

Intracardiac flow visualization: current status and future directions

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Non-invasive cardiovascular imaging initially focused on heart structures, allowing the visualization of their motion and inferring its functional status from it. Colour-Doppler and cardiac magnetic resonance (CMR) have allowed a visual approach to intracardiac flow behaviour, as well as measuring its velocity at single selected spots. Recently, the application of new technologies to medical use and, particularly, to cardiology has allowed, through different algorithms in CMR and applications of ultrasound-related techniques, the description and analysis of flow behaviour in all points and directions of the selected region, creating the opportunity to incorporate new data reflecting cardiac performance to cardiovascular imaging. The following review provides an overview of the currently available imaging techniques that enable flow visualization, as well as its present and future applications based on the available literature and on-going works.

Keywords

Intracardiac flow • Flow mapping • Multimodality imaging • Vortex flow

Introduction

In the last few years, we have witnessed a growing interest in understanding flow behaviour inside cardiac chambers. This has become possible due to the wake of new technologies that have expanded our options in cardiovascular imaging to include the chance to visualize and analyse the complex flow distribution inside the heart and to use its potential to the diagnosis of cardiac function. With this whole new perspective come new concepts and technologies of which this article provides a general overview.

Understanding intracardiac flow: the role of vortices

Although there have been numerous attempts to accurately describe myocardial fibre architecture, its precise distribution remains to be elucidated. However, fibre orientation and function has been described to be a major determinant of blood flow orientation in cardiac chambers, ¹ therefore, playing an essential role in cardiac performance. ² This distribution generates marked changes of blood flow direction and magnitude when passing through the atria and ventricles. Kilner et al. ³ used multi-slice cardiac magnetic resonance

(CMR) to illustrate the asymmetries and direction changes of flow through the heart chambers resulting in a redirection of the momentum of blood flow towards the next cavity. One of these changes in flow motion is the appearance of vortices, regions of accumulated vorticity, a property of a fluid particle based on its local angular velocity that describes its tendency to rotate. A vortex is, therefore, a circular or elliptical-shaped rotating mass of fluid spinning around a virtual central axis.

Vortices form as follows: when blood flows through a tubular structure, fluid layers at the centre of the jet move faster than those adjacent to the containing boundaries due to friction (Figure 1A). When boundaries disappear or abruptly expand, this friction-generated shear stress generates a swirling tendency of the peripheral layers of fluid to spin away from the central jet (Figure 1B). This generation of vorticity can organize in compact regions as vortices, a situation given in cardiac chambers. A clear example is the vortex ring that forms along the tips of the mitral leaflets which, seen in a two-dimensional (2D) plane, shows a stronger anterior component and a weaker posterior one (Figure 1C).

It is assumed that vortices play an important role in normal cardiac function, keeping blood in motion inside cardiac chambers, preserving momentum, avoiding excessive dissipation of energy, facilitating inflow into the ventricle, and redirecting it towards the aortic

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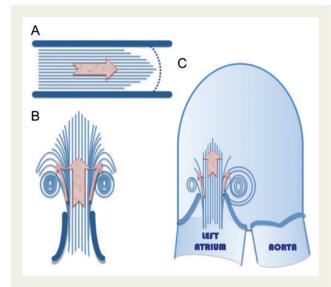


Figure 1 A fluid moving inside a straight vessel presents higher velocities in its centre and slower in the external fluid layers due to friction (A). The difference in flow velocity generates a tendency of the fluid to spin away from the central jet that causes swirling flow motion when the limiting boundaries expand (B). This situation appears in cardiac chambers when the filling inflow passes through the atrio-ventricular valve into the ventricle, where this swirling tendency organizes in vortices (\mathcal{C}).

valve. 3,4 These flow patterns in the left heart have shown differences related to age, gender, blood pressure, and ventricular geometry, as shown in Figure 2. 5

