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# Diagnosis and Surveillance of Aortic Root Dilation

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## Abstract

Aortic root dilation (AoD) imparts increased risk of aortic complications such as dissection, rupture, and valvular regurgitation. Multiple etiologies of AoD exist, such as Marfan syndrome, bicuspid aortic valve, Ehler-Danlos syndrome, infections, and idiopathic conditions. Due to the variety of clinical conditions that can result in AoD, and the risks associated with worsening AoD, a thorough understanding of the pathophysiology of AoD, noninvasive imaging modalities, and pharmacologic therapies is critical. This chapter will review the various etiologies of AoD, pathophysiological basis of each disease entity, overview of the diagnosis of AoD, noninvasive imaging modalities employed for detection and surveillance, pharmacological therapies used in the prevention and management, and the factors that guide intervention such as surgical repair.

**Keywords:** aortic root, enlargement, dilation, aneurysm, noninvasive imaging

## 1. Introduction

Aortic root dilation (AoD) is frequently an incidentally discovered, asymptomatic finding that is seen on various imaging modalities [1]. The anatomy of the aortic root includes the annulus, sinuses of Valsalva, sinotubular junction and ascending aorta [1], with the size being a function of a patient's biologic variables such as height, age, BSA, and gender [1, 2]. However, while natural variations in the size of the aortic root are well known, the identification of progression from normal to pathologic AoD is a key clinical diagnosis that carries significant cardiovascular risk including aortic dissection, rupture, valvular regurgitation and cardiac tamponade [1, 3–5]. The etiology of pathological AoD is varied, ranging from congenital, infectious, autoimmune, and idiopathic conditions; and influences the medical and surgical management [1, 5]. Due to the variety of clinical conditions that can result in AoD, and the risks associated with worsening AoD, a thorough understanding of the pathophysiology of AoD, noninvasive imaging modalities and pharmacologic therapies is critical. The aim of this chapter is to review the most common conditions associated with AoD, appropriate imaging modalities, and treatment strategies to manage AoD.

## 2. Etiologies of aortic root dilation

Multiple etiologies of AoD exist such as Marfan syndrome, bicuspid aortic valve, Loeys-Dietz and Ehler-Danlos syndromes, idiopathic conditions, hypertension,

infections, and inflammatory disorders. In this chapter, we will discuss the various etiologies categorized into two standardized groups—genetically-mediated and nongenetically mediated AoD.

## **2.1 Genetically-mediated aortic root dilation**

Genetically-mediated aortic root dilation or enlargement is the leading cause of thoracic aortic aneurysms. Marfan syndrome (MFS), the prototype condition for AoD, and bicuspid aortic valve has led to a greater understanding of AoD pathophysiology, pharmacologic treatment, timing of surgical intervention and optimal surveillance strategies with noninvasive imaging [6].

### *2.1.1 Marfan syndrome*

MFS is one of the most common hereditary disorders of connective tissues and is characterized by manifestations in cardiovascular, skeletal, and ocular systems [7]. MFS is the most common genetic cause of thoracic aortic aneurysms (TAAs). Its inheritance is almost exclusively autosomal dominant and mostly involves a mutation of the fibrillin-1 (FBN1) gene encoding the connective tissue structural protein fibrillin-1 [8]. The widely accepted incidence of Marfan syndrome is ~1 in 5000 individuals [9].

Although the inheritance pattern is predominantly autosomal dominant, rare cases of autosomal recessive FBN1 gene mutations has been described [10]. While patients with Marfan phenotypes usually have an affected family member, 25% of the cases are sporadic due to *de novo* mutations [9]. In addition, in <10% of Marfan cases, no mutation of FBN1 was determined [11]. Since it was first identified as the main cause of Marfan syndrome, FBN1 mutations, depending on how it is mutated, were linked to a variety of syndromes and phenotypes [12]. Animal studies investigating the pathophysiology of the disease demonstrated over-expression of TGF- $\beta$  in the mitral valve preceding prolapse, the aorta associated with dilatation, skeletal muscle associated with myopathy, and the dura leading to ectasia [12]. Later, mutations in TGF-beta receptor 2 (TGFB2) and TGFB1 genes were identified in some patients with Marfan phenotypes and subsequently implicated in the disease process in FBN1 mutation negative individuals [13–15]. These genes were also linked to another condition later, namely Loeys-Dietz syndrome (LDS) [14].

The diagnosis of Marfan syndrome is established by using a combination of clinical manifestations, family history, and the presence of FBN1 mutation. In order to facilitate accurate recognition of the syndrome and improve patient management and counseling, a set of defined clinical criteria, called the Ghent nosology was developed [16] and later revised [17] (**Table 1**). Apart from the genetic testing for FBN1 mutation, Ghent nosology uses a systemic score calculation using clinical manifestations of Marfan and an aortic root dilatation Z-score (see noninvasive imaging below).

