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EVALUATION OF HEMOLYTIC POTENTIALS BY EULERIAN APPROACH IN CENTRAL VENOUS ACCESS FOR HEMODIALYSIS

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Abstract. Despite some advantages over others vascular access methods, the use of central venous catheter (CVC) has been associated with risks for patient health, such as hemolysis. The aim of the present work is to evaluate the hemolytic potential of the blood flow by numerical simulations in central venous catheter for hemodialysis by Eulerian approach. The simulations were carried out in transient regime covering two cardiac cycles. The geometry of central veins was obtained by computed tomography images of a healthy 74-year-old male patient. It was used a CVC MedCOMP/HEMO-CATH model with a dialysis flow of 0.0053 kg/s. The K-ω SST (Shear Stress Transport) was used to model turbulence and the Carreau-Yasuda model of non-Newtonian fluid for blood behavior was adopted. Linear hemolysis index (HI_L) power law model was implemented as a transport equation. It was observed that the HI_L was critical close to the venous orifices of the catheter due to disturbances in the blood flow, such as increased shear stress and recirculation, generated by the outflow jets and the presence of the catheter. The Eulerian approach proved to be a qualitatively useful tool in the development of central venous catheter design.

Keywords: Hemodialysis, Central Venous Access, Central Venous Catheter, Hemolytic Potential, Computational Fluid Dynamics, Blood Flow.

1. INTRODUCTION

Central Venous Catheter (CVC) represents a form of vascular access to perform the hemodialysis procedure and it is in increasing use around the word (Lucas *et al*., 2019; Neves *et al*., 2020; Allon *et al*., 2017). The increase in the use of CVC is due to the advantages that this device has over others vascular access methods, such as ease of insertion, unnecessary maturation time, availability for immediate use and painless dialysis process (Peng *et al*., 2017; Mokrzycki and Lok, 2010).

However, the prolonged use of CVC for the treatment of patients with chronic kidney disease is connected to the spread of some complications, for example, infections, thrombus formation and hemolysis (Peng *et al*., 2017; Lucas *et al*., 2019). Hemolysis, which is the process of red blood cells (RBC) rupture with the release of hemoglobin in the blood plasma, can lead to a reduction in the patient life expectancy, morphological changes, functional biochemical changes and complete disruptions of blood cells (Taskin *et al*., 2012). Therefore, the quantification of hemolytic potential became a criterion for the development of cardiovascular device designs (Lacasse *et al*., 2007).

The increased spread of hemolysis is associated with a significant change in the blood flow pattern due to the presence of the central venous catheter (Ho *et al*., 2020; Mareels *et al*., 2007). This disturbance in the hemodynamic can generate a change in the shear stress field that RBC is subjected, and this can change the hemolytic potential in the

central venous system (Costa *et al*., 2020; Lucas *et al*., 2014). Mareels *et al*. (2007), for example, shows that changes in catheter tip design cause changes in the shear stress field through experimental protocol and numerical simulations.

Several attempts have been made to develop a mathematical model to accurately quantify the hemolysis (Faghih and Sharp, 2019; Taskin *et al*., 2012; Lacasse *et al*., 2007). Giersiepen *et al*. (1990) presented an empirical Power Law model to predict the damage of red blood cells, defining a parameter called hemolysis index (*HI*), depending on two blood flow parameters: shear stress and exposure time to these stresses. The *in vitro* experiments were carried out under Couette flow conditions to study 25 aortic valve prostheses.

Numerical models based on computational fluid dynamics (CFD) is a tool that appears as an alternative for the assessment of hemodynamic factors that influence RBC (Gonçalves *et al*., 2020a). This tool is characterized by relatively low cost and for being a non-invasive technique (Lucas *et al*., 2014; Gonçalves *et al*., 2019; Gonçalves *et al*., 2020a). Furthermore, it is possible to implement mathematical models to calculate the hemolytic potential in computational models.

