Aortic Morphology and Function in Ehlers Danlos Syndrome Type IV

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Introduction

Ehlers Danlos Syndrome type IV (EDS IV) is a rare, genetic disorder of type III collagen, an important structural component of the artery wall. Individuals with EDS IV have a significant lifetime risk to develop aneurysmal dilatation, dissection or rupture of the medium and large arterial vessels. Arterial rupture is a common cause of death in affected individuals. Currently, no methods predict the risk to develop an aneurysm or rupture in individuals with EDS IV. In an effort to identify potential MRI markers that might herald increasing risk of rupture, we compared the morphology of the aorta in individuals with EDS type IV to age-matched unaffected siblings.

Methods

Fifteen adult subjects with molecular confirmation of EDS type IV (*COL3A1* mutation) and 8 unaffected siblings were consented for an MRI study. All participants were imaged on a 1.5T MRI scanner (GE Signa) with a protocol that included an axial 2D time-of-flight angiographic survey from the arch to the iliac bifurcation (TR= 11.9; TE= 2.8; thickness = 4mm; FOV=32cm; matrix=256x256), high-resolution, axial black-blood (DIR) fast spin echo (FSE) images of the infrarenal aorta (TR= 800; TE= 16.7; thickness= 4mm; FOV=32cm; matrix=320x320), and breath-held CINE phase contrast images of the ascending and descending aorta at the point of bifurcation of the pulmonary trunk and of the infrarenal abdominal aorta (TR = 13.3 TE = 6.4; FOV=320cm; matrix = 128x64; views per segment = 4; VENC=150).

Data were analyzed using a custom software program for vascular MRI analysis. Diameter was measureed along the entire length of the descending and abdominal aorta from the 2D TOF images. Additionally, the diameter of the aortic root was measured from a late diastolic magnitude image from the CINE PC series. Aorta wall thickness was measured from the black blood FSE images using an algorithm adapted from carotid wall thickness measurements [1]. Finally, pulse propagation velocity was assessed using the CINE PC images as described in [2].

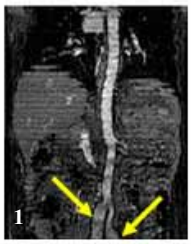
Results

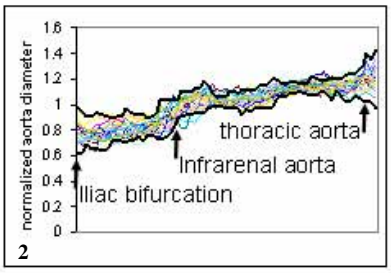
No aortic aneurysms were observed in any subjects, although aneurysms were noted in branch vessels of several subjects (Fig. 1). Fig. 2 shows the aorta diameter measurements from the EDS subjects, normalized by the overall average diameter of each. Black curves indicate two standard deviations of variation measured from the normal controls. No appreciable deviations of the EDS subjects from normal are apparent. Fig. 3 compares the diameter of the aortic root to that of the descending thoracic aorta. Black bars show the 95% confidence region derived from the normal subjects, indicating that the aortic root was out of proportion to the thoracic aorta in two subjects with EDS. The aortic root appeared prominent in these individuals. Aorta wall thickness showed no difference between subjects (mean = 1.52 mm) and controls (mean = 1.50) although wall thickness was correlated with age (R=0.67) and aorta diameter (R = 0.40). Pulse propagation velocity for normal subjects (Fig. 4) was consistent with previous reports in the literature and showed an age dependence (R=0.83) very similar to past reports [2]. For subjects with type IV EDS (Fig. 5), however, pulse propagation velocity was highly variable and showed no appreciable age dependence (R=0.15).

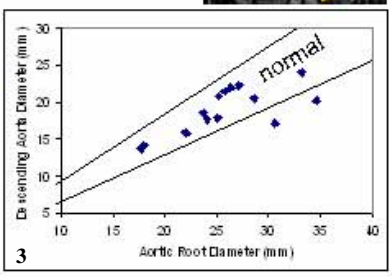
Conclusions

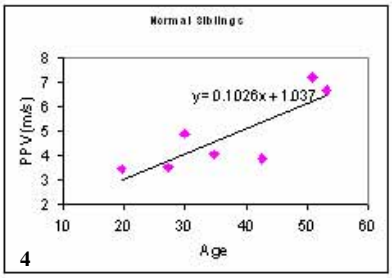
Overall, aortic morphology was surprisingly consistent between EDS subjects and controls in terms of descending aorta diameter, abdominal aorta diameter and aorta wall thickness. Two subjects had aortic root enlargement, a known risk factor for dissection [3]. The clearest differences were found in pulse propagation velocity, where the EDS subjects, in contrast to controls, did not show age dependence. In Marfan syndrome, elasticity is frequently reduced [4], which would lead to an elevated pulse propagation velocity. In that context, our finding suggests that different primary alterations in aortic matrix can alter aortic elasticity and influence the risk of dissection or rupture. Close follow up of those with increased propagation may determine if such measurements have predictive value and may help to identify therapies, such as those recently composed for the vascular component of Marfan syndrome.

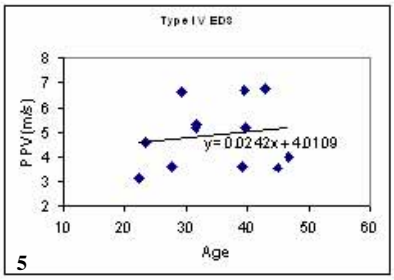
Figures: 1) reformatted axial MRA showing bilateral iliac aneurysms (arrows), 2) normalized aorta diameters of 15 EDS patients with 95% bounds from normal controls indicated in black, 3) descending aorta versus aortic root diameters compared to 95% bounds from normal controls, 4) pulse propagation velocity versus age for normal controls compared to 5) EDS patients.











References

[1] Underhill et al., *JMRI*. 24:379-87, 2006.
[2] Rogers et al., *JACC*. 38:1123-9, 2001.
[3] Meijboom et al.,*AJC*. 96:1441-4, 2005.
[4] Baumgartner et al., *JTCS*. 132:811-9, 2006.