Chapter

Internal Flow Choking in Cardiovascular System: A Radical Theory in the Risk Assessment of Asymptomatic Cardiovascular Diseases

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Abstract

The theoretical discovery of Sanal flow choking in the cardiovascular system (CVS) demands for interdisciplinary studies and universal actions to propose modern medications and to discover new drugs to annul the risk of flow-choking leading to shock-wave generation causing asymptomatic-cardiovascular-diseases. In this chapter we show that when blood-pressure-ratio (BPR) reaches the lower-critical-hemorrhage-index (LCHI) the flow-choking could occur in the CVS with and without stent. The flow-choking is uniquely regulated by the biofluid/blood-heat-capacity-ratio (BHCR). The BHCR is well correlated with BPR, blood-viscosity and ejection-fraction. The closed-form analytical models reveal that the relatively high and the low blood-viscosity are cardiovascular-risk factors. In vitro data shows that nitrogen, oxygen, and carbon dioxide gases are predominant in fresh blood samples of the human being/*Guinea-pig* at a temperature range of 37–40 °C (98.6–104 °F). In silico results demonstrate the occurrence of Sanal flow choking leading to shock wave generation and pressure-overshoot in CVS without any apparent occlusion. We could conclude authoritatively, without any *ex vivo* or *in vivo* studies, that the Sanal flow choking in CVS leads to asymptomatic-cardiovascular-diseases. The cardiovascular-risk could be diminished by concurrently lessening the viscosity of biofluid/blood and flow-turbulence by increasing the thermal-tolerance level in terms of BHCR and/or by decreasing the BPR.

Keywords: asymptomatic cardiovascular disease, biofluid choking, BHCR, risk factors, sanal flow choking

1. Introduction

The cardiovascular system (blood circulatory system) is an internal fluid flow loop with multiple branches, transport nutrients and oxygen to all cells in the body.

The center of the cardiovascular system (CVS) is the heart, which is accountable to pump blood through the complex network of viscoelastic vessels, viz., arteries, veins and capillaries. Blood flow in CVS is inherently an unsteady phenomenon experiencing with transient events. Blood flow begins when the heart relaxes between two heartbeats. Due to the cyclic nature of the heart the velocity and pressure of the internal fluid (blood/biofluid) circulating through the viscoelastic vessels varies with time. Blood flow in CVS is typically laminar but due to its pulsatile nature makes possible the flow transition to turbulent. Furthermore, the variations in the fluid flow properties and vessel geometry due to pathophysiological reasons, including the seasonal effects, contribute for the transition of laminar flow to turbulent.

Diseases of the CVS are manifold in gravity and microgravity environment (human spaceflight) and afflict millions of patients worldwide including cases of: coronary artery disease (CAD), ischemic gangrene, abdominal aortic aneurysms, moyamoya disease, and stroke. A few of these dysfunctions are reported to be the end result of atherosclerosis, characterized by plaque accumulation within the walls of the arteries. Atherosclerotic cardiovascular disease (CVD) is the leading cause of death for both men and women. There is no clear age cut point for defining the onset of risk for CVD, which is corroborated from the clinically detected elevated risk factor levels and subclinical abnormalities of adolescents as well as young adults. The hemodynamic characteristics of blood flow have long been thought to play an important role in the pathogenesis of atherosclerosis. In light of the discovery of internal flow choking in CVS [1, 2], the hemodynamic characteristics of blood flow need to be examined in detail for exploring the causes and effects of flow choking in gravity and microgravity environment for an authentic conclusion in the risk assessment of asymptomatic cardiovascular diseases.

Heart failure (HF) is the cardiovascular epidemic of the 21st century [2]. Although there has been significant advancement in the diagnosis, prognosis, treatment and prevention of HF with reduced ejection fraction (EF), the morbidity and mortality are still extensive. This is particularly true due to the Covid-19 pandemic (www.escardio.org). The EF is a blood flow measurement in percentage (%), specifying how much blood the left ventricle pumps out with each contraction. The EF measurement under 40% may be an indication of HF or cardiomyopathy. An EF from 41–49% may be considered as "borderline" cases having the history of stroke (memory effect). A normal heart's EF may be between 50–70%. An EF value higher than 75% generally indicates hypertrophic cardiomyopathy (HCM), which could affect people of any age [2]. HCM is reported as a cause of acute HF particularly in young people, including young athletes. Although all these percentage demarcations of the EF are meaningful for the diagnosis, until the discovery of the Sanal flow choking the EF estimations were not supported by any closed-form analytical model for taking brilliant clinical decisions case by case. The recent theoretical discovery of the Sanal flow choking [1, 2] provides an insight for the risk assessment of asymptomatic cardiovascular diseases. Moreover, the Sanal flow choking model could generate universal benchmark data for predicting the condition of internal flow choking in CVS for taking an authentic conclusion on the desirable EF in terms of blood flow percentage for healthy subjects for reducing the risk of acute-heart-failure. The European Society of Cardiology (ESC) reported (2020) that patients with cardiovascular risk factors and established cardiovascular disease (CVD) represent a vulnerable population when suffering from the Covid-19. It is important to note that patients with cardiac injury in the context of Covid-19 have an increased risk of morbidity and mortality.

The acute-heart-failure is an event rather than a disease [3, 4]. Therefore, many researchers argued for a radical change in thinking and in therapeutic drug

development through multidisciplinary research [1–6]. Of late, Kumar et al. [2] reported conclusively that the transient event causing the acute-heart-failure is due to the phenomenon of internal flow choking (biofluid/Sanal flow choking) at a critical total-to-static pressure ratio. Internal flow choking is a compressible fluid flow effect caused by the blockage factor, which occurs at a critical blood-pressure-ratio (BPR), irrespective of the incoming flow velocity. In the CVS, the total pressure is considered as systolic blood pressure (SBP) and the static pressure is denoted as diastolic blood pressure (DBP). The physical situation of internal flow choking in the micro/nanoscale fluid flows in the circulatory system is more susceptible at microgravity condition due to altered variations of blood viscosity, turbulence and the BPR (SBP/DBP). During a long-term human spaceflight mission, the major factor that affects cardiovascular dysfunctions is the absence of gravity [6]. Cardiovascular changes in actual spaceflight differ from those in stimulations such as head-down bedrest or dry immersion [7]. The changes in the cardiovascular system begin solely with the fluid shift associated with microgravity, followed by the decreased circulatory blood volume, cardiac size, and aerobic capacity, and the most prominent symptom, postflight orthostatic intolerance. These symptoms are generically known as "cardiovascular deconditioning" [7–11]. Microgravity environment decreases plasma volume and increases the hematocrit compared with the situation on the earth surface, which increases the relative viscosity of blood. Since blood viscosity strongly depends on hematocrit there are possibilities of an early flow choking in microgravity environment due to an enhanced boundary layer blockage [6].

