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Review article

The future of cardiovascular magnetic resonance imaging in thoracic aortopathy: blueprint for the paradigm shift to improve management

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ABSTRACT

Thoracic aortopathies result in aneurysmal expansion of the aorta that can lead to rapidly fatal aortic dissection or rupture. Despite the availability of abundant non-invasive imaging tools, the greatest contemporary challenge in the management of thoracic aortic aneurysm (TAA) is the lack of reliable metrics for risk stratification, with absolute aortic diameter, growth rate, and syndromic factors remaining the primary determinants by which prophylactic surgical intervention is adjudged. Advanced cardiovascular magnetic resonance (CMR) techniques present a potential key to unlocking insights into TAA that could guide disease surveillance and surgical intervention. CMR has the capacity to encapsulate the aorta as a complex biomechanical structure, permitting the determination of aortic volume, morphology, composition, distensibility, and fluid dynamics in a time-efficient manner. Nevertheless, current standard-of-care imaging protocols do not harness its full capacity. This state-of-the-art review explores the emerging role of CMR in the assessment of TAA and presents a blueprint for the required paradigm shift away from aortic size as the sole metric for risk-stratifying TAA.

1. Introduction

The healthy aortic wall functions as a robust biomechanical structure, loading and unloading cardiac volume efficiently and reliably. To achieve this, the molecular and cellular environment of the aorta is monitored and stabilized through a complex interplay between vascular wall cells and the extracellular matrix (ECM) [1]. This homeostatic process is altered in a variety of disease states, collectively described as aortopathies in which the aortic wall becomes weak and susceptible to damage (Fig. 1). Thoracic aortopathies result in aneurysmal dilatation of the aorta known as thoracic aortic aneurysms (TAA), which develop due to imbalances in ECM synthesis and degradation that are predominantly driven by dysregulation of transforming growth factor beta 1 (TGFβ) signaling, fibrillin fragmentation, and metalloproteinase activation (Fig. 2) [1].

TAA manifest clinically as acute aortic syndromes (AAS)—dissection or rupture—that are life-threatening with mortality 80% in sufferers

Abbreviations: 2D, two-dimensional; 3D, three-dimensional; 4D, four-dimensional; AAS, acute aortic syndrome; AI, artificial intelligence; BAV, bicuspid aortic valve; CFD, computational fluid dynamics; CTA, computed tomography angiography; ECM, extracellular matrix; IRAD, International Registry of Acute Aortic Dissection; MRI, magnetic resonance imaging; OSI, oscillatory shear index; PET, positron emission tomography; PWV, pulse wave velocity; TAA, thoracic aortic aneurysm; USPIO, ultrasmall superparamagnetic iron oxide; WSS, wall shear stress; CMR, cardiovascular magnetic resonance; TGFβ, transforming growth factor beta; TSP1, thrombospondin; FBN, fibrillin; MMP, matrix metalloproteinase; MRA, magnetic resonance angiography; BOOST, Bright-blood and black-blOOd phase SensiTive inversion recovery; HASTE, half-Fourier single shot turbo spin echo

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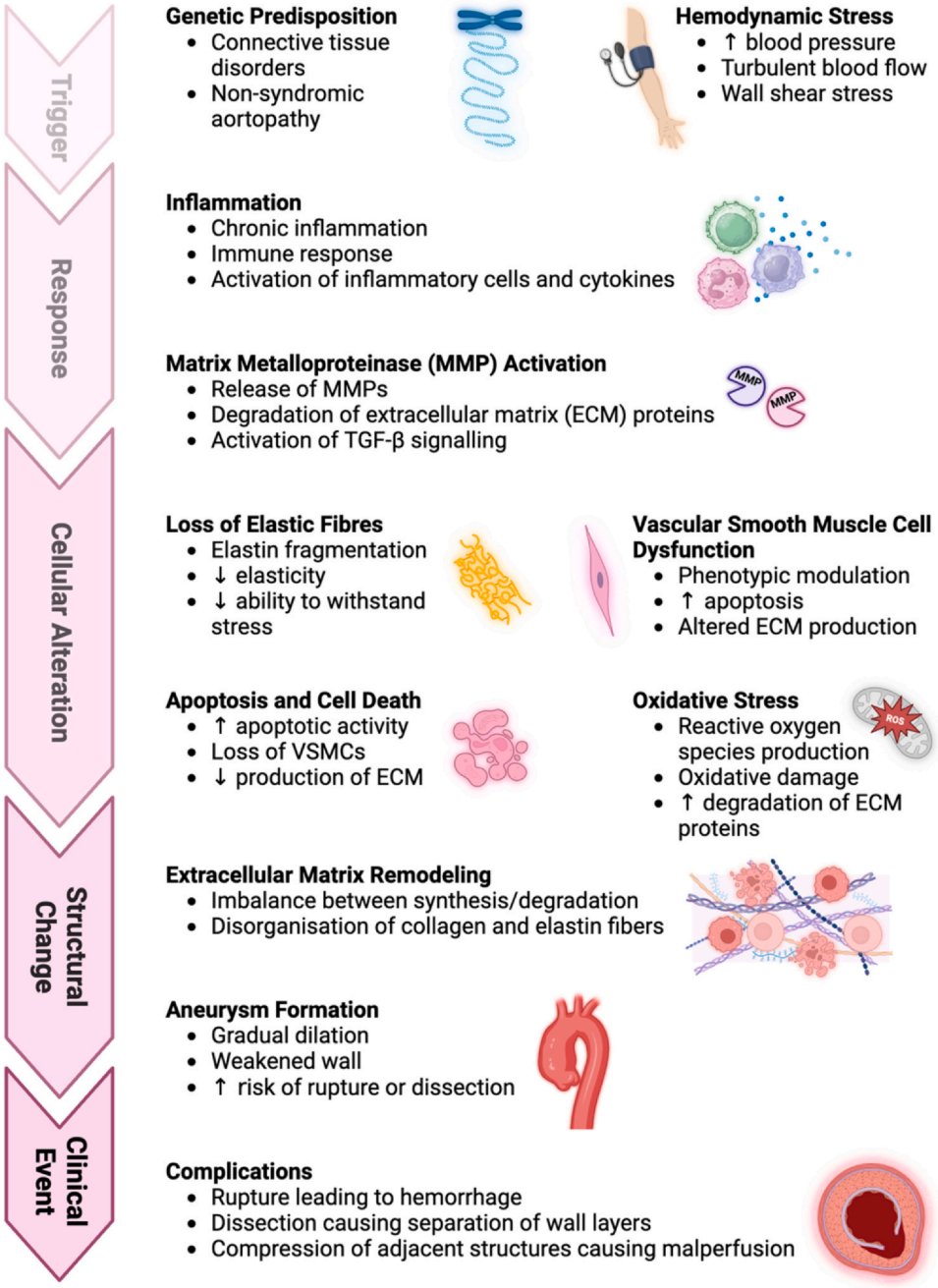