There are two approaches of computational methods available: Lagrangian and Eulerian. The Lagrangian approach is able to calculate the shear stress history on RBC, which allow the quantification of previous damage. However, the results obtained by the Lagragian approach depend on the number of pathlines used and how the integration is carried out (Taskin *et al*., 2012). On the other hand, Eulerian approach has the advantage of producing predictions that cover the entire computational domain with a single solution, because this approach is described by a partial differential equation (Lacasse *et al*., 2007). Nevertheless, this approach is still a target of doubts in the academic community due to some limitations present in the model (Ho *et al*., 2020). The Eulerian approach has been used in different studies to estimate hemolysis in different vascular devices, such as blood pump and hemodialysis cannulas (Taskin *et al*., 2012; Garon and Farina, 2004; Heck *et al*., 2017).

The aim of this study was to evaluate the hemolytic potential in central venous access for hemodialysis, using the Eulerian approach, through computational fluid dynamics. Moreover, was sought to contribute to the advancement of the central venous catheter design, through the analysis of hemodynamic behavior, in particular the factors related to hemolysis. In this way, it was be analyzed the critical regions of disruption of erythrocyte along the computational domain caused by the presence of the catheter, as well as due to the outflow jets through the venous orifices of CVC.

2. MATERIALS AND METHODS

2.1 Geometry

The methodology proposed by Machado *et al*. (2018) for the acquisition of the geometry of the central veins was adopted. The geometry was acquired by computed tomography (CT) of a male healthy patient, 74 years old. The procedure was approved by the Comitê de Ética em Pesquisa/Universidade Federal de Minas Gerais (CEP-UFMG) under process number CAAE 02405712.5.1001.5149.

The geometry has been simplified similar to Costa *et al.* (2020) study. Through the medical image processing software, InVesalius3®, it was possible to separate a three dimensions anatomical structure of the region of interest. In addition, the geometry was filtered, that is, bone tissue surfaces and other unwished noises were removed.

The next step was to edit the geometry in Autodesk Meshmixer®. In this software, cleaning, smoothing and removal of surface imperfections were performed, as well as the ramifications of central venous system, such as the subclavian and external jugular veins, to reduce the computational cost of the simulations.

With the aim of facilitate the generation of the mesh and reduce the computational cost, the edited geometry of the venous system was simplified in order to make it symmetrical, that is, the three-dimensional curvatures of the central venous system were removed.

SolidWorks software (SolidWorks, Inc., Concord, MA, USA) was used to generate the geometry of a MedCOMP/HEMO-CATH model clinical catheter (Harleysville, PA, USA). Figure 1a shows the geometry of the CVC indicating the arrangement of arterial and venous orifices, while Figure 1b shows the geometry used in the simulation.
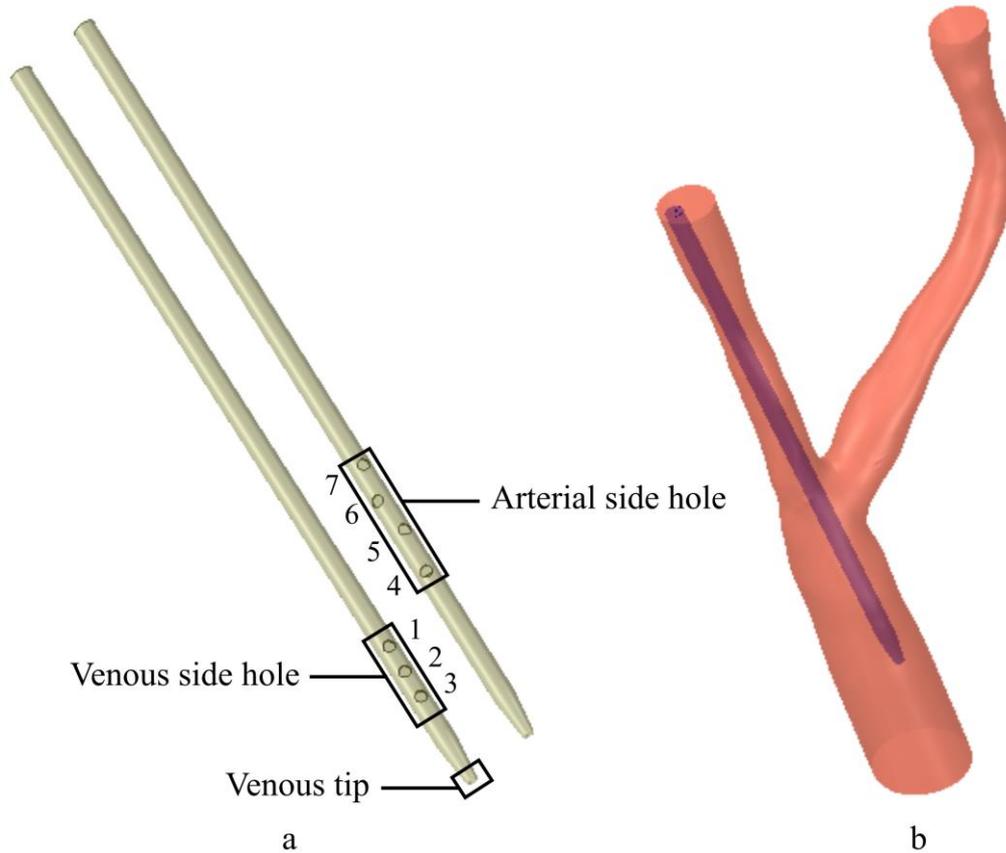
Figure 1. Central venous catheter geometry (a). CVC inserted into the central veins (b).

