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Intra-aneurysmal high-resolution 4D MRI flow imaging for hemodynamic imaging markers in intracranial aneurysm instability

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ABSTRACT

BACKGROUND AND PURPOSE: Prediction of aneurysm instability is crucial to guide treatment decisions and to select appropriate patients with unruptured intracranial aneurysms (IAs) for preventive treatment. High resolution four-dimensional magnetic resonance (4D MRI) flow imaging and 3D quantification of aneurysm morphology could offer insights and new imaging markers for aneurysm instability. In this cross-sectional study, we aim to identify 4D MRI flow imaging markers for aneurysm instability by relating hemodynamics in the aneurysm sac to 3D morphological proxy parameters for aneurysm instability.

MATERIALS AND METHODS: In 35 patients with 37 unruptured IAs, a 3T MRA and a 7T 4D flow MRI scan was performed. Five hemodynamic parameters - peak-systolic (WSS_{MAX}) and time-averaged wall shear stress (WSS_{MEAN}), oscillatory shear index (OSI), mean velocity, and velocity pulsatility index (vPI) - were correlated to six 3D morphology proxy parameters of aneurysm instability - major axis length, volume, surface area (all three size parameters), flatness, shape index, and curvedness - by Pearson's correlation with 95% confidence intervals (CI). Scatterplots of hemodynamic parameters that correlated with IA size (major axis length) were created.

RESULTS: WSS_{MAX} and WSS_{MEAN} correlated negatively with all three size parameters (strongest for WSS_{MEAN} with volume ($r = -0.70$, 95% CI -0.83 to -0.49)) and OSI positively (strongest with major axis length ($r = 0.87$, 95% CI 0.76 to 0.93)). WSS_{MAX} and WSS_{MEAN} correlated positively with shape index ($r = 0.61$, 95% CI 0.36 to 0.78 and $r = 0.49$, 95% CI 0.20 to 0.70 , respectively) and OSI negatively ($r = -0.82$, 95% CI -0.9 to -0.68). WSS_{MEAN} and mean velocity correlated negatively with flatness ($r = -0.35$, 95% CI -0.61 to -0.029 and $r = -0.33$, 95% CI -0.59 to 0.007 , respectively) and OSI positively ($r = 0.54$, 95% CI 0.26 to 0.74). vPI did not show any statistically significant correlation.

CONCLUSIONS: Out of the five included hemodynamic parameters, WSS_{MAX} , WSS_{MEAN} , and OSI showed the strongest correlation with morphological 3D proxy parameters of aneurysm instability. Future studies should assess these promising new imaging marker parameters for predicting aneurysm instability in longitudinal cohorts of IA patients.

ABBREVIATIONS: IA = intracranial aneurysm; 3D = three dimensional; 4D MRI flow = four-dimensional Magnetic Resonance Imaging flow; TOF-MRA = Time-of-flight Magnetic Resonance Angiography; WSS = wall shear stress; WSS_{MAX} = WSS calculated at peak systole; WSS_{MEAN} = time averaged WSS; OSI = oscillatory shear index; vPI = velocity pulsatility index

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SUMMARY SECTION

PREVIOUS LITERATURE: Studies have shown a correlation of 3D morphological parameters, including size related parameters, as well as flatness, curvedness and shape index with aneurysm instability. Identifying additional imaging markers is crucial for assessing aneurysm instability and optimizing treatment decisions. The current progress in 4D MRI flow imaging enables in vivo detection of hemodynamics, including WSS_{MAX} , WSS_{MEAN} , OSI, mean velocity and vPI in the aneurysm sac itself. To our knowledge, no study identified 7T 4D MRI flow imaging markers for aneurysm instability by relating hemodynamics in the aneurysm sac to the aneurysm 3D morphology proxy parameters for aneurysm instability.

KEY FINDINGS: In our study, WSS_{MAX} showed the strongest correlation with area ($r = -0.69$, 95% -0.83 to -0.47), WSS_{MEAN} showed the strongest correlation with volume ($r = -0.70$, 95% -0.83 to -0.49) and OSI showed the strongest correlation with major axis length ($r = 0.87$, 95% CI 0.76 to 0.93)

KNOWLEDGE ADVANCEMENT: This study is an important first step to a better understanding of hemodynamics in the pathophysiological process of aneurysm instability and demonstrates possible new hemodynamic imaging markers for aneurysm instability.

