



Clinical Applications of the 4D Flow Technique in the Hemodynamic Evaluation of Congenital Heart Diseases

Aplicación clínica de la técnica 4D Flow en la evaluación hemodinámica de cardiopatías congénitas



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Summary

4D Flow technique refers to MR images acquired through a phase contrast angiography retrospective sequence, in which blood velocity data are obtained in three directions, in a 3-dimensional space, and through all of the cardiac cycle. With the 4D flow images, the regional and global dynamics of blood flow can be quantitatively analyzed through hemodynamic measurements, such as: average, maximum and minimum velocity, average flow, forward and regurgitation flow, ejection volume, and mathematical approximations to pressure gradients and shear forces in vessel walls; It also allows analyze qualitatively the temporal evolution of complex blood flow patterns through flow lines, particle tracers, 3D velocity graphs and vectors; representations that describe the trajectory of the blood, over time, in the cardiovascular system. These characteristics make the technique have many potential applications in clinical practice, as it provides information on the function and status of the patient's cardiovascular system. In this study we evaluated with the 4D flow technique some congenital pathologies: pulmonary stenosis, patent ductus arteriosus, and aortic stenosis.

Resumen

La técnica 4D Flow hace referencia a las imágenes de resonancia magnética (RM) adquiridas mediante una secuencia retrospectiva de angiografía contraste de fase, en la cual se obtienen datos de la velocidad de la sangre en las tres direcciones, en un espacio de 3 dimensiones (3D) y a través de todo el ciclo cardíaco. Con las imágenes obtenidas mediante 4D Flow se puede evaluar de forma cuantitativa la dinámica regional y global del flujo sanguíneo con medidas hemodinámicas, tales como: velocidad promedio, máxima y mínima, flujo latido promedio, flujo de avance y regurgitante, volumen de eyección, y aproximaciones matemáticas a los gradientes de presión y fuerzas de cizallamiento en las paredes de los vasos; además, permite analizar cualitativamente la evolución temporal de los complejos patrones de flujo sanguíneo por medio de líneas de flujo, trazadores de partículas, gráficas de velocidad 3D y vectores; representaciones que describen la trayectoria de la sangre, a través del tiempo, en el sistema cardiovascular. Estas características permiten que la técnica tenga muchas aplicaciones potenciales en la práctica clínica, ya que brindan al especialista información valiosa sobre la función y el estado del sistema cardiovascular del paciente. A continuación se evalúa mediante 4D Flow, en algunas patologías congénitas: estenosis valvular pulmonar, conducto arterioso persistente y estenosis aórtica.

Introduction

The diagnosis and study of congenital cardiopathies represent a great radiological challenge due to their

anatomical and functional complexity (1). Today, many diagnoses are made in the prenatal period with fetal echocardiography, and postnatal follow-up is done

using transthoracic echocardiography or, in specific cases, transeophageal echocardiography. These methods, being non-invasive, inexpensive and widely available, remain the first line of diagnosis and follow-up. One of its major limitations is that it is operator-dependent, which leads to greater inter- and intra-operator variability and is associated with diagnostic errors. This limitation could be reduced with rigorous training. Complementary methods using ionizing radiation, such as conventional angiography or coronary angiography and tomography, should be used with caution in order to reduce the harmful effects of accumulated radiation doses. Especially since these patients require periodic follow-up, and will be subjected to repeated imaging studies and interventions throughout their lives (2).

Cardiac magnetic resonance imaging (MRI) is a non-invasive, reproducible, sensitive and specific method for the diagnosis and follow-up of congenital heart disease. Among its many advantages are the facts that it does not use ionizing radiation, allows an anatomical and functional evaluation and, unlike the other methods, allows tissue characterization with different sequences. As it is a method of higher cost, requiring sedation assisted by an anesthesiologist (under protocol in children under 6 years of age, and in selected cases in patients from 6 to 10 years of age), and long evaluation times, it is not considered the gold standard method for initial diagnosis, but in many cases is the method of choice for post-surgical follow-up. Technological advances make this diagnostic method increasingly simple, with shorter acquisition times and more robust protocols, to obtain complete anatomical, functional and tissue characterization information. Sequences such as the 4-Dimensional Flow technique (4D Flow) are opening up the field of application of cardiac MRI (3), which allows for the evaluation of flow in heart valves, vascular structures and implanted ducts, in three planes and in time (4D). The following describes the experience in the application of the 4D Flow technique for the qualitative evaluation of three different congenital heart diseases: pulmonary valve stenosis, patent ductus arteriosus and aortic stenosis.