2.2 Hemolytic potential model

The Eulerian numerical model used to calculate the hemolytic potential was based on the empirical model proposed by Giersiepen *et al.* (1990). Equation (1) describes this mathematical model.

$$HI(\%) = \frac{\Delta Hb}{Hb} = C\,\tau^{\alpha} t^{\beta}, \tag{1}$$

Where, τ is shear stress and t is exposure time. C, α and β are constants obtained through of an experimental data regression. *HI* represents the hemoglobin released (*ΔHb*) with respect to the total blood hemoglobin (*Hb*). Lacasse *et al.* (2007) proposes the following transport equation for calculating the hemolytic potential.

$$\frac{\partial HI_L}{\partial t} + (\mathbf{u} \cdot \nabla)HI_L = \delta\,A\,\tau^{\frac{\alpha}{\beta}}(1 - HI_L), \tag{2}$$

Where $HI_L = HI^{\frac{1}{\beta}}$ is the linear hemolysis index with respect to time (*t*), $\mathbf{u}$ is the velocity vector, $A = (C/100)^{\frac{1}{\beta}}$ and δ considers the limit value of shear stress (τ_s) necessary to produce hemolysis, given by:

$$\delta = \begin{cases} 0 \text{ if } \tau < \tau_s \\ 1 \text{ if } \tau \geq \tau_s \end{cases}, \tag{3}$$

Wherein, the value generally used for τ_s is 25 Pa (Lacasse *et al.*, 2007).

2.3 Numerical solution

The simulations to obtain the linear hemolysis index in the central venous access for hemodialysis were performed using the ANSYS-Fluent® 19.2 software (ANSYS-Fluent Inc., Lebanon, NH, USA). It was considered incompressible and transient flow covering two complete cardiac cycles of 0.8 s. Regarding the characteristics of the blood, the value of 1060 kg/m^3 was used for the density (Gonçalves *et al.*, 2019; Gonçalves *et al.*, 2020a, Silva *et al.*, 2020), and for the

rheological behavior of the blood it was adopted the Carreau-Yasuda model for non-Newtonian fluid. Table 1 presents the values that were used for the parameters of the Carreau-Yasuda model.

Table 1. Parameter values of the Carreau-Yasuda model.

Maximum Viscosity (kg/m.s)	Minimum Viscosity (kg/m.s)	Power-Law index	Time Constant (s)
0.0035	0.0560	0.3568	3.3130

The K-ω SST (Shear Stress Transport) turbulence model was adopted. To comply with the Courant-Friedrichs-Lewis criterion, a time step of 0.002 s was used, resulting in 400 time steps for each complete cardiac cycle of 0.8 s. As a convergence criterion, a numerical residual less than 10^{-4} was considered. The flow inside the CVC was considered in steady state with a mass flow rate of 0.0053 kg/s, as in the clinical procedure of hemodialysis. Equation (2) was implemented in the ANSYS-Fluent® 19.2 software to calculate the HI_L.

