3-4-2008

Mechanical Properties of Aneurysms of the Descending Human Aorta

Peter Lin

Mechanical Properties of Aneurysms of the Descending Human Aorta

A Thesis Submitted to the

Yale University School of Medicine

in Partial Fulfillment of the Requirements for the

Degree of Doctor of Medicine

By

Peter C. Lin

2007

ABSTRACT

Objective: Treatment decisions for aortic aneurysms are currently based on size criteria originally developed in the 1960s, even though we now have more sophisticated methods that can refine interventional criteria. In this project, we applied engineering principles in order to generate a comprehensive picture of the mechanical properties of descending thoracic aortic aneurysms, including their ability to deform in response to pressure, as well as the stresses that cause wall stretch or rupture. Our goal was to use these mechanical properties to understand, explain, and predict the tendency of descending aneurysms to rupture or dissect.

Methods: Using an epi-aortic ultrasound probe intra-operatively, we measured aortic wall thickness during systole and diastole, circumference during systole and diastole, and blood pressure on 12 patients undergoing elective resection of their descending aortic aneurysms. From these measurements, we calculated the distensibility, wall stress, elastic modulus (E_{inc}), and pulse wave velocity (PWV) for the neck (narrow portion) and belly (widest portion) of fusiform aneurysms. We compared these mechanical properties between the neck and belly of descending aortic aneurysms with a paired t-test, as well as between ascending and descending aortic aneurysms with an unpaired t-test.

Results: The average aneurysm belly was 4.1 cm in diameter compared to 2.7 cm in the neck ($p = 0.0002$). Distensibility was higher in the neck than the belly ($p = 0.02$), the wall stress was higher in the belly ($p = 0.01$), and E_{inc} was non-significantly higher in the belly ($p = 0.08$). There was no significant difference in PWV ($p = 0.33$). There were no significant differences in any of the mechanical properties between descending and ascending aortic aneurysms.

Conclusion: Larger aneurysms are at increased risk of rupture because 1) they experience greater circumferential wall stress tending to expand the lumen, and 2) they are less distensible with a higher elastic modulus which indicates they have less reserve stretch capacity. We also showed that different sections of the same aneurysm behave differently but that the ascending and descending aortic aneurysms behave similarly. These findings have implications on the validity of using mechanical parameters to predict the natural course of aortic aneurysms. Finally, we demonstrated that there may be better ways to predict aortic rupture or dissection than current standards using diameter or growth rate alone.

ACKNOWLEDGEMENTS

I would like to thank Dr. John Elefteriades for sharing his infinite wisdom as a thesis advisor and research mentor, Dr. Raj Modak for his help in data collection and organization, Ms. Marianne McCarthy for her essential role as a facilitator and coordinator, and Dr. George Koullias for his study on ascending aortic aneurysms and for sharing his data for comparison. This project was conducted in collaboration with Maryann Tranquilli, RN, and the esteemed Dr. Paul Barash.

I am also grateful to the Office of Student Research at the Yale University School of Medicine for awarding a Student Research Fellowship in the summer of 2004.

TABLE OF CONTENTS

INTRODUCTION

The aorta plays an active role in blood circulation throughout the human body. Through pulsations with each heart beat, the aorta buffers stroke volume and propagates the pulse pressure during diastole. However, the ability of the aorta to withstand constant forces and stresses exerted by circulating blood often leads to long-term changes in its mechanical properties which can manifest as structural and functional changes. These changes occur even under normal physiologic conditions as a result of aging, in which the aorta modestly dilates in a process called ectasia. In contrast, various insults or congenital defects may result in pathology of the human aorta. Common culprits resulting in diseased aorta include aging, infection, inflammation, trauma, collagen vascular disease, and atherosclerotic disease, ultimately leading to formation of aortic aneurysms, a condition which has epidemiologic consequences.

Approximately 15,000 deaths annually in the United States can be attributed to aortic aneurysms (1). With a mortality and morbidity at less than 5%, elective surgical treatment of aortic aneurysms results in significantly improved outcomes compared to emergency treatment for a ruptured aneurysm which has a very high mortality. About 40% of patients with ruptured aneurysms do not survive long enough to reach the hospital. Of those who do survive long enough to come to medical attention, only about 50% survive the immediate perioperative period (2,3). For these reasons, treatment of aortic aneurysms has focused on early intervention in order to preclude catastrophic results such as aneurysm rupture or aortic dissection.

Classification

In the most general sense, an aneurysm refers to a focal dilation of a blood vessel compared to its previous diameter or adjacent tissue. When applied to the abdominal aorta, most authors agree that a dilation of greater than 3.0 cm is considered aneurysmal (4), representing approximately 50% dilation compared to average aortic tissue which measures 2.0 cm in diameter. Aortic aneurysms are frequently classified according to morphology or location.

Based on morphology, aortic aneurysms can be either fusiform (common) or saccular (uncommon). A fusiform aneurysm is a cylindrical dilation affecting the entire circumference of the aorta. These types of aneurysms are commonly but not always associated with atherosclerotic disease. These aneurysms have a "belly," corresponding to the aneurysmal section of the largest diameter, and a "neck," which refers to the narrow zone between the belly and normal aortic tissue. Saccular aneurysms, which are less common than fusiform aneurysms, are outpouchings of the aorta. A short neck often connects saccular aneurysms to the aorta.

Aortic aneurysms may also be classified based on their location as thoracic, thoracoabdominal, or abdominal. These represent diverse disease processes, and the clinical presentation, natural history, and treatment decisions are different for each of these segments. Representing 3% of aortic aneurysms, thoracoabdominal aneurysms are sometimes grouped with abdominal aortic aneurysms, although thoracoabdominal aneurysms are also often considered a separate class that require special considerations for surgical repair including possible re-implantation of the origins of visceral arteries. In contrast, ascending thoracic aneurysms are often asymptomatic and uncommonly result from atherosclerotic disease unless atherosclerosis is also present elsewhere. For purposes of this study, descending thoracic as well as thoracoabdominal aortic aneurysms were classified as descending aortic aneurysms, all of which arise distal to the origin of the left subclavian artery.

Pathology

It is important to note that the thoracic aorta behaves quite differently from the abdominal aorta as a result of different biochemical compositions. The thoracic aorta generally has a significantly higher collagen and elastin content as well as a higher collagen to elastin ratio than the abdominal aorta. Moreover, vascular smooth muscle cells originate from the neural crest in the ascending aorta and from the mesoderm and endothelial cells in the descending aorta (5). Finally, the majority of descending aortic aneurysms are associated with atherosclerosis (6), and these aneurysms are characterized by remodeling of the extracellular matrix, mainly due to a net excess of proteolysis and an inflammatory infiltrate.

On a molecular level, components of the extracellular matrix, most notably elastin and collagen, play the largest role in the "passive" mechanical properties of the aorta, which give the aorta its strength and allow the aorta to stretch (7). On the other hand, vascular smooth muscle cells affect the "active" mechanical properties, which maintain hemostasis and control blood pressure but only provide slight contributions to the strength of the vessel (7).

Physiologically, the contribution of the matrix components to aortic properties is controlled by a balance between proteinases that degrade these proteins and their inhibitors. In an aneurysmal state, the tissue appears to undergo matrix disruption due to cytokine-induced proteinase synthesis and activation without compartmentalization or sufficient endogenous inhibition (7). Further disruption of the tunica media results in decreased numbers of vascular smooth muscle cells and loss of wall strength (8). This loss of wall strength is eventually reflected in weakening of the aorta, which several authors have studied in the context of the aorta's mechanical properties.

Treatment

Nonsurgical options in the treatment of aortic aneurysms include close observation with serial examinations, while incorporating medical therapies such as smoking cessation and beta blocker therapy, both of which may slow aneurysm expansion. Surgical elective treatment for aortic aneurysms is replacement of the aneurysm with a prosthetic graft, although endovascular repair is considered in selected patients who represent high surgical risks.

Currently, indications for elective repair include symptomatic aneurysms regardless of diameter or growth rate, diameter greater than 5.5 cm, and rapid rate of aneurysm expansion. For thoracic aneurysms, an acceptable cutoff for surgical resection is 5.5 cm for ascending aneurysms and 6.5 cm for descending aortic aneurysms (9). Many studies have demonstrated that the risk of rupture strongly correlates with aneurysm size, with a marked increase in risk once the aneurysm reaches 5.5 cm in diameter (10,11). With an annual risk of rupture estimated at 0.5 to 5% for aneurysms less than 5.0 cm (11), many vascular surgeons have adopted this diameter as a cutoff for elective repair. Regarding rate of expansion, a small aneurysm regardless of location that expands at greater than 0.5 cm over six months of follow-up is considered to be at high risk of rupture (13). Although this current standard of care has been validated through studies looking at risk of rupture or dissection, we believe that outcomes can be further improved through a better understanding of the mechanical properties of aneurysms, either through mathematical modeling as other authors have done, or through calculation from direct measurements as we have done in this study.

Investigations on the Development of Aortic Aneurysms

These guidelines identifying candidates for surgical repair of aortic aneurysms grew from early work beginning in the 1960s that first identified size as a major criterion for risk of aneurysm rupture (14,15). However, we can now apply engineering principles to better understand aortic aneurysms (16), and this has been accomplished in various investigations that characterized aneurysms based on molecular analysis, mathematical models, strength testing, and noninvasive ultrasonographic tracings. For instance, molecular analyses of resected aortic aneurysms have shown that the increased stiffness of aneurysmal aortic tissue is likely due to a reduction in elastin content (19, 24).

In contrast to molecular analysis, mathematical models have attempted to explain the growth and structural weaknesses of aneurysms in terms of increased stiffness and decreased wall strength (7,8,12). In one study, Watton, et al. modeled the abdominal aorta as a two-layered cylindrical membrane using nonlinear elasticity and a physiologically realistic constitutive model (12). This model addressed collagen remodeling in the context of aneurysm growth, and this model's predicted rate of aortic dilation was consistent with those observed *in vivo*. However, this model did not predict changes in wall thickness, thus precluding the ability to estimate stress distribution and possibly rupture of the aneurysm.

Combining modeling with *ex vivo* measurements, Raghaven, et al. performed uniaxial tensile testing of excised human aneurysmal and nonaneurysmal abdominal aortic specimens and used a mathematical model to quantify the elastic response (20). The authors concluded that the difference between aneurysmal and normal aorta may be due to a difference in recruitment and loading of collagen fibers, and that AAA rupture may be related to a reduction in tensile strength.

While these mathematical models provide great insights into the development of aortic aneurysms, it is also clinically important to have the ability to non-invasively examine the properties of a patient's aneurysm. A promising method to accomplish this is through ultrasonographic echo tracings, which has been used in previous studies to demonstrate increased stiffness of aneurysmal tissue (21,22).

However, reaching the full potential of ultrasonography as a clinical tool will probably require combining engineering principles with ultrasonographic measurements. Indeed, many studies have already elucidated the role of mechanical properties in the pathology of the aorta while also demonstrating the validity of mechanical properties to predict aneurysm rupture (17,18). For instance, a prospective six-center study of 210 patients showed that a change in distensibility, as calculated from ultrasonographic tracings, may be a more powerful predictor of risk of rupture of infrarenal AAA than using diameter alone (17). This study, however, was limited by the fact that its cohort either was not offered or refused surgical repair of their aneurysm, thus limiting the ability to generalize the results of the study to people definitively requiring repair.

Although these previous studies have applied engineering principles to describe the characteristics and growth of aortic aneurysms, to the best of our knowledge, no studies have based their biomechanical analysis on direct *in vivo* epi-aortic measurements. When taken on patients requiring aneurysm repair, these *in vivo* epi-aortic measurements provide the advantage of being able to correlate the aorta's mechanical profile (distensibility, E_{inc}, wall stress, and pulse wave velocity) to varying degrees of definite pathology and dilation. Most significantly, this may lead to eventually using non-invasive echo tracings to determine an aneurysm's specific mechanical profile to guide future therapy.

Mechanical Properties

To expand upon these previous studies, we have examined *in vivo* mechanical properties of descending aortic aneurysms in patients undergoing elective repair. While a prior study characterized the mechanical properties of ascending aortic aneurysms (22), no such studies have yet been published on the properties of the descending aortic aneurysm. Specifically, we aimed to look at the distensibility, wall stress, and elastic modulus (E_{inc}) which have been demonstrated to give a comprehensive mechanical profile of aortic aneurysms (22). Additionally, we look at the pulse wave velocity in descending aortic aneurysms which reflects aortic stiffness and has been related to risk of rupture (23).