INTRODUCTION

Unruptured intracranial aneurysms (IA) have a prevalence of approximately 3% in the general adult population.¹ While most aneurysms stay stable during lifetime, rupture leads to subarachnoid hemorrhage with severe consequences, including a 35% case fatality rate and 35% dependency in survivors.² Preventive treatment by endovascular or neurosurgical approaches can prevent subarachnoid hemorrhage but carries a significant risk of complications.³ Therefore, in clinical decision making, the aneurysm rupture risk has to be weighed against the treatment complication risk. Currently, it is difficult to predict IA rupture. While IA size is one of the main predictors of aneurysm instability, a significant portion of ruptured aneurysms is small in size, since small aneurysms by far outnumber larger ones.^{3,4,5} Identifying additional imaging markers beyond size is crucial for assessing aneurysm instability and optimizing treatment decisions.

Since hemodynamics play an important role in the development of aneurysms and aneurysm instability,⁶ high resolution four-dimensional (4D) flow imaging performed on 7T MRI might serve as a possible method to identify aneurysm instability.⁷ The current progress in 4D MRI flow imaging enables in vivo detection of hemodynamics in the aneurysm sac itself. Recent advancements have also enabled three-dimensional (3D) quantification of aneurysm morphology. Studies have shown a correlation of 3D morphological parameters, including major axis length, volume, and surface area (size parameters) as well as flatness, curvedness, and shape index with aneurysm instability. In this way, these morphology parameters can play a role as proxy parameters for aneurysm instability.^{4,5,8,9}

The aim of this study is to identify 4D MRI flow imaging markers for aneurysm instability by relating hemodynamics in the aneurysm sac to the aneurysm 3D morphology proxy parameters for aneurysm instability.

MATERIALS AND METHODS

Study population

This cross-sectional study consisted of a consecutive series of patients undergoing clinical routine follow up imaging for an unruptured and untreated IA in the period between June 2021 and July 2022. All patients met the in- and exclusion criteria of this study. Inclusion criteria were patients over 18 years old with unruptured IAs larger than 4mm. Patients who were pregnant or who had previous treatment for an additional IA were excluded. Clinical care consisted of a 3T MRA TOF follow up scan. As part of this study, an additional 7T 4D MRI flow scan was performed at the University Medical Center Utrecht, The Netherlands. This was on the same day as the 3T MRA TOF scan in patients who gave informed consent for this study and did not have a contraindication for 7T MRI. The local ethics review committee approved the study.

MRI Protocol

The 3T (Philips Healthcare, Best, The Netherlands) MRA scans were performed using a 32-channel head coil. The protocol included a 3D T1-weighted gradient echo time-of-flight (TOF) MRA acquisition with the following scan parameters: FOV 200 (Feet-Head) x 200 (Left-Right) x 80 (Anterior-Posterior) mm³, acquired spatial resolution 0.5 x 0.5 x 0.5 mm³, TR/TE = 22/3.4ms, flip angle = 18° and acquisition duration around 5 minutes. The 7T MRI (Philips Healthcare, Best, The Netherlands) examinations were performed using an 8-channel volume transmit coil in quadrature mode and 32-channel receive coil (Nova Medical, Houston, United States) for the acquisition of 4D flow data. The 4D flow scan was performed using the Amsterdam University Medical Center 'PROspective Undersampling in multiple Dimensions' (PROUD) software patch, which enables a pseudospiral ky/kz-plane acquisition scheme designed for incoherent undersampling with a variable sampling density.¹⁰ A 4D phase-contrast (PC) MRI acquisition was performed with the field-of-view encompassing the IA and its parent vessel. Retrospective gating was performed using a peripheral pulse unit for heartbeat detection. Parameters for the 4D PC MRI scan were as follows: angulated coronal FOV 190 (Feet-Head) x 190 (Right-Left) x 20 (Anterior-Posterior) mm³, acquired and reconstructed resolution of 0.5 x 0.5 x 0.5 mm³, TR/TE = 7.0/2.2, velocity encoding sensitivity 50 cm/s, flip angle 10°, nominal acceleration factor 7, and 12 reconstructed cardiac phases (i.e., reconstructed temporal resolution 83ms for a heart rate of 60 bpm). A previous study¹¹ investigated that WSS increases with more spatial resolution in experimental phantom studies. For this reason, we used the high acquired spatial resolution of 0.5 mm x 0.5 mm x 0.5 mm which is made possible by the under-sampling technique used and more importantly by the surplus of signal from 7 tesla. To improve field homogeneity, vendor-supplied image-based shimming was performed using second-order terms, before acquiring the 4D flow scan. Acquisition duration was 10 minutes. Datasets were reconstructed with the pipeline developed for the PROUD data by Amsterdam University Medical Center, using the BART toolbox.¹² The reconstruction pipeline included phase subtraction and background phase correction in MRecon (Gyrotools, Zurich, Switzerland).