The coupled algorithm was used for the Pressure-Velocity coupling. For spatial discretization of the momentum it was used the second order Upwind method. The implicit second order scheme for the temporal discretization was adopted. The second order upwind method for turbulent kinetic energy and for the specific dissipation rate was used. The first order upwind method for the linear hemolysis index discretization was considered. Lastly, the PRESTO! scheme for the pressure discretization was used. In the ANSYS-fluent software the continuity discretization is based on the method presented by Rhie and Chow (1983).

2.4 Mesh convergence tests

The mesh convergence tests were carried out in a transient regime. For the analysis of mesh convergence, the pressure and velocity results were monitored in four planes close to the tip and lateral orifices of the catheter, since these are regions of greater gradients of these variables. The meshes were refined by doubling the number of elements until the differences in the mean values, for pressure and velocity, in the considered planes, were close to 5%. Table 2 shows the characteristics of the tested meshes and Table 3 shows the relative errors in the four analyzed planes.

Table 2. Characteristics of tested meshes.

	Mesh 1	Mesh 2	Mesh 3
# Elements	839864	1651824	3648883
# Nodes	286231	552404	1226046

Table 3. Relative errors in the four analyzed planes.

Relative Error: Velocity		
Plane	**Mesh 2 – Mesh 1**	**Mesh 3 – Mesh 2**
Venous hole 1 (%)	3.34	1.83
Venous hole 2 (%)	1.92	3.93
Arterial hole 4 (%)	1.79	5.52
Close to Venous tip (%)	3.83	3.11
Relative Error: Pressure		
Plane	**Mesh 2 – Mesh 1**	**Mesh 3 – Mesh 2**
Venous hole 1 (%)	0.58	0.69
Venous hole 2 (%)	1.28	0.92
Arterial hole 4 (%)	1.64	1.10
Close to Venous tip (%)	0.52	0.39

For the tested meshes, it can be seen that they met the criterion previously established, that is, the differences were less than 5%. Nevertheless, it was adopted the use of mesh 2, because mesh 1 did not meet the converge criterion of 10^{-4} in numerical residuals.

2.5 Boundary conditions

The velocity at the inlets of the central veins, that is, right and left jugular veins, were determined from the average of the flow rates curves in the superior vena cava from the studies of Markl *et al.* (2011) and Mynard and Smolich (2015). The flow rates used to calculate the velocity in the right and left jugular veins were considered equal to the half

of the total flow rate in the superior vena cava, and this justified by the scarcity of data in the literature and the lack of consensus, present in the studies (Gonçalves *et al.*, 2019; Gonçalves *et al.*, 2020a; Marr *et al.*, 2018; Lucas *et al.*, 2014).