Distensibility reflects the ability of the aorta to change its diameter in response to changes in intraluminal pressure. Distensibility reflects compliance at a given pressure, but we did not examine compliance *per se* because compliance (change in cross sectional area for a change in pressure) only gives information about the aorta as a static structure and depends heavily on vessel geometry.

A higher distensibility means that the diameter of the vessel changes to a greater extent between systole and diastole. Distensibility is an innate property of the aorta that depends on elastin and collagen content in the wall of the aorta. At lower pressures, elastin is primarily responsible for distensibility and recoil, compared to higher pressures when collagen provides tensile strength and stiffness (24). Alternatively, distensibility can be viewed as the ability of the aorta to absorb energy during systole and to subsequently release that energy during diastole, aiding in blood flow during both parts of the cardiac cycle. Clinically, distensibility has shown promise as an indicator of risk of aneurysm rupture. As previously mentioned, a recent study has shown that a change in distensibility was a significant predictor of risk of rupture independent of diameter (17).

Another measure of wall stiffness is the incremental elastic modulus (E_{inc}), which represents the tangent of the stress / strain curve of the aortic wall (22). It can be loosely viewed as the amount of stress required to stretch a material. Therefore, the same amount of circumferential stress (perpendicular to the wall) causes less deformation in a wall with a high E_{inc} than in a wall with low E_{inc}. Being able to predict the diameter at which circumferential stress exceeds elastic modulus may help to avoid catastrophic aortic rupture or dissection (22).

In contrast to distensibility and elastic modulus which directly reflect wall stiffness, pulse wave velocity (PWV) is an indirect reflection of wall compliance. During systole, contraction of the left ventricle dilates the aortic wall and creates a pulse wave that travels down the arterial walls in advance of blood flow. A wall with higher compliance absorbs a greater amount of the pulse wave energy, thus decreasing pulse wave velocity. In other words, a higher PWV indicates lower compliance, and an aorta that mimics a metal pipe would have the highest PWV.

The usefulness of PWV has been demonstrated in several studies, including one investigation that calculated PWV in nonaneurysmal aortic tissue (descending thoracic aorta) proximal to the site of these patients' infrarenal AAA repair (23). Based on Doppler ultrasonographic measurements, this study found that patients who underwent emergent repair for AAA rupture had a lower aortic PWV and higher compliance compared to patients who underwent elective AAA repair. These data had possible epidemiologic implications because they potentially explain the paradox of a non-decreasing incidence of ruptured AAAs even with an increased number of elective surgical procedures. Specifically, this study's authors concluded that aneurysms with a high compliance and low PWV might undergo faster growth and earlier rupture, thereby preventing early diagnosis and treatment of the aneurysms. Because PWV has been widely used as a marker of wall stiffness (23,25,26) and has helped to provide possible insights into aneurysm growth (23), we have included PWV in our analysis.

Whereas distensibility, E_{inc}, and PWV all describe the general "stiffness" of an aorta or aneurysm, no characterization is complete without including the stress on the aorta. Therefore, we determined circumferential wall stress, which is the force exerted by circulating blood on the aortic wall per unit of surface area. Unlike shear stress whose vector runs parallel to the vessel wall, circumferential wall stress results in forces exerted perpendicular to the aortic wall, leading to pulsations in the diameter of the aorta. The energy is absorbed largely by stretching of elastin and collagen fibers in the wall, a phenomenon also called strain. When the wall stress surpasses the aorta's ability to counteract the force, the wall ruptures or dissection occurs. This means that the ultimate ability of an aorta to withstand aneurysm formation, or for an aneurysm to resist rupture and dissection, is based on a balance between its strength, elasticity and wall stress.

STATEMENT OF PURPOSE AND HYPOTHESIS

The purpose of this study was to create a better understanding of the mechanical changes underlying the pathology of descending aortic aneurysms in humans (distal to the origin of the left subclavian artery) as well as the structural failures leading to aneurysm rupture or dissection. In order to accomplish this, we used *in vivo* human aortic measurements to calculate distensibility, wall stress, elastic modulus (E_{inc}), and pulse wave velocity of descending fusiform aortic aneurysms. We analyzed the relationship among these mechanical properties with each other and with aneurysm diameter in order to understand differences between the neck and belly of aortic aneurysms, as well as differences between the descending and ascending aorta. Our hypotheses are the following:

1. A greater degree of pathological wall stretch is associated with increased stiffness of the descending human aorta. As a result, the belly of descending aortic aneurysms will have a lower distensibility, higher E_{inc}, and higher PWV than the neck of the same aneurysm. Similarly, larger aneurysms will have a lower distensibility, higher E_{inc}, and higher PWV than smaller aneurysms.
2. As circumferential wall stress is largely dependent on vessel geometry, the belly of descending aortic aneurysms will experience greater wall stress than the neck, and larger aneurysms will experience greater wall stress than smaller aneurysms.
3. Because the descending and ascending aortas have different wall compositions, their mechanical properties (distensibility, E_{inc}, PWV, and wall stress) will be significantly different.

METHODS

Patient Group

This study included 12 patients who underwent elective resection of descending thoracic and thoracoabdominal aortic aneurysms at Yale-New Haven Hospital between October 2003 and September 2004. Surgical candidates were identified for aneurysm resection after finding aortic aneurysms on imaging studies or after patients sought medical attention for symptomatic aortic aneurysms. Computed Tomography (CT) scans, if not already performed, were taken of these patients to confirm the pre-operative anatomy and size of the aneurysms. Using current standards of practice, patients underwent resection for symptomatic aneurysms, for aneurysms greater than 5.5 cm in diameter, and for aneurysms with a growth rate greater than 1.0 cm over the previous year. This study excluded patients with aortitis or known connective tissue disorders such as Marfan syndrome. We also excluded patients whose aneurysms extended to the aortic arch or ascending aorta. This study was approved by the Human Investigations Committee of Yale University (Protocol # 0301023874, *Mechanical Properties of the Aorta by Epi-aortic Echo*).

General Surgical Techniques and Epi-aortic Echocardiography

Patients were given general anesthesia with a double lumen endotracheal tube. A radial artery line was placed in order to continuously monitor blood pressure throughout the surgery, and this line also provided continuous blood pressure readings when we took epi-aortic ultrasonographic measurements.

The incision was either a left lateral or posterolateral thoracotomy that began in the fourth to sixth intercostal space. After careful surgical dissection, the aneurysm was exposed as fully as possible and measurements for this study were taken. This occurred before cannulation of the distal vasculature in preparation for cardiopulmonary bypass. Because measurements occurred before bypass, the body temperature was still within normal physiologic range at the time of epi-aortic measurements.

Measurements were taken as follows. First, a 6- to 15-MHz echocardiographic probe (Phillips model 21390A, Andover, Mass) was connected to a standard ultrasonographic station (Phillips series 5500). After the probe was coated with ultrasonographic gel, it was inserted into a sterile plastic sheath. A cushion constructed of a sterile surgical glove finger filled with normal saline allowed the transmission of ultrasonic waves between the probe and aortic tissue, thus avoiding interference from any potential gas interface. Once the probe was held in place by the surgeon (the principal investigator of this study), various measurements were taken by the attending anesthesiologist. These values were the diameter and wall thickness of the aneurysm, taken at the peak of systole and at diastole. Systolic and diastolic blood pressures were recorded from a pressure transducer connected to a cannulated radial artery. To maximize accuracy and reproducibility, three separate ultrasonographic measurements were taken during three separate cardiac cycles for each patient.

Once representative aortic cross-sections were identified in the two-dimensional mode, measurements were taken in triplicate from the M-mode display with the distance cursor. In eight patients, measurements were taken both at the narrow zone (neck) and widest accessible portion (belly) of the aneurysm.

After measurements were taken and recorded, the surgeon proceeded with the remainder of the aneurysm resection according to standard surgical technique. A prosthetic graft connected the remaining sections of aorta after resection of the aneurysm.

When possible, the author of this study was present in the operating room as a surgical assistant or to help with ultrasonographic measurements.

Calculation of Mechanical Properties

For our analysis, we compared the aneurysm neck to the aneurysm belly, and descending aortic aneurysms to ascending aortic aneurysms (see Appendix C). The author of this thesis created a computer spreadsheet in Microsoft Excel in order to calculate the distensibility, wall stress, elastic modulus, and pulse wave velocity (Table 1, below). The suitability of the equations used in this investigation were determined after reviewing current literature on mechanical properties of the aorta and other elastic vessels (17,22,25,27). The final version of this spreadsheet automatically calculated the aforementioned mechanical properties based on the epi-aortic ultrasonographic measurements and simultaneous blood pressure readings. The equations used to calculate mechanical properties are listed in Appendix A.

Mechanical property	Units
Distensibility	$mmHg^{-1}$
Wall stress	kPa
Elastic modulus	kPa
Pulse wave velocity	m/s

Table 1. Units of the mechanical properties presented in the current investigation.

Ascending Aortic Data

The data on ascending aortic aneurysms were previously published by George Koullias, et al (22). John Elefteriades was the principal investigator in Koullias's ascending aneurysm study as well as the original descending aneurysm study presented here. The data collection technique using an epi-aortic probe was very similar in both studies, involving direct epi-aortic ultrasonographic measurements through a sterile sheath taken before cannulation and cardiopulmonary bypass.

Statistical Analysis

The Student's paired t-test using a two-tailed distribution comparing the belly to the neck of aortic aneurysms was calculated in Microsoft Excel with the TTEST function. Aortic aneurysms that only included belly but no neck measurements (due to intra-operative limitations) were excluded from the paired t-tests. The unpaired t-test assuming unequal variances was used to determine statistical differences between mechanical properties of ascending and descending aortic aneurysms. Best fit lines were calculated with the least squares method in Microsoft Excel.

RESULTS

Patient Demographics

This study included adult men and women, with a male predominance (Table 2). The age range for patients with aortic aneurysms was 48 to 75 years, with a mean age of 61.2 years. The average diameter of the belly of the aneurysms was 4.1 cm and the average diameter of the neck was 2.8 cm.

Number of patients with aneurysms	12
Male:Female	9:3
Age (years)	61.2 ± 4.2
Age ranges	48 - 75
Avg belly diameter (cm)	4.1 ± 0.3
Avg neck diameter (cm)	2.8 ± 0.2

Table 2. Demographic data of patients undergoing resection for descending aortic aneurysms. Data are presented as mean ± SEM where applicable.

Overall Differences Between Neck and Belly of Aortic Aneurysms

	Aneurysm belly	**Aneurysm neck**	**p-value**
Systolic diameter (cm)	4.1 ± 0.3	2.7 ± 0.2	0.00018
Distensibility ($mmHg^{-1}$)	0.0029 ± 0.0008	0.0037 ± .0009	0.022
Wall Stress (kPa)	147 ± 19	98 ± 15	0.008
Elastic modulus (kPa)	1330 ± 516	820 ± 262	0.083
Pulse wave velocity (m/s)	6.7 ± 1.4	7.0 ± 0.9	0.334

Table 3. Average values for the mechanical properties of the neck and belly of descending aortic aneurysms. Data are presented as mean ± SEM. P-values are based on Student's paired t-test between the aneurysm neck and belly.

The distensibility, elastic modulus and pulse wave velocity (PWV) all reflected upon the stiffness of the aorta, and all three parameters indicated that the belly was stiffer than the neck (Table 3). On average, the neck had a distensibility of 0.0037 $mmHg^{-1}$, which was 28% higher than in the belly where the average distensibility was 0.0029 $mmHg^{-1}$. This difference was statistically significant ($p = 0.02$). The average elastic modulus was 820 kPa in the aneurysm neck compared to 1330 kPa in the aneurysm belly. This represented a 50% difference and indicated that the belly had less reserve stretch capacity. Although this average difference was greater than the average difference in distensibility, the difference in elastic modulus did not reach statistical significance ($p = 0.083$). Finally, the pulse wave velocity is inversely related to compliance, and this property again suggested that the belly is stiffer than the neck, but this difference was not as clear as for the distensibility and elastic modulus. The average PWV was only 8% higher in the aneurysm belly than in the aneurysm neck and there were no statistically significant differences in these two parts of the aneurysm ($p = 0.334$). Taken together, the results for distensibility, elastic modulus, and PWV show that the belly of an aneurysm is less able to deform or change its geometry as a way to accommodate increases in pressure or strain.

