



## Review

# Diagnostic and prognostic significance of cardiovascular vortex formation



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## ABSTRACT

Various forms of vortex formation in the cardiovascular system convey valuable information regarding the function of heart and great vessels. The vortex ring that forms during systole in the aortic sinus is the first that was recognized and the asymmetric transmitral vortex ring that forms in the left ventricle during diastole has been most commonly used for diagnosis and follow up of heart failure patients. Adverse vortex interaction in the heart can also occur due to valvular regurgitation and may have energetic consequences to the heart. Furthermore, vortices do exist in other chambers such as the right ventricle and may even arise in the great arteries and veins due to congenital heart disease. Here, we summarize diagnostic and prognostic significance of vortices and vortex imaging in the heart, their applications in clinical medicine, and discuss how these flow features can be used to assess functional status of the heart.

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## Introduction

Presence of vortices in the heart is a phenomenon that was first proposed by Leonardo Da Vinci in 1513. Illustrated in his drawings,

he portrayed the aortic valve leaflets being closed due to a symmetric vortex ring formed at the sinuses of Valsalva by the end of systole. The subject was not discussed further until recent years when a vast interest was reborn for studying these flow features in different chambers of the heart. These efforts were initiated by Bellhouse whose *in vitro* experiments suggested the presence of a vortex ring in the left ventricle (LV) [1]. Later on, several studies discussed the role of these vortices on blood flow momentum and energy transfer [2–5], and on that basis, some proposed diagnostic indices that can be used for clinical grading

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of the diastolic function [6]. Although, this was just the beginning, thanks to advances in cardiac imaging, different types of vortices were found in other heart chambers such as the right ventricle (RV) [7] and the atria [8–10].

The clinical application of transmitral vortex has been the main interest of these studies. Whether these flow structures reveal significant information regarding the functional status of the heart has been a question worth answering. The clinical significance of vortices was initially suggested by Gharib et al. [11] who demonstrated that major aspects of cardiac function can be “uniquely and sensitively” reflected in the optimization of early diastolic vortex formation based on the data of 110 volunteer subjects. Following the same direction, researchers graded the abnormal rapid filling phase in a group of 62 patients with diastolic dysfunction and concluded that vortex formation can be efficiently used in the clinical setting to distinguish among different grades of diastolic dysfunction [6]. Other studies discussed the application of vortex imaging in heart failure [12–14], assessment of heart valves [14–18], RV flow [19], and in congenital heart diseases [20–22].

Fredriksson et al. [23] discussed an asymmetric vortex ring surrounding the tricuspid inlets during the early and late diastolic phases, and emphasized the significance of this flow feature during normal function of the right heart. There are also hypotheses on the asymmetric redirection of blood in atrial and ventricular cavities of the looped heart in humans [24], which suggest that the asymmetries and curvatures of the looped heart have potential fluid dynamic advantages to prevent thrombus formation by affecting the flow arriving at arterial branches, thus facilitating the evolution of large and dynamically-active vertebrate animals.

This review aims to summarize diagnostic and prognostic significance of vortices and vortex imaging in the heart along with their applications in clinical medicine, and discusses how these flow features can be used to assess functional status of the heart.

### Vortex imaging to study heart failure

There are growing interests in the clinical applications of intracardiac flow analysis in various fields of cardiology. Intracardiac flow analysis is useful in evaluating the current disease status, selection of treatment strategy, assessment of response to therapy, and prediction of future clinical outcomes in patients with heart failure (HF). Therefore, in conjunction with the conventional structural and functional parameters, vortex flow analysis may contribute to the optimal management of patients with HF.

The form and dynamics of vortical flow within the LV reflect the pathophysiological link between diastolic filling and systolic ejection and have been shown to be an important predictor of adverse outcomes among patients with chronic HF [25–27]. Thus, vortex imaging can be used as a powerful tool to predict clinical outcomes in these groups of patients. Here we outline the application of vortex imaging in a variety of cardiac conditions that may lead to HF.

*Dilated cardiomyopathy (DCM)* is anatomically characterized by chamber enlargement that leads to systolic dysfunction. DCM is a good example for which intracardiac flow analysis can lead to further clinical information because its low systolic function defined by conventional ejection fraction (EF) is often misleading and not directly correlated with patients' symptoms and functional status [28,29]. In an early clinical study using echocardiographic particle imaging velocimetry (Echo-PIV), Hong et al. demonstrated the clear differences between the vortex flow in normal subjects versus DCM patients [27]. The vortex morphology in patients with abnormal LV systolic function is consistently shorter, wider and rounder compared to normal controls. Furthermore, vortex pulsatility was

found to be significantly lower in patients with DCM. Through this study, Hong et al. showed that vortex flow analysis using Echo-PIV is feasible, reproducible and can distinguish between normal and abnormal ventricular systolic function [29].

In the context of vortex flow, kinetic energy fluctuation (KEF) represents the degree of regularity in flow or turbulence. A recent study has shown that in patients with congestive heart failure and systolic dysfunction, KEF serves as an independent predictor for major adverse cardiac events (MACE) including death, heart transplantation, hospitalization due to heart failure, and significant ventricular arrhythmia that require admission. There was an inverse correlation between the two, with higher KEF associated with a lower risk for MACE (Fig. 1) [30].

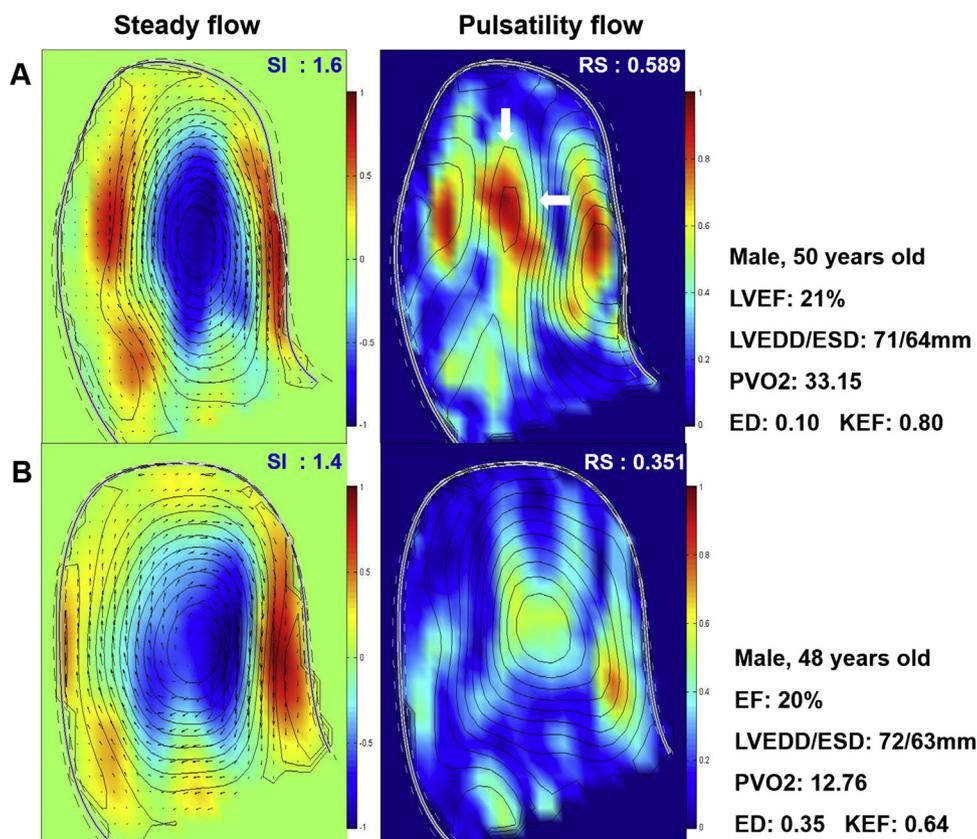
*Ischemic cardiomyopathy:* One of the most promising applications of vortex imaging in HF patients lies in the prediction of LV thrombus formation due to acute anterior wall myocardial infarction (MI). LV apical thrombus formation is a major complication in patients with LV dysfunction following an anterior MI. Although thrombus formation mechanisms are diverse, abnormalities in apical contraction and consequent changes in the fluid dynamics would lead to stagnant flow in the LV apex, which predispose to thrombus formation in these patients [31]. However, conventional echocardiographic parameters are insufficient for predicting post-MI apical thrombus formation [25]. Son et al. showed that the intraventricular vortex flow analysis is useful in evaluating the future risk of thrombus formation after acute anterior MI [13]. In particular, they showed that lower values of vortex depth and pulsatility power are strongly associated with LV apical thrombus formation. This prospective study also proposed higher incidence of LV thrombus formation in patients showing poor vortical flow pattern when diagnosed with anterior MI. These results suggest the possibility of vortex-guided anticoagulation therapy in the future [13].

