properties of the fluid, leading to more efficient and effective operation of the equipment. However, it can also result in increased pressure drop and turbulence, which can be detrimental to the performance of the system [9], [12].

Clinical Implications. In coronary artery anatomy with multiple smooth and soft curves, the rotational flow may be better in flowing at a faster speed while still maintaining orderly transport. However, if the speed exceeds a limit, turbulence may occur.

FLOW SEPARATION AT A CURVE (KELVIN-HELMHOLTZ INSTABILITY)

Angiographic Description. When the blood flow reaches a bifurcation, such as where the distal left main artery (LM) divides into the left anterior descending artery (LAD) and the left circumflex artery (LCX), the primary flow continues downstream after hitting the bifurcating center or the carina. At the same time, the flow near the outer curve experiences deceleration and may become stagnant. (Figure 5) What is the clinical meaning of the above observations?

ChatGPT Perspective. The Kelvin–Helmholtz instability is a fluid instability that occurs when there is velocity shear in a single continuous fluid or a velocity difference across the interface between two fluids. This separation of flow occurs when the flow of liquid in a pipe or over a surface becomes unstable and separates from the surface. This can cause a reduction in flow rate, an increase in pressure drops, and even damage to the pipe or equipment due to vibration and turbulence. When the speed of the peripheral layer becomes too low compared with the flow of the central layers, vortex shedding occurs as vortices or eddies form after the curve or in the wake of the object (Figure 6) [9].

Clinical Implications. The recirculation flow at the exit slope of a large side branch of a bifurcation is a hydraulic mechanism that typically occurs at the outer curve of the ostium of the LCX (Figure 7). However, if the recirculation flow becomes a vortex and transforms into a disorganized turbulent flow, this lesion can grow significantly. To prevent this outcome, control of HTN by medications, especially with beta-blockers would decrease the gradient at the origin (the aortic root) and the end (the distal coronary artery), resulting in slower speed across the lesion. Lower speeds lead to less gradient between central and peripheral layers, reducing the likelihood of recirculation or vortex formation.

BOUNDARY LAYER

Angiographic Description. In the proximal segment of a large coronary artery, it is common for the peripheral layers to become thick and stagnant, resulting in a phenomenon known as the boundary layer. What are the causes and the clinical meaning of these boundary layers? (Figure 8)

Hydraulic Perspective. When a fluid enters a pipe, viscous effects will develop due to the pipe wall. The region where viscous effects are important is referred to as the boundary layer [5].

ChatGPT Perspective. If the boundary layer of a coronary flow is too thick, it can lead to reduced shear stress on the endothelial cells of the intima layer. Shear stress is the frictional force exerted by the flowing blood on the endothelial cells and is an important stimulus for the release of nitric oxide, which plays a critical role in regulating vascular function and health. When the shear stress is too low due to a thick boundary layer, it can lead to endothelial dysfunction, which is characterized by a reduction in the production and release of nitric oxide and an increase in the production of reactive oxygen species and pro-inflammatory