One of the major causes of mortality and clinical hallmark of Marfan syndrome is aortic root dilation and related complications such as dissection, rupture and/or aortic valvular regurgitation. Aortic root dilation is typically first identified on echocardiography in 60–80% of Marfan patients [18]. Therefore, surveillance echocardiography has been routinely used to serially monitor aortic dimensions. If the aortic root diameter is above 4.5 cm in adults, aortic dilation rates are above 0.5 cm/year, and/or significant aortic insufficiency is already present, more frequent monitoring is recommended [6] (see Diagnosis and Surveillance of Aortic Root Dilation below for more detailed guidelines).

Patients with family history of Marfan disease
• Ectopia lentis
• Systemic score $\geq 7$
• Aortic root dilatation Z-score
$\geq 2$ in patients above 20 years old
$\geq 2$ in patients below 20 years old
Patients without family history of Marfan disease
• Aortic root dilatation Z-score $\geq 2$ and Ectopia lentis
• Aortic root dilatation Z-score $\geq 2$ and FBN1 mutation
• Aortic root dilatation Z-score $\geq 2$ and systemic score $\geq 7$
• Ectopia lentis and FBN1 mutation associated with aortic root dilatation

**Table 1.**  
 Revised Ghent nosology.

### 2.1.2 Bicuspid aortic valve

Bicuspid aortic valve is one of the most frequent congenital heart anomalies in adults, affecting 0.9–2% of the population [19]. Most cases of bicuspid aortic valve are familial and studies show that heritability of the disease is ~90% making it an autosomal dominant pattern with incomplete penetrance [20]. Bicuspid aortic valve can occur alone or with other congenital cardiovascular disorders such as coarctation of the aorta, supra- or subvalvular aortic stenosis, and ventricular septal defect [21].

The diagnosis is often established by transthoracic echocardiogram (TTE), which has high sensitivity (~92%) and specificity (~96%) [22]. TTE is also useful for surveillance of potential complications of bicuspid aorta such as aortic stenosis, aortic dilation, aortic regurgitation, and infective endocarditis [23]. Given the risk of inheritance, first degree relatives are also recommended to be screened with TTE [21].

Prevalence of aortic dilation in patients with bicuspid aortic valve disease ranges from 20 to 84% depending on the criteria used in different studies [24]. The risk of aortic dilation increases with age and the risk of dissection increases as the aortic diameter increases [25, 26]. When the aortic root diameter is above 4.5 cm, there is a family history of aortic dissection, or aortic diameter change is rapid it is recommended to perform echocardiogram annually [21]. More frequent surveillance is recommended for patients with aortic root diameters approaching surgical thresholds (see Surgical Interventions section below).

### 2.1.3 Loeys-Dietz syndrome

Loeys-Dietz syndrome (LDS) is a rare congenital syndrome characterized by hypertelorism (widely spaced eyes), a split uvula or cleft palate, tortuous arteries and aortic aneurysms. LDS shares many features with Marfan syndrome [14]. Most of the LDS cases are sporadic or show an autosomal dominant pattern of inheritance [14].

The incidence and prevalence of the disease is still not well established.

Loeys-Dietz syndrome was initially classified into two subtypes based on the severity of the cutaneous and craniofacial features but later was divided into six subtypes stratified by genotypes [27]. These subtypes are labeled 1–6 and associated with mutations in TGFBR1, TGFBR2, SMAD3, TGFB2, TGFB3, SMAD2, respectively [27]. Type 1 and type 2 are the most commonly seen subtypes with frequencies of 20 and 55% among all subtypes, respectively [28].

Aortic root dilation is a hallmark feature of this disease entity and is frequently seen in patients (~80%) [29]. Another vascular manifestation is aneurysms throughout the arterial tree. This is a concerning clinical manifestations of the disease and can cause aggressive arteriopathy; therefore, early operative intervention at ascending aortic diameters of  $\geq 42$  mm is recommended [30].

#### *2.1.4 Ehler-Danlos syndrome*

Ehlers-Danlos syndromes (EDS) are a heterogeneous and relatively rare group of connective tissue disorders characterized by skin hyperextensibility, joint hypermobility, and tissue fragility [31]. Ehler-Danlos syndrome can present with a variety of clinical manifestations and can be caused by different kinds of genetic mutations. Overall prevalence of EDS is ~1 in 5000 and EDS hypermobile (hEDS) is the most common type [31].

Vascular complications can be seen with different types of EDS; however, it is most commonly seen in type IV (vascular or arterial ecchymotic type; vEDS), characterized by an autosomal dominant mutation in COL3A1 (collagen, type III,  $\alpha$ -1 gene) encoding type III procollagen [32]. Up to 80% with vEDS patients suffer from vascular complications by the age 40 years [32]. Therefore EDS patients, especially vEDS, patients should be routinely evaluated for aortic root disease. These patients are recommended to undergo elective operation at smaller diameters (4.0–5.0 cm) to avoid acute dissection or rupture. Patients with a growth rate of more than 0.5 cm/year in an aorta that is <5.5 cm in diameter are recommended to be considered for operation [33].

## **2.2 Nongenetic**

### *2.2.1 Idiopathic*

Aortic root dilation is an established phenomenon that has shown strong correlations to key pathobiological factors such as age, body surface area (BSA), height and gender. The correlation of aortic root size with age and BSA were initially described in the development of screening nomograms using M-mode echocardiograms [34]. Follow up studies with 2D echocardiography further validated these correlations, allowing for the development of nomograms for normal patient populations or adjusted for patients with underlying congenital disorders (i.e., Marfan syndrome) [2, 35]. These studies evaluating AoD by echocardiograms are further supported by reviews of autopsy data that show clear correlations to key pathobiological factors such as increased age and height with AoD [36].

Despite the validation of age as being correlated strongly with AoD, the mechanism of age on the development of AoD still remains an area of active research. One of the predominant hypotheses is based on the idea of cyclic stress, and how the aorta degrades through gradual mechanical decline of elastin proteins [37]. Elastic arteries, namely the aorta, are estimated to dilate by 10% with each beat [38]. It is hypothesized that the shear stress over a normal lifetime results in the degradation of elastic lamella, resulting in arterial dilation and stiffening [38]. This is corroborated by histologic data demonstrating damage to medial elastin of the proximal aorta [38]. Furthermore, there is evidence to suggest that in the absence of risk factors such as hypertension or atherosclerosis, the aortic wall undergoes age-associated reprogramming that is proinflammatory promotes progression of arterial disease [39]. Wang et al. demonstrated in pathologic samples of aortas that age correlated with increased smooth muscle cell invasion, and increased production of downstream angiotensin II mediators [39].

In addition to age and BSA, gender is another key factor which can increase the risk and progression of AoD [40]. In the Framingham study of 1849 men and 2152 women, not currently diagnosed with cardiac disease or having a cardiac history, aortic root was 2.4 mm smaller in women than men with m-mode echocardiography [40]. A systematic review in 2014 of 10,741 patients with hypertension revealed men had a significantly higher incidence of AoD relative to women [41].

In conclusion, a series of biological variables are correlated with AoD, and it is important to take these into account as they are potential confounders or contributors in the evaluation of patients with pathologic AoD. Even exercise capacity has been correlated with AoD, with a recent meta-analysis showing that athletes defined by participation in National Collegiate Athletic Association (NCAA) or international equivalent had an aortic root diameter that was larger than nonathletic controls [42], and a statistically significant increase by measurement of sinuses of Valsalva and aortic root annulus [42]. It is important to understand the significance of biological variables such as age, height, BSA, or gender to fully evaluate pathologic AoD without the influence of known confounders.

### 2.2.2 HTN

Hypertension is a well-known risk factor for aortic dissection, and in some studies, it is estimated to factor into roughly half of the overall risk for aortic dissection [43]. A recent prospective cohort study of 30,447 patients, 86% of patients who developed aortic dissection had hypertension [4]. However the relationship between hypertension and AoD is not as clearly established. In a Framingham study of 3195 patients, there was no relationship between the development of AoD with hypertension [44]. A subsequent follow up study of Framingham participants evaluating aortic root diameter was positively correlated with mean arterial pressure, but negatively associated with pulse pressure, indicating that the mechanism behind AoD is more complicated [45]. Moreover, investigations have shown that in patients with other comorbidities for AoD, such as, Turner syndrome, hypertension is significantly associated with increased prevalence of AoD [45]. This has led to interesting insights into the cyclic stress hypothesis of the development of AoD [43]. If AoD develops due to chronic shear stress, then it would be expected that AoD is correlated with higher pulse pressure (PP), which would presumably lead to greater stress and aortic dilation [43]. However, studies have reported an inverse relationship between AoD and PP [43]. Additionally a systematic review in 2014 showed that in a population of 10,791 hypertensive patients, 9.1% had AoD with a significant gender skew toward men [41]. However there was no significant correlation of mean arterial pressure or pulse pressure values and AoD [41]. While hypertensive patients have a higher incidence of AoD, the mechanism remains to be further investigated. Moreover, these unclear correlations between MAP, PP, and AoD suggest that the aorta is not static, but a dynamic structure whose response to stress, such as hypertension, is still being elucidated [43].

### 2.2.3 Infections

Since the first mass production of penicillin in 1945, the modern era of antibiotics has resulted in a decrease in the prevalence of mycotic aneurysms due to bacterial infections in developed countries [46, 47]. However they can still be found in developing countries, and are rare but well described causes of mycotic aneurysms [46]. Most common pathogens include *Salmonella*, *Staphylococcus* and *Streptococcus pneumoniae*, and while rare have been in the pathogenesis of mycotic aneurysms of the aortic root [46, 48, 49]. Other common bacteria include *Mycobacterium*

*tuberculosis* and *Treponema pallidum*, which will be discussed below, and more rare causes include *Listeria*, *Bacteroides*, *Clostridium septicum*, and *Campylobacter jejuni* [46]. With the majority of bacterial aortitis, aneurysm development is generally saccular, and *Salmonella* has been reported in case studies to predominantly affect the abdominal aorta than the thoracic [46, 48]. Infections with Staphylococcal species generally are related to underlying aortic valve infections, but have been reported to progress into aneurysms of the aortic root [46, 49].

#### 2.2.3.1 *Treponema pallidum*

*Treponema pallidum*, a sexually transmitted spirochete which is the causative organism of syphilis, is a well characterized cause of aortitis [46, 50, 51]. Cardiovascular involvement is limited to late stage, or tertiary syphilis, and generally occurs 5 to upwards of 40 years after primary infection [50, 51]. Aortitis, and aneurysm development is due to invasion of the vasa vasorum, resulting in obliterative endarteritis that leads to degradation of the aortic media [50, 51]. The chronic inflammation results in fibrosis of the intima, a phenomenon known as “tree-barking” that ultimately progresses to aneurysm development. In an autopsy study in 1960 of 51 aortic aneurysms secondary to syphilitic aortitis, 7.8% were found at the sinuses of Valsalva and 29.4% involved the ascending aorta, representing a majority of the sample [52]. This predominance to the ascending thoracic aorta have been further corroborated in later studies, however the detailed echocardiographic analysis of syphilitic aortitis, specifically in relation to AoD is limited due to the rarity of the disease presentation [46, 50].

#### 2.2.3.2 *Tuberculosis*

Tuberculosis is a relatively common infection especially in developing countries [53]. *Mycobacterium tuberculosis*, the causative pathogen, is a known cause of mycotic aortic aneurysms [46, 50]. Pathogenesis of tuberculous mycotic aneurysm is believed to be due to lymphatic spread or hematogenous seeding, and mortality rates are reported as high as 60% in patients who develop this complication [50]. While more commonly affecting the distal aortic arch and descending aorta, there are case reports detailing aortic root aneurysms due to tuberculosis [50, 54].

#### 2.2.3.3 *HIV*

There have been case reports proposing an association between aortic aneurysms and HIV [50]. In a variety of these cases the causes are generally multifactorial, as the majority of cases have reported coinfections (Q fever and leishmaniasis) or comorbid autoimmune conditions (giant cell arteritis) [55, 56]. It is still an area of investigation as to whether there is a true association, and there is sparse data showing a relationship with AoD.

### 2.2.4 *Inflammatory disorders*

#### 2.2.4.1 *Ankylosing spondylitis*

Ankylosing spondylitis, a seronegative spondyloarthropathy, is a chronic, progressive rheumatologic disorder, and was one of the first found to be associated with aortitis [50, 57]. The proposed mechanism of AoD in ankylosing spondylitis is fibrous growth development along the intima, which leads to subsequent weakening [57]. Prior TEE studies further evaluated the prevalence of AoD in ankylosing

spondylitis, and 82% of patients with ankylosing spondylitis had aortic root abnormalities [58]. Specifically, 61% of patients had aortic root thickening and 25% of patients had AoD [58]. AoD in these populations is a relatively common phenomenon and is associated with significant cardiac morbidity [45, 57].

#### *2.2.4.2 Relapsing polychondritis*

Relapsing polychondritis is another autoimmune disorder, which is a multisystem inflammatory disorder that primarily affects the cartilaginous structures of the body [59]. Cardiovascular involvement is common, estimated to be the second most frequent cause of death and can result in aneurysm development in 5% of cases of both thoracic and abdominal aorta [50, 59]. AoD has been known to occur, albeit rare, with cases of requiring surgical revision after the development of aortic regurgitation [60, 61].

#### *2.2.4.3 Takayasu arteritis*

Takayasu arteritis is a chronic granulomatous large vessel vasculitis, predominantly found in pediatric populations [50, 62]. A rare disorder, the pathogenesis is characterized by granulomatous panarteritis that can affect the entirety of the aorta and major branches, however predominantly affects the common carotid and subclavian artery [62]. While rare, there are reports of AoD from Takayasu arteritis resulting in aortic regurgitation [63, 64].

#### *2.2.4.4 Giant cell arteritis*

Giant cell arteritis is a large vessel vasculitis that is characterized by chronic granulomatous inflammation [50]. While commonly affecting carotid, temporal and vertebral arteries, it has been known to affect the ascending aorta, at times resulting in dissection or aortic valve insufficiency [50]. The development of AoD from GCA may be influenced by other comorbid conditions such as HIV; however, this association is currently only supported with case reports [55].

#### *2.2.5 Other*

##### *2.2.5.1 Left ventricular hypertrophy*

Additionally left ventricular hypertrophy is reported to be positively correlated with AoD. Early retrospective reviews of echocardiographic studies have shown a positive relationship between LVH and AoD, and this has been further supported in subsequent systematic reviews [41, 65]. Patients with AoD with concomitant left ventricular hypertrophy are shown to have an increased risk of adjusted cardiovascular events [66]. However as with previous studies, the exact mechanism between LVH and AoD is still being determined.

## **3. Diagnosis and surveillance of aortic dilation**

### **3.1 Clinical manifestations**

Aortic root dilation is typically a silent disease, with most cases being diagnosed incidentally on imaging. AoD can become symptomatic as the aneurysm enlarges. Aortic root aneurysms grow at an average of 1–4 mm/year [5], with a faster rate



of growth noted in patients with bicuspid aortic valves, Marfan syndrome, ESRD, male gender, and smokers [5, 67]. When the aneurysm enlarges to the point of compressing surrounding structures the patient may begin to observe symptoms—the most common of which is chest pain, seen in up to 75% of patients [5, 68]. Other nonspecific symptoms can include back pain, abdominal pain and fatigue (though only present in 5% of patients).

Additionally, patients may present with symptoms secondary to complications of a dilated aortic root such as aortic insufficiency and congestive heart failure. Thus, patients can develop dyspnea as the presenting symptom of aortic root dilation up to 40% of the time [68]. Other presenting symptoms may be related to the complications noted in **Table 2** [69–74].

### 3.1.1 Complications of aortic root dilation

Acute aortic emergencies that occur secondary to aortic root dilation include dissection, rupture, and aortic insufficiency. As the aortic root diameter increases, the risk for aortic dissection and rupture rises [75]. Aortic dissections are the most common acute aortic emergencies [76], and can be classified depending on the segment of the aorta affected: type A dissections involve the ascending aorta (seen in aortic root dilation), while type B dissections are those that occur distal to the left subclavian artery.

Aortic dissection most commonly presents with acute onset chest pain that may radiate to the back. The character of the pain has traditionally been described as ripping or tearing in nature, however over half of patients may instead complain of sharp pain [77]. In addition, geriatric populations are less likely to have an acute onset of pain [78]. Physical exam findings that may be present include unequal blood pressures in the upper extremities, a new diastolic murmur indicative of acute aortic regurgitation, or muffled heart sounds secondary to tamponade (with proximal extension of the dissection). Imaging may be notable for widening of the mediastinum on CXR [77]. In order to aid in the diagnosis of a dissection, an aortic dissection detection risk score (ADD-RS) has been developed. The score is comprised of three categories: the presence of high risk conditions such as Marfan syndrome, the presence of typical symptoms (such as abrupt onset chest pain), and the presence of physical exam findings such as unequal blood pressure readings in the upper extremities. Each group is given a score of 1 if a feature is present, and the total score helps pave the next steps of workup—a score of 0 can be followed by diagnostic workup of other pathologies, while scores of 2–3 should be followed by expedited workup and immediate surgical consultation for possible aortic dissection [79].

Complication of aortic root aneurysm	Presenting symptom
Aortic insufficiency, aortic regurgitation	Dyspnea, diastolic murmur, congestive heart failure symptoms
Aortic dissection	Sharp chest pain, may radiate to the back
Thromboembolism	Symptoms of stroke
Compression of tracheal or bronchus	Hemoptysis, cough, recurrent pneumonitis
Compression of left recurrent laryngeal nerve	Hoarseness
Compression of superior vena cava	Signs of superior vena cava syndrome
Compression of esophagus	Dysphagia

**Table 2.**  
*Complications and presenting symptoms of aortic root dilation.*

Aortic rupture is also an acute and life-threatening complication of aortic root dilation. It can present similarly to aortic dissection with regards to chest pain, however rupture can lead to severe and abrupt hypotension. Moreover, contingent with the site of rupture the patient may have symptoms such as hemoptysis [80] (if there is rupture into the lung), hematemesis [81] (if there is rupture into the esophagus), or cardiogenic shock [82] (if there is rupture into the pericardial cavity with resultant tamponade physiology).

Aortic root dilation may also lead to aortic insufficiency. Roughly 30% of aortic insufficiency is now recognized as being caused by aortic root dilation, surpassing the incidence of any valvular cause [83]. The pathophysiology is related to stretching of the aortic valve annulus secondary to aortic root dilation, which results in incomplete closure of the aortic leaflets during diastole. Unfortunately, at the onset of aortic regurgitation, patients may be asymptomatic; therefore, congestive heart failure can develop when the regurgitant valve goes unnoticed.

### *3.1.2 Impact/burden on public health*

While aortic root aneurysms are known to grow at an average of 1–4 mm/year [5], it is difficult to ascertain how fast an individual's aortic root aneurysm will grow, therefore necessitating surveillance imaging. The frequency of surveillance imaging recommended is dependent on the etiology of the aortic root dilatation as well as its size, with genetically mediated aortic disease having a lower threshold for more frequent (biannual) imaging [84]. At the very least however patients are recommended to have annual imaging for aortic root dilation to closely monitor the aortic diameter. The impact that frequent imaging (CT, MR angiography or echocardiography) has on public health is likely significant, with cumulative costs. In addition, any patient with a bicuspid aortic valve should be screened for a thoracic aortic aneurysm, as well as screening all first-degree family members of a patient with genetic conditions such as Marfan syndrome [85].

## **3.2 Noninvasive imaging**

The aortic root is the most proximal segment of the aorta. It extends from the annulus of the aortic valve to the sinotubular junction (STJ). It is composed of the left, right, and non coronary sinuses of Valsalva. The diameter of the aorta decreases as it moves distally. The aortic root is assessed using multimodality imaging techniques. These include transthoracic echocardiogram (TTE), cardiac magnetic resonance imaging (cMRI), and cardiac computed tomography angiography (cCTA).

### *3.2.1 Transthoracic echocardiogram*

TTE is widely used for the detection and monitoring of aortic root pathology. Early studies established age- and sex-specific nomograms for aortic root measurements [86]. These studies used the motion mode (M-mode) of TTE, in which the amplitude of the ultrasound pulses amplitudes is converted to corresponding level on gray-scale imaging [86]. Using the M-mode, the American Society of Echocardiography (ASE) has recommended using the leading-edge to leading-edge approach for measuring the aortic root [87]. Later studies used 2D TTE and obtained reference measurements of the aortic root. This is now preferred over M-mode images, which may be off-axis and are subject to aortic motion that may produce erroneous measurements.

On echocardiogram, the aortic root diameter is typically measured in the parasternal long-axis view from the right coronary sinus to the opposite sinus of Valsalva. When unable to obtain the long axis view, the parasternal short axis view may provide more accurate measurements. However, universal landmarks to measure the root in this view have not been established. Some suggest measuring the diameter from the right coronary sinus to the opposite commissure. These measurements are typically performed at end diastole, as this represents the resting aortic diameter [88]. In adults, these measurements correlate with age and body size. In addition, the aorta is about 2 mm larger in men compared to women due to differences in body size [89]. Normal values stratified by body surface area and age have been published by the ASE [87].

Importantly, TTE is limited by its two-dimensional images and thus does not give a complete depiction of the aortic root. It is also limited by patient factors that limit the visualization windows and thus aortic root measurement. Since the aorta is not a straight tube, it can be imaged obliquely leading to over-estimation of its true diameter. Newer modalities, such as cMRI and cCTA, can provide three-dimensional images.

### *3.2.2 Cardiac magnetic resonance imaging*

Despite ECG-gated CT being the most accurate modality for evaluating the thoracic aorta, it is limited by the radiation and contrast exposure. This is particularly important in younger patients with connective tissue disorders that require serial follow up imaging. Cardiac MRI provides an alternative approach for imaging the thoracic aorta including the aortic root and is considered the preferred modality in select groups. It can be performed with ECG gating to provide motion-free evaluation of the aorta. In addition, young patients, in whom this is more commonly used, can hold their breath for longer periods, allowing acquisition of images with high spatial resolution.

Cardiac MRI evaluation of the aorta does not require contrast use. MRI sequences used include balanced steady-state free precession (SSFP) sequences, fast imaging employing steady-state acquisition (FIESTA), true fast imaging with steady-state precession (FISP), and balanced fast-field echo (FFE) sequences. These sequences provide a high signal-to-noise ratio and adequate contrast between vessel wall and blood pool [90]. When used with ECG gating and contrast enhanced MRA, images tend to have less artifact, higher resolution, and overall short imaging time. Another approach is to use ECG gating 2D balanced SSFP sequence that is oriented perpendicular to the aortic root in two planes to assess the aortic valve and root throughout the cardiac cycle. In addition, prospective ECG gating and respiratory navigation with three-dimensional balanced SSFP sequences can provide 3D aortic imaging without contrast administration [91, 92].

It is important to note that different methods of aortic measurement have been described and guidelines are less well defined. Aortic root measurements can be challenging given different approaches. Burman et al. found in the Framingham Heart Study that cusp-commissure dimensions better corresponded with reference echocardiographic aortic root measurements [89, 93]. This best correlated with study measurements after averaging the three end-diastolic cusp-commissure measurements [93]. In addition, there is a lack of consensus with regard to measurements used (inner lumen only versus lumen and wall) and whether measurements should be adjusted to body surface area, sex, and age.

### *3.2.3 Cardiac computed tomography*

Although TTE is widely used for the imaging and surveillance of aortic root, cardiac computed tomography angiography (cCTA) is currently the most commonly

used technique for the study of the thoracic aorta. Main advantages of cCTA are fast scanning times, low artifact sensibility, and wide availability including emergency rooms operating 24 h [94].

The new generation CT scanners acquire high-resolution 3D datasets of the thoracic aorta, showing sensitivities up to 100% and specificities of 98–99% [95]. ECG synchronization is vital for detailed assessment of the aortic root anatomy since it allows suppression of pulsation artifacts [96]. ECG gating also allows viewing images in a particular phase of the cardiac cycle. Unfortunately, the ECG-gated technique can increase the acquisition time and required breath-hold time. In order to minimize the increased acquisition times, employment of a 64 or wider ECG-gated row detector system is suggested [95, 97].

Modern CT scanners can be used to employ several different cardiac synchronization methods such as prospective ECG triggering where images are only acquired during a specified portion of the cardiac cycle, starting at a predetermined delay from the R wave; retrospective ECG gating where the desired cardiac phase is selected retrospectively from the raw data [95, 97]. The details of each technique will not be discussed in this chapter; however, it is important to determine the advantages and disadvantages of different techniques. The main limitations of CT are related to the radiation exposure and the use of iodinated contrast media and different techniques come at a higher cost of each limitation.

For the surveillance of aortic root, any technique can be used and be useful; therefore, the technique with the least amount of radiation exposure should be selected such as prospective sequential triggering without padding, retrospective gating with tube-current modulation optimized for diastolic-phase datasets only, or a prospectively triggered high-pitch helical acquisition [95, 97]. Retrospective ECG gating acquires redundant helical CT data which allows the reconstruction of images at different cardiac phases and providing detailed images which can be useful in complicated cases and pre-/post-operative imaging since pseudoaneurysm or small leaks which are some of the most common complications of aortic root surgery can only be detected during a specific phase of the cardiac cycle. Iodinated contrast-media is another risk related to CT imaging given the risk of contrast induced nephropathy and allergic reactions of various severity. Surveillance CT data for the dimensions of aortic root can be acquired without contrast injection; however, a complete endoluminal evaluation can only be achieved by the injection of contrast-medium [97].

It is standard of care to monitor the size of aortic aneurysms that are below surgical threshold, <5.5 cm for nongenetic aneurysms and <5.0 cm for genetically-mediated aneurysms [98]. In general, physicians should be conscientious about patient cumulative radiation exposure as there is evidence that it can increase cancer incidence and cancer mortality [99]. One study estimated that ionizing radiation exposure results in 0.7% of total expected baseline cancer incidence and 1% of total cancer mortality. These rates increase with greater cumulative exposure [99]. Therefore, physicians should opt to perform serial CT imaging with longer intervals in the most appropriate patients. A study investigating patients with moderate-risk thoracic aortic aneurysms (defined as size <5.0 cm) showed that patients with aneurysms below 4.3 cm had overall lower risk of significant aneurysm growth or size reaching surgical threshold. Thus, the authors suggested that these subset of patients undergo surveillance CT scans less frequently.

#### **4. Management and prevention of aortic root dilation**

Management focuses on slowing the rate of growth and the complications of aortic root dilation. The line of management that is chosen for a patient depends on

symptoms and size of the aneurysm. For patients who are asymptomatic and have root dilation <55 mm, medical management is advised. In patients with Marfan syndrome or a bicuspid aortic valve, the cut off of  $\leq 50$  mm is used for medical management [1, 100].

## **4.1 Medical management**

### *4.1.1 Beta blockers*

The use of beta blockers has shown a survival benefit in patients with aortic root dilation secondary to Marfan syndrome [101]. While data on survival benefits for patients with bicuspid aortic valves is sparse, the common practice is to also prescribe beta blockers given that both conditions share a similar pathology and therefore both are likely to benefit from beta blockade. The mechanism by which beta blockers slow the progression of aortic root dilation is through their negative inotropic and chronotropic effects, reducing the peak left ventricular ejection rate and therefore decreasing shear stress and the rate of aortic dilation [102].

### *4.1.2 Other agents for blood pressure control*

The goal blood pressure for patients with thoracic aortic aneurysms is <130/80 mmHg. In patients who cannot tolerate beta blockers, calcium channel blockers (CCB) are an alternative group of medications available. While less studied as compared to beta blockers, CCB have also been found to reduce the rate of aortic root dilation [103]. Other agents that can be used for additional blood pressure control include ACE-inhibitors and ARBs.

### *4.1.3 Management of other cardiovascular risk factors*

In order to reduce the risk for complications such as aortic dissection, patients should be counseled on smoking cessation, and cessation of drugs that increase aortic wall stress such as cocaine or other stimulants. In addition patients should have dyslipidemia well controlled, which can be achieved through the use of atorvastatin 40–80 mg daily in individuals with aortic root aneurysms [104, 105].

### *4.1.4 Lifestyle modifications and pregnancy*

Patients should be counseled on avoiding high intensity and collision sports, such as boxing and cycling. Instead patients should take part in low dynamic sports, such as golf [5, 106]. Pregnancy should be avoided in patients with Marfan syndrome with an aortic diameter >40 mm, if a patient does choose to become pregnant however there must be close follow up with surveillance imaging of the aortic diameter [5, 101].

## **4.2 Surgical management**

### *4.2.1 Indications for surgery*

Emergent surgical interventions are indicated for management of an aortic dissection or rupture, or a symptomatic aneurysm. In addition, surgical repair can be performed electively in high risk patients to prevent propagation of an aneurysm (**Table 3**). Indications for elective surgical intervention include the absolute size of the aneurysm—if the diameter is over 55 mm, or over 50 mm in patients with Marfan syndrome or bicuspid valves. Other indications for elective surgery include if the rate

Emergent surgical repair	Elective surgical repair
<ul style="list-style-type: none"> <li>• Aortic rupture</li> <li>• Aortic dissection</li> <li>• Symptomatic aortic root dilation (may represent an impending rupture)</li> </ul>	<ul style="list-style-type: none"> <li>• Aortic dilation &gt;55 mm</li> <li>• Aortic dilation &gt;50 mm in individuals with Marfan syndrome or bicuspid valves</li> <li>• Rate of growth &gt;10 mm/year</li> <li>• Aortic insufficiency (decision largely based on diameter of aortic dilation)</li> </ul>

**Table 3.**  
*Indications for emergent and elective surgical repair of aortic root dilation.*

of growth of an aneurysm surpasses 10 mm/year, and if there is concurrent aortic insufficiency [1, 100]. In addition, patients who undergo aortic insufficiency repair who have concurrent aortic root dilation should be considered for aortic replacement at the time of their surgery—that is since 25% of patients with aortic root diameters >40 mm will eventually also require intervention for their aortic aneurysm [107].

#### 4.2.2 Surgical interventions

As opposed to supra-avalvular aortic aneurysms, aortic root aneurysms involve the coronary ostia as well as the aortic valve, which have implications on the type of surgical procedure available for patients. There are two approaches for a surgical intervention: radical and conservative. In a radical surgical intervention the patient's aortic valve and root are replaced (commonly referred to as the Bentall procedure), whereas in conservative interventions only the aortic root is replaced [108].

The Bentall procedure involves replacing the aortic valve with a prosthetic valve, and thus has the caveat of requiring indefinite anticoagulation [5]. If patients have a high bleeding risk it may therefore be worthwhile investigating replacement of the aortic root while preserving the valve. In addition, it is important to note that a large number of patients with aortic root dilation are young (secondary to its association with Marfan syndrome), and therefore lifelong anticoagulation in cases such as these confers a cumulative bleeding risk. Preserving the aortic valve while surgically treating the aortic root dilatation is made possible by the development of two surgical procedures: the first is removing the aortic root while keeping the valve intact. The second method is through re-implantation of the aortic valve [5]. Both the Bentall procedure as well as aortic valve-preserving procedures have been shown to have comparable short and long-term outcomes with regards to the risk of death and valve associated complications. The main difference however is that patients undergoing valve sparing operations were significantly more likely to develop moderate to severe aortic regurgitation later [108].

In patients with both severe aortic stenosis and ascending aortic aneurysm, undergoing surgical aortic valve replacement (sAVR) and concomitant surgical intervention for aortic aneurysms above 4.5 cm is recommended by the American College of Cardiology (ACC) foundation guidelines [84]. However, in high-risk surgical patients, undergoing a transcatheter aortic valve replacement (TAVR) has become an alternative approach that obviates the need for parallel surgical aortic aneurysm intervention. This raises the concern for the safety of TAVR catheter-based delivery system in patients with aortic aneurysms since intraoperative rupture or dissection risk potentially increases. However, a clinical study showed that TAVR does not increase intraoperative aortic dissection/rupture risk or mortality with a median follow-up of 14 months [109]. Therefore, there are no recommendations against performing TAVR in patients with ascending aortic aneurysms.

## **Conflict of interest**

None.

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