In the outlet of the central veins geometry it was considered that the pressure at the outlet of the superior vena cava is equal to the pressure of the right atrium (Mynard and Smolich, 2015). Figure 2 illustrates the curves for the two variables used in the boundary conditions.
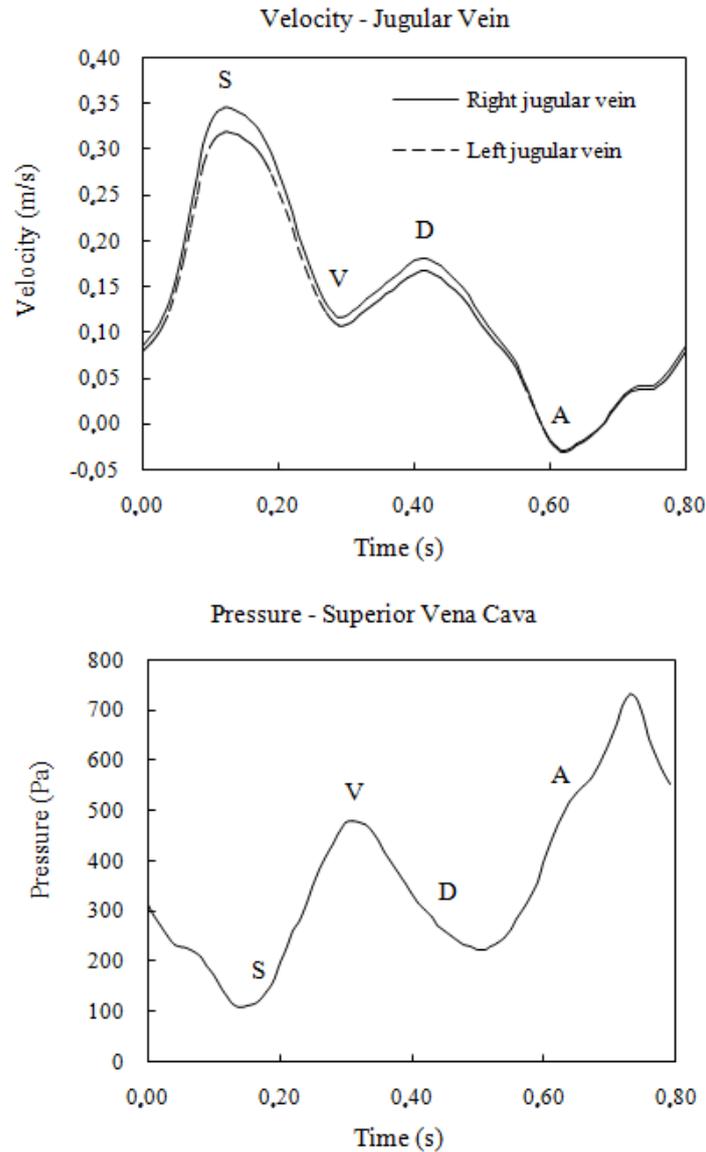

Figure 2. Velocity inlets and pressure outlet curves in the central veins. The instants of the cardiac cycle that occur to atrial contraction (A), systole (S), transitional wave (V) and diastole (D) are indicate.

Non-slip condition in the walls of the veins and the catheter was adopted. For the HI_L, a zero value was considered in the domain inlets, $HI_L = 0$, and zero flux of this variable in the walls and in the outlet of the computational domain, $\frac{\partial HI_L}{\partial n} = 0$.

3. RESULTS AND DISCUSSION

Figure 3 indicates the regions with the highest hemolytic potentials, in the computational domain, by iso-volumes of HI_L, obtained at the time of maximum velocity of the cardiac cycle ($t = 0.14$ s). These iso-volumes represent three-dimensional regions of the HI_L distributions above previously specified values.
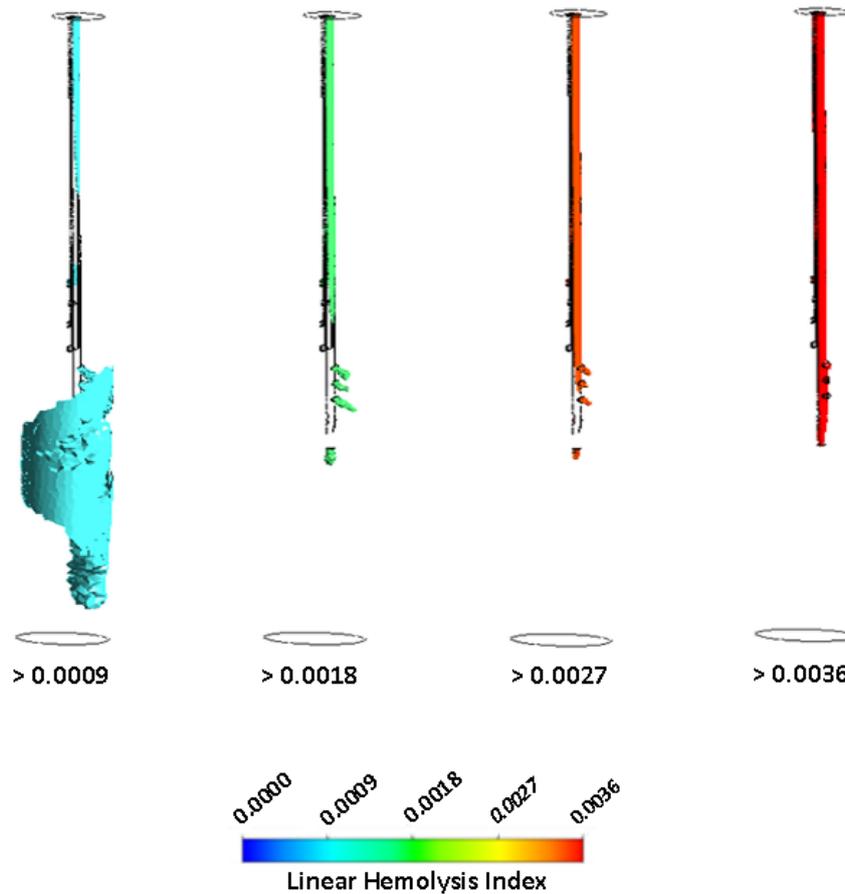
Figure 3. Iso-volumes of HI_L.