Human blood is a compressible fluid with different degrees of the compressibility percentage because the specific volume (or density) of blood does change with temperature and/or pressure [1, 2]. Therefore, the specific heat at the constant-pressure (C_p) is always higher than the specific heat at the constant-volume (C_v) of all human blood. The ratio of C_p and C_v is defined as the blood-heat-capacity-ratio (BHCR), which is an important parameter determining the thermal-tolerance level of blood [2]. The specific heat capacity depends on the number of degrees of freedom and each independent degree of freedom permits the particles to store thermal energy and as a result the BHCR will be always greater than one. It corroborates that blood is a compressible fluid and internal flow choking in CVS could occur at a critical BPR irrespective of hypertension or hypotension. Traditionally hypertension is considered as a cardiovascular-risk-factor in patients with systemic autoimmune and chronic inflammatory diseases. Until the theoretical discovery of the internal flow choking in CVS there were no authentic conclusions to support whether hypertension or hypotension is more risk with regards to the hemorrhagic stroke and acute myocardial infarction [1, 2]. The fact is that an acute-heart-failure could occur in both hypertension or hypotension patient because the controlling parameter of this event is the blood-pressure-ratio (BPR). In brevity, attaining the critical BPR is considered as the risk factor for asymptomatic cardiovascular diseases. At the threshold of the internal choking condition, a minor oscillation in BPR for both *hyper* and *hypo* subjects is likely to aggravate the cardiovascular risk. In light of the discovery of internal flow choking in CVS [1, 2], the classic definition of the hypertension causing cardiovascular risk is largely arbitrary [SBP ≥140 and/or DBP ≥90 mmHg]. The prevailing cardiovascular risk data remains challenging owing to the fact that the internal flow choking could occur in both hypertension or hypotension subjects once SBP/DBP reaches the critical BPR. The internal flow choking could happen anywhere in CVS including capillaries, vasa vasorum and/or nanoscale vessels. Capillaries are tiny blood vessels connecting arteries to veins. These blood vessels carry oxygen and nutrients to individual cells throughout the body. The vasa vasorum is a network of small blood vessels that are found in large

veins (e.g., the venae cavae) and arteries such as the aorta and its branches. These small vessels serve to provide blood supply and nourishment for tunica adventitia and outer parts of tunica media of large vessels. Arteries deliver blood from the heart to the rest of the body and Veins return the blood back to the heart from the rest of the body. It is important to note that the pressure inside of arteries is very different from the pressure inside of veins. The pressure created by the heart pushes the blood through the arteries and the pressure inside the arteries is directly related to the blood pressure. The pressure in the veins is very low. Of late Kumar et al. [2, 3] reported that not the pressure but the magnitude of the blood-pressure-ratio (BPR) is the risk factor for acute-heart-failure and the brain hemorrhage because at the choked flow condition there are possibilities of the occurrence shock wave and pressure-overshoot in any vessel with divergent and/or bifurcation region causing aneurysm or wall tearing.

A brain hemorrhage is a type of stroke. It is caused by an artery in the brain bursting and causing localized bleeding in the surrounding tissues. Brain arteriovenous malformations (AVMs) are abnormal connections of arteries and veins [12]. An AVM can develop anywhere in the body, but occurs most often in the brain. Brain AVMs are a leading cause of the hemorrhage in children and young adults, although they can cause other morbidities such as seizures, focal neurological deficits, and headaches. There is usually high flow through the feeding arteries, nidus, and draining veins, which may result in rupture and intracranial hemorrhage, the most severe complication of an AVM. Clinically, brain AVMs are technically challenging and resource-intensive to manage with the available therapeutic modalities and often require multi-modal therapy. The factors influencing risk of hemorrhage associated with sporadic brain AVM is still poorly understood. It has already been established that blood/biofluid is a compressible viscous fluid and internal flow choking can occur anywhere in CVS at a critical BPR causing asymptomatic hemorrhage. In light of the theoretical discovery of the phenomenon of internal flow choking in nano scale fluid flows [1, 2], further studies on the pathogenesis of asymptomatic intracranial hemorrhage is envisaged [13]. Briefly, the concept of internal flow choking in blood circulatory system provides an insight for the diagnosis, prognosis, treatment and prevention of the asymptomatic coronary artery disease (CAD) and peripheral artery disease (PAD).

2. Internal flow choking

Internal flow is a flow for which the fluid is bounded by walls. Internal flow choking is a compressible fluid flow effect and a fluid dynamic condition in wall-bounded systems associated with the venturi effect. Admittedly, when a flowing fluid at a given pressure and temperature passes through a constriction (such as the throat of a convergent-divergent (CD) nozzle or a valve in a pipe) into a lower pressure environment the fluid velocity increases for meeting the continuity condition set by the law of nature, viz., the law of conservation of mass. The conservation of mass (continuity) is a fundamental concept of physics and it tells us that at the steady state condition the mass flow rate through a tube is a constant and equal to the product of local density, local velocity, and local cross-sectional area of the tube. The local cross-sectional area can alter due to the boundary layer blockage (i.e., boundary layer displacement thickness) as a result of the viscous flow effect. The cardiovascular system or hemodynamic process is said to be in a steady state if the state variables which define the behavior of the system or the process are unchanging in time.

All fluids in nature are viscous and compressible [1] and prone to create boundary layer over the bounding walls altering the effective geometric shape of the tube. The magnitude of boundary layer blockage depends up on the rheology of fluid and the type of flow featuring from laminar, transitional to turbulent flow characteristics. Boundary layer is the layer of fluid in the immediate vicinity of a bounding surface where the effects of viscosity are significant in the flow. Note that because of the greater velocity gradient at the wall the frictional shear stress in a turbulent boundary layer is greater than in a purely laminar boundary layer. And as a result, the turbulent boundary layer thickness will be higher than laminar boundary layer thickness. The main known parameter characterizing laminar–turbulent transition is the *Reynolds number*, which is defined as the ratio of inertial forces to viscous forces within a fluid which is subjected to the relative internal movement due to different fluid velocities. The transition to turbulence can occur over a range of *Reynolds numbers*, depending on many factors, including the wall surface roughness, heat transfer, vibration, noise, and other disturbances. The parameters influencing the local *Reynolds number* in a tube are local density, local viscosity, local velocity and the local diameter (a characteristic length). In fact, a decade before, blood was treated as a Newtonian fluid but later the established viscoelastic properties make human blood non- Newtonian [14, 15]. It depends on the elastic behavior of red blood cells. For compressible fluids, viscosity depends on temperature and varies very slowly with low pressure levels. It is an established fact that viscosity variations of fluids will be significant at high pressure levels and low temperature. The viscosity of water increases exponentially with decrease in temperature and is affected by the type and concentration of solutes. Although many empirical laws are available for predicting viscosity of gases, there is no established law for predicting the viscosity of blood in all directions as it possesses anisotropic characteristics. Anisotropy just refers to the properties of a material being directionally dependent. Many biological fluids have elements of anisotropy, because they are made of different cells and plasma that react differently to stresses. For example, blood has to flow in arteries and veins, which range in size from very large to extremely small under pressure pulses emanating from the heart. So the corpuscles in the blood vary in shape along the flow direction and in transverse directions. When they have to squeeze through a tiny vessel, they are extremely distorted and the "fluid" becomes highly anisotropic. Since Newton's law of viscosity is not a fundamental law of nature; and in light of the theoretical discovery of the Sanal flow choking in the CVS, it is desirable to establish a mathematical model to predict accurately the directionally dependent viscosity of blood at various pathophysiological ranges of pressure and temperature for a credible decision making on the possibilities of the occurrence of internal flow choking in the circulatory circuit *a priori*. Such a model will be useful for a credible risk assessment of asymptomatic cardiovascular diseases through in silico methodology with compressible viscous flow models.

