Computational Flow Dynamics Analysis of Pelvic and Abdominal Veins Using CT, Venography, and Duplex Imaging

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Abstract

Using modeling and computational flow dynamics, a methodology has been formulated which could potentially be used to assess the risk of re-thrombosis in DVT patients. Using patient imaging data in the form of computational tomography (CT), Venography, and Duplex Imaging in conjunction with computational flow dynamics (CFD), the relationship was investigated between blood flow properties and the likelihood of stent stenosis. By constructing a 3D model of patient venous anatomy and performing CFD analysis, pressure, wall shear force, velocity, and flow data were obtained on individual veins to perform a comparative study of patients who developed thrombus following stent placement and patients who did not. Comparing patient imaging data through modeling helped to determine which blood flow parameters were significant to rethrombosis. A number of statistical tests were performed on the velocity, pressure and shear stress outputs from the CFD models, and found both pressure and velocity data to be markedly varied between patients who would develop stenosis and those who would not. Additionally, the areas of greatest curvature were identified along the iliac vein, and significant differences were found between the blood flow on the interior and exterior portions of the vein. These methods can be applied to larger patient data sets in the future, hopefully providing insight towards the optimal course of treatment for DVT patients.

Keywords: deep vein thrombosis, computational flow dynamics, computational modeling, re-thrombosis

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Introduction

Deep vein thrombosis (DVT) is a serious medical condition, which if left untreated can result in severe pain, clinical complication, and in some cases, death. DVT, though preventable and treatable if diagnosed early, can be challenging to address. Treatment methods include anticoagulants as well as venous stenting procedures in chronic DVT patients. Clinical estimates of re-thrombosis of stents is between 10-20% for the 6-12 month period following placements [1]. The anatomical features and blood flow parameters which contribute most to re-thrombosis, or stenosis, are not yet clear. In the Iliac vein specifically, which is responsible for draining a large portion of blood from the leg and pelvic region, stenosis has been observed to form preferentially on the interior (or lesser) portion of the curved section of the vein. Thus, degree of curvature has been noted to be a potentially influential feature when assessing likelihood of stenosis. To better understand this phenomenon and improve the prognosis of stenting procedures, a deeper understanding of the factors which contribute to rethrombosis are needed. Computational modeling methods, such as computational flow dynamics, CFD, can be used to analyze patient imaging data and examine blood flow in more detail.

CFD has a wide array of usages in mechanical and fluidics engineering, and can be a powerful tool for clinical research. By collecting routine imaging scans, such as CT, image annotating tools can be used to reconstruct the pelvic venous anatomy as a 3D model. CFD has been used in recent years for modeling of individual patient venous and arterial anatomy, and is being explored as a method of aiding interventional treatment. Models can be derived using patient-specific parameters, and have the benefit of allowing many simulated tests without further patient involvement. The methods used to simulate specific tissues have been improving as many models have included the non-uniform properties of various tissues as well as the unique viscoelastic behaviors exhibited in the body. Modeling opens opportunities in clinical spaces to study phenomena which may have previously required extensive and invasive procedures.

To assess the risk of developing stenosis, biochemical factors from hematological profiles have been used, however the anatomy and blood flow of the venous anatomy has not been explored extensively. While many physiological factors and behaviors likely influence risk of developing thrombus, examining the relationship between blood flow and stenosis may provide a more precise and focused method of assessing risk. While the relationship between the physiological and mechanical characteristics of veins and the development of DVT has been explored through CFD, this research aims to expand on the specific blood flow properties which may be most influential when characterizing risk [2]. The methods used also aim to address the influence of curvature on blood flow properties and risk.

Materials and Methods

Preparation of 3D Model for CFD Analysis

To construct 3D models of the stented portions within patient veins, imaging data in the form of CT was primarily used. The CT data was able to be viewed in an image analysis software called 3DSlicer, which is used to visualize and annotate clinical data. Using a slice-by-slice method, the stented region of the iliac vein was hand selected, using a fine point paint tool, to ensure likeness to the patient anatomy as seen in Figure 1A. The vein could then be viewed as a 3D volume, and edited to correct any selection errors, as seen in Figure 1B. The 3D model constructed in Slicer was then exported as an OBJ file for further processing in Autodesk Maya. Maya was used to edit the initial volume by removing the inlets and outlets, which was necessary to perform CFD. The ends of the vein were flattened by first retopologizing the mess to generate polygonal regions that were able to be selected and removed from the end surface of the vein. Once these sections had been removed the hole present at the end of the vein was filled with a level plane, which can be seen in Figure 1C. Using the multi-cut tool in Maya, both the inlet and outlet of the vein were selected within the mesh and removed from the volume. The edited volume was then exported from Maya as an STL file and loaded into ICEM CFD for meshing. The faces of the model had to be manually selected and defined from the generated mesh.