1. 4D Flow

The 4D Flow technique is based on the Phase Contrast Angiography (PCA) sequence, which is made up of retrospective two-dimensional (2D) acquisitions synchronized with the cardiac cycle (PCA 2D movie). The main application of this 2D technique is to measure the speed of blood in a single plane and obtain hemodynamic parameters, such as flows, volumes and velocities, which allow mathematical calculations of peak pressure gradient based on Bernoulli's formula.

The PCA 2D movie technique can be extended to a three-dimensional spatial acquisition, with the purpose of encoding the speed of the blood in the three directions of the Cartesian system and in different phases of the cardiac cycle. For this reason, it is necessary to code the blood flow in the x, y, and z axes by acquiring four sequences, three speed-sensitive and one reference (Figure 1). This technique is known as "4D Flow" because of its four-dimensional (three spatial and one temporal) acquisition characteristic.

The 4D Flow technique refers to MRI images acquired through a retrospective sequence of phase contrast angiography, in which data is obtained on the speed of blood in three directions, in a three-dimensional (3D) space and throughout the cardiac cycle (4). With the images obtained by 4D Flow (Figure 2), the regional and global dynamics of blood flow can be quantitatively evaluated by means of hemodynamic measures such as average, maximum and minimum speed, average beat flow, advance and regurgitant flow, ejection volume, and mathematical approximations of pressure gradients and shear forces; It also allows the qualitative analysis of the temporal evolution of complex blood flow patterns by means of flow lines, particle tracers, 3D velocity graphs and vectors, representations that describe the trajectory of blood through time (5-7). These characteristics make the technique have many potential applications in clinical practice, as they provide the specialist with valuable information about the function and condition of the patient's cardiovascular system.

The 4D Flow technique has great clinical potential as a tool for the study of patients with congenital cardiopathies, since it allows quantitative and qualitative analyses of the hemodynamic behaviour of the blood and its relationship with cardiac and vascular structures (8-10).

1.1 Data acquisition

4D Flow images were acquired in 3 patients, each with a different congenital heart disease: pulmonary stenosis, patent ductus arteriosus, and aortic stenosis. Using a 1.5T resonator (Philips, Achieva), we obtained Balance-FFE movie sequences, 2D and 4D flow quantification images with the 4D Flow technique, T2 black blood images and angioresonance images with 3D contrast medium.

The 4D Flow images were acquired with the following parameters: Field of View (mm) = 350 × 350, Voxel size (mm) = 2.5 × 2.5, slice thickness (mm) = 5, slices = 48, TR (ms)/TE (ms) = 4/2.1, Venc (cm/s) = 200-150, SENSE (factor) = 2, Flip angle (degrees) = 6, Phases = 16, additionally the data were performed with free breathing, electrocardiographic synchronization and a torso-cardiac coil.

1.2 Data processing

All data obtained with the 4D Flow technique was exported from the resonance equipment in an image format called PAR-REC. They were then processed on a workstation using the GTFlow software (Gyrotools LLC, Zurich, Switzerland), which allows the blood velocity to be calculated for each voxel in the three coordinated axes and in all phases of the heart cycle. Subsequently, three-dimensional representations of blood flow can be generated and the corresponding haemodynamic variables calculated.

The processing of 4D Flow images is summarized as follows: first, the vascular structures in the magnitude images are segmented using a thresholding method, second, a 3D isosurface is created based on the previous segmentation, and finally, the isosurface is used to generate a certain number of seeds or particles, which correspond to the points where the blood velocity data are calculated in the phase images.

