Very Low and High Blood Viscosity Are Risk Factors for Internal Flow Choking Causing Asymptomatic Cardiovascular Disease

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Very Low and High Blood Viscosity Are Risk Factors for Internal Flow Choking Causing Asymptomatic Cardiovascular Disease

Short Title: High thermal tolerance level reduces the cardiovascular risk

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Abstract

Background

The truly popular consequence of management with the blood-thinning-drug, causation of lower blood-viscosity (BV), is bleeding and very frequently asymptomatic-hemorrhage (AH) and the acute-heart-failure (AHF) happen without any preceding symptoms.

Objectives

Our aim was to develop an infallible closed-form analytical model for demonstrating the proof of the concept of the Sanal flow choking in cardiovascular system (CVS) causing AH and AHF by correlating the blood pressure ratio (BPR), biofluid/blood-heat-capacity-ratio(BHCR), blood viscosity(BV), stenosis (in terms of vessel cross-sectional area (VCA)) and ejection fraction(EF). For establishing the proof of the concept we were planned *in vitro* and *in silico* studies.

Methods

The closed-form-analytical-methodology is used herein to establish the proof of the concept of Sanal-flow-choking. *In vitro* method is invoked for the speciation analyses of blood samples of healthy subjects (human being/Guinea pig) for the BHCR estimation. *In silico* method is used for demonstrating the asymptomatic pressure-overshoot in an artery due to the Sanal flow choking and shock wave generation.

Results

The closed-form analytical, *in vitro* and *in silico* results are presented herein to establish the proof of the concept of internal flow choking in CVS causing cardiovascular risk without prejudice to the *percutaneous coronary intervention* (*PCI).* The analytical models reveal that the relatively high and low BV are risk factors of AH and AHF. *In*

vitro study shows that nitrogen(N_2), oxygen(O_2), carbon dioxide(CO_2) and argon(Ar) gases are predominant in fresh-blood samples of the healthy human-being and *Guinea-pig* at a temperature range of 37-40^0 C (98.6-104^0 F), which increases the risk of flow-choking leading to AH and AHF. The thermal-tolerance level in terms of BHCR of *Guinea-pig* is found higher than the human being. In silico results demonstrated the Sanal flow choking and shock wave generation in an artery with the divergent/bifurcation region.

Conclusions

An overdose of blood-thinning drug for reducing the blood-viscosity(BV) augments *Reynolds number* leading to high-turbulence and enhanced boundary-layer-blockage(BLB), which increases the chances of cavitation and the *Sanal-flow-choking* leading to the shock wave and pressure-overshoot causing *memory effect* (stroke history) in viscoelastic vessels. Designing the precise blood-thinning regimen is vital for attaining the desired therapeutic efficacy and negating undesirable flow-choking leading to AH and AHF. Herein we established that the disproportionate blood-thinning treatment increases the risk of the *Sanal-flow-choking* due to the enhanced BLB factor. The cardiovascular risk could be diminished by concurrently lessening the BV and flow turbulence by rising thermal-tolerance-level in terms of BHCR or by decreasing the BPR.

Condensed Abstract

Herein, we provide a proof of the concept to establish that such asymptomatic diseases are due to the boundary-layer-blockage (BLB) induced flow choking (Sanal-flow-choking) at a critical blood-pressure-ratio (BPR). When the pressure of the nanoscale-fluid increases, *average-mean-free-path* decreases and thus, the *Knudsen number* reduces

leading to a no-slip boundary condition with compressible-viscous (CV) flow effect. *Sanal-flow-choking* is a CV flow effect creating a physical situation of the *sonic-fluid-throat,* at a critical BPR. We concluded that AH and AHF are transient-events due to flow-choking, and not an illness. The cardiovascular risk could be diminished by concurrently lessening the BV and flow turbulence by rising thermal-tolerance-level in terms of BHCR or by decreasing the BPR.

Introduction

The acute-heart-failure (AHF) is reported as the biggest killer globally over the centuries. Very frequently, the fatal AHF happens without prior indications of coronary artery obstruction (angina). According to the WHO [1], the *Ischemic heart disease* (IHD) [2] and the *asymptomatic hemorrhage (AH) / stroke* are the world's biggest killers. M.Packer [3] categorically reported that the acute-heart-failure (AHF) is a transient episode and not an illness and put forward a coherent claim for multidisciplinary research for drugs-discovery [4]. Of late (May 2020), V.R.S.Kumar et al. [5] reported in a connected paper that such an event instigating the AHF is due to an internal flow choking (biofluid and/or Sanal flow choking) in the cardiovascular system (CVS), which happens at a critical systolic-to-diastolic blood-pressure-ratio (BPR). It could occur without prejudice to the *Percutaneous Coronary Intervention* (*PCI).* The real scientific truth is that, at a critical BPR, the internal flow choking occurs anywhere in the CVS with sudden expansion/divergence, vasospasm or bifurcation regions (see Fig.1(a-f) – the central illustration). The critical fact is that the internal biofluid/blood flow choking is uniquely regulated by its heat-capacity-ratio (HCR). The *Sanal flow choking* phenomenon is established as the *fluid-throat* induced internal flow choking in the real world flows

(continuum and non-continuum) due to the compressible viscous flow effect [5-11]. An internal flow choking due to BV variations and turbulence in CVS leads to cavitation, shock wave generation and transient pressure-spike. Internal flow choking could happen in all vessels including *vasa vasorum* and nanoscale tubes. The fact is that when the pressure of the *nanoscale fluid flow*/non-continuum-flows increases, *average-mean-free-path* decreases and thus, the *Knudsen number* reduces leading to a no-slip boundary condition with compressible viscous (CV) flow effect. The *Sanal-flow-choking* is a CV flow effect creating a physical situation of *sonic-fluid-throat,* at a critical systolic to diastolic blood pressure ratio (SBP/DBP), due to the boundary layer blockage (BLB). The concepts of *Sanal flow choking* [5] is well correlated herein with the existing concepts in the biological sciences for finding possible solutions for reducing the risk of *biofluid/Sanal flow choking* leading to AH and AHF.