In contrast to the other mechanical properties, wall stress does not reflect the stiffness of the aorta but it does provide information regarding the tendency of circulating blood to stretch the aorta. We found that there were statistically significant differences in localized wall stress at the aneurysm neck and belly ($p = 0.008$). The wall stress was, on average, 50% greater at the aneurysm belly than at the neck, which means that the belly was exposed to greater stresses that could have altered its structural integrity.

Just as important as understanding differences between the neck and belly of aortic aneurysms is understanding variations in these mechanical properties with changes in diameter. These relationships are described in the following sections.

Distensibility

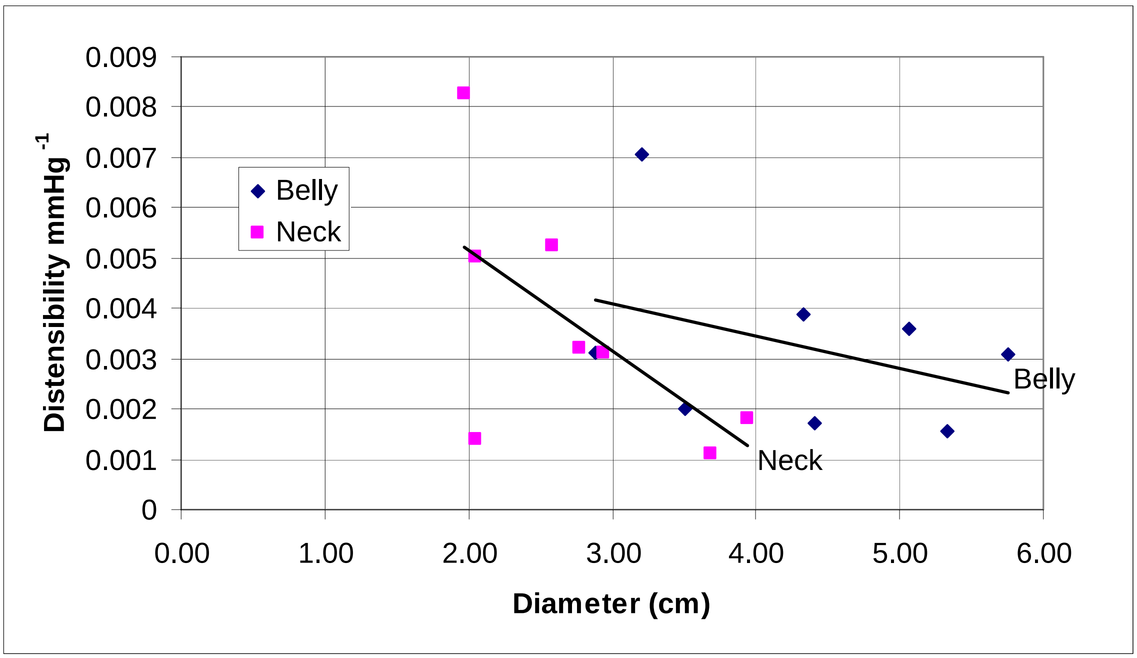

Figure 1. Relationship between the distensibility of different parts of descending aortic aneurysms to the maximal systolic diameter of the aneurysm.

We found that in general, larger aneurysms were less distensible than smaller aneurysms, which meant that smaller aneurysms had a greater ability to expand in response to pressure (Figure 1). We also found that the neck was usually more distensible than the belly even though there was some overlap in size between the groups. Specifically, above a diameter of approximately 3 cm, the distensibility of the neck was similar to the distensibility of the belly. A second similarity between the neck and belly is that the entire range of distensibility was similar for these two parts of aortic aneurysms. On the other hand, a change in diameter had a greater effect on distensibility in the neck than in the belly of the aneurysm, as indicated by a greater magnitude of the slope of the neck equation compared to the belly equation:

$$Distensibility(belly) = -0.34 \times diameter + 0.0043$$
$$Distensibility(neck) = -2.00 \times diameter + 0.0091$$

<u>Wall Stress</u>

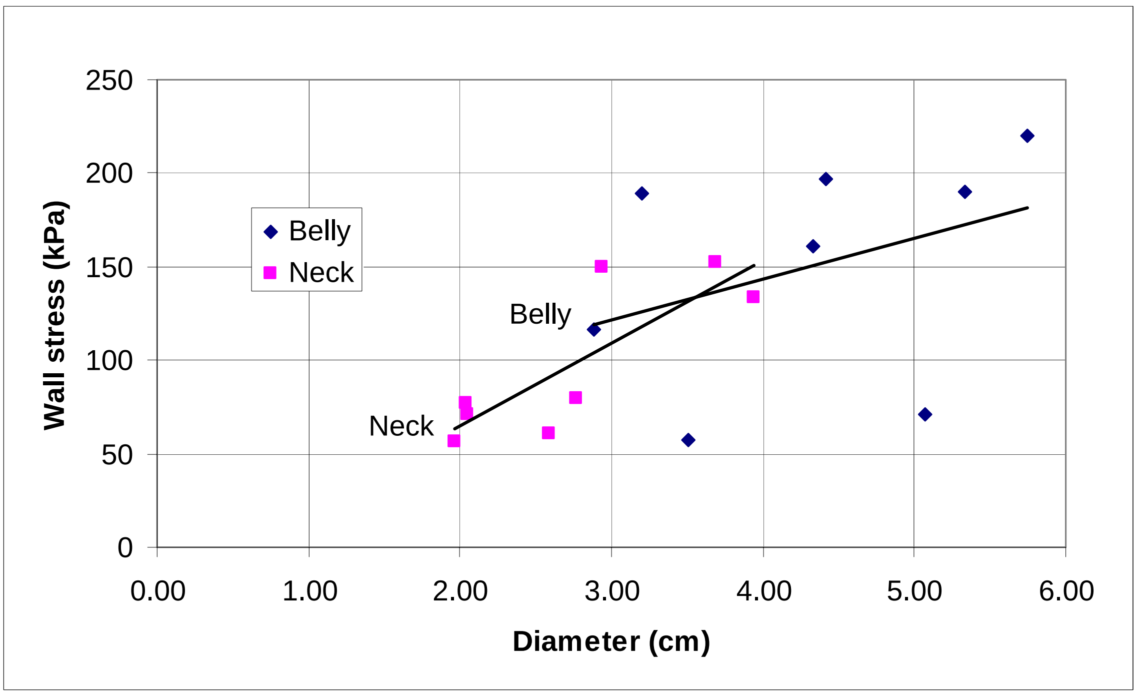

Figure 2. The relationship between circumferential wall stress and maximal systolic diameter shows a linear relationship for both the neck and belly of descending aortic aneurysms.

The wall stress increased in a roughly linear relationship with increases in aneurysm diameter (Figure 2). Quantitatively, the relationship can be described with the following two equations.

$$WallStress(neck) = 17 \times diameter + 79$$
$$WallStress(belly) = 44 \times diameter - 24$$

Some authors have shown the validity of using a single linear equation to describe the relationship between wall stress and diameter regardless of wall pathology (27), and we also combined our data to form a single plot, resulting in the following overall equation for wall stress.

$$WallStress(neck \ \& \ belly) = 29 \times diameter + 26$$

An important note is that, even though the plots for the neck and belly of aortic aneurysms can be combined into a single graph, the fact that the belly has larger diameters means that the belly will naturally experience greater wall stress.

Recognizing that wall stress is highly dependent on the blood pressure, we extrapolated our data in order to determine the wall stress on the aortic aneurysms at blood pressures that might be reached in daily activities. The intra-operative systolic blood pressure was maintained between approximately 90 and 110 mmHg, so we re-calculated wall stress at a blood pressure of 220 mmHg. This is a typical blood pressure in someone performing strenuous activities (such as lifting weights) or in a stressful situation. The results of this extrapolation are shown in Figure 3 (below). Wall stress is markedly increased at higher blood pressures, and the biggest aneurysms experience the largest increase in wall stress.

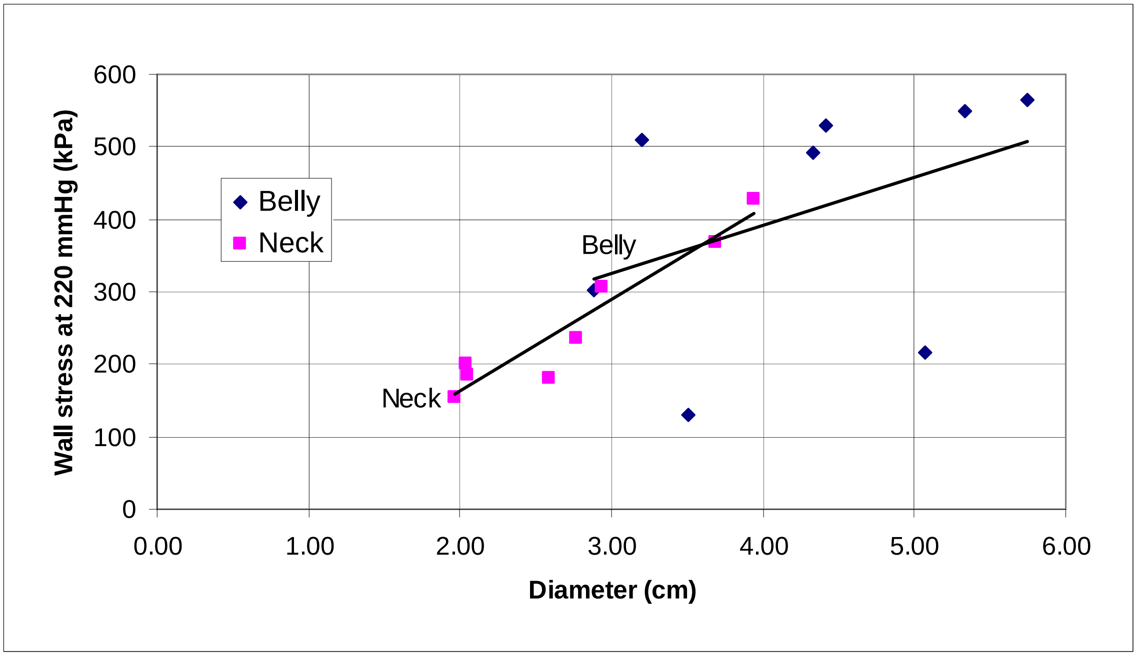

Figure 3. The extrapolated relationship between wall stress of descending aortic aneurysms versus maximal systolic diameter at a hypothetical blood pressure of 220 mmHg.

Elastic Modulus (E_{inc})

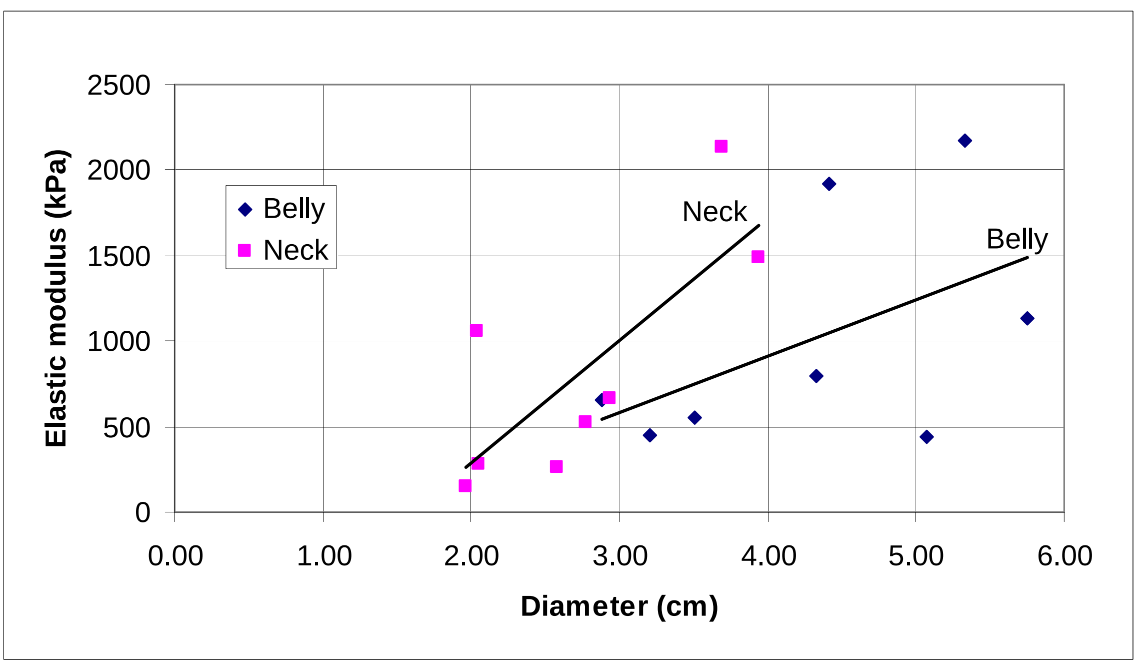

Figure 4. Relationship between the incremental elastic modulus of different parts of descending aortic aneurysms to the maximal systolic diameter of the aneurysm.