Morphology proxy parameters

In total, six 3D-quantified morphology parameters were derived: major axis length, volume, surface area (size parameters), flatness (axis length ratio), curvedness (local morphology) and shape index. 3D morphologic measurements were performed as described in detail in a previous study and morphology parameters are visualized in this same study.⁵ Shape index is a rotation and translation invariant measure which describes the topology of the UIA surface. The values of the shape index ranges from -1 to 1, which correlates with a concave (or "cup" shape) or convex (or "dome" shape) respectively. For example, a shape index of 0.3 (on a scale between -1 to 1) indicates a more subtle convex shape of the aneurysm in comparison to a shape index of 0.9 which describes a more definite convex shape.⁵ Segmentations of the IAs were made on the 3T TOF-MRAs by manually drawing contours per imaging slice around the IA, using an in-house-developed software implemented in MeVisLab (MeVis Medical Solutions, Bremen, Germany), by an experienced neuroradiologist (I.v.d.S. with 15 years of experience). Following the segmentation, the software employed a marching cubes algorithm to fit a mesh around the IA. This mesh was then used to calculate the aneurysm's volume and surface area. Next, the major, minor, and least axis of the IA were calculated

using principal component analysis. From these principal components, various morphology parameters were calculated according to the Image Biomarker Standardization Initiative (IBSI) guidelines.¹³

Hemodynamic parameters

We quantified five hemodynamic parameters (wall shear stress (WSS)_{MAX}, WSS_{MEAN}, the oscillatory shear index (OSI), mean velocity, and velocity pulsatility index (vPI)) in the aneurysmal sac. The reconstructed 4D flow datasets were analyzed by RvT (with >4 years of 4D flow analysis experience) using CAAS MR Solutions v5.1.2 software (Pie Medical Imaging, Maastricht, The Netherlands) (Figure 1). CAAS automatically generates the centerline and perpendicular slices for the region of interest along the complete circle of Willis from the internal carotid artery towards the smaller cerebral arteries. These perpendicular slices were visually checked and automatically propagated over all time points of the cardiac cycle to create volumetric flow rate traces and velocity traces over the cardiac cycle. The blood flow velocity pulsatility index (vPI = (Velocity_{max}-Velocity_{min})/Velocity_{mean}) was calculated from each velocity trace. The inter- and intra-observer reliability of the analysis with the CAAS software in the CoW has been tested previously with good to very good reproducibility and repeatability (ICC = 0.65–0.96).¹⁴ WSS was calculated using the segmentations performed for the 3D aneurysm morphology quantification, and previously described software in Matlab R2018a, by multiplying the wall shear rate by the dynamic viscosity of blood (3.2 x 10⁻³ Pa·s).¹¹ We performed two types of WSS calculations: WSS calculated at peak systole (WSS_{MAX}) and time-averaged WSS (WSS_{MEAN}), in which the WSS is expressed as the average over the cardiac cycle. The WSS_{MAX} and WSS_{MEAN} were expressed as the spatial mean value (Figure 1). The oscillatory shear index was defined as the fluctuation of WSS over one cardiac cycle. OSI is a non-dimensional parameter and ranges from 0 (no change) to 0.5 (oscillating flow).¹⁵

Sample size calculation

To detect a minimum correlation coefficient value of 0.5, with a desired type II error of 10% and alpha of 0.05, a sample size of 37 aneurysms is sufficient.¹⁶

Statistical analysis

The normality of the data was tested using the Kolmogorov-Smirnov test of normality. We calculated Pearson's correlation coefficient *r* with 95% confidence intervals (CI) to study relationships between the five hemodynamic parameters (WSS_{MAX}, WSS_{MEAN}, OSI, mean velocity and vPI) and the six morphologic proxy parameters (major axis length, volume, surface area, flatness, shape index, and curvedness). Additionally, we visualized the relationship between the hemodynamic parameters that correlated with IA size (major axis length) by creating scatterplots. Statistical analyses were performed in IBM Statistics Package of Social Sciences (SPSS) (Version 25, IBM, Armonk, NY, USA).

RESULTS

Baseline characteristics

In total, 35 patients (10 men, mean age 66 ± 9) with 37 unruptured IAs were scanned. The aneurysms had a mean major axis length ± standard deviation of 7.0 ± 1.7 mm (range 4.4 – 10.3 mm). The most common aneurysm location was the middle cerebral artery (46%), followed by the anterior communicating artery (27%), the internal carotid artery (22%), and the basilar artery (5%). Other baseline patient and IA characteristics (location, morphology, and hemodynamics) are summarized in Table 1. The outcomes of IA morphologic and hemodynamic parameters are given in mean values and standard deviations.

