ORIGINAL ARTICLE

3D Analysis of Geometry and Fluid Dynamics During Presurgical Planning of Patients with Single Ventricle and Heterotaxy Syndrome in Pre-Fontan-Kreutzer Stage

Análisis 3D de la geometría y fluidodinámica durante el planeamiento prequirúrgico de los pacientes con ventrículo único y síndrome de heterotaxia en el estadio pre Fontan-Kreutzer

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ABSTRACT

Background: The aim of the Fontan-Kreutzer procedure is to obtain a balanced distribution of hepatic venous flow to both lungs in order to achieve a favorable long-term clinical condition. These patients, due to the continuous passive hepatic venous flow to the lungs develop long-term liver disease, (cirrhosis), plastic bronchitis or protein-losing disease. If there is an unbalanced distribution of hepatic venous flow to the lungs, arteriovenous fistulas in the pulmonary parenchyma begin to develop, leading to decreased arterial oxygen saturation.

Objective: The aim of this study was to predict and avoid an unbalanced distribution of hepatic venous flow to the lungs after total cavopulmonary connection surgery at the Fontan-Kreutzer stage through the use of fluid dynamics analysis.

Methods: Two patients with a single ventricle and complex anatomy were studied and underwent pre-surgical planning by modeling in three dimensions (3D) the digital shape of the anatomic segmentation through the DICOM format of the contrast-enhanced axial computed tomography. Then, the model of the virtual surgery was performed to apply computational fluid dynamics to the chosen surgical technique, in order to evaluate the balanced distribution of hepatic venous flow to the lungs.

Results: Computational fluid dynamics applied in the different proposed surgical techniques to complete the total cavopulmonary connection in the Fontan-Kreutzer stage predicted a distribution of 60% to 65% hepatic venous flow to the right pulmonary artery and 35% to 40% to the left pulmonary artery.

Conclusions: The 3D reconstruction methodology of each patient's anatomy combined with computational fluid dynamics modeling obtained by the present interdisciplinary group, allowed developing different surgical scenarios specific to the patients under study. The physics approach of a medical problem has allowed favorable results and constitutes a systematic method towards the application of precision medicine. This personalization has the advantages of studying in advance the anatomy of the patients in virtual form, essential for proposing different surgical scenarios and optimizing surgical times. The evaluation of physiological quantities for different scenarios by means of simulation, enabled the approximation of hepatic venous flow distribution to both lungs, determining which strategy minimizes or avoids fistula formation in the patient. This has a direct impact on the improvement of long-term outcomes after completing the total cavopulmonary connection at the Fontan-Kreutzer stage.

Keywords: Fluid dynamics - Fontan Kreutzer

RESUMEN

Introducción: En la cirugía de Fontan-Kreutzer se busca obtener una distribución equilibrada del flujo venoso hepático hacia ambos pulmones para lograr una condición clínica favorable a largo plazo. Estos pacientes, debido al flujo continuo pasivo venoso hepático

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hacia los pulmones desarrollan a largo plazo enfermedad hepática (cirrosis), bronquitis plástica o enfermedad perdedora de proteínas. Si se produce una distribución desbalanceada del flujo venoso hepático hacia los pulmones comienzan a desarrollarse fistulas arteriovenosas en el parénquima pulmonar, que llevan a la disminución de la saturación arterial de oxígeno.

Objetivo: Predecir y evitar una desbalanceada distribución del flujo venoso hepático hacia los pulmones después de la cirugía de conexión cavo-pulmonar total en el estadio de Fontan-Kreutzer a través de utilizar el análisis de la fluidodinámica.

Material y métodos: Dos pacientes con ventrículo único con anatomía compleja fueron estudiados y se realizó en ellos el planeamiento prequirúrgico modelando en 3 dimensiones (3D) la forma digital de la segmentación anatómica a través del formato DICOM de la tomografía axial computada con contraste. Luego se realizó el modelo de la cirugía virtual para poder aplicar a la técnica quirúrgica elegida la fluidodinámica computacional que permite evaluar la distribución balanceada del flujo venoso hepático hacia los pulmones.