The incremental elastic modulus directly varied with the diameter of the aneurysm (Figure 4). As stated earlier, however, there was only a non-significant difference in elastic modulus between the neck and belly of aneurysms ($p = 0.083$). A change in diameter appeared to have a greater effect on E_{inc} of the neck than on E_{inc} of the belly, and the slope of E_{inc}/diameter was almost 2.5 times greater for the aneurysm neck than aneurysm belly. Moreover, in those cases when the aneurysm belly was small (< 3.5 cm), we found that the elastic modulus was similar to the elastic modulus in similar-sized aneurysm necks. It was at the larger diameters (> 3.5 cm) that the elastic modulus of the neck was much greater than the elastic modulus of the belly, accounting for the difference in the separate plots. These plots can be characterized by the following two linear equations:

$$E_{inc}(neck) = 249 \times diameter + 310$$
$$E_{inc}(belly) = 712 \times diameter - 1130$$

<u>Relationship Between E_{inc} and Wall Stress</u>

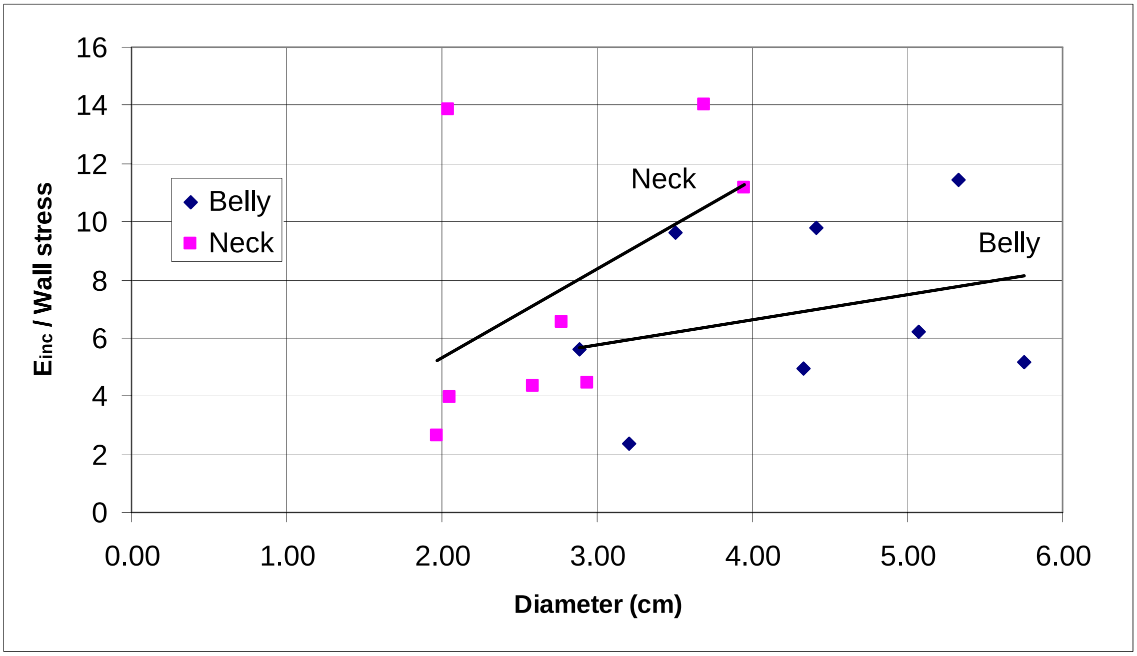

Figure 5. Relationship between E_{inc}/Wall stress to maximal systolic diameter of descending aortic aneurysms. E_{inc} = elastic modulus. E_{inc} and wall stress are both measured in units of pressure so E_{inc}/wall stress is unitless.

Figure 5 illustrates how E_{inc} / wall stress varied according to diameter. Using linear regression analysis, we found that this relationship could be described by the following equations:

$$\frac{E_{inc}}{WallStress} = 3.1 \times diameter - 0.8 \text{ (aneurysm neck)}$$

$$\frac{E_{inc}}{WallStress} = 0.6 \times diameter + 4.2 \text{ (aneurysm belly)}$$

As diameter increased, the E_{inc}/Wall stress relationship increased much more dramatically in the neck than in the belly of aortic aneurysms. In other words, because the slope of this relationship is greater than 1.0 for the neck of aneurysms, E_{inc} increases at a greater rate than wall stress for aneurysms of larger diameter. On the other hand, because the slope is less than 1.0 for the belly of aneurysms, E_{inc} increases at a slower rate than wall stress as diameter increases. Because this was a cross-sectional study, our results were valid for aneurysms of different sizes, but our study did not address whether E_{inc}/wall stress would follow the same pattern as an aneurysm grows.

We addressed this limitation of a cross-sectional study by directly comparing the relationship between E_{inc} and wall stress, and we plotted E_{inc} as a function of wall stress. As Figure 6 (below) shows, as the wall stress increases, the elastic modulus also increases in any part of the aneurysm. However, a major difference between the neck and the belly is that the elastic modulus in the neck increases to a greater extent with an increase in wall stress for any aneurysm. Therefore, within the limits of standard error and measurement uncertainty, our data indicate that all aneurysm bellies follow the "belly" line in Figure 6 and all aneurysm necks follow the "neck" line. This implies that as an aneurysm enlarges, the wall stress increases throughout the aneurysm (as shown by Figure 2), and most significantly, E_{inc} of the belly is unable to increase to the same extent that E_{inc} of the neck increases.

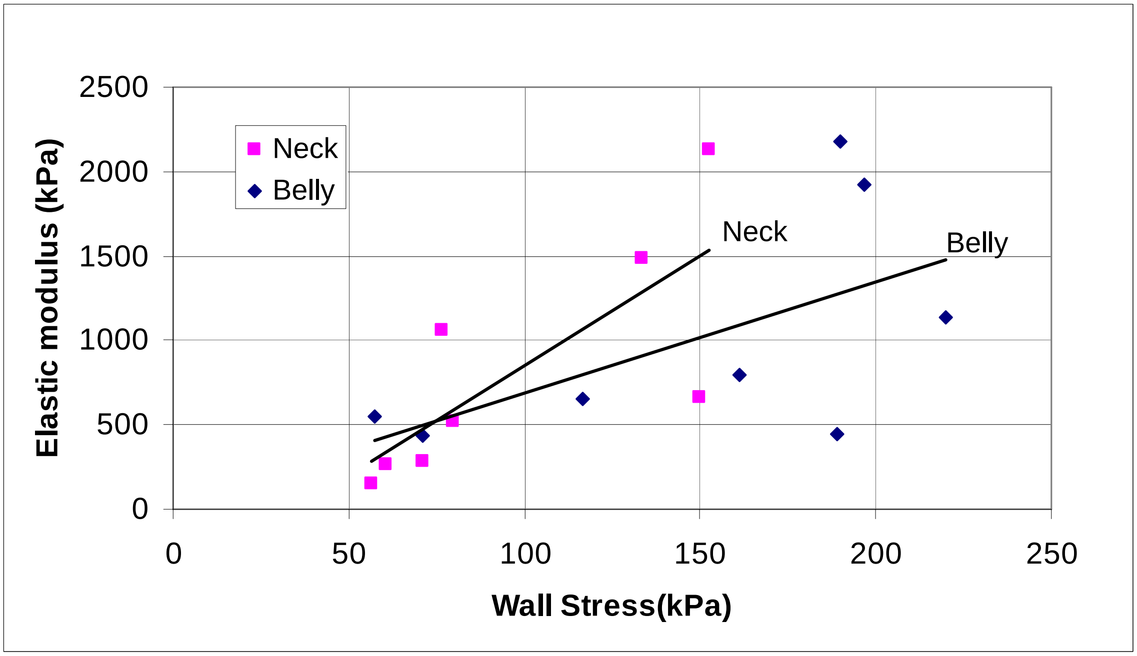

Figure 6. Relationship between elastic modulus and wall stress in the neck and belly of descending aortic aneurysms.

Pulse Wave Velocity (PWV)

The final mechanical property that we calculated in this study was pulse wave velocity (Figure 7)

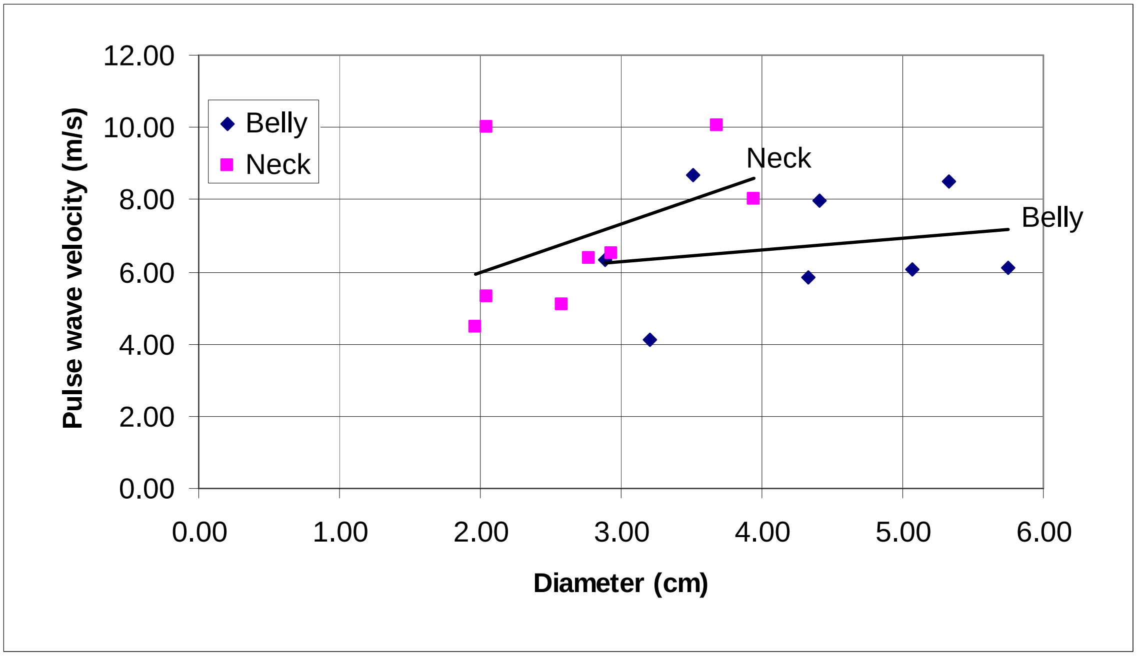

Figure 7. Relationship between pulse wave velocity and maximal systolic diameter of different sections of aneurysms of the descending aorta.

Similar to our other calculated characteristics, a change in diameter was associated with a greater change in the pulse wave velocity in the neck of descending aortic aneurysms than in the belly. Interestingly, the pulse wave velocity in the belly and neck of aneurysms was quite similar within the entire range of diameters. The PWV ranged from 4.1 m/s to 8.7 m/s in the belly, and it ranged from 4.5 m/s to 10.0 m/s in the neck, and these values were statistically indistinguishable ($p = 0.334$).