### Application of vortex imaging in cardiac resynchronization therapy

In selected groups of HF patients with low EF and left bundle branch block, cardiac resynchronization therapy (CRT) has been shown to be effective in terms of predicting the prognosis and quality of life [32]. However, even by using advanced diagnostic techniques, selecting patients who are potential responders to CRT remains challenging for the reasons that are not completely understood [33]. Several studies have clearly shown the key role of echocardiography in assessing mechanical dyssynchrony before CRT [33,34]. However, due to the large variability of results, currently there is no recommended echocardiographic parameter for selection of patients undergoing CRT [35]. To overcome the limitations of conventional echocardiography, vortex flow analysis has been considered as a potentially useful tool according to several studies [36,37], including the recent one by Cimino et al. that showed significant worsening in flow-derived parameters in non-responder patients compared to responders to CRT [38].

### Vortex formation in the right heart

The RV function represents an important determinant for clinical outcome following several cardiac conditions including but not limited to congenital heart diseases (CHDs) [30,39–41]. The peculiar shape of the RV is elusive to most visualization methods and its physiological relevance is not yet completely understood. Accordingly, several questions remain unanswered, such as the relevance of the RV's wide excursion of the free wall with respect to thickening of the intraventricular septum during RV contraction, functional role of the RV inflow and outflow tracts geometry, and coupling of the RV and the pulmonary artery (or aorta) in case of a



**Fig. 1.** Left ventricular (LV) vortex flow pattern in dilated cardiomyopathy. (A) A patient without event; (B) a patient with non-sustained ventricular tachycardia. Both patients showed comparable LVEF and LV size. However, patient A showed higher pulsatility and kinetic energy fluctuation and less energy dissipation compared to patient B. SI, sphericity index; RS, relative strength; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end diastolic dimension; ESD, end systolic dimension; PVO2, peak oxygen consumption; ED, energy dissipation; KEF, kinetic energy fluctuation.

systemic RV in hypoplastic left heart syndrome (HLHS). These unknowns have led to different hypotheses on the RV mechanical and physiological functions [42].

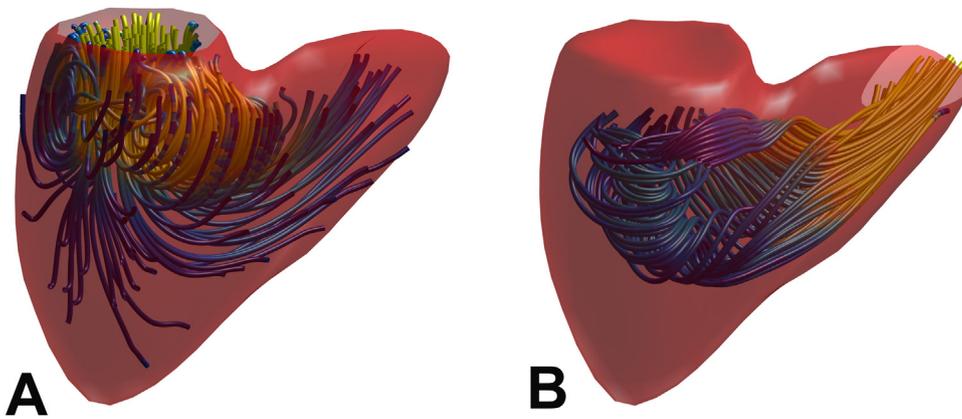
Due to its asymmetrical shape and anatomical location, RV structure and flow cannot be clearly visualized by conventional 2D echocardiography techniques. The RV's complex shape limits the information that can be acquired from echocardiography to assess its function. In general, quantifying the RV based on geometrical assumptions are only partially reliable and those information must be combined with the results obtained by multiple views to infer more reliable information [43]. More recently, the advent of 3D echocardiography permits a more comprehensive evaluation of RV geometry. Nevertheless, the availability of reliable quantification methods is still limited, or at the experimental level [44–46]. Contrary to LV whose fluid dynamics have been vastly studied, the role of fluid dynamics in RV function is yet largely unknown. Several studies using echocardiography, phase-contrast cardiac magnetic resonance (so-called “4D-Flow MR”) and numerical simulations have explored LV fluid dynamics [28,47,48]. However, the field has not yet progressed at a comparable pace for the RV. It is believed that the main reason would be the lack of techniques that can reliably map the flow in such a complex geometry. We have summarized the current-state-of-the-art on RV fluid dynamics and provided our perspectives for future studies.

**RV fluid dynamics:** The flow through the RV develops a diastolic 3D vortex that originates from the tricuspid jet that eventually rotates about an axis oriented along the RV outflow tract in systole. During the early 1990s, Peskin and McQueen performed the first numerical simulations of the flow in the entire heart including the RV [49]. Although those studies were primarily focused on

methodological improvements, they showed the complexity of the swirling motion in the RV with a rotational flow observed from multiple views [50]. A decade later, studies based on the segmentation of animal-dedicated 3D echocardiography evidenced the vortex ring formation behind the tricuspid valve whose circulation diminishes in the dilated RVs [51].

Methodological advances in studying RV fluid dynamics progressed to be more feasible in the advent of 4D-Flow MRI that permits direct measurements of time-resolved blood velocities with good spatial resolution. Visualizations with 4D-Flow MR have shown that in healthy subjects the blood entering the RV produces a vortex ring through the tricuspid valve during diastole, and then, this rotating body of blood passes into the RV outflow tract while the RV apex exhibits relatively low blood velocities. This pattern is associated with an efficient blood transit where almost half of the ejected volume is from the blood that directly flows from the right atrium (RA) toward the pulmonary valve [23]. Accordingly, the blood flow kinetic energy efficiently transfers from the RV inflow to the RV outflow tract. These observations suggest that, contrary to the LV, the wide motion of the atrioventricular plane toward the RV base significantly boosts the normal early RV filling even more than apical suction, and implies that the E-wave velocity measured at the tip of the tricuspid valve would be lower than its analogous at the mitral side [52].

