

COVID-19 Pandemic: High BPR and Low BHCR are Risk Factors of Asymptomatic Cardiovascular Diseases

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ABSTRACT

A critical review has been carried out herein for correlating the phenomenon of internal flow choking (biofluid / Sanal flow choking (PMCID: PMC7267099)) and asymptomatic cardiovascular risk of COVID-19 patients. We show that when systolic-to-diastolic Blood-Pressure-Ratio (BPR) reaches the Lower-Critical-Hemorrhage-Index (LCHI) the internal flow choking could occur in the Cardiovascular System (CVS) with and without plaque/occlusion. The critical BPR for flow choking is uniquely regulating 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 (CVR) factors. In vitro data shows that nitrogen, oxygen, and carbon dioxide gases are predominant in fresh blood samples of the human being and Guinea-pig at a temperature range of 37-40 °C (98.6-104 F). *In silico* results demonstrated the occurrence of Sanal-flow-choking at a critical BPR leading to shock wave generation and pressure-overshoot in CVS causing memory effect (stroke history). The asymptomatic cardiovascular-risk of COVID-19 patients and others 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; Covid-19; BHCR; Risk factors; Sanal flow choking

INTRODUCTION

Coronavirus (COVID-19) is a pandemic disease and plays foremost community health angst. A few examinations have archived contamination with SARS CoV-2, the infection causing COVID-19, in patients who never have side effects (asymptomatic) and in patients not yet suggestive (presymptomatic) [1,2]. The epidemiology of COVID-19 stated that the susceptibility of the coronavirus infection was found in all age people. The European Society of Cardiology (ESC) reported (2020) that subjects with cardiovascular-risk factors and proven cardiovascular disease (CVD) denote an exposed population when agonizing from the COVID-19 [3]. ESC also added that subjects with cardiac injury in the perspective of COVID-19 have an enhanced risk of illness and demise. Although the disease can affect any age group, elderly and patients with comorbidities are at risk for severe disease. Many reported risk factors over the decades are flexible and account for

the majority of the population's attributable risk for Myocardial Infarction (MI). Cardiovascular disease (CVD) risk stratification decides if traditional risk factors for CVD is present [3]. Reported that the low Biofluid/Blood-Heat-Capacity-Ratio (BHCR) and high systolic-to-diastolic Blood-Pressure-Ratio (BPR) are the asymptomatic cardiovascular risk factors of COVID-19 patients and others [3-7]. Note that the physical situation of internal flow choking (Biofluid/Sanal flow choking) is very high in COVID-19 patients having high BPR and low BHCR [3,4]. The Chinese Center for Disease Control and Prevention identified comorbidities such as cardiovascular disease, diabetes mellitus, chronic respiratory disease, hypertension, and cancer to be associated with the adverse outcome of COVID-19 [8,9]. As the pandemic progresses, healthcare systems all over the world are being challenged. COVID-19 is an infectious disease, putting a great challenge to health worldwide, which will probably continue until an effective drug is discovered or group immunity is succeeded. In this mini-review we are focusing

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on the asymptomatic cardiovascular diseases of COVID-19 patients and providing insight for drug discovery for increasing the thermal tolerance level of COVID-19 patients and others by increasing the BHCR and/or decreasing the BPR for prohibiting the flow choking in the cardiovascular system (CVS). Please see Figure 1, the central illustration pertaining to flow choking.