Comparison Between Ascending and Descending Aortic Aneurysms

In addition to comparing the belly to the neck of descending aortic aneurysms, we also compared mechanical properties of descending aortic aneurysms to the corresponding mechanical properties of ascending aortic aneurysms from a study published by Koullias, et al (22) (Tables 4 and 5).

	Descending neck	Ascending neck	p-value
Systolic diameter (cm)	2.7 ± 0.2	3.1 ± 0.04	0.29
Distensibility ($mmHg^{-1}$)	0.0037 ± .0009	0.0041 ± 0.0002	0.71
Wall Stress (kPa)	98 ± 15	102 ± 2.5	0.79
Elastic modulus (kPa)	820 ± 262	900 ± 61.3	0.81

Table 4. Differences in mechanical properties in the neck of descending and ascending aortic aneurysms. Data are presented as mean ± SEM. P-values were calculated using the unpaired t-test with two tails assuming unequal variances.

	Descending belly	Ascending belly	p-value
Systolic diameter (cm)	4.1 ± 0.3	4.3 ± 0.05	0.58
Distensibility ($mmHg^{-1}$)	0.0029 ± 0.0008	0.0022 ± 0.0001	0.36
Wall Stress (kPa)	147 ± 19	132 ± 3.4	0.49
Elastic modulus (kPa)	1330 ± 516	1400 ± 57	0.88

Table 5. Differences in mechanical properties in the belly of descending and ascending aortic aneurysms. Data are presented as mean ± SEM. P-values were calculated using the unpaired t-test with two tails assuming unequal variances.

Table 4 (neck) and Table 5 (belly) indicate that there were no statistically significant differences in mechanical properties of descending and ascending aortic aneurysms. Appendix B includes graphs representing the relationship between distensibility versus diameter, wall stress versus diameter, and elastic modulus versus diameter for corresponding parts of descending and ascending aortic aneurysms.

DISCUSSION

Summary

Although our understanding of the mechanisms behind the development of aortic aneurysms has increased dramatically over the last several decades, ruptured aortic aneurysms remain a significant cause of mortality and morbidity. In 2004, the Center for Disease Control reported that aortic aneurysms were the 18th overall leading cause of mortality in the United States and the 14th leading cause in people over 55 years old (28). Perhaps more alarmingly, however, is the fact that as the elderly population in the United States continues to rise, the number of people undergoing elective as well as emergent repair of ruptured aortic aneurysms has remained steady over the last decade (29). It has been suggested that this reflects the fact that patients with a high aortic compliance undergo a faster aneurysm growth and early rupture, which precludes early diagnosis and treatment (23).

Because aneurysms behave differently, a "one size fits all" approach to managing aneurysms based on size criteria can lead to suboptimal management. To avoid this pitfall, our ultimate goal was to elucidate mechanical properties of aneurysmal tissue in the descending human aorta in order to identify aneurysms at risk for rupture. We accomplished this goal by first demonstrating significant differences in distensibility and wall stress, and clear but non-statistically significant differences in elastic modulus, between the neck and belly of descending aortic aneurysms. Second, we showed that the differences between ascending and descending aortas and aneurysms may be minor when examining mechanical properties, even though the ascending and descending aorta have different wall compositions. This could imply that knowledge gained from one part of the aorta may help us understand other parts of the aorta.

Neck and Belly of Aneurysms

Regarding differences between the neck and belly of descending aortic aneurysms, we demonstrated the following points:

1. Larger aneurysms are stiffer than smaller aneurysms. A lower distensibility in larger aneurysms means they are less able to accommodate increases in pressure with reversible wall deformation, and a higher E_{inc} in larger aneurysms means they have been stretched closer to their limits than smaller aneurysms.
2. The neck and belly of aneurysms, even within the same size range, behave quite differently, and the section of an aneurysm (neck or belly) trumps vessel diameter in determining elasticity and stiffness. Specifically, there was overlap in the diameter of the large aneurysm necks with the diameter of the small aneurysm bellies between approximately 3 and 4 cm. In these cases, distensibility and E_{inc} of the aneurysm neck better followed the neck equations better than belly equations; the same generalization also held true for the aneurysm belly.
3. Although there were significant differences in the wall stress of the belly and neck, it appears that the predominant factor influencing wall stress was vessel diameter rather than section of aneurysm (unlike distensibility and E_{inc}).
4. Pulse wave velocity (PWV) was not significantly different in the neck and belly of descending aortic aneurysms, which is probably because the belly had insufficient length to detect a change in pulse wave velocity

These conclusions on distensibility, elastic modulus, and wall stress support the current standard of operating on aneurysms once they reach a certain size due to greatly increased risk of rupture. This is because a larger aneurysm size magnifies two risk factors for aneurysm rupture: decreased ability of the wall to withstand stress due to stiffness, and a greater wall stress. In other words, larger aneurysms become increasingly less able to withstand the increased stresses that accompany their greater diameters.

Our conclusions regarding aortic stiffness are supported by other studies which have shown that thoracic aneurysmal tissue has greater stiffness and less tensile strength than normal tissue (24) and that decreased distensibility is associated with increased risk of rupture (17). Likewise, our conclusions on wall stress being strongly dependent on diameter alone are supported by a study by Okamoto, et al that showed circumferential stress depends on aortic diameter and systolic blood pressure but not on age or clinical diagnosis (27). To the best of our knowledge, though, our study is the first that demonstrated the relationship between these theoretical mechanical weaknesses to actual epi-aortic measurements of aortic aneurysms *in vivo*, thus providing even stronger support for the conclusion that mechanical weakness of the descending aorta leads to aneurysm formation and possibly rupture or dissection.

Risk of Rupture or Dissection

While we have shown that determining mechanical properties of descending aortic aneurysms provides invaluable insights into their pathology, this study also showed that we can predict theoretical risk of rupture. To do this, we compared each patient's wall stress to the elastic modulus, and we also compared wall stress to experimentally determined aneurysm wall strength. Published literature suggests that ruptured aneurysmal tissue has a wall strength anywhere from 477 kPa to 823 kPa (20,30,31) Perhaps the most relevant wall stress in current literature was determined by Fillinger, et al, who found that a peak wall stress greater than 400 kPa in an aneurysm 5.5 cm in diameter had a 20% annual risk of rupture (31), and that a wall stress a peak stress greater than 450 kPa regardless of diameter had a 4% annual risk of rupture (32). These numbers correspond extraordinarily well with our data, which suggest that at a diameter of 5.0 cm, aneurysms begin to experience a wall stress of 450 kPa (Figure 3). Not coincidentally, published literature shows that aneurysms between 4 and 5 cm have an annual rupture risk of 0.5 to 5%, whereas those between 5 and 6 cm have an annual rupture risk of 3 to 15% (11); these data refer to abdominal aortic aneurysms but still provide estimates for the risk of rupture of descending thoracic aneurysms. In other words, previous literature has shown a dramatic increase in rupture risk in aneurysms greater than 5.0 cm, while separate studies have demonstrated that 450 kPa represents maximal wall strength of an aortic aneurysm; our analysis provides the link between these studies because we have shown that 5.0 cm aneurysms are commonly exposed to wall stresses of 450 kPa.

We believe that we can further refine our ability to predict an aneurysm's ability to endure wall stress without rupturing by comparing elastic modulus and wall stress together (Figures 5 and 6). As expected, this ratio decreases as diameter increases, which explains why larger vessels are usually at greater risk of rupture than smaller vessels. Larger vessels encounter a disproportionately larger circumferential stress compared to smaller vessels because the slope of (E_{inc}/wall stress) versus diameter (Figure 5) is less than one, implying that larger vessels have less stretch reserve. Theoretically, this means the stiff aneurysm is one that does not distend with pressure and is likely to rupture, as opposed to the flexible aneurysm which distends under stress and is thus more resilient to rupture. Since the E_{inc} to wall stress ratio basically represents the ability of a vessel wall to withstand pressure compared to the wall stress that it actually encounters, we could even go so far as to propose that this ratio may help to determine surgical candidates (Figure 8, below).

Possible New Method to Identify Operative Candidates

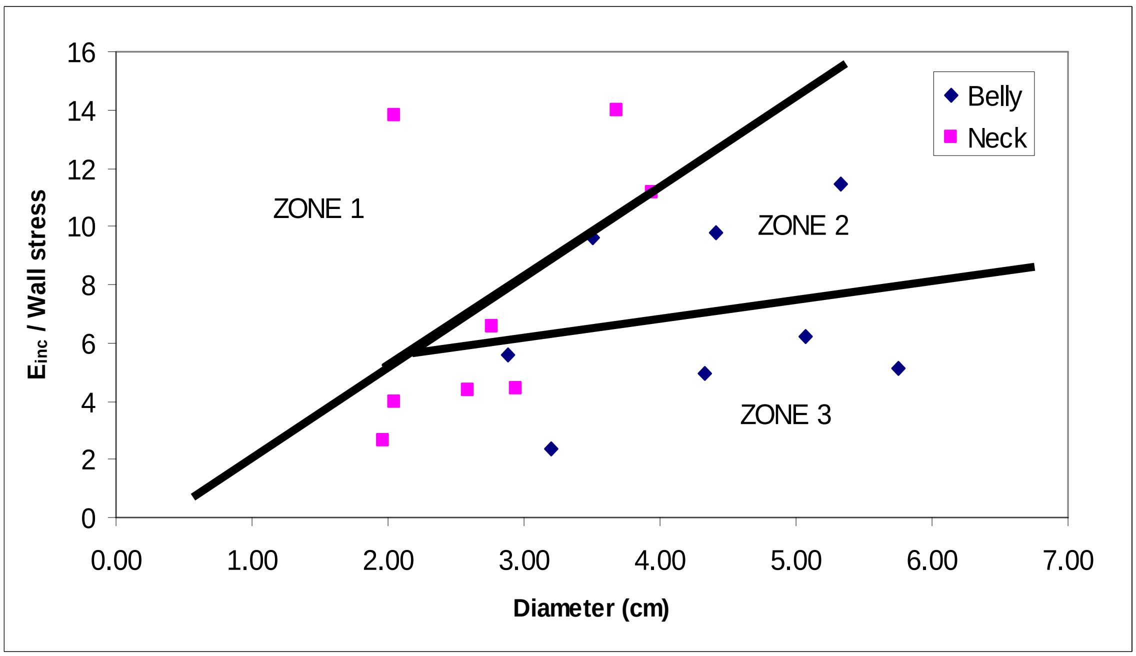

Figure 8. Proposed zones describing the behavior of descending aortic aneurysms. Each zone represents a different level of risk for aneurysm rupture. Zone 1 = low risk, Zone 2 = indeterminate risk, Zone 3 = high risk.

The independent and dependent variables are the same in Figure 8 and our earlier E_{inc}/Wall stress versus diameter graph (Figure 5), but Figure 8 includes three different zones representing different risks of rupture. In this figure, Zone 1 has excellent negative predictive value in ruling out the possibility that a dilated portion of aorta behaves like the belly of an aneurysm, as no belly data points lie within this area.

Therefore, if E_{inc}/wall stress for a patient clearly falls into Zone 1, a patient's enlarged aorta is unlikely to behave like the belly of an aneurysm but rather behave more like the neck of an aneurysm with its associated stronger elastic properties and resistance to rupture. These patients are unlikely to need urgent surgery and can probably be conservatively managed with medical therapies and close follow-up.

In contrast to Zone 1, Zone 3 represents those patients whose enlarged aortas behave like the belly of an aneurysm regardless of the belly diameter. Excluding patients with connective tissue disorders, we doubt that any normal-diameter, non-aneurysmal aorta would fall into Zone 3 because they have a normal biochemical composition and mechanical properties. Indeed, this speculation is supported by our data because no aneurysm with a small belly (less than approximately 3 cm) falls into Zone 3. In potential follow-up studies to the current investigation, it would be most interesting to test whether non-aneurysmal aortas in people with connective tissue disorders fall into Zone 3.