Resultados: La fluidodinámica computacional predijo en las distintas técnicas quirúrgicas propuestas para completar la con¬exión cavo-pulmonar total en el estadio Fontan-Kreutzer una distribución del flujo venoso hepático hacia la arteria pulmonar derecha de 60 % a 65 % y a la rama izquierda de 35 % a 40 %.

Conclusión: La metodología de reconstrucción 3d de la anatomía de cada paciente combinada con el modelado por fluido dinámica computacional obtenida por el presente grupo interdisciplinario, permitió modelar diferentes escenarios quirúrgicos específicos para los pacientes en estudio. La aproximación desde la física de un problema médico permitió obtener resultados favorables y constituir un método sistemático hacia la aplicación de la medicina de precisión. Esta personalización presenta las ventajas de estudiar con antelación la anatomía de los pacientes en forma virtual, esencial para proponer diferentes escenarios quirúrgicos y optimizar los tiempos en cirugía. La evaluación de cantidades fisiológicas para diferentes escenarios, mediante simulación, permitió aproximar la distribución del flujo venoso hepático hacia ambos pulmones permitiendo determinar qué estrategia minimiza o evita la formación de fistulas en el paciente. Esto tiene un impacto directo en la mejora de los resultados a largo plazo luego de completar la conexión cavo-pulmonar total en el estadio de Fontan-Kreutzer.

Palabras clave: Fluidodinámica - Fontan-Kreutzer

INTRODUCTION

Newborns have 50% distribution of blood flow towards the cephalic part of the body due to the proportion of the head in relation to the body. When they begin to walk, the metabolic demand of the muscles causes the cardiac output to increase by up to 70% to the lower limbs. For this reason, the therapeutic strategy of the single ventricle leading to univentricular correction consists of a stepwise approach. At 3 to 6 months old, the superior vena cava is connected to the pulmonary artery (Glenn surgery), to increase the effective pulmonary flow and thus blood oxygenation. Then, when the patient starts to walk and the relative cardiac output towards the cephalic region decreases with respect to that of the lower limbs, it is considered necessary to connect the inferior vena cava to the pulmonary artery. This technique, known as the Fontan-Kreutzer procedure, separates the pulmonary from the systemic circulation, improving the effective pulmonary flow and allowing the survival of patients with univentricular hearts. For this circulation to be effective it requires an adequate anatomy with low pressures both in the pulmonary tree as in the single ventricle, since blood circulates by gravity in the inspiratory and expiratory phase depending on the difference between atmospheric and intrathoracic pressures.

In the Fontan-Kreutzer procedure, the aim is to obtain a balanced distribution of hepatic venous flow to both lungs to achieve a favorable long-term clinical condition. These patients, due to the continuous passive hepatic venous flow to the lungs develop long-term liver disease (cirrhosis), plastic bronchitis or protein-losing disease, generating failure of the Fontan system. (1) Balanced distribution reduces the formation of pulmonary arteriovenous malformations and prevents the decrease of arterial oxygen saturation. It also minimizes the loss of blood flow energy to the lungs and avoids the associated thrombosis due to certain localized high and low shear stress sites on the walls of the total cavopulmonary connection system in the Fontan-Kreutzer stage. The hepatic factor is a molecule or an undetermined metabolite essential in this process. If there is an unbalanced distribution of hepatic venous flow to the lungs, absence of the passage of this hepatic factor through the lung tissue takes place and arteriovenous fistulas begin to develop in the lung parenchyma, leading to decreased oxygenation of arterial blood. (2)

Although long-term complications are multifactorial, they may be related to the geometric design of the total cavopulmonary connection affecting the hemodynamic resistance and the balance of hepatic venous flow distribution to the lungs. (3-6)

In patients in whom the hepatic venous flow is to one lung, arteriovenous malformations develop in the contralateral lung. Patients who are prone to the development of arteriovenous fistulas have a 32% to 85% chance of developing them, due to lack of hepatic factor flow through the lungs before performing the total cavopulmonary connection in the Fontan-Kreutzer stage. (7)

In patients with complex anatomy for the total cavopulmonary connection it is difficult to estimate blood flow distribution, taking into account 2 or 3 flow inlets, then the passage of blood through a total cavopulmonary connection with an angled geometry, and that finally flow is distributed in a balanced and equitable way through two pathways to both lungs.