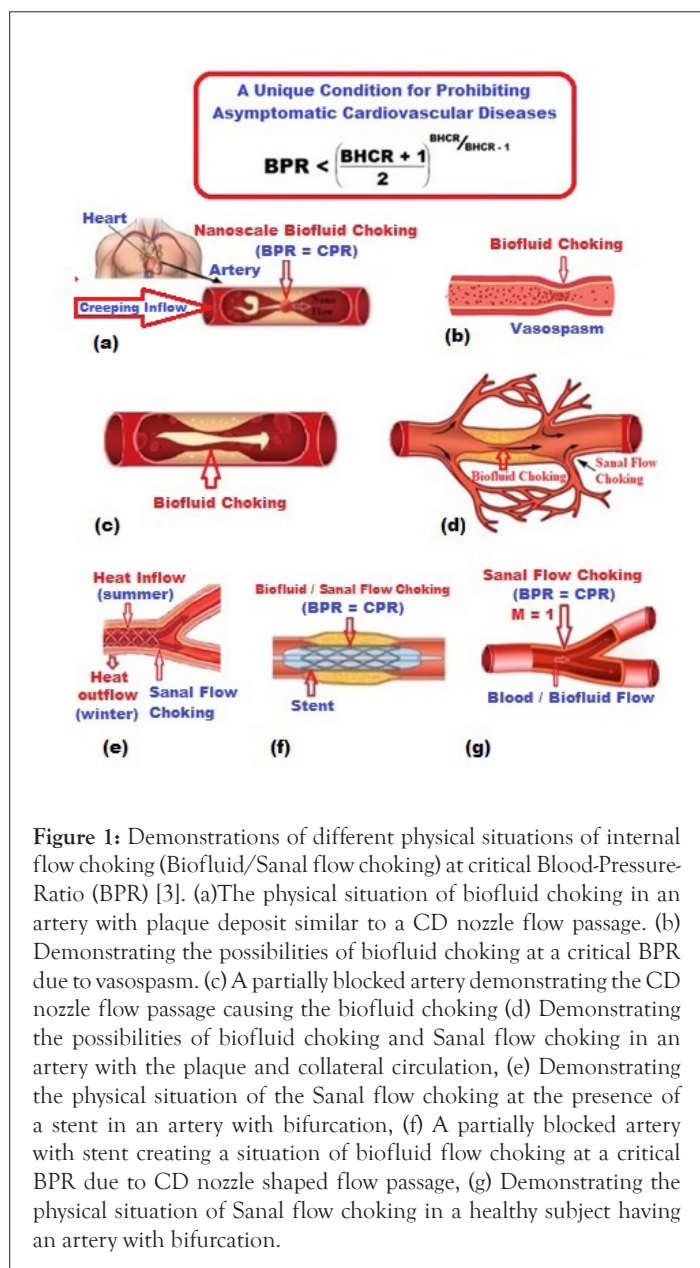


Figure 1: Demonstrations of different physical situations of internal flow choking (Biofluid/Sanal flow choking) at critical Blood-Pressure-Ratio (BPR) [3]. (a)The physical situation of biofluid choking in an artery with plaque deposit similar to a CD nozzle flow passage. (b) Demonstrating the possibilities of biofluid choking at a critical BPR due to vasospasm. (c) A partially blocked artery demonstrating the CD nozzle flow passage causing the biofluid choking (d) Demonstrating the possibilities of biofluid choking and Sanal flow choking in an artery with the 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 Sanal flow choking in a healthy subject having an artery with bifurcation.

LITERATURE REVIEW

Acute Heart Failure (AHF) is reported as the biggest killer globally over the centuries and heart failure is the cardiovascular epidemic of the 21st century [3,10]. It is reported that COVID-19 patients are more susceptible to AHF. The truly popular consequence of management with the blood-thinning drug, causing to lower blood viscosity is bleeding and very frequently asymptomatic hemorrhage and acute heart failure happens without any preceding symptoms in COVID-19 patients and others. Milton Packer [11] reported that acute heart failure is an event and not an illness and put forward a coherent claim for multidisciplinary research and a paradigm shift in thinking in the therapeutic drug development with a focus on the chemistry of drugs [11,12]. This is particularly inevitable at this juncture due

to the COVID-19 pandemic and associated cardiovascular risk [3-7]. Discovered that such a transient episode leading to asymptomatic cardiovascular disease is due to the internal flow choking (Figures 1a-1g). There are two types of internal flow choking in CVS viz., biofluid choking and Sanal flow choking (PMID: 32837737, PMCID: PMC7267099). Biofluid flow choking occurs in CVS due to the plaque induced Convergent-Divergent (CD) nozzle flow effect and/or due to vasospasm or any other type of occlusion. The Sanal flow choking occurs due to the boundary layer persuaded sonic fluid-throat effect (see Figure.2) at a critical systolic-to-diastolic blood pressure ratio (SBP/DBP), which is defined as the Critical Pressure Ratio (CPR) [3,4].

The closed-form analytical model (see Equation 1) clearly indicated the condition for prohibiting internal flow choking in CVS. Equation 1 represents the Lower-Critical-Hemorrhage-Index (LCHI), which can be estimated from the lowest value of the BHCR of evolved gases in the CVS. The Upper Critical Hemorrhage Index (UCHI) can be evaluated (see Equation 2) from the specific heat of blood at Constant Pressure (C_p) and the specific heat of blood at Constant Volume (C_v). These models reveal that COVID-19 patients with gas embolism or having low BHCR must always maintain their BPR less than the LCHI for prohibiting the internal flow choking and associated cardiovascular diseases.

$$BPR = \frac{SBP}{DBP} < LCHI = \left(\frac{(BHCR)_{evolved\ gases\ with\ the\ lowest\ BHCR} + 1}{2} \right) \left(\frac{(BHCR)_{upper}}{(BHCR)_{lower} - 1} \right) \quad (1)$$

$$UCHI = \left(\frac{(BHCR)_{blood} + 1}{2} \right) \left(\frac{(BHCR)_{upper}}{(BHCR)_{lower} - 1} \right) \quad (2)$$

In light of the discovery of Sanal flow choking in the cardiovascular system [3,4] the thermal tolerance of the COVID-19 patient's blood needs to be examined in terms of BHCR for the risk assessment of asymptomatic cardiovascular diseases. The fact is that the critical BPR for internal flow choking in the Cardiovascular System (CVS), in gravity and microgravity condition [5], is exclusively decided by the BHCR [3-7]. The BHCR is well correlated with BPR, blood-viscosity, ejection-fraction and Sanal flow choking, which are supporting with the clinical findings worldwide [3].

