In Vivo Quantification of Aortic Stiffness in Abdominal Aortic Aneurysm Patients using MR Elastography: A Longitudinal Study

Primary Author: Huiming Dong[1], MS (dong.449@osu.edu)

Department of Biomedical Engineering, The Ohio State University; Department of Radiology; The Ohio State University Wexner Medical Center.

Introduction

Abdominal aortic aneurysm (AAA) is an abnormal vascular dilation of the abdominal aorta. Although the disease usually progresses without significant symptom, AAA can eventually lead to life-threatening aortic rupture, making it a leading cause of death in the United States [1].

Clinically, AAAs with diameter≥5.0 cm are considered high-risk, suggesting a higher chance of rupture when compared to those with diameter<5.0 cm. However, several studies have shown that small AAAs (<5.0 cm) can also rupture, demonstrating that diameter is a poor indicator for rupture potential [2-4]. Darling and colleagues reported that the rupture rate for AAAs<5.0cm can be as high as 12.8% whereas that for AAAs>5.0cm is only 40% [5]. Nicholls et al. observed that approximately 10% small AAAs ruptured among 161 patients who had been admitted to the University of Washington Medical Center in a ten-year period [6]. According to Hall et al., up to 23% small AAAs rupture, suggesting that solely using AAA diameter for rupture risk evaluation is not reliable and can lead to delayed intervention of high-risk small AAAs as well as unnecessary repairs of the stable large AAAs [7].

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Aortic stiffness is also known to be closely associated with a variety of cardiovascular comorbidities such as atherosclerosis, aortic aneurysm, aging-related vascular degradation, etc. [8-11]. Recently, aortic stiffness has been suggested as a better alternative in rupture risk assessment as it can provide critical information about the overall AAA mechanical integrity. Pulse wave velocity (PWV) is the current gold standard for estimating the stiffness of the aorta [12]. However, it has several major limitations. First, peripheral wave-based measurements such as the carotid-femoral PWV method measures pulse wave from peripheral arteries which is a poor reflection of the central aortic pulse wave [13]. Second, it is challenging to obtain the true aortic wall thickness, diameter, and pulse wave pass length that are required to correctly derive aortic stiffness from PWV [14]. In addition, PWV only provides a global measure of aortic stiffness and does not provide temporal and spatial estimates [15].

MR elastography (MRE) is a novel phase-contrast based MR technique for estimating the shear stiffness of soft tissues. It has been demonstrated that it is feasible to non-invasively evaluate aortic stiffness in vivo in healthy volunteers [16-17], AAA patients [18] and large animal models [19] using aortic MRE. Despite the effort in studying relationships between aortic stiffness and cardiovascular diseases, a longitudinal study has not been performed in which AAA stiffness and diameter variation are serially tracked during the course of AAA development using MRE. Moreover, the correlation between AAA stiffness and diameter remains unknown.

Therefore, the aim of this work is to serially follow AAA patients every 6 months to obtain MRE-measured AAA stiffness for understanding the variation of stiffness and diameter during the development of the disease.

Methods

In this study, 37 AAA patients were recruited. Each patient was serially scanned for every 6 months. **Table I** summarizes the number of patients and their visits.

All MR imaging was performed on a 3T MR scanner (Tim Trio, Siemens Healthcare, Erlangen, Germany) using a rapid GRE MRE sequence [20]. Patients were scanned in head first-supine position as demonstrated in **Figure 1.** The imaging parameters included: TE= 10.18ms, TR =14.29ms. FOV=400x400mm^2; matrix size=256x256; slice thickness=6mm; No. of slices=3; mechanical frequency=60Hz; motion encoding gradient frequency=60Hz; three-directional motion encoding; No. of phase offsets=4.

Aortic MRE data were processed using MRElab (Mayo Clinic, Rochester, MN). The first harmonic displacement data were filtered using a fourth order Butterworth band-pass filter with cutoffs of 1-40waves/FOV to eliminate noise wave reflections. Subsequently, a local-frequency estimation (LFE) inversion was performed on the 3D volumetric MRE dataset to obtain spatial frequencies from the filtered displacement data in each motion encoding direction [21]. The reported stiffness is then calculated by a weighted combination of stiffness in all three directions. Assuming soft tissue density to be 1gm/cm^3, the effective shear stiffness can then be calculated by

$$\mu = f_{mech}^2 / f_{sp}^2 \text{ (Eq. 1)}$$

where f_{MECH} is the mechanical frequency and f_{sp} is the spatial frequency. The effective stiffness obtained using LFE is equivalent to solving the Helmholtz equation under the assumptions of infinite medium, incompressibility of the tissue, local homogeneity and no attenuation [22]. The reported effective stiffness value in this study is a weighted combination of stiffness from all encoding directions.