This has led to improvements in preoperative planning and has given rise to new multidisciplinary work methodologies that combine medical knowledge with the complementary use of tools such as multimedia design of virtual surgeries, and the use of computational fluid dynamics. (8-12)

The novelty of this work is that we were able to plan the surgical treatment of these patients in a personalized way in a public hospital in Argentina with an interdisciplinary group of cardiovascular surgeons, cardiologists, imaging technicians, nuclear physicists and engineers, electronic engineers and multimedia designers.

OBJECTIVE

The aim of this study was to predict and prevent an unbalanced distribution of hepatic venous flow to the lungs after total cavopulmonary connection surgery at the Fontan-Kreutzer stage, by using fluid dynamics analysis.

METHODS

The three dimensional (3D) anatomy of two patients was reconstructed using the DICOM of the computed tomography (CT) scan, adding the 3D design of the selected surgical technique based on the premise of making the straightest and shortest possible connection between the inferior vena cava and the pulmonary artery branches. Computational simulations of fluid dynamics were subsequently performed to estimate the inflow to the Fontan system and the distribution of hepatic flow to both pulmonary artery branches. (Table 1) Defining the hemodynamic conditions for blood flow simulation is a great challenge. In our hospital, echocardiography and catheterization are usually performed for the presurgical evaluation of a patient candidate for total cavopulmonary connection in the Fontan-Kreutzer stage. DICOM data from a CT or magnetic resonance imaging (MRI) scan are required for 3D modeling of the anatomy and eventual design of the virtual surgery. Certain hemodynamic data are necessary for the computer simulation, such as the inflows to the model to be evaluated (single or bilateral Glenn, inferior vena cava or suprahepatic veins, azygos vein, etc.) and the pressure values in the different points of the system. For the latter, we considered the values measured by invasive catheterization. Flows are shown in Table 2. We initially used echocardiography-calculated flows by measuring the velocity time integral (VTI). Flow values are absolutely variable according to the patient's condition; for example, the systemic venous return flow varies significantly during inspiration or expiration or during apnea. In this study, we used the echocardiographic VTI to estimate blood flow calculated as the product of the average velocity and the cross-sectional area of the vessel. (13) Since flow is pulsatile and its velocity varies along the cross-sectional area of the vessel, there is a velocity distribution (flow velocity profile). An average velocity value is obtained by adding all the velocities within the Doppler spectral envelope (velocity time integral). The cross-sectional area is obtained by echocardiography and compared with the CT measurements of the anatomy.

For venous flows, average velocities are measured during several cardiac cycles established by the electrocardiogram, as well as heart rate, and then flow through that vessel is calculated in liters/minute. To consider total flow, the systemic cardiac output was also measured by aortic VTI. (13)

Reconstruction of the anatomical models

Slicer (Kitware, USA) was used for image processing, segmentation and 3D reconstruction, (14) and algorithms from the ITK library (Insight Software Consortium, USA) were developed. (15)

We worked with Blender (Netherlands) (16) to adapt the Fontan procedure connections to the reconstructed 3D models. These were used for computational fluid dynamics calculations. After the virtual surgery, the anatomical model and the proposed surgical reconstruction were loaded into a self-developed online virtual browser to be analyzed in detail and discussed in a clinical surgical meeting.

Patient number 1 had a sequential and segmental analysis of the cardiac anatomy in which an atrial situs inversus, ventricular L-loop and L position of the aorta were observed. The diagnostic methods used were echocardiogram, contrast-enhanced CT, catheterization, and 3D reconstruction, showing a single ventricle with tricuspid atresia and pulmonary atresia (Figure 1).