Based on Figure 3, it is possible to verify that close to the tip and the venous orifices of the catheter was the region with the highest linear hemolysis index. These results suggest that hemolysis increase is more associated with catheter outflow jets. Figure 4 and Figure 5 shows that the distribution of shear stress is more evident in those locations, which was also verified by Gonçalves (2020b), thus those areas with higher shear stresses are critical for the rupture of blood cells. Other studies have also identified that, close to the venous orifices of the catheter, is a favorable zone for vortices formation, flow separation and recirculation, which could be related to the increase in exposure time in this region (Lucas *et al.*, 2013; Lucas *et al.*, 2014).

Figure 4 presents a comparison of the linear hemolysis index field with the shear stress field. The analyzed variables were obtained in XY planes defined close to the tip and passing through the centers of the catheter lateral orifices, also at time $t = 0.14$ s. Next to each plane, the average values (Mn) of these variables in the respective planes are also indicated.

Regarding the HI_L distribution it can be seen that the pattern was similar to the shear stress distributions. Thus, in points where there are high values of shear stress, it presented a greater potential for hemolysis. It was observed that the distribution of shear stress was more evident near the tip and the venous orifices of the catheter, that is, in planes P1, P2, P3 and P4. As a result, HI_L was also more evident in these planes, that is, hemolysis was more critical close to the venous orifices of the central venous catheter. Quantitatively, it should be noted that the P2 plan was the most critical, in average values, for the two quantities discussed, among the four mentioned planes.