Analytical Methodology

Using the compressible flow theory, the following closed-form analytical models (see Eqs.1-5) have been developed for correlating the BHCR, BPR, blood-kinematic-viscosity (BKV), blood-density (BD), diastolic-blood-pressure (DBP), hydraulic-diameter of the vessel (HDV), the vessel cross-sectional area (VCA), blood/biofluid velocity (LVB), Reynolds number (*Re*), boundary-layer-blockage (BLB) and ejection-fraction in terms of biofluid/blood flow rate (BFR) for predicting the risk of flow-choking in cardiovascular system (CVS) causing AH and AHF.

Equations 1 & 2 are two independent conditions for maintaining an unchoked flow condition in the CVS. Note that when the flow Mach number (M) reaches one flow gets choked. Therefore, it is mandatory to retain the flow Mach number always less than one

for prohibiting the internal flow choking in CVS, which is reflected in Eq.2, Eq.2a and Eq.2b. Note that Eq.2(a) and Eq.2b are the corollary of Eq.2, which explains the role of the vessel blockage in terms of VCA and the ejection fraction in terms of BFR on the risk of flow choking leading to AH and AHF.

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

$$M < 1 \quad (2)$$

$$\frac{(\boldsymbol{Re})(\boldsymbol{BKV})}{\boldsymbol{HDV}} \left[\frac{BD}{(BHCR)\ (DBP)}\right]^{1/2} < 1 \quad (2a)$$

$$\left[\frac{(BFR)_{local}\ (BV)_{local}}{(BHCR)_{lowest}\ (DBP)\ (VCA)_{local}}\right]^{1/2} < 1 \quad (2b)$$

$$LCHI = \left(\frac{(BHCR)_{lowest}+1}{2}\right)^{BHCR_{lowest}/BHCR_{lowest}-1} \quad (3)$$

$$UCHI = \left(\frac{(BHCR)_{blood}+1}{2}\right)^{(BHCR)_{blood}/(BHCR)_{blood}-1} \quad (4)$$

Note that for prohibiting the internal flow choking in CVS all subjects must maintain BPR lower than the *lower-critical-hemorrhage-index* (LCHI), which could be estimated from the lowest value of the BHCR of evolved gases in the CVS (see Equation 3). For instance, if carbon dioxide is the dominant gas in the CVS it is mandatory to maintain BPR lower than 1.8257 for creating an unchoked flow condition for prohibiting the shock wave generation and pressure-overshoot causing the AH and AHF. The LCHI can be estimated

through *in vitro* study aiming for finding the dominant gases evolved from blood samples of each subject (*human being or animal*) at different thermal levels. The *upper critical hemorrhage index* (UCHI) can be predicted (see Equation 4) from the specific heat of blood at constant pressure (C_p) and the specific heat of blood at constant volume (C_v), estimated using the *Differential Scanning Calorimeter - Perkin Elmer DSC 8000*.

The boundary-layer-blockage (BLB) in the blood vessels can be influenced by the variations in the biofluid viscosity and the BHCR of the flowing gas / nano plasma. The Eq.(5) correlates the artery diameter (d_i), the corresponding inflow Mach number (M_{inlet}), the axial Mach number (M_{axial}), and the BHCR, which is derived from compressible flow theory [5-7].

$$BLB = \left[1 - \left[\frac{M_{inlet}}{M_{axis}} \right]^{1/2} \left[\frac{1 + \left(\frac{BHCR - 1}{2} \right) M_{axis}^2}{1 + \left(\frac{BHCR - 1}{2} \right) M_{inlet}^2} \right]^{\frac{BHCR+1}{4(BHCR-1)}} \right] d_i \qquad (5)$$

The previous researchers, in general, assumed that the human blood is an incompressible fluid (i.e., $C_p = C_v$). That is patently not true as the human blood specific volume (or density) does change with temperature or pressure. At the *Sanal flow choking* condition, the creeping flow will get accelerated in a uniform cross-sectional area duct due to the area blockage caused by the boundary-layer-displacement-thickness (i.e., the blockage factor). The total 3D boundary layer blockage (TBLB) at the *Sanal-flow*-choking condition ($M_{axis} = 1$) for *diabatic* flows is obtained as (see Eq.5a) [5-7],

$$TBLB\Big|_{@\ sonic-fluid-throat} = \left[1 - M_{inlet}^{1/2} \left[\frac{2}{(BHCR)_{lowest} + 1} \left(1 + \frac{(BHCR)_{lowest} - 1}{2} M_{inlet}^2 \right) \right]^{\frac{(BHCR)_{lowest}+1}{4(1-(BHCR)_{lowest})}} \right] d_i \qquad (5a)$$

149 The blockage factor in the blood vessels could change due to the seasonal effects as a
150 consequence of the differences in the blood viscosity [5-17]. If the blood vessel geometry
151 is similar to the CD nozzle shape (see **Fig.1(a-f)**), the *Sanal flow choking* leads to shock
152 wave generation and transient pressure-spike [5-7]. This physical situation could be
153 predicted through credible multidisciplinary *in silico* models [5,6] verified and validated
154 at the *Sanal flow choking* condition. The **Fig.2** shows (solution of Eq.5a) the SANAL
155 chart pertaining to a case of gas embolism with carbon dioxide as the dominant gas. It
156 clearly indicates that irrespective of the percentage blockage of the artery, the critical
157 BPR determines the risk of the biofluid/*Sanal flow choking* leading to an acute-heart-
158 failure. The *Sanal chart* also shows that a decrease in the blockage factor reduces the
159 flow Mach number, which reduces the risk of internal *flow choking*. Note that for
160 prohibiting the internal *flow choking* all subjects must maintain BPR always lower than
161 the LCHI. Our analytical model proves that the *stents* could reduce the risk of the heart
162 attack but it is not better than drugs owing to the fact that the biofluid/*Sanal flow choking*
163 could occur with and without stent (see **Fig.1(d-f)**). The self-explanatory equations (see
164 Eqs. 1-5), derived from the compressible flow theory [5-7], are highlighting various
165 influencing parameters for prohibiting the biofluid/*Sanal flow choking* in the artery. Note
166 that the ejection fraction (EF) is reflected in Eq.2(b) in terms of biofluid/blood flow rate
167 (BFR). It is evident from the closed-form-analytical model (see Eq.2b)) that the EF is not
168 the lone parameter for declaring the risk of AHF. It is coupled with the local vessel cross-
169 sectional area (VCA), local biofluid/blood velocity (BV), $(BHCR)_{lowest}$ and the DBP. In
170 high risk subjects (BPR close to LCHI and/or Mach number close one) a slight oscillation
171 in the BPR predisposes to the choking and the unchoking phenomena leading to

