

# How can Four-Dimensional Magnetic Resonance Imaging Improve the Diagnosis of Heart Disease?

Ciaran Grafton-Clarke<sup>1,2</sup>, Liandra Ramachenderam<sup>2</sup>, Gareth Matthews<sup>1,2</sup>, Jordi Broncano<sup>3</sup>, Pankaj Garg<sup>1,2,\*</sup> 

<sup>1</sup>Norwich Medical School, University of East Anglia, Norwich, UK

<sup>2</sup>Norfolk and Norwich University Hospitals, Norwich, UK

<sup>3</sup>Hospital San Juan de Dios, HT Médica, Córdoba, Spain

\*Correspondence: [p.garg@uea.ac.uk](mailto:p.garg@uea.ac.uk) (Pankaj Garg)

## Abstract

This review describes the evolution and enhanced diagnostic capabilities introduced by four-dimensional (4D) flow cardiac magnetic resonance (CMR) in cardiovascular imaging. It charts the historical advancements from echocardiography through to two-dimensional phase-contrast magnetic resonance imaging (2D-PC MRI), culminating in the adoption of 4D flow MRI. This technique affords exhaustive, time-resolved, three-dimensional visualisations of intracardiac and vascular blood flow, refining the accuracy of cardiovascular assessments over traditional methods, especially in complex anatomical settings. The review elaborates on the capacity of 4D flow MRI to offer unparalleled insights into flow dynamics, vessel wall interactions, and cardiac function, thereby enhancing disease detection, risk stratification, and therapeutic evaluations. It accentuates the impact of 4D flow MRI on modern cardiological practices, highlighting its pivotal role in advancing diagnostics and patient management in the context of diverse cardiovascular pathologies.

**Key words:** 4D flow MRI; valvular heart disease; pulmonary hypertension; heart failure; echocardiography; 2D-PC MRI

Submitted: 1 July 2024 Revised: 30 August 2024 Accepted: 9 September 2024

## Introduction

Blood flow within the heart and major arteries is inherently pulsatile, multidimensional, and multidirectional. Its accurate assessment is crucial for evaluating cardiovascular hemodynamics (Secomb, 2016). Echocardiography, a cornerstone in heart disease diagnostics, underwent significant advancements during the 1960s and 70s (Edler and Lindström, 2004).

In the 1960s, continuous wave Doppler technology was introduced, which allowed for the measurement of blood flow velocities along the entire path of the ultrasound beam (Coman and Popescu, 2015). This technique was particularly valuable for assessing peak velocities and pressure gradients in valvular heart disease. The 1970s brought the development of pulse wave Doppler, which enabled precise localisation of blood flow measurements at specific points (Pereira et al, 2015). This advancement was especially useful for evaluating the hemodynamic impact of valvular heart disease and assessing diastolic function.

### How to cite this article:

Grafton-Clarke C, Ramachenderam L, Matthews G, Broncano J, Garg P. How can Four-Dimensional Magnetic Resonance Imaging Improve the Diagnosis of Heart Disease? *Br J Hosp Med.* 2024. <https://doi.org/10.12968/hmed.2024.0382>

Copyright: © 2024 The Author(s).

In the late 1980s, two-dimensional phase-contrast magnetic resonance imaging (2D-PC MRI) emerged as a major advancement in cardiovascular imaging. 2D-PC MRI is a non-invasive imaging technique that allows for the measurement of blood velocity in multiple directions across a plane. Unlike traditional Doppler echocardiography, which relies on angle-dependent assumptions, 2D-PC MRI offers angle-independent velocity measurements. This means 2D-PC MRI can provide accurate flow information, even when the direction of flow is complex or when it is difficult to align the imaging plane with the blood flow, such as in areas with turbulent flow or vessels with unusual geometries (Garcia et al, 2019). However, despite these advantages, one notable limitation of 2D-PC MRI is its relatively lower spatial resolution compared to echocardiography. Spatial resolution refers to the ability of an imaging modality to distinguish small structures that are close together. The lower spatial resolution of 2D-PC MRI affects its ability to assess small anatomical features or subtle structural abnormalities.

The next evolution in cardiac MRI was the development of four-dimensional flow (4D flow MRI) in the early 2000s. 4D flow MRI is an advanced imaging technique that captures three-dimensional spatial data and three-dimensional velocity data of blood flow. This information is encoded in each pixel within the heart and vessels over the complete cardiac cycle (time being the fourth dimension) (Gorecka et al, 2022). In simpler terms, 4D flow MRI provides a comprehensive view of how blood moves in all directions within the heart and major vessels over time.

Initially, 4D flow MRI faced challenges such as lengthy acquisition times (over one hour) and complex data processing. However, advancements in acceleration methods, including parallel imaging techniques, have significantly improved its feasibility. Parallel imaging involves the use of multiple receiver coils that simultaneously capture different portions of the image, thereby reducing the time needed to acquire the complete dataset (Bissell et al, 2023). Further improvements in motion compensation techniques, which correct for the movement of the heart during the scan, and valve tracking capabilities, which ensure accurate measurement of flow through moving heart valves, along with the enhancements in MRI hardware and post-processing software, have transformed 4D flow MRI into a practical and versatile imaging tool. These advancements have revolutionised the ability to diagnose and monitor cardiovascular conditions, providing unprecedented insights into flow patterns, vessel wall interactions, and cardiac function that were previously unattainable with traditional imaging techniques. Table 1 provides a comparison between echocardiography, 2D-PC MRI, and 4D flow MRI.

Four-dimensional flow MRI offers several important benefits. One major advantage is the ability to select any region within the three-dimensional (3D) data volume retrospectively, meaning that clinicians can analyse different areas of interest after the initial scan without needing to perform additional imaging. This unrestricted planar access permits retrospective flow measurements, enhancing the flexibility and utility of the data collected.

**Table 1. Differences between echocardiography, 2D-PC MRI and 4D flow MRI.**

Feature	Echocardiography	2D-PC MRI	4D flow MRI
Measurement type	PW: Blood flow velocity at specific points CW: High-velocity blood flow along a single line	Velocity and flow quantification across a plane	Velocity and flow quantification in 3D over time
Dimensionality	1D (along ultrasound beam)	2D (in a defined plane)	4D (3D spatial + time)
Spatial resolution	PW: Resolution depends on sample volume, typically 1–2 mm in depth and width CW: Measures along a single line, so no depth resolution	It can resolve flow within a single plane, typically with a 1–3 mm spatial resolution. Thickness depends on the imaging protocol, but often 5–8 mm	Typically 1–3 mm spatial resolution in all three dimensions. Voxel size varies, often 1–22 mm isotropic, enabling detailed flow visualisation
Temporal resolution	High (frame rate >50 Hz)	Moderate (temporal resolution 40–50 ms)	Moderate (temporal resolution 40–50 ms)
Field of view	Limited to the beam path	Limited to cross-section region of interest	Truly unlimited and can cover the entire heart
Clinical applications	PW: Peak velocity, time-velocity integral, valve area CW: Peak velocity, pressure gradient, valve area	Flow quantification, shunts, valvular assessment	Comprehensive flow dynamics, complex flow patterns, and haemodynamic assessment
Advantages	Real-time, high temporal resolution, easy to perform	Quantitate flow assessment, directionality, and phase encoding. Fast acquisition	Comprehensive flow assessment, visualisation of complex flow patterns. Not radiographer-dependent
Limitations	PW: Angle-dependent, limited sample volume, aliasing CW: Angle-dependent, no depth resolution, aliasing	Requires longer acquisition time, breath-holds needed, limited to 2D planes	Time-consuming data acquisition and processing, high computational requirements
Patient preparation	Minimal	Requires MRI-compatible environment, breath-holding	

Aliasing: a phenomenon where velocities exceeding the Nyquist limit are incorrectly represented as lower velocities. Breath-holding: a common requirement in MRI imaging to minimise motion artefacts by asking patients to hold their breath during image acquisition. Field of view: the extent of the observable area that an imaging modality can capture at one time. Spatial resolution: the ability of an imaging modality to distinguish small details. Temporal resolution: the ability of an imaging modality to capture fast-moving structures by taking images in rapid succession. Voxel size: the smallest distinguishable box-shaped part of a three-dimensional image. 2D-PC MRI, two-dimensional phase-contrast magnetic resonance imaging; 4D flow MRI, four-dimensional flow magnetic resonance imaging; PW, pulse-wave Doppler; CW, continuous-wave Doppler; 1D, one-dimensional; 3D, three-dimensional.