In patient number 2, the sequential and segmental analysis of the cardiac anatomy performed using echocardiogram, contrast-enhanced CT, cardiac catheterization, and 3D reconstruction of the geometry led to a diagnosis of atrial situs ambiguous, ventricular L loop, and L position of the aorta (right aortic arch) with an unbalanced right-dominant atrioventricular canal with pulmonary atresia and moderate atrioventricular valve insufficiency in the Glenn stage (Figure 2). Figure 3 A shows the left Glenn system in cardiac catheterization together with the anatomy of the pulmonary arteries, 3 B the right Glenn system together with the branches of the pulmonary arteries and 3 C the ambiguous drainage of the inferior vena cava into the single atrium.

Computational Fluid Dynamics

The domain of the study system, defined by the geometric model, is approximated by tetrahedral elements generated by GMSH (C Geuzaine & J-F Remacle, U Liege, Belgium), a generator of finite element meshes. (17) To model the hemodynamic behavior of blood in this system, the continuity and the Navier-Stokes equations (conservation of momentum

Table 1. Hepatic venous flow distribution to right and left branches of pulmonary artery predicted by computational fluid dynamics

Patient	Sex	Age	Estimated systemic flow (L/min)	Hepatic flow to the right pulmonary artery (%)	Hepatic flow to the left pulmonary artery (%)
1. Lateral Tunnel	M	3 years and 10 months	1.86	60	40
2. Extracardiac Tube	M	3 years	2.05	65	35

and mass) are solved. Profiles developed for the velocities (Dirichlet) obtained from VTI and Neumann type measurements for the pressures at the inlets were established. For the outlets Dirichlet-type floating pressure values and Neumann type for the velocities were used. The conditions on the walls were non-sliding. As a result of the simulation, the velocity and pressure components that satisfy these equations were obtained. The results presented were solved with the open-source software OpenFOAM, (18) initially using the SIMPLE (Semi Implicit Method for Pressure Linked Equation) algorithm in steady state. However, it is common for the steady state solution to be unstable and convergence with acceptable tolerances is not achieved, in which case a transient solution is obtained with a PISO (Pressure Implicit with Splitted Operators) type algorithm. This algorithm is limited by the need to keep the Courant number <1 to produce stable solutions, restricting the time step to be used and increasing the simulation time to excessive values. Finally, using a combination of both algorithms, known as PIMPLE, the time step can be increased to reach Courant numbers of around 20, resigning some precision in the temporal evolution, but maintaining the flow values at the outlets. The Courant number is the flow velocity by the time step divided by the mesh size. If it equals 1, it means that the fluid passes through one cell in one time step.

The hepatic venous flow distribution (HFD) was estimated from computational fluid dynamics simulations. It is defined as the ratio of blood flow in the inferior vena cava and the right and left pulmonary arteries and is calculated by tracking particles in the flow lines. This value is considered favorable for distribution values between 40% and 60% for both pulmonary arteries. We studied these clinical metrics in conjunction with flow structures and pressure drops to elucidate the mechanisms that lead to greater energy dissipation or a certain distribution of hepatic flow. To estimate the value of the hepatic venous flow distribution, a software was developed that calculates and displays the trajectory lines for a given set of particles that travel through the simulated fluid.

This quantity is calculated by the time integral of the velocity field components obtained from the computational fluid dynamics calculation. By visually counting these lines, the percentage of hepatic venous flow distribution towards the pulmonary artery branches is estimated. This can be observed in Figure 4 A, which displays the velocity distribution in the pulmonary artery branches with an extracardiac tube in patient 1. Figure 4 B shows the velocity distribution in the pulmonary arteries with a lateral caval tunnel in patient 2. To perform calculations, we assume that the vessel walls are rigid; (19-21) and that the parameters related to the efficiency of the total cavopulmonary connection, such as the power loss and distribution of the hepatic venous flow in a patient

Table 2. Flow and VTI data by echocardiography

	Structure	Diameter (cm)	VTI (cm)	Radius (cm)	Radius² (cm²)	Area (cm²)	Volume (cm³)	Average speed (m/s)	Flow (L/min)
Patient 1	SVC/Glenn	0.8						0.22	0.67
	IVC	1.2						0.15	1.05
	RPA	1.0							
	LPA	0.9						0.14	0.55
	Aorta	16.5						0.18	2.14
Patient 2	Right Glenn	0.7	21	0.35	0.1225	0.35	8.1		0.69
	Left Glenn	0.5	25	0.25	0.0625	0.20	4.9		0.42
	IVC	0.8	22	0.4	0.16	0.50	11.0		0.94
	Aorta	1.7	8.5	0.85	0.7225	2.27	19.3		1.64

Echocardiographic flow and VTI data.
IVC: inferior vena cava; LPA: left pulmonary artery; RPA: right pulmonary artery; SVC: superior vena cava; VTI, velocity time integral.