ICEM CFD was used to define the segments of the volume which would represent the inlet, outlet, and wall of the vein when performing CFD. Segments were selected and renamed as the appropriate faces of the vein. Curves were generated around both the inlet and outlet of the vein and the fluid body was defined within the volume. An example of a bounded and region specified mesh model can be seen in Figure 1D.

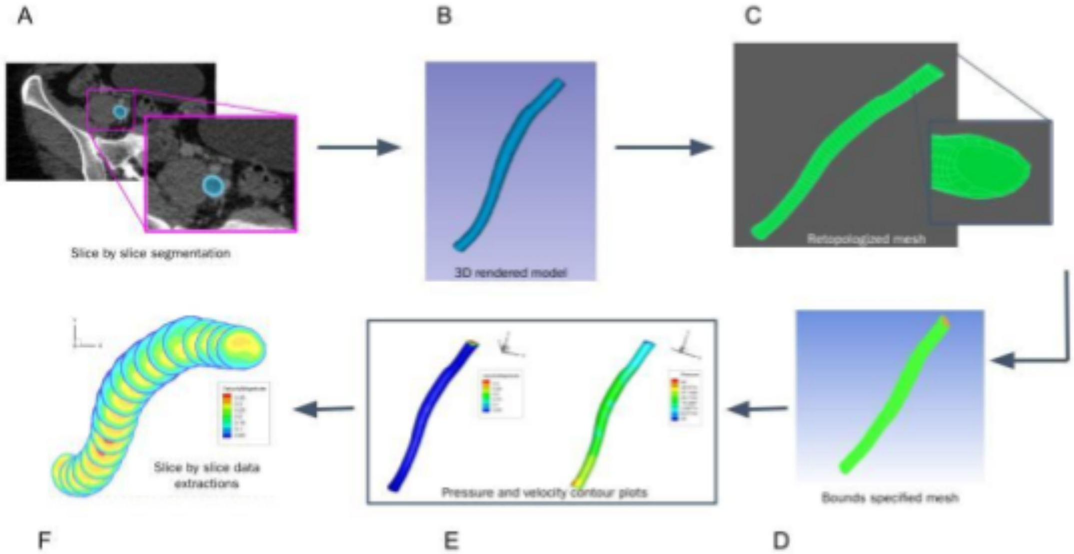

Figure 1. Pipeline for Model Generation, CFD, and Data Analysis.
(A) Slice by slice segmentation of each z-axis slice. (B) 3D rendered model, viewed as a volume in 3D space. (C) Mesh prepared for Autodesk Maya with flattened ends. (D) Bounded and region specified mesh. (E) Output contour plots for velocity and pressure. (F) Slice by slice data extraction, showing all slices of the vein.

Curvature Calculation

The curvature of each vein was calculated by first identifying the coordinates (x,y,z) of the centerpoint in each slice of the vein, from inlet to outlet. The matrix generated by this data was then imported into MATLAB and used in a custom function curvature.m, which was provided by our advising team. The function provided output vectors for three variables: cumulative arc length (C), radius of curvature (R), and curvature vector (k). The local or scalar curvature was then determined to be 1/R.

Data Visualization

Data visualization was performed in TecPlot 360º. The solution data was exported from ANSYS Fluent after the simulation was complete as a .cgns file. Contour plots for each of the three parameters being studied (velocity, pressure and wall shear stress) were generated using a small rainbow color scale, which can be seen in Figure 1E. Data analysis was performed on each slice by extracting the data from various z axes for each of the three parameters, which can be seen in Figure 1F. A probe tool was used to determine the exact values for the data at specific points throughout the slices.

Limitations and Assumptions

The accuracy of the model depends heavily on the assumptions made. The stented vein was assumed to be rigid because it was unknown which stent brands and types were used which might affect the mechanical properties of each patient's stent. A fixed velocity input was used in the CFD at the inlet of the vein based on measurements taken by duplex ultrasound at the femoral head at the end of the stenting procedure. The fixed inlet velocity was required as the blood velocity profile changes throughout the cardiac cycle so an average of the patient's intravascular blood velocity was used [3]. Additionally, it was assumed that there was constant blood viscosity and density. The values used for viscosity and density were 0.00278 kg/m*s and 1060 kg/m^3 based on the literature, respectively [4], [5]. Finally,a K-omega turbulence model was used in the CFD to mimic the normal flow of blood through the cardiovascular system. These four main assumptions impose limits on the validity of the model. Compounding errors of these can lead to a model that is not representative of what is happening physiologically in the iliac vein.

Results

CFD Model Output – In Stent Re-Thrombosis

The first group of patients studied were those that developed thrombus inside the stented region, detected in a follow-up CT scan. Immediately after an angioplasty stenting procedure had been performed a preliminary CT scan was performed in order to confirm appropriate flow inside the stent as well as to confirm the lack of thrombus inside the stent. Ideally, the flow inside the stented region in the preliminary scan should represent normal physiological venous flow, as the vein is no longer occluded. In order to understand which factors most contribute to the development of thrombosis, three parameters were analyzed, venous velocity, pressure, and wall shear stress. By extracting data from each slice of the vein, trends for each of the three parameters can be seen in Figure 2 below. From the inlet at slice 1 to the outlet at slide 20, there is a linear decrease in the maximum velocity and venous pressure. In addition, the maximum wall shear stress remains constant and very minimal from inlet to outlet.