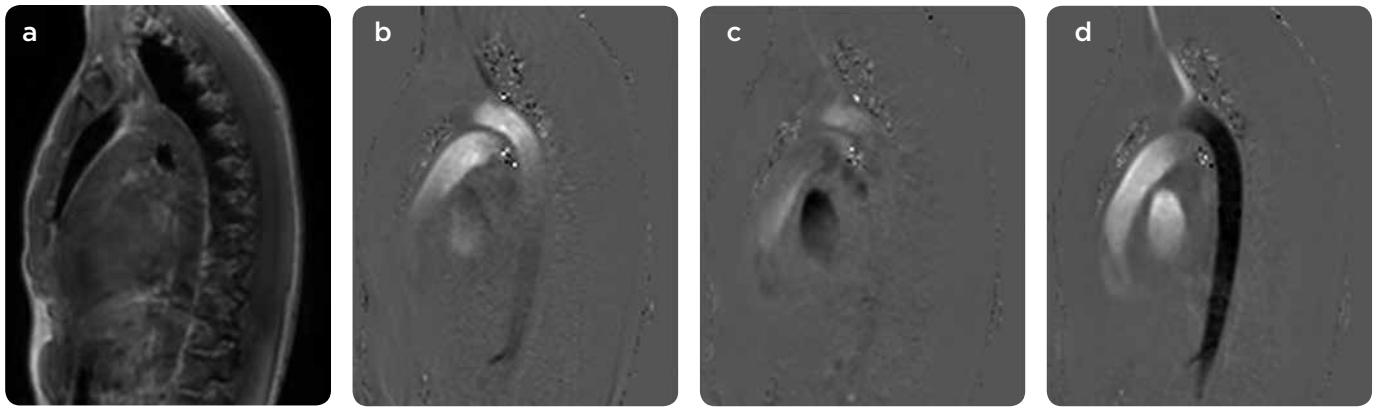


Figure 1. The 4D Flow technique needs to acquire four three-dimensional data sets: one for magnitude and three for flow coding. a) Sagittal shear magnitude. b-d) Images representing the coding of blood velocity in the three directions of space. The intensity of the pixels represents the speed and direction of the blood. Coding addresses: (b) antero-posterior, (c) right-left and (d) head-foot.

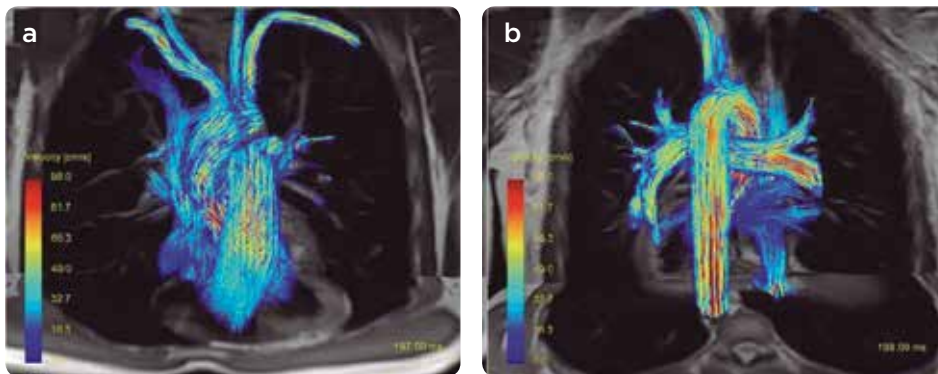


Figure 2. 3D representation of blood flow patterns in the heart and large vessels. 4D Flow sequence superimposed (recorded) with anatomical images. a) Anterior/posterior view. b) Posterior/previous view. The speed of the blood is color-coded.

