Assessment of Computational Histopathology in Thoracic Aortic Aneurysm

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Background and Hypothesis: Thoracic aortic aneurysm (TAA) histopathology includes elastic fiber (EF) abnormalities, mucoid extracellular matrix (MECM) accumulation, and smooth muscle derangement in the aortic medial layer. While semi-quantitative grading of these characteristics is a standard practice, computational characterization of medial layer components may facilitate novel quantitative analyses at higher throughput. We hypothesized that computational results would correlate with results of semi-quantitative grading of aortic histopathology.

Experimental Design: Formalin-fixed, paraffin-embedded human aortic tissue sections were stained with Movat's pentachrome to characterize aortic microstructure. Sections were also immunostained for nitrotyrosine residues to assess oxidative stress. Samples were initially graded semi-quantitatively by two independent blinded readers. Next, computational histopathology software was used a) to quantify the proportions of EF, MECM, and cellular area in the medial layer of pentachrome-stained sections and b) to quantify the distribution and intensity of positive nitrotyrosine staining in immunostained sections. Association between semi-quantitative grading and computed values was tested with ANOVA.

Results: The cohort included 74 participants who underwent prophylactic aortic replacement for TAA and 23 healthy controls. The mean age was 54±17 years. On average, EFs accounted for 49% (range 6-90%) of medial tissue area, whereas MECM accounted for 25% (1-73%). The overall semi-quantitative grade of medial degeneration severity was associated with decrease in EF fraction ($p=0.02$). The grade of EF thinning also strongly correlated with decrease in EF fraction ($p=1 \times 10^{-6}$). Meanwhile, grade for accumulation of MECM was associated with increase in MECM ($p=0.004$). Increased semi-quantitative grading for nitrotyrosine levels was associated with increased nuclear signal optical density ($p=9 \times 10^{-10}$) and greater percentage of cells labeled as strongly positive ($p=8 \times 10^{-10}$).

Conclusion and Potential Impact: We observed significant correlations between computed quantitative values and semi-quantitative grading. This suggests that computational histopathology is a valid method for investigation of human TAA tissues.