arrhythmia. Most heart valve problems involve the aortic and mitral valves, possibly because of its geometric shape similar to CD nozzle flow passage. *Further discussion to valve problems, aneurysm and arrhythmia is beyond the scope of this article.* Note that the biofluid/*Sanal flow choking* could create unusual pressure-overshoot in vessels with divergent/bifurcation regions [5-7], which increases *memory effects* (stroke history) leading to artery tear in the subsequent stroke.

In vitro Methodology

We have estimated the heat capacity ratio (HCR) of blood, obtained from the healthy human being and one *Guinea pig* living in the southern part of the Indian union, using the *Differential Scanning Calorimeter (DSC) - Perkin Elmer DSC 8000*. *Samples are collected from healthy subjects after the informed consent. All the experimental methods reported herein are in accordance with relevant guidelines and regulations. Please note that the ethical committee approval is not required by the national legislation of Indian union for conducting the blood sample test of healthy human being and animals reported herein, which are applicable to all the authors and their affiliated institutions in India.* We confirm that all experimental protocols were approved by the National Centre for Combustion Research and Development (NCCRD) of Indian Institute of Science (IISc) for the blood sample tests of healthy human being and animals. *Also note that for the randomized studies the blood bank who supplied blood samples of healthy subjects obtained the written and informed consent from all the healthy human being prior to the test conducted at NCCRD/IISc, India.* The *in vitro* methodology is available at https://osf.io/p7kmg [10]. **Table-1** shows the estimated *UCHI* of healthy human being of age 23-56. **Figure 3** shows the mass spectrum of N_2, O_2, and CO_2 evolved as a function

of both time and temperature obtained from blood sample tests of healthy subjects (human being and *Guinea pig).* The mass spectrometer used in the present study is Perkin Elmer SQ8T, which uses the Electron Impact detector. During our comprehensive *in vitro* studies, we have noticed that the gases evolved from the fresh blood sample depends on the blood temperature, heating rate, blood group, age and the blood pressure value. It is evident from **Fig.3** that CO_2 is the dominant gas for human being whereas nitrogen gas is dominant in the blood sample of *Guinea pig.* The estimated LCHI of all healthy human being is found 1.82, which is based on the evolved dominant carbon dioxide gas (BHCR = 1.289). In the case of *Guinea pig,* the LCHI is estimated as 1.89, which is based on the dominant nitrogen gas (BHCR = 1.4). We found that there are variations in the heat capacity of blood samples collected in three different Vacutainers of same healthy subjects. The *anticoagulant* reduces the BHCR and susceptible to an early biofluid choking in blood vessels, including *vasa vasorum,* causing high risk of *hemorrhage* and heart attack. The most popular consequence of medication with anticoagulant drug is bleeding.

It is crystal clear from **Fig.3** that the possibilities of the *Sanal flow choking* in the animal (*Guinea pig*) is lower than in the human being at the same temperature level as the HCR of the main gas generated in the animal is found constantly higher than the human being. The mass spectrum of N_2 is observed greater in *Guinea pig* whereas in the healthy human being CO_2 is observed greater. The HCR of N_2 is 1.4 and that of CO_2 is 1.289. It corroborates that at the same thermal loading condition, the artery of *Guinea pig* gets choked only at a BPR of 1.8929 and the artery of the healthy human being gets an early choking at a BPR of 1.8257. Therefore, we concluded 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 of the human being is important for reducing the risk of AHF due to the Covid-19 or otherwise.

In Silico Methodology

In an effort to demonstrate the BLB induced *Sanal flow choking* we have carried out *in silico* studies with creeping inflow conditions (a case with gas embolism) using a validated flow solver [6] and demonstrated the pressure overshoot at the downstream region of an artery with a divergent region (see **Fig.4**) causing *hemorrhage* and/or *heart attack* as the case may be. The preliminary *in silico* results (see **Fig.4**) show the *Sanal flow choking* and the shock-wave 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**.** It corroborates that the phenomenon of biofluid/*Sanal-flow-choking* is a paradigm shift in the diagnostic sciences of acute-heart failure.

Statistical analysis

All *in vitro* studies were carried out independently at least six times for repeatability and also for establishing that the data generated are in agreement with the true value in each independent experiment. *In silico* studies are carried out after the code validation.

Outcomes

In vitro study proved that the specific heat of blood at constant pressure (C_p) is always higher than the specific heat at constant volume (C_v). Therefore, the validity of the analytical models (Eqs.1-4) derived from the compressible flow theory for predicting the risk of flow choking leading to AH and AHF presented herein is established. During the *Hyphenated techniques* at the atmospheric pressure we have detected predominantly N_2, O_2,