For all other aneurysms in Zone 3, our study suggests that patients should probably undergo surgery. If our analysis is correct, then patients in Zone 3 are those at greatest risk of rupture. For prognosis, these patients are also at the greatest risk for worsening their mechanical profile. This is because the E_{inc}/Wall stress ratio is less than 1.0 for the aneurysm belly, which means that as the aneurysm grows the E_{inc}/Wall stress ratio will become less favorable, unless the elastin and collagen content somehow changes beneficially. Additional studies could confirm that the elastin and collagen content is relatively stable, providing additional evidence that patients in Zone 3 probably need surgery regardless of aneurysm size. A longitudinal study on patients whose small-diameter aneurysms fall into Zone 3 would allow us to test whether this proposed Zone classification is indeed clinical useful or not.

Finally, Zone 2 represents the blending of properties of the belly and neck of aortic aneurysms. Our analysis has shown that the majority of this area is composed of aneurysm bellies. As this area probably encompasses both pathologic and normal aortas, it would be interesting to longitudinally follow those aortas or aneurysms that fall into this category. Because we do not know the natural outcomes of these aneurysms, we tentatively conclude that the prognosis and surgical candidacy of these patients are indeterminate.

This scheme to divide aneurysms into three groups may provide a new way to look at the aneurysms. At the very least, it shows that diameter alone does not adequately distinguish aneurysms from each other.

Pulse Wave Velocity

One reason we included PWV in our analysis was that it is ubiquitous in the literature on atherosclerosis and wall stiffness (23,25,26). However, we found that the PWV could not distinguish neck from belly. This is consistent with our understanding of PWV because we know that compliance (as reflected in the PWV) depends on vessel geometry, which in turn strongly depends on degree of atherosclerosis. In our study, it is very likely that the aneurysm neck and belly had similar degrees of atherosclerosis, possibly explaining why they were statistically indistinguishable. Perhaps more significantly, while an aneurysm may measure several centimeters in length, the belly of aneurysms may not be long enough to permit detection of a change in PWV. Based on our findings on E_{inc} and distensibility, we surmise that atherosclerosis notwithstanding, the most likely reason there were no significant differences in PWV was that the length of the belly was not long enough to measure a change in PWV. Therefore, in identifying mechanical properties of thoracic aneurysms, whose pathology involves atherosclerosis less frequently than abdominal aneurysms, PWV may be less useful than distensibility, wall stress, and E_{inc} because these latter characteristics do not depend on vessel geometry and may be less affected by atherosclerosis or tube length.

Aneurysms of the Ascending and Descending Aorta

Although this study showed that mechanical properties of descending aortic aneurysms are not statistically different from a related study's data on ascending aortic aneurysms, there may still be differences between these two sections of the aorta (Tables 2 and 3). We expected to see differences because the thoracic aorta behaves differently from the abdominal aorta, and the pathogenesis of ascending aneurysms is different from the pathogenesis of abdominal aortic aneurysms. Regarding the development of thoracic aortic aneurysms, the term cystic medical necrosis describes the triad of loss of smooth muscle cells, diminished number of elastic fibers, and accumulation of proteoglycans; on the other hand, abdominal aortic aneurysms have been primarily associated with atherosclerosis (5). Both types of aneurysms do demonstrate loss of vascular smooth muscle cells and destruction of matrix elastic fibers (5).

Since we already know that many factors influence the mechanical properties of elastic vessels, there are several explanations why our measured mechanical properties were not statistically different between ascending and descending aortic aneurysms. Obviously, it is quite possible that these studies simply lacked enough power. Nevertheless, based on our results showing such striking similarities in mechanical properties, we can reasonably speculate and even expect that a more powerful study might reveal statistical significance but would also show that these mechanical properties still remained similar to each other. Another explanation as to why the ascending and descending data were similar could be that differences only arise when comparing the ascending aorta to the distal descending aorta (such as the abdominal aorta). In any case, because of the similarities in mechanical properties, our study suggests that we should consider managing proximal descending aneurysms as though they were ascending aneurysms.

Limitations to this study

This study would have benefited from the inclusion of control data on normal descending aortas (see Appendix C), but we still believe we have thoroughly demonstrated some important insights based on comparing the belly and neck of descending aneurysms, and by comparing ascending to descending aortic aneurysms. As a result of this study, we do have a better understanding of the behavior of descending aortic aneurysms, both in terms of appreciating the mechanical failure of descending aortic aneurysms and in terms of helping to unify some of the abundant literature describing these aneurysms.

A second issue that must be addressed is the use of linear regression analysis instead of higher-order analysis to describe the mechanical properties of aneurysms, but based on other published literature we do not think this was a source of significant error. We already know that at lower pressures, elastin plays a larger role than collagen in providing strength and recoil, but collagen more heavily influences the behavior of the aorta at higher pressures and diameters (24). This means that a simple linear model is not adequate to predict the behavior of elastic arteries at extreme pressures. If our range of diameters and pressures had been greater than in the current study, then indeed it would have been more appropriate to use a nonlinear model. However, recent nonlinear mathematical modeling on the growth of aortic aneurysms that account for elastin and collagen behavior, as well as progressive fiber recruitment, showed that the pressure-diameter relationship is linear to a first order approximation when the blood pressure was less than approximately 120 mmHg (12). By corollary, our calculated mechanical properties resulting from data obtained at pressures below 120 mmHg would also behave in a linear relationship to vessel diameter. Fortunately, the intra-operative systolic blood pressures ranged between 90 and 110 mmHg, validating our assumption of linear behavior.

Another potential but unlikely source of systematic error in our study was the assumption that the radial blood pressure satisfactorily reflected central blood pressure. It has been well documented since 1955 that blood pressures taken through radial artery cannulation tend to be greater than central blood pressures (33), but on the other hand, the difference in radial and central blood pressure is minimal before cardiopulmonary bypass and significant only after bypass (33,34). Using standard fluid-filled transducers during narcotic anesthesia but before cardiopulmonary bypass, Pauca, et al. found that the radial mean arterial pressure (MAP) and diastolic artery pressure (DAP) consistently and accurately reflected central aortic pressure (34). On the other hand, the pre-bypass radial systolic artery pressure (SAP) overestimated aortic SAP by 10 to 35 mmHg in 50% of patients. However, this difference was most pronounced at systolic blood pressures higher than those seen in our patient population, which were generally less than 100 mmHg.

Because our measurements were taken before bypass and because the systolic blood pressures were less than 100 mmHg, our pre-bypass measurements are probably accurate. Nevertheless, we recalculated the mechanical properties allowing for the worst case scenario with a 10% overestimation in central blood pressure, and found minimal changes. Perhaps the strongest evidence that our calculated mechanical properties match those of the actual aorta is the fact that our data match mechanical properties based on mathematical modeling. For instance, Okamoto, et al. calculated wall stress and other mechanical properties using a cylindrical model of the aorta. The wall stress versus diameter graphs are similar whether they are based on Okamoto's mathematical model or our epi-aortic measurements (Figure 9) (27).

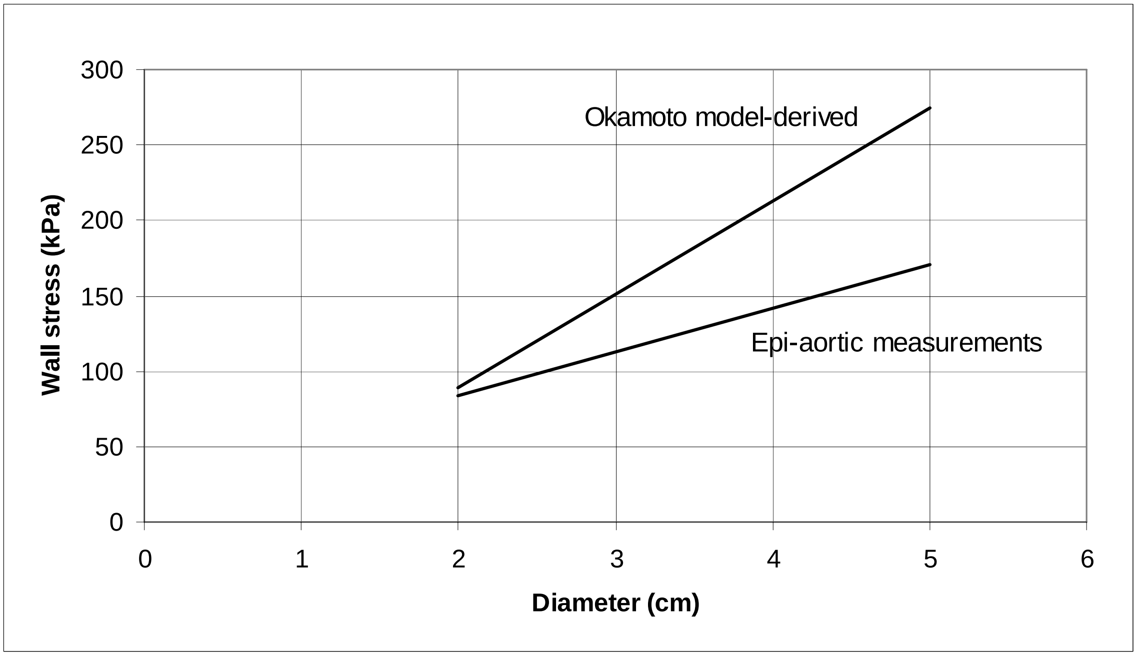

Figure 9. Wall stress, as determined by epi-aortic measurements or mathematical model, as a function of diameter. "Epi-aortic measurements" model is derived from epi-aortic ultrasonographic measurements. "Okamoto model-derived" is derived from a cylindrical mathematical model of the aorta.[27]

Conclusion

In summary, we have reported mechanical properties of descending human aortic aneurysms (distal to the left subclavian artery) based on epi-aortic measurements taken *in vivo* at the time of surgical resection. Our results showed that larger aneurysms are at increased risk of rupture because 1) they experience greater circumferential wall stress tending to expand the lumen, and 2) they are less distensible with a higher elastic modulus which indicates they have less reserve stretch capacity. We also showed that different sections of the same aneurysm behave differently but that the ascending and descending aortic aneurysms behave similarly. These findings have implications on the validity of using mechanical parameters to predict the natural course of aortic aneurysms.

Finally, while we did suggest a new scheme to risk stratify descending aortic aneurysms based on the relationship between the elastic modulus and wall stress, the real significance of this study was the demonstration that there are better ways to identify aneurysm weakness and potential rupture than current standards using diameter or growth rate alone.

In the future, for aortic mechanics to be utilized in pre-operative surgical decision making, the data need to be accessible non-operatively and non-invasively. We are currently performing a research investigation to confirm that transesophageal echocardiography, a common clinical technique, can obtain mechanical property measurements which correlate with those ascertained via epi-aortic measurements. We look forward to a future in which surgical decision making is made not just based on aneurysm size, but also based on aortic mechanical properties (distensibility, E_{inc}, wall stress, and E_{inc}/wall stress ratio). We believe that mechanical properties will likely permit better informed decision making.

REFERENCES

1. American Heart Association: Heart Disease and Stroke Statistics—2003 Update. http://www.americanheart.org/downloadable/heart/ 10461207852142003HDSStats Book.pdf

2. Farooq MM, Freischlag JA, Seabrook GR, Moon MR, Aprahamian C, Towne JB. Effect of the duration of symptoms, transport time, and length of emergency room stay on morbidity and mortality in patients with ruptured abdominal aortic aneurysms. Surgery 1996;119(1):9-14.

3. Thomas PR, Stewart RD. Abdominal aortic aneurysm. Br J Surg 1988;75(8):733-6.

4. Ouriel K, Green RM, Donayre C, Shortell CK, Elliott J, and DeWeese JA. An evaluation of new methods of expressing aortic aneurysm size: relationship to rupture. J Vasc Surg 1992;15(1):12-8; discussion 19-20.

5. Guo DC, Papke CL, He R, and Milewicz DM. Pathogenesis of thoracic and abdominal aortic aneurysms. Ann New York Aca Sci 2006;1085:339-52.

6. Dillon ML, Young WG, Sealy WC. Aneurysms of the descending thoracic aorta. Ann Thorac Surg 1967;3:430–8.

7. Goodall S, Crowther M, Bell PR, and Thompson MM. The association between venous structural alterations and biomechanical weakness in patients with abdominal aortic aneurysms. J Vasc Surg 2002;35(5):937-42.

8. He CM and Roach MR. The composition and mechanical properties of abdominal aortic aneurysms. J Vasc Surg 1994;20(1):6-13.