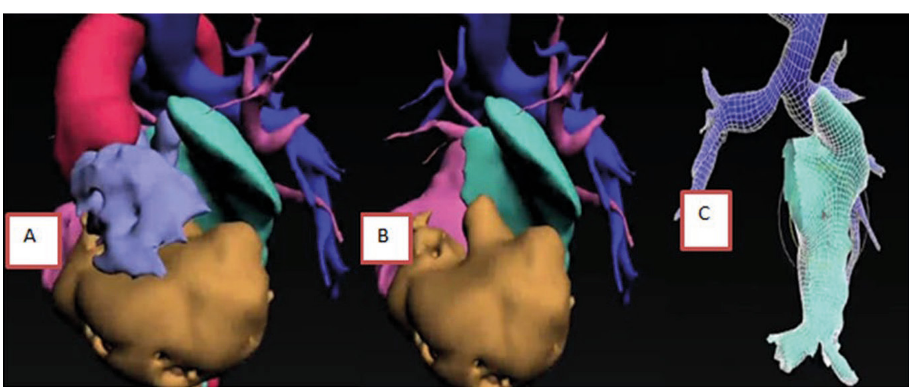

Fig. 1 Patient 1. **A** and **B**: 3D reconstructed images showing in an anterior view the aorta exiting in L-position from the single ventricle of left morphology (pearly colored structure). In Fig. **A**, **B** and **C** the drainage of the suprahepatic veins in a position of atrial situs inversus is shown in turquoise. The pulmonary branches to the Glenn system are seen in blue

with an intraatrial rerouting do not change significantly compared to using a fluid-structure interaction model. We also assume that blood behaves as an incompressible Newtonian fluid, with a constant viscosity of 3.71 mPas and a density of 1060 kg/m. The boundary conditions for the hemodynamics of a single ventricle broadly include the vessel walls and ends. (22) For the vessel ends, boundary conditions given by the clinical measurements described above will be imposed and we will assume flow rate values averaged over one or more cardiac cycles. We assume that the conditions of both the systemic flow rate and the inlet distribution are preserved before and after surgery (the physiological conditions in the rest of the system do not change). (23-31)

RESULTS

Computational fluid dynamics in the different surgical techniques proposed to complete the total cavopulmonary connection in the Fontan-Kreutzer stage predicted a distribution of the hepatic venous flow towards the right pulmonary artery of 60% to 65% and to the left pulmonary artery of 35% to 40%. (Table 1).

Distribution of hepatic venous flow

Figure 5 A shows the simulation of the hepatic flow distribution in patient 1 with an extracardiac tube technique resulting in 65% of the hepatic venous flow

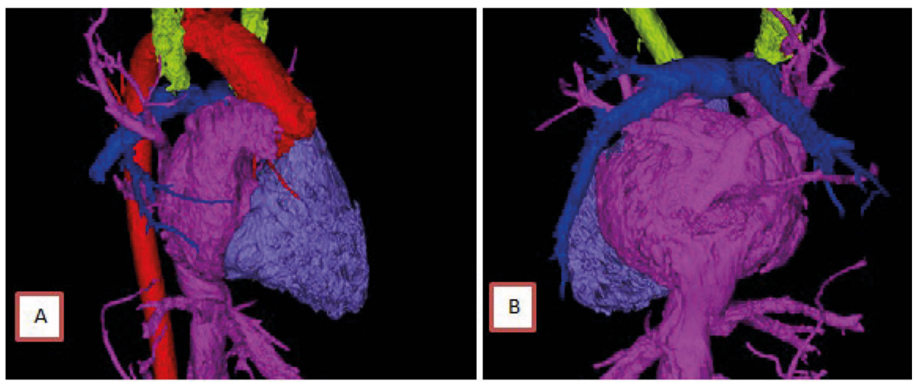

Fig. 2. Patient 2. **A** and **B**: 3D reconstruction image. The single atrium receiving the pulmonary veins and the inferior vena cava can be seen in fuchsia. B shows the ambiguous drainage of the inferior vena cava into the single atrium. In both figures, the geometries of the two Glenn systems draining into the pulmonary artery structure (blue) are visualized in light green. The ventricular L-loop is also seen in the purple structure. The L position of the aorta is seen in red.