The planes that cut the CVC arterial orifices (P5, P6, P7 and P8) presented the highest mean values of shear stress. However, they were the planes with the lowest mean values of linear hemolysis index. This can be explained by analyzing Figure 5, where iso-surfaces for shear stress for instant $t = 0.14$ s are illustrated. It was observed that regions where there were high shear stresses present small extensions, being restricted in the venous lumen of the catheter. This fact can contribute for the small particle exposure time to this stresses level, causing these lower values for HI_L. Furthermore, Gonçalves (2020b) showed that this region is not characterized by presenting recirculation at this instant of the cardiac cycle, which also contribute to the reduction of exposure time. This effect is more visible for the last arterial orifice of the CVC (P8).
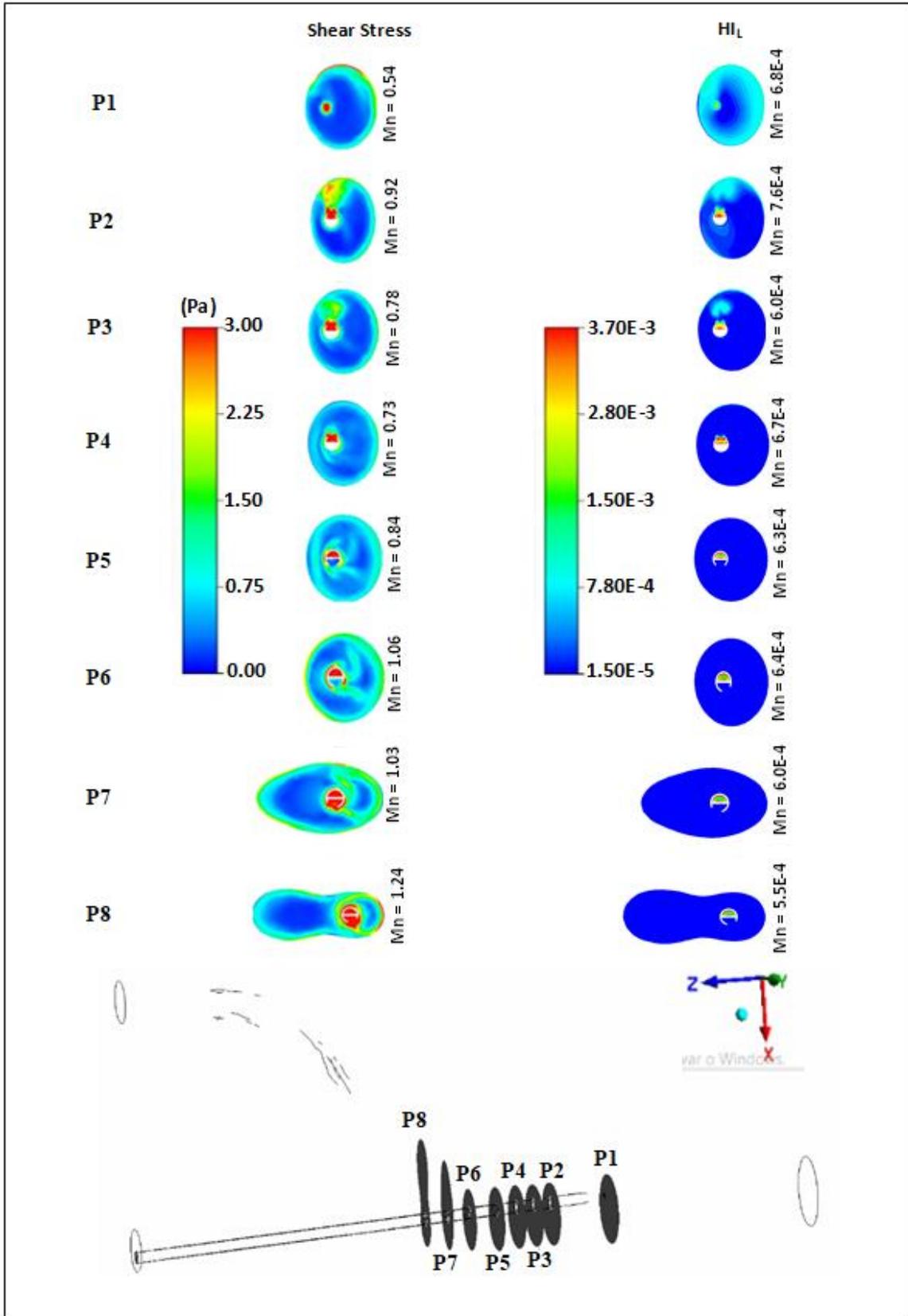
Figure 4. Shear stress and HI_L for planes that cut the centers of the CVC orifices.
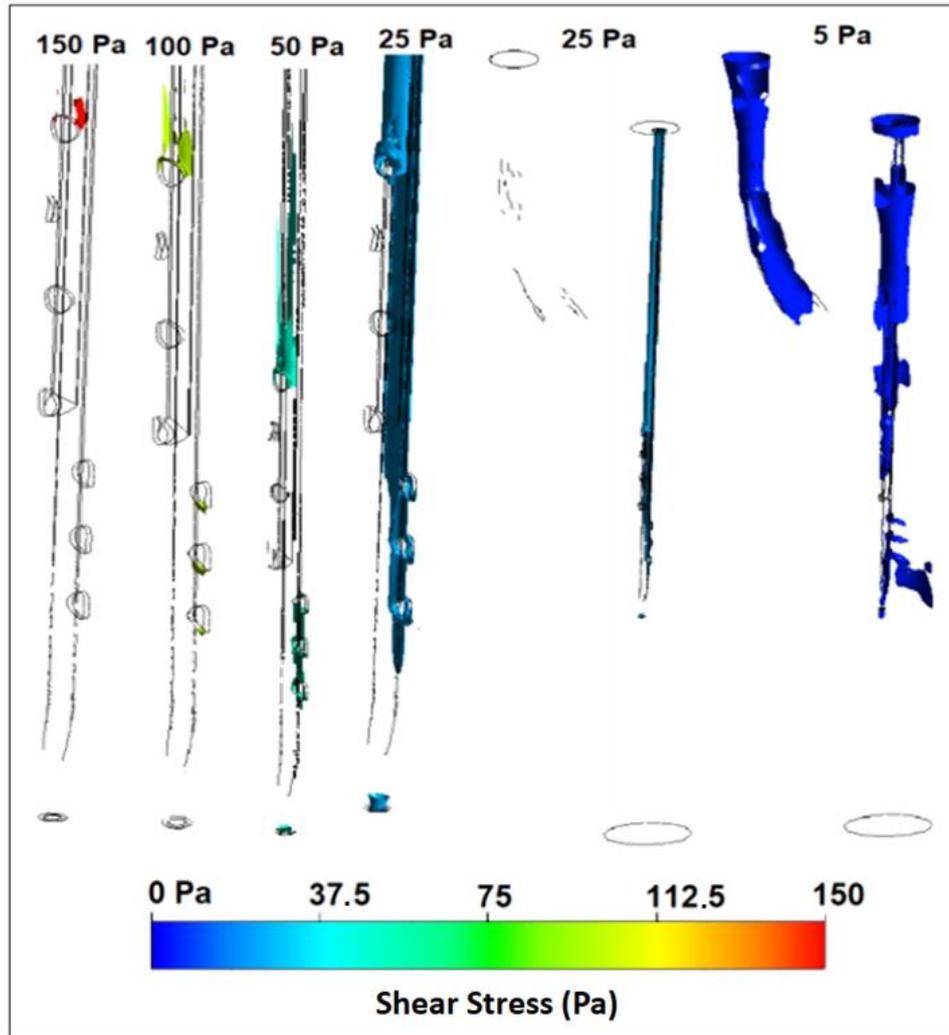
Figure 5. Iso-surfaces of shear stress.