The Sanal-flow-choking [3,4] could happen in any blood-vessel without an iota of the symptom of the plaque (see Figure 2). The Sanal flow choking phenomenon is established as the boundary-layer-blockage persuaded internal flow choking in the CVS due to the compressible viscous flow effect [3,4,13]. The internal flow choking due to blood viscosity variations and turbulence in CVS leads to cavitation, shock wave generation and transient pressure-spike leading to memory effect (stroke history) and asymptomatic cardiovascular diseases. The safe condition for prohibiting the flow choking in the CVS is stipulated by the analytical model presented herein as Equation 1.

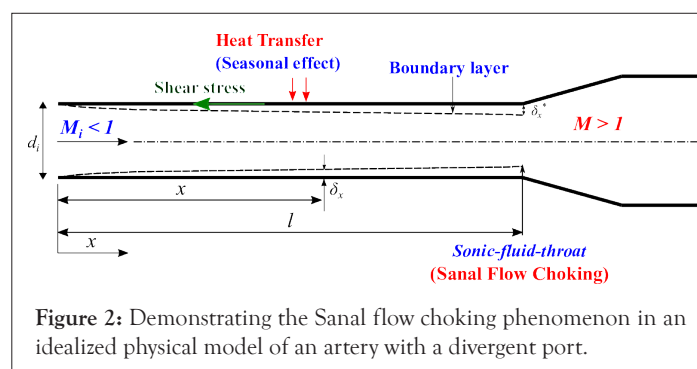


Figure 2: Demonstrating the Sanal flow choking phenomenon in an idealized physical model of an artery with a divergent port.

Traditionally hypertension is considered as a cardiovascular risk factor in patients with systemic autoimmune and chronic inflammatory diseases. It has been reported that [3-7] an acute-heart-failure could occur in both hypertension or hypotension patient because the controlling parameter of this event is the Blood-Pressure-Ratio (SBP/DBP). Furthermore, an increase in blood viscosity is considered as a major cardiovascular risk factor. The very common after-effect of administration with the blood-thinning-drug, causing to lower blood-viscosity, is bleeding and very frequently asymptomatic hemorrhage and acute heart failure happen without any preceding symptoms. This is particularly true for COVID-19 patients [3]. Reported that while decreasing the blood viscosity the Reynolds number will increase and the flow becomes turbulent, which increases the Boundary-Layer-Blockage (BLB) causing an early Sanal flow choking. This theoretical finding proves conclusively that high blood viscosity and low blood viscosity are risk factors of internal flow choking leading to asymptomatic cardiovascular diseases. Indeed, BLB 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. Therefore, the risk of flow choking in the CVS due to viscosity variations would be high during the winter than in the summer season [14,15]. According to a focused update [16] and guidelines of AHA/ACC/HRS, a new generation blood-thinning drug, non-vitamin K oral anticoagulants (NOACs), is now suggested as the favored substitute to warfarin for reducing the risk of stroke allied with Atrial Fibrillation (AFib). Note that large swings in BPR create periodic choking and unchoking phenomena causing AFib or an irregular heartbeat (arrhythmia). Further discussion pertaining to arrhythmia is beyond the scope of this review paper.

Note that using the lopsided blood thinning medicine to reduce the blood viscosity only makes the turbulence worse and increases the chances of cavitation and flow choking because the BLB factor will be more for turbulent flow than laminar flow [3,4]. These findings are corroborated with clinical reports and open literature [17-50]. Therefore, we have to discover a drug which is capable to reduce simultaneously viscosity and turbulence for meeting the conflicting requirements. In light of the discovery of the Sanal flow choking phenomenon in CVS, this conflicting requirement can be achieved by discovering a drug capable to increase the BHCR and/or decrease the BPR.

In vitro study data reveals that blood of healthy subjects evaporates at a temperature range of 37-40 °C (98.6-104 F) and generates carbon dioxide gas, which increases the risk of internal flow choking in the CVS. The single phase in silico results (Figure 3) reveal that the transient pressure-overshoot occurs at the Sanal flow choking condition due to gas embolism leading to the generation of shock waves in CVS causing memory effect (stroke history). Therefore, it is desirable, rather necessary, and perhaps inevitable to monitor ambulatory blood pressure in terms of BPR and the thermal tolerance level in terms of BHCR of high risk COVID-19 patients. Such an effort for knowing the BPR and BHCR of each and every subject will be helpful for the diagnosis, prognosis, treatment and prevention of the asymptomatic cardiovascular risk of COVID-19 patients and the community as a whole.