Recent studies have pointed to a single parameter defining key aspects of vortex development, vortex formation time (VFT), as a strong index of cardiac health⁶ and effective fluid transport.⁷ VFT, a dimensionless parameter expressing the duration of early diastole and, hence, reflecting the quality of ventricular filling, is correlated with transmitral thrust and mitral annulus recoil, and is, therefore, considered to be a powerful tool to assess diastolic performance.^{8–10} The VFT index has already demonstrated its applicability in detecting alterations in transmitral flow efficiency and relation to prognosis of heart failure patients.¹¹

Visualizing intracardiac flow: available techniques

Studying intracardiac flow has been possible with the development and application of new techniques. Overcoming significant technical challenges, CMR- and echocardiography-based applications have started to show its potential for research and clinical applications (*Table 1*).

Flow visualization through echocardiographic imaging

The low cost, wide availability and possibility to perform real time evaluation of flow motion with relatively short post-processing

times has fostered the development of ultrasound-based flow visualization techniques and drives the current efforts to explore its clinical relevance and applicability. Several initiatives have emerged to overcome the limitations inherent to conventional ultrasound techniques in potentially visualizing flow motion. However, several challenges remain unresolved, such as technical limitations in the accurate detection of all flow velocities present in cardiac chambers, due to a 2D visualization of three-dimensional (3D) flow, although approaches to a 3D echo-based flow visualization have been reported. With regard to the latter, CMR has been used as the standard for *in vivo* comparison, but the potential inaccuracies when comparing instantaneous with averaged flow are a matter of concern. 14,15

Echocardiographic particle image velocimetry

Echocardiographic particle image velocimetry (Echo-PIV) is based on the use of ultrasound tracking groups of contrast agent particles. Motion patterns are detected through a frame-by-frame analysis of the distribution of contrast particles throughout the analysed region, which generates data on flow direction and velocity. Echo-PIV has proved to accurately reproduce intracardiac flow behaviour both *in vitro* and *in vivo* in various clinical settings. However, limitations on the detection of high velocities due to the need for very high frame rates, not achievable with currently available ultrasound devices, have hindered its further development and potential clinical applicability.

Vector flow mapping

Vector flow mapping (VFM), based on colour-Doppler data, solves the obstacle of angle-dependency through mathematical calculations based on echo-dynamography. This consists of a series of equations aimed at converting a 2D distribution of measured axial velocities (parallel to the ultrasound beam) and estimated radial velocities (perpendicular to the former ones) into a plane of vortical and nonvortical flow vectors. 16 The application of specific functions to infer flow velocity vectors includes two main assumptions: first, that flow along each scan radius is laminar, and, therefore, can be decomposed into vortical and non-vortical components; secondly, that through-plane flow is minor or non-existent. In spite of these two important assumptions, VFM has proved to be a reasonably accurate tool for depicting and measuring in vitro generated flow structures. 17 An example of the flow and vortex visualization is provided in Figure 3. Current efforts in the development of VFM algorithm are aimed at enabling 3D flow characterization. Additional limitations such as time and spatial resolution and optimal Nyquist limit adjustment to avoid aliasing without missing relevant low-velocity flow data come from its Doppler-based character.

Combination of colour-Doppler data with speckle tracking

Combination of colour-Doppler data with speckle tracking complemented by applying the continuity equation to yield cross-beam velocity information has also been successful in depicting intraventricular vortex flow behaviour, ¹⁸ as shown in *Figure 4*. The limitations of this technique include those inherent to Doppler and