Secondly, the analysis of 4D flow acquisitions allows for a comprehensive assessment of blood flow that extends beyond basic phase-contrast parameters, such as the speed, volume, and direction of blood. As an advanced imaging technique, 4D flow MRI can estimate the hemodynamic effects at the interface between blood and other tissue types, such as myocardium and vessel walls, as well as visualise flow signatures within the cardiac structures (Crandon et al, 2017). Examples of hemodynamic parameters that can be derived from 4D flow data include kinetic energy (energy of blood flow due to its motion), wall shear stress (a frictional force that blood flow exerts on the inner walls of vessels), viscous energy loss (energy dissipation due to the internal friction within a fluid as it flows), and the presence of vortex formations (a measure of the ‘spinning’ motion of flow) (Demirkiran et al, 2022; Kaur et al, 2020). These tools have clear translational benefits. Research using 4D flow MRI is advancing the understanding of how abnormalities in blood flow correlate with symptoms and disease prognosis. This technology allows clinicians to identify specific ‘flow signatures’, unique patterns of blood flow, that can be used to diagnose disease, stratify risk for important clinical outcomes, and monitor the hemodynamic response to treatment (Zhuang et al, 2021).

Moreover, 4D flow MRI is a versatile clinical tool with diverse applications across a range of disease states. For example, it can assess abnormal flow dynamics, such as those occurring in stenotic regions, regurgitant jets, or turbulence. Understanding these dynamics can provide critical information on the severity of disease and guide clinical decisions, including the need for surgical intervention (Gorecka et al, 2022).

Another application is the visualisation of complex flow phenomena, such as vortex formation (circular flow patterns), helical flows (a spiral-like twisting of flow that can indicate changes in blood vessel structure or function), and intracardiac flow disturbances (abnormal flow patterns within the heart chambers). The advanced imaging capabilities are particularly useful in predicting outcomes for patients with conditions such as pulmonary arterial hypertension, where the precise characterisation of blood flow can inform the likely disease trajectory and the effectiveness of therapeutic interventions (Ota et al, 2022).

In this article, we review the application of 4D flow MRI across several key cardiovascular disease states, including valvular heart disease, aortopathies, and pulmonary arterial hypertension. We highlight the value of 4D flow MRI in offering detailed anatomical and functional insights, which are crucial for the accurate assessment of these conditions. We hope this synthesis of relevant and up-to-date literature underscores the transformative potential of 4D flow MRI, which is applicable to all practitioners providing care to patients with cardiovascular disease.

## Clinical Utility of 4D Flow MRI in Aortic Valve Disease

Aortic valve disease is the most common form of valvular heart disease, affecting approximately 5% of individuals over the age of 65 (Lindroos et al, 1993; Rajamannan et al, 2011). Accurate detection and grading of disease severity are cru-

cial, as these assessments directly influence clinical decisions, including whether to proceed with surgical intervention (Benjamin et al, 2018).

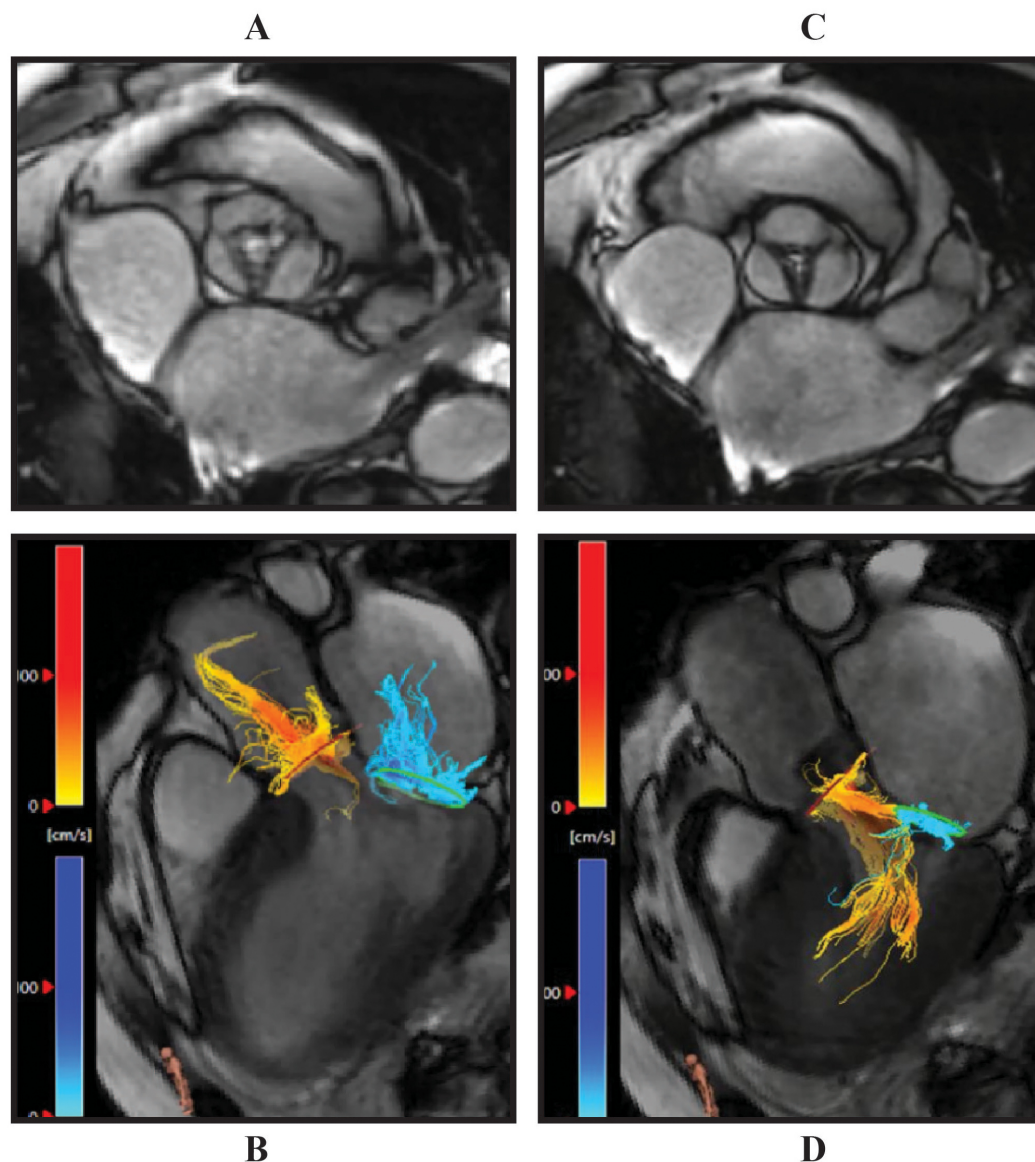
Aortic stenosis (AS) is most commonly the result of age-related degeneration, which leads to an obstruction of forward blood flow through the aortic valve. When the disease progresses to a severe state, AS significantly impacts morbidity and mortality (Blanken et al, 2018). Key biomarkers used to determine the severity of AS include peak systolic blood flow velocities (the maximum speed and direction of blood during the systolic period), transvalvular gradient (the difference in pressure between the left ventricle (LV) and the aorta during blood ejection), and aortic valve area.

Echocardiography, the primary diagnostic tool for AS, measures these biomarkers but has limitations. Its accuracy can be compromised by geometric assumptions, such as assuming that heart valves are perfectly circular or that the shape of the ventricular chamber is ellipsoidal. Additionally, flow misalignment can occur when the direction of blood flow is not parallel to the ultrasound beam, which can lead to inaccuracies, especially in cases of eccentric flow patterns (where blood flows abnormally off-centre through the valve) or dynamic flow jets (flow patterns that vary in response to changing cardiac conditions) (Garcia et al, 2003). Similarly, 2D-PC MRI, which captures blood flow in only one direction, often underestimates flow rates and peak velocities compared to echocardiography due to its limited ability to account for complex flow dynamics (Adriaans et al, 2020; Søndergaard et al, 1993).