241 CO_2, Ar and one undefined composite gas (m/z = 28.5) in blood samples of healthy
242 subjects at various intensity at the temperature range of 37-40^0 C (98.6-104^0 F) and above.
243 We observed that the gasification temperature of healthy *Guinea pig* blood is higher than
244 the healthy human being. The BHCR of healthy subjects taken from the EDTA and
245 Lithium Heparin tubes was found significantly lower (31-32 %) than the fresh blood
246 samples of the same healthy subjects tested within 5 minutes of collection. We observed
247 that CO_2, the gas with the lowest HCR is relatively and consistently higher in the healthy
248 males than the healthy male *Guinea pig* of four weeks old (see **Fig.3**). Note that HCR of
249 CO_2 is 1.289, therefore a subject with gas embolism, with CO_2 as the dominant gas, the
250 biofluid choking occurs (see Eq.1) at a BPR of 1.8257, which is the *lower critical*
251 *hemorrhage index* (LCHI). It reveals that patients who are taking blood-thinning
252 medication must maintain their BPR always less than 1.8257, as dictated by Eq.1, for
253 reducing the risk of internal flow choking leading to *asymptomatic vascular diseases.*
254 The closed-form analytical model, *in vitro* and *in silico* study results reported herein
255 reveal that for a healthy-life all human being/animals with the high BPR inevitably have
256 high BHCR for reducing the risk of AHF by prohibiting biofluid/Sanal-flow-choking
257 heading to shock wave generation and transient pressure-spike causing memory effect
258 (stroke history). The preliminary single phase *in silico* results (see **Fig.4**) show the
259 phenomenon of Sanal-flow-choking and shock waves generation at the subsonic inflow
260 condition (creeping flow) leading to the transient pressure-overshoots (stroke) in the
261 downstream zone of an artery with a divergent port.

Results

We discovered that at a critical blood-pressure-ratio (BPR), the internal-flow-choking occurs anywhere in the cardiovascular system (CVS) with sudden expansion/divergence/ bifurcation or vasospasm regions. The critical fact is that the internal-flow-choking is uniquely regulated by *BHCR*. Analytical findings reveal that the relatively high and low BV are cardiovascular risk factors. Herein we established that the disproportionate blood-thinning treatment increases the risk of *internal flow choking* due to the enhanced boundary-layer-displacement-thickness (boundary layer blockage (BLB) factor) due to an increase in flow turbulence in the CVS due to an increase in *Reynolds number* (*Re*) as a consequence of relatively low blood viscosity (BV).

Discussion

Through closed-form analytical models (see Eqs.1-4) we could correlate the BHCR, BPR, BV and EF along with other parameters contributing for internal flow choking. The infallible closed-form analytical models shed light on finding solutions for decreasing the risk of AH and AHF due to biofluid choking and/or Sanal flow choking leading to shock wave generation (see Fig.1(a-f).

Mostly, in the CVS blood flow is considered as laminar. When taking blood thinning drugs, the whole BV reduces and as a consequence *Re* rises and the laminar flow could be disordered and convert to turbulent. The flow turbulence enhances the deficit of energy in the type of friction, which increases the BLB in the vessels and generates heat and augment the internal energy affecting a reduction in BHCR, which is corroborated

283 with *in vitro* results. Additionally, turbulence enhances the perfusion pressure essential
284 to push the blood flow.

285 Viscosity variations are depending on the shear rate or shear rate history of the
286 blood/biofluid, which could vary due to seasonal effects too [12-34]. Blood temperature
287 decreases during the *winter* season resulting an increase in blood viscosity and the
288 inverse effect happens during the *summer* season [6]. It corroborates that the BLB factor
289 causing the *Sanal flow choking* [5] would alter due to the BV variations as a consequence
290 of the blood-thinning medication and/or the seasonal effects [6]. Indeed, BLB induced
291 biofluid/Sanal flow choking is more prone during the winter season than the summer
292 season due to the higher BV at the relatively low blood temperature. It leads to say that
293 the risks of flow choking leading to AH and AHF would be high during the winter than in
294 the summer season, which is corroborating with literature data [6,17].

295 Eq.1 reveals that the critical ratio of BPR for flow choking is an exclusive function
296 of BHCR. It is crystal clear from Eq.2a that stenosis (an abnormal narrowing of the
297 passage of a blood vessel, i.e., a decrease in hydraulic diameter of the blood vessel) could
298 increase the risk of flow choking. Eq.2a also tells us that stent implant for increasing the
299 hydraulic diameter could decrease the risk of flow choking but not a permanent solution
300 for reducing the risk of AHF, without having proper control on the other parameters
301 highlighted herein (see Eqs.1, 2, 2a & 2b).

302 It is important to note that though all the existing percentage demarcation of the EF
303 are meaningful for the diagnosis, until the dissemination of this article these findings
304 were not supported by any closed-form analytical model for an authentic conclusion.
305 Eq.2(b) explains the desirable BFR or EF for forecasting the risk of AHF. Eq.2(a-b) is

showing the correlation of the EF in terms of local BFR of normal heart and the other controlling parameters (geometric, fluid dynamics and thermodynamic properties of blood/biofluid). It is evident from Eq.2(a-b) that the risk factor depends on the coupled effects of the EF, the local VCA, BHCR, DBP and the local BV. It is evident from these mathematical models that at a constant VCA and DBP a decrease in BHCR and an increase in *Reynolds number* jointly or individually, increases the possibilities of internal flow choking. Apparently (see Eq.2a) an increase in *kinematic viscosity* increases the possibilities of flow choking. On the contrary, an increase in *kinematic viscosity* decreases the possibilities of flow choking by reducing the *Reynolds number*. It reveals that there is a safe range of blood viscosity for prohibiting the flow choking of each and every subject, which depends up on the coupled effects of the other controlling parameters (see Eqs.1, 2, 2a & 2b) for flow choking. Therefore, the dose of blood-thinning drugs must be prescribed subjected to the condition prescribed in Eqs.2a & 2(b).