Table I. Summary of Patients and Visits

No. of Visits to the Scanner	No. of Patients Followed	Mean AAA Stiffness (kPa)
First Scan	37	7.85±2.51
Second Scan	13	8.39±1.79
Third Scan	7	7.29±1.44
Fourth Scan	4	10.28±0.32
Fifth Scan	1	10.73

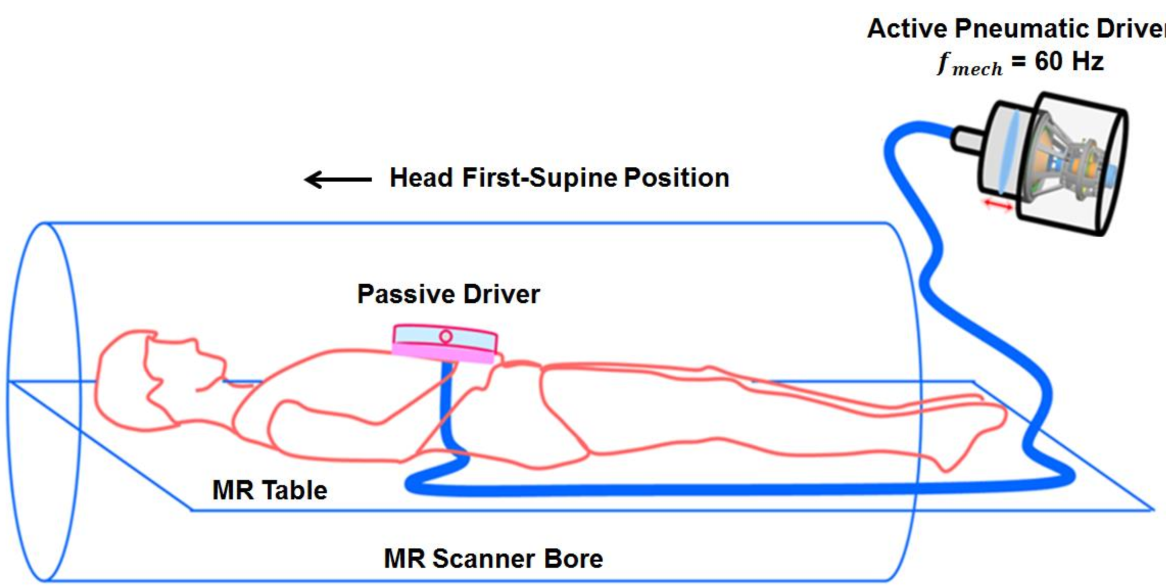

Figure 1. Experimental Set-Up for Aortic MRE. Aortic MRE measurements were performed in AAA patients using head first-supine position. Mechanical waves were generated via an active pneumatic driver placed outside the scan room. A passive driver was placed in the abdomen region of patients and the driver was connected to the active driver through plastic tube. The mechanical wave frequency was 60 Hz to achieve optimal tissue penetration and spatial resolution.

Results

Both AAA diameter and stiffness increased as the disease progressed in one patient. **Figure 2** demonstrates the magnitude images in sagittal view, wave images and the corresponding stiffness maps of the same patient during his 3 serial visits. The AAA diameters were 5.6cm, 5.8cm and 5.9cm for these 3 visits, respectively. The mean AAA stiffness measured by MRE was 6.10±2.53kPa, 8.34±3.26kPa and 10.26±5.14kPa.