Eulerian model has the advantage of obtaining the hemolysis index at each point of the studied fluid domain. This can contributes to assist in the design and analysis of clinical devices to estimate the hemolytic potential, since it allows mapping the critical regions throughout the computational domain. Nevertheless, the Eulerian model cannot be used to determine the exact concentration of blood cell disruptions, being used only for a qualitative analysis, because the empirical model of the *HI* was determined for Couette flow, however the blood flow is exposed to different magnitudes of shear stress, which can vary in time and space (Haniel *et al*., 2019).

Moreover, Grigioni *et al*. 2004 indicates that the Power Law models, to predict the hemolytic potential, are suitable only for laminar flow. Thus, recent studies are focusing on developing more accurate models in a wider range of flow regimes, for example, Wu *et al*. (2019) relates the hemolysis index to the energy dissipation rate for this purpose.

Finally, it should be noted that the present work also has the limitation of not having experimental data to compare with the result presented here to validate the numerical model. Furthermore, fluid-structural interactions were not considered in the simulations to verify the influence of veins deformations and the displacement of CVC on the variables discussed previously. However, the fluid dynamic analysis is performed with rigid walls, and under these conditions the shear stress tends to be higher (Lin *et al*., 2017). Therefore, it is possible that the HI values are overestimated, since these two quantities are directly related.

4. CONCLUSION

Numerical models based on computational fluid dynamics allow the investigation o hemodynamic parameters that can influence hemolysis in a non-invasive way at a relatively low cost. This tool can be used to assist healthcare professionals, so that clinical procedures are performed with greater efficiency, ensuring safety and comfort for the patient. It was possible to verify that the Eulerian model can qualitatively indicate the most critical regions for

hemolytic potential. As a result, this model can help the development of CVC designs to reduce the incidence of hemolysis.

The results showed that high values of the linear hemolysis index are concentrated in regions close to the venous orifices of the CVC, that is, hemolysis in the hemodialysis procedure is more influenced by the outflow jets of the catheter. This occurs, because these regions are characterized by high shear stresses and high recirculation, which increase the exposure time to these stresses.

Nevertheless, it is necessary to carry out experimental tests in order to compare the results of this work. In addition, is necessary to perform simulations considering fluid-structural interactions to analyze whether the mechanical behavior of the veins significantly interferes in the HI_L fields.

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