4D flow MRI offers a more comprehensive solution for evaluating aortic valve disease by incorporating three velocity-encoded directions (x, y, and z). This means that it can measure blood flow velocity in three dimensions, capturing the full complexity of blood movement through the heart and vessels. One significant advantage of 4D flow MRI is its ability to retrospectively select the highest velocity site for quantification, making it particularly effective for assessing multiple and eccentric jets (jets not aligned along a straight path). This capability results in more accurate measurements of peak velocities and mean transvalvular gradients, thereby avoiding the underestimation of these parameters that often occurs with 2D-PC imaging (Adriaans et al, 2020; Blanken et al, 2018; Garcia et al, 2019). Furthermore, pressure gradient assessment across the aortic valve using 4D flow MRI is consistent with invasive measurements and, when compared to Doppler echocardiography, it shows superior agreement with results obtained from invasive catheterisation (Grafton-Clarke et al, 2022). This makes 4D flow MRI a valuable tool for non-invasive yet highly accurate evaluation of aortic valve diseases.

The precision of 4D flow MRI is particularly advantageous in situations with dynamic and eccentric flow patterns, as it can more accurately capture the nuances of blood flow. This enhanced accuracy is crucial for better assessing the severity of AS, especially in cases where the stenosis is not uniform or where the flow patterns are highly complex. Fig. 1 illustrates a case of degenerative stenotic valvular heart disease, where the patient has both aortic stenosis and regurgitation, as well as mitral regurgitation. In this example, flow acceleration through the stenotic lesion can be observed, along with adaptive left ventricular hypertrophy. Importantly, during diastole, aortic regurgitation competes with mitral inflow, restricting the opening

of the anterior mitral valve leaflet. The degree of spatial flow delineation provided by 4D flow is not achievable with continuous-wave, pulse-wave, or colour Doppler echocardiography.



**Fig. 1. Application of 4D flow MRI streamline visualisation in valvular heart disease.** In systole (A,B), there is flow acceleration in the aorta, with irregular thickening of the tips of the aortic valve leaflets. There is also retrograde flow through the mitral valve, consistent with mitral regurgitation. In diastole (C,D), there is regurgitation through the aortic valve, with a jet directed towards the anterior leaflet of the mitral valve that is restricting mitral inflow (blue streamlines).

Additionally, the 4D flow MRI's ability to measure turbulent kinetic energy (TKE) offers further insight into the hemodynamic impact of AS. TKE quantifies the energy loss due to turbulence, providing information about how efficiently blood flows through a stenotic valve (Mansoor and Garcia, 2023). This comprehensive hemodynamic quantification can be particularly valuable for understanding patient symptoms and assessing the potential impact on cardiac function (Binter et

al, 2017). For example, a study has shown that left ventricular blood flow kinetic energy, as measured using 4D flow MRI, correlates with exercise performance during the six-minute walk test (Elhawaz et al, 2021). The same research indicates that impaired left ventricular kinetics before aortic surgery can predict adverse remodeling following valvular intervention. This highlights the role of 4D flow MRI as a marker of functional status, as well as a predictor of outcome following surgical intervention.

Aortic regurgitation (AR) occurs when the aortic valve leaflets fail to close properly, resulting in the backflow of blood from the aorta into the left ventricle. AR is most frequently caused by age-related degeneration of the valve. Precise grading of AR is essential for appropriate clinical management, as it helps determine the timing of valve repair or replacement to prevent progressive heart damage and worsening symptoms. Alongside traditional 2D echocardiography, which remains the standard diagnostic tool in the United Kingdom, 4D flow MRI has emerged as a valuable diagnostic tool. 4D flow MRI demonstrates exceptional sensitivity (100%) and specificity (98%) for AR detection and is particularly effective in overcoming the challenges posed by eccentric jets and non-circular valve orifices that can complicate echocardiographic assessments (Chelu et al, 2016; Crandon et al, 2017).

4D flow MRI offers valuable hemodynamic insights that go beyond those offered by conventional imaging modalities. By capturing both qualitative and quantitative data, 4D flow provides detailed information on complex flow dynamics, such as peak velocity, flow volume and regurgitant fraction. These parameters are crucial for evaluating aortic valve function and understanding the progression of aortic valve disease. Moreover, 4D flow MRI uniquely characterises intricate patterns of disturbed flow, including helical flow patterns that may increase the risk of aortic dilatation and dissection (Hope et al, 2009), vortex formation associated with abnormal shear stress (force exerted parallel to the vessel wall), potentially leading to valve degeneration (Takehara et al, 2020), and flow eccentricity, which can impact valve durability and function (Farag et al, 2019). These capabilities underscore the utility of 4D flow MRI in clinical settings, spanning pre-operative assessments, post-operative evaluations, and risk stratification. In these contexts, 4D flow MRI offers more accurate quantification of the regurgitant fraction and better prediction of symptoms and clinical outcomes compared to echocardiography (Myerson, 2021; Ranard et al, 2023).

Furthermore, 4D flow MRI's ability to detect left ventricular remodelling, an adaptive response of the heart to volume overload caused by AR, is useful (Elhawaz et al, 2021). Recognising these changes early can guide timely intervention, potentially preventing significant ventricular damage and reducing the risk of complications such as heart failure (Vollema et al, 2019). The consistency and reliability of 4D flow MRI are further enhanced by its adherence to the conservation of mass principle (a core concept in fluid dynamics stating that mass cannot be created or destroyed in a closed system), ensuring that measurements of blood flow are not only precise but also reproducible across different imaging sessions and patient positions (Juffermans et al, 2021; Roes et al, 2009; Westenberg et al, 2008). This

reproducibility is crucial for both clinical research and routine patient care, as it provides consistent and reliable data that support therapeutic decisions.

