Thoracic Aorta Displacement and Strain Analysis Using Spiral Cine DENSE MRI

Melissa Valdman

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Faculty Member 1:
Printed: John N. Oshinski
Signature: [Signature] (12/14/17)

Faculty Member 2:
Printed: Degiang Qiu
Signature: [Signature] 12/14/2017
Abstract

Aneurysms are the 18th most common cause of death in the United States, and patients with connective tissue disorders are at particularly high risk of developing these lesions. Understanding more about the structural and biological properties that play a role in the formation of aneurysms could be vital to their early detection and prevention. In this study, we compare displacement and strain data from six patients who have connective tissue disorders (e.g., Marfan Syndrome, Loeys-Dietz Syndrome, or Ehlers-Danlos) and eight patients with healthy aortas using spiral cine DENSE MRI in order to differentiate the mechanical properties of healthy vs. diseased aortas and to understand the properties associated with different stages of aneurysm formation. We predict that patients with connective tissue disorders will demonstrate larger total displacement and strain along the aortic wall. These results will help differentiate the mechanical properties of healthy aortas and aortas associated with connective tissue disorders, as well as understand the properties associated with different stages of aneurysm formation.
Introduction

Out of every 100,000 patients, six to ten are found to have thoracic aortic aneurysms (TAA) annually [1]. Mortality is associated with aneurysmal rupture which is caused by the degradation of the aortic wall. The current method for determining rupture risk, and thus the need for surgery, is based on the diameter of the aneurysm. Surgical intervention is suggested at aortic diameters of 5.5 cm or above unless the patient has a preexisting condition. Patients with a family history of aneurysms, a bicuspid aortic valve, Marfan Syndrome, or other connective tissue disorders require intervention earlier at a suggested 5.0 cm diameter. However, some aneurysms rupture below these diameters and some never rupture above these diameters [2]. To effectively predict the risk of rupture, there needs to be a better understanding of the altered structural and biological properties of the aortic wall in aneurysms and not just its overall size [3]. A better understanding of these properties may be gained by analyzing aortas at a higher risk of developing these lesions before and after the aneurysm forms.

Aneurysm Formation

Aneurysms form due to damage to the cells and extracellular matrix of the aortic wall, most notably the loss of elastin and functional smooth muscle cells. Vascular remodeling is the response of the body to this tissue damage. Vascular remodeling is often indicated by changes in stiffness of the aortic wall [4]. To improve the accuracy of predicting rupture risk, morphologic and mathematical analyses of TAA geometry have been proposed. These methods can give a better estimate of wall stress, which plays an important role in determining rupture risk. A previous study used a three-dimensional computer modeling technique to calculate the wall stress of thoracic aortic aneurysms. The model used three components to make the stress calculation: the geometry of the TAA, the mechanical behavior of the tissue, and the blood pressure. In comparison to current
methods of determining rupture risk, this model was an improvement. While the model focused on the mechanical properties of the TAA, which are essential in understanding rupture risk, it failed to consider another key element - the biological properties of the aneurysm. One of the key components of the model is the mechanical behavior of the tissue derived from a material model. This piece of the model does not consider the complexity and heterogeneity of the TAA. The biological and structural elements of the aneurysm tissue are key in rupture potential, but they are also complex and vary patient-specifically and between different spatial segments of an aneurysm [2].

**Aortic Heterogeneity**

The aorta is not structurally uniform throughout its length, which means different parts could be more prone to aneurysm formation. For example, the thoracic aorta has a higher content of elastin, and the thoracic aorta undergoes changes due to aging earlier than the thoracic aorta [3]. These heterogeneities mean that stresses may vary depending on the region of the aorta. Furthermore, aneurysms have been shown to have different material properties at different locations within the lesion. By understanding these heterogeneities, predicting early changes indicative of the beginning of lesions may be possible, targeted treatments can be produced, and accurate models can be created to predict rupture. While studies have shown that heterogeneity exists in different regions of the aorta along its length, there are few studies that have explored the potential for heterogeneity around the circumference of the aorta.

**MRI**

A major challenge in assessing the heterogeneous material properties of the aorta is the difficulty in quantifying the displacement and strain of the aortic wall in vivo. One possible solution is the recent development of DENSE (displacement-encoding with stimulated echoes)
MRI [5]. DENSE is most commonly used in imaging of the myocardium but there has been one study that used it in the ascending aorta, although it was not used to calculate strain [6]. In our study, spiral cine DENSE imaging is used to calculate the displacement and strain of the thoracic aortic wall and see how these measurements differ based on the circumferential position.