Correlations between hemodynamics and morphology

All hemodynamic and morphological parameters were normally distributed. WSS_{MAX} and WSS_{MEAN} correlated negatively with the three size-related parameters: major axis length (*r* = -0.67, 95% CI -0.82 to -0.44 and *r* = -0.64, 95% CI -0.80 to -0.40, respectively); volume (*r* = -0.67, 95% CI -0.82 to -0.44 and *r* = -0.70, 95% CI -0.83 to -0.49, respectively); and area (*r* = -0.69, 95% CI -0.83 to -0.47 and *r* = -0.67, 95% CI -0.82 to -0.44, respectively). OSI correlated positively with the size-related parameters, including major axis length (*r* = 0.87, 95% CI 0.76 to 0.93), volume (*r* = 0.77, 95% CI 0.59 to 0.88), and area (*r* = 0.76, 95% CI 0.58 to 0.87).

WSS_{MAX} and WSS_{MEAN} correlated positively with shape index (*r* = 0.61, 95% CI 0.36 to 0.78 and *r* = 0.49, 95% CI 0.20 to 0.70, respectively) and OSI correlated negatively with shape index (*r* = -0.82, 95% CI -0.90 to -0.68). OSI correlated positively with flatness (*r* = 0.54, 95% CI 0.26 to 0.74). WSS_{MEAN} correlated negatively with flatness (*r* = -0.35, 95% CI -0.61 to -0.029). No correlations were found between mean velocity or vPI and the morphologic parameters, except for mean velocity, which correlated negatively with flatness (*r* = -0.33, 95% CI -0.59 to -0.007).

Correlation between hemodynamic parameters and morphological 3D proxy parameters of aneurysm instability is shown in Table 2 and is visualized in Figure 2. Scatterplots for the relationships of WSS_{MEAN}, WSS_{MAX} and OSI with aneurysm size are shown in Figure 3.

DISCUSSION

In this study, we demonstrated that the 4D flow hemodynamic parameters WSS_{MAX} , WSS_{MEAN} and OSI showed the strongest correlation with 3D morphological parameters that are proxy-parameters of aneurysm instability, as described in previous literature. No correlations were found between mean velocity or vPI and the morphologic parameters, except for a modest negative correlation of mean velocity correlating with flatness.

A study using 3T 4D flow imaging to correlate aneurysm hemodynamics to IA morphological parameters size and size ratio in 70 unruptured IAs, showed a negative correlation between the WSS_{MEAN} and IA size-related parameters.^{14,17} This is consistent supports with our findings with 7T MRI. In previous literature, both low WSS and high WSS have been associated with aneurysm instability, a paradox that has yet to be clarified.^{6,18} Our findings support the low WSS theory, which states that low WSS pressure along the vessel wall causes damage to endothelial cells and that vascular remodeling occurs due to pro-inflammatory changes, enhancing the development of IAs.¹⁸

One study¹⁹ on morphological and hemodynamic risk factors for aneurysm rupture investigated the morphological and hemodynamic parameters of 23 aneurysms ≥ 7 mm, consisting of 11 unruptured and 12 ruptured aneurysms. This study used 3D rotational angiography and computational fluid dynamics (CFD) to analyze all IAs. The WSS_{MEAN} was found to be lower and the OSI to be higher in ruptured (instable) aneurysms in comparison to the unruptured aneurysms, and therefore, they were regarded as indicators of rupture risk.¹⁹ The findings in this study are in line with our findings that WSS_{MEAN} and OSI are correlated significantly with morphology proxy parameters of IA instability.

Whereas the literature is consistent regarding the size parameters (IA major axis length, volume and area) and shape index in relation to IA instability, the interpretation of flatness remains challenging due to contradictory findings in the literature. One study found that an increase in flatness, measured over time, is associated with aneurysm instability⁵, while another study found low flatness, measured at baseline, to be associated more with instable aneurysms.⁴ In our study WSS_{MEAN} , OSI and mean velocity correlated significantly with flatness although the correlations between the hemodynamic parameters with flatness were less strong compared to other morphological parameters. This might be due to the contradictory association of flatness as proxy parameters for IA instability. Besides, according to the sample size calculation, the minimum correlation coefficient of significance was 0.5. Both WSS_{MEAN} and mean velocity had a correlation coefficient falling below 0.5, hence indicating unclear clinical relevance.

