Morphometric Analysis of Elastic Matrix Structural Changes in Abdominal Aortic Aneurysm (AAA) Patients with Large Aneurysms

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ABSTRACT
Abdominal aortic aneurysms (AAAs) pose a significant health threat due to the risk of fatal rupture, primarily driven by the gradual expansion of the abdominal aorta. The pathogenesis involves the breakdown of elastin, a crucial extracellular matrix protein, attributed to the upregulation of matrix metalloproteinases (MMPs) and compensatory collagen synthesis. Despite current medical and surgical interventions, the disease progresses. This study focuses on advancing morphometric analysis through previous studies by quantifying critical collagen parameters such as diameter, perimeter length, and tortuosity alongside parameters such as elastin, laminin, and fibronectin in AAA samples from patients undergoing surgical repair. Utilizing a computer-based morphometry technique, AAA tissue samples were analyzed. The morphometric parameters were computed to access variations associated with demographies such as gender, smoking history, thrombus presence, atherosclerosis, diabetes, and chronic kidney disease. Notably, 81% of the tissue samples were from male patients aged between 55 and 85 years, revealing differences in various parameters, particularly in 82% of males with aortic dissection. These findings suggest potential benefits on elastin, emphasizing the need for further exploration. In conclusion, this research contributes crucial data for understanding tissue analysis in the context of AAA, laying groundwork for regenerative approaches in aortic injury. Ultimately, with the future direction of creating a database to predict when patients would need to undergo surgery with the data collected.

INTRODUCTION
- AAA: Localized, rupture prone expansions of abdominal aorta
- Caused due to chronic proteolytic activity owing to the increase in proteolytic enzyme called MMPs
- Proteolysis breaks down elastic matrix that provides vessel stretch and recoil
- Adult vascular cells are not able to regenerate elastin naturally
- Goal: To develop strategies for in situ regenerative repair of elastin
- What is the need? A quantitative method of elastin fiber morphometry assesses this which gives information about the status and function of elastin in AAAs and its correlation to morphological and physiological aspects of AAAs.
- This would also enable prediction of elastic fiber fate and AAA rupture risk besides identifying targeted outcomes of regenerative therapies.
- This study employs a computer-based morphometric technique developed in our lab to quantify the critical parameters of elastic fibers in the tissue sample collected from AAA patients undergoing surgical repair.
- Specific Aim: To compare the critical morphometric parameters of elastic fibers like area, aspect ratio, maximum diameter, maximum diameter, perimeter length and tortuosity of different demographic criteria of the patients including age, sex, presence/absence of other conditions like atherosclerosis.

METHODS
- The aorta tissue was donated by the patients undergoing open AAA repair surgery at the Heart and Vascular Institute of Cleveland Clinic.
- Patient’s demographic criteria was extracted using the Red Cap database.
- For morphometric analysis, the tissue was washed with PBS as received. 1/3 of the tissue was fixed overnight in 4% PFA at 4°C.
- Next, the tissue was paraffin embedded and sectioned as 6 μm microsections per slide and one slide per subject.
- The sections were then stained with modified Hart Stain. (1 volume of Wieger’s iron resorcin fuchsin and 9 volumes of 1% hydrochloric acid in 70% ethanol)
- The sections were scanned using a whole slide scanner and morphometry was done using Image Pro software.

RESULTS

- Demographics data suggests that male patients are definitely more vulnerable to develop AAAs than females and smoking is a major contributing factor for the development of AAA pathology because a total of 84% of patients have smoking history either present or past.
- Atherosclerosis in 88% patients is in agreement with literature describing pathophysiological progression of AAA since atherosclerotic plaques blocks the entry of nutrients to the cells leading to cell death, elastin degradation and progression of AAAs.
- Studies show that progression of CKD and AAA is attributed to common matrix metalloproteinases like MMP-2,8,9. Hence, it is more likely that CKD can lead to AAA or vice versa.
- We compared the morphometry data between the patients with and without AD in this work because AAA is followed by AD in many patients because severe aortic bulge increases the risk of a tear in the aortic lining, creating a false lumen and leading to AD3. So we wanted to see these changes in elastic fiber with increasing severity of aneurysm.
- Increased % area of elastin (Fig 4B) suggests more fragmented elastin in the patients with AD. While no difference in mean was seen in other parameters), the data trend shows higher variability of critical parameters like Diameter Max and Perimeter Length suggesting some pathologial changes in the elastic matrix with the presence of AD.

DISCUSSION

- Morphometric analysis comparing AAA patients with and without Aortic Dissection (AD) (Fig 4A) elastin quantity was significantly higher in patients receiving an AD.

FUTURE WORK
- Collect tissue samples from patients at St. Luke’s.
- Analyze future data.
- Create a database that allows the demographics to be inputted and to predict how degraded the elastin is based on our parameters and current data.

REFERENCES

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