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Assessment of Aortic Stenosis Severity by Cardiovascular Magnetic Resonance

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ABSTRACT

Cardiovascular magnetic resonance (CMR) has become a valuable tool to corroborate aortic stenosis (AS) severity when echocardiography assessment is discordant. Moreover, CMR can provide useful complementary information about AS severity and hemodynamic markers. In particular, the use of advanced 4D flow CMR allows a comprehensive assessment of complex flow alterations produced by AS. This review provides an overview of the added value obtained by standard 2D flow and advanced 4D flow quantification for AS severity assessment and discusses the advantages and disadvantages of current clinical metrics. This includes an introduction of promising new hemodynamic markers, and discusses how these novel makers may identify potential complications and disease progression in patients with AS.

Keywords: aortic stenosis, cardiovascular magnetic resonance, flow quantification.

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RESUMEN

La imagenología de resonancia magnética cardiovascular (RMC) se ha establecido como una importante herramienta para corroborar la severidad de la estenosis aórtica (EA) cuando el examen por ecocardiografía es contradictorio. Además, la RMC puede proveer importante información complementaria con respecto a la severidad de la EA y diversos indicadores hemodinámicos. En particular, el uso de técnicas avanzadas de flujo en 4D por RMC permite una extensiva evaluación de las complejas alteraciones de flujo provocadas por la presencia de la EA. Este artículo de revisión describe de manera detallada el valor agregado obtenido en la práctica clínica con el uso de las técnicas de medición de flujo bidimensionales, así como las técnicas avanzadas de flujo en 4D para la cuantificación y evaluación de la severidad de la EA. De igual modo, se discuten las ventajas y desventajas de los parámetros clínicos comúnmente utilizados para la estratificación de la severidad de la EA. Además, incluye una introducción a nuevos y prometedores índices hemodinámicos, discute su utilidad para la identificación de potenciales complicaciones y de progresión de la EA *in vivo*.

Palabras clave: estenosis aórtica, resonancia magnética cardiovascular, cuantificación de flujo.

INTRODUCTION

Aortic stenosis (AS) is a multifaceted disease, with a prevalence of 2-3% in populations older than 80 years old [1], and which involves atherosclerotic- and elastocalcinosis-like processes affecting the aortic valve opening (via narrowing or obstruction) and motility [2], [3]. Transthoracic echocardiography (TTE) is the primary imaging technique for the assessment of AS severity as indicated in the ACC/AHA/ESC guidelines [4]-[6]. However, in patients with inadequate TTE quality or discordant results, cardiovascular magnetic resonance (CMR) can be used to corroborate the AS severity, to assess ventricular function and volume, and to estimate myocardial fibrosis/hypertrophy [7]-[9]. In particular, flow imaging by ECG-gated 2D phase contrast (PC) CMR offers the opportunity to quantify flow-derived parameters with higher reproducibility than TTE [8]. It has also been shown that CMR is more diagnostic than 2D echocardiography in determining the presence of congenital defects, such as bicuspid aortic valve [10].

CMR flow imaging techniques and analytic tools have rapidly evolved in recent years and today permit a comprehensive assessment of changes in aortic hemodynamics associated with aortic valve disease. This paper reviews the current clinical metrics using 2D flow velocity measurements, introduces emerging 2D flow and advanced 4D flow hemodynamics markers, and future perspectives in the assessment of AS severity.

STANDARD OF CARE: AS ASSESSMENT

Cardiac auscultation remains the most widely used method of screening by evaluating the cardiac murmurs related to valvular heart diseases. The production of acoustic noise related to murmurs is due to 3 main factors: (1) high blood flow rate through normal or abnormal orifices; (2) forward flow through a narrowed or irregular orifice into a dilated vessel or chamber; (3) backward or regurgitant flow through an incompetent valve. Heart murmurs

are an important clue for the diagnosis of AS in asymptomatic patients. In particular midsystolic (systolic ejection) murmurs, often crescendo-decrecendo, occurs when the blood is ejected across the aortic valve. An increase of intensity depends in part on the velocity of the blood flow across a narrowed area, thus it may be a sign of stenosis. On detection, the imaging modality of choice is TTE which can evaluate cardiac morphology, dimension, volumes, function, and the severity of the valve obstruction. In comparison to other imaging modalities, TTE is fast, cheap, portable, and widely available in the clinic. In general, the main parameters of interest are peak transvalvular velocity, peak/mean pressure gradient (PG), and aortic valve effective orifice area (EOA) [4], [6], [11], Table 1. Nonetheless, a comprehensive evaluation of valve morphology is essential to fully characterize the presence and/or severity of valve stenosis and to understand disease progression. This includes the documentation of the presence of congenital anomalies, degree of leaflet thickening and calcification, presence and extent of commissural fusion, and any fibrocalcific remodelling of the subvalvular apparatus. Therapeutic decisions are also guided by assessment of left ventricular function which is accomplished with the measurement of: systolic and diastolic diameters, wall thickening and motion, ejection fraction, masse, and geometrical remodelling.

The utility of TTE must be balanced with the known challenges of this imaging powerful modality. For example, care must be exercised when measuring morphologic and hemodynamic parameters. Morphological measurements are limited by acoustical windows and inappropriate transducer alignment, such as for valve planimetry. These limitations are also especially important in the left ventricular outflow tract (LVOT) where the lumen dimensions are necessary for EOA computation [3], [12]. Additional care must be exercised for the measurement of LVOT and transvalvular hemodynamic parameters which are also affected by transducer position and acoustic window [4], [6], [13]-[15]. Since velocity measurements are used to estimate pressure gradients using the simplified Bernoulli equation ($4 \times V^2$) [4], any error in the velocity measurement is propagated by the square when calculating pressure gradient. Moreover, the clinical measurement of EOA has a high variability with TTE for each of the three measurements (LVOT area, LVOT and transvalvular velocity-time integrals) required for its estimation [4]-[6]. Studies have shown that in experienced laboratories LVOT and transvalvular velocity measurements have a very low intra- and inter-observer variability (3-4%) [4]; however, LVOT dimensional variability is higher (5-8%) and often requires corroboration by other imaging modalities. Finally, stroke volume (SV) measurement in the LVOT assumes laminar flow and a flat velocity profile, which is often not the case in patients with AS. As result, SV measurement may be under- or over-estimated in such scenarios [4], [6], [13]-[15].