Fig. 1. Mechanism underlying the development of thoracic aortic aneurysms. *TGFβ* transforming growth factor beta 1, *VSMC* vascular smooth muscle cells

[2]. Incidences of TAA appear to be rising [3], likely owing to improved diagnostic approaches, with abundant non-invasive imaging tools for assessment including echocardiography, computed tomography angiography (CTA), and magnetic resonance imaging (MRI) [4]. Nevertheless, the greatest contemporary challenge in the management of TAA is the lack of metrics beyond aortic diameter for risk stratification to guide preventative surgery.

Though there is robust evidence supporting the correction of aortic dimensions to body size [5–8], guidelines advocate for prophylactic surgical intervention based on absolute aortic diameter, along with growth rate and the presence of genetic predispositions [9]. A key limitation of utilizing absolute aortic diameter is that it does not represent the three-dimensional (3D) pathological process underlying TAA or adjust to individual characteristics, an approach especially important in quantifying fusiform aneurysms [10]. Nevertheless, acute complications are rare in ascending non-syndromic TAA of moderate dilatation, but the incidence sharply rises to 3–7% per year when the diameter exceeds 60 mm [11,12]. To avoid aneurysmal expansion beyond these critical points, guidelines recommend preventative surgery for an ascending thoracic aortic diameter of 55 mm, or lower in the presence of connective tissue disorders, family history, AAS, or concomitant bicuspid aortic valve (BAV) [9].

Despite this link between severe TAA dilatation and unfavorable outcomes, most dissections appear to occur at aortic diameters below guideline recommendations for prophylactic surgical correction. The International Registry of Acute Aortic Dissection (IRAD) [13], a multinational database of over 7300 aortic dissection cases, found that 60% of patients had aortic diameters below the threshold for prophylactic surgery, implying that current guidelines designed to mitigate dissection risk fail to prevent most real-world events. Additionally, since the aorta dilates after the onset of dissection, it is likely that the number of events that would have been prevented based on current diameter cut-

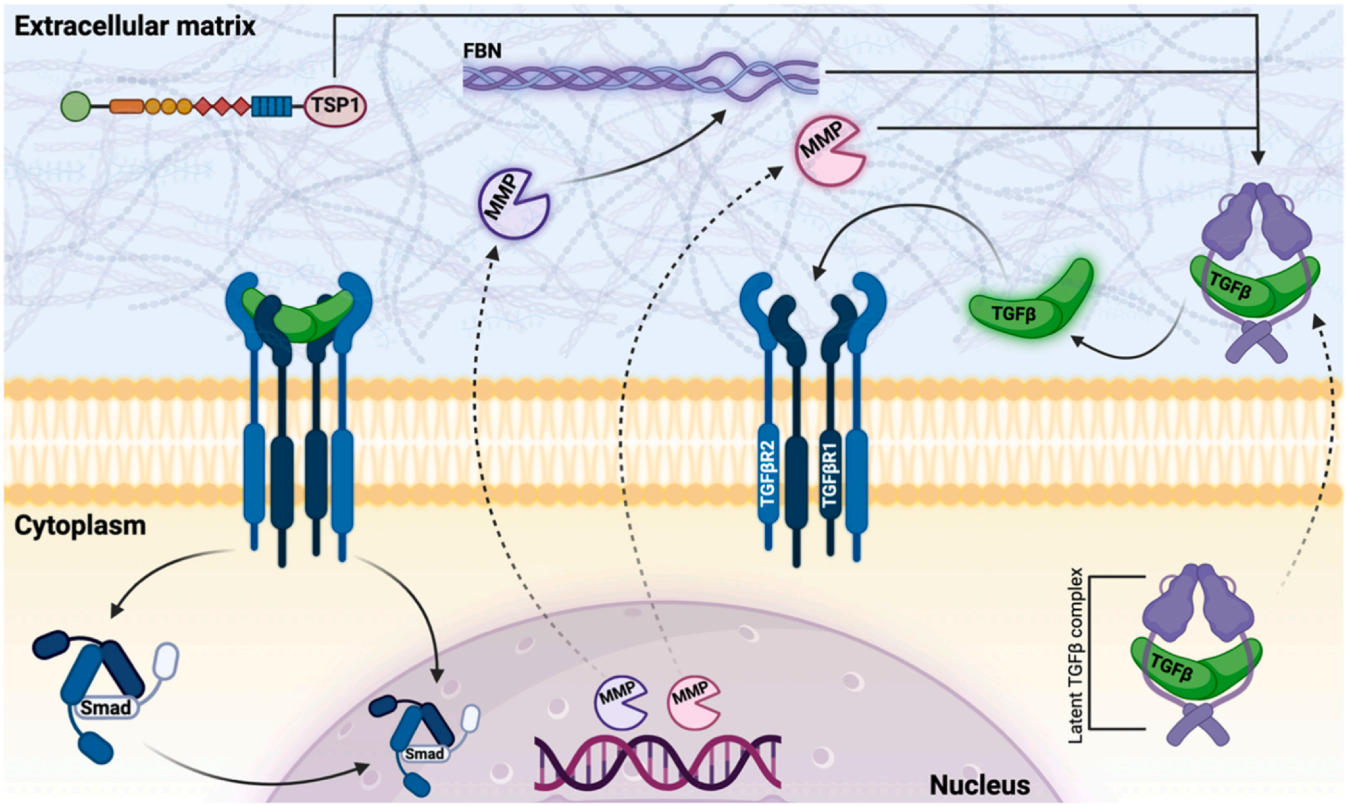

Fig. 2. Key molecular pathway signaling driving extracellular matrix degradation and thoracic aneurysm formation. Transforming growth factor beta 1 (TGFβ) signaling plays a crucial role in the development of thoracic aortic aneurysms. Within the extracellular matrix (ECM), TGFβ is normally kept in an inactive state, bound to latency-associated peptides and further stabilized by ECM components. Various proteases including matrix metalloproteinases (MMP), thrombospondin (TSP1), and fibrillin (FBN) fragments can cleave latent TGFβ complexes, releasing active TGFβ into the ECM to bind with its subunits (TGFβR1 and TGFβR2). Binding of TGFβ results in Smad protein phosphorylation and nuclear translocation of Smad complexes, driving gene activation and MMP release. Within the ECM, MMPs cause proteolysis and resultant pathological degradation of the ECM, as well as further release of active TGFβ through direct (cleavage of latent TGFβ complexes) and indirect (MMP-associated fragmentation of fibrillin) pathways. *MMP* matrix metalloproteinase

offs is even lower than those represented in IRAD [14]. This hypothesis has been recently corroborated in a nationwide echocardiographic cohort, which demonstrated that although severe TAA affords a nearly 30-fold increased risk of aortic death; over 90% of the population who experienced aortic mortality did so at diameters that were less than severely dilated prior to their indexed events [15].

This pattern has been described as “the aortic paradox” and reinforces the core statistical principle that event rates are a function of both the likelihood of an event and the population numbers in which it occurs. That is, despite a grossly increased probability of aortic dissection in severely dilated TAA, given its low incidence, the much larger population who have non-severely dilated aortas experience the majority of fatal aortic dissections [15]. Hence, although aortic diameter predicts AAS on a population level, these metrics alone are insufficient to identify individual risk. Nevertheless, it is questionable if lowering the thresholds for surgical intervention alone would bear a long-term mortality benefit as it may expose a considerable number of patients with smaller TAA and thus, minimal yearly risk of dissection to morbidity and mortality associated with elective surgery. To improve patient care and outcomes, diagnosis must therefore move beyond aortic dimensions as a sole metric and toward determining volume, morphology, composition, distensibility, and fluid dynamics within the aorta.

Cardiovascular magnetic resonance (CMR) presents a promising imaging candidate to provide the required shift in paradigm if we are to improve patient management in TAA. It is a superior tool for imaging cardiovascular structures and large arteries, owing to its high spatial resolution and soft-tissue contrast [16,17], and has excellent correlation with histology in aortic disease [18,19]. Additionally, CMR can be coupled with emerging contrast agents to provide an understanding of the underlying pathological processes and disease activity (Graphical Abstract).

Current standard-of-care for CMR of TAA typically involves magnetic resonance angiography (MRA), diaphragmatic navigator-gated 3D whole heart bright-blood imaging, assessment of cardiac function, and two-dimensional (2D) late gadolinium enhancement (LGE) of the myocardium with an aortic valve stack and flows, despite having time-efficient capabilities beyond these conventions (Table 1) [20]. Given the current limitations for reliable risk stratification coupled with advances in aortic imaging using CMR, attention has turned to the application of novel CMR-based sequences to better understand aortic disease and develop a more holistic approach to understanding its pathophysiology. This review will look at emerging CMR applications that seek to enhance assessment of aortic disease by moving beyond aortic dimensions to understand TAA morphology, aortic wall composition, biomechanics, and molecular changes which may be applied to improve risk stratification and guide management for patients.

2. The aorta in 3D: length, volume, and morphology

A key limitation of absolute aortic diameter is that it does not represent the 3D pathological process underlying TAA. Axial aneurysmal expansion and morphologic deformation are not comprehensively assessed by site-specific aortic diameter measurements, which may not necessarily be present in this form of remodeling [21], strengthening the case for multidimensional growth measurements. Recent studies have demonstrated that with the use of CMR, it is possible to determine anatomical regions that exhibit dilatation more precisely and

Table 1
Sequences, timing, and capacity of standard-of-care versus a proposed protocol for MRI in aortopathy.

	Standard-of-care	Proposed protocol
Sequences, order of acquisition, and time (min)		
	1. Localizer (1) 2. HASTE (1) 3. Cine: cardiac, aortic valve (5) 4. 2D aortic flow (1) 5. MRA (2) 6. EGE—myocardium (1) 7. 3D whole heart (8) 8. 2D LGE—myocardium (10)	1. Localizer (1) 2. Cine: cardiac, aortic valve, AA/DA at MPA (6) 3. iT2Prep-BOOST (8) 4. 4D flow (10) 5. 3D LGE—myocardium + thoracic aorta (8)
Total time (min)	29	33
Data obtained		
Myocardium		
LV/RV volumetry and function	+	+
Fibrosis	+	+
Aortic valve		
Morphology	+	+
Function	+	+ +
Aortic measurements		
Luminal diameter/area	+	+
Volumetry	+	+
Morphology	+	+
Aortic biomechanics		
Stiffness	−	+
Distensibility	−	+
Wall shear stress	−	+
Aortic wall composition		
Thickness	+	+
Plaque burden	+	+
Plaque phenotype	+	+ +
Intramural hematoma	+	+ +
Fibrosis	−	+

AA ascending aorta, *DA* descending aorta, *MPA* main pulmonary artery, *MRA* magnetic resonance angiography, *EGE* early gadolinium enhancement, *LGE* late gadolinium enhancement, *LV* left ventricular, *RV* right ventricular, *2D* two-dimensional, *3D* three-dimensional, 4D four-dimensional, *HASTE* half-Fourier single shot turbo spin echo, *BOOST* Bright-blood and black-blOOd phase SensiTive inversion recovery

reproducibly than manual measurements [22,23]. This allows for the identification of regions with expansion beyond the aortic segments measured according to expert recommendations [4]. These insights highlight how CMR permits 3D visualization of the aorta which can facilitate morphologic, length, and volume calculations that are essential in surgical planning and may enhance risk assessment.

In cases of aortic dissection, entry tears predominantly occur in the circumferential direction, which acts along the length of the vessel and leads to tears perpendicular to the direction of the force [24]. Despite these post-mortem findings, longitudinal stress is the primary driver of aneurysmal development, a consequence of the pressure generated by the heart with each beat. Longitudinal elasticity is a major component of the Windkessel effect, the physiological state driving aortic mechanical function [25], with elongation of the aorta purported to reflect a loss of longitudinal elasticity and increased stress on the intima [26]. Studies have demonstrated that aortic longitudinal strain is a predictor of aortic events in patients with Marfan syndrome [27], and that elevated longitudinal wall stress in non-genetic patients predicts the site of the entry tear before aortic dissection [28]. Thoracic aortic length can be determined on CMR by measuring the length from the aortic annulus or sinotubular junction to the origin of the innominate artery, though using the aortic annulus rather than the sinotubular junction accounts for difficulties in determining the site of the latter when effacement has ensued [29]. Recently, thoracic aortic aneurysmal length beyond 13 cm has been demonstrated to confer an approximately 5-fold greater risk of AAS in both non-genetic and genetic aortic disease compared to aneurysms of < 9 cm in length, with a hinge point of 11 cm serving as a potential intervention criterion to avoid adverse events [30].

Aneurysmal volume provides a more comprehensive measurement than aortic length alone and offers additional insights into the severity and progression of TAA. While the formula for aortic volume calculation (π[diameter/2]^2 $\times$ length) assumes a cylindrical geometry, more accurate methods exist through the use of 3D CMR data. Specifically, volumetric analysis can be refined by summing the voxels within the segmented aneurysm, providing a more precise assessment that accounts for the often irregular shapes of aortic aneurysms. This approach is especially important for non-cylindrical aneurysms, such as saccular types, which have been shown to carry a higher risk of rupture compared to fusiform aneurysms.

When indexed to body surface area or height, volumetric measurements facilitate improved quantitative assessments for both presurgical monitoring and postoperative surveillance. Although aortic diameter and length are already predictive of AAS [29], combining these measurements into a voxel-based volumetric analysis improves the sensitivity and accuracy of these predictive models. In fact, the sensitivity of aortic volume for predicting AAS has been shown to be up to seven times higher than that of maximal aortic diameter alone, while maintaining high reproducibility [31]. The inclusion of both accurate volumetry and aneurysm morphology in routine TAA surveillance strengthens the case for its application in clinical practice.

Similar discrepancies have been found with regard to aortic tortuosity and morphology, where the degree of ascending aortic deformation has been shown to increase the likelihood of aneurysmal expansions [32–34]. Aortic tortuosity can be readily determined by CMR using 3D whole heart and MRA sequences, and has been associated with a higher rate of aortic events in patients with Marfan syndrome [35]. However, the clinical uptake of tortuosity assessment is currently limited by an absence of data supporting its predictive utility in non-genetic AAS and the lack of a universal method for its measurement. In general, the main limitation of applying CMR to comprehensively define the aortic size, volume, and shape in 3D is the absence of age and anthropometric adjusted reference values and the time required to

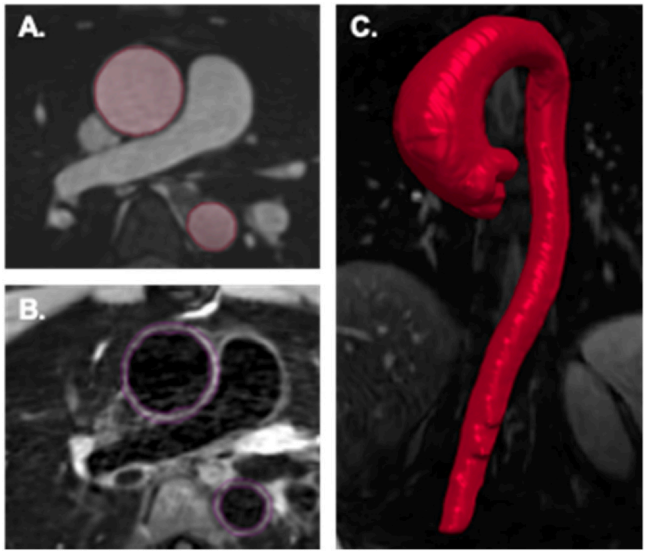

Fig. 3. AI segmentation of the aorta. Axial views of the ascending and descending aorta at the right pulmonary artery using bright (A) and dark (B) blood sequences. Corresponding AI segmentation of the lumen (A) and aortic wall (B) is displayed in red and purple circles. A 3D image of the aorta can be extracted based on the segmentation in (A), as shown in (C), which can then be applied to determine aortic length, degree of tortuosity, and quantify volume. *3D* three-dimensional, *AI* artificial intelligence

obtain these measures. Prospective studies aimed at standardizing methods and determining population-specific reference ranges coupled with the continued integration of machine learning and artificial intelligence (AI) into CMR software and practice will hasten their clinical uptake (Fig. 3) [36–38].

3. Aortic biomechanics: stiffness, distensibility, and wall shear stress

3.1. Aortic stiffness and distensibility

Aortic stiffness and distensibility relate to how the aorta responds to changes in pressure and volume during the cardiac cycle. Aortic stiffness refers to the resistance of the aorta to deformation and is associated with increased rigidity of the arterial walls [39]. Distensibility relates to the ability of the aorta to expand in response to increased pressure and volume following cardiac systole and is a measure of elasticity and compliance of the aortic wall [40].

CMR assessment of aortic stiffness can be measured by pulse wave velocity (PWV) on phase-contrast sequences. PWV represents the speed at which the pressure wave travels along the aorta, with stiffer arteries transmitting these waves faster. CMR can be applied to image the aorta at two different locations and then measure the time it takes for the pulse wave to travel between these points. This traditional method of measuring PWV is limited as it only measures PWV across two specific sites and when various aortic segments need to be examined, would require assessment at multiple levels. Consequently, the quantification of PWV has been introduced through the implementation of four-dimensional (4D) flow sequences (see below). This approach has shown a strong correlation with 2D PWV [41] and affords the advantage of continuously evaluating the biomechanical properties of the entire aorta in a single acquisition. Using these sequences, an increase in aortic stiffness has been shown to be associated with aging [42]. Additionally, other studies have demonstrated that the biomechanical properties of the aorta are similar in both bicuspid and tricuspid aortic valves regardless of the degree of dilation, and different from those with Marfan syndrome who have generally higher aortic stiffness [43–45].

Aortic distensibility is determined by aortic cine imaging whereby cross-sectional area change is quantified in diastole and systole to determine aortic compliance. However, similar to traditional PWV assessment, this method only establishes aortic distensibility in specific aortic segments and not throughout an entire region. Therefore, other methods that assess the entire aortic volume, or a combination of parameters such as local distensibility with longitudinal strain, should be implemented to achieve a more comprehensive evaluation. Sequences to determine stiffness and distensibility are acquired rapidly by CMR and have been associated with cardiovascular outcomes [46–49], with evidence of additional utility in TAA sub-populations including those with Marfan and Turner syndrome, as well as in cases of morphologically BAV [50–53].

3.2. Wall shear stress

CMR flow assessment relies on phase-contrast techniques to acquire image contrast between moving and stationary protons. The underlying concept is based on the feature of protons to accumulate a phase shift that is proportional to the speed at which they move along a magnetic gradient field. Traditionally, phase contrast has been acquired using a 2D acquisition that encodes velocity in one principal direction and is available on all modern magnetic resonance imaging (MRI) systems as an integral part of clinical protocols assessing blood flow and cardiac and valve function in the heart and large vessels [54]. Recent advances have led to the acquisition of time-resolved, 3D, three-directional encoded velocity data. This technique is commonly referred to as 4D flow and provides detailed flow visualization within the aorta to allow flow quantification at any location within an acquired volume [55]. Furthermore, the obtained velocity data can be incorporated with computational fluid dynamics to reliably estimate wall shear stress (WSS).

WSS refers to the force per unit area ($N/m^2/Pa$) exerted by blood flow on the aortic endothelium and is an important parameter in understanding its hemodynamic conditions, which has been demonstrated to remain constant in subjects irrespective of increasing TAA size [56]. Blood flow induces a drag between the outermost layer of blood and the inner layer of the vascular wall in contact with blood and vascular WSS can affect both the functional and the structural integrity of endothelial cells [57]. MRI-derived 4D flow to determine WSS predicts histopathological and biomechanical changes in the aortic wall in patients with TAA [58–60], adding to the understanding of the complex flow patterns distal to the aortic valve and guiding understanding of the mechanism underlying aortic dilation (Fig. 4) [61].

Determination of aortic WSS involves considering blood flow dynamics (velocity profile and laminar flow) and vascular geometry, as shear stress is directly proportional to the velocity gradient (change in velocity with respect to distance) and inversely proportional to the vessel radius. In simplified scenarios, laminar flow through a cylindrical conduit can be determined by the Hagen-Poiseuille equation to estimate shear stress (τ) ($\tau = 4\eta(Q/\pi r^3$, where η is the viscosity of blood, Q is the volumetric flow rate, and r is the radius of the vessel) [62]. WSS can then be calculated as the product of the viscosity and the velocity gradient near the vessel wall and expressed as $WSS = \tau/\rho$, where ρ is the blood density. However, this model does not account for aortic anatomical variances which require more sophisticated computational fluid dynamics to determine WSS. Computational fluid dynamics takes into account aortic geometry, valve function, non-uniform velocity profiles, and fluid properties to provide more accurate estimations of WSS [63], and can be employed following 4D flow CMR to analyze and simulate blood flow patterns within the cardiovascular system [64].

The role of WSS in aortic pathology has been most extensively studied in patients with BAV. In these patients, increased flow eccentricity through the aortic valve [65–67], greater vorticity [68,69], and consequently increased WSS have been described [70–72], especially in those with aortic valve stenosis [73]. This pattern of increased WSS varies depending on valve morphotype and the pattern of ascending

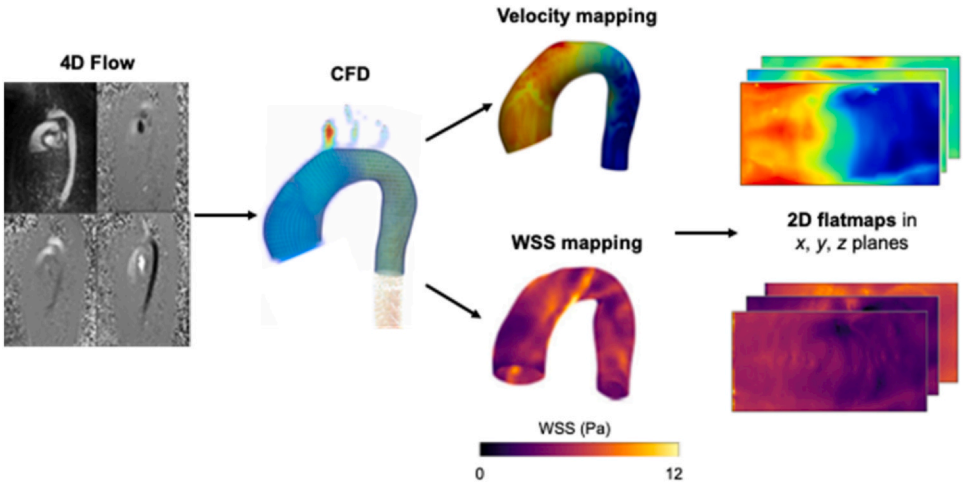

Fig. 4. Workflow of wall shear stress acquisition by 4D flow CMR. Following 4D flow sequence acquisition, the aorta can be segmented and computational fluid dynamics (CFD) applied. An automated registered mesh of the aorta can be derived and applied by CFD, following which spatial coordinates (in the x, y, z planes) of each mesh node can be used to calculate velocity and wall shear stress maps in 3D and as 2D flatmaps. Though CFD is not required for velocity mapping, which can be performed in real-time and is therefore more time efficient, it may lack resolution, noise control, and predictive capabilities in which case CFD can be complementary. *2D* two-dimensional, *3D* three-dimensional, *4D* four-dimensional, *CMR* cardiovascular magnetic resonance, *WSS* wall shear stress

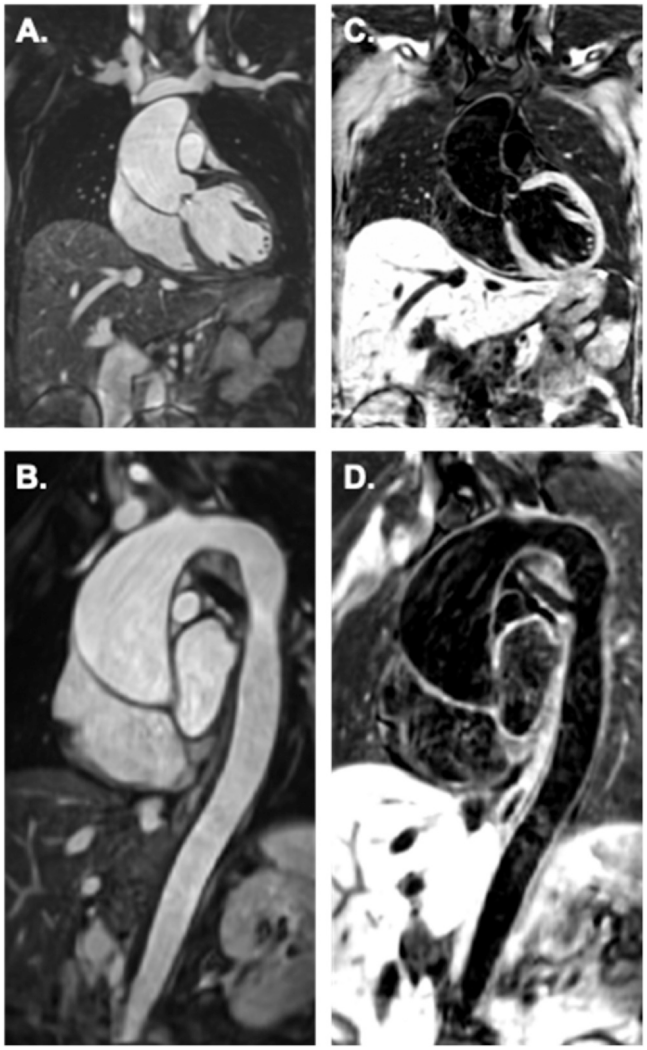

Fig. 5. iT2Prep-BOOST sequence in thoracic aortopathy. Simultaneous bright (A and B) and dark (C and D) blood imaging using the iT2Prep-BOOST sequence in the coronal and sagittal planes in a patient with fusiform aneurysm of the thoracic ascending aorta. This single sequence can be utilized to determine the presence and degree of aneurysmal dilatation on the bright-blood imaging as well as identify underlying pathological processes involving the aortic wall using dark blood imaging. *BOOST* Bright-blood and black-blOOd phase SensiTive inversion recovery

aortic dilation. Furthermore, various prospective longitudinal studies have demonstrated a relationship between flow eccentricity and increased WSS with aortic dilation [74,75], and WSS angle has been shown to be predictive of aortic growth [76]. All of this makes this parameter highly relevant in the follow-up of these patients, especially in patients with genetic aortic diseases, as there are few predictors of events beyond diameter. In patients with Marfan syndrome or Loeys Dietz syndrome, alterations in flow beyond the aortic root have been demonstrated and could be related to its dilation [77,78].

Another parameter gaining relevance in patients with arterial dilation is the oscillatory shear index (OSI). The OSI measures the degree to which WSS changes direction during the cardiac cycle and is used as an indicator of disturbed WSS. Several studies have correlated this parameter with the development of thoracic aneurysms and its role in aortic dilation [71,79], though more information is needed to establish its role in ascending aortic dilation [80].

Though increased WSS determined by 4D flow correlates with histopathological changes seen in TAA, there are limited data demonstrating its utility in predicting TAA aneurysmal progression and risk of future aortic events; however, data in the abdominal aortic aneurysm population appear favorable [81,82]. Prospective studies should seek to explore the clinical utility of 4D flow in predicting TAA sequelae to strengthen the case for its routine performance.

4. Aortic wall composition

Applying CMR to understand aortic wall architecture allows for an enhanced understanding of the associated risk factors driving progressive aortic expansion and events. It is understood that aortic flow alterations are linked to structural changes in the aortic wall that predispose it to dilation [58,83]. Therefore, the presence of eccentric flow, rotational flow, and increased WSS are associated with ultrastructural changes at the intima and media layers, contributing to aortic dilation [84–86]. As discussed, CMR can assess aortic flow alterations, and it also enables evaluation of changes in the composition of the aortic wall. CMR can be utilized to determine aortic wall thickness, the presence of aortitis, cystic medial necrosis, plaque burden, and its phenotype as well as the presence of intramural hematoma, providing insights into risk stratification and implications for clinical outcomes relating to aortic disease [87–91]. Moreover, the development of advanced MRI sequences permits the assessment of aortic wall dimensions and architecture in a time-efficient manner, providing valuable ancillary information in TAA with practical applicability.

In particular, recently developed simultaneous bright- and black-blood aortic imaging shows improved image quality compared to conventional T2-prepared balanced steady-state free precision and

half-Fourier single shot turbo spin echo (HASTE) sequences with comparable measurements for aortic wall and lumen dimensions and is on average 4 min (40%) faster with the additional provision of black-blood images (Fig. 5) [92]. This iT2Prep-BOOST sequence has been applied in patients with TAA to demonstrate its utility beyond current standard-of-care sequences and can be coupled with 3D whole heart LGE sequences to assess fibrosis within the aortic wall [92,93]. The clinical value of LGE for diagnosing myocardial fibrosis and informing clinical decision-making is well-established [94,95]. Nevertheless, the utility of LGE CMR to assess aortopathy is yet to be elucidated despite the knowledge that cystic medial necrosis and associated ECM expansion through the accumulation of proteoglycans and loss of smooth muscle cells are central processes driving the development aortopathy and aortic events, making these regions more likely to retain LGE than healthy aortic tissue. Prospective trials looking at aortic LGE are needed to determine the utility of its quantification and relationship to clinical progression of TAA. Furthermore, the combined investigation of flow alterations and arterial composition changes could be significant for a more comprehensive understanding of the progression of aortic dilation.

5. Molecular imaging in aortopathy

Molecular MRI can be facilitated using probes with gadolinium chelators and ultrasmall superparamagnetic iron oxide (USPIO) or coupled with positron emission tomography (PET) to provide an understanding of pathobiological activity in TAA. Novel PET tracers targeting calcification as a surrogate of elastin loss and fibrosis (^{18}F-NaF) as well as inflammation and thrombus (^{18}F-FDG) have been applied in vivo and correlate with expanding aortic aneurysms and dissection [96–98], with multiple pre-clinical probes currently under investigation [99–101]. It is worth noting that PET-based imaging approaches come with additional cost, feasibility, and radiation exposure that may potentially limit their wider uptake into clinical practice. In this vein, USPIO-enhanced CMR may be more pragmatic. USPIO can identify macrophages and is considered a surrogate measure of vessel wall inflammation in aortic aneurysm [102], which in human trials has been demonstrated to predict abdominal aneurysm expansion, rupture, and surgical repair [103].

Gadolinium-based molecular probes remain at the pre-clinical stage [104], with limitations in their in vivo application deferred by more stringent pathways to clinical translation when compared to PET-based agents that can be administered at significantly lower doses and cost; enhancing their safety profile and scalability. Notwithstanding, in the pre-clinical setting collagen, elastin and tropoelastin sensing molecular probes have been demonstrated to reliably identify rapidly expanding aneurysms and predict rupture [105–107]. The potential utility of molecular imaging to identify disease-specific pathological processes relating to TAA could provide an understanding of disease activity which is currently not afforded in aortic imaging and may be applied to stratify risk, survey TAA, and guide intervention.

6. Conclusion

There is now substantiative evidence identifying that absolute aortic dimensions in TAA are insufficient in predicting patient-specific risk of future AAS [13,15]. These findings challenge the utility of current guideline recommendations for preventative aortic surgery in asymptomatic patients [9], which are limited in the main by an absence of data supporting other reliable predictors. Moreover, its 3D distribution allows for the assessment of aortic growth maps, providing information on the dilation of different aortic regions beyond the determination of a single diameter [22]. CMR has the advantage of providing better soft-tissue contrast allowing for the characterization of the vascular wall beyond that afforded by CTA or echocardiography, making it a superior candidate for aortic assessment in non-emergent cases [16,17]. Additionally, CMR offers valuable insights into the biomechanical properties of the aorta [4], providing the necessary tools to move beyond aortic size as the lone standard in guiding clinical decision-making and personalizing patient management. Owing to the development of novel imaging sequences and the rapidity of their acquisition, CMR to assess this complex biomechanical structure can be delivered in roughly the same time taken to perform current standard-of-care aortic imaging with prognostic applications beyond conventional protocols (Table 1). This review provides an outline of the CMR-based tools that can be utilized to identify high-risk disease features that could warrant earlier intervention, facilitating a paradigm shift to a more comprehensive understanding of the aorta and the pathological processes underlying TAA.

Given the complex heterogeneity of TAA, it is worth highlighting that certain sequences embedded within the proposed CMR approach may be of greater clinical utility in certain cases. Genetic factors ranging from syndromic to heritable aortopathies drive TAA, as well as anatomical variations such as BAV. Conversely, patients can develop aneurysms from environmental and degenerative changes related to aging, hypertension, and smoking as well as local factors such as prior cardiac surgeries where the aorta has been cross-clamped or from infective, granulomatous, and autoimmune disorders [108]. Due to these variances in etiology, certain MRI sequences may be more beneficial in predicting risk for specific TAA sub-populations; such as 4D flow in BAV or aortic deformation and fibrosis in Marfan syndrome. Accordingly, it is logical that prospective studies seek to enroll specific TAA cohorts to discern the efficacy of the proposed sequences within sub-populations.

6.1. Limitations

There are some limitations to the proposed protocol contained within the review (Table 1) that should be considered, these relate primarily to workflow optimization and offline reconstruction. First, the current workflow from image acquisition to analysis is not fully streamlined for some of the sequences described. Such processes currently rely on various software platforms and manual intervention, which can be time-consuming and cumbersome. For such a protocol to be adopted on a wider scale and to enhance generalizability and reproducibility, the development of integrated software solutions is necessary. Such advances will allow more seamless transition from scanner output to analysis, reducing operator dependency and facilitating efficient clinical use across centers. Second, the inclusion of 4D flow CMR presents challenges due to the need for CFD modeling. Though CFD is not necessarily required for velocity mapping, it can allow for enhanced assessment in complex cases. The caveat of CFD remains the long computation times and offline reconstruction of scanner data, which limits application and increases complexity in the clinical setting. Moving forward, improvements in computational efficiency and automated reconstruction methods to streamline 4D flow assessment would improve uptake and usability.

6.2. Future directions

The prevalence of AAS is increasing independent of an aging population [109], and despite a high, and under-recognized mortality rate [9,110], AAS are rare because of the relatively low prevalence of TAA [111], making prospective studies using the proposed CMR sequences challenging. As such, multicentered prospective trials using enriched cohorts from specialized aortic centers will be the most fruitful in confirming the utility of novel CMR approaches in predicting outcomes in TAA. Additionally, surrogate measures such as the rapidity of TAA progression may be considered a pragmatic short-term clinical endpoint to support the more widespread use of this imaging strategy in the first instance. If we are to improve upon current diagnostic strategies in aortopathy, standardization of such a CMR approach will increase uptake and clinical realization. It is hoped that this review will serve as a step towards encouraging collaboration and application of emerging

MRI techniques for the assessment of TAA, providing the necessary tools to potentially move beyond absolute aortic size in clinical practice.

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Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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