The blood/biofluid compressibility effects on mass flow rate have some surprising results. At a particular total condition, there is a maximum limit of mass flow that occurs when the flow Mach number is equal to one (i.e., local flow velocity equal to the local velocity of sound). The limiting of the mass flow rate is called choking of the flow, which occurs at the sonic fluid flow condition (i.e., Mach number (M) equal to one). It is important to note that although the fluid velocity reaches sonic condition and becomes choked, the mass flow rate is not choked. The mass flow rate can still be increased if the upstream pressure is increased as this increases the density of the gas entering the orifice. Internal flow choking occurs when sonic velocity is reached at the constriction section. And the flow becomes

independent from downstream conditions. In other words, internal flow choking occurs in CVS at a critical blood pressure ratio (SBP/DBP), which is governed by the biofluid/blood heat capacity ratio (BHCR).

$$BPR = \frac{SBP}{DBP} = \left(\frac{BHCR+1}{2}\right)^{BHCR/BHCR-1} \quad (1)$$

The analytical model (Eq. (1)) derived from the compressible flow theory [1, 5, 16, 17] dictates the exact condition of internal flow choking in CVS. It is pertinent to note that if the blood vessel is having the shape of a convergent-divergent (CD) nozzle due to occlusion, stenosis, vasospasm and/or the effect of boundary layer blockage (**Figure 1**) there are possibilities of the generation of shock waves and transient pressure-overshoot in the downstream region of the vessel after attaining the internal flow choking condition (Eq. (1)) as a result of supersonic flow development. Occlusion of the blood vessel causing internal flow choking may be due to atherosclerotic plaque, an embolised blood clot, necrosis or a foreign body presence. According to the law of nature, with a mathematical proof [5, 16], for a compressible fluid to expand isentropically from subsonic (M < 1) to supersonic (M > 1) speeds, it must flow through a convergent-divergent duct or a CD-shaped streamtube [5, 6, 16, 17] experiencing with a physical situation of internal flow choking at a critical BPR (**Figure 2**). The critical BPR for internal flow choking is governed by the BHCR as dictated by Eq. (1). There are two types of internal flow choking in CVS viz., biofluid choking and Sanal flow choking. Biofluid flow choking occurs in CVS due to the plaque induced CD nozzle flow effect and/or due to vasospasm (**Figure 1(a–d)**) or any other type of occlusion. A vasospasm is the narrowing of the arteries caused by a persistent contraction of the blood vessels, which is known as vasoconstriction. Vasospasms can affect any area of the body including the brain (cerebral vasospasm) and the coronary artery (coronary artery vasospasm). The Sanal flow choking phenomenon is established as the fluid-throat induced internal flow choking due to the boundary layer formation in the real world flows (continuum/non-continuum) owing to the compressible viscous flow effect [1, 2]. The Sanal flow choking creates a physical situation of boundary layer blockage persuaded biofluid flow choking of the circulatory circuit at a critical systolic-to-diastolic blood pressure ratio (BPR) in all the subjects with and without any plaque (**Figure 1(d–g)**) and/or apparent occlusion.

The internal flow choking is a new theoretical concept in biological science applicable to continuum and non-continuum biofluid flows. As the pressure of the nanoscale biofluid/non-continuum-flows rises, average-mean-free-path diminishes and thus, the *Knudsen number* lowers heading to a zero-slip wall-boundary condition with compressible viscous flow effect, which increases the risk of cardiovascular diseases. Eq. (1) tells us that low BPR, high BHCR or high thermal tolerance of blood reduces the risk of internal flow choking, which in turn reduces the possibilities of shock wave generation and pressure overshoot causing asymptomatic cardiovascular diseases. At a critical BPR, the Sanal flow choking occurs anywhere in the CVS, including micro/nanoscale vessels with sudden expansion/divergence or bifurcation regions. The Sanal flow choking leads to supersonic flow development heading to the shock wave generation in viscoelastic vessels creating memory effect (stroke history). It occurs due to the boundary layer persuaded convergent-divergent (CD) duct shape of the flow passage (**Figure 3**).

The shock wave can occur anywhere at any time in the supersonic flow when there is a flow compression due to streamtube effect or geometric effect or any