The results obtained from MRI complemented by the numerical simulation, *in vitro* experiments and endocardial geometry reconstructed from 3D echocardiography have shown formation of an initially-compact trans-tricuspid vortex ring during early diastole (Fig. 2A) [7,19,53]. This vortex ring is partly dissipated due to interaction with the RV septum and breaks into a weakly turbulent flow pattern with an underlying rotation due to the



**Fig. 2.** Streamlines inside a healthy right ventricle model obtained from numerical simulation. (A) During diastole, the incoming flow gives rise to the formation of a vortex structure with a relatively ring shape. (B) During systole, the vortex gets mostly dissipated and its rotational tendency turns into a helical flow along the axis of the right ventricular outflow tract. The streamlines are color-coded based on kinetic energy from low (blue) to high (yellow).

remaining portion of the vortex. During systole, this background rotation gives rise to a helical motion spinning out along the RV outflow tract (Fig. 2B).

#### Abnormal vortical flow in congenital heart disease

Echocardiography is a well-established method for the diagnosis and follow-up of children as well as adult patients with CHD. However, RV assessment that plays a crucial role in many CHD conditions can be challenging by only relying on echocardiography, particularly after several re-operations that are common in CHD patients. In various CHDs, the RV can be of very different shapes resulting in a diverse blood flow patterns whose physiological relevance are not completely understood. Recent advances in MRI-based phase-contrast flow measurements have widened the scope of MRI's clinical applications beyond the functional measurements and follow-up to quantify the hemodynamics and risk stratification in CHD patients [22,54–56]. In particular, development of 4-dimensional flow MR imaging (4D-Flow MRI) has uniquely provided the possibility of quantifying the blood flow dynamics including vortex formation [57].

**Vortex formation in the Fontan circulation:** Fontan physiology is characterized by a single functioning pumping chamber that takes advantage of passive venous return blood flow to the lungs. Fontan circulation is considered the palliative state after multiple (usually three) corrective surgeries in CHD patients, e.g., in tricuspid atresia or the hypoplastic left heart syndrome (HLHS), in whom a biventricular repair is not possible. In Fontan circulation, the function of the single ventricle (SV) represents an important factor for the clinical outcome and long-term survival [58,59]. More recently, it has been shown that cardiac function, and not respiration, is the driving force of the venous return flow in patients with HLHS whereas respiration is the crucial factor for the blood flow amplitude in the vena cava [60]. Therefore, comprehensive imaging and analysis of blood flow dynamics can lead to better understanding of the altered blood flow in this iatrogenic univentricular circulation. Vortex formation in the venous side of the Fontan circulation can be observed in the Fontan tunnel of patients with a lateral tunnel where the atrial part is often dilated [61,62] or at the site of the cavopulmonary connections. The *in vivo* visualization of such vortices can be best achieved by using 4D-Flow MRI [61,63]. Although computer simulations have been used for quantification of vortices with blood flow pathlines in the Fontan circulation [61,64], 4D-Flow MRI has the greatest potential to reliably map the flow in the complex Fontan circulation and overall in CHD patients.

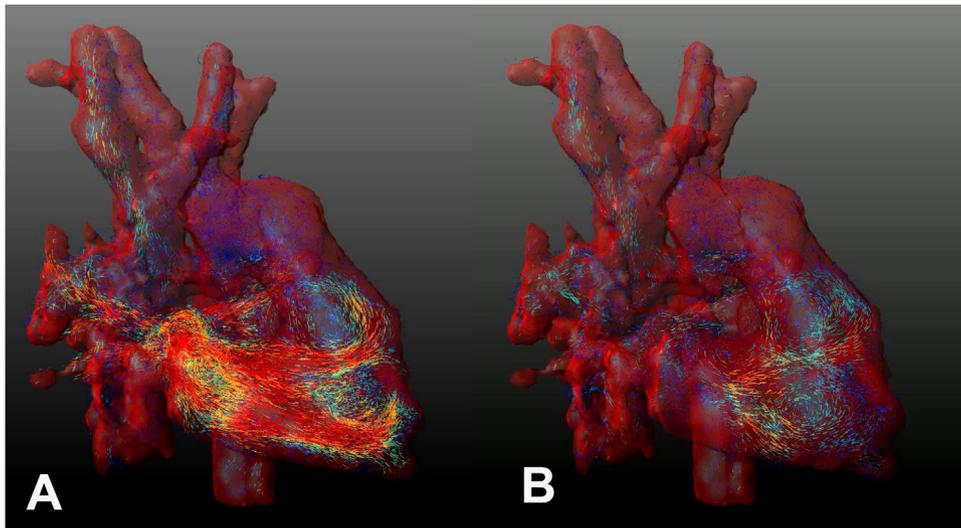
The advantage of vortex formation and optimal arrangement in total extracardiac cavopulmonary connection has been quantitatively studied *in vitro* by Amodeo et al. [65]. They reported that the total extracardiac cavopulmonary connection with left-sided diversion of the inferior vena caval conduit anastomosis leads to a central vortex that regulates the caval flow and provides a relatively more energy-efficient flow pattern compared to the total extracardiac cavopulmonary connection with directly-opposed cavopulmonary anastomoses [65].

In single ventricle physiology where the RV serves as the systemic ventricle e.g. in the HLHS, the vortex formation within the single ventricle has not been thoroughly studied yet. In Fig. 3A, we show an example of the diastolic blood flow across the tricuspid valve in a single ventricle of a HLHS patient with Fontan circulation whose ejection fraction is within normal range with no detectable tricuspid regurgitation. Using 4D-Flow MRI, formation of a vortex ring in the RV during diastole as well as its dissipation by end-systole can be observed (Fig. 3B). To date, the clinical significance of these vortices as surrogate for RV diastolic function (or their role in energy dissipation and blood flow momentum) is unknown.

The RV's complex shape and function in CHD patients is an important determinant for blood flow dynamics, which may have implications on the long-term clinical outcome of these patients. To understand the cause and effect between form and function, future prospective studies need investigate how specific shapes of the RV inflow and outflow tracts and the coupling of the RV and the neo-aorta in HLHS in CHD patients affect the patients' outcome.

**Tetralogy of Fallot:** Tetralogy of Fallot (TOF) is a common form of cyanotic CHD with a prevalence of 3.4 per 10,000 live births in the United States [66] and accounts for approximately 6.8% of live-born patients with CHD [67]. TOF presents as a heterogeneous range of phenotypes whose major anatomical features are pulmonary and subpulmonary stenosis or atresia, a subaortic ventricular septal defect (VSD), and RV hypertrophy. Although total repair during infancy reduces the risk of several complications [68,69], pulmonary regurgitation (PR) and RV dilation frequently occur even years after the TOF repair. These adverse outcomes are particularly more common in subjects with transannular patch and RV outflow tract (RVOT) dilation [70]. 4D-Flow MRI provides additional information on blood flow profiles, e.g., vortex formation in the pulmonary artery [71,72].