9. Coady MA, Rizzo JA, Hammond GL, Kopf GS, and Elefteriades JA. Surgical intervention criteria for thoracic aortic aneurysms: a study of growth rates and complications. Ann Thorac Surg 1999; 67(6):1922-6; discussion 1953-8.

10. Powell JT, Greenhalgh RM. Small abdominal aortic aneurysms. N Engl J Med 2003; 348(19):1895-901.

11. Brewster DC, Cronenwett JL, Hallett JW, Johnston KW, Krupski WC, and Matsumura JS. Guidelines for the treatment of abdominal aortic aneurysms. Report of a subcommittee of the Joint Council of the American Association for Vascular Surgery and Society for Vascular Surgery. J Vasc Surg 2003;37(5):1106-17.

12. Watton PN, Hill NA, Heil M. A mathematical model for the growth of abdominal aortic aneurysms. Biomechan Model Mechanobiol 2004; 3:98–113.

13. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, et al. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower

extremity, renal, mesenteric, and abdominal aortic). Circulation 2006; 113:e463.

14. Szilagyi DE, Smith RF, DeRusso FJ, Elliott JP, Sherrin FW. Contribution of abdominal aortic aneurysmectomy to prolongation of life. Ann Surg 1966; 164:678.

15. Foster JH, Bolasny BL, Gobbel WG, and Scott HW. Comparative study of elective resection and expectant treatment of abdomianl aortic aneurysm. Surg Gynecol Obstet 1969; 129:1.

16. Boudoulas H, Toutouzas PK, Wooley CF (Eds.). Functional Abnormalities of the Aorta. Futura Publishing Company. Armonk, NY. 1996.

17. Wilson KA, Lee AJ, Hoskins PR, Fowkes FG, Ruckley CV, and Bradbury AW. The relationship between aortic wall distensibility and rupture of infrarenal abdominal aortic aneurysm. J Vasc Surg 2003; 37:112-7.

18. Vorp DA, Raghauer ML, Webster MV. Mechanical wall stress in abdominal aortic aneurysm: influence of diameter and asymmetry. J Vasc Surg 1998; 27:632-9.

19. Sumner DS, Iokanson DE, Strandness DE Jr. Stress-strain characteristics and collagen-elastin content of abdominal aortic aneurysms. Surg Gynecol Obstet 1970; 147:211-4.

20. Raghavan ML, Webster MW, Vorp DA. Ex vivo biomechanical behavior of abdominal aortic aneurysm: assessment using a new mathematical model. Ann Biomed Eng 1996; 24:573-82.

21. Sonesson B, Hansen F, and Lanne T. Abdominal aortic aneurysm: a general defect in the vasculature with focal manifestations in the abdominal aorta. J Vasc Surg 1997; 26:247-54.

22. Koullias G, Modak R, Tranquilli M, Korkolis DP, Barash P, and Elefteriades JA. Mechanical deterioration underlies malignant behavior of aneurysmal human ascending aorta. J Thorac Cardiovasc Surg 2005; 130(3):677-83.

23. Russo L. Thoracic aortic compliance as a determinant of rupture of abdominal aortic aneurysms. Ann New York Aca Sci 2006. 1085:363-6.

24. Vorp DA, Schiro BJ, Ehrlich MP, Juvonen TS, Ergin MA, and Griffith BP. Effect of aneurysm on the tensile strength and biomechanical behavior of ascending thoracic aorta. Ann Thorac Surg 2003; 75:1210–4.

25. Blacher J, Asmar R, Djane S, London GM, and Safar ME. Aortic pulse wave velocity as a marker of cardiovascular risk in hypertensive patients. Hypertension 1999; 33(5):1111-7.

26. Bank AJ and Kaiser DR. Smooth muscle relaxation: effects on arterial compliance, distensibility, elastic modulus, and pulse wave velocity. Hypertension 1998; 32(2):356-9.

27. Okamoto RJ, Xu H, Kouchoukos NT, Moon MR, and Sundt TM. The influence of mechanical properties on wall stress and distensibility of the dilated ascending aorta. J Thorac Cardiovasc Surg 2003; 126(3):842-50.

28. Centers for Disease Control and Prevention. Web-based Injury Statistics Query and Reporting System: Leading causes of death reports, 1999—2004. http://webapp.cdc.gov/sasweb/ncipc/leadcaus10.html

29. Cowan JA, Dimick JB, Henke PK, Rectenwald J, Stanley JC, and Upchurch GR. Epidemiology of aortic aneurysm repair in the United States from 1993 to 2003. Ann N Y Aca Sci 2006; 1085:1-10.

30. Di Martino E, Bohra A, Vande Geest J, Gupta N, Makaroun M, Vorp D. Biomechanical properties of ruptured versus non-ruptured Abdominal Aortic Aneurysm wall tissue. in Biomedical Engineering Society Annual Fall Meeting. Philadelphia, PA. 2004.

31. Fillinger MF, Raghavan ML, Marra SP, Cronenwett JL, and Kennedy FE. In vivo analysis of mechanical wall stress and abdominal aortic aneurysm rupture risk. J Vasc Surg 2002; 36(3):589-97.

32. Fillinger MF, Marra SP, Raghavan ML, et al: Prediction of rupture risk in abdominal aortic aneurysm during observation: Wall stress versus diameter. J Vasc Surg 2003; 37:724-732.

33. Kroeker EJ, Wood E H . Comparison of the simultaneously recorded central and peripheral arterial pressure pulses during rest, exercise and tilted position in man. Circ Res 1955; 3:623-32

34. Pauca AL, Wallenhaupt SL, Kon ND, Tucker WY. Does radial artery pressure accurately reflect aortic pressure? Chest 1992; 102:1193-1198.

35. Nichols WW and O'Rourke MF. McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles. 5th ed. London, England: Hodder Arnold; 2005.

36. Chen CH, Nevo E, and Fetics B. Estimation of central aortic pressure waveform by mathematical transformation of radial tonometry pressure: validation of generalized transfer function. Circulation 1997; 95:1827-1836.

37. Mignini MA, Piacentini E, and Dubin A. Peripheral arterial blood pressure monitoring adequately tracks central arterial blood pressure in critically ill patients: an observational study. Critical care (London, England) 2006; 10(2):R43.

38. Long A, Rouet L, Bissery A, Rossignol P, Mouradian D, and Sapoval M. Compliance of abdominal aortic aneurysms evaluated by tissue Doppler imaging: correlation with aneurysm size. J Vasc Surg 2005; 42(1):18-26.

APPENDIX A

A1. Distensibility of an elastic vessel

$$Dist(P) = \frac{1}{LCSA_{syst}} \times \frac{\Delta LCSA}{\Delta P}$$

$$LCSA_{syst} = \pi \times \left(\frac{D}{2}\right)^2$$

$$\Delta P = BP_{syst} - BP_{diast}$$

Where:

D = Lumen diameter
$LCSA_{syst}$ = Luminal cross sectional area during systole
P_{syst} = Systolic blood pressure
ΔLCSA = change in luminal cross sectional area between systole and diastole
ΔP = pulse pressure
BP_{syst} = systolic blood pressure
BP_{diast} = diastolic blood pressure

A2. Wall stress

In our analysis, wall stress is calculated at peak systole because that is the point of the cardiac cycle at which the aorta undergoes the greatest amount of stress and, according to current theories, is therefore the most important wall stress to determine.

$$WS_{syst} = \frac{2 \times LCSA_{syst} \times P_{syst}}{WCSA}$$

$$WCSA = WT_{syst} \times (\pi \times D)$$

Where:

WS = Wall stress
$LCSA_{syst}$ = Luminal cross sectional area during systole
P_{syst} = Systolic blood pressure
[MCSA = surface area of the aortic wall cross sectional area]
WCSA = surface area of the aortic wall cross sectional area
WT_{syst} = Aortic wall thickness during systole
D = Lumen diameter

A3. Incremental Elastic Modulus

The incremental elastic modulus is defined as the slope of the stress / strain relationship of the aortic wall.

$$E_{inc} = \frac{3}{Dist(P)} \times \frac{1 + LCSA_{syst}}{WCSA}$$

Where:

E_{inc} = Incremental elastic modulus
Dist(P) = distensibility at a pressure P, as defined above
$LCSA_{syst}$ = Luminal cross sectional area during systole
WCSA = surface area of the aortic wall cross sectional area

A4. Pulse Wave Velocity

The pulse wave velocity (PWV) was calculated using the Moens-Koertewig equation:

$$PWV = \left(\frac{E_{inc} \times h}{2\rho \times r} \right)^{1/2}$$

Where:

ρ = Blood density
R = Vessel radius
E_{inc} = Elastic modulus
h = Wall thickness

APPENDIX B

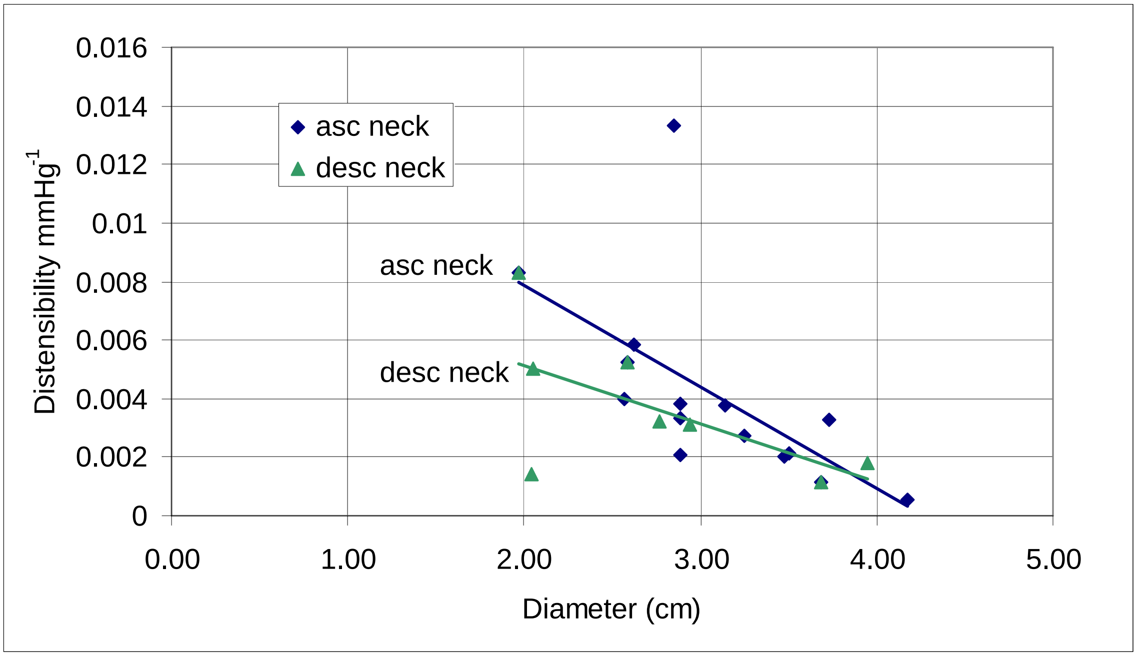

Figure B1. Relationship between distensibility and diameter of the neck of ascending and descending aortic aneurysms. Desc = descending aortic aneurysm. Asc = ascending aortic aneurysm.