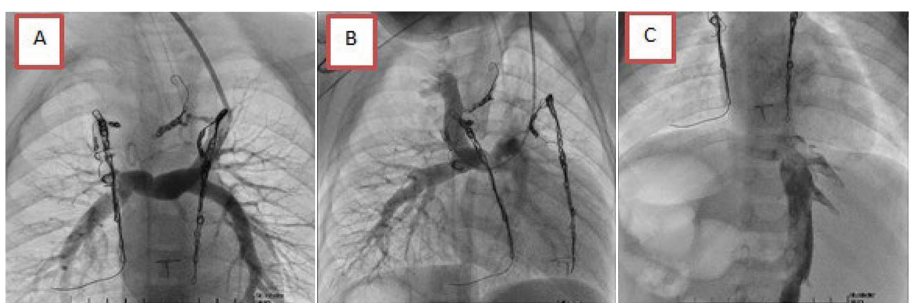

Fig. 3. A: The left Glenn system is observed in cardiac catheterization along with the anatomy of the pulmonary arteries. **B:** the right Glenn system is seen together with the branches of the pulmonary arteries. **C:** the ambiguous drainage of the inferior vena cava is seen in the single atrium.

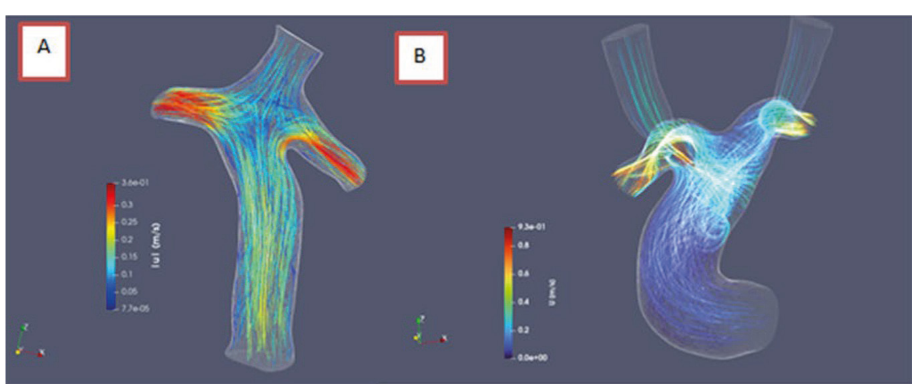

Fig. 4. A: Distribution of velocities in the pulmonary arteries with an extracardiac tube in patient 1. **B:** Distribution of velocities in the pulmonary arteries with a caval lateral tunnel in patient 2.

to the right pulmonary artery and 35% of the hepatic flow to the left pulmonary artery using a systemic flow rate of 1.86 liters/minute. Figure 5B shows that in patient 2 the fluid dynamics simulation indicates that with the Fontan technique of lateral caval tunnel the hepatic flow is distributed 60% to the right pulmonary artery and 40% to the left pulmonary artery using a systemic inflow rate of 2.05 liters/minute.

Both patients had a satisfactory postoperative outcome with 95% oxygen saturation and survival was 100% at discharge. Due to the excellent 4-year evolution we are extending this presurgical planning to patients with a single ventricle and complex anatomy and physiology. Neither of these two patients developed pulmonary arteriovenous fistulas.

DISCUSSION

Patients with a diagnosis of single ventricle present a wide range of anatomical variations that pose a challenge to plan and predict the ideal surgical reconstruction for the Fontan-Kreutzer procedure. Prospective virtual modification of the patient's anatomy to simulate a surgical approach combined with computational modeling provided information on the physiological impact of different surgical decisions.