Note that using 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. The flow turbulence increases the deficit of energy in the form of friction, which increases the BLB in blood vessels and generates heat and augment the internal energy causing a decrease in the BHCR, which is vulnerable to an early flow choking in the CVS. Based on the above findings we established herein that the *uneven blood-thinning* drugs increase the risk of internal flow choking triggering AHF, which is supporting with the established laboratory index, International normalized ratio (INA). More specifically, an overdose of drugs for blood-thinning medication increases the *Reynolds number* leading to the high turbulence level

in the vessel and as a result the laminar flow could be disturbed and becomes turbulent causing an early internal flow choking (biofluid and/or *Sanal flow choking)* causing a transient sharp pressure-spike due to the generation of shock waves at the creeping inflow condition without any iota of symptoms of the plaque in an artery with sudden expansion / divergence / bifurcation / vasospasm (**see Fig.1 as the Central Illustration**). More specifically, internal flow choking could occur in nanoscale vessels and also in the coronary artery without prejudice to the *Percutaneous Coronary Intervention* (*PCI).* Note that when the pressure of the *nanofluid* increases, the *average mean free path* decreases and thus, the *Knudsen number* reduces leading to a no-slip boundary condition with compressible viscous flow effect. The *Sanal-flow-choking* is a CV flow effect, which is established as the flow choking caused by the BLB at the creeping inflow condition at a critical pressure ratio. Briefly, the prediction of internal flow choking in CVS is a scientific breakthrough and a paradigm shift in the diagnostic science of *asymptomatic* vascular diseases. *Sanal flow choking* leads to the shock-wave generation followed by pressure overshoot causing tearing of the blood vessels. The tearing depends on the *memory effects* (stroke history) and the thermoviscoelatic properties of the vessel. This basic research paper, originated from the chemical rocket science [6], aims to discover the fundamental cause(s) of bleeding while taking blood-thinning drugs and propose possible conditions for reducing the risk of internal flow choking causing AH and AHF.

Note that large swings in BPR create periodic choking and unchoking phenomena causing atrial fibrillation (*AFib)* or an irregular heartbeat (*arrhythmia*). In light of *the Covid-19 pandemic*, the thermal tolerance level of blood needs to be examined in terms of variations in the BHCR for the risk assessment of the ischaemic heart disease. The

European Society of Cardiology (ESC) reported (2020) that subjects with CVR factors and proven cardiovascular disease (CVD) denote an exposed population when agonizing from the *Covid-19*. ESC also added that subjects with cardiac injury in the perspective of *Covid-19* have an enhanced risk of illness and demise (www.escardio.org). This article sheds light for exploring new avenues in biological science for discovering new blood-thinning drugs for reducing the risk of flow choking causing AH and AHF [9, 11, 33,35]. We concluded that the cardiovascular treatment should be targeted based on blood pressure ratio (BPR), instead of blood pressure levels alone, in chronic heart failure patients [34].

The sporadic internal flow *choking,* due to significant fluctuations in BPR, heading to transient pressure-overshoots created throughout the life-span in the CVS create the vessel walls more stiff due to *memory effects* (stroke history). Such physical situations in any viscoelastic vessels are prone to rupture in the subsequent internal flow choking and shock wave development. Briefly, we have reported conclusively herein (see Eq.1) that high BPR and low BHCR are risk factors for flow choking.

Conclusions

The uneven usage of blood-thinning medication will increase the *Reynolds number*, which produces high turbulence level creating enhanced boundary layer blockage causing an early biofluid/Sanal flow choking. We concluded through infallible closed-form analytical models that relatively **high blood viscosity** and relatively **low blood viscosity** are risk factors for an early flow choking causing AH and AHF, which is correlating with the established index INA. Therefore, the real effect of viscosity on flow choking needs to be established for taking preventive strategies for reducing the risk of AH and AHF.

On this rationale, it is essential, rather needed, perhaps inevitable to declare a condition for prohibiting the flow choking in the CVS, which we have presented herein in terms of blood viscosity, density, *Reynolds number*, BHCR, BPR, DBP and stenosis (vessel geometry). 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 vascular diseases.* In high risk subjects (*BPR close to the LCHI*) a slight oscillation in the BPR predisposes to the choking and the unchoking phenomena, which could lead to *arrhythmia*. In a nutshell, we have proved conclusively that the high-BHCR reduces the risk of flow choking as dictated by Eq.1, which is an indisputable physical condition, without any *ex vivo* or *in vivo* model support, for prohibiting *asymptomatic stroke* in any vessel [20-23]. We concluded that 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 and pressure overshoot (36-39). We corroborated herein that, the AHF is a transient episode and not an illness.

Study limitations

Conducting *in vivo* studies in all subjects require ethical clearance.

Translational Outlook

Large randomized blood sample tests for BHCR estimation along with the BPR measurement, adequately in all seasons in all blood groups, across the globe are needed

for discovering new drugs capable to increase the BHCR and/or decrease the BPR in all seasons for reducing the risk of *internal flow choking* in all subjects.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Code availability statement

The mathematical algorithm used for generating analytical results are available with the author VS. The code used for generating *in vitro* results are available with the authors RSB and CO. The code used for generating the *in silico* results is available with the authors NC and AS. The raw data required to reproduce the results are available with the corresponding author and could be shared upon reasonable request.

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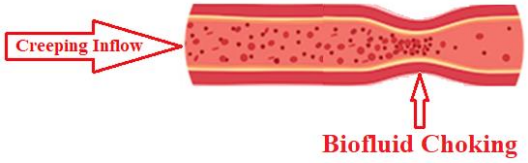
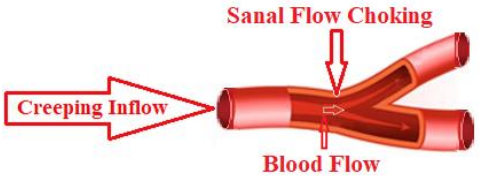
The Central Illustration for the Drugs Discovery

(a)

(b)



(c)



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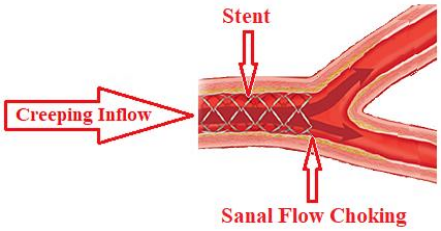

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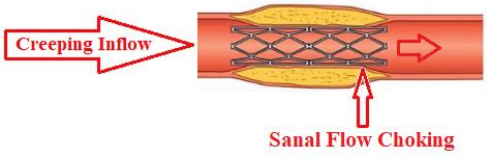


(f)

Figure 1(a-f). Demonstration of various physical situations of the Internal flow choking (Biofluid/Sanal flow choking) in the cardiovascular system without prejudice to the Percutaneous Coronary Intervention (PCI).