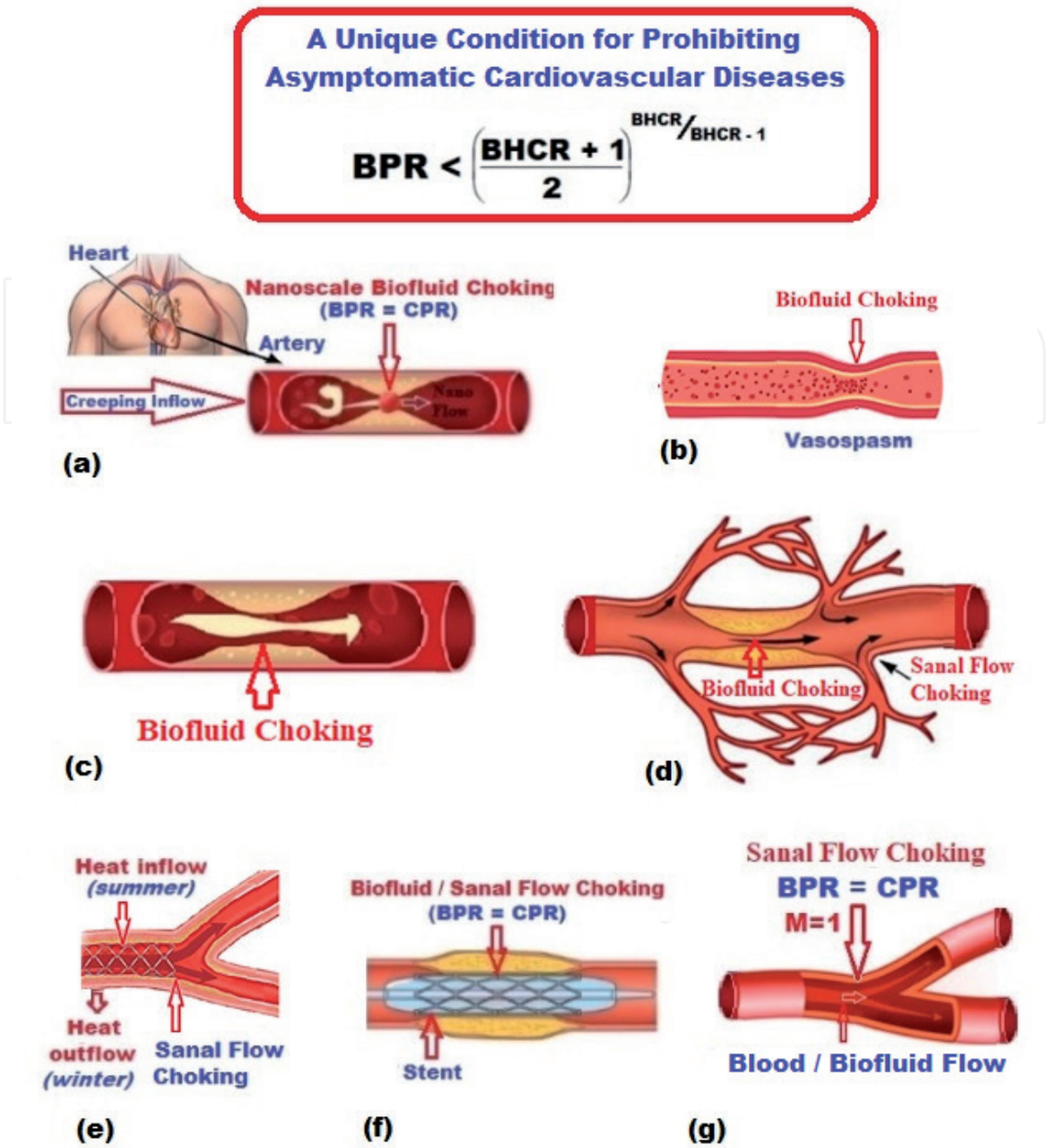

Figure 1.
Demonstrations of different physical situations of internal flow choking (biofluid/Sanal flow choking) at a critical blood-pressure-ratio (BPR) [1]. (a) physical situation of biofluid choking in an artery with plaque deposit similar to a CD nozzle flow passage, (b) demonstrating the possibilities of biofluid choking at a critical BPR due to vasospasm, (c) a partially blocked artery demonstrating the CD nozzle flow passage causing biofluid choking, (d) demonstrating the possibilities of biofluid choking and Sanal flow choking in an artery with plaque and collateral circulation, (e) demonstrating the physical situation of the Sanal flow choking at the presence of a stent in an artery with bifurcation, (f) a partially blocked artery with stent creating a situation of biofluid flow choking at a critical BPR due to CD nozzle shaped flow passage, (g) demonstrating the physical situation of the Sanal flow choking in a healthy subject having an artery with bifurcation.

other flow disturbance. Normal shock waves create very sharp transient pressure-overshoot in CVS, which leads to bulging or tearing of vessels. The tearing (hemorrhagic stroke) or bulging of vessels (aneurysm) depend on the memory effect (stroke history) and relaxation modulus of the viscoelastic vessels. Memory effect depends on the strength of the shock wave and the associated occurrence of the transient pressure-overshoot over the years due to the frequent fluctuations in BPR, due to various reasons, ranging from unchoked to choked biofluid flow conditions. Note that large oscillations in BPR leads to *arrhythmia*. Most heart valve problems

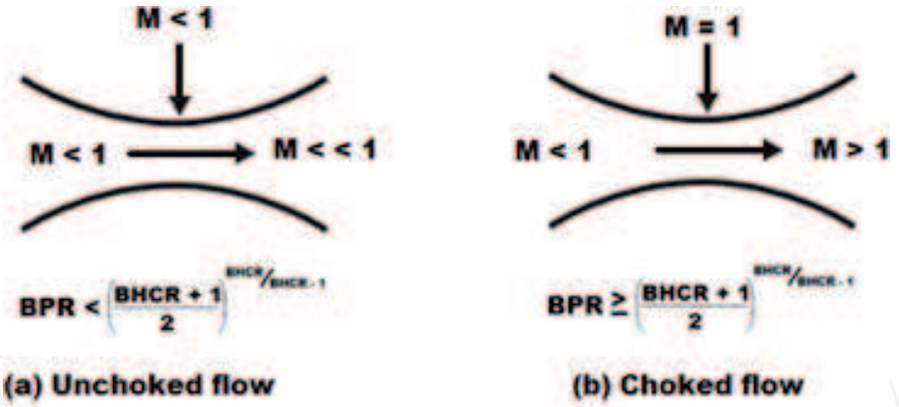

Figure 2.
Demonstrating the physical situation of the internal flow choking and unchoking condition in a CD duct or a CD shaped streamtube.

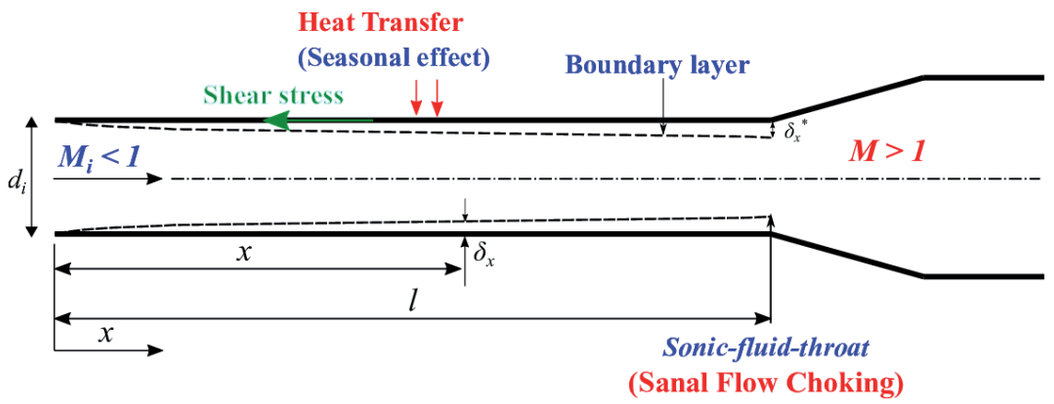

Figure 3.
Demonstrating the Sanal flow choking phenomenon in an idealized physical model of an artery with a divergent port.

involve the aortic and mitral valves, possibly because of its geometric shape similar to a convergent-divergent (CD) duct flow passage [2, 6]. All these deliberations lead to establish herein that the internal flow choking is an undesirable phenomenon in CVS as it leads aneurysm, hemorrhagic stroke, moyamoya disease, myocardial infarction. The significant clinical aspect is that; the internal flow choking is uniquely regulated by the biofluid/blood heat-capacity-ratio (BHCR). Of late V.R.S.Kumar et al. [2] correlate the BHCR with BPR, blood viscosity (BV) and ejection fraction (EF) for establishing the concept of internal flow choking causing asymptomatic cardiovascular diseases for taking brilliant clinical decisions in case by case manner [18–30].