The first systematic application of RV fluid dynamics in a clinical context was shown in patients with repaired TOF (r-TOF) using echo-PIV [73]. This study was performed in 4-chamber-view,



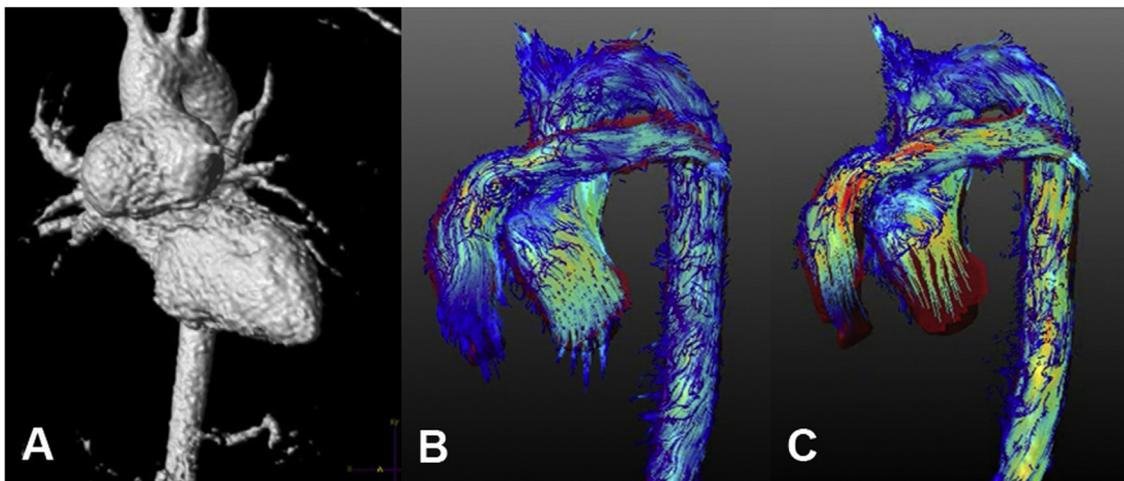
**Fig. 3.** Flow in the single ventricle of a HLHS patient with Fontan circulation is acquired by 4D-flow MRI (right anterior oblique view). (A) Diastolic vortex ring developed from the trans-tricuspid jet; (B) vortex dissipation at end-systole.

which only shows a partial view of the complex 3D RV flow. Nevertheless, the study demonstrated that flow pattern in patients with TOF generates higher circulation and reduced energy dissipation, which are assumed to be related to ventricular enlargement and changes in the chamber compliance. These results evidence the need to introduce simple comprehensive descriptions of the RV fluid dynamics in global terms to be used for clinical evaluations.

Under normal conditions, hemodynamic forces are directed along the base-apex direction in diastole, and they rotate toward the RVOT during systole with no significant component in the transversal direction between the septum and the free wall [47,74]. It is expected that deviations from this natural dynamic balance may lead to abnormal RV function even during the early stages of dysfunction. More recent studies have shown that in TOF patients with pulmonary regurgitation, RV blood motion is altered in a way that affects hemodynamic forces and leads to a disturbed pattern of kinetic energy [75,76]. These effects are assumed to disturb the balance of intraventricular pressure in presence of tricuspid valve regurgitation due to the backward flow directed toward the RVOT.

*Vortex formation in the great arteries:* Dextro-transposition of the great arteries (D-TGA) is the second most frequent cyanotic congenital cardiovascular malformation, usually requiring arterial switch operation (ASO) in the neonatal period [77,78]. The current routine surgical technique for ASO includes the Lecompte technique, which is characterized by transferring the pulmonary artery bifurcation in front of the ascending aorta [79].

It has been previously shown that patients who undergo Lecompte technique present with vortex formation, supranatural helical blood flow, and a reduced indexed cross-sectional area of the left pulmonary artery compared to the patients after spiral reconstruction (complete anatomical correction) [80]. Fig. 4 compares the pathline reconstruction in a TGA patient after ASO and Lecompte technique using GTFLOW software (GyroTools GmbH, Winterthur, Switzerland). Abnormal vortices are formed (arrows) in the often-dilated aortic sinus (Fig. 4A and B) and pulmonary artery (Fig. 4C). Lalezari et al. [81] demonstrated that the neo-aortic root after ASO, which is originally the root of the pulmonary artery, has histomorphological deficiencies in collagen content and myocardial support that may explain the dilatation of the neo-aortic root (Fig. 4A) and consequently the typical flow pattern with vortex



**Fig. 4.** Transposition of the great arteries after arterial switch operation. (A) Anterior–posterior view: long-term follow-up with MRI shows a significantly dilated aortic sinus in contrast-enhanced magnetic resonance-angiography (MRA); (B) lateral view: vortex formation in the distal pulmonary arteries (arrow) in early systole; (C) lateral view: vortex formation in the aortic sinus in late systole.

formation in the aortic sinus (Fig. 4C). Due to the steep angle between the main pulmonary artery and left and right pulmonary artery branches after ASO with Lecompte technique, an accelerated systolic blood flow can usually be observed along with vortex formation in the distal main pulmonary artery (Fig. 4B).

Using 4D-Flow MRI, Riesenkampff et al. [82] analyzed the blood flow patterns in the aorta and pulmonary trunk of TGA patients. They compared 29 patients with repaired transposition, concordant atrioventricular and discordant ventriculoarterial connection, to 8 healthy volunteers. They found that contrary to the healthy control groups, helicity was absent in all TGA patients, independent of the type of operation. They also reported that partial helices were observed in the ascending aorta of 58% of patients after arterial switch. In the pulmonary trunk, laminar flow was mainly observed in healthy volunteers and in patients after arterial switch, whereas vortex formation was present in 88% of patients after atrial redirection (Mustard or Senning Operation [83,84]), which is considered a historic surgical technique [82].

### Abnormal vortical flow in heart valve disease

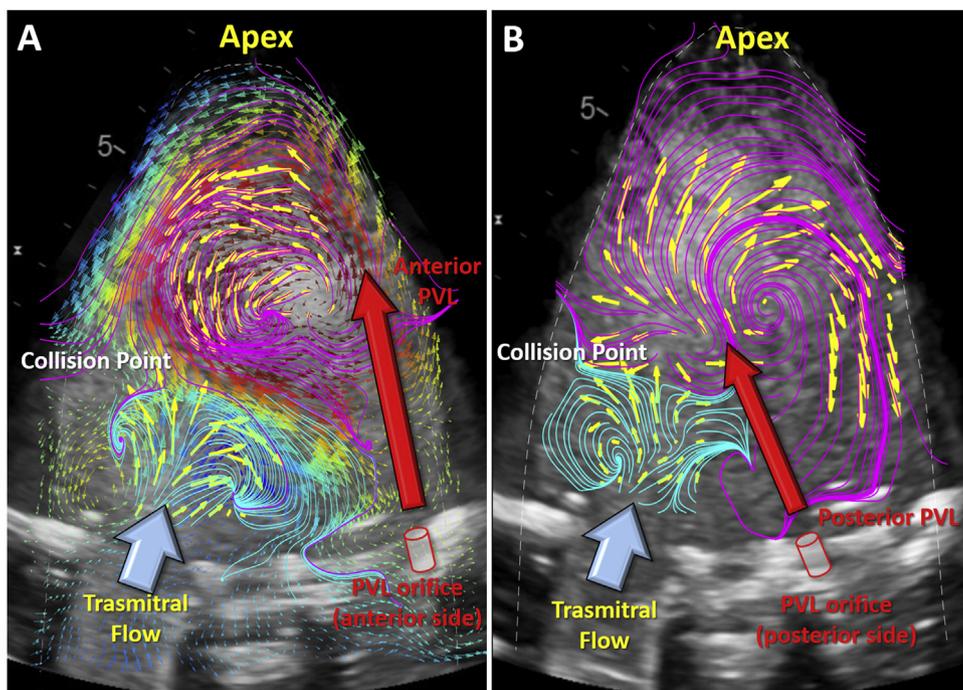
Heart valve diseases are in various types and each type affects vortex formation in a unique form. Abnormal fluid dynamics situations due to aortic regurgitation (AR), aortic stenosis (AS), and mitral regurgitation (MR) directly and indirectly affect transmitral vortex formation. Additionally, vortex formation can be easily affected due to the severity of valve insufficiency, valve morphology, blood pressure, and cardiac output. Here we summarize *in vivo* and *in vitro* studies on abnormal vortex formation induced by heart valve diseases.