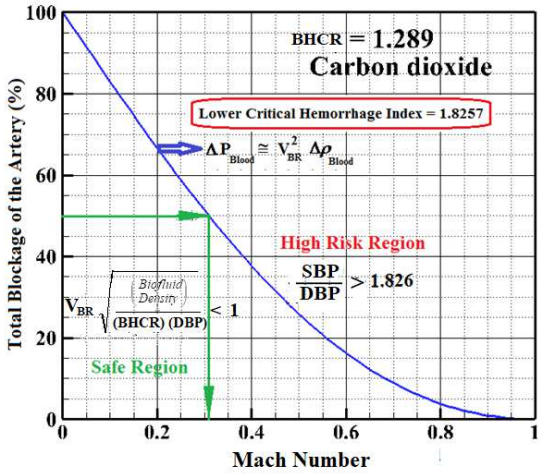
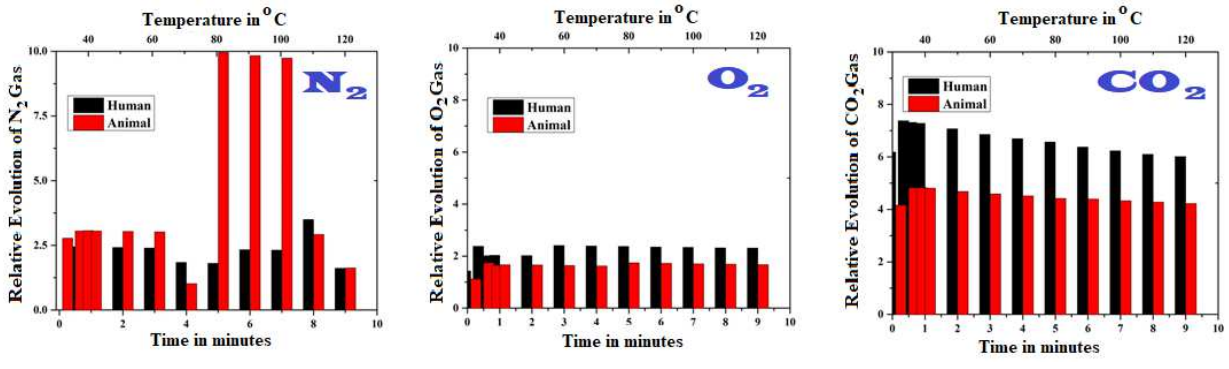


Fig.2 *SANAL Chart*: Condition for prohibiting AH and AHF



(a) (b) (c)

Fig. 3(a-c) Mass spectrum of N_2, O_2, and CO_2 evolved as a function of both time and temperature obtained from blood samples of healthy subjects.

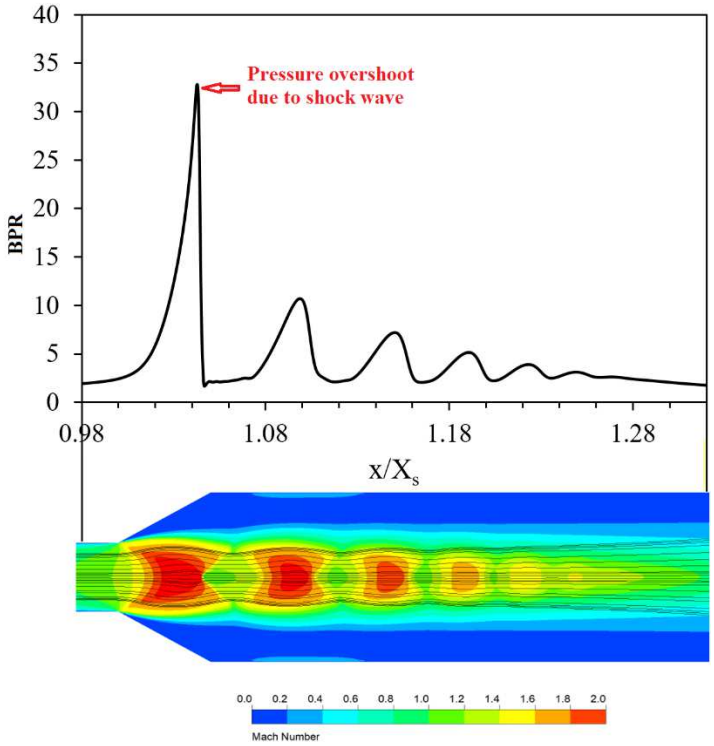


Fig. 4 In silico results show the Sanal-flow-choking and shock waves generation at the subsonic inflow condition (creeping flow) leading to the transient pressure overshoots (stroke) in the downstream region of an artery *(where tissue death (infarction) occurs)* with divergent port as a result of the CD nozzle flow effect (a case with gas embolism).

Table-1 Prediction of the *UCHI* from the heat capacity ratio of fresh blood samples of healthy human being of age 23-56.

Batch No.	***Blood Group***	***SBP/ DBP***	***BPR***	***BHCR***	***UCHI @ 37.5° C***
3073	O+	150/90	1.666	3.5	3.11
3074	A+	120/70	1.714	2.76	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	2.64

Author Contributions

VRSK: Conceptualization, analytical modeling, manuscript drafting; **SKC:** In vitro conceptualization, manuscript editing; **PKR:** In vitro conceptualization, manuscript editing; **RSB:** *In vitro* and data generation; **NC:** *In vitro*, *in silico* and project support, **VS:** Modeling and simulation support, **AS:** *In silico* simulation support, **CO:** Resources