3. Analytical methodology

The analytical prediction of the Sanal flow choking [1, 2] is a breakthrough in biological science, which creates a radical change in the diagnostic sciences of asymptomatic cardiovascular diseases because the various causes of the Sanal flow choking are complementing with all the established concepts in the medical sciences [2]. The concepts of Sanal flow choking is reviewed herein for highlighting pragmatic solutions for reducing the risk of internal flow choking leading to shock wave generation causing asymptomatic cardiovascular diseases. The whole blood viscosity is popularly the one of Virchow's triad, which is a recognized concept pronounces the three wide types of causes that are believed to interpose to thrombosis

causing cardiovascular complications, viz., hypercoagulability, hemodynamic changes (stasis, turbulence), endothelial injury/dysfunction. Furthermore, it is well known that blood is a non Newtonian fluid [2] as blood viscosity changes due to fluid force, seasonal effects and blood thinning medications.

Viscosity variations are depending on the shear rate or shear rate history of the blood/biofluid, which could vary due to local effects too. Blood temperature decreases during the winter season resulting an increase in blood viscosity and the inverse effect happens during the summer season [5, 18]. It corroborates that the boundary-layer-blockage (BLB) factor causing the Sanal flow choking would alter due to the blood viscosity variations as a consequence of the blood-thinning medication and/or the seasonal effects [2, 18]. Indeed, boundary-layer-blockage induced internal flow choking is more prone during the winter season than the summer season due to the higher blood viscosity at the relatively low blood temperature. It leads to say that the risks of internal flow choking leading to asymptomatic cardiovascular diseases would be high during the winter than in the summer season [5, 18]. It is important to note that disproportionate blood-thinning medication will increase the Reynolds number, which produces the high-turbulence-level creating enhanced boundary-layer-blockage (BLB)-factor causing an early internal flow choking. Therefore, we can establish that relatively high blood viscosity and low blood viscosity are risk factors for an early internal flow choking in cardiovascular system (CVS) causing asymptomatic stroke/hemorrhage and acute heart failure, which is correlating with the established index, viz., International normalized ratio (INR). Therefore, the real effect of viscosity on internal flow choking in CVS needs to be established through randomized clinical trials for taking preventive strategies for reducing the risk of asymptomatic hemorrhage and acute heart failure. On this rationale, it is essential, rather needed, perhaps inevitable to declare an exact condition for prohibiting the internal flow choking in the CVS, in terms of viscosity, density, Reynolds number, biofluid/blood-heat-capacity-ratio (BHCR), blood-pressure-ratio (BPR), the ejection fraction in terms of biofluid/blood flow rate (BFR), and stenosis (vessel geometry), which are accomplished through the closed-form analytical models (Eqs (2), (3)). Eqs (2), (3) are declaring the unchoked flow condition in the CVS, which could predict the cardiovascular risk for taking a conclusive clinical decision on each and every subject in all seasons. Accurate estimation of the parameters highlighted in Eqs (2), (3) are absolutely required for the future health care management of all subjects aiming for prohibiting asymptomatic cardiovascular diseases.

$$\left[\frac{(BFR)_{local} V_{local}}{(BHCR)_{lowest} (DBP) A_{local}}\right]^{1/2} < 1 \qquad (2)$$

$$\frac{(Reynolds\ number)(kinematic viscosity)}{Hydraulic\ diameter\ \ of\ \ the\ \ vessel}\left[\frac{Blood\ Density}{(BHCR)(DBR)}\right]^{1/2} < 1 \qquad (3)$$

It is evident from Eq. (1), and Eqs (2), (3) that a decrease in BHCR, DBP and the vessel diameter increases the cardiovascular risk, which is correlating with the existing clinical findings [2, 18, 28, 29]. Eq. (1) also reveals that an increase in systolic blood pressure (SBP) increases the cardiovascular risk (CVR). Briefly, an increase in BPR increases the CVR. Eq. (1) and Eqs (2), (3) are two independent and complementing conditions set for prohibiting the internal flow choking in the CVS. Eq. (2) is an offshoot of Eq. (3), which highlights the coupled effect of

thermo-fluid dynamics properties of biofluid/blood along with the vessel blockage in terms of the hydraulic diameter. Note that nanoscale fluid flow system with apparently high-risk blockage (**Figure 1(a)**) must always maintain the flow Mach number less than one as dictated by Eqs (2) and (3) for negating the undesirable internal flow choking causing shock wave generation and pressure-overshoot in the CVS leading to acute myocardial infarction. In such cases the flow Mach number can be retained always less than one by keeping BPR always less than the lower critical hemorrhage index (LCHI), which can be achieved by increasing the BHCR through drugs or otherwise. Analytical model (Eq. (2)) proves that the stents could reduce the risk of the heart attack but no better than drugs for increasing the BHCR owing to the fact that the Sanal flow choking could occur with and without stent. The impeccable analytical models presented herein as Eqs (2), (3) reveal that the usage of blood-thinners without increasing the BHCR create high risk of bleeding and stroke. The fact is that the blood-thinner decreases the viscosity and increases the *Reynolds number*, which augments the turbulence level causing an enhanced boundary layer blockage, which predisposes for an early flow choking. The flow turbulence enhances the deficit of energy in the type of friction, which increases the boundary layer blockage in the vessels and generates heat and augment the internal energy affecting a reduction in BHCR. Additionally, turbulence enhances the perfusion pressure essential to push the blood flow, which creates an early undesirable Sanal flow choking in the circulatory system.