**Aortic regurgitation and paravalvular leak:** Aortic regurgitant jet flows backward into the LV, which leads to volume overload, elevation of end-diastolic pressure, and LV enlargement. A recent *in vitro* study using Echo-PIV has quantified how AR jet affects intraventricular flow field [85]. The regurgitant jet flowing into the LV through the center of aortic valve impinges the inferolateral

wall of the LV and interferes with the transmitral vortex formation that eventually leads to an increase in intraventricular energy dissipation. As the severity of AR progresses from trace to moderate, the energy dissipation accentuates. In another *in vitro* study, Morisawa et al. reported that paravalvular leak (PVL) after transcatheter aortic valve replacement leads to abnormal intraventricular vortex formation and disturbed fluid dynamics condition [86]. Furthermore, they showed that the location of PVL orifice strongly affects the vortex interaction between the PVL jet and transmitral flow (Fig. 5). Compared to the anterior PVL, posterior PVL generates more significant flow disturbance with and increased flow kinetic energy, which suggests that posterior PVL has more negative impact on intraventricular fluid dynamics.

**Aortic stenosis and bicuspid aortic valve:** Restriction in aortic valve opening because of AS leads to abnormal flow field downstream of the valve. AS due to bicuspid aortic valve results in complex vortex formation in the ascending aorta because of its eccentric orifice. Few studies have described how bicuspid aortic valve affects the fluid dynamics in aorta. Through *in vitro* experiments and using particle image velocimetry (PIV), Saikrishnan et al. showed that the location of the valve orifice strongly affects the vortex formation in the aortic sinus and ascending aorta [87]. The eccentric orifice location results in eccentric ejected jet, which forms a high velocity vortex with larger turbulent kinetic energy compared to control trileaflet valves. In another study, Kimura et al. computationally analyzed how transvalvular jet through a bicuspid aortic valve influences the aortic flow field [88]. According to their study, bicuspid AS leads to helical blood flow in the ascending aorta and increases the wall shear stress in the greater curvature of the proximal ascending aorta. Their results corroborate with other studies on helical blood flow in the ascending aorta of patients with bicuspid aortic valve [89,90].

**Mitral regurgitation:** MR is commonly diagnosed by echocardiography and patients with severe MR ultimately need surgical or interventional treatment. In moderate or severe MR, massive regurgitant jet streaming into the left atrium (LA) leads to LA enlargement and increased LA pressure, which sometimes result in



**Fig. 5.** Intraventricular vortex interaction in presence of paravalvular leak (PVL). (A) Anterior PVL jet streams into an LV model alongside the anterior wall and travels toward the apex. The PVL jet forms a counterclockwise vortex at the vicinity of the apex and collides with transmitral flow. (B) Posterior PVL jet streams toward the posterior left ventricular wall, forms a large clockwise vortex and ultimately collides with the transmitral flow and significantly disturbs the LV flow field.

atrial fibrillation. MR jets are heterogenous and vastly complex because their form and direction vary and can be easily affected by the LV systolic function as well as LA morphology and mitral leaflets. Therefore, a general description of LA fluid dynamics in MR patients is considerably challenging. Dyverfeldt et al. analyzed LA vortex formation in five patients with prolapse of posterior mitral leaflet using 4D-Flow MRI and compared those with healthy control subjects [91]. They reported a distinct form of vortex formation in the vicinity of inflow from the left pulmonary vein during both systole and diastole, whereas in patients with MR, the dominant systolic vortex occurred near the route of the MR jet alongside the atrial septum that led to a boost in turbulent kinetic energy.

**Vortex formation through mechanical heart valves:** The form and function of the vortices due to the mechanical heart valves (MHVs) are far from normal. Unlike bioprosthetic heart valves (BHVs), the MHVs' rigid leaflets boost the flow turbulence, which increases energy dissipation.

Faludi et al. described the intraventricular vortex formation in patients with a bileaflet mechanical mitral position *versus* healthy control subjects using echo-PIV [16]. Based on the echocardiogram's three-chamber view, transmitral flow entering the LV forms a clockwise vortex, and then the rotating blood flow is redirected toward the LV outflow tract at the end diastole. In contrast, in patients with a bileaflet MHV, a counterclockwise vortex is formed at the end diastole before flowing across the LV center towards the LV outflow tract. Other studies have reported that the flow through the MHVs is strongly affected by the valve design (*i.e.* mono or bileaflet), leaflet opening angle, and valve orientation [92–94].