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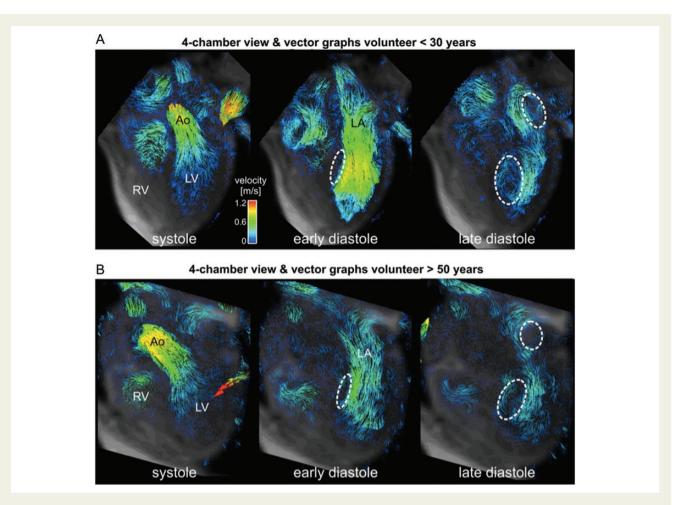


Figure 2 Vector graph visualization of intracardiac blood flow in a young (A) and an old (B) healthy volunteer. The formation of diastolic vortex flow in the LA and LV is indicated by the dashed circles. Note the reduced diastolic in-flow velocities (colour coding) and less prominent vortex flow in the older volunteer. LA, left atrium; RV, right ventricle; Ao, aorta.

speckle tracking, as well as the ones previously mentioned affecting echocardiographic flow visualization tools. By neglecting throughplane information, this technique has calculated to miss $\sim\!15\%$ of flow when compared with CMR.

Flow visualization through magnetic resonance imaging

The intrinsic motion sensitivity of MRI can be used to image vessels with flow-sensitive CMR techniques, also termed phase contrast (PC) MR angiography, or to directly acquire and quantify blood flow in the major vessels or inside the heart chambers.¹⁹

Flow-sensitive 2D CMR

The basic principle of PC-CMR relies on the intrinsic sensitivity of the MR signal to motion. PC-CMR is most frequently applied in its basic form using PC data acquired in a 2D imaging plane positioned at a user-selected location. The MR-signal phase in this 2D imaging plane is directly affected by blood flow, which can be used to spatially and temporally measure blood flow velocity along flexibly selectable

encoding directions. To measure and analyse pulsatile blood flow, data acquisition is synchronized with the cardiac cycle using the ECG signal. This gating allows for the reconstruction of images representing anatomy and flow over the duration of a heartbeat (also termed CINE imaging). Two-dimensional CINE PC-CMR in the thoracic region is typically performed during a breath-hold that potentially limits spatial and/or temporal resolution.

Two-dimensional CINE PC-CMR methods require appropriate control of flow encoding sensitivities, a user-controlled variable referred to as velocity sensitivity (venc), which represents the maximum velocity that can be encoded. Thus, accurate flow quantification requires some prior knowledge of the expected peak blood flow velocities to prevent the appearance of aliasing. The acquired 2D CINE PC-CMR data can be used for flow quantification as illustrated in Figure 5, enabling the calculation of flow-time curves, net flow, mean velocities, peak velocities, and retrograde fraction.

Four-dimensional flow CMR

The combination of 3D spatial encoding and PC-CMR offers the possibility of isotropic high spatial resolution and thus the ability to measure and visualize the temporal evolution of complex flow and

	Echo-PIV	VFM	CMR	
Data source	Echocardiographic tracking of groups of contrast agent particles	Calculation of laminar and vortical flow components from Colour-Doppler	Influence of flow motion on MR-signal phase: phase contrast	
Main advantages				
	Low cost Wide availability Shorter examination times		Higher spatial resolution with full 3D coverage	
Limitations				
	Inherent to conventional echocardiographic examinations (acoustic shadowing, technically difficult examinations, etc.)		Intracardiac devices not suitable for CMR studies Longer examination times	
	Need for the use of contrast agents Requiring frame rates of 60–150 fps for adequate detection of high velocities	Lacking 'in vivo' validation study Underestimation of velocities in vortex areas perpendicular to ultrasound beam	Limited temporal resolution (poor flow characterization in brief phases of cardiac cycle) Flow data are averaged over several cardiac cycles	
Sources of error				
	Cross-plane migration of contrast agent particles Manual contour detection	Manual de-aliasing Manual definition of endocardial borders	Eddy current effects Maxwell terms Gradient field distortions	
Accuracy				
High velocities	Limited: affected by frame rate (upper limit of \sim 60 cm/s)	Accurate visualization. May require adjustment of Nyquist limit or manual de-aliasing	Accurate visualization, although selectable velocity sensitivity (venc) requires some prior knowledge of	
Low velocities	Accurate visualization	Underestimation. Nyquist limit adjustment and focus on smaller areas may improve the detection but introduces noise through the detection of cardiac wall motion	the expected velocity values	