Keeping these measurement challenges in mind, EOA assessment by TTE may be not feasible in up to 20-30% of patients due to the described limitations. Furthermore, often there are discrepancies between EOA severity and pressure gradient [16], [17]. Thus, the care provider should be aware of the intrinsic limitations and uncertainty of the technique regarding stenosis severity and thus therapeutic management strategies. In addition, if TTE measurements are not feasible or are discordant, it is important to confirm the stenosis severity with other, ideally non-invasive, non-ionizing, diagnostic modalities. For this reason, CMR has become an alternative imaging technique to corroborate TTE measurements and may provide additional information concerning stenosis severity.

ROLE OF CMR FOR THE ASSESSMENT OF AORTIC VALVE STENOSIS

For the assessment of AS, CMR offers a range of different pulse sequences. For example, steady-state free precession (SSFP) allows for the visualization of valve/ventricle anatomy and motion (Fig. 1). Turbo spin echo (T1 weighted, T2 weighted, fat saturation) and inversion

Table 1. Current and emerging flow-derived parameters in the assessment of aortic stenosis.

Parameter	Criteria for Severity	Utility and advantage	Limitations	Image modality
Valvular obstruction				
Peak jet velocity †	> 4 m/s	Easy to measure Low inter/intra-observer variability High specificity	Highly flow dependant Overestimates LV energy loss in patients with small aortas May underestimate stenosis severity in low-flow conditions	TTE, CMR
Mean pressure gradient †	> 40 mmHg	Same as peak jet velocity	Same as peak jet velocity	TTE, CMR
Valve jet angle/ displacement *	NA	Same as peak jet velocity Reflects stenosis severity and LV remodelling	Same as peak jet velocity	CMR
Effective orifice area (EOA) †	≤ 1 cm^2	Less flow dependant than pressure gradient or peak velocity	Susceptible to measurement errors using continuity equation May under/over-estimate stenosis severity in patients with hypertension, and low-flow states	TTE, CMR
EOA$_i$= EOA/BSA	≤ 0.6 cm^2/m^2	Represent intrinsic severity of valve obstruction	May overestimate stenosis severity in obese patients	TTE, CMR
EOA kinetic *	NA	Same as EOA. Opening and closing slopes characterize stenosis severity and its effect on LV function	Same as EOA Needs high temporal resolution	TTE, CMR
Vorticity magnitude *	NA	Quantify rotational flow magnitude Characterize shear layer separation regions	May be noise due to velocity derivative computation Needs high spatial resolution	CMR

Energy loss index (ELI) = $[(EOA \times A_{Ao})/(EOA + A_{Ao})]/BSA$	$\leq$ 0.5 - 0.6 cm^2/m^2	Less flow dependant than gradient or peak velocity Considers pressure recovery and is similar to EOA measured by catheter Reflects LV energy loss caused by stenosis Should be measured in patients with small aortas	Same as EOA	TTE, CMR
Stroke work loss (SWL) = $100 \times (\Delta P_{mean}/SBP + \Delta P_{mean})$	$> 25\%$	Less dependent than gradient or peak velocity	May underestimate stenosis severity and LV energy loss in patients with hypertension	TTE, CMR
Turbulent kinetic energy *	NA	Similar to ELI Local measurement of irreversible turbulent energy dissipation	May be affected by partial volume velocity measurements Needs balanced 4D flow measurements	CMR
Viscous energy loss *	NA	Quantifies viscous energetic dissipation due to stenosis severity. Independent of pressure recovery	May be affected by velocity derivative computation	CMR
Vascular load				
Systemic arterial compliance (SAC) = SV_i/(SBP-DBP)	$\leq$ 0.6 ml. $mmHg^{-1}.m^{-2}$	Most frequent cause of increased arterial load Can unmask hypertension in patients pseudo-normalized blood pressure	Susceptible to measurement errors	TTE, CMR
Systemic vascular resistance (SVR) = 80×MBP/CO	$> 2{,}000$ $dyne.s.cm^{-5}$		Susceptible to measurement errors	TTE, CMR
Global hemodynamic load				
Valvulo arterial impedance (Z_{va}) = $(SBP + \Delta P_{mean})/SV_i$	> 4.5 mmHg. $ml^{-1}.m^2$	Represents global (valvular+arterial) load imposed on LV May be superior to predict occurrence of symptoms and events	Susceptible to measurement errors Does not differentiate load contribution (valvular vs. arterial)	TTE, CMR
Flow pattern				
Helicity *	NA	Characterize complex rotation flow patters	Typically visually quantified	CMR
Vortical feature *	NA	Visualize structural flow organization	Same as vorticity magnitude	CMR
Wall shear stress *	NA	Quantifies the friction force of the flowing blood at the arterial wall	May be affected by velocity derivative computation. Needs high spatial resolution	CMR

A_{Ao}: Ascending aorta surface; BSA: Body surface area; CMR: Cardiovascular magnetic resonance; CO: Cardiac output; DBP: Diastolic blood pressure; LV: left ventricle; MBP: Mean blood pressure; NA: Not Available; SBP: Systolic blood pressure; SV_i: Stroke volume indexed to BSA; TTE: Transthoracic echocardiography. † Included in international guidelines for the aortic stenosis assessment; * emerging parameter using cardiovascular magnetic resonance.