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## References

- Bellhouse BJ. Fluid mechanics of a model mitral valve and left ventricle. *Cardiovasc Res* 1972;6:199–210.
- Dabiri JO, Gharib M. The role of optimal vortex formation in biological fluid transport. *Proc Biol Sci* 2005;272:1557–60.
- Kheradvar A, Gharib M. On mitral valve dynamics and its connection to early diastolic flow. *Ann Biomed Eng* 2009;37:1–13.
- Kheradvar A, Gharib M. Influence of ventricular pressure drop on mitral annulus dynamics through the process of vortex ring formation. *Ann Biomed Eng* 2007;35:2050–64.
- Kheradvar A, Milano M, Gharib M. Correlation between vortex ring formation and mitral annulus dynamics during ventricular rapid filling. *ASAIO J* 2007;53:8–16.
- Kheradvar A, Assadi R, Falahatpisheh A, Sengupta PP. Assessment of transmitral vortex formation in patients with diastolic dysfunction. *J Am Soc Echocardiogr* 2012;25:220–7.
- Falahatpisheh A, Pedrizzetti G, Kheradvar A. Three-dimensional reconstruction of cardiac flows based on multi-planar velocity fields. *Exp Fluids* 2014;55:1–15.
- Rodríguez Muñoz D, Markl M, Moya Mur JL, Barker A, Fernández-Golfín C, Lancellotti P, et al. Intracardiac flow visualization: current status and future directions. *Eur Heart J Cardiovasc Imaging* 2013;14:1029–38.
- Ishizaki U, Nagao M, Shiina Y, Fukushima K, Takahashi T, Shimomiya Y, et al. Prediction of Fontan-associated liver disease using a novel cine magnetic resonance imaging “vortex flow map” in the right atrium. *Circ J* 2018;82:2143–51.
- Gaeta S, Dyverfeldt P, Eriksson J, Carlhäll C-J, Ebberts T, Bolger AF. Fixed volume particle trace emission for the analysis of left atrial blood flow using 4D Flow MRI. *Magn Reson Imaging* 2018;47:83–8.
- Gharib M, Rambod E, Kheradvar A, Sahn DJ, Dabiri JO. Optimal vortex formation as an index of cardiac health. *Proc Natl Acad Sci U S A* 2006;103:6305–8.
- Abe H, Caracciolo G, Kheradvar A, Pedrizzetti G, Khandheria BK, Narula J, et al. Contrast echocardiography for assessing left ventricular vortex strength in heart failure: a prospective cohort study. *Eur Heart J Cardiovasc Imaging* 2013;14:1049–60.
- Son J-W, Park W-J, Choi J-H, Houle H, Vannan MA, Hong G-R, et al. Abnormal left ventricular vortex flow patterns in association with left ventricular apical thrombus formation in patients with anterior myocardial infarction: a quantitative analysis by contrast echocardiography. *Circ J* 2012;76:2640–6.
- Kheradvar A, Houle H, Pedrizzetti G, Tonti G, Belcik T, Ashraf M, et al. Echocardiographic particle image velocimetry: a novel technique for quantification of left ventricular blood vorticity pattern. *J Am Soc Echocardiogr* 2010;23:3102–11.
- Charonko J, Kumar R, Stewart K, Little W, Vlachos P. Vortices formed on the mitral valve tips aid normal left ventricular filling. *Ann Biomed Eng* 2013;41:1049–61.
- Faludi R, Szulik M, D'Hooge J, Herijgers P, Rademakers F, Pedrizzetti G, et al. Left ventricular flow patterns in healthy subjects and patients with prosthetic mitral valves: an in vivo study using echocardiographic particle image velocimetry. *J Thorac Cardiovasc Surg* 2010;139:1501–10.
- Zhang H, Zhang J, Zhu X, Chen L, Liu L, Duan Y, et al. The left ventricular intracavitary vortex during the isovolumic contraction period as detected by vector flow mapping. *Echocardiography* 2012;29:579–87.
- Markl M, Draney MT, Miller DC, Levin JM, Williamson EE, Pelc NJ, et al. Time-resolved three-dimensional magnetic resonance velocity mapping of aortic flow in healthy volunteers and patients after valve-sparing aortic root replacement. *J Thorac Cardiovasc Surg* 2005;130:456–63.
- Mangual JO, Domenichini F, Pedrizzetti G. Describing the highly three dimensional right ventricle flow. *Ann Biomed Eng* 2012;40:1790–801.
- Geiger J, Markl M, Herzer L, Hirtler D, Loeffelbein F, Stiller B, et al. Aortic flow patterns in patients with Marfan syndrome assessed by flow-sensitive four-dimensional MRI. *J Magn Reson Imaging* 2012;35:594–600.
- Frydrychowicz A, Markl M, Hirtler D, Harloff A, Schlenk C, Geiger J, et al. Aortic hemodynamics in patients with and without repair of aortic coarctation: in vivo analysis by 4D flow-sensitive magnetic resonance imaging. *Invest Radiol* 2011;46:317–25.
- Rickers C, Kheradvar A, Sievers H-H, Falahatpisheh A, Wegner P, Gabbert D, et al. Is the Lecompte technique the last word on transposition of the great arteries repair for all patients? A magnetic resonance imaging study including a spiral technique two decades postoperatively. *Interact Cardiovasc Thorac Surg* 2016;22:817–25.
- Fredriksson AG, Zajac J, Eriksson J, Dyverfeldt P, Bolger AF, Ebberts T, et al. 4-D blood flow in the human right ventricle. *Am J Physiol Heart Circ Physiol* 2011;301:H2344–50.
- Kilner PJ, Yang G-Z, Wilkes AJ, Mohiaddin RH, Firmin DN, Yacoub MH. Asymmetric redirection of flow through the heart. *Nature* 2000;404:759–61.
- Hong G-R, Kim M, Pedrizzetti G, Vannan MA. Current clinical application of intracardiac flow analysis using echocardiography. *J Cardiovasc Ultrasound* 2013;21:155–62.
- Pedrizzetti G, Domenichini F. Nature optimizes the swirling flow in the human left ventricle. *Phys Rev Lett* 2005;95:108101.
- Hong G-R, Pedrizzetti G, Tonti G, Li P, Wei Z, Kim JK, et al. Characterization and quantification of vortex flow in the human left ventricle by contrast echocardiography using vector particle image velocimetry. *JACC: Cardiovasc Imaging* 2008;1:705–17.
- Kim I-C, Hong G-R, Pedrizzetti G, Shim CY, Kang S-M, Chung N. Usefulness of left ventricular vortex flow analysis for predicting clinical outcomes in patients with chronic heart failure: a quantitative vorticity imaging study using contrast echocardiography. *Ultrasound Med Biol* 2018;44:1951–9.
- Kim I-C, Hong G-R. Intraventricular flow: more than pretty pictures. *Heart Fail Clin* 2019;15:257–65.
- Wheeler M, Leipsic J, Trinh P, Raju R, Alaamri S, Thompson CR, et al. Right ventricular assessment in adult congenital heart disease patients with right ventricle-to-pulmonary artery conduits. *J Am Soc Echocardiogr* 2015;28:522–32.
- Beppu S, Izumi S, Miyatake K, Nagata S, Park YD, Sakakibara H, et al. Abnormal blood pathways in left ventricular cavity in acute myocardial infarction. Experimental observations with special reference to regional wall motion abnormality and hemostasis. *Circulation* 1988;78:157–64.
- Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA, et al. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). *Eur Heart J* 2013;34:2281–329.
- Auricchio A, Tang AS, Merkely B, Wilkoff BL, Blomström-Lundqvist C, Israel C, et al. 2012 EHRA/HRS expert consensus statement on cardiac resynchronization therapy in heart failure: implant and follow-up recommendations and management: a registered branch of the European Society of Cardiology (ESC), and the Heart Rhythm Society; and in collaboration with the Heart Failure Society of America (HFSa), the American Society of Echocardiography (ASE), the American Heart Association (AHA), the European Association of Echocardiography (EAE) of the ESC and the Heart Failure Association of the ESC (HFA). Endorsed by the governing bodies of AHA, ASE, EAE, HFSa, HFA, EHRA, and HRS. *Europace* 2012;14:1236–86.
- Dohi K, Suffoletto MS, Schwartzman D, Ganz L, Pinsky MR, Gorcsan III J. Utility of echocardiographic radial strain imaging to quantify left ventricular dyssynchrony and predict acute response to cardiac resynchronization therapy. *Am J Cardiol* 2005;96:112–6.
- Chung Eugene S, Leon Angel R, Tavazzi L, Sun J-P, Nihoyannopoulos P, Merlino J, et al. Results of the Predictors of Response to CRT (PROSPECT) Trial. *Circulation* 2008;117:2608–16.