motion patterns in a 3D volume. In this context, ECG synchronized 3D PC CMR using three-directional velocity encoding (also termed '4D flow MRI') can be employed to visualize and quantify 3D blood flow characteristics in the heart and vessels. ^{20,21} A number of recent methodological improvements (parallel imaging, adaptive respiration control with increased efficiency, etc.) permit the acquisition of 4D flow CMR data with full-volumetric coverage of the heart within reasonable scan times of the order of 8–15 min. ^{22,23} Given the exam duration, systems allowing monitoring of breathing pattern in parallel to the data acquisition have been developed.

To visualize complex, three-directional blood flow within a 3D volume, various visualization tools, including 2D vector-fields, 3D streamlines, and time-resolved 3D particle traces have been proposed. It is also possible to retrospectively quantify blood flow velocities and volumes at user-selected locations of interest within the 3D volume. In addition to the previously mentioned flow measurement parameters, more advanced quantification methods and algorithms have been presented in the literature. These include the derivation of wall shear stress, pulse wave velocity, pressure difference, or turbulent kinetic energy. ^{26–30}

Figures 6 and 7 illustrate the use of 4D flow CMR for the visualization and quantification of 3D blood flow in the heart and pulmonary system, respectively.

One of the main limitations associated with CMR flow visualization comes from the fact that the information is generated from averaged flow values over several cardiac cycles. Other limitations are related to the several effects that can introduce imperfection in the resulting PC-CMR data, which cause errors in velocity measurements. Major sources of inaccuracy in velocity-encoded images include eddy current effects, Maxwell terms, and gradient field distortions. If uncorrected, all three effects can severely distort the measured three-directional velocities and thus result in distortion of 3D streamlines and 3D particle traces, which might lead to incorrect flow pattern visualization and, subsequently, to false conclusions regarding flow characteristics. It is important to keep in mind that such phase offset errors exhibit a substantial and non-linear increase with increasing distance from the iso-centre of the MR system.

Defining flow study: regions and parameters

So far, the study of intracardiac flow behaviour has aimed at providing a better understanding of both physiological and pathological situations, as well as to explore potential new tools to better diagnose clinical entities and optimize their treatment. Many of these studies are

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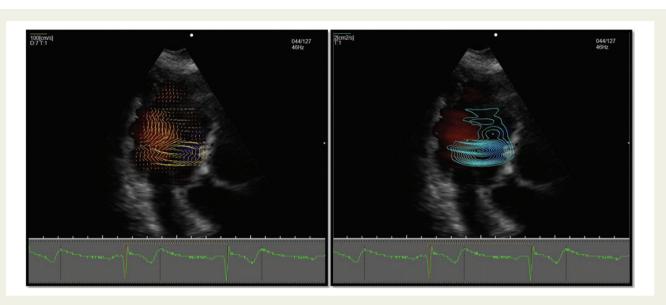


Figure 3 VFM provides two main visualization modes: (i) On the left, vector display shows the direction and intensity of flow velocity in each point of the scanned area through yellow arrows proportional in length to flow velocity. (ii) On the right, vortex visualization mode displays round lines indicating the presence of a vortex, with higher line density corresponding to areas of more intense flow. Both vector and vortex scale and density can be adjusted by the user.