The closed-form analytical, in vitro and in silico studies reviewed herein corroborate 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 code solving using a reliable blood viscosity model capable to capture the memory effect (stroke

history) is a meaningful task for predicting a priori the asymptomatic cardiovascular disease with credibility.

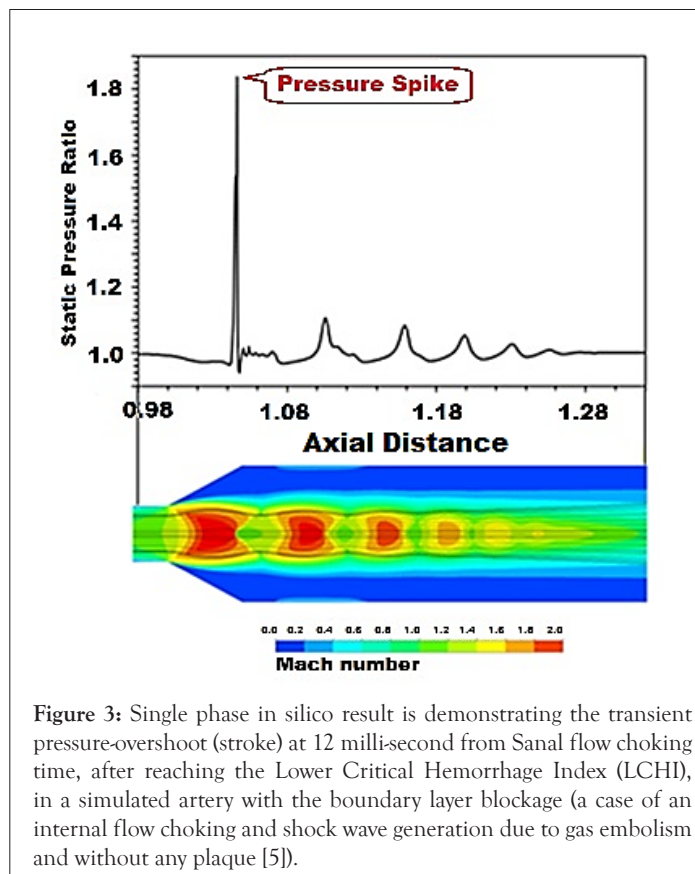


Figure 3: Single phase in silico result is demonstrating the transient pressure-overshoot (stroke) at 12 milli-second from Sanal flow choking time, after reaching the Lower Critical Hemorrhage Index (LCHI), in a simulated artery with the boundary layer blockage (a case of an internal flow choking and shock wave generation due to gas embolism and without any plaque [5]).

DISCUSSION AND CONCLUSION

The theoretical discovery of Sanal-flow-choking (PMCID: PMC7267099) 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 internal flow choking leading to shock wave generation causing asymptomatic-cardiovascular-diseases. We concluded that the Sanal flow choking is the fundamental cause of asymptomatic cardiovascular diseases in COVID-19 patients and others. The possibilities of internal flow choking in the human being is higher than the animal (male Guinea pig) under the same thermal loading condition as the BHCR of the dominant gas evolved in the animal (Guinea pig) is found consistently higher than the human being. The major in vitro finding is that, blood of healthy subjects evaporates at a temperature range of 37-40°C (98.6-104 F) and generates carbon dioxide gas, which increases the risk of flow choking in the CVS. The critical BPR for the internal flow choking is uniquely regulated by the BHCR. Therefore, increasing the BHCR and/or decreasing the BPR are possible options for reducing the risk of flow choking causing the asymptomatic cardiovascular risk. We concluded that discovering a single drug capable to suppress the turbulence level and enhance the BHCR or prescribing a companion medicine along with the traditional blood-thinning medications are predestined for meeting the conflicting requirements (i.e., decrease viscosity and turbulence simultaneously) of all the subjects for reducing the asymptomatic cardiovascular risk of COVID-19 patients, astronauts/cosmonauts and others without any prejudice. We concluded that designing the precise blood thinning regimen is vital for attaining the desired therapeutic efficacy and negating undesirable flow choking leading to asymptomatic cardiovascular diseases. For a

healthy-life all subjects with high-BPR inevitably have high-BHCR for reducing the risk of the internal flow choking.

SIGNIFICANCE STATEMENT

This review article sheds light for exploring new avenues in biological science for discovering new drugs for reducing the risk of internal flow choking causing asymptomatic cardiovascular diseases of COVID-19 patients and others.

CONFLICT OF INTEREST

The authors declare no conflict of interest in every sphere.

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