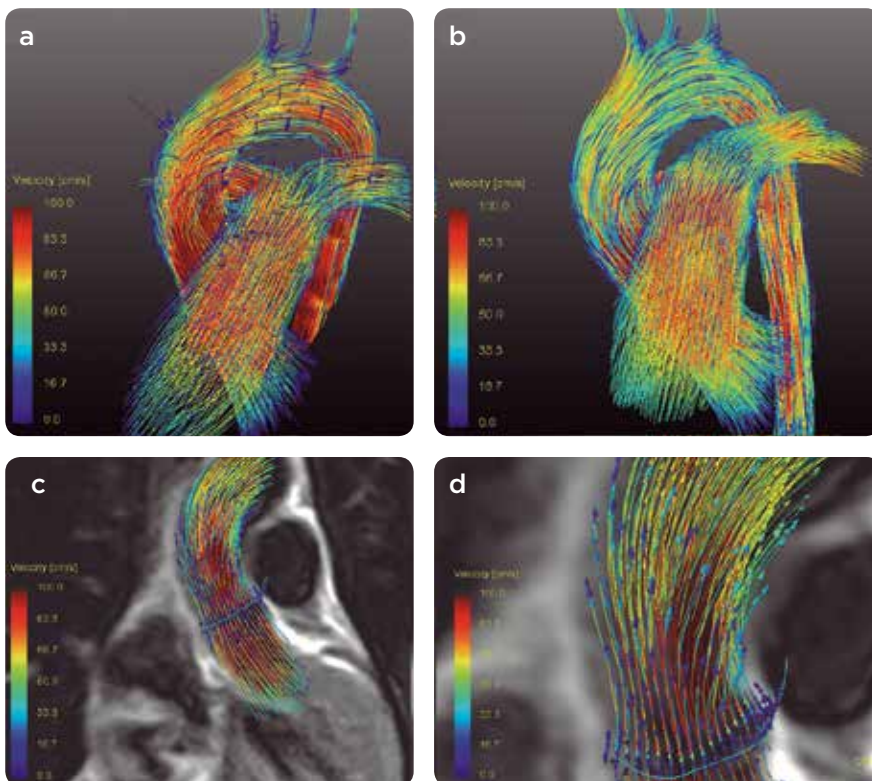


Figure 3. Qualitative analysis of the 4D Flow technique. a) Flow lines in the aorta and pulmonary arteries. b) Visualization using particle tracers. c) Particle tracers in the ascending aorta generated from a region of interest, cut at the level of the pulmonary artery. d) Vector representation of the particle tracers in the same region of interest described in (c).

1.3 Data analysis: 3D representation

The images acquired with the 4D Flow technique allow us to visualize the movement of blood through three-dimensional representations throughout the cardiac cycle and to perform a qualitative analysis of the complex blood flow patterns in a patient (Figure 3). The most common representations are described below.

- » Flow Lines: Allow visualizing the flow velocity field at each time point. Flow lines provide, through a field representation, the trajectory of fluid particles (blood) at each point in time. This provides an overview of the blood flow pattern (11).
- » Particle tracers: Allow visualizing the trajectory of the fluid particles in the velocity field through time. This representation depends on the position and time point of the particle in the cardiac cycle. Particle tracers are used to analyze the temporal evolution of blood flow patterns during the cardiac cycle (12).

1.4 Data analysis: quantification

An important advantage of the 4D Flow technique lies in the retrospective quantification of the hemodynamic parameters that can be obtained in any location of the three-dimensional images. For the quantification of the flow parameters it is possible to select cuts at any angle and locate them perpendicularly to any vessel or heart structure. 4D Flow allows you to perform hemodynamic calculations in contours or regions of interest, such as: Average, maximum and minimum speed, peak speed, average flow, forward and regurgitant flow, regurgitant fraction, systolic volume and systolic distance, among others. Additionally, it allows to analyze the values at each time point of the cardiac cycle and to perform calculations for individual voxels. On the other hand, data from the 4D Flow technique allows mathematical approximations to be made of pressure gradients in vascular structures and to calculate the shear forces on the vessel wall produced by blood flow. The graphs of some quantitative measures are shown in figure 4

2. Case presentation

The 4D Flow technique was successfully used in the cardiovascular MRI protocol in each of the following heart diseases: pulmonary valve stenosis, patent ductus arteriosus, and aortic stenosis. In addition, the 4D Flow images were used to obtain three-dimensional representations of the evolution of blood flow in the large vessels of the heart using particle tracers. The three cases are presented below to illustrate the usefulness of this technique..

2.1 Case 1

28-year-old male, with a history of heart murmur since childhood. Hospitalized for chest pain and dyspnea. The physical examination showed systolic murmur at lung focus and hypertrophic osteoarthropathy of the fingers of the upper limbs. Acute coronary syndrome was ruled out with electrocardiogram (ECG) and enzyme measurements. Echocardiography was performed where dilation and hypertrophy of the right ventricle was observed, with no signs of a short circuit from

left to right. Cardiac MRI was performed for anatomical and functional characterization (Figure 5).

2.2 Case 2

18-year-old female. History of Down syndrome and cyanotic congenital heart disease; with impaired functional class now with stage 3 New York classification (NYHA) and atypical chest pain. Physical examination found systolic murmur in aortic focus, perioral and distal cyanosis. In previous echocardiography reports there was a patent ductus arteriosus and suspicion of Eisenmenger syndrome. MRI is performed for anatomical and functional characterization (Figure 6).