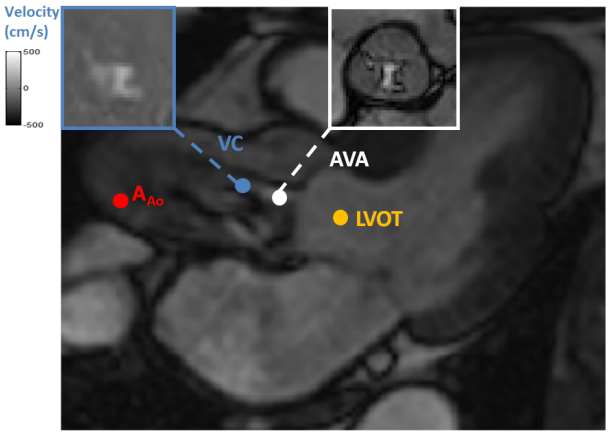

Fig. 1. Fluid mechanics of the aortic valve. Schematic representation of the left ventricle, aortic valve and ascending aorta. The blood flows from the left ventricular outflow tract (LVOT) through the aortic valve (AVA indicates anatomic aortic valve area) and is spatially accelerated to the vena contracta (VC) position, where the blood then decelerates and diverges within the ascending aorta (A_{Ao}). The cross-sectional area of VC corresponds to the valve effective orifice area (EOA). Magnetic resonance velocity measurements at VC (10 mm from the aortic valve) are indicated in a blue square. Notice that AVA $\gg$ EOA.

recovery techniques are used to characterize valve masses [18], [19]. Phase-contrast (PC) MRI is employed to quantify blood flow velocity in flexibly selectable 2D imaging planes above, and below the aortic valve. The primary use of CMR flow velocity measurements is to corroborate the standard measures obtained by TTE such as peak velocity, transvalvular peak/mean PG, and valve EOA [4], [7]-[9], Table 1.

PC-MRI relies on the intrinsic motion sensitivity of MRI which can be used to image vessels as that employed by phase contrast MR-angiography, but also to quantify blood flow velocities. Using appropriate velocity encoding gradients, flow or tissue motion dependant phase effects can be used to measure two datasets with different velocity dependant signal phases at otherwise identical acquisition parameters. Subtraction of the two resulting phase images allows the quantitative assessment of the underlying blood velocities (Fig. 2). The velocity encoding gradients can be applied along arbitrary directions to capture the nature of blood flow in any orientation within the imaging slice. Thus, stationary objects (e.g. static tissue) within the slice have a null net phase and moving objects (e.g. blood flow) have a net phase or phase shift proportional to blood velocity in the measured direction. Measured velocities in the predominant blood flow direction appear bright and flow opposite direction in dark (Fig. 2B). Velocity mapping requires an adequate selection of velocity encoding sensitivity (also termed 'V_{enc}') to avoid velocity aliasing (phase shift $> 180^o$). To synchronize phase contrast measurements with pulsatile flow, data acquisition is gated to the cardiac cycle and time resolved (CINE) images are collected to depict the dynamics of blood flow during the cardiac cycle. Following data acquisition, PC-MRI generates 2 set of images: time-resolved magnitude and phase difference (velocity) images that depict vessel anatomy and blood flow over the cardiac cycle. Magnitude images are used for anatomic orientation and boundary vessel identification for the quantification of peak/mean velocity and blood flow from the velocity images (Fig. 3).

Pressure gradients across the aortic valve can be estimated by the simplified Bernoulli equation ($4 \times V^2_{peak}$), where mean PG is obtained by averaging V_{peak} from each time frame over systole. It has been demonstrated that PC velocity mapping can accurately measure velocities over 5 m/s selecting adequate velocity encoding sensitivity [20]. However, in clinical practice 2D PC often underestimates PG measured by TTE [7]-[9], [21], due to local signal loss, background noise, velocity aliasing, inadequate plane positioning and temporal resolution [22]-[26]. A promising metric for AS severity assessment is valve EOA [8], [9], [27], [28]. Valve EOA can be estimated by CMR using the continuity equation (EOA=SV/VTI_{Ao}) [8], [9], [29], where SV is the stroke volume and VTI_{Ao} is the velocity-time integral over valve ejection period downstream of the aortic valve (Fig. 3). The left ventricular SV can be estimated based on multi-slice short axis CINE SSFP images covering the entire left ventricle,

which is considered the gold standard [30]. Alternatively, PC MRI in the LVOT can be used by multiplying each pixel velocity and area to estimate the instantaneous flow volume (Fig. 3). It is important to differentiate the valve EOA from the anatomic valve area (AVA). The AVA corresponds to the physical opening of aortic valve, often measured by valve planimetry, and EOA corresponds to the hemodynamic opening of aortic valve at vena contracta position where V_{peak} is located (Fig. 1). AVA is usually greater than EOA and they are physically related by the contraction coefficient (CC=EOA/AVA). It should be noted that a similar AVA may have a different EOA. This is relevant for differentiating tricuspid from bicuspid valve hemodynamics and AS severity [31].

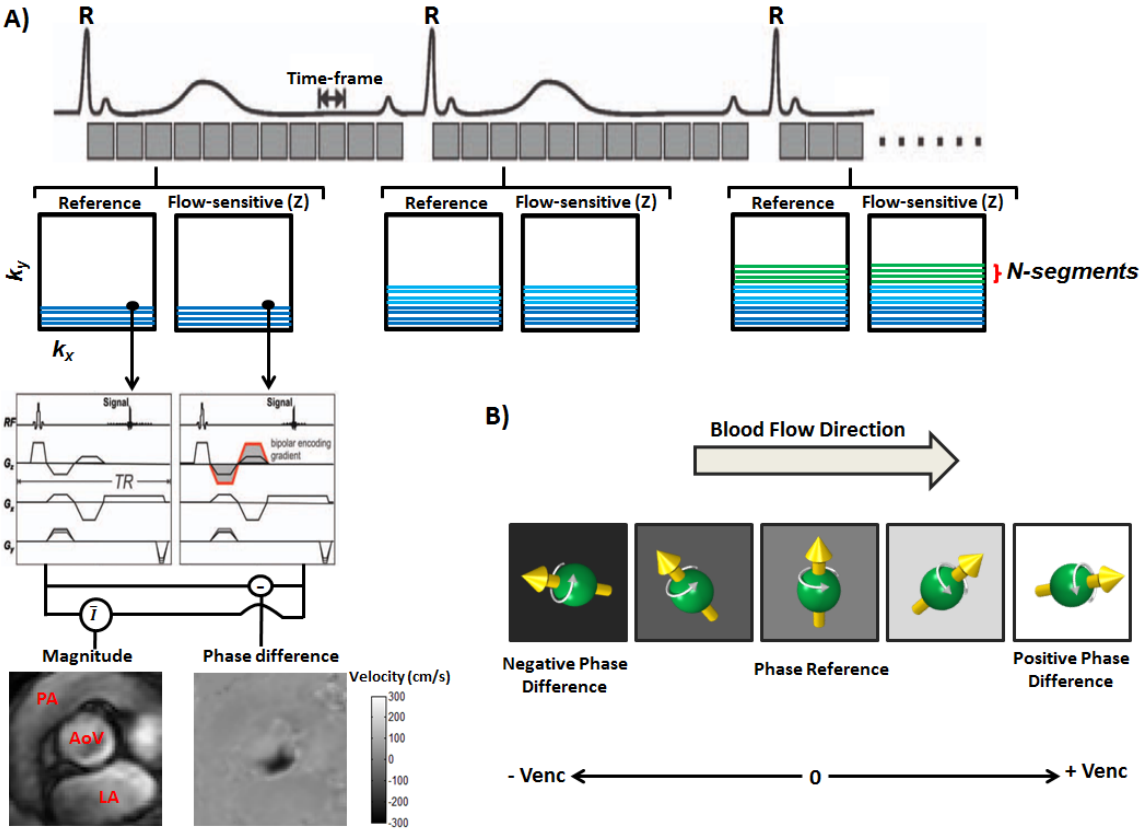

Fig. 2. Standard 2D CINE PC MRI with one-directional through-plane (Z) velocity encoding. Panel A: A reference and velocity sensitive scan (bipolar encoding gradient) are acquired in direct succession. Magnitude images are calculated by averaging both scans and the subtraction provides phase difference images that contain quantitative blood flow velocities, as shown in a 2D slice above and parallel to the aortic valve (AoV), pulmonary artery (PA) and left atrium (LA). Due to time constraints, the MR data cannot be acquired during a single heartbeat, thus velocity data are collected over several cardiac cycles. The measurement is synchronized with the cardiac cycle using an ECG-gated k-space segmented data acquisition. For each heartbeat and time-frame only a subset of N-segments of all required phase-encoding steps are measured. The procedure is repeated until the entire dataset is acquired. The selection of the number of phase-encoding lines (N-segments) determines the temporal resolution (*i.e.*, time to collect data for a single time-frame) and a total scan time of the acquisition. Panel B: The presence of aortic stenosis will require the selection of higher velocity sensitivities (V_{enc}), from 200 to 500 cm/s, for a proper flow measurement. Blood flow velocities in the predominant blood flow direction will appear bright and blood flow velocities in the opposite direction will appear dark. Notice that velocities exceeding V_{enc} range will produce aliasing within the image.

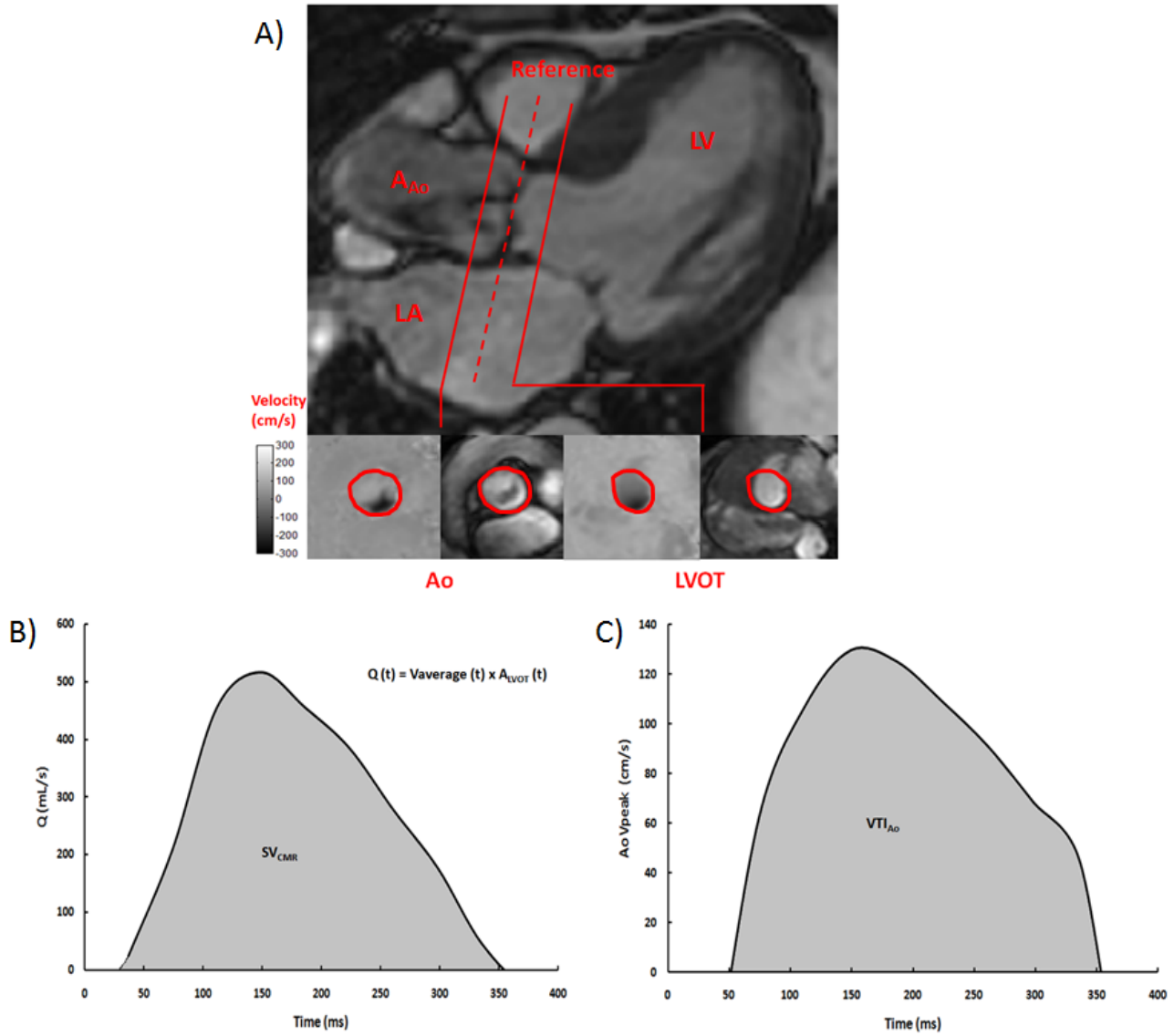

Fig. 3. CMR image planes used for aortic valve measurements. Panel A: Flow velocity map was acquired at two image planes, one located at left ventricular outflow tract (LVOT) and the second at aortic level (Ao) downstream of the aortic valve plane (reference). Red contours in Ao and LVOT planes define the region of interest (ROI) for flow velocity measurements. Panel B: Measurement of stroke volume (SV) during systole at LVOT, ROI appears red in panel A. The change in instantaneous flow (Q) at the ROI is calculated as follows: Q(t) = average velocity (t) $\times A_{LVOT}$, where A_{LVOT} is the cross-sectional area of the LVOT. The SV is estimated by the flow-time integral during systole. Panel C: Peak velocity measurement over systole used for aortic velocity-time integral (VTI_{Ao}) at Ao, ROI appears red in panel A. The VTI_{Ao} is the area under the velocity curve. Both SV and VTI_{Ao} are needed for the valve effective orifice area estimation by continuity equation. Ascending aorta: A_{Ao}; Left atrium : LA; Left ventricle: LV.

EMERGING 2D HEMODYNAMIC MARKERS

Previous TTE studies have suggested that valve opening and closing kinetic analysis, i.e. the temporal changes of EOA during systole, can provide incremental prognostic information beyond standard EOA as computed by the continuity equation [32]-[34]. However this

analysis is cumbersome, time consuming, and may lead to measurement errors using TTE. Aortic valve PC velocity measurements allow the instantaneous computation of EOA using the time-resolved version of the continuity equation (EOA[t]=Q[t]/$V_{Ao-peak}$[t]), where Q[t] is the instantaneous flow at LVOT and $V_{Ao-peak}$[t] is the instantaneous peak velocity of transvalvular flow [28], [35]. In particular, EOA opening slope has been associated with plasma level of NT pro-brain natriuretic peptide (BNP) which has been shown to be a powerful predictor of outcome in patients with AS [36], [37]. Recently, it has been shown that the estimation of aortic valve EOA by CMR using a vorticity-derived jet shear layer detection (JSLD) method avoids the need for SV measurement and is less variable than other flow-derived EOA approaches [27]. This vorticity-derived method shows the potential usefulness of advanced fluid mechanics parameters in the assessment of AS severity using 2D PC measurements.

A recent study suggests that aortic valve flow jet angle/displacement may provide complementary hemodynamic information in patients with isolated AS severity [38]. Angle and displacement were associated to left ventricular function, geometric remodelling and valvulo-arterial impedance, a powerful marker of AS prognosis. In particular, a Cox risk analysis suggested that valve angle may be closely related to aortic valve replacement event. This parameter may play an important role in valve-related aortic diseases; further details are presented in the 4D flow section.

It should be noted that standard 2D PC techniques provide one-directional "through plane" velocity encoding measurements, the image quality may be degraded by noise and/or due to inadequate selection of the $V_{enc.}V_{enc}$ and signal-to-noise ratio (SNR) in the corresponding magnitude images are inversely related ($V_{noise} \approx V_{enc}/SNR$). It is recommended to keep a V_{enc} as low as possible to optimize velocity noise and improve image quality but above the maximal expected velocity to avoid aliasing [39], [40].

ADVANCED 4D FLOW HEMODYNAMIC MARKERS

One of the major limitations of 2D PC measurements is the need to select of a 2D image plane. Full volumetric 3D coverage with three-directional velocity measurements as accomplished by recently introduced 4D flow MRI techniques can help eliminating these limitations [39], [40]. The acquisition of a 3D data volume in combination with 3-directional velocity encoding requires longer acquisition times (up to 15-20 mins) during free-breathing (Fig. 4). Respiration control strategies such as navigator gating are thus necessary to avoid motion effects.