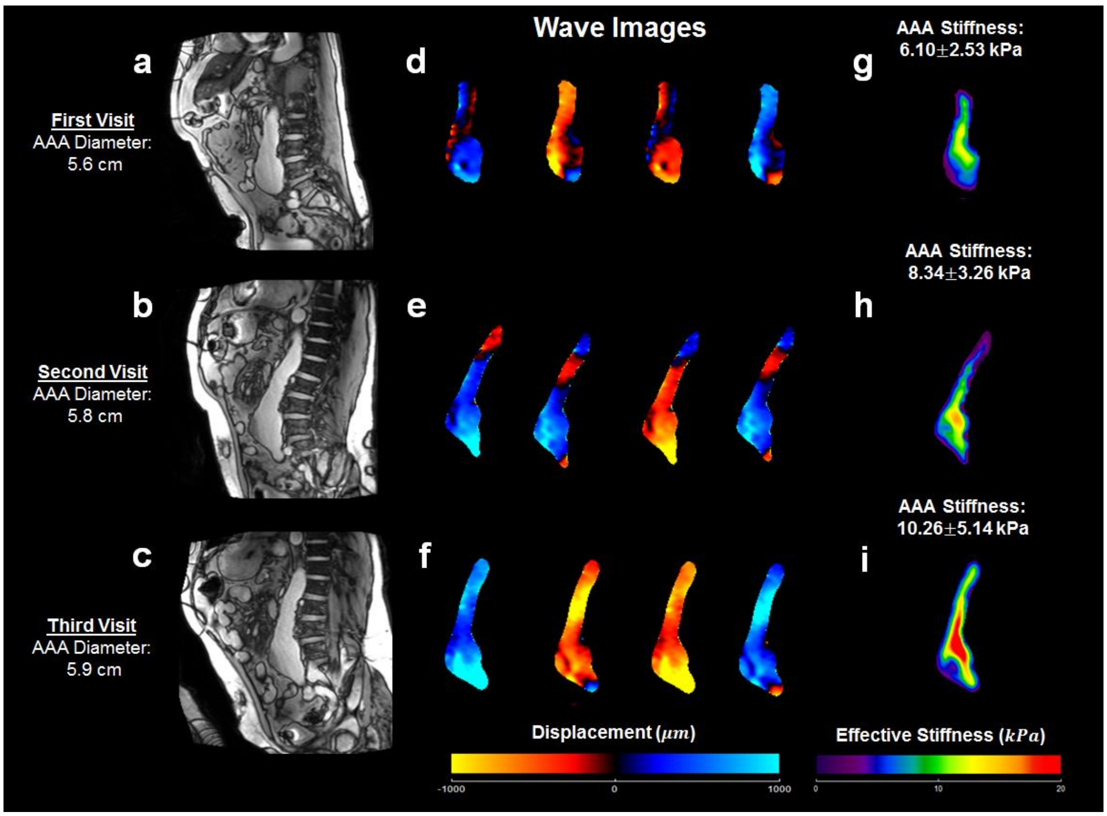

Figure 2. Aortic MRE Measurements in One Patient during 3 Serial Visits. Magnitude images in sagittal view (a-c) of the same patient from his 3 serial visits were displayed to demonstrate the disease progression. The AAA diameter increased from 5.6 cm to 5.8 cm during his 3 visits. Snapshots of propagating waves along readout direction (i.e., the vertical direction) at four different time points in the abdominal aorta were shown (d-f). The mean aortic stiffness increased as the disease developed. The mean aortic stiffness measured by MRE (g-i) was 6.10±2.53 kPa, 8.34±3.26 kPa and 10.26±5.14 kPa for first to third visit, respectively.

AAAs with similar diameters have different stiffness. **Figure 3** displays AAAs with various diameters and stiffness values from different patients. Small AAAs (i.e., AAAs<5.0cm) were not necessarily more compliant than large AAAs (i.e., AAAs>5.0cm) and vice versa, indicating that AAA diameter may not be an adequately accurate indication of the mechanical integrity of aneurysms, and aortic stiffness is independent of AAA diameter.

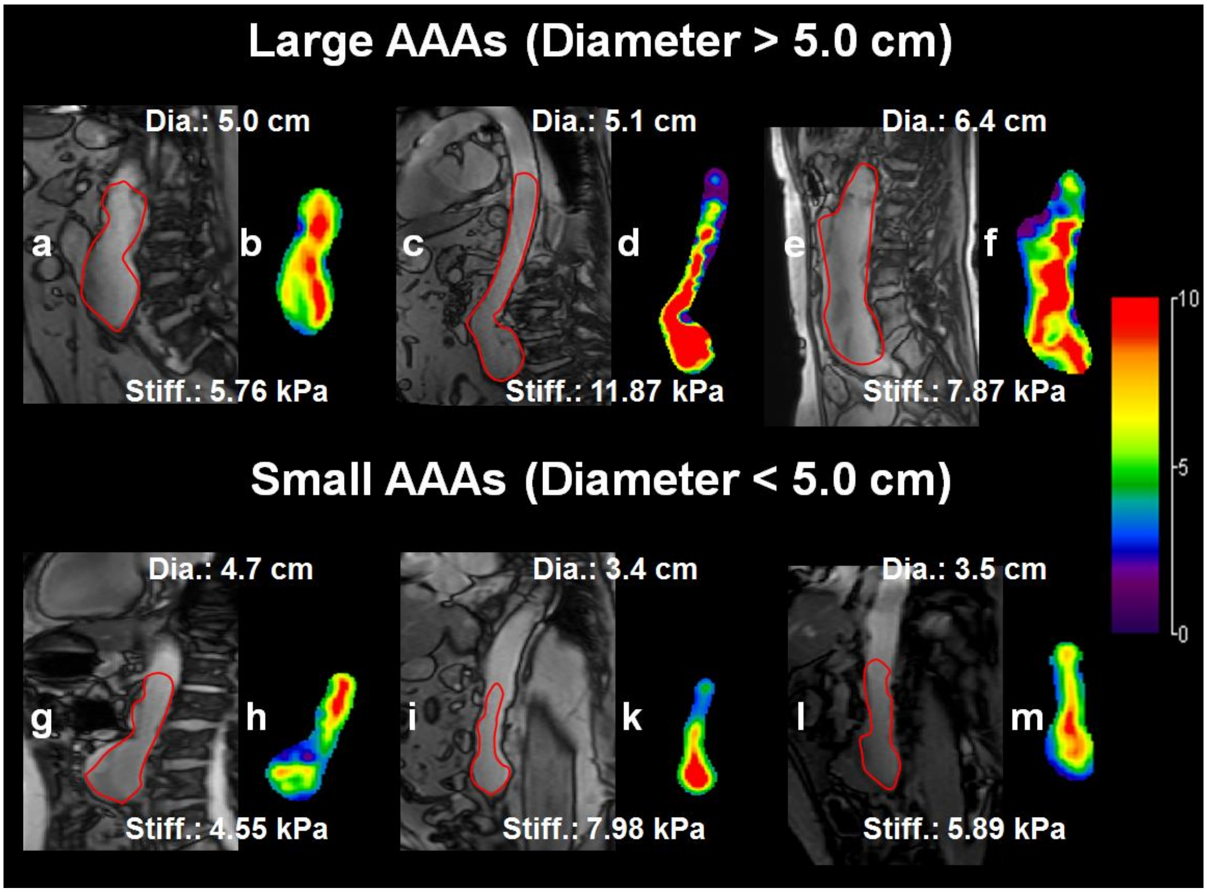

Figure 3. Aortic Stiffness and AAA Diameters in Different Patients. Magnitude images in sagittal view and stiffness maps of AAAs with different diameters were demonstrated in the figure. Small AAAs (i, k) were not necessarily more compliant than large AAAs (a, b) and vice versa. Moreover, AAAs with similar diameters could have considerably different mean aortic stiffness (a, b vs. c, d), demonstrating that AAA diameter may not be an adequately accurate indication of the mechanical integrity of aneurysms, and aortic stiffness is independent of AAA diameter.

The stiffness of AAA is significantly higher than that of remote AAA region (i.e., the normal portion of the abdominal aorta) during patients' first visit, (p<0.0001). **Figure 4** demonstrates aortic stiffness and AAA diameter variation of all patients of different visits. The mean aortic stiffness is 4.94±1.69kPa, 7.85±2.51kPa, 8.39±1.79kPa, 7.29±1.44kPa, 10.28±0.32kPa and 10.73kPa for remote AAA region at visit 1and for AAA at visit 1 to visit 5, respectively. There is no significant difference in AAA diameter among different visits. The mean AAA diameter is 4.68±1.36cm, 4.18±0.74cm, 4.24±0.93cm, 4.52±1.09cm and 4.09cm for visit 1 to visit 5, respectively.