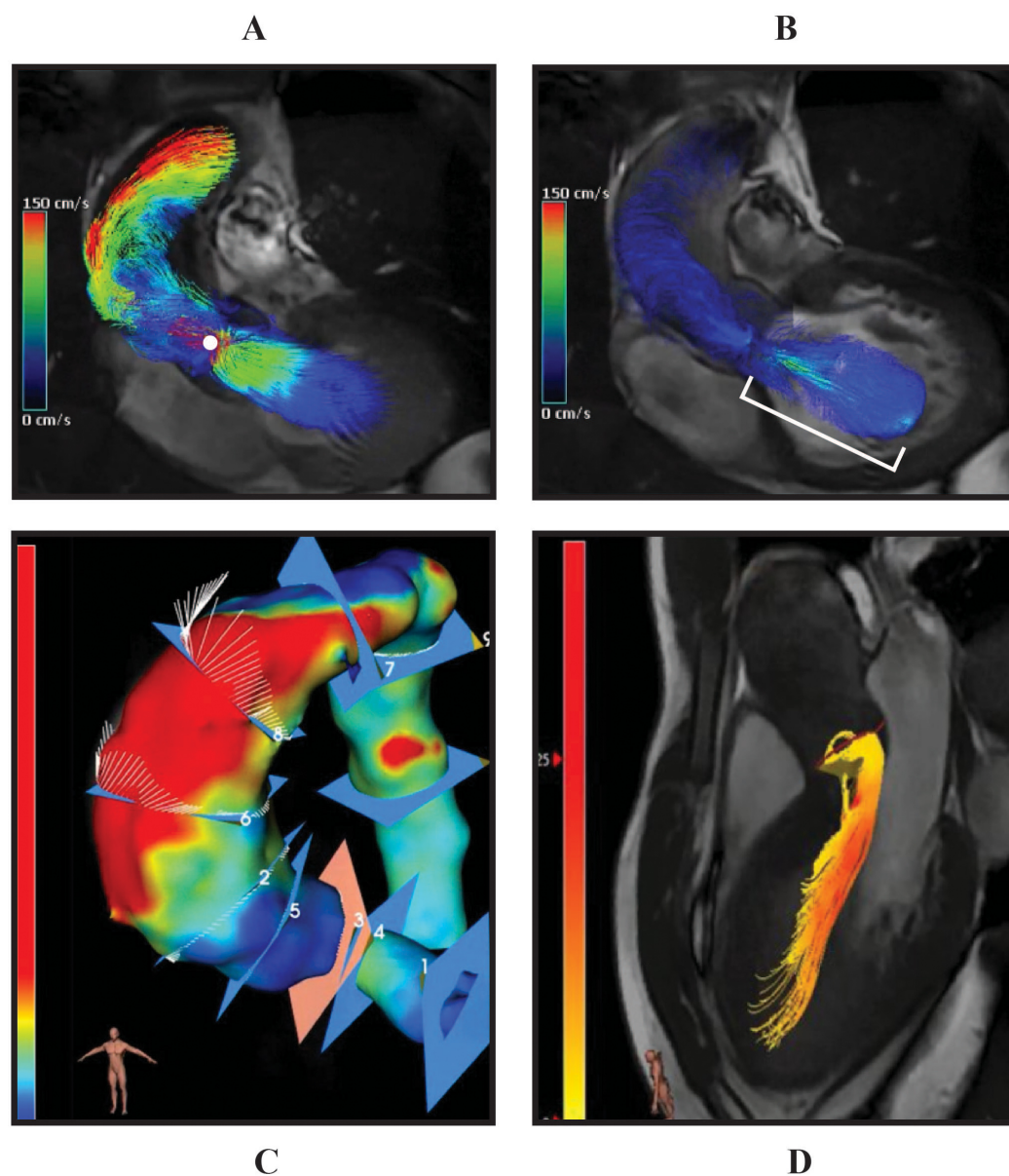
Bicuspid aortic valve (BAV) is the most common congenital valvular heart disease, affecting approximately 1–2% of the population. This condition is characterised by having only two cusps in the aortic valve. BAV can be associated with aortic stenosis (AS), aortic regurgitation (AR), both, or neither (Evangelista Masip et al, 2022). AS is the most prevalent dysfunction among older adults with BAV, occurring when the valve leaflets become thickened or calcified, restricting blood from the left ventricle to the aorta. On the other hand, BAV-related AR is more commonly seen in younger individuals. This typically results from annular dilatation (enlargement of the valve ring), cusp retraction (pulling back of the valve leaflets), or prolapse (displacement of a leaflet into the left ventricle), with severe AR occurring in up to 30% of these individuals (Evangelista Masip et al, 2022).

4D flow MRI, particularly when combined with valve tracking techniques, provides superior quantification of AR and offers higher reproducibility compared to echocardiography, especially in the presence of eccentric jets (Kammerlander et al, 2019; Myerson et al, 2012). BAV is a leading cause of mixed aortic valve disease (AR + AS), accounting for up to 50% of patients undergoing valve repair (Unger et al, 2018). In these cases, unequal transvalvular flow can make traditional quantification methods, such as echocardiography, inadequate for accurate assessment (Cawley et al, 2009). 4D flow MRI offers a unique approach to this challenge by enabling the simultaneous quantification of AS and AR using valve tracking in different locations of the aortic root complex, all while adhering to the conservation of mass principle. Fig. 2 represents a case of bicuspid aortopathy as shown by 4D flow MRI, with both aortic stenosis and regurgitation demonstrated. Fig. 3 shows a case of a unicommissural aortopathy, characterised by an eccentric aortic jet associated with aortic stenosis, as well as severe aortic regurgitation.

## Application of 4D Flow MRI in Disease of the Mitral Valve

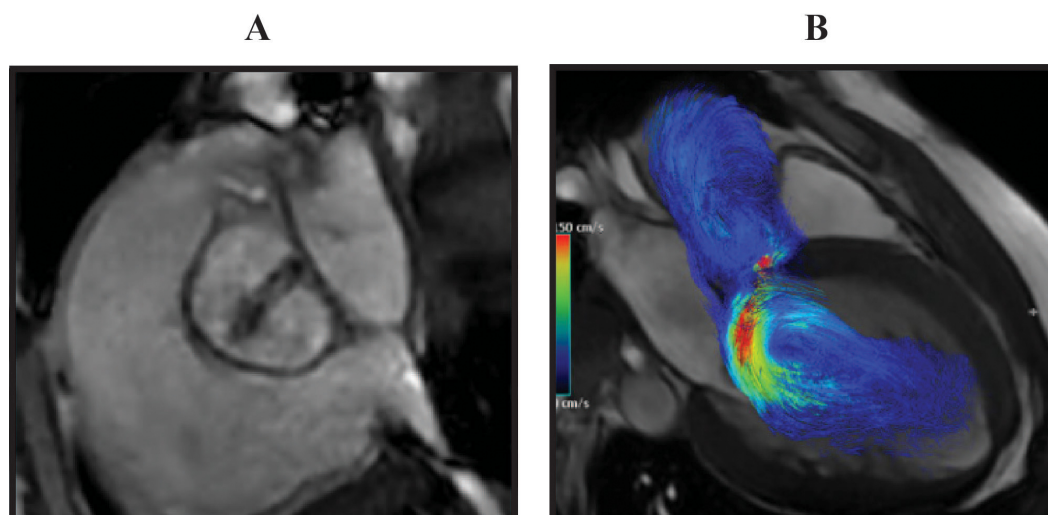
Mitral regurgitation (MR) is the most prevalent form of left-sided valvular heart disease (VHD). MR occurs when the mitral valve does not close properly, allowing blood to flow backwards from the left ventricle into the left atrium. It is classified as primary when caused by anatomical abnormalities or direct damage to the mitral valve itself, such as rheumatic disease or mitral valve prolapse, and secondary when it results from LV dysfunction or dilatation (enlargement of the left ventricle). Treatment strategies, either surgical valve repair or intervention, depend on symptoms, regurgitation severity, LVEF ( $\leq 60\%$ ), and LV end-diastolic diameter ( $\geq 45$  mm) (Blanken et al, 2018). Although echocardiography is typically the initial imaging modality for MR assessment, it can face challenges due to the presence of multiple or eccentric jets and the complex, mobile, saddle-shaped anatomy of the mitral valve (Gorecka et al, 2024).

MRI has shown greater accuracy and reproducibility in quantifying MR compared to echocardiography, making it a valuable alternative, particularly when transtho-



**Fig. 2.** Role of 4D flow MRI in aortic valve disease and aortopathy. (A) In the three-chamber slice (left atrium, left ventricle, and outflow tract), the position of peak velocity is easily identified (white circle). Large vortex formation can be seen in the mid-ascending aorta. This produces abnormal wall shear stress on the aortic arch (C). (B) In diastole, regurgitant flow can be seen entering the left ventricle through the aortic valve. Within the aorta, there is holo-diastolic retrograde flow. (D) Valve tracking increases the accuracy of measuring aortic regurgitation.

raic echocardiography results are inconclusive (Zoghbi et al, 2017). However, direct 2D-PC imaging often overestimates transmitral flow due to through-plane motion (motion of the heart during imaging that affects accuracy) and may produce inconsistent results with variable mitral regurgitant jets (Fidock et al, 2019). In contrast, the indirect 2D-PC method, which calculates MR by subtracting the forward flow in the ascending aorta from the LV systolic volume, avoids these challenges and performs better in forecasting mitral valve surgery referrals, post-operative LV remodelling, and all-cause mortality (Myerson et al, 2016; Penicka et al, 2018).



**Fig. 3. Role of 4D flow MRI in congenital aortic valve disease.** Aortic Uni-commissural aortic valve (A). (B) Three-dimensional streamline demonstrates severe aortic regurgitation with intra-cardiac vortical flow. The regurgitant jet causes fluttering of the mitral valve (Austin Flint phenomenon).

4D flow MRI has proven to be a feasible and reproducible method for assessing MR, accurately quantifying mitral flow even in patients with atrial fibrillation and across different scan types or protocols. It supports both direct and indirect quantification methods (Fidock et al, 2019; Gorecka et al, 2024). Retrospective valve tracking in 4D flow MRI provides superior accuracy and lower variation in assessing net forward flow (Juffermans et al, 2021). The indirect 4D flow method (subtracting 4D flow-derived aortic stroke volume from 4D flow-derived mitral forward flow) demonstrates superior reproducibility compared to 2D-PC methods and aligns with the precision of invasive transoesophageal echocardiography for MR. A recent study highlights that flow tracking, rather than valve tracking, provides more accurate quantification in severe MR, enhancing the evaluation of regurgitant volume and its differentiation from aortic flow (Blanken et al, 2018). Transthoracic echocardiography tends to underestimate regurgitant volume in MR while overestimating it in mitral valve prolapse (Marsan et al, 2009).