**Connective Tissue Disorders**

Connective tissue disorders weaken the aortic wall, which increases the risk for aneurysm formation. Connective tissues provide structure and support throughout the entire body, but they are especially paramount to the aorta. The aortic wall must be strong, yet elastic enough to withstand the constant pressure and high shear stress from blood flow. These two properties are found within the connective tissues which are composed of different proteins (e.g., Elastin, Fibrillin, CTGF, etc.). Various connective tissue disorders are results of mutations which alter the normal function of these proteins. Three connective tissues were looked at in this study. The first, Marfan syndrome, is a genetic disorder in which fibrillin is abnormally formed. Its effect on the aorta is prominent since fibrillin helps with the aortic wall’s structure and durability. Loeys-Dietz Syndrome is also a genetic disorder which affects tissue growth factor beta receptors 1 and 2. These protein mutations can cause unstable tissue in the aortic wall. The last disorder considered in this study is Ehlers-Danlos Syndrome, which is a group of genetic disorders characterized by hypermobile joints, hyper extensible skin, and fragile tissue [7].
Materials and Methods

2D spiral cine DENSE images were obtained on a 3T Siemens Prisma scanner from five patients who have Marfan Syndrome, Loeys-Dietz Syndrome, or Ehlers-Danlos Syndrome. These scans were all from the patient’s thoracic aorta. They are taken either in the distal aortic arch just distal to the left subclavian artery or in the mid-descending thoracic aorta behind the left atrium. Each 2D DENSE series consists of a standard magnitude image and two phase images in which the phase data within each pixel is directly proportional to the displacement of the tissue within that pixel from a reference state. By using diastole as the reference, multiple time points can be imaged to track the displacement of the aortic wall throughout the cardiac cycle.

In order to calculate the displacement and strain of the aortic wall, DENSE data was processed using custom MATLAB code. In brief, aortic wall displacement of each pixel in reference configuration is tracked through all time points. From the tracked displacement data, the Green strain can be calculated according to \( E = \frac{1}{2} (H + H^T + H^T \cdot H) \) where \( H \) is the referential displacement gradient. Multiple custom noise reduction techniques such as special and time soothing are implemented. The plot is created using the peak strain over sixteen sectors and shows the heterogeneity across the aortic wall.

In this IRB-approved study, there are eight control healthy patients and six patients that have connective tissue disorders (e.g., Marfan Syndrome, Loeys-Dietz Syndrome, or Ehlers-
Danlos) differing in severity. Some of these patients have aneurysms, others are starting to form aneurysms, and some do not have aneurysms at all. By comparing the circumferential strain and displacement of each of these groups to healthy patients, we can see how these values differ based on the stage of aneurysm formation. The patients can then be further characterized based on aortic wall strain values, which predict the onset of aneurysm formation.

**Preliminary Results**

Initial results were gathered from two Marfan patients and compared to two healthy patients of similar age and gender used as controls. The first Marfan patient was a 37 year old female with mitral valve disease. She showed a mean strain value of 15.1% which was higher than the control 37 year old female who had a strain value of 8.2%. The distribution of values (Figure 3) was similar to the old and young patient controls.

The second Marfan patient was a 56 year old male with no cardiovascular complications. He had a mean strain value of 7.2% which was similar to the control 58 year old male who had a strain value of 8.9%. The distribution of values (Figure 3) was also similar to the old patient controls.

![Figure 3: Peak strain distributions. White arrow shows the location of the vertebra. (A) Control, 37 year old female, (B) control, 58 year old male, (C) Marfan syndrome, 37 year old female, (D) Marfan syndrome, 56 year old male.](image)
Discussion

The aorta becomes stiffer and less compliant with age and based on results from the healthy patients alone, the mean strain distribution is different in older patients (> 50 years old) compared to younger patients (< 50 years old). For the control group, in older patients, we see the largest strain in the median wall or the wall immediately counterclockwise of the spine vertebra, while in younger patients, the largest strain is in the greater curvature which is immediately clockwise of the spine vertebra. This is most likely due to the high sheer the greater curvature undergoes daily from blood hitting it as it goes over the aortic arch. The greater curvature fatigues faster than the other parts of the wall and looses elastin which makes it less compliant in older people.

The first Marfan patient was young and had cardiovascular complication most likely due to her Marfan syndrome. The mean strain results were much higher than the controls, and the mean strain distribution was a hybrid between the young and old patient controls. This patient showed evidence of an early increase in strain in the median wall. The second Marfan patient had Marfan syndrome but did not have any complications to go with it even at the age of 56. The mean strain values and the distribution of strain values were similar to that of the control. From this, we see that Marfans that does not affect the cardiovascular system also does not affect aortic wall strain values, while Marfans that does affect the cardiovascular system will affect the strain values. More patient data will need to be analyzed to accept or reject the hypothesis.
References