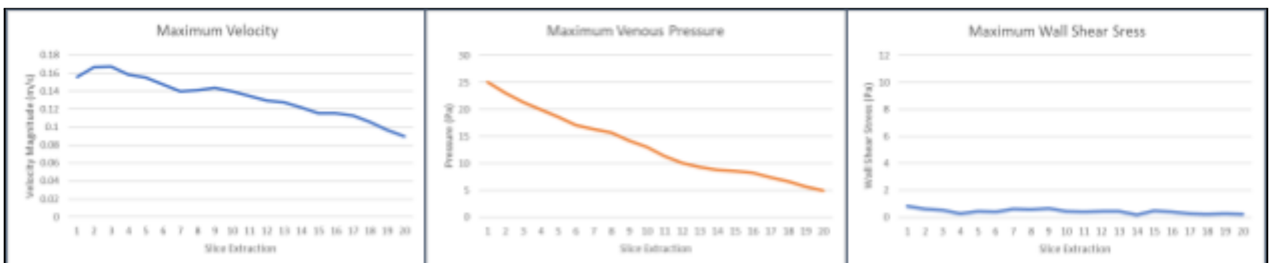

Figure 2. Flow Dynamics After Stenting. Output graphs for maximum velocity, pressure, and wall shear stress through each slide of the vein in a preliminary scan of the patient group that developed re-thrombosis.

In a routine follow-up CT scan, the patient had developed thrombus inside the stented region, so the impact of this occlusion on the flow dynamics was analyzed. The same three parameters were studied and the results for maximum velocity, pressure and wall shear stress can be seen in Figure 3. As shown by the clear irregularities in each of the three parameters, this suggests that the stent is fully or partially occluded by slice 13.

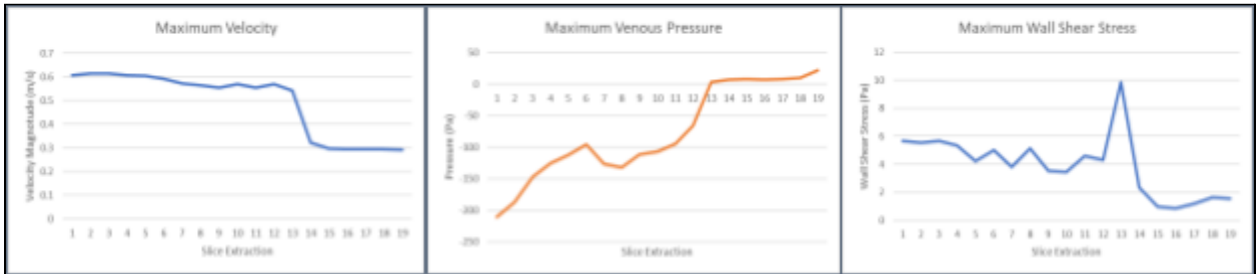

Figure 3. Flow Dynamics at Follow-up Scan with Thrombosis. Output graphs for maximum velocity, pressure, and wall shear stress through each slide of the vein in a follow-up CT scan of the patient group that developed re-thrombosis.

In order to determine if one or more of the parameters being studied could be used as a predictive measure of thrombus formation inside of the stented region, comparisons between these data sets from the preliminary scan to follow-up CT scan were made. Using a paired t-test with a significance level of 0.05, it was found that there is a significant difference in the maximum velocity magnitude between the preliminary and follow-up CT scan with thrombus formation. Specifically, the velocity magnitude found from the follow-up scan was much greater in magnitude and nonlinear compared to the preliminary scan where the velocity was linearly decreasing. The comparison between these two data sets can be seen in Figure 4.

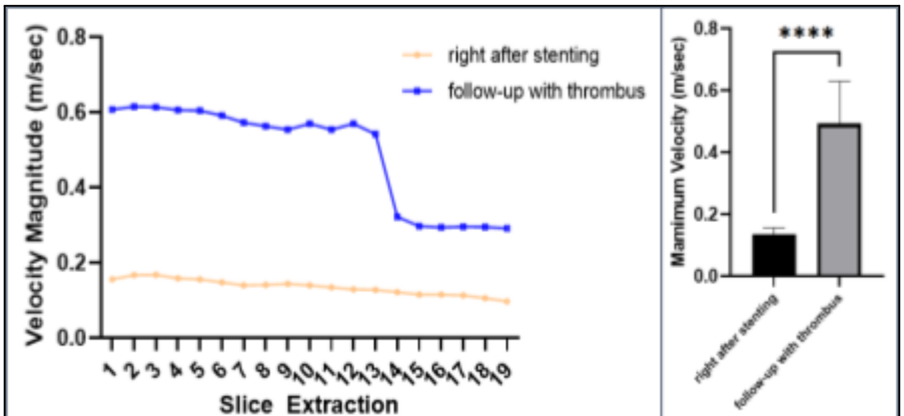

Figure 4. Comparison of Maximum Velocity between Preliminary and Follow-up Scans with Thrombosis. Comparison in maximum velocity magnitude between the preliminary and follow-up CT scans. Data was compared using a paired t-test with a significance level of 0.05.