- [36] Pedrizzetti G, Martiniello AR, D'Onofrio A, Caso P, Bianchi V, Tonti G. Changes in electrical activation modify the orientation of left ventricular flow momentum: novel observations using echocardiographic particle image velocimetry. *Eur Heart J Cardiovasc Imaging* 2015;17:203–9.
- [37] Zorzi A, Muraru D, Corrado D, Bertaglia E, Badano L, Siciliano M, et al. Cardiac resynchronization therapy by multipoint pacing improves response of left ventricular mechanics and fluid dynamics: a three-dimensional and particle image velocimetry echo study. *Europace* 2016;19:1833–40.
- [38] Cimino S, Palombizio D, Cicogna F, Cantisani D, Reali M, Filomena D, et al. Significant increase of flow kinetic energy in “nonresponders” patients to cardiac resynchronization therapy. *Echocardiography* 2017;34:709–15.
- [39] Leary PJ, Kurtz CE, Hough CL, Waiss M-P, Ralph DD, Sheehan FH. Three-dimensional analysis of right ventricular shape and function in pulmonary hypertension. *Pulm Circ* 2012;2:34–40.
- [40] Haddad F, Hunt SA, Rosenthal DN, Murphy DJ. Right ventricular function in cardiovascular disease, Part I. *Circulation* 2008;117:1436–48.
- [41] Baumgartner H, Bonhoeffer P, De Groot NMS, de Haan F, Deanfield JE, Galie N, et al. ESC Guidelines for the management of grown-up congenital heart disease (new version 2010): the Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC). *Eur Heart J* 2010;31:2915–57.
- [42] Sengupta PP, Narula J. RV form and function: a piston pump, vortex impeller, or hydraulic ram? *JACC Cardiovasc Imaging* 2013;6:636–9.
- [43] Lang RM, Badano LP, Mor-Avi V, Afzal J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;28:1–39.e14.
- [44] Fernández-Golfín C, Zamorano JL. Three-dimensional echocardiography and right ventricular function. The beauty and the beast? *Circ Cardiovasc Imaging* 2017;10:e006099.
- [45] Nagata Y, Wu VC-C, Kado Y, Otani K, Lin F-C, Otsuji Y, et al. Prognostic value of right ventricular ejection fraction assessed by transthoracic 3D echocardiography. *Circ Cardiovasc Imaging* 2017;10:e005384.
- [46] Muraru D, Spadotto V, Cecchetto A, Romeo G, Aruta P, Ermacorà D, et al. New speckle-tracking algorithm for right ventricular volume analysis from three-dimensional echocardiographic data sets: validation with cardiac magnetic resonance and comparison with the previous analysis tool. *Eur Heart J Cardiovasc Imaging* 2016;17:1279–89.
- [47] Töger J, Arvidsson PM, Bock J, Kanski M, Pedrizzetti G, Carlsson M, et al. Hemodynamic forces in the left and right ventricles of the human heart using 4D flow magnetic resonance imaging: Phantom validation, reproducibility, sensitivity to respiratory gating and free analysis software. *PLoS ONE* 2018;13:e0195597.
- [48] Pedrizzetti G, Domenichini F. Left ventricular fluid mechanics: the long way from theoretical models to clinical applications. *Ann Biomed Eng* 2015;43:26–40.
- [49] Peskin CS, McQueen DM. Cardiac fluid dynamics. *Crit Rev Biomed Eng* 1992;20:451–9.
- [50] Peskin CS, McQueen DM. Fluid dynamics of the heart and its valve. In: Othmer HG, Adler FR, Lewis MA, Dallon JC, editors. *Case studies in mathematical modeling: ecology, physiology, and cell biology*. Englewood Cliffs, NJ: Prentice Hall; 1997. p. 309–37.
- [51] Paspouliarides A, Shu M, Shah A, Womack MS, Glower DD. Diastolic right ventricular filling vortex in normal and volume overload states. *Am J Physiol Heart Circ Physiol* 2003;284:H1064–72.
- [52] Carlsson M, Heiberg E, Toger J, Arheden H. Quantification of left and right ventricular kinetic energy using four-dimensional intracardiac magnetic resonance imaging flow measurements. *Am J Physiol Heart Circ Physiology* 2011;302:H893–900.
- [53] Mangual JO, Domenichini F, Pedrizzetti G. Three dimensional numerical assessment of the right ventricular flow using 4D echocardiography boundary data. *Eur J Mech B/Fluids* 2012;35:25–30.
- [54] Geiger J, Markl M, Stiller B, Arnold R. Impaired continuity of flow in congenital heart disease with single ventricle physiology. *Interact Cardiovasc Thorac Surg* 2011;12:87–90.
- [55] Romeih S, Aguib H, Yacoub M. Utility of 4D flow mapping in Eisenmenger syndrome with pulmonary atresia. *Cardiol Young* 2016;26:1581–9.
- [56] Geiger J, Hirtler D, Gottfried K, Rahman O, Bollache E, Barker AJ, et al. Longitudinal evaluation of aortic hemodynamics in Marfan syndrome: new insights from a 4D flow cardiovascular magnetic resonance multi-year follow-up study. *J Cardiovasc Magn Reson* 2017;19:33.
- [57] Markl M, Kilner PJ, Ebberts T. Comprehensive 4D velocity mapping of the heart and great vessels by cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2011;13:7.
- [58] Cohen MS, Dagaincourt N, Zak V, Baffa JM, Bartz P, Dragulescu A, et al. The Impact of the left ventricle on right ventricular function and clinical outcomes in infants with single right ventricle anomalies up to 14 months of age. *J Am Soc Echocardiogr* 2018;31:1151–7.
- [59] Ohye RG, Schranz D, D'Udekem Y. Current therapy for hypoplastic left heart syndrome and related single ventricle lesions. *Circulation* 2016;134:1265–79.
- [60] Gabbert DD, Hart C, Jerosch-Herold M, Wegner P, Ravesh MS, Voges I, et al. Heart beat but not respiration is the main driving force of the systemic venous return in the Fontan circulation. *Sci Rep* 2019;9:2034.
- [61] Restrepo M, Tang E, Haggerty CM, Khiabani RH, Mirabella L, Bethel J, et al. Energetic implications of vessel growth and flow changes over time in Fontan patients. *Ann Thorac Surg* 2015;99:163–70.
- [62] Hart C, Gabbert DD, Pardun E, Kramer H-H, Voges I, Rickers C, et al. Anatomical and functional assessment of the intra-atrial lateral tunnel in the Fontan circulation. *Eur J Cardiothorac Surg* 2013;44:462–7.
- [63] Trusty PM, Restrepo M, Kanter KR, Yoganathan AP, Fogel MA, Slesnick TC. A pulsatile hemodynamic evaluation of the commercially available bifurcated Y-graft Fontan modification and comparison with the lateral tunnel and extracardiac conduits. *J Thorac Cardiovasc Surg* 2016;151:1529–36.
- [64] Bove EL, de Leval MR, Migliavacca F, Guadagni G, Dubini G. Computational fluid dynamics in the evaluation of hemodynamic performance of cavopulmonary connections after the norwood procedure for hypoplastic left heart syndrome. *J Thorac Cardiovasc Surg* 2003;126:1040–7.
- [65] Amodeo A, Grigioni M, Oppido G, Daniele C, D'Avenio G, Pedrizzetti G, et al. The beneficial vortex and best spatial arrangement in total extracardiac cavopulmonary connection. *J Thorac Cardiovasc Surg* 2002;124:471–8.
- [66] Parker SE, Mai CT, Canfield MA, Rickard R, Wang Y, Meyer RE, et al. Updated national birth prevalence estimates for selected birth defects in the United States, 2004–2006. *Birth Defects Res A Clin Mol Teratol* 2010;88:1008–16.
- [67] Rauch R, Hofbeck M, Zweier C, Koch A, Zink S, Trautmann U, et al. Comprehensive genotype-phenotype analysis in 230 patients with tetralogy of Fallot. *J Med Genet* 2010;47:321–31.
- [68] van de Wall EE, Mulder, Barbara JM. Pulmonary valve replacement in patients with tetralogy of Fallot and pulmonary regurgitation: early surgery similar to optimal timing of surgery? *Eur Heart J* 2005;26:2614–5.
- [69] Dietl CA, Cazzaniga ME, Dubner SJ, Perezbalino NA, Torres AR, Favaloro RG. Life-threatening arrhythmias and RV dysfunction after surgical repair of tetralogy of Fallot. Comparison between transventricular and transatrial approaches. *Circulation* 1994;90(5 (Pt 2)):II7–12.
- [70] Shin HJ, Park Y-H, Shin YR, Park HK, Choi JY, Jung JW, et al. Factors associated with progression of right ventricular enlargement and dysfunction after repair of tetralogy of Fallot based on serial cardiac magnetic resonance imaging. *Eur J Cardiothorac Surg* 2016;50:464–9.
- [71] Köhler B, Gasteiger R, Preim U, Theisel H, Gutberlet M, Preim B. Semi-automatic vortex extraction in 4D PC-MRI cardiac blood flow data using line predicates. *IEEE Trans Vis Comput Graph* 2013;19:2773–82.
- [72] Vasanawala SS, Hanneman K, Alley MT, Hsiao A. Congenital heart disease assessment with 4D flow MRI. *J Magn Reson Imaging* 2015;42:870–86.
- [73] Kutty S, Li L, Danford DA, Houle H, Datta S, Mancina J, et al. Effects of right ventricular hemodynamic burden on intraventricular flow in tetralogy of Fallot: an echocardiographic contrast particle imaging velocimetry study. *J Am Soc Echocardiogr* 2014;27:1311–8.
- [74] Arvidsson PM, Töger J, Carlsson M, Steding-Ehrenborg K, Pedrizzetti G, Heiberg E, et al. Left and right ventricular hemodynamic forces in healthy volunteers and elite athletes assessed with 4D flow magnetic resonance imaging. *Am J Physiol Heart Circ Physiol* 2016;312:H314–28.
- [75] Sjöberg P, Töger J, Hedström E, Arvidsson P, Heiberg E, Arheden H, et al. Altered biventricular hemodynamic forces in patients with repaired tetralogy of Fallot and right ventricular volume overload because of pulmonary regurgitation. *Am J Physiol Heart Circ Physiol* 2018;315:H1691–702.
- [76] Sjöberg P, Bidhult S, Bock J, Heiberg E, Arheden H, Gustafsson R, et al. Disturbed left and right ventricular kinetic energy in patients with repaired tetralogy of Fallot: pathophysiological insights using 4D-flow MRI. *Eur Radiol* 2018;28:4066–76.
- [77] Prêtre R, Tamisier D, Bonhoeffer P, Mauriat P, Pouard P, Sidi D, et al. Results of the arterial switch operation in neonates with transposed great arteries. *Lancet* 2001;357:1826–30.
- [78] De Praetere H, Vandecasteele J, Rega F, Daenen W, Marc G, Eyskens B, et al. 20 years of arterial switch operation for simple TGA. *Acta Chir Belg* 2014;114:92–8.
- [79] Lecompte Y, Zannini L, Hazan E, Jarreau MM, Bex JP, Tu TV, et al. Anatomic correction of transposition of the great arteries. *J Thorac Cardiovasc Surg* 1981;82:629–31.
- [80] Sievers H-H, Putman LM, Kheradvar A, Gabbert D, Wegner P, Scheewe J, et al. 4D flow streamline characteristics of the great arteries twenty years after Lecompte and direct spiral arterial switch operation (DSASO) in simple TGA. *Glob Cardiol Sci Pract* 2016;2016:201629.
- [81] Lalezari S, Hazekamp MG, Bartelings MM, Schoof PH, Gittenberger-de Groot AC. Pulmonary artery remodeling in transposition of the great arteries: relevance for neo-aortic root dilatation. *J Thorac Cardiovasc Surg* 2003;126:1053–60.
- [82] Riesenkampff E, Nordmeyer S, Al-Wakeel N, Kropf S, Kutty S, Berger F, et al. Flow-sensitive four-dimensional velocity-encoded magnetic resonance imaging reveals abnormal blood flow patterns in the aorta and pulmonary trunk of patients with transposition. *Cardiol Young* 2014;24:47–53.
- [83] Houck CA, Teuwen CP, Bogers AJJC, de Groot NMS. Atrial tachyarrhythmias after atrial switch operation for transposition of the great arteries: treating old surgery with new catheters. *Heart Rhythm* 2016;13:1731–8.
- [84] Baysa SJ, Olen M, Kanter RJ. Arrhythmias following the Mustard and Senning operations for dextro-transposition of the great arteries: clinical aspects and catheter ablation. *Cardiac Electrophysiol Clin* 2017;9:255–71.
- [85] Okafor I, Raghav V, Condado JF, Midha PA, Kumar G, Yoganathan AP. Aortic regurgitation generates a kinematic obstruction which hinders left ventricular filling. *Ann Biomed Eng* 2017;45:1305–14.
- [86] Morisawa D, Falahatpisheh A, Avenatti E, Little SH, Kheradvar A. Intraventricular vortex interaction between transmitral flow and paravalvular leak. *Sci Rep* 2018;8:15657.
- [87] Saikrishnan N, Yap C-H, Milligan NC, Vasilyev NV, Yoganathan AP. In vitro characterization of bicuspid aortic valve hemodynamics using particle image velocimetry. *Ann Biomed Eng* 2012;40:1760–75.