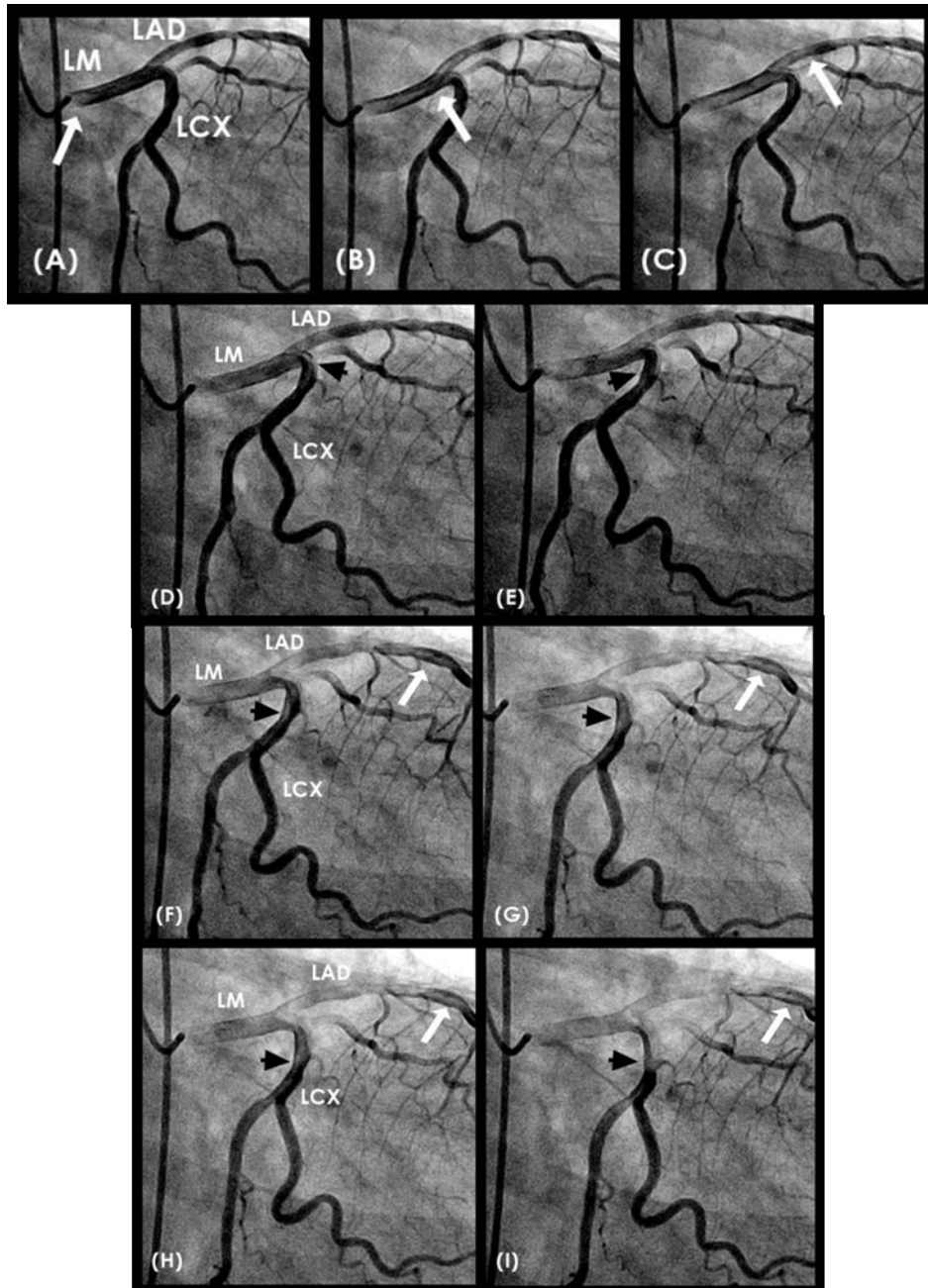


FIGURE 5. Coronary Flow at a Curve. This is a series of nine consecutive images of a left coronary angiogram. The left main artery (LM), the left anterior descending artery (LAD), and the left circumflex artery (LCX) are filled with black contrast. The blood in white moves in, displaces the contrast, shows the movement of the blood and its characteristics. All images are filmed at 15 images per second, or each image = 0.067 seconds or 67 milliseconds.

(A) The flow begins to enter the LM, as a white arrowhead at the ostium of the LM (arrow). This is the beginning (first image) of diastole.

(B) The blood (in white) is seen at the proximal LAD, (arrow) while it is only at the ostium of the LCX. This is the second image of diastole.

(C) The blood is seen further down the mid LAD (arrow) while it is still at the ostium of the LCX. This is the 3rd image of diastole.

(D) In a higher magnification of the images, the flow at the LM looks turbulent. The flow is at the ostium of the LCX, and preferentially turns at the curve along the carina (arrowhead). This is the 4th and last image of diastole.

(E) The blood is at the proximal and mid LAD, while at the LCX, the blood just barely enters the LCX on the carina side. There is a thick layer of contrast at the outer curve of the LCX, opposite to the carina (arrowhead). This is the beginning of the separation layer. This is the first image of systole.

(F) At this stage, the blood moves more slowly at the mid LAD (white arrow) because this is the 2nd image of systole while at the LCX. The blood is still at the ostial and proximal segments. The separation layer is still prominent with some elements of white blood (arrowhead). This is the evidence of recirculating or swirling flow at the separation layer.

(G) The flow on the carina border is still homogeneously white, even though the speed is slow because this is during systole. At the same time, there is turbulent movement of the blood (mixing of black and white) inside the separation layer (arrowhead).