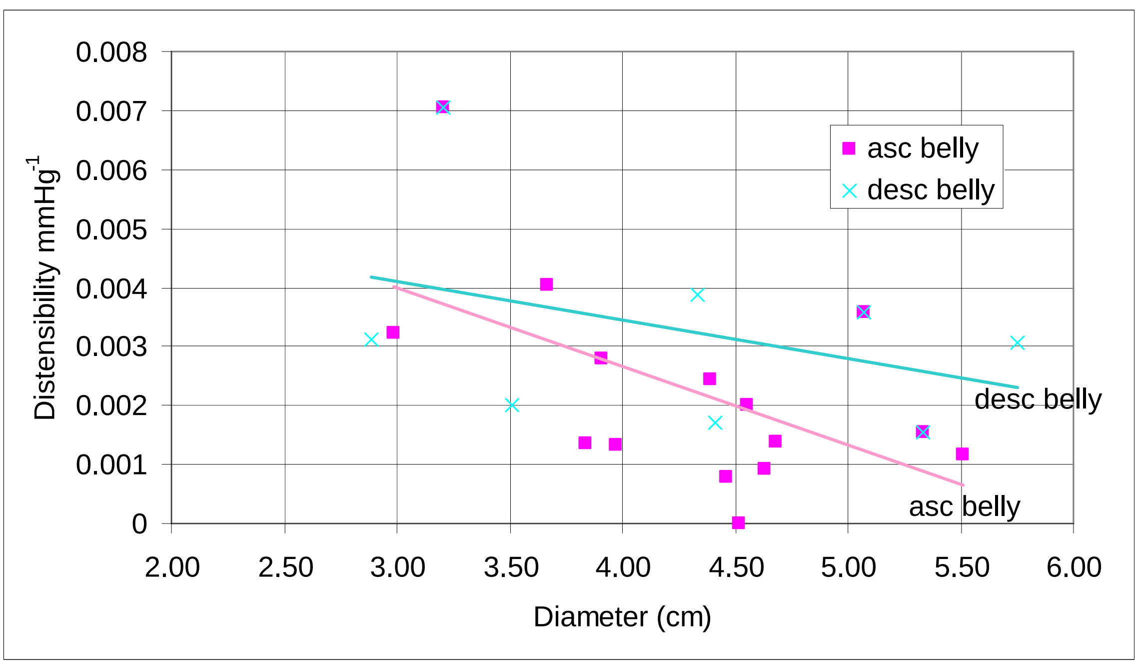

Figure B2. Relationship between distensibility and diameter of the belly of ascending and descending aortic aneurysms. Desc = descending aortic aneurysm. Asc = ascending aortic aneurysm.

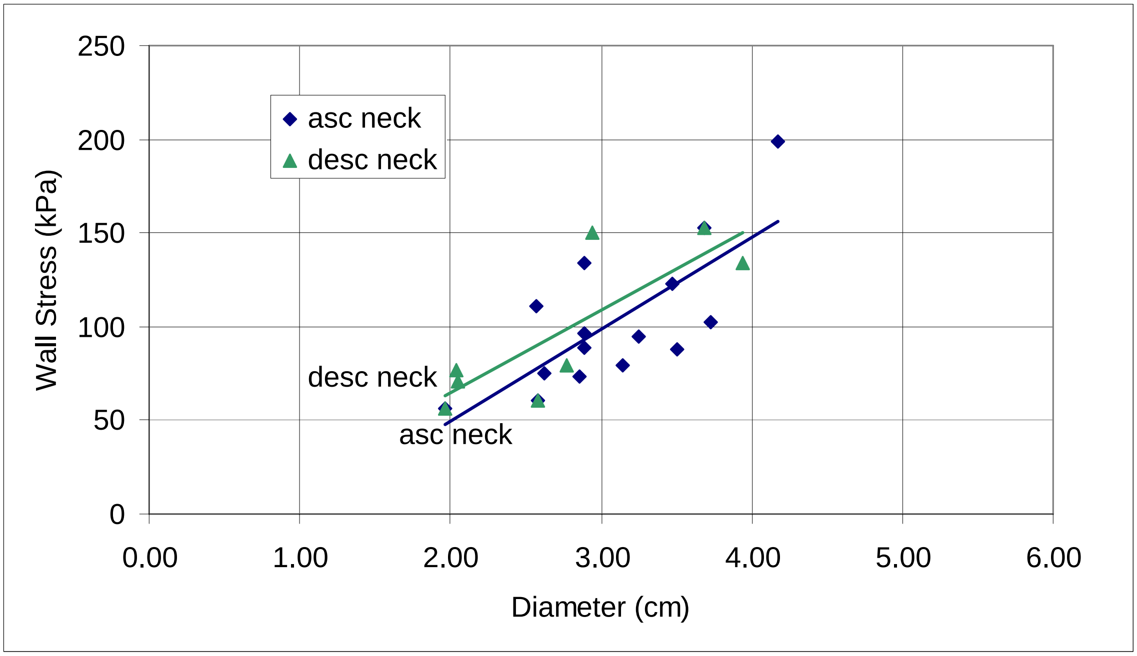

Figure B3. Relationship between wall stress and diameter of the neck of ascending and descending aortic aneurysms. Desc = descending aortic aneurysm. Asc = ascending aortic aneurysm.

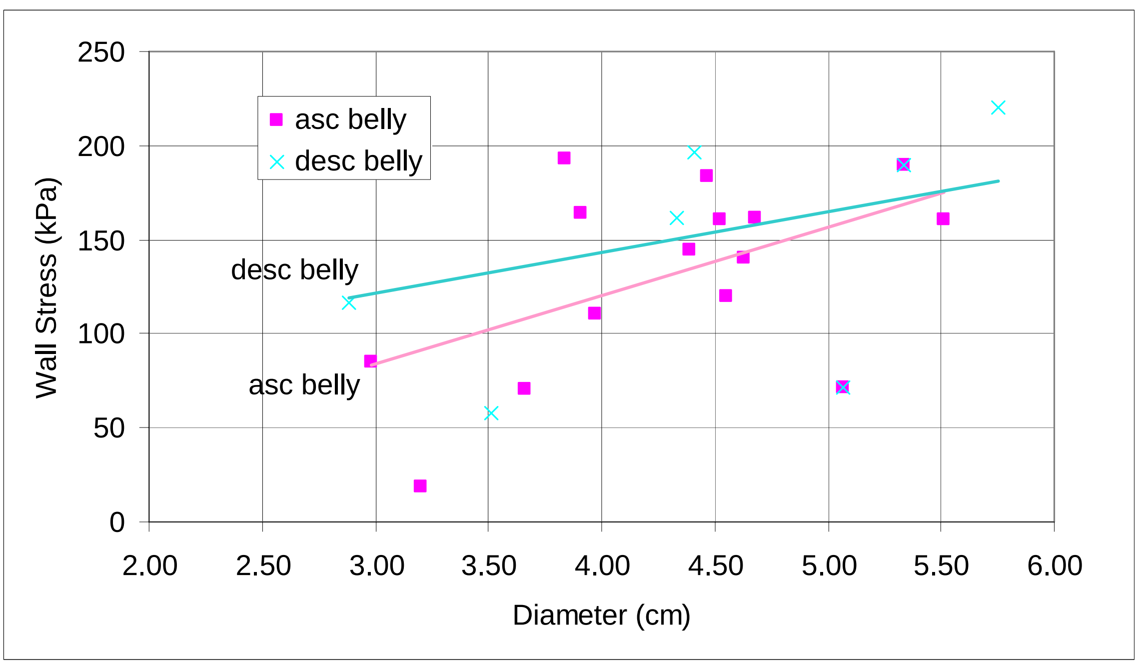

Figure B4. Relationship between wall stress and diameter of the belly of ascending and descending aortic aneurysms. Desc = descending aortic aneurysm. Asc = ascending aortic aneurysm.

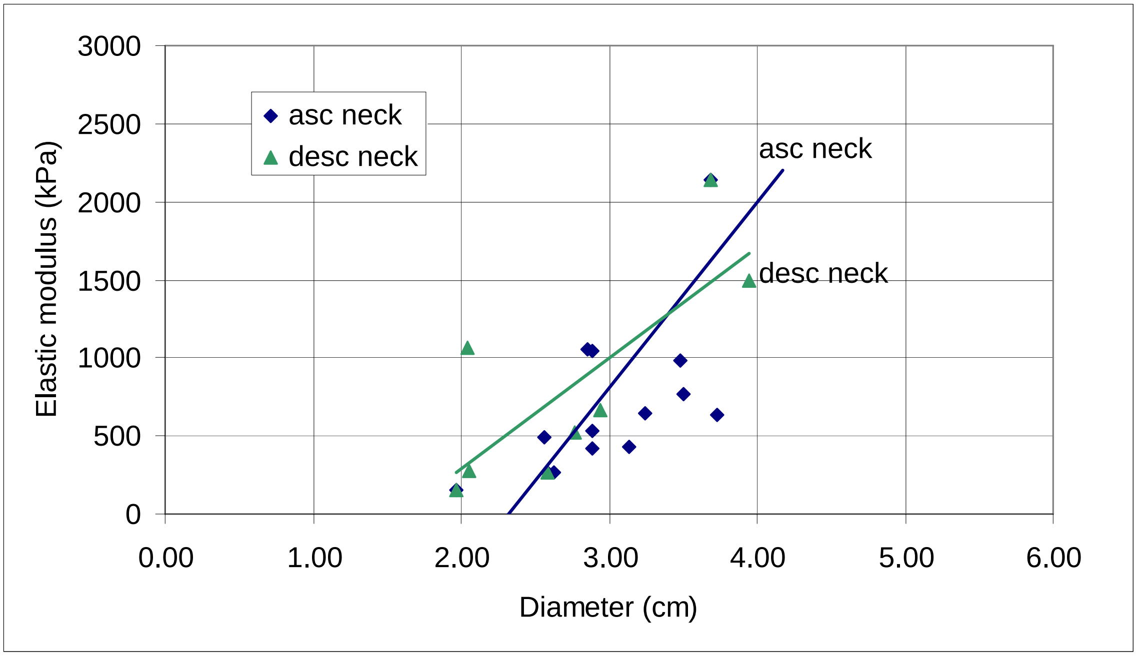

Figure B5. Relationship between elastic modulus and diameter of the neck of ascending and descending aortic aneurysms. Desc = descending aortic aneurysm. Asc = ascending aortic aneurysm.

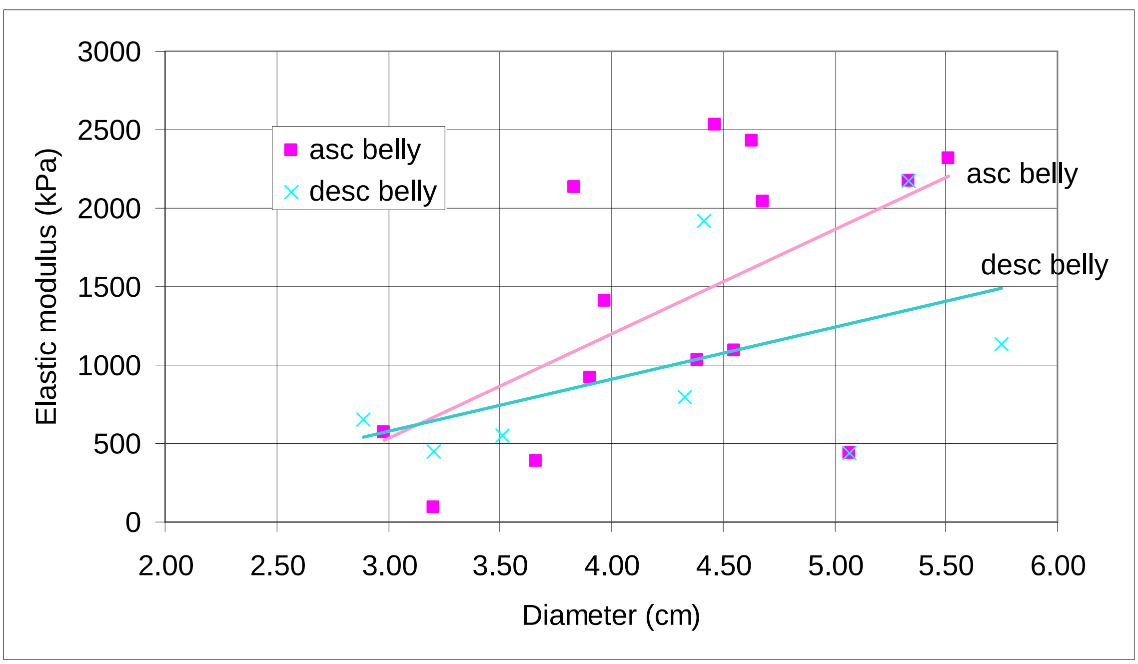

Figure B6. Relationship between elastic modulus and diameter of the belly of ascending and descending aortic aneurysms. Desc = descending aortic aneurysm. Asc = ascending aortic aneurysm.

APPENDIX C

Control Data on Normal Descending Aortas

We were unable to obtain control data before the submission deadline for this thesis due to unavoidable delays with the Human Investigations Committee re-approval process. This study has been recently re-approved, and the comparison between descending aortic aneurysms and normal aortas will be presented in a future paper.