**Results**

Idealized aneurysms of 3 representative shape index values (ASI = 2, 4, 6) were generated for 5 diameters (z-score = 6, 8, 10, 12, 14) at three positions along the right coronary artery (RCA) and one position in the left anterior descending (LAD) for a total of 40 cases. Hemodynamic simulation results were isolated over aneurysmal regions to identify the effects of shape, diameter, and position on local hemodynamic conditions.

**Hemodynamic Variations with Shape and Size**

Hemodynamic parameter distributions at the vessel wall have been hypothesized to be an effective way to assess aneurysm hemodynamics. Broadly, we expect similarly shaped aneurysms to give rise to similar hemodynamic behaviors; further, we expect that increases in Z-score correspond to decreases in fluid velocity and the potential for turbulence or recirculation. Indeed, these expectations are reflected qualitatively in distributions of TAWSS over the vessel surface (Figure \_\_\_). We observe that surface hemodynamic patterns vary consistently with respect to increasing Z-score, with overall decrease in TAWSS as the diameter increases. Additionally, for each value of ASI, aneurysms appear to bear similar spatial distributions of TAWSS.

To understand hemodynamic variations with geometric parameters, distributions of hemodynamic parameters are quantified in an aggregate manner, revealing that multiple combinations of aneurysm shape and size can produce similar hemodynamics. First, the average TAWSS over each aneurysm surface is computed and plotted with respect to ASI, stratified by aneurysm Z-score (Figure \_\_\_\_). As shape index increases (i.e. more elongated aneurysms), and as Z-score increases, average TAWSS declines. While in the LAD, the lowest values appear in the longest aneurysms of largest diameter, with relatively steep negative trend overall, average values in the RCA remain relatively similar; the lowest values are observed in aneurysms with ASI = 4.

The fractional aneurysm surface area exposed to TAWSS values less than a critical threshold is another aggregate measure that has been proposed for evaluating CAA hemodynamics and stratifying patient risk [CITATION]. A plot of fractional area exposed to low TAWSS as a function of ASI, again stratified by aneurysm Z-score is given in Figure \_\_\_. We observe that for aneurysms in both the RCA and LAD, the fractional area under 1 dyne/cm2 increases as either of Z-score or ASI increase. Notably, the longest aneurysms of moderate Z-score (ASI = 6, Z-score = 8) produce similar values to shorter aneurysms of largest Z-score (ASI = 2, Z=score = 14). As with average TAWSS, multiple combinations of aneurysm shape and diameter can produce similar hemodynamics.

Residence Time (RT1), the time fluid parcels spend within an aneurysm, can also be used to understand CAA hemodynamics. We observe that RT1 varies consistently with respect to aneurysm shape and diameter (Figure \_\_\_). Increased RT1 relative to the baseline, computed in the original vessel without artificial aneurysms, indicates that all aneurysms regardless of size and shape exhibit fluid accumulation, likely due to recirculation and stagnation. While the small aneurysm diameter (Z-score = 6) produces little variation in RT1 as the aneurysm lengthens, higher values of Z-score tend to also magnify the effects of increasing aneurysm length. As with average TAWSS and fractional TAWSS-exposed area, the relationship between RT1 and aneurysm geometry indicates that multiple combinations of aneurysm shape and size can illicit similar hemodynamic behavior.

**Aneurysm Position and Hemodynamics**

Aneurysms generated in proximal, medial, and distal positions along the RCA enable comparison of hemodynamics as a function of position. Computing time-dependent flow rate into each aneurysm indicates that for each position, flow into the aneurysm is independent of size, but decreases with position along the centerline (Supplemental Figure \_\_\_\_) due to the presence of additional branches diverting blood flow. Despite variation in flow rate, Figure \_\_\_\_ depicts similar levels of TAWSS in aneurysms of the same shape (ASI = 2). Proximal RCA aneurysms exhibit comparatively little variation in average TAWSS as Z-score increases, relative to medial and distal locations. Average TAWSS increases in medial aneurysms relative to proximal and distal positions, though fractional surface area exposed to low TAWSS exhibits little variation with respect to aneurysm geometry.

While average TAWSS and fractional TAWSS-exposed area exhibited inconsistent variation with respect to aneurysm position, RT1 increases consistently with respect to position (Figure \_\_\_). In particular, the largest, most distal aneurysm (Z-score = 14) has significantly increased RT1 relative to all other aneurysms of the same shape. Supp. Fig. \_\_ indicates that flow rates are identical for aneurysms in the same position regardless of diameter; especially given low variation in baseline RT1 with position, inlet flow rate differences fail to explain increased RT1 distally, as well as changes in RT1 with increased aneurysm size. This suggests that increased aneurysm size promotes pronounced recirculation in distal aneurysms relative to proximal or medial positions, enabling greater variation in RT1 with respect to aneurysm diameter.

To further investigate hemodynamic mechanisms underlying the non-linear relationship between average TAWSS and aneurysm position, we investigated average WSS over the cardiac cycle. We observe that in proximal and medial aneurysms of ASI=2 in the RCA, values of average WSS are ranked in decreasing order by Z-score over the cardiac cycle (Fig \_\_\_). However, in aneurysms in the distal RCA, intermediate values of Z-score (8, 10, 12) correspond to consistently increased values of average WSS compared to both low and high values (Z-score = 6, 14) throughout much of the cardiac cycle. This behavior can be understood through visualization of fluid velocity within the aneurysm.

Velocity streamlines through aneurysm cross sections reveal that inflow jet through the aneurysm expansion produces different impingement behaviors against the vessel wall (Figure \_\_\_). Aneurysms of the same position feature similar inflow jet patterns, producing the similar surface distributions of TAWSS as seen in Figure \_\_\_. In proximal and medial cases, increases in Z-score did not significantly alter inflow jet impingement area; however, in the distal cases, increases in Z-score alter the angle of the inflow jet, resulting in differing patterns of recirculation. These changes correspond to the WSS trends observed in Figures \_\_\_, \_\_\_, \_\_\_ and the RT1 trends observed in Figure \_\_\_. Further, these inflow jet patterns explain how average TAWSS can increase in medial aneurysms without altering the fractional surface area exposed to low TAWSS (Figures \_\_\_, \_\_\_).

Examining average TAWSS, fractional TAWSS-exposed area, and RT1 indicates that aneurysm diameter, shape, and position jointly determine aneurysm hemodynamics. Further, we find that aneurysm position influences hemodynamics by influencing inflow jet patterns, suggesting that local vessel curvature may be an effective low-dimensional predictor of hemodynamic behavior.

**Vessel Curvature and Hemodynamics**

**Clinical Predictive Value**

[map clinical data onto plots]

**Discussion**

The importance of accurate risk stratification methods for patients with CAAs secondary to KD is well understood. Indeed, studies over the last several years have shown the AHA’s diameter-based algorithm for initiation of systemic anticoagulation to be insufficient for effectively predicting patient risk. Although these studies have explored the potential for patient-specific simulations to reveal key hemodynamic predictors underlying thrombotic risk, the variability of these predictors with respect to patient anatomy and aneurysm geometry has remained unclear.

Our idealized aneurysm models indicate that Z-score remains a strong predictor of hemodynamic behavior. Within Figures \_\_\_ , we can still see the role of diameter – there are consistent trends in average TAWSS and RT1 with respect to Z-score at each level of ASI. However, Z-score alone is insufficient to determine hemodynamic behavior – shape and position, also, are influential (Fig. \_\_\_\_\_).

Fraction of aneurysm surface area exposed to low TAWSS has been used to construct a decision boundary for KD patient risk classification that is more predictive of thrombosis than aneurysm diameter [CITATION]. Thus, we assess the distribution of TAWSS over the surface as one potential surrogate for hemodynamic behaviors that may underlie thrombosis. Results exemplified by Figure \_\_\_ show aneurysms with constant diameter but with different aspect ratios, or with constant aspect ratio and varying diameter, can furnish substantially different hemodynamic environments. These consistent variations suggest that a combination of shape parameters may be sufficiently predictive of aneurysm hemodynamics, potentially reducing need for computationally expensive 3D simulations.