4D flow measurements allow a retrospective plane quantification analysis of imaged cardiac structures. Furthermore, the use of advanced visualization tools with 4D flow data facilitates analysis of complex blood flow patterns, such as highly helical flow commonly observed in the presence of valve disease [41]. The volumetric interrogation of 3D blood flow velocities permits the computation of advanced parameters capable of characterizing valve-related flow effects such as vorticity, JSLD, helicity (in the form of localized normalized helicity, LNH), flow angle, wall shear stress (WSS), and energy loss (turbulent and viscous). It has been suggested that complex flow patterns may play a role in endothelial cell signaling and valvular fiber organization by inducing functional changes within the cells and altering the stimulation of other internal structures such as G-protein and kinase receptors or iron channels [42]-[44].

Flow helicity is typically assessed using 3D flow visualization strategies such streamlines, flow vectors or time-resolved 3D pathlines (Fig. 5). A more effective and representative analysis may be performed using vortical and LNH features. Vorticity-derived features allow for the quantification of JSLD and LNH parameters, and visualization of complex flow patterns. The direct estimation of EOA using a 4D flow JSLD method is an example of a vorticity-derived parameter (Fig. 5) [45], [46]. A recent study demonstrated that LNH features can visualize plug flow organization

in different numerical setups [47], [48]. Similar results can be obtained using 4D flow MRI measurement in the context of valve-related aortic diseases (Fig. 6), allowing a more comprehensive analysis of flow organization due to AS severity. As indicated in the previous section, recent studies have suggested an association between transvalvular jet flow angle and the aortic dilation rate and WSS alteration using 4D flow MRI measurements in patients with bicuspid valves [49], [50]. A recent sub-study of multicenter SEAS study demonstrated that transvalvular energy loss, measured by TTE, may provide independent and additional prognosis information in asymptomatic AS patients rather than conventional TTE measures [51]. In this context, recent studies proposed two methods, turbulent kinetic energy (TKE) dissipation and viscous energy losses (VEL), to compute of energy loss using 4D flow MRI data [52], [53]. Both TKE and VEL may provide further information that traditional energy loss computed with TTE in AS patients. However, larger studies are needed to assess the diagnostic value of both parameters.

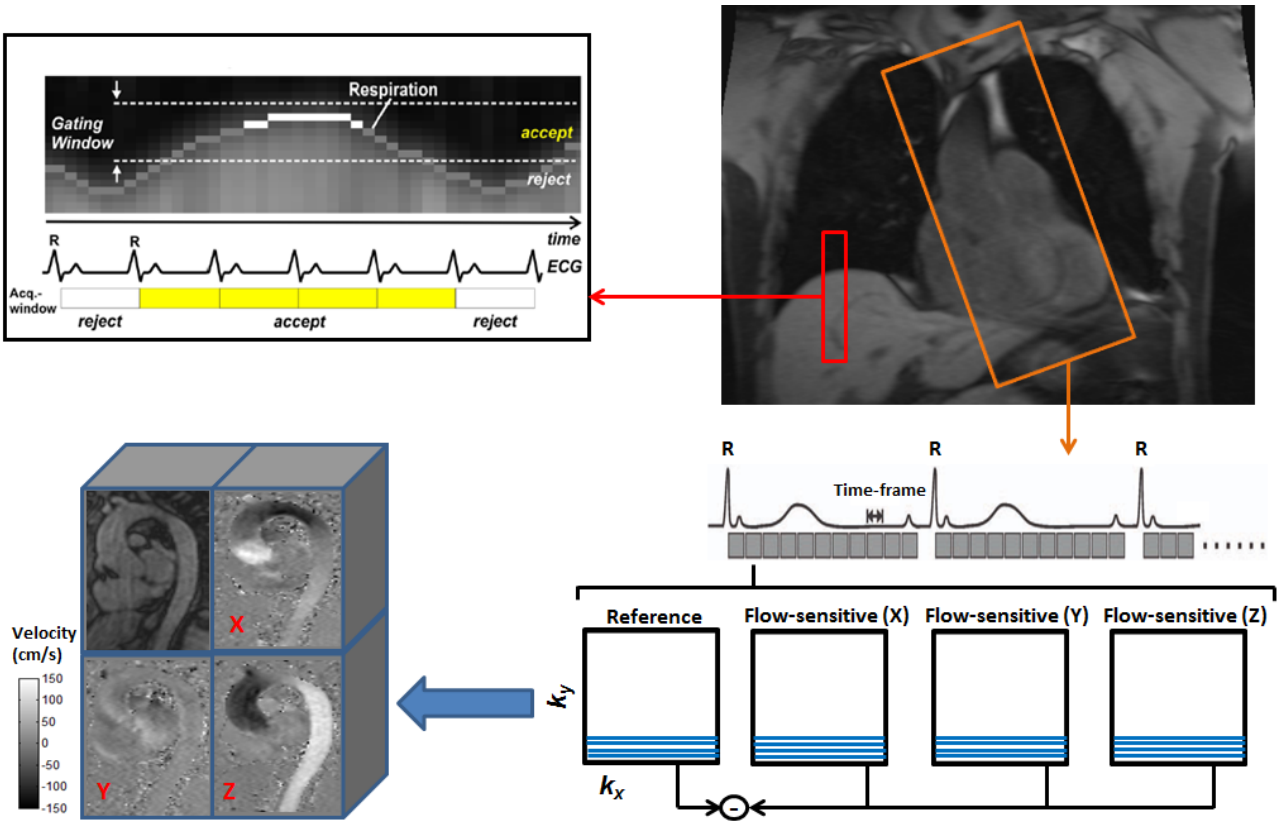

Fig. 4. Schematic of 4D flow of the thoracic aorta. For each time frame, four 3D raw datasets are collected to measure three-directional blood flow velocities (Vx, Vy, Vz) with a reference scan and three velocity-encoded acquisitions. For applications in the aorta or pulmonary systems a typical TR on the order of 5-6 ms, spatial resolution = 2 × 2 × 2 mm^3, Venc = 100-150 ms, Segments = 2, parallel imaging with R = 2, navigator efficiency = 50%-80% results in a total scan time of approximately 15-20 minutes with a temporal resolution of 40-50 ms.

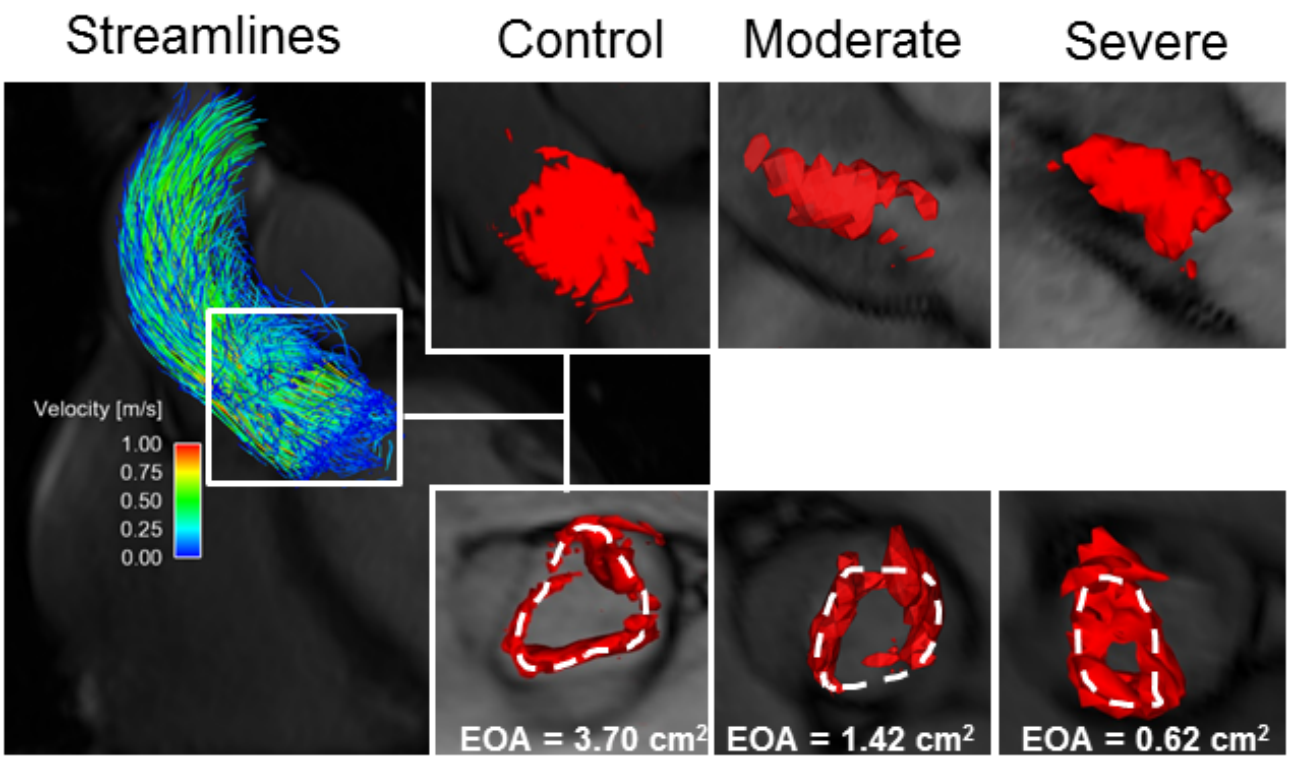

Fig. 5. Aortic valve effective orifice area assessment using jet shear layer detection method. Figure shows three different cases (control, moderate and severe aortic stenosis) using valve area estimation with the 4D flow jet shear layer detection (JSLD) method at peak systole. The first column illustrates the aortic flow velocity streamlines at peak systole; the second column shows a 3D lateral view and top valve view of JSLD structure (red iso-surface) computed from 4D flow MRI data at peak systole for a control subject; the third column shows a 3D lateral view and top valve view of JSLD at peak systole for a moderate aortic stenosis patient; the fourth column shows a 3D lateral view and top valve view of JSLD at peak systole for a severe aortic stenosis patient.

CURRENT CHALLENGES AND FUTURE PERSPECTIVES

Depending on the choice of imaging modality, different limitations and challenges are encountered during the acquisition and analysis of flow for the assessment of AS severity and valve-related diseases. The TTE estimation of most hemodynamic parameters of AS severity (*i.e.*, peak velocity, peak/mean PG, and valve EOA) requires the measurement of SV, which might be subject to several measurement errors, such as image foreshortening or poor image quality of LVOT. Hence, the accurate measurement of flow is mandatory to assess and interpret AS severity parameters. In addition, the standard TTE hemodynamic parameters of AS severity do not take in consideration the influence of pressure recovery phenomenon, the interaction with systemic arterial hypertension, and transvalvular flow rate variability [3]. New TTE parameters, such as the energy loss index (Table 1), have been proposed to consider the pressure recovery that might occurs downstream of the stenotic valve. In particular, patients with moderate to severe AS and small aortas are subject of pressure recovery effect [3], [54]. Patients with AS often have concomitant valve regurgitation, and in both scenarios aortic compliance may be reduced thereby increasing the hemodynamic burden of the LV and the mechanical stress on the aortic valve. An emerging TTE measurement of the arterial load on the LV is the valvulo-arterial impedance, Table 1. It has been proposed that the measurement of aortic compliance and valvulo-arterial impedance by TTE or CMR may better assess the interaction between the ventricular,

valvular and arterial factors, and therefore improve the risk stratification in patients with AS [3]. The main pitfall of all hemodynamic parameters of AS severity, regardless the imaging technique, is the dependence on the trasvalvular flow magnitude which may vary patient from patient and/or follow-up visit of the same patient [55]. In particular the PG, the most frequent used parameter, is directly related to the square of the transvalvular velocity magnitude and may lead to a significant underestimation of AS severity in patients with low-flow rate. Patients with "pseudo-severe" AS at low-flow conditions have the tendency to mask the "true" AS severity and represent a challenging population for therapeutic decision [3]. In these cases, stress testing (exercise or dobutamine challenge) can further aid in the stratification of this patient group. Beyond the assessment of the native aortic valve, same hemodynamic parameters (*i.e.*, PG and EOA) can be used to evaluate implanted prosthetic valves (bioprosthetic valves, new generation of transcatheter valves or TAVIs, and mechanical monoleaflet and bileaflet valves) performance using both 2D and 4D flow MRI [56]-[60]. In general, bioprosthetic valves can be scanned as the native valve. However, a specific limitation may exist for mechanical valves and TAVIs, the metallic components of some prosthesis will present a challenge due to the signal void that they can create. Several studies have shown that signal void was found within the valve but no further downstream of the valve jet where the measurements are performed [56]-[60]. In particular, the single use of a single plane downstream of the valve is suggested [60] due to the difficulty of flow measurement at the LVOT with mechanical heart valves. The flow MRI clinical assessment of prosthetic valves, as a complement of TTE follow-up, may be useful for the early detection of malfunction [58] or valve hemodynamic deterioration.

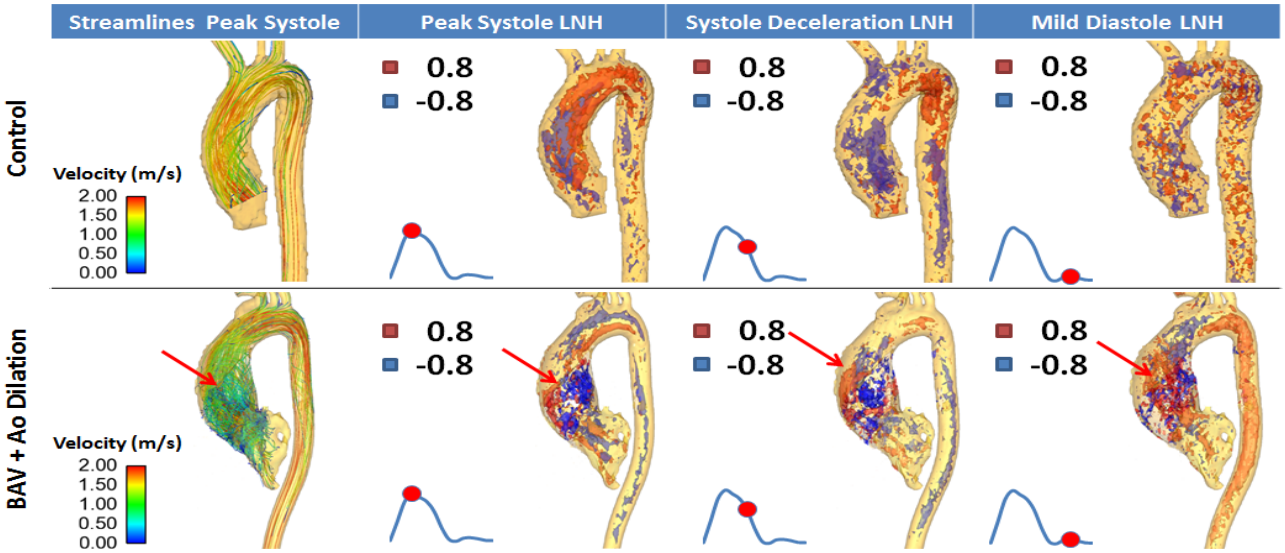

Fig. 6. Aortic flow helicity. The horizontal panels show a control subject and a patient with bicuspid aortic valve (BAV) and aortic (Ao) dilation (> 4 cm). The first column illustrates the aortic flow velocity streamlines at peak systole; the second column shows 3D localized normalized helicity (LNH, positive spin in red, negative spin in blue) features at peak systole; the third column shows 3D LNH features during systole deceleration and fourth column shows 3D LNH features mid-diastole. Localized, tightly coherent, and temporally long LNH structures (red arrow) illustrate the high complex vortex flow alterations which occur during cardiac cycle.

The emerging 2D and advanced 4D hemodynamic markers obtained using CMR, Table 1, represent an initial effort to overcome TTE parameter limitations, may be used to further understand of AS severity hemodynamics, and enhance risk stratification and clinical decision management of these patients. However, it is important to emphasise that further validation in large prospective studies are needed before implementing them in clinical routine. Regarding 4D flow MRI, new strategies focus on sequence design and hardware development (e.g. short echo time, k-space sampling and parallel imaging [61]-[64]), which have the potential to improve acquisition time and make 4D flow measurement fit clinical schedules and time demands. In addition to long acquisition times, advanced 2D and 4D flow parameters often need time-consuming dedicated post-processing for data analysis. The need of more automated assessment for clinical workflow is crucial. Tools and dedicated software most be developed to standardize the measurement of advanced hemodynamic markers and, more important, the translation of those measurements into longitudinal clinical studies evaluating AS severity outcome.

CONCLUSIONS

Quantitative assessment of aortic stenosis severity using cardiovascular magnetic resonance flow imaging is rapidly progressing and will positively impact clinical practice in the near future. In particular, advanced flow techniques such as 4D flow MRI provide a unique and intuitive flow visualization and quantification of several hemodynamic markers. However, current acquisition time and processing strategies need to be streamlined in order to be incorporated in clinical practice. The data presented in this review provides an overview of the potential for these new flow-derived parameters to further the aid in the assessment of AS severity. Nonetheless, larger prospective studies are needed to evaluate the association of advanced hemodynamic markers with patient outcome in valve-related diseases.

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