- [88] Kimura N, Nakamura M, Komiya K, Nishi S, Yamaguchi A, Tanaka O, et al. Patient-specific assessment of hemodynamics by computational fluid dynamics in patients with bicuspid aortopathy. *J Thorac Cardiovasc Surg* 2017;153:S52–62.e3.
- [89] Vergara C, Viscardi F, Antiga L, Luciani GB. Influence of bicuspid valve geometry on ascending aortic fluid dynamics: a parametric study. *Artif Organs* 2012;36:368–78.
- [90] Barker AJ, Markl M, Bürk J, Lorenz R, Bock J, Bauer S, et al. Bicuspid aortic valve is associated with altered wall shear stress in the ascending aorta. *Circ Cardiovasc Imaging* 2012;5:457–66.
- [91] Dyverfeldt P, Kvitting J-PE, Carlhäll CJ, Boano G, Sigfridsson A, Hermansson U, et al. Hemodynamic aspects of mitral regurgitation assessed by generalized phase-contrast MRI. *J Magn Reson Imaging* 2011;33:582–8.
- [92] Su B, Kabinejadian F, Phang HQ, Kumar GP, Cui F, Kim S, et al. Numerical modeling of intraventricular flow during diastole after implantation of BMHV. *PLoS ONE* 2015;10:e0126315.
- [93] Van Rijk-Zwikker GL, Delemarre BJ, Huysmans HA. The orientation of the bileaflet CarboMedics valve in the mitral position determines left ventricular spatial flow patterns. *Eur J Cardiothorac Surg* 1996;10:513–20.
- [94] Querzoli G, Fortini S, Cenedese A. Effect of the prosthetic mitral valve on vortex dynamics and turbulence of the left ventricular flow. *Phys Fluids* 2010;22:041901.