In severe MR secondary to mitral valve prolapse, flow tracking marginally improves agreement on regurgitant volume compared to the 4D flow indirect method. Additionally, 4D flow MRI-derived regurgitant volume correlates with the extent of post-operative LV reverse remodelling in primary MR (Gorecka et al, 2024). The extent of MR quantified by 4D flow MRI is independently associated with microvascular obstruction in post-reperfused ST-segment elevation myocardial infarction, a prognostic factor related to adverse outcomes independently of infarct size (Assadi et al, 2022).

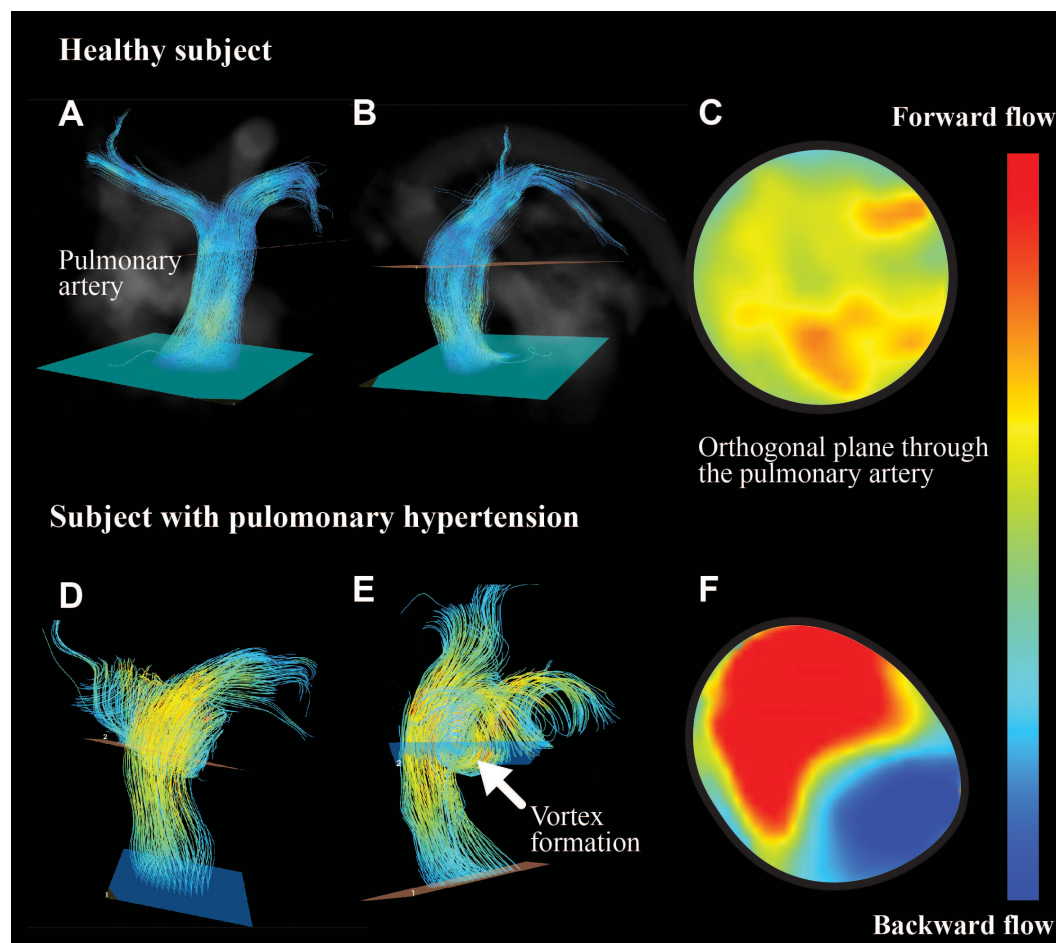
## 4D Flow MRI and its Applications in Pulmonary Artery Hypertension and Right-Heart Disease

Pulmonary hypertension (PH) is a heterogeneous disease characterised by a mean pulmonary artery pressure  $\geq 20$  mmHg, as measured using right-heart catheterisation (RHC), which is considered the gold standard for diagnosis. PH is a significant global health issue, affecting approximately 1% of the population worldwide. MRI is recognised as one of the most important tests in PH due to its ability to provide detailed insights into both cardiac morphology and function, and more recently, pulmonary flow dynamics. Complex flow characteristics can be measured with 4D flow MRI. These include eccentricity (a measure of flow displacement from a perfectly circular cross-section), vorticity (local spinning motion of fluid as it flows along a path), and helicity (a measure of the topological complexity of the flow field, quantifying the degree of ‘tangling’ of fluid flow lines in space).

In health, pulmonary arterial blood flow is laminar, meaning it flows smoothly in parallel layers. However, in patients with increased mean pulmonary artery pressure (mPAP), the flow often becomes vortical. This is demonstrated in Fig. 4. The presence and time-persistence of vortices in the main pulmonary artery are both diagnostic and prognostic indicators of PH. In the study by [Reiter et al \(2015\)](#), a strong correlation was found between the percentage of cardiac phases with vortex formation and mPAP, suggesting that the more frequent the vortex formation, the higher the mPAP. In another study, the duration of vortex formation had a higher diagnostic yield for detecting elevated pulmonary artery pressure than conventional echocardiographic parameters (i.e., peak systolic tricuspid regurgitation pressure gradient) ([Ramos et al, 2020](#)). The helical component of pulmonary artery blood flow has also been shown to be deranged in patients with pulmonary hypertension ([Schäfer et al, 2017](#)). These distinct flow characteristics have been linked to cardiac inefficiency ([Wang et al, 2021](#)). While our understanding of the significance of this is not well developed, future research will offer further insight into the diagnostic potential of full haemodynamic characterisation.

4D flow MRI also allows for the visualisation of wall shear stress (WSS) within the pulmonary arteries. WSS is a dynamic frictional force generated by blood flow along the surface of the vascular wall ([Tang et al, 2012](#)), which plays an important role in vascular wall remodelling. A recent study has shown that low WSS in the pulmonary arterial trunk is indicative of PH ([Terada et al, 2016](#)). Furthermore, research comparing healthy individuals with those having PH has demonstrated that patients with PH exhibit lower peak systolic velocities, peak flow, stroke volume, and WSS ([Ota et al, 2022](#)). [Singh et al \(2020\)](#) found that right ventricular (RV) flow measurements provided incremental value over RV ejection fraction for discriminating adverse RV remodelling and impaired exercise capacity in patients with PH. This evidence reinforces the potential of 4D flow MRI as a comprehensive tool for assessing the severity of PH and for monitoring disease progression and therapeutic response.

In summary, 4D flow MRI can provide complementary diagnostic information in the assessment of patients presenting with suspected PH. Future directions



**Fig. 4. Role of 4D flow MRI in pulmonary hypertension (PH).** 4D flow MRI pulmonary artery flow velocity streamline visualisation in a patient without PH (A–C) and a patient with PH (D–F). In health, systolic flow is laminar (A,B), and there is no reversal of flow during systole (C). In PH, pulmonary flow is turbulent and vortical (D,E), and there is a notable reversal of flow during systole (F).

include the need to evaluate the incremental role of 4D flow MRI, in addition to its role as a tool to monitor therapeutic responses.

## Other Applications of 4D Flow MRI

### Congenital Heart Disease

The clinical utility of 4D flow MRI in congenital heart disease (CHD) lies in its ability to provide detailed hemodynamic information, significantly enhancing the capabilities of traditional imaging modalities. Unlike conventional methods, which often require multiple scans and may be limited by their two-dimensional perspective, 4D flow MRI captures a single 3D volume of the heart and blood vessels. This comprehensive imaging approach allows for faster scans and enables retrospective analysis, improving both efficiency and accuracy. 4D flow MRI is particularly effective in visualising intricate flow patterns such as vortices, helices, and shunts (Rizk, 2021).