Figures

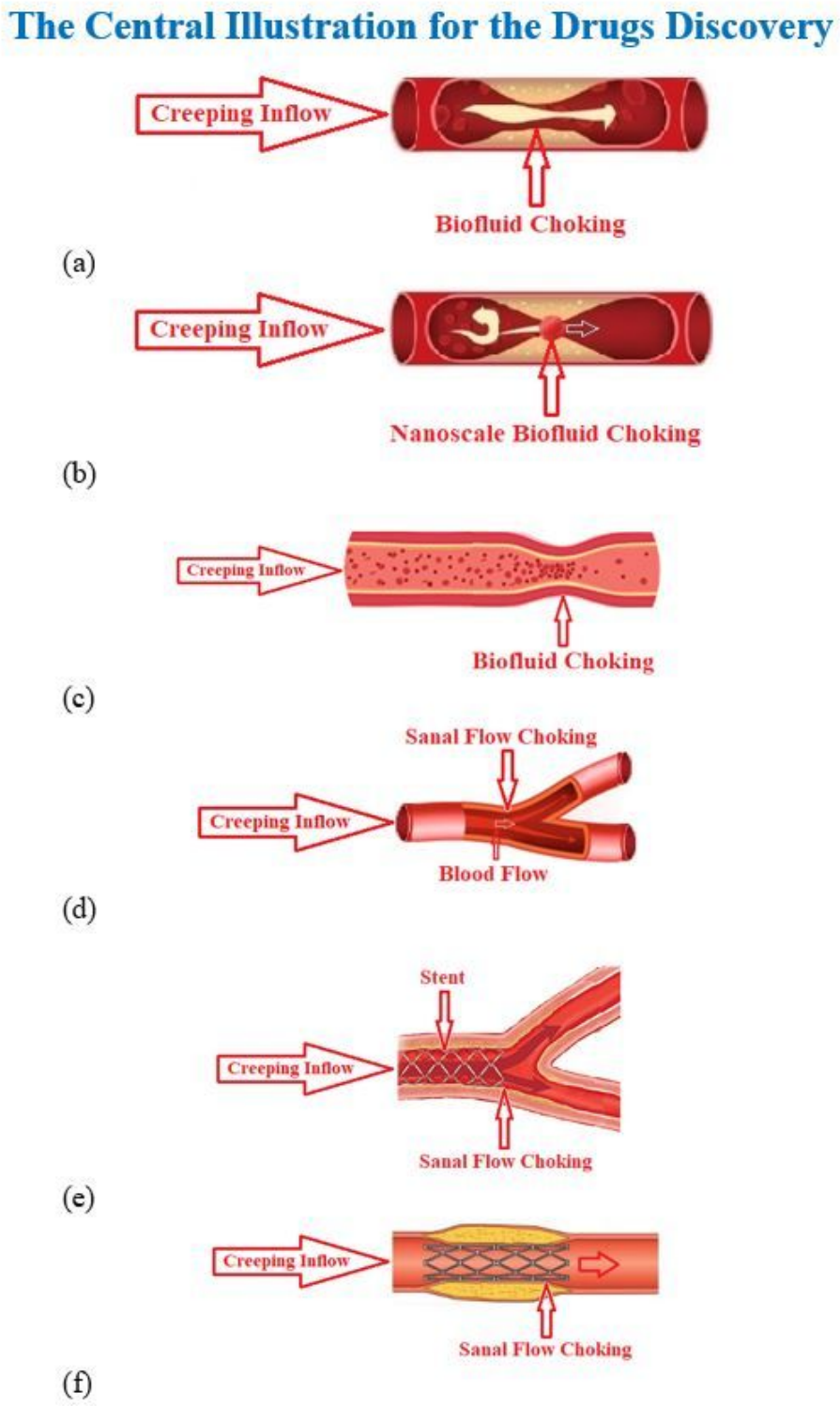


Figure 1

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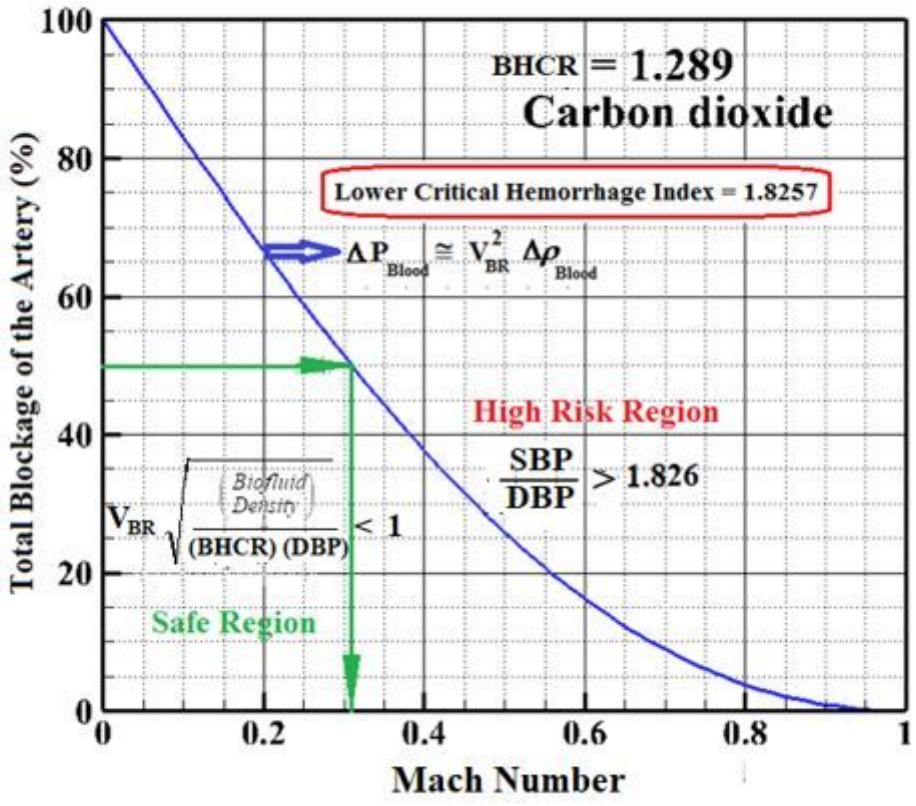