3.1 Lower critical hemorrhage index

In order to avoid internal flow choking in CVS an unchoked–fluid-flow condition must be maintained throughout the circulatory system. It could be achieved by maintaining the BPR always lower than the lower-critical-hemorrhage-index (LCHI), which is dictated by the lowest value of the BHCR (Eq. (4)) of the evolved gases from blood or foreign gases entered in the CVS. Air can enter in veins and arteries during surgical procedures. It has been reported that non meticulous brain surgeries result in an air embolism. Significant venous air embolism may develop acutely during the perioperative period due to a number of causes such as during head and neck surgery, spinal surgery, improper central venous and hemodialysis catheter handling, etc. The trend of using self-collapsible intravenous (IV) infusion bags instead of the conventional glass or plastic bottles has several advantages, one of them being protection against air embolism [31].

$$BPR < LCHI = \left(\frac{(BHCR)_{evolved\ gases\ with\ the\ lowest\ BHCR} + 1}{2} \right)^{(BHCR)_{lowest} / (BHCR)_{lowest}^{-1}} \tag{4}$$

$$UCHI = \left(\frac{(BHCR)_{blood} + 1}{2} \right)^{(BHCR)_{blood} / (BHCR)_{blood}^{-1}} \tag{5}$$

Note that BHCR of CO_2 is lower than air, which creates an early internal flow choking. For instance, if CO_2 is the dominant gas in the CVS it is mandatory to maintain BPR lower than 1.82, within the pathophysiological range of human temperature, for creating an unchoked flow condition for prohibiting the shock wave generation [1] causing asymptomatic cardiovascular diseases due to transient pressure-overshoot. Note that BHCR of CO_2 decreases from 1.31 @ 0 °C to 1.281

@ 100 °C. Eq. (4) shows that the BHCR is having the bearing on all the parameters highlighted in Eqs (2), (3) for prohibiting the internal flow choking. The fact is that at the choked flow condition the critical-BPR is a unique function of BHCR. Briefly, the LCHI can be predicted (Eq. (4)) using the lowest value of the BHCR among the dominant gases present in the CVS of each subject (human being or animal).
The upper critical hemorrhage index (UCHI) can be predicted (Eq. (5)) from the specific heat of blood at constant pressure (C_p) and the specific heat of blood at constant volume (C_v) using the differential scanning calorimeter [6].

4. In vitro methodology

In vitro data [6] shows that nitrogen (N_2), oxygen (O_2), and carbon dioxide (CO_2) gases are predominant in fresh blood samples of the human being/*Guinea-pig* at a temperature range of 37–40 °C (98.6–104 °F), which increases the risk of internal flow choking leading to the asymptomatic cardiovascular risk. It is evident from the reported results (**Figure 4**), exceeding the thermal tolerance level, that the possibilities of internal flow choking in the human being is higher than the animal (*Guinea pig*) under the same thermal loading condition as the BHCR of the dominant gas evolved in the animal is found consistently higher than the human being. As a result, the LCHI is higher for the healthy male *Guinea pig* as dictated by the Eq. (4). The mass spectrum of N_2 is reported higher in animal whereas in human being CO_2 is found higher [1, 6]. The BHCR of N_2 is 1.4 and that of CO_2 is 1.289 at a temperature of 300 K (80.33 F). At this thermal loading condition, an early internal flow choking occurs in the human artery at a BPR of 1.82 compared to an animal (*Guinea pig*) artery at a BPR of 1.89. It proves that the thermal tolerance level of the healthy *Guinea pig* is higher and the cardiovascular risk is lower than the human being under identical conditions. Therefore, increasing the thermal tolerance level in terms of BHCR of the human being is an important factor for reducing the risk of asymptomatic cardiovascular diseases caused by the shock waves as a result of internal flow choking. **Figure 5** is demonstrating the percentage variations of evolved gases (viz., N_2 -m/z = 28, O_2 -m/z = 32, CO_2 -m/z = 44, Ar -m/z = 40, an unknown composite gas -m/z = 28.5), from blood samples of four different healthy human beings and one healthy male *Guinea pig* of four weeks old, during the hyphenated technique at a blood temperature of 40 °C (104° F). The estimated UCHI of healthy human being of age 23–56 with different blood group is presented in **Table 1**.

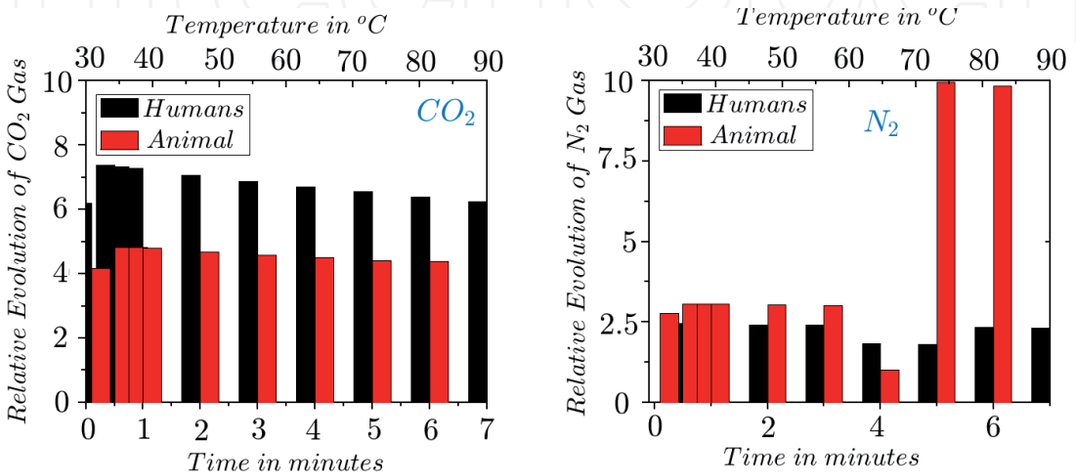

Figure 4.
The mass spectrum of CO_2 and N_2 evolved as a function of both time and temperature in the blood samples of healthy subjects [1].