In comparing the maximum pressure magnitude through each slice of the vein, there was a statistically significant difference between the preliminary and follow-up CT scans. As shown in Figure 5, the maximum pressure found in the follow-up scan is much lesser in magnitude and nonlinear.

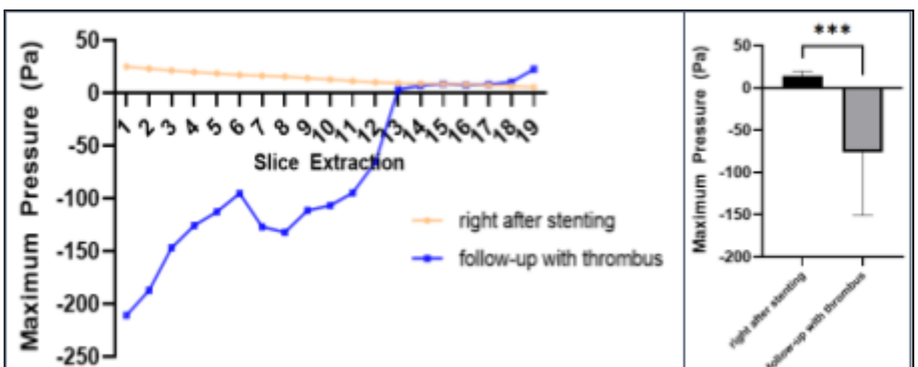

Figure 5. Comparison of Maximum Pressure between Preliminary and Follow-up Scans with Thombosis. Comparison in maximum pressure magnitude between the preliminary and follow-up CT scans. Data was compared using a paired t-test with a significance level of 0.05.

Finally, when the maximum wall shear stress was compared between the preliminary and follow-up CT scans, it was found that there is a significant difference between the two data sets, with the magnitude of the follow-up being greater in magnitude and nonlinear. The sharp spike in wall shear stress suggests that the stented region is fully occluded by that point, adding additional stress to the wall of the vein.

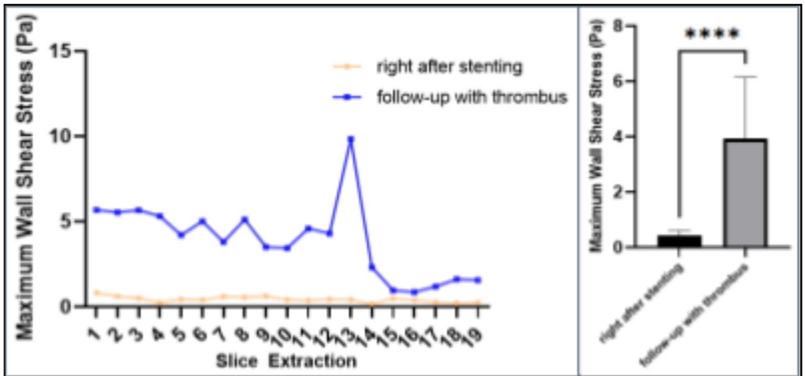

Figure 6. Comparison of Maximum Wall Shear Stress between Preliminary and Follow-up Scans with Thrombosis. Comparison in maximum wall shear stress magnitude between the preliminary and follow-up CT scans. Data was compared using a paired t-test with a significance level of 0.05.

CFD Model Output – Lack of In Stent Re-Thrombosis

The second group of patients analyzed were those that did not develop thrombus inside of the stented region after some follow-up time, as detected by a CT scan. The same three parameters were analyzed, velocity magnitude, pressure magnitude, and maximum wall shear stress. As can be seen in Figure 7, the maximum velocity remains relatively constant from inlet to outlet as does the maximum wall shear stress, and a steady decrease in venous pressure was observed in this case.

Figure 7. Flow Dynamics at Follow-up Scan without Thrombosis. Output graphs for maximum velocity, pressure, and wall shear stress through each slide of the vein in a follow-up CT scan of the patient group that did NOT develop re-thrombosis.