Figure 2

SANAL Chart: Condition for prohibiting AH and AHF

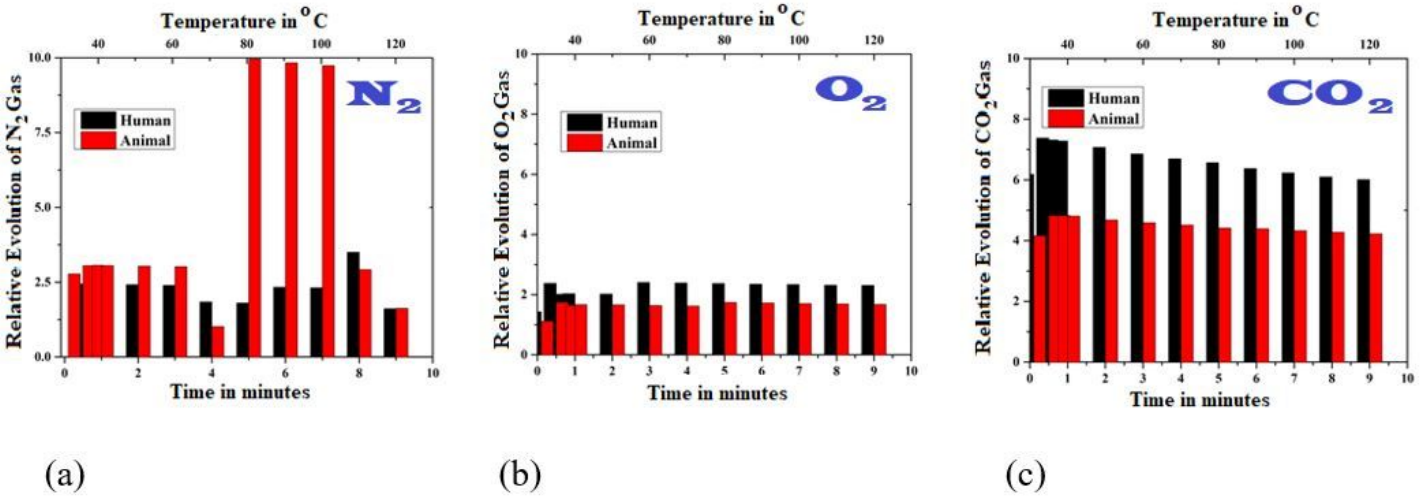

Figure 3

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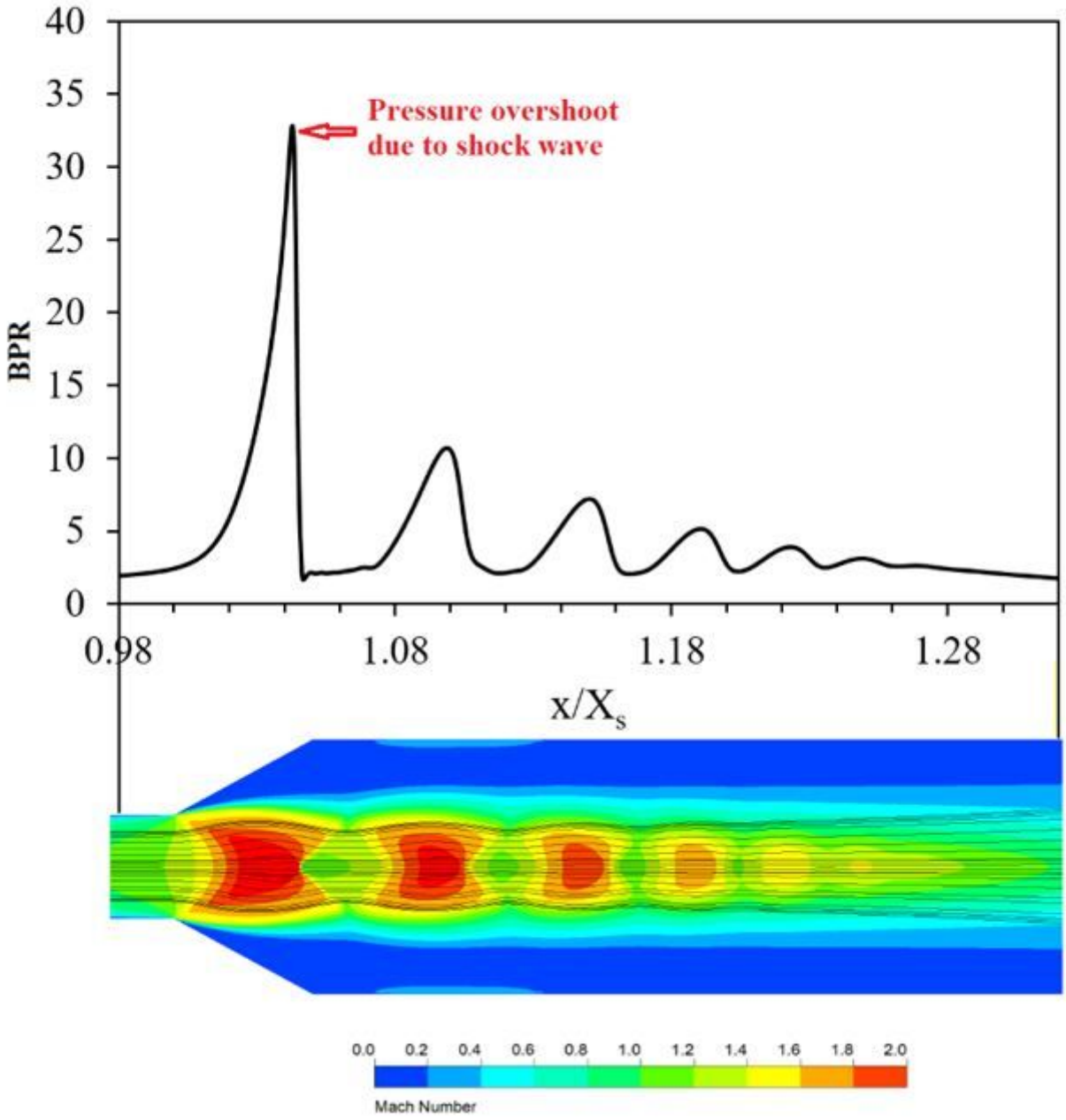

Figure 4

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