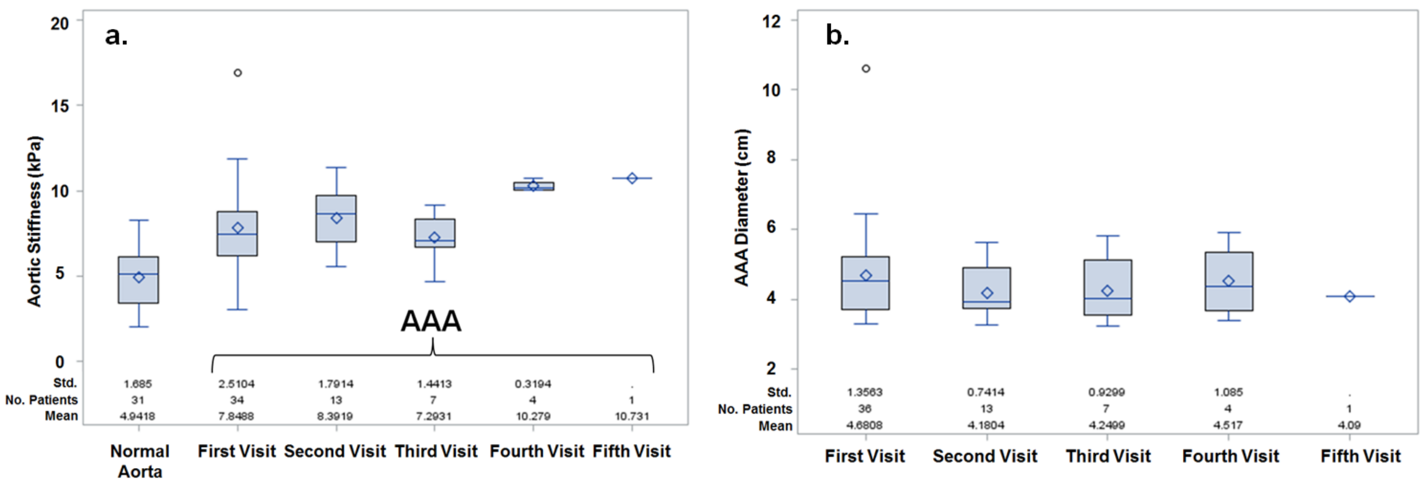

Figure 4. Variation in Aortic Stiffness and AAA Diameter. Aortic stiffness varied during the serial follow-ups, indicating changes in the mechanical integrity of AAA wall (a). The stiffness of AAA is significantly higher than that of remote AAA region (i.e., the normal portion of the abdominal aorta) during patients' first visit, (p<0.0001). There is no significant difference in AAA diameter among different visits (b).

There is no significant correlation observed between MRE-derived aortic stiffness and AAA diameter with Pearson correlation coefficient=-0.048 (*p*=0.726). **Figure 5** displays the scatter plot of aortic stiffness and AAA diameter, demonstrating that the overall mechanical integrity of AAA is not correlated to its size.

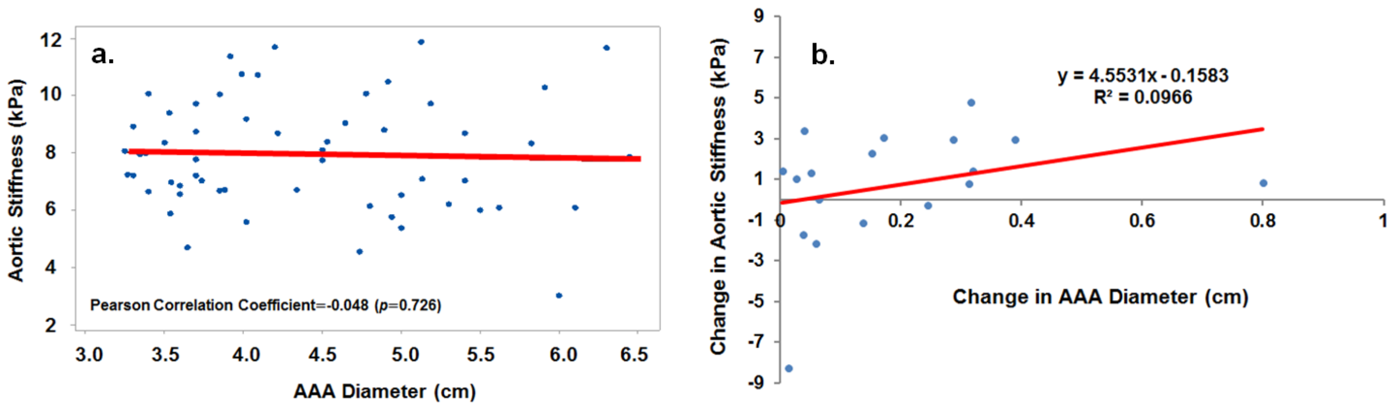

Figure 5. Correlation between Aortic Stiffness and AAA Diameter. (a) shows that there was no significant correlation observed between MRE-derived aortic stiffness and AAA diameter with Pearson correlation coefficient=-0.048 (p=0.726). Additionally, (b) demonstrates that the change in aortic stiffness did not correlated the change in AAA diameter (R^2=0.0966), suggesting that AAA diameter was independent of the aortic stiffness and thus could not provide adequate insight of rupture potential.

Conclusion

MRE demonstrated that aortic stiffness varied during the serial follow-ups, indicating changes in AAA wall integrity. There is no correlation found between aortic stiffness and AAA diameter, suggesting that AAA diameter may not correctly indicate the mechanical integrity of aneurysms. Therefore, aortic MRE is a potential tool for AAA diagnosis and more accurate rupture risk assessment.

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