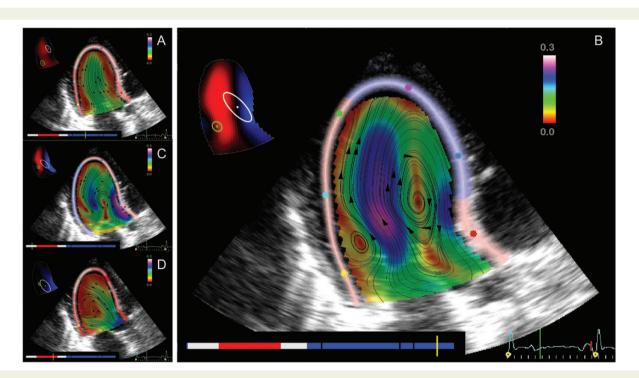


Figure 4 Through a combination of strain and speckle tracking, flow visualization as developed by Bermejo et al. provides a visualization where streamlines represent velocity direction; colour bar represents codification of velocity values. A schematic figure with vortex cores location can be seen on the upper left corner: clockwise vortex (in white) and counter-clockwise vortex (in green). The bottom-left colour bar indicates the phase of the cardiac cycle [red: ejection; blue: filling; white: isovolumic periods; during filling black marks indicate (left-to-right) the instants of peak-E wave velocity, A-wave onset, and peak-A wave velocity].

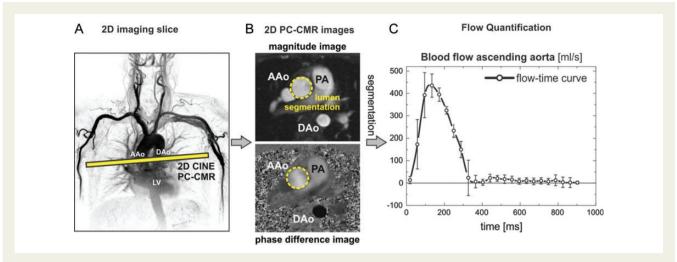


Figure 5 (A) Blood flow quantification in the aorta using a 2D CINE PC-CMR acquisition placed immediately distal to the aortic valve plane and encoded for through-plane velocities. (B) After data acquisition and reconstruction of magnitude and phase difference images, the vessel contours of the AAo are identified by lumen segmentation to quantify time-resolved blood flow. (C) Flow-time curves in the ascending aorta above the aortic valve averaged over 10 normal healthy subjects (error bars = inter-individual variation of blood flow). AAo, ascending aorta; PA, pulmonary artery; DAo, descending aorta.

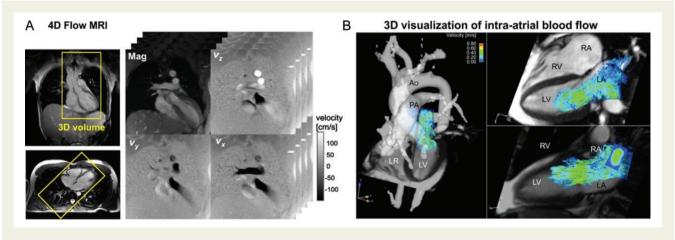


Figure 6 Four-dimensional flow MRI and visualization of 3D flow. (A) Four-dimensional flow MRI raw data comprises information along all three spatial dimension, three velocity directions (vx,vy,vz), and time spanning the cardiac cycle. (B) Co-registered four-chamber CINE images and 3D flow visualization in the atrium and ventricle during mitral in-flow.

still hindered by the ongoing development of visualization techniques, reduced number of patients, and uncertainty about the real significance of measured parameters. However, some have already provided interesting results (*Table 2*).

Left ventricle vortex flow and its relation with systolic and diastolic function

LV has, by far, been the cardiac region to serve as a reference for the development of these techniques, from a silicon LV replica³¹ to the most of the published work related to clinical entities. Studied parameters can be grouped as related to vortex size, intensity, and position:

Vortex size: regardless of the variations among different studies, vortex size or shape (depth, length, width, area, and sphericity index) seem to be associated with LV systolic function,³² even more in specific moments of cardiac cycle, such as isovolumetric contraction.³³

Vortex flow intensity: measured as relative strength, pulsation correlation, maximum circulating flow or delay in acquiring its maximum energy vortex intensity has been associated with both systolic and diastolic dysfunction, wider QRS complexes, and larger end-systolic longitudinal diameters. 32-34

Vortex position: a persistent apical vortex during ejection has been associated with LV systolic dysfunction.³⁵ Other studies have shown that the incidence, location, and extent of vortex flow

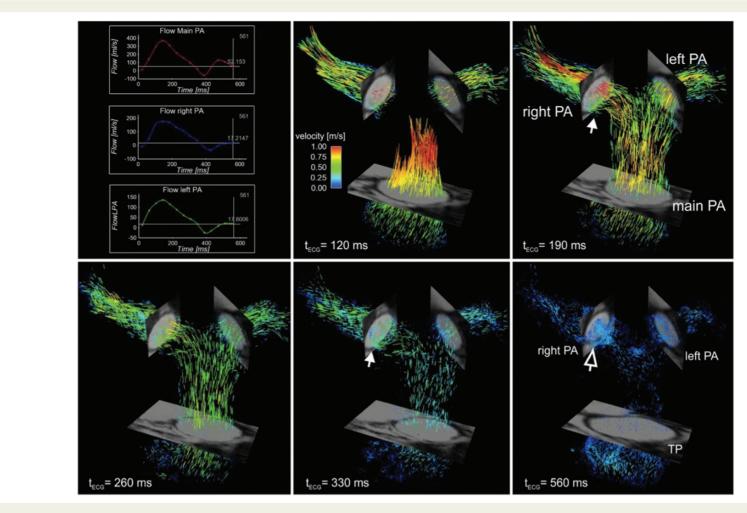


Figure 7 Three-dimensional blood flow visualization in the pulmonary system based on time-resolved 3D pathlines in a normal volunteer. Systolic pulmonary outflow with high blood flow velocities (red colour) is followed by lower diastolic flow with mild helix flow (solid white arrows) and mild retrograde flow (open white arrow) in the right pulmonary artery. Top left: retrospective flow quantification was employed to calculate flow-time curves in the main, right, and left pulmonary artery. PA, pulmonary artery.

Region	Measured parameter	Correlation	Technique		
Left ventricle	Vortex size				
	↓Length ↓Depth ↓Sphericity index ↑Width	Decreased LV systolic function	Echo-PIV, VFM		
	Vortex intensity				
	↓Relative strength ↓Pulsation correlation ↑Time to peak kinetic energy ↓Flow volume	LV systolic dysfunction LV diastolic dysfunction Wider QRS, LV dilation	Echo-PIV, VFM		
	Vortex location				
	Persisting at apex during ejection	LV systolic dysfunction	VFM		
Right ventricle	Blood residence time RV systolic function Differential regional function RV function in pulmonary hypertension		CMR, 3D-ech		
Left atrium	Vortex formation	Prevention of blood stasis	CMR		
Valve disease Atrial septal defects Aortic coarctation	Cross-flow quantification	Solid correlations with haemodynamic or imaging gold standards	CMR, VFM		

inside the LV were markedly altered in patients with dilated cardiomyopathy. 5,36

LV vortices' presumed role in energy preservation seems to be related to a combination of their location, size, and intensity. As previously mentioned, VFT provides a good basis for analysing the generation of vortices and how this influences its haemodynamic significance. However, direct visualization and quantification techniques seem to provide a whole different range of parameters that may also determine different aspects of cardiac performance. In addition, other determinants of flow patterns inside the LV non-vortex related, such as a direct flow within the LV from the left atrium through the aortic valve, has shown to be decreased in patients compared with healthy volunteers.³⁷

Right ventricular flow

Advances in the study of right ventricular (RV) 3D flow have been made lately, showing a relation between RV ejection fraction and blood residence time in it. 38