Simulations performed before the interventions were useful in achieving a successful approach that was demonstrated by the surgical technique used in each patient; however, using magnetic resonance imaging we have been unable to perform a study of the distribution of hepatic venous flow to the lungs after each intervention. Given the variation in the balance of hepatic venous flow and pulmonary vasculature resistance in the patients studied, as well as the experience of several pediatric surgeons and cardiologists who have performed flow simulation for patients diagnosed with a single ventricle, it is clear that it is not possible to predict hepatic flow distribution based on clinical experience alone, even at large centers with substantial experience with these patients. Factors that determine the distribution of hepatic venous flow to the lungs include the position of the systemic veins (single or bilateral superior vena cava side), the inferior vena cava side, the number of suprahepatic veins and the distance from their output orifice to the single atrium, the angulation of the veins as they enter the pulmonary arteries, and the balance of flow between the different venae cavae and other hemodynamic factors.

It should be noted that the assembly of the interdisciplinary group is a hard teamwork of many hours, with professionals from different scientific fields in our country, and entails continuous learning to be able to use these tools in the clinical setting of patients within a public hospital. A very important point is the 3D design of the surgical technique to achieve a model as close as possible to the geometric reality of the anatomy of each patient. (32,33) The close collaboration between the engineers of the modeling team and the surgeons is essential to translate the details of the surgical approach planned by the surgeons into the virtual model.

CONCLUSION

The 3D reconstruction methodology of the anatomy of each patient combined with the computational fluid dynamics modeling obtained by this interdisciplinary group, allowed designing different surgical scenarios specific to the patients under study. The physics approach of a medical problem has provided favorable results and constitutes a systematic method towards the application of pre-operative medicine. This customization offers the advantages of studying the patient's anatomy in advance in a virtual way, which is essential

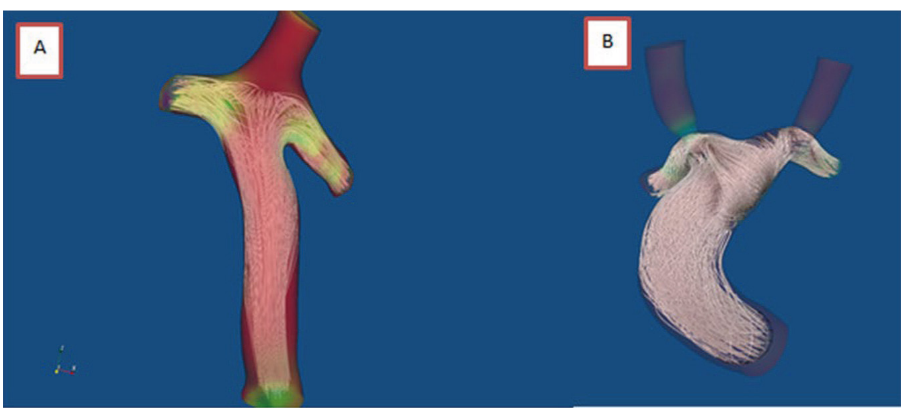

Fig. 5 Distribution of hepatic venous flow to pulmonary arteries. **A:** The simulation of the hepatic flow distribution in patient 1 using an extracardiac tube technique shows a distribution of 65% of hepatic venous flow to the right pulmonary artery and 35% of hepatic venous flow to the left pulmonary artery with a systemic flow rate of 1.86 liters/minute. **B:** The fluid-dynamics simulation in patient 2 shows that with the caval lateral tunnel technique, the hepatic flow is distributed 60% to the right pulmonary artery and 40% to the left pulmonary artery, using a systemic inflow of 2.05 liters/minute.

for proposing different surgical scenarios and optimizing procedural times. The evaluation of physiological quantities for different scenarios through simulation, allowed the approximation of hepatic venous flow distribution to both lungs, determining which strategy minimizes or avoids the formation of fistulas in the patient. This has a direct impact on improving long-term outcomes after completing the total cavopulmonary connection at the Fontan-Kreutzer stage.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web).

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