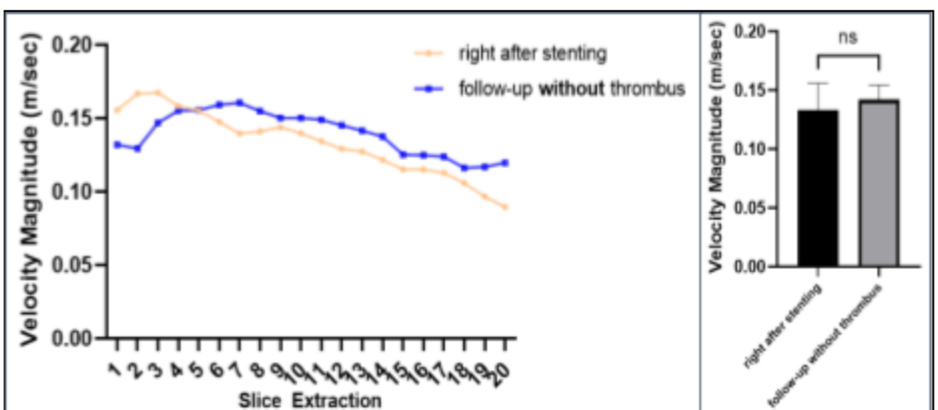

Figure 8. Comparison of Maximum Velocity between Preliminary and Follow-up Scans without Thrombosis. Comparison in maximum velocity magnitude between the preliminary and follow-up CT scan without thrombus formation. Data was compared using an unpaired t-test with a significance level of 0.05.

Given that it would be expected that the flow dynamics of this case to be most similar to those found in the preliminary scan from the patient that did develop thrombus, comparisons were made between this follow-up CT scan without thrombus formation to the preliminary scan from a patient that did develop thrombus. In comparing the maximum velocity between the two scans, using an unpaired t-test with a significance level of 0.05, there was no significant difference found between the two data sets. This comparison can be seen in Figure 8.

When comparing the maximum pressure through each slice from the inlet to outlet, it was determined that there was a significant difference between the two data sets, although the trends seen in each data set are consistent, with a steady decrease in pressure. The comparison between the maximum pressure between preliminary and follow-up scans can be seen in Figure 9.

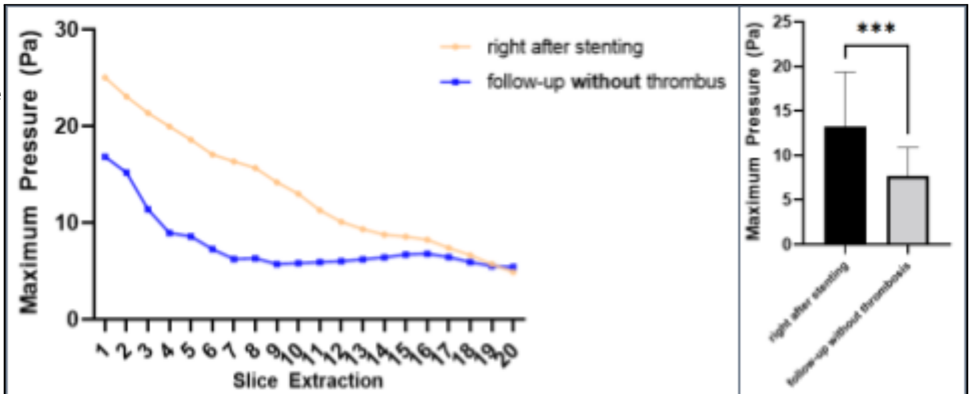

Figure 9. Comparison of Maximum Pressure between Preliminary and Follow-up Scans without Thrombosis. Comparison in maximum pressure magnitude between the preliminary and follow-up CT scan without thrombus formation. Data was compared using an unpaired t-test with a significance level of 0.05.

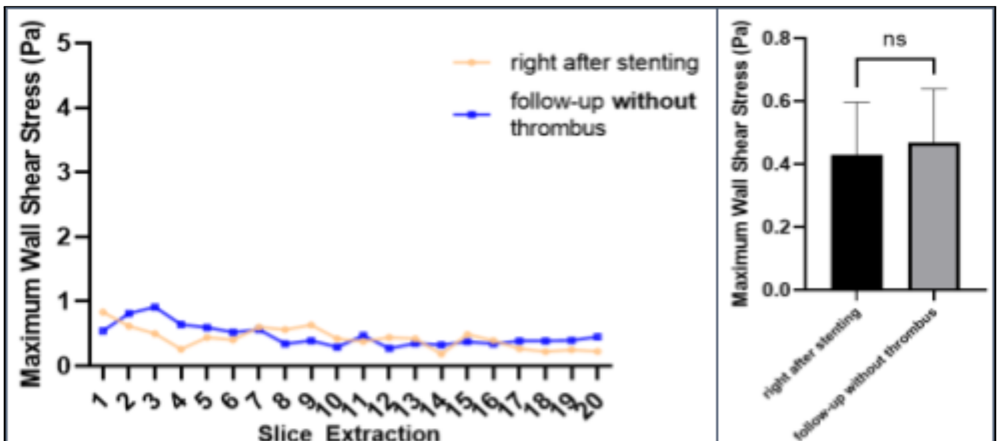

Figure 10. Comparison of Maximum Wall Shear Stress between Preliminary and Follow-up Scans without Thrombosis. Comparison in maximum wall shear stress between the preliminary and follow-up CT scan without thrombus formation. Data was compared using an unpaired t-test with a significance level of 0.05.