Additionally, varying both shape and diameter can give rise to similar hemodynamic parameters. This suggests that the effectiveness of TAWSS-thresholded area for patient risk stratification lies in its ability to capture critical hemodynamic features that are not strictly dependent on aneurysm shape or diameter alone. In comparison, averaging TAWSS over the surface of the aneurysm also affords a single-dimensional summary of aneurysm hemodynamics, but struggles to capture both variations in time and sacrifices knowledge of spatial distribution (Figure \_\_\_). Contextualized by the relatively decreased clinical utility of average TAWSS [CITATION], the lossy nature of this aggregate measure suggests insufficiency in representing the hemodynamic features relevant for determining thrombotic risk.

We also investigated changes in RT1 as aneurysm shape, diameter, and position vary. We find that RT1 increases consistently as Z-score, shape index increase, and as position becomes more distal. A relationship between residence time and thrombosis has been hypothesized for both cerebral and coronary aneurysms [CITATION, Sengupta 2014]. Here, however, RT1 increases intuitively with both aneurysm length and diameter. Given relatively well-developed inlet jets as illustrated in Fig \_\_ that may be unrealistic in true patient anatomies, it is difficult to determine whether these trends are a characteristic of the RT1 parameter, or whether geometric similarity between all smooth, symmetric idealized aneurysms in this study inhibits analysis of RT1’s ability to quantify nuanced hemodynamics.

Although we have systematically investigated the role of shape parameters on aggregate measures of aneurysm hemodynamics, further work should continue to investigate the potential for low-dimensional representations of aneurysm geometry towards predicting CAA hemodynamics as a surrogate for improving clinical predictive value. Known correlations between aneurysm hemodynamic and geometric features suggest potential to link clinical measurements easily obtained from echocardiography or other routine imaging modalities with patient outcome. Such approaches may form the basis for more sophisticated geometry-based risk stratification methods supporting clinical decision- making in assessment of KD patients.

Further, we demonstrate the potential for modification of patient-specific vascular models and artificial aneurysm generation for systematic evaluation of the relationship between anatomy and hemodynamics. Extending the methodlogy in [CITATION], we first illustrate that controlled variation in aneurysm shape, diameter, and position may produce predictable variation in hemodynamic parameters. Indeed, assumptions such as axisymmetric aneurysm radius, high degree of surface smoothness, and single aneurysm per vessel limit degree of clinical realism. However, manipulating key parameters such as length, diameter, and position were sufficient to enable systematic variation of aneurysm hemodynamics. We demonstrate that systematic evaluations enable closer interrogation of inconsistent variations in hemodynamic parameters, highlighting vessel curvature as an additional geometric parameter influencing hemodynamics (Fig \_\_\_).

The effects of aneurysm shape, diameter, and position were systematically investigated through the use of artificial aneurysms produced in the same baseline coronary tree.

Our systematic studies of relationship between aneurysm shape, diameter, and position and aneurysm hemodynamics confirms that diameter alone is insufficient in predicting aneurysm hemodynamics – shape and position are also key factors. Indeed, systematic variation in shape and diameter indicate that multiple combinations of aneurysm shape and diameter can illicit similar average TAWSS and fractional low TAWSS-exposed area values. Previous work also showed that these aggregate measures of aneurysm hemodynamics serve as promising mechanisms for stratification of patient thrombotic risk [CITATIONS]. Given that aneurysms of varying shape and diameter combinations can produce similar hemodynamics, then,

Previous work has shown that average TAWSS and fractional low TAWSS-exposed area cutoffs served as promising mechanisms for stratification of patient thrombotic risk [CITATIONS]. determining that multiple combinations of aneurysm shape and diameter could illicit similar average TAWSS and fractional low TAWSS-exposed area values, we

These temporal variations in average WSS are difficult to identify through aggregate functions of TAWSS alone.

Plotting aggregate hemodynamic parameters with respect to volume shows a strong linear relationship.

Discussion

Given potential clinical significance of consistently low shear in relation to flow stagnation and thrombosis,