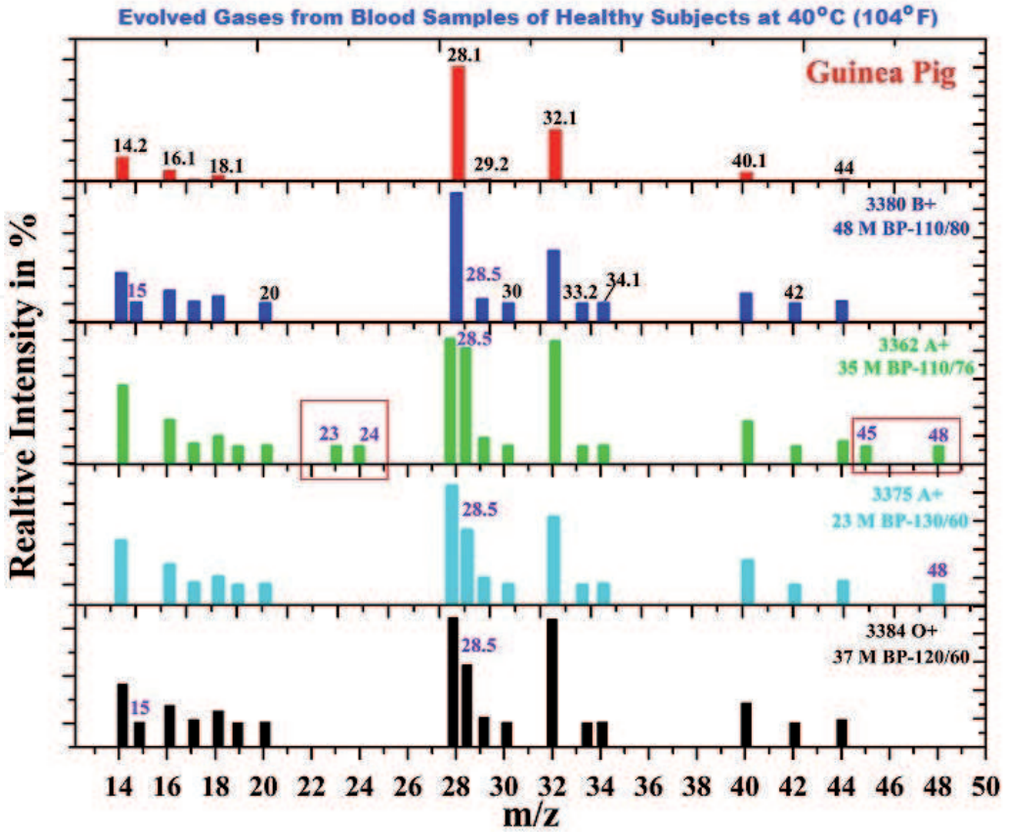

Figure 5.
Demonstrating the percentage variations of evolved gases (viz., N_2-m/z = 28, O_2 m/z = 32, CO_2-m/z = 44, Ar-m/z = 40, an unknown composite gas - m/z = 28.5) from the blood samples of four different healthy human beings and one Guinea pig during the hyphenated technique at a blood temperature of 40 °C (104° F) [2].

Batch No.	Blood Group	SBP/DBP	BPR	BHCR	UCHI @ 37.5° C
3073	O+	150/90	1.666	3.500	3.110
3074	A+	120/70	1.714	2.760	2.691
3078	B-	150/90	1.666	2.7292	2.709
3080	O+	150/90	1.666	2.9935	2.824
3082	A+	140/96	1.458	2.6759	2.640

Table 1.
Prediction of the UCHI from the heat capacity ratio of fresh blood samples of healthy human being of age 23–56 [2].

5. In silico methodology

Over the decades, bio-medical researchers have been relying on *in silico* simulation to model and cognize the natural mechanisms behind the creation and evolution of hemodynamic disorders. It has been recognized that the *wall-shear-stress* exerted on the walls of the blood vessel due to the flow of blood/biofluid is one of the main pathogenic factors leading to the occurrence of such disorders. The magnitude and distribution of the *wall shear stress* in a blood vessel can provide an insight into the locations of possible aneurysm growth. Furthermore, blockages that build up over time can be predicted by having a qualitative understanding of the flow profile. *In silico* methods can be used for modeling and understanding such vital internal flows. Obviously, the insights gained from the three-dimensional (3D)

multi-phase *in silico* simulation can help design patient-specific treatments and forecast asymptomatic cardiovascular risk. In this book chapter, as a proof of the concept of fluid-throat persuaded shock waves, we are highlighting the single phase *in silico* results (**Figure 6**) demonstrating the Sanal flow choking phenomenon followed by pressure-overshoot in an idealized physical model of a blood vessel with divergent region (see **Figure 3**) with working fluid as gas. The modeling of non-Newtonian behavior of blood flow is an important task in any *in silico* simulation with fluid-structural interaction for forecasting asymptomatic cardiovascular diseases. Additionally, a realistic time-varying boundary condition need to be implemented in order to mimic the pulsatile nature of diabatic flow (flow involves transfer of heat) of blood in a thermo-viscoelastic vessel.

The in silico result presented in **Figure 6** is clearly demonstrating the phenomenon of the Sanal-flow-choking and the shock-waves generation at the subsonic inflow condition (creeping flow) leading to the transient pressure-overshoots (stroke) in the downstream region of an artery with divergent port. **Figure 6** provides the proof of the concept of fluid-throat persuaded flow choking in the CVS. The closed-form analytical prediction of the 3D blockage factor [1] at the sonic-fluid-throat location is a useful tool for the *in vitro* and *in silico* experiments in both the continuum and non-continuum flows with due consideration of heat transfer effects (real-world fluid flow effect). Note that the phenomenon of Sanal flow choking is a paradigm shift in the diagnostic sciences of asymptomatic CVD. Therefore, development of a multi-phase, multispecies, viscoelastic fluid-structural interactive *in silico* model capturing the memory effect (stroke history) is a meaningful objective for predicting *a priori* asymptomatic cardiovascular diseases with credibility [2]. Such an effort will be helpful for the diagnosis, prognosis, treatment and prevention of the hemorrhagic stroke and the acute heart failure of each and every subject with confidence.

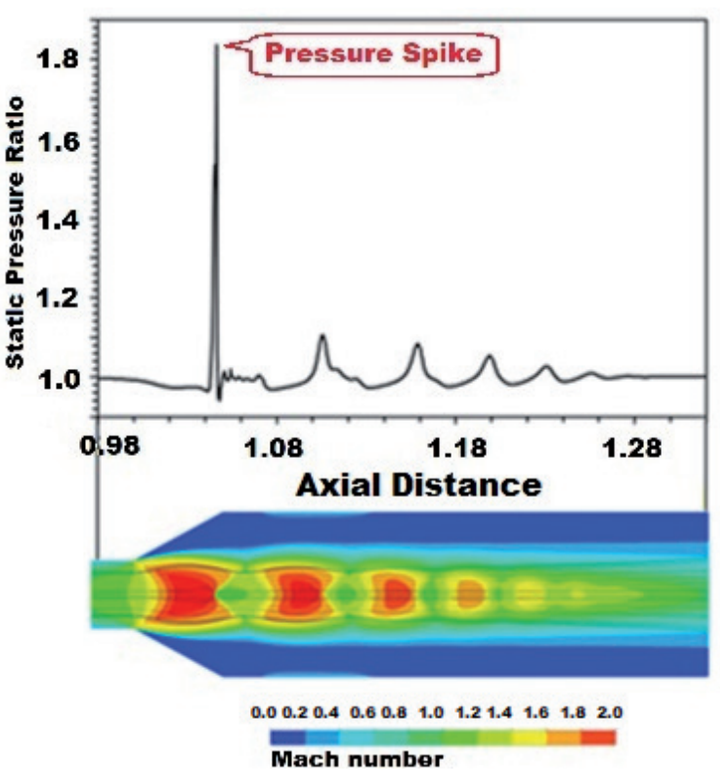

Figure 6.
Single phase in silico *result is demonstrating the transient pressure-overshoot (stroke) at 12 milli-second from Sanal flow choking time, after reaching the lower critical hemorrhage index (LCHI), in a simulated artery with the boundary layer blockage (a case of an internal flow choking and shock wave generation due to gas embolism and without any plaque [5]).*