2.3 Case 3

16-year-old male with a history of childhood asthma. He's manifesting multiple episodes of palpitations and syncope. A regular tachycardia of narrow QRS complexes that responded to adenosine was documented by ECG. The ECG shows signs of severe pulmonary hypertension and a bivalve aortic valve. An electrophysiological study was carried out in which automatic tachycardia of the union, a finding associated with congenital cardiopathies, was evident. It was decided to perform cardiovascular MRI to assess cardiopathy not visualized by ECG and right ventricle (Figure 7).

3. Clinical applications

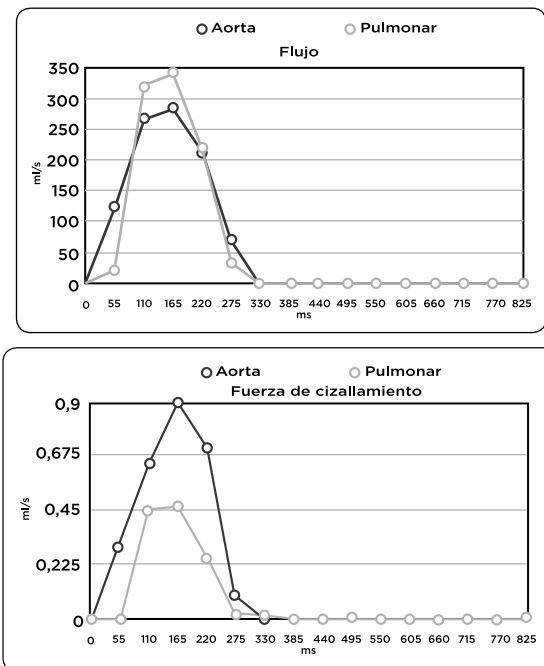


Figure 4. Quantitative measurements obtained by the 4D Flow technique in the aorta and pulmonary artery in a specific section of each artery. Upper: graphs of blood flow in the arteries, lower: the average shear force exerted on the vessel wall by the passage of blood. The blue line represents the aorta and the green represents the pulmonary artery. The x-axis of the graphs corresponds to the length of the subject's cardiac cycle.