4D flow MRI has progressed our understanding of specific CHD conditions. For instance, in patients with repaired tetralogy of Fallot, 4D flow MRI can quantify pulmonary regurgitation, evaluate velocity and pressure gradients across the pulmonary valve, and assess right ventricular size and function (Warmerdam et al, 2022). In cases of aortic coarctation, it characterises the coarcted segment and measures peak velocity and pressure gradients (Hope et al, 2010). For partial anomalous pulmonary venous return, it provides detailed anatomical information and quantifies pulmonary and systemic arterial flow, which is essential for calculating the shunt fraction and evaluating ventricular size and function preoperatively (Christopher et al, 2020).

### Atrial Fibrillation Thromboembolic Event Risk

Thromboembolic events in atrial fibrillation (AF) typically originate from thrombi that form in the left atrium (LA). Understanding the flow dynamics within the left atrium is key to assessing the risk of thrombus formation and subsequent stroke risk. A study has shown that certain markers, such as LA peak velocity and vorticity are reproducible, temporally stable, and robust to changes in rhythm and heart rate. LA blood stasis correlates with higher stroke risk (as estimated using the CHA2DS2-VASc score (Congestive Heart failure, Age, Atherosclerosis, Diabetes mellitus, Stroke, Vascular disease, sex)) (Lee et al, 2014). These markers provide a non-invasive readout of LA hemodynamics that are potentially mechanistically relevant to thrombus formation and embolic stroke (Spartera et al, 2021).

### Intra-Cardiac Energy Profiles

Evaluating intra-cardiac energy profiles is crucial for understanding cardiac efficiency and dysfunction, especially in heart failure. A study shows that heart failure patients with mild LV remodelling have impaired inflow kinetic energy preservation compared to healthy individuals. Additionally, myocardial infarction reduces average LV kinetic energy throughout the cardiac cycle, indicating altered energy dynamics in LV dysfunction (Garg et al, 2018). Within this population, 4D flow can detect subtle changes in cardiac function, even in those with preserved ejection fraction.

## Conclusion

4D flow MRI represents a significant advancement in cardiovascular imaging by providing comprehensive, time-resolved, three-dimensional data of blood flow during the complete cardiac cycle. This technology enhances diagnostic accuracy for complex flow patterns and offers detailed insights into hemodynamic parameters such as turbulent kinetic energy, wall shear stress, and vorticity. Future directions include further refinement of imaging techniques to reduce scan times and improve accessibility. 4D flow MRI sits alongside traditional methods like echocardiography and 2D-PC MRI, complementing them with its ability to visualise and quantify complex blood flow dynamics, thereby offering a huge potential for improving disease detection, risk stratification, and therapeutic monitoring. Its integration into clinical practice promises to enhance the precision of cardiovascu-

lar assessments and support more tailored treatment strategies. Continued research and technological advancements will likely expand its clinical applications, making it an indispensable tool in modern cardiology.

### Key Points

- Unlike echocardiography, which can struggle with complex or eccentric jets, 4D flow MRI provides detailed three-dimensional visualisation of blood flow over time, enhancing the assessment of valvular heart disease.
- 4D flow MRI parameters such as turbulent kinetic energy and wall shear stress offer more precise insights than 2D-PC MRI, which is limited to a single plane.
- By providing accurate measurements of regurgitant volumes and peak velocities, 4D flow MRI has the potential for more precise diagnosis and better prediction of patient outcomes compared to traditional methods.

## Availability of Data and Materials

All data generated or analyzed during this study are included in this article.

## Author Contributions

CGC and PG designed and planned the paper. LR, GM and JB performed literature search and planned the content. CGC and LR drafted the initial manuscript. PG, GM and JB provided the figures and did final edits to the manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

All data presented in the figures are derived from the PREER-CMR registry, which has received ethical approval from the REC (reference number: 21/NE/0149). All patients involved in the study provided informed opt-out consent.

## Acknowledgement

Not applicable.

## Funding

This research received no external funding.

## Conflict of Interest

PG is a clinical advisor for Pie Medical Imaging and Medis Medical Imaging. PG consults for Anteris and Edwards Lifesciences. All other authors have no conflicts of interest to declare.

## References

- Adriaans BP, Westenberg JJM, van Cauteren YJM, Gerretsen S, Elbaz MSM, Bekkers SCAM, et al. Clinical assessment of aortic valve stenosis: Comparison between 4D flow MRI and transthoracic echocardiography. *Journal of Magnetic Resonance Imaging*. 2020; 51: 472–480. <https://doi.org/10.1002/jmri.26847>
- Assadi H, Grafton-Clarke C, Demirkiran A, van der Geest RJ, Nijveldt R, Flather M, et al. Mitral regurgitation quantified by CMR 4D-flow is associated with microvascular obstruction post reperfused ST-segment elevation myocardial infarction. *BMC Research Notes*. 2022; 15: 181. <https://doi.org/10.1186/s13104-022-06063-7>
- Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, et al. Heart Disease and Stroke Statistics-2018 Update: A Report From the American Heart Association. *Circulation*. 2018; 137: e67–e492. <https://doi.org/10.1161/CIR.0000000000000558>
- Binter C, Gotschy A, Sündermann SH, Frank M, Tanner FC, Lüscher TF, et al. Turbulent Kinetic Energy Assessed by Multipoint 4-Dimensional Flow Magnetic Resonance Imaging Provides Additional Information Relative to Echocardiography for the Determination of Aortic Stenosis Severity. *Circulation. Cardiovascular Imaging*. 2017; 10: e005486. <https://doi.org/10.1161/CIRCIMAGING.116.005486>
- Bissell MM, Raimondi F, Ait Ali L, Allen BD, Barker AJ, Bolger A, et al. 4D Flow cardiovascular magnetic resonance consensus statement: 2023 update. *Journal of Cardiovascular Magnetic Resonance*. 2023; 25: 40. <https://doi.org/10.1186/s12968-023-00942-z>
- Blanken CPS, Farag ES, Boekholdt SM, Leiner T, Kluin J, Nederveen AJ, et al. Advanced cardiac MRI techniques for evaluation of left-sided valvular heart disease. *Journal of Magnetic Resonance Imaging*. 2018; 48: 318–329. <https://doi.org/10.1002/jmri.26204>
- Cawley PJ, Maki JH, Otto CM. Cardiovascular magnetic resonance imaging for valvular heart disease: technique and validation. *Circulation*. 2009; 119: 468–478. <https://doi.org/10.1161/CIRCULATIONAHA.107.742486>
- Chelu RG, van den Bosch AE, van Kranenburg M, Hsiao A, van den Hoven AT, Ouhlous M, et al. Qualitative grading of aortic regurgitation: a pilot study comparing CMR 4D flow and echocardiography. *The International Journal of Cardiovascular Imaging*. 2016; 32: 301–307. <https://doi.org/10.1007/s10554-015-0779-7>
- Christopher A, Olivieri L, Cross R, Ramakrishnan K, Loke YH. 4-Dimensional Flow by Cardiac Magnetic Resonance Informs Surgical Planning in Partial Anomalous Pulmonary Venous Return. *JACC. Case Reports*. 2020; 2: 672–677. <https://doi.org/10.1016/j.jaccas.2020.02.012>
- Coman IM, Popescu BA. Shigeo Satomura: 60 years of Doppler ultrasound in medicine. *Cardiovascular Ultrasound*. 2015; 13: 48. <https://doi.org/10.1186/s12947-015-0042-3>
- Crandon S, Elbaz MSM, Westenberg JJM, van der Geest RJ, Plein S, Garg P. Clinical applications of intracardiac four-dimensional flow cardiovascular magnetic resonance: A systematic review. *International Journal of Cardiology*. 2017; 249: 486–493. <https://doi.org/10.1016/j.ijcard.2017.07.023>
- Demirkiran A, Hassell MECJ, Garg P, Elbaz MSM, Delewi R, Greenwood JP, et al. Left ventricular four-dimensional blood flow distribution, energetics, and vorticity in chronic myocardial infarction patients with/without left ventricular thrombus. *European Journal of Radiology*. 2022; 150: 110233. <https://doi.org/10.1016/j.ejrad.2022.110233>
- Edler I, Lindström K. The history of echocardiography. *Ultrasound in Medicine & Biology*. 2004; 30: 1565–1644. [https://doi.org/10.1016/S0301-5629\(99\)00056-3](https://doi.org/10.1016/S0301-5629(99)00056-3)
- Elhawaz A, Archer GT, Zafar H, Fidock B, Barker N, Jones R, et al. Left ventricular blood flow kinetic energy is associated with the six-minute walk test and left ventricular remodelling post valvular intervention in aortic stenosis. *Quantitative Imaging in Medicine and Surgery*. 2021; 11: 1470–1482.

- <https://doi.org/10.21037/qims-20-586>
- Evangelista Masip A, Galian-Gay L, Guala A, Lopez-Sainz A, Teixido-Turà G, Ruiz Muñoz A, et al. Unraveling Bicuspid Aortic Valve Enigmas by Multimodality Imaging: Clinical Implications. *Journal of Clinical Medicine*. 2022; 11: 456. <https://doi.org/10.3390/jcm11020456>
- Farag ES, Vendrik J, van Ooij P, Poortvliet QL, van Kesteren F, Wollersheim LW, et al. Transcatheter aortic valve replacement alters ascending aortic blood flow and wall shear stress patterns: A 4D flow MRI comparison with age-matched, elderly controls. *European Radiology*. 2019; 29: 1444–1451. <https://doi.org/10.1007/s00330-018-5672-z>
- Fidock B, Barker N, Balasubramanian N, Archer G, Fent G, Al-Mohammad A, et al. A Systematic Review of 4D-Flow MRI Derived Mitral Regurgitation Quantification Methods. *Frontiers in Cardiovascular Medicine*. 2019; 6: 103. <https://doi.org/10.3389/fcvm.2019.00103>
- García D, Dumesnil JG, Durand LG, Kadem L, Pibarot P. Discrepancies between catheter and Doppler estimates of valve effective orifice area can be predicted from the pressure recovery phenomenon: practical implications with regard to quantification of aortic stenosis severity. *Journal of the American College of Cardiology*. 2003; 41: 435–442. [https://doi.org/10.1016/s0735-1097\(02\)02764-x](https://doi.org/10.1016/s0735-1097(02)02764-x)
- Garcia J, Barker AJ, Markl M. The Role of Imaging of Flow Patterns by 4D Flow MRI in Aortic Stenosis. *JACC. Cardiovascular Imaging*. 2019; 12: 252–266. <https://doi.org/10.1016/j.jcmg.2018.10.034>
- Garg P, Crandon S, Swoboda PP, Fent GJ, Foley JRJ, Chew PG, et al. Left ventricular blood flow kinetic energy after myocardial infarction - insights from 4D flow cardiovascular magnetic resonance. *Journal of Cardiovascular Magnetic Resonance*. 2018; 20: 61. <https://doi.org/10.1186/s12968-018-0483-6>
- Gorecka M, Bissell MM, Higgins DM, Garg P, Plein S, Greenwood JP. Rationale and clinical applications of 4D flow cardiovascular magnetic resonance in assessment of valvular heart disease: a comprehensive review. *Journal of Cardiovascular Magnetic Resonance*. 2022; 24: 49. <https://doi.org/10.1186/s12968-022-00882-0>
- Gorecka M, Cole C, Bissell MM, Craven TP, Chew PG, Dobson LE, et al. 4D Flow Cardiac MR in Primary Mitral Regurgitation. *Journal of Magnetic Resonance Imaging*. 2024. (online ahead of print) <https://doi.org/10.1002/jmri.29284>
- Grafton-Clarke C, Njoku P, Aben JP, Ledoux L, Zhong L, Westenberg J, et al. Validation of aortic valve pressure gradient quantification using semi-automated 4D flow CMR pipeline. *BMC Research Notes*. 2022; 15: 151. <https://doi.org/10.1186/s13104-022-06033-z>
- Hope MD, Meadows AK, Hope TA, Ordovas KG, Saloner D, Reddy GP, et al. 4D flow evaluation of abnormal flow patterns with bicuspid aortic valve. *Journal of Cardiovascular Magnetic Resonance*. 2009; 11: P184.
- Hope MD, Meadows AK, Hope TA, Ordovas KG, Saloner D, Reddy GP, et al. Clinical evaluation of aortic coarctation with 4D flow MR imaging. *Journal of Magnetic Resonance Imaging*. 2010; 31: 711–718. <https://doi.org/10.1002/jmri.22083>
- Juffermans JF, Minderhoud SCS, Wittgren J, Kilburg A, Ese A, Fidock B, et al. Multicenter Consistency Assessment of Valvular Flow Quantification With Automated Valve Tracking in 4D Flow CMR. *JACC. Cardiovascular Imaging*. 2021; 14: 1354–1366. <https://doi.org/10.1016/j.jcmg.2020.12.014>
- Kammerlander AA, Wiesinger M, Duca F, Aschauer S, Binder C, Zotter Tufaro C, et al. Diagnostic and Prognostic Utility of Cardiac Magnetic Resonance Imaging in Aortic Regurgitation. *JACC. Cardiovascular Imaging*. 2019; 12: 1474–1483. <https://doi.org/10.1016/j.jcmg.2018.08.036>
- Kaur H, Assadi H, Alabed S, Cameron D, Vassiliou VS, Westenberg JMM, et al. Left Ventricular Blood Flow Kinetic Energy Assessment by 4D Flow Cardiovascular Magnetic Resonance: A Systematic Review of the Clinical Relevance. *Journal of Cardiovascular Development and Disease*. 2020; 7: 37. <https://doi.org/10.3390/jcdd7030037>
- Lee DC, Markl M, Fluckiger J, Ng J, Carr JC, Collins JD, et al. Left atrial blood stasis by 4D flow MRI correlates with stroke risk estimation by CHA2DS2-VASc score. *Journal of Cardiovascular Magnetic Resonance*. 2014; 16: O51.
- Lindroos M, Kupari M, Heikkilä J, Tilvis R. Prevalence of aortic valve abnormalities in the elderly: an echocardiographic study of a random population sample. *Journal of the American College of Cardiology*. 1993; 21: 1220–1225. [https://doi.org/10.1016/0735-1097\(93\)90249-z](https://doi.org/10.1016/0735-1097(93)90249-z)