6. Summary and conclusions

Although the diagnostic sciences have been advanced significantly during the last eight decades [32–40], until the theoretical discovery of the Sanal flow choking, the real occurrence of acute-heart-failure was poorly understood, largely for the reason that it was an under diagnosis condition [2]. Now the real cause of an acute-heart-failure comes to the foreground [1, 2]. All the findings reported in this chapter are complementing with the clinical data causing asymptomatic cardiovascular diseases. Analytical models, *in vitro* and *in silico* results presented herein corroborated that a vaccination or a single drug could reduce the risk of hemorrhagic stroke and acute heart failure [1, 2]. It could be achieved by increasing the BHCR and/or decreasing the BPR. We recognized through this comprehensive review that the internal flow choking, leading to the shock-wave generation and the transient pressure spike in a blood vessel, is the fundamental cause of asymptomatic cardiovascular diseases including hemorrhagic stroke and acute heart failure. Now the precipitating factor for the plaque rupture has come to the foreground. We concluded that the boundary-layer-blockage persuaded Sanal flow choking could occur anywhere in the circulatory circuit with gas embolism when BPR reaches LCHI. The boundary-layer-blockage-factor depends on the BHCR, flow Mach number, biofluid viscosity and turbulence, which could alter due to seasonal changes, variations in lipoprotein and other contributing factors. The greater the reduction in low-density lipoprotein (LDL) cholesterol, the lower the risk of stroke. The shock wave due to the Sanal flow choking could disrupt an atherosclerotic plaque or coronary artery wall. In a nutshell, the discovery of the biofluid/Sanal flow choking is a paradigm shift in the diagnostic sciences of coronary artery disease (CAD) and peripheral artery disease (PAD).

In vitro study shows that nitrogen (N2), oxygen (O2), carbon dioxide (CO2), and argon (Ar) gases are predominant in fresh blood samples of healthy subjects at a temperature range of 37 – 40 °C (98.6 – 104 °F), which enhances the chances of internal flow choking (with or without any coronary artery stent) leading to pressure-overshoot and acute heart failure. This physical situation is more dangerous in Covid-19 patients, which could lead to cardiac epidemic. We observed through *in vitro* study that (**Figure 4**), CO_2, the gas with the lowest heat capacity ratio (HCR), is relatively and consistently higher in the healthy males than the healthy male *Guinea pig* of four weeks old. It reveals that as a preventive measure for all subjects with a low BHCR, including patients who are taking blood-thinning medication must maintain their BPR always less than 1.82, as dictated by Eq. (4), for reducing the risk of asymptomatic CVD.

We concluded that a single anticoagulant drug capable to suppress the turbulence level and enhance the BHCR or a companion medicine along with the traditional blood-thinning medications is predestined for meeting the conflicting requirements (i.e., decrease viscosity and turbulence simultaneously) of all the subjects for reducing the risk of asymptomatic hemorrhage (AH) and acute heart failure (AHF). In high risk subjects, (i.e., BPR is very close to the LCHI), a slight oscillation in the BPR predisposes to the choking and the unchoking phenomena, which could lead to arrhythmia and memory effect. Briefly, this study sheds light for exploring new avenues in biological science for discovering new blood-thinning drugs for reducing the risk of internal flow choking causing asymptomatic cardiovascular diseases [1, 2]. The cardiovascular treatment should be targeted based on blood pressure ratio (BPR), instead of blood pressure levels alone, in chronic heart failure patients. We concluded that the risk of internal flow choking heading to asymptomatic cardiovascular diseases could be decreased by concurrently reducing blood viscosity and turbulence by enhancing the BHCR and/or reducing the BPR.

The discovery of the Sanal flow choking phenomena calls for continuous ambulatory blood pressure (BP) and thermal level monitoring in high risk patients in the diagnosis and preventive management of asymptomatic cardiovascular diseases. The continuous blood pressure and thermal level measurement could be done in a more pragmatic way by using a wearable BP monitor with the temperature sensor in the modern form of a wristwatch. Analytical methods such as machine learning could definitely enhance the accuracy and advance daily wearable device-based diagnoses [41–49]. Recent studies on heart failure management in gravity and microgravity environment (during the long human spaceflight) corroborate that the physical situation of the Sanal flow choking phenomena calls for continuous ambulatory BP and thermal-level monitoring in astronauts'/cosmonauts [6, 41–50]. Note that the Sanal flow choking is more susceptible at microgravity condition due to altered variations of blood viscosity, turbulence and the BPR. Microgravity environment decreases plasma volume and increases the hematocrit compared with the situation on the earth surface, which increases the relative viscosity of blood. We concluded that for a healthy-life all subjects (human being/animals) in the earth and in the outer space with high BPR necessarily have high BHCR. We also concluded that for reducing the cardiovascular risk, all the astronauts/cosmonauts should maintain the BPR lower than the lower critical hemorrhage index (LCHI) as dictated by the lowest heat capacity ratio (HCR) of the gas generating from the biofluid/blood for prohibiting the internal flow choking during the space travel. We recommend all astronauts/cosmonauts should wear ambulatory blood pressure and thermal level monitoring devices similar to a wristwatch throughout the space travel for the diagnosis, prognosis and prevention of internal flow choking leading to asymptomatic cardiovascular diseases. The scientific objective of this study and review was to discover the correlation between the thermal tolerance level in terms of BHCR, the BPR, blood viscosity, ejection fraction (EF) and the cardiovascular risk leading to AH and AHF, which we could achieve herein. We concluded that designing the precise blood thinning regimen is vital for attaining the desired therapeutic efficacy and negating undesirable flow choking leading to acute-heart failure. For a healthy-life all subjects with high-BPR inevitably have high-BHCR for reducing the risk of the internal flow choking (biofluid/Sanal flow choking) triggering the AHF due to the shock wave generation. We corroborated that, the acute-heart-failure (AHF) is a transient episode and not an illness. In a nutshell, a single drug capable to increase BHCR and/or decrease the BPR could reduce the risk of asymptomatic cardiovascular diseases without any prejudice.

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