Assessment of cross-orifice flow

Flow visualization techniques open new options to quantify flow across regurgitant, stenotic or artificial valves, ^{21,39–41} atrial septal defects, or aortic coarctation ^{42–45} with reasonable accuracy. Recent studies have shown that 4D flow MRI can provide new insights into the impact of aortic valve disease on changes in aortic haemodynamics such as significant changes in wall shear stress associated with bicuspid aortic valves. ⁴⁶

Other

Applications include the detection of areas of potential thrombus formation due to slow or stagnant flow, ⁴⁷ left atrial flow, ^{15,48} or changes

in flow motion in paced rhythms.⁴⁹ Several groups have reported advances in the analysis of blood flow through artificial valves, blood flow characteristics in the thoracic aorta,^{50,51} peripheral vessels,⁵² carotid arteries,⁵³ large intracranial arteries,⁵⁴ as well as flow in the pulmonary and venous systems.⁵⁵

Conclusions

A series of technical advances have opened the possibility to visualize and analyse intracardiac blood motion, generating new options to investigate flow patterns that provide additional information to the functional status of the heart. One of the main determinants of intracardiac flow is vortex behaviour, which has already shown to be associated with optimal cardiac performance.

Results from initial studies already demonstrate the potential of these techniques to detect pathologically altered flow characteristics and identify new patho-mechanisms for the development of cardiac and vascular disease. Ongoing improvements in the accuracy and feasibility of the available techniques together with a growing knowledge on the main determinants of blood flow in the cardiovascular system should lead us to finding the right parameters to incorporate to our current range of diagnostic tools.

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Conflict of interest: none declared.

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IMAGE FOCUS

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Cardiac involvement in Becker muscular dystrophy: role of cardiovascular magnetic resonance

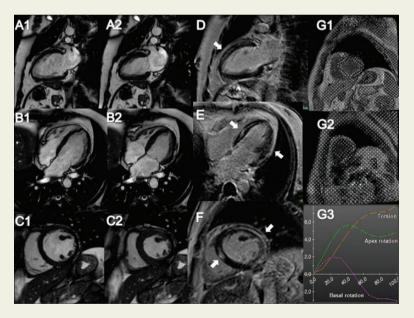
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We report the case of a 40-year-old male known carrier of the Becker muscular dystrophy (BMD) who presented with fatigue in the outpatient clinic. Echocardiographic examination revealed a regional inferior left ventricular (LV) wall motion abnormality (Supplementary data online, *Movie S1*).

A cardiovascular magnetic resonance imaging study (CMR) was indicated, showing a near dilated left ventricle with hypokinesia in the midinferolateral and lateral segments ($Panels\ A1-C2$) in the SSFP cine images (Supplementary data online, $Movies\ S2-S4$) and mild depression of LV ejection fraction. Late gadolinium enhancement (LGE) imaging ($Panel\ D-F$) depicted extensive mesocardic fibrosis in the mid-septum and lateral wall, with a distribution pattern similar to the observed in similar cases. CMR tagging sequences ($Panels\ G1-G3$) showed a



reduced (8°) LV myocardial torsion (LVT) between the base and the apex (Supplementary data online, Movie S5).

Although our case presented already with LV dysfunction, mid-wall myocardial fibrosis and reduced LVT can be present at early stages of the disease, before the onset of cardiac symptoms, making contrast enhanced CMR an accurate imaging technique to detect early cardiac impairment in patients with BMD.

Systolic and diastolic CMR images of the LV longitudinal long-axis (A1 and A2), horizontal long-axis (B1 and B2) and short-axis views (C1 and C2). LGE CMR images of the longitudinal long-axis (D), horizontal long-axis (E) and short-axis (E) views. Arrows indicate the myocardial fibrosis regions. Basal (E) and apical (E) views of tagged CMR images and curves showing LVT impairment (E).

Supplementary data are available at European Heart Journal – Cardiovascular Imaging online.

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