- Mansoor O, Garcia J. Clinical Use of Blood Flow Analysis through 4D-Flow Imaging in Aortic Valve Disease. *Journal of Cardiovascular Development and Disease*. 2023; 10: 251. <https://doi.org/10.3390/jcdd10060251>
- Marsan NA, Westenberg JJM, Ypenburg C, Delgado V, van Bommel RJ, Roes SD, et al. Quantification of functional mitral regurgitation by real-time 3D echocardiography: comparison with 3D velocity-encoded cardiac magnetic resonance. *JACC. Cardiovascular Imaging*. 2009; 2: 1245–1252. <https://doi.org/10.1016/j.jcmg.2009.07.006>
- Myerson SG, d'Arcy J, Christiansen JP, Dobson LE, Mohiaddin R, Francis JM, et al. Determination of Clinical Outcome in Mitral Regurgitation With Cardiovascular Magnetic Resonance Quantification. *Circulation*. 2016; 133: 2287–2296. <https://doi.org/10.1161/CIRCULATIONAHA.115.017888>
- Myerson SG, d'Arcy J, Mohiaddin R, Greenwood JP, Karamitsos TD, Francis JM, et al. Aortic regurgitation quantification using cardiovascular magnetic resonance: association with clinical outcome. *Circulation*. 2012; 126: 1452–1460. <https://doi.org/10.1161/CIRCULATIONAHA.111.083600>
- Myerson SG. CMR in Evaluating Valvular Heart Disease: Diagnosis, Severity, and Outcomes. *JACC. Cardiovascular Imaging*. 2021; 14: 2020–2032. <https://doi.org/10.1016/j.jcmg.2020.09.029>
- Ota H, Kamada H, Higuchi S, Takase K. Clinical Application of 4D Flow MR Imaging to Pulmonary Hypertension. *Magnetic Resonance in Medical Sciences*. 2022; 21: 309–318. <https://doi.org/10.2463/mrms.rev.2021-0111>
- Penicka M, Vecera J, Mirica DC, Kotrc M, Kockova R, Van Camp G. Prognostic Implications of Magnetic Resonance-Derived Quantification in Asymptomatic Patients With Organic Mitral Regurgitation: Comparison With Doppler Echocardiography-Derived Integrative Approach. *Circulation*. 2018; 137: 1349–1360. <https://doi.org/10.1161/CIRCULATIONAHA.117.029332>
- Pereira T, Correia C, Cardoso J. Novel Methods for Pulse Wave Velocity Measurement. *Journal of Medical and Biological Engineering*. 2015; 35: 555–565. <https://doi.org/10.1007/s40846-015-0086-8>
- Rajamannan NM, Evans FJ, Aikawa E, Grande-Allen KJ, Demer LL, Heistad DD, et al. Calcific aortic valve disease: not simply a degenerative process: A review and agenda for research from the National Heart and Lung and Blood Institute Aortic Stenosis Working Group. *Circulation*. 2011; 124: 1783–1791. <https://doi.org/10.1161/CIRCULATIONAHA.110.006767>
- Ramos JG, Fyrdahl A, Wieslander B, Reiter G, Reiter U, Jin N, et al. Cardiovascular magnetic resonance 4D flow analysis has a higher diagnostic yield than Doppler echocardiography for detecting increased pulmonary artery pressure. *BMC Medical Imaging*. 2020; 20: 28. <https://doi.org/10.1186/s12880-020-00428-9>
- Ranard LS, Bonow RO, Nishimura R, Mack MJ, Thourani VH, Bavaria J, et al. Imaging Methods for Evaluation of Chronic Aortic Regurgitation in Adults: JACC State-of-the-Art Review. *Journal of the American College of Cardiology*. 2023; 82: 1953–1966. <https://doi.org/10.1016/j.jacc.2023.08.051>
- Reiter G, Reiter U, Kovacs G, Olschewski H, Fuchsjäger M. Blood flow vortices along the main pulmonary artery measured with MR imaging for diagnosis of pulmonary hypertension. *Radiology*. 2015; 275: 71–79. <https://doi.org/10.1148/radiol.14140849>
- Rizk J. 4D flow MRI applications in congenital heart disease. *European Radiology*. 2021; 31: 1160–1174. <https://doi.org/10.1007/s00330-020-07210-z>
- Roes SD, Hammer S, van der Geest RJ, Marsan NA, Bax JJ, Lamb HJ, et al. Flow assessment through four heart valves simultaneously using 3-dimensional 3-directional velocity-encoded magnetic resonance imaging with retrospective valve tracking in healthy volunteers and patients with valvular regurgitation. *Investigative Radiology*. 2009; 44: 669–675. <https://doi.org/10.1097/RLI.0b013e3181ae99b5>
- Schäfer M, Barker AJ, Kheyfets V, Stenmark KR, Crapo J, Yeager ME, et al. Helicity and Vorticity of Pulmonary Arterial Flow in Patients With Pulmonary Hypertension: Quantitative Analysis of Flow Formations. *Journal of the American Heart Association*. 2017; 6: e007010. <https://doi.org/10.1161/JAHA.117.007010>
- Secomb TW. Hemodynamics. *Comprehensive Physiology*. 2016; 6: 975–1003. <https://doi.org/10.1002/cphy.c150038>
- Singh I, Oliveira RKF, Heerdt P, Brown MB, Faria-Urbina M, Waxman AB, et al. Dynamic right ventricular function response to incremental exercise in pulmonary hypertension. *Pulmonary Circulation*. 2020; 10:

2045894020950187. <https://doi.org/10.1177/2045894020950187>
- Søndergaard L, Hildebrandt P, Lindvig K, Thomsen C, Ståhlberg F, Kassir E, et al. Valve area and cardiac output in aortic stenosis: quantification by magnetic resonance velocity mapping. *American Heart Journal*. 1993; 126: 1156–1164. [https://doi.org/10.1016/0002-8703\(93\)90669-z](https://doi.org/10.1016/0002-8703(93)90669-z)
- Spartera M, Pessoa-Amorim G, Stracquadanio A, Von Ende A, Fletcher A, Manley P, et al. Left atrial 4D flow cardiovascular magnetic resonance: a reproducibility study in sinus rhythm and atrial fibrillation. *Journal of Cardiovascular Magnetic Resonance*. 2021; 23: 29. <https://doi.org/10.1186/s12968-021-00729-0>
- Takehara Y, Isoda H, Takahashi M, Unno N, Shiiya N, Ushio T, et al. Abnormal Flow Dynamics Result in Low Wall Shear Stress and High Oscillatory Shear Index in Abdominal Aortic Dilatation: Initial in vivo Assessment with 4D-flow MRI. *Magnetic Resonance in Medical Sciences*. 2020; 19: 235–246. <https://doi.org/10.2463/mrms.mp.2019-0188>
- Tang BT, Pickard SS, Chan FP, Tsao PS, Taylor CA, Feinstein JA. Wall shear stress is decreased in the pulmonary arteries of patients with pulmonary arterial hypertension: An image-based, computational fluid dynamics study. *Pulmonary Circulation*. 2012; 2: 470–476. <https://doi.org/10.4103/2045-8932.105035>
- Terada M, Takehara Y, Isoda H, Uto T, Matsunaga M, Alley M. Low WSS and High OSI Measured by 3D Cine PC MRI Reflect High Pulmonary Artery Pressures in Suspected Secondary Pulmonary Arterial Hypertension. *Magnetic Resonance in Medical Sciences*. 2016; 15: 193–202. <https://doi.org/10.2463/mrms.mp.2015-0038>
- Unger P, Pibarot P, Tribouilloy C, Lancellotti P, Maisano F, Iung B, et al. Multiple and Mixed Valvular Heart Diseases. *Circulation. Cardiovascular Imaging*. 2018; 11: e007862. <https://doi.org/10.1161/CIRCIMAGING.118.007862>
- Vollema EM, Singh GK, Prihadi EA, Regeer MV, Ewe SH, Ng ACT, et al. Time course of left ventricular remodelling and mechanics after aortic valve surgery: aortic stenosis vs. aortic regurgitation. *European Heart Journal. Cardiovascular Imaging*. 2019; 20: 1105–1111. <https://doi.org/10.1093/ehjci/jez049>
- Wang L, Liu M, Zhang PY, Dai JZ, Ma HY, Tao XC, et al. Analysis of right ventricular flow with 4-dimensional flow cardiovascular magnetic resonance imaging in patients with pulmonary arterial hypertension. *Quantitative Imaging in Medicine and Surgery*. 2021; 11: 3655–3665. <https://doi.org/10.21037/qims-20-1267>
- Warmerdam EG, Neijzen RL, Voskuil M, Leiner T, Grotenhuis HB. Four-dimensional flow CMR in tetralogy of fallot: current perspectives. *The British Journal of Radiology*. 2022; 95: 20210298. <https://doi.org/10.1259/bjr.20210298>
- Westenberg JJM, Roes SD, Ajmone Marsan N, Binnendijk NMJ, Doornbos J, Bax JJ, et al. Mitral valve and tricuspid valve blood flow: accurate quantification with 3D velocity-encoded MR imaging with retrospective valve tracking. *Radiology*. 2008; 249: 792–800. <https://doi.org/10.1148/radiol.2492080146>
- Zhuang B, Sirajuddin A, Zhao S, Lu M. The role of 4D flow MRI for clinical applications in cardiovascular disease: current status and future perspectives. *Quantitative Imaging in Medicine and Surgery*. 2021; 11: 4193–4210. <https://doi.org/10.21037/qims-20-1234>
- Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, et al. Recommendations for Noninvasive Evaluation of Native Valvular Regurgitation: A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Magnetic Resonance. *Journal of the American Society of Echocardiography*. 2017; 30: 303–371. <https://doi.org/10.1016/j.echo.2017.01.007>