(H) Now, the blood is still at the mid LAD (white arrow), while at the LCX, there is more turbulence at the separation layer (arrowhead). The reason for the slow speed at the LAD is because the flow is in systole (3rd image of systole).

(I) At this stage, the antegrade flow in the proximal LCX is larger, more prominent, and occupies more than half of the proximal LCX. The separation layer at the proximal LCX is now limited to a thin layer. The black color of the separation layer is more homogenous. It may be due to reversed flow during systole (arrowhead). The slow movement of the blood at the LAD and reversal flow at the LCX are due to contraction in systole. This image is the 4th image of systole.

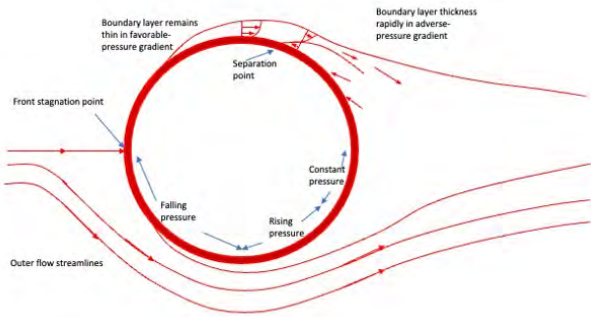


FIGURE 6. Schema of the flow at a curve. At the exit curve, there is a separation of flow due to the higher velocity of the upper layers and slower velocity at the lower layers. (adapted from reference [6])

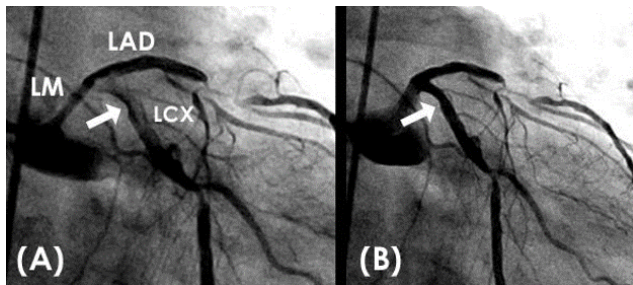


FIGURE 7. Slow Growth Lesion. (A) There is a thick boundary layer (white arrow). (B) At the same location of the boundary layer, as the whole artery in full contrast, there is a subtle narrowing of the proximal segment of the left circumflex artery (LCX), which is a slow growth lesion compared with the lesions in the mid left anterior descending artery and mid-LCX (red arrow).

cytokines. These changes can lead to a variety of pathological processes, including vasoconstriction, increased platelet aggregation, and recruitment of inflammatory cells to the vessel wall. Over time, these processes can contribute to the development and progression of atherosclerosis [13], [14].

CONCLUSION

In the study of flow in pipes or biomedical systems, laminar flow is the standard that is most efficient without damaging walls and components of the system. However, not

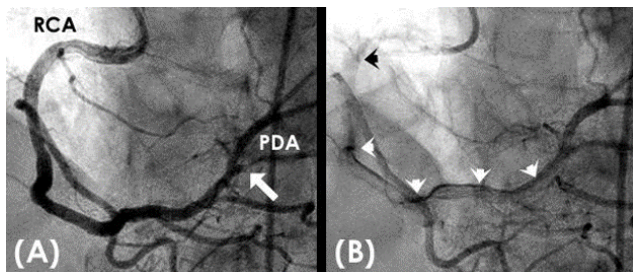


FIGURE 8. Right Coronary Artery Angiogram. (A) This was the right coronary artery (RCA) angiogram of a patient with uncontrolled diabetes, smoking, and high levels of low-density lipoprotein (LDL)-cholesterol. Her troponin level was high. There was a severe lesion at the ostium of a posterior descending artery (PDA) branch (white arrow). (B) There was a minimally thick boundary layer along the inner curve (short arrows).

all pipes or arteries, or veins are straight. The fluid or blood needs to navigate the mild or acute curves, cross the smooth or rough surfaces of the inner lumen, or flow in the same direction or against the main flow. Through these changes in the systems, the laminar flow needs to accommodate and change its flow patterns so the transportation of fluid or material can be successful. This review emphasizes the metamorphosis of laminar flow in various environments of pipes or tubes in biomedical systems in order to conserve energy and transport efficiently. Further research on the role of laminar flow and its metamorphoses could help in the clinical implication of these results.

CONFLICTS OF INTEREST

None of the authors have conflicts of interest to declare.

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