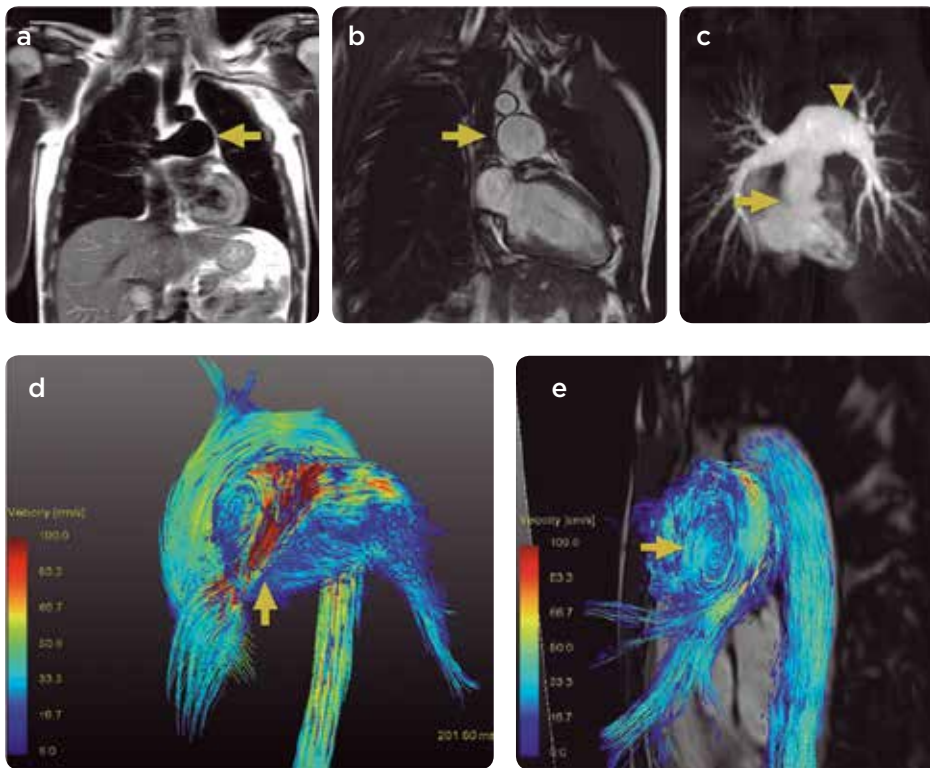


Figure 5. Case 1. a) Black blood image, coronal cut. b) Image obtained from a Balance-FFE film sequence on long axis. a and b) Marked dilation of the left pulmonary artery (arrows), with a diameter of 39 mm. c) Multiplanar reconstruction of the pulmonary circulation phase contrast angiography sequence, where pulmonary valve stenosis (arrow) and post-sterotic dilation of the trunk of the pulmonary artery, with a diameter of 38 mm, and the left pulmonary artery (arrowhead) are observed. d) Image obtained by 4D Flow: increased blood velocity (red) in the area of valvular stenosis (arrow) and turbulent flow patterns in the left pulmonary artery. The speed of the blood is coded according to the colour scale. e) Representation of the blood flow by means of particle tracers using the 4D Flow technique. Note how the blood moves in a "whirlpool" in the left pulmonary artery (arrow).

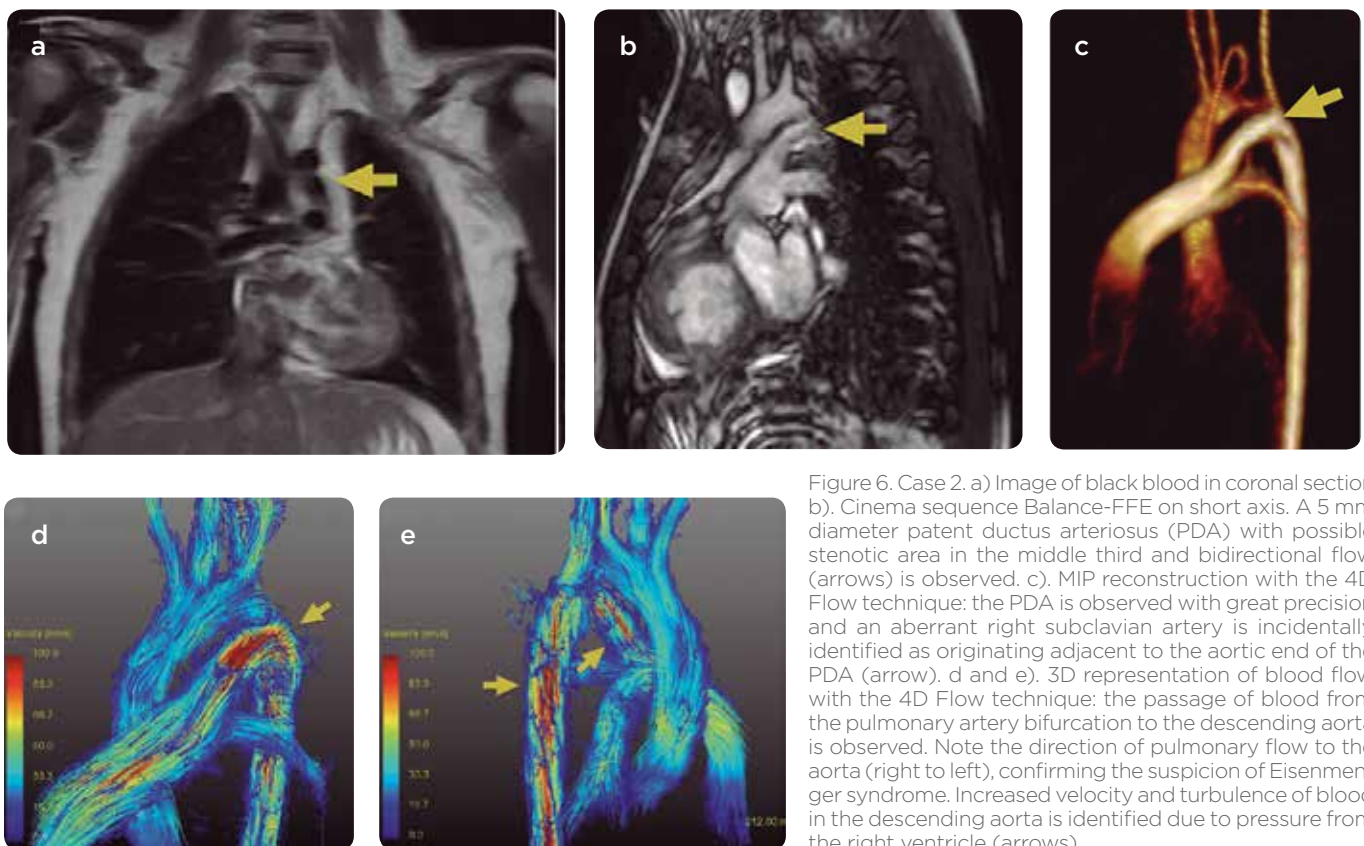


Figure 6. Case 2. a) Image of black blood in coronal section b). Cinema sequence Balance-FFE on short axis. A 5 mm diameter patent ductus arteriosus (PDA) with possible stenotic area in the middle third and bidirectional flow (arrows) is observed. c). MIP reconstruction with the 4D Flow technique: the PDA is observed with great precision and an aberrant right subclavian artery is incidentally identified as originating adjacent to the aortic end of the PDA (arrow). d and e). 3D representation of blood flow with the 4D Flow technique: the passage of blood from the pulmonary artery bifurcation to the descending aorta is observed. Note the direction of pulmonary flow to the aorta (right to left), confirming the suspicion of Eisenmenger syndrome. Increased velocity and turbulence of blood in the descending aorta is identified due to pressure from the right ventricle (arrows).

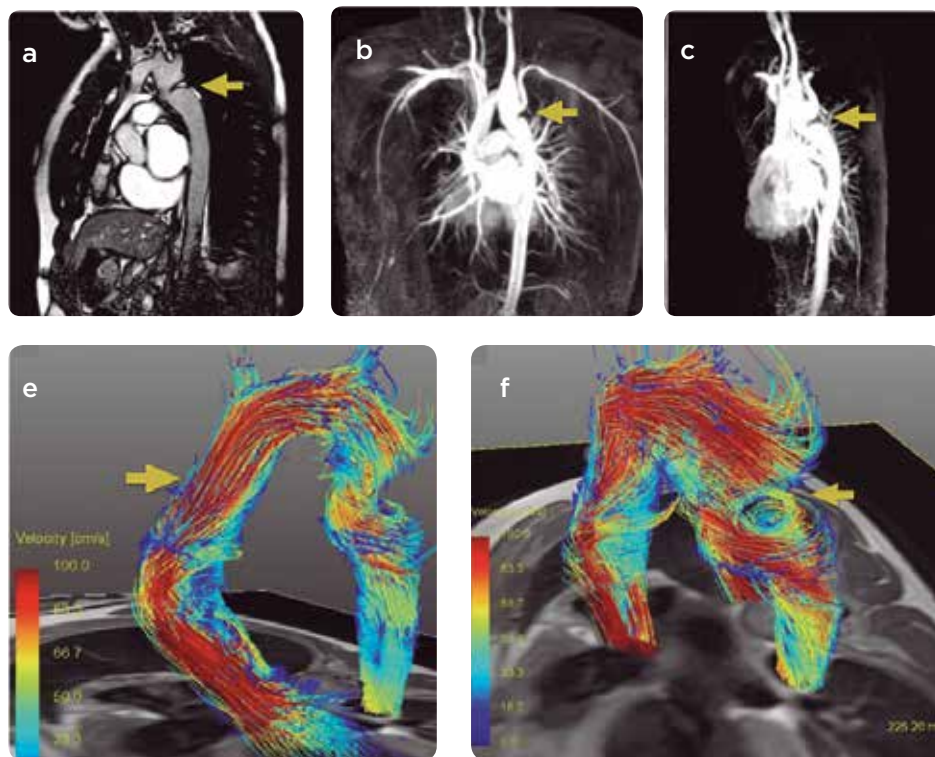


Figure 7. Case 3. a) Balance-FFE cinema sequence in a parasagittal cut on the aorta axis. b and c) Coronal and sagittal reconstructions of contrast dye angiography sequences in systemic arterial phase. Significant coarctation of the descending aorta (arrow) is observed, with a distal aortic arch diameter of 27 mm, coarctation of 18 mm and post-sterotic dilation of 26 mm. d and e) Reconstructions obtained through the 4D Flow technique overlaid with anatomical black blood images. The tortuous configuration of the ascending aorta and the turbulent blood flow through it are observed. Subsequently, a decrease in blood velocity in the descending aorta distal to the coarctation site and the helical and tortuous flow pattern that is generated after coarctation is passed is demonstrated.

Although the 2D phase contrast technique is currently considered the gold standard for the study of blood flow, the planning of this sequence is considered highly operator-dependent because the accuracy of hemodynamic data varies when the acquisition plane and structure of interest are not perpendicular. The acquisition of the 2D sequence requires less time than the 4D Flow technique; however, the latter offers a greater capacity for qualitative and quantitative analysis (13). The 4D Flow technique allows for a three-dimensional representation of blood flow patterns at each stage of the cardiac cycle. Additionally, it allows the estimation of blood flow and velocity parameters, hemodynamic biomarkers, such as shear stress in blood vessel walls and pressure gradients, without the need for intravenous contrast media (14). Another great advantage of this technique is the capacity for retrospective multiplanar analysis that is performed in the post-processing of the images, after the patient is removed from the equipment, which allows quantifying the blood flow in any arbitrary plane and in any angulation, without the need to acquire new images (15).

The 4D Flow technique can be particularly useful in congenital heart diseases where it is necessary to calculate flow variables through multiple vessels. In addition, applications have been reported in vascular stenosis, valvular lesions, and aortic coarctations, which demonstrate the potential of the technique to reveal important information about the spatio-temporal dynamics of turbulent cardiovascular flows (16,17).

Several authors have documented in previous studies the multiple clinical applications of the 4D Flow technique in the area of cardiovascular MRI. Hope et al (18) found that the risk of aneurysm formation in patients with bivalve aorta can be stratified by quantifying the shear forces obtained with 4D Flow. This allows the diagnosis

and possible interventions in the ascending aorta of these patients to be carried out with greater objectivity. In addition, with the 4D Flow technique it is possible to quantify abnormal flow and hemodynamic loading, so the risk of vascular pathology can be defined including the possibility of presenting an aneurysm or dissection before clinical manifestations occur (18).

Other examples mention the usefulness of 4D Flow in the study of pulmonary circulation, in clinical scenarios such as tetralogy of Fallot (19) or in patients with short circuits from left to right with risk of pulmonary hypertension. Additionally, it is possible to evaluate the patient's post-surgical state, analyze the flow patterns after the intervention and evaluate the efficiency of the different cavopulmonary anastomosis (20).

With regard to the evaluation of portal circulation and renal arteries, Markl et al (6) have described the potential of the 4D Flow technique to quantify blood flow in patients with portal hypertension and in the planning or monitoring of individuals with renal transplantation. Similarly, the 4D Flow technique allows the assessment of flow patterns, velocity and shear forces in aneurysms, arteriovenous malformations, carotid bulbs and other extra and intracranial territories, such as the carotid siphon, which are difficult to quantify by Doppler ultrasound (21-24).

4. Limitations

Current major limitations of 4D Flow include spatial resolution, time resolution, and total acquisition time. The latter is the main limitation for the implementation of the technique in clinical practice. From 5 to 15 min depending on the anatomical region, also depending

on the patient's respiratory and heart rate (retrospective acquisition). On the other hand, the sequence time increases significantly when a higher spatial or temporal resolution is required (25). However, acceleration methods have been proposed for image acquisition that include, according to the MRI team, parallel imaging, sampling strategies that perform correlations in the space-time domain, and radial acquisitions of k-space (26-28).

It is important to mention that 4D Flow is a highly complex technique (13), which, added to the lack of standardized protocols for image acquisition, image processing methodologies and structured reports that include both quantitative and qualitative information, means that this technique can be implemented, for the time being, in MRI centers with experience in advanced imaging techniques and with an interdisciplinary group of professionals.

It is important to mention that the 4D Flow technique is not included in the Mandatory Health Plan in Colombia, therefore, the institutions that decide to include it in their portfolio of services will have to assume the cost of the technique as an added value to the examination by which the patient was referred.

5. Conclusion

The 4D Flow technique allows the adequate qualitative evaluation of blood flow in different cardiac pathologies and a better understanding of the behavior of blood flow in congenital cardiopathies, for which reason it has become a tool with great clinical potential in cardiovascular MRI studies by providing information on blood flow patterns and quantification of hemodynamic variables.

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