Finally, when comparing the maximum wall shear stress between these two data sets, it was observed that there was a nonsignificant difference, as the wall shear stress from both cases was constant and close to zero, as expected. This comparison can be seen in Figure 10.

Curvature Analysis

The original hypothesis for this project was that the development of thrombus inside the stented region was either attributed to changes in one of the three parameters studied, or that it could be attributed to some feature of the venous anatomy. Specifically, it was hypothesized that the thrombus was more likely to occur on the interior or lesser curve as opposed to the greater curve, in the region of greatest curvature. An image that shows the difference between the interior and exterior regions of the curve can be seen in Figure 11.

By identifying the center point of each slice and using a MATLAB function to calculate the local curvature for each vein, the region of greatest curvature was identified. The region of greatest curvature for each of the three cases previously studied, a preliminary and follow-up scan for a patient that did develop thrombus as well as a follow-up scan from a patient that did not develop thrombus, can be seen below in Figure 12. The region of greatest curvature is identified on the graph by the slices in between the black vertical lines and then can be seen on the physical model by the black rings around the 3D model.

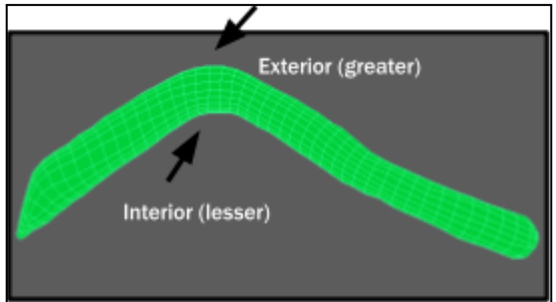

Figure 11. Interior vs Exterior Curve Explanation. Image that shows the regions of the interior and exterior curves.

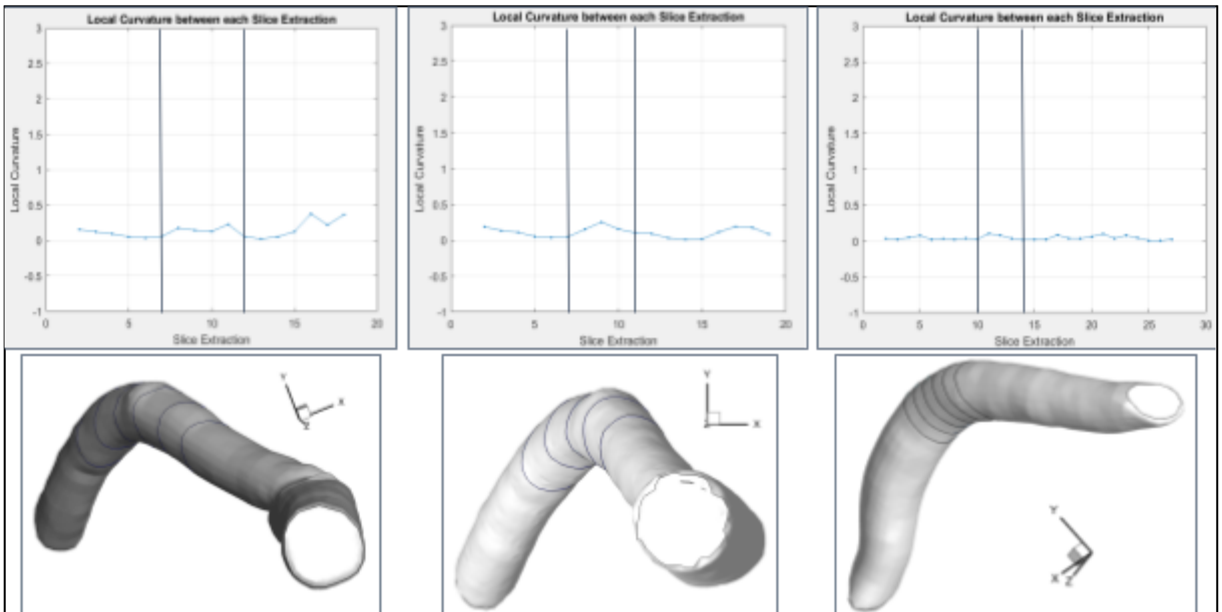

Figure 12. Local Curvature Calculation and Identification. Output graphs for local curvature between each slice of the segmented vein. The region of greatest curvature can be identified by the black, vertical lines on the graph as well as in the 3D model but the concentric black rings in the curve.

In order to determine if the tendency of thrombus to occur on the lesser curve of the vein was in fact accurate, each slice within the region of greatest curvature was analyzed by extracting values for maximum velocity and pressure on the interior and exterior region of the curve. When analyzing the maximum velocity on the interior and exterior regions of the curve from data taken directly after stenting, a significant difference was observed between these two regions, where the velocity on the exterior was greater in magnitude. Given that the group knew this patient would develop thrombosis inside of the stented region in a follow-up, the velocity magnitude on the interior of the curve was expected to be less, which was observed. In addition, the same phenomena were observed for the maximum pressure through the vein, where the pressure was found to be greater on the exterior curve as opposed to the interior. The curvature analysis for data collected directly after angioplasty stenting can be seen in Figure 13.

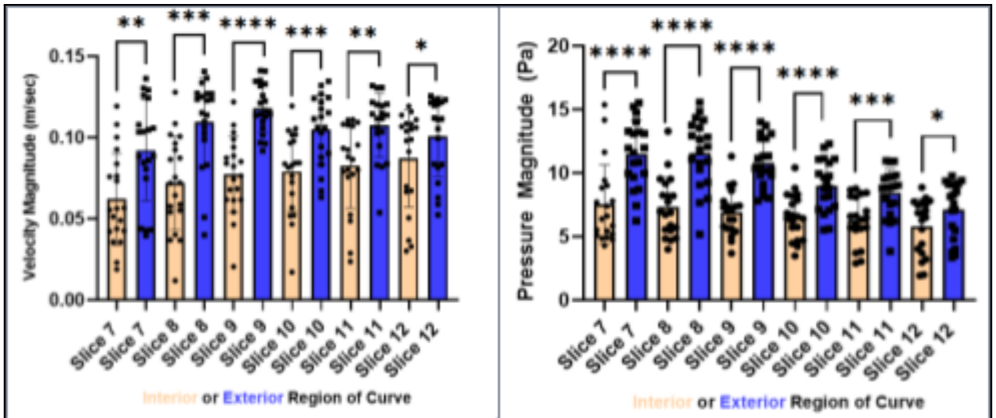

Figure 13. Curvature Analysis after Stenting. Comparisons between the interior and exterior curve of the vein in the region of greatest curvature for both velocity and pressure magnitude. Images were generated from data directly after stenting for a patient who would develop re-thrombus.

The same analysis was performed for the case where thrombus had occurred, as determined by a routine follow-up CT scan. Both significant and nonsignificant differences were observed for the velocity magnitude between the interior and exterior curves. As the suggested region of full occlusion is approached, which occurs at slice 13, the significance is minimal as would be expected because the flow is disrupted and the space for blood to flow through is narrower. In addition, when analyzing the maximum pressure through each slide within the region of greatest curvature, significance differences were observed between the interior and exterior regions, with that significance dwindling as the region of full occlusion approached. The curvature analysis for data collected from a follow-up CT scan after the patient developed re-thrombosis can be seen in Figure 14.

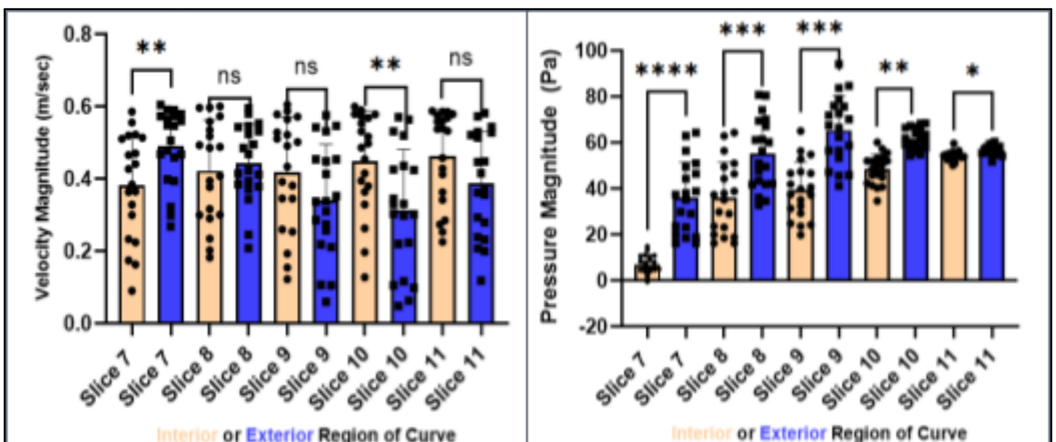

Figure 14. Curvature Analysis at Follow-up With Thrombosis. Comparisons between the interior and exterior curve of the vein in the region of greatest curvature for both velocity and pressure magnitude. Images were generated from data taken from a follow-up CT scan in a patient with re-thrombosis.

The analysis was extended to the case where thrombus did not occur, as determined by a follow-up CT scan. Both significant and nonsignificant differences between the interior and exterior regions of the curve, although the significance was minimal. In addition, extremely statistically significant differences were seen between the pressure magnitude on the interior and exterior curves of the vein. The curvature analysis for data collected from a follow-up scan when the patient had not developed re-thrombosis can be seen in Figure 15.

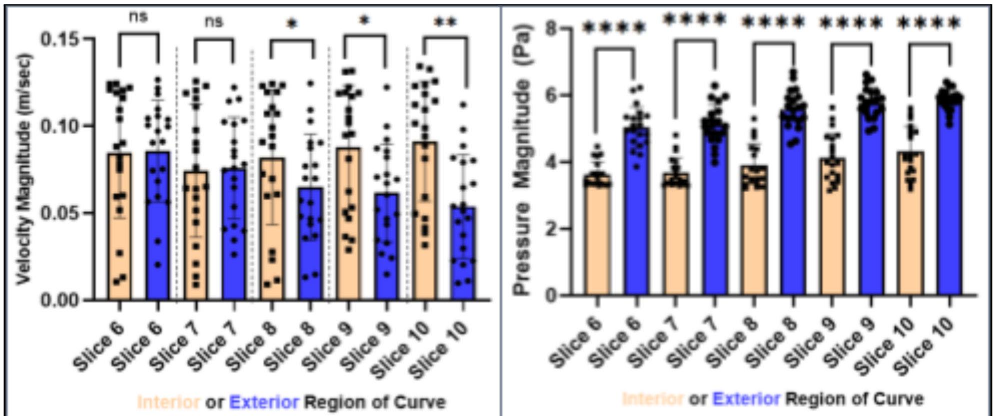

Figure 15. Curvature Analysis at Follow-up Without Thrombosis. Comparisons between the interior and exterior curve of the vein in the region of greatest curvature for both velocity and pressure magnitude. Images were generated from data in a follow-up CT scan from a patient who did not develop re-thrombosis.

Discussion

Interpretation of Results

After analyzing the pressure, velocity, and wall shear stress of patients who developed thrombus and those who did not, as well as performing curvature analysis, the velocity and pressure are likely important indicators of the risk of rethrombosis. It has also been determined that the difference in fluid flow between the interior and exterior portions of the curved region of the Iliac is likely responsible for the preferential thrombus formation on the interior curve. In comparing the pressure and velocity CFD results from case 2 prior to thrombus formation and case B, which did not develop thrombus, there were significant differences observed in the maximum pressure throughout the vein. This indicates that pressure may be a determinant of the blood flow patterns which contribute to thrombus formation. How these differences in maximum pressure are specifically influenced by anatomy is still unclear; however, efforts to regulate maximum venous pressure may be explored for limiting thrombus formation.

The curvature analysis within each slice produced both significant and nonsignificant results; however, in general as the approximate region of occlusion was reached in each vein, the differences in maximum pressure and velocity magnitude were significant in most cases. This indicates that curvature impacts the blood flow patterns experienced throughout the vein. While curvature may not definitively increase risk of thrombosis, it was observed that between the case that did not develop stenosis and the case that did, differences in velocity magnitude were much more significant between the interior an exterior curves in the stented vein which would eventually thrombose. With a larger sample size of cases, additional consistency of these trends displayed would allow for a more full understanding of the impact curvature and blood flow have on thrombus formation.

Future Directions

The methods and analysis performed could be applied to a larger sample of patient data sets to confirm or elaborate on the observations found in our work. Additionally, the complexity of the model could be improved upon to more accurately represent the conditions in which thrombus forms. The thrombus formation itself was not modeled, as it was beyond the scope of the project. Using CFD to model the thrombus formation along with the blood flow could improve the accuracy of the simulation results. Other parameters outside of maximum pressure, velocity magnitude, and wall shear stress will be needed to be computed in future work to fully understand the changes in blood flow throughout stenosis. The mechanical properties of the stented vein itself could be modified to more accurately represent venous tissue which has been reinforced with a stent. Different stent materials could be examined for variations in mechanical behavior which could impact blood flow.

When considering stenosis, there are many biochemical and hormonal signals which impact thrombus formation. While blood flow is significant to thrombosis, the addition of studying the signals which influence the coagulation cascade would create a more complete understanding of the physiological environment in which thrombus forms. Nano-scale engineering could be utilized to deter thrombus formation on the stent itself through various active material coatings.

In addition to the cases which CFD was performed and analyzed on, a number of other patient venous models have been constructed which could be simulated in future work. With a larger pool of cases, the results of CFD could be used to solidify our observations and inform future research efforts. While the methods were largely for exploratory research, the results of a large enough sample size could potentially inform clinical procedure. Stenting placement and stent dimensions could be tailored to individual patient needs, particularly those who are at a high risk, improving the long term prognosis of DVT. Additionally, being able to determine if an individual is at high risk for re-thrombosis could help patients and clinicians prepare for further treatment as well as streamline the usage of diagnostic imaging.

Conclusion

The importance of blood flow in thrombus formation was demonstrated through the computational fluid dynamic model and slice by slice analysis. Statistical analysis was performed to determine the pressure and velocity data to be statistically significant between patients who would develop stenosis and those who would not at a follow-up computed tomography scan. The regions of greatest curvature were identified in the iliac veins and found significant differences between the interior and exterior of the vein for the blood flow. In future work, this method can be applied to a larger number of patients to provide insight on stenting procedures to reduce risk of stenosis.

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