Mean velocity was not correlated to other morphological parameters, which is in line with another study in which they could not demonstrate any significant association with velocity and IA size.¹⁷ Therefore mean velocity might be less valuable as a new imaging marker for IA instability.

A correlation between vPI and IA rupture was described in a retrospective cohort of four ruptured IAs, whereby pulsatility and non-sphericity were the only consistent predictive risk factors before and after rupture for all four IAs.²⁰ We found no correlations between vPI and any of the morphology parameters. The small number of IA's and the difference in study design of the aforementioned study regarding the precise location of measurements and the pulsatility calculation steps could explain the differences.

No studies have been performed relating hemodynamic parameters to shape index of the aneurysms. A reason for this might be that shape index is not one of the IBSI parameters, but rather describes the local shape of the aneurysm. However, since shape index is related to IA instability,⁵ our study provides new insights and information by demonstrating that WSS_{MAX} and OSI both correlated to the parameter shape index.

Gadolinium enhancement of the IA wall or aneurysm wall enhancement (AWE) is another potential imaging marker that is associated with aneurysm instability in cross-sectional studies. A recent multicenter longitudinal cohort study on AWE and risk of aneurysm growth and rupture showed that AWE predicts aneurysm growth or rupture during short-term follow-up, but not when adjusting for aneurysm size.²¹ To our knowledge, three studies relating IA wall enhancement to both 3D quantified morphology and hemodynamics have been performed in this topic.^{22,23,24} These three studies all had a different study design and the 3D morphology characteristics were not defined according to the IBSI guidelines. Furthermore, the hemodynamic assessment was performed with CFD modeling and not with 4D flow imaging, impeding comparison with our findings. Currently no consensus exists on the relationship between morphology, hemodynamics and wall enhancement. The correlation between the latter is of added value for developing an optimized imaging strategy for IAs and should be assessed in future studies.

A recent systematic review²⁵ investigated the relation between computational fluid dynamics in the CoW and IA formation, growth, or rupture in three case series of 13 aneurysms in total. Due to limited number of cases and the heterogeneity between the three different case series, no conclusions were drawn on the relation between hemodynamics, the development and instability or rupture of unruptured IAs. The reviewed studies in this systematic review all had a cross sectional design, which does not allow one to determine if the differences in hemodynamics are the cause or the consequence of IA rupture.

The strengths of this study were the ultra-high field 7T MRI 4D flow with 0.5 mm isotropic 4D flow datasets within 10 minutes of scan time with increased SNR and resolution compared to 3T MRA. The advantage of 7T 4D flow imaging in measuring hemodynamics is that it provides, in vivo quantification of hemodynamics with inclusion of the time dimension which allows the calculation of time resolved parameters such as oscillatory shear index and WSS_{MAX} . This would not have been possible in comparison to 3D methods as TOF. By providing supporting evidence that 4D hemodynamic measures correlate with morphological parameters, we aimed to elucidate the pathological process of aneurysm formation.¹⁴ Moreover, we correlated our in vivo intra-aneurysmal hemodynamics with 3D-quantified IA morphology parameters that are correlated to aneurysm instability. These 3D-quantified morphology parameters were calculated on the basis of definitions in accordance with the IBSI guidelines.¹³

This study has some limitations. The cross-sectional study design does not allow us to draw conclusions on the relation between hemodynamic parameters and IA instability over time. Future studies should be of longitudinal design and investigate the dynamic interaction between hemodynamics and IA instability over time and study the prognostic value of all hemodynamic and IBSI standardized 3D morphology parameters in prediction of IA growth and IA rupture. Next, future translational studies should explore the applicability of 7T 4D flow results on the clinically used 3T scanner, enabling the acquisition of hemodynamic studies in larger populations. This study included IAs with a size >4 mm, and therefore, it does not allow us to draw conclusions for aneurysms with a size smaller than 4 mm. Finally, according to our sample size calculation, we had statistical power to demonstrate a correlation of 0.5 or higher. Therefore, the clinical relevance of correlation coefficients being lower than 0.5 is unclear.

CONCLUSIONS

In conclusion, in this study we demonstrate that 4D flow hemodynamics WSS_{MAX} , WSS_{MEAN} , and OSI correlated strongest with morphological parameters that are proxy-parameters of aneurysm instability. This study is an important first step to a better understanding of hemodynamics in the pathophysiological process of aneurysm instability and demonstrates possible new hemodynamic imaging markers for aneurysm instability.

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Tables and figures

Table 1. Patient and intracranial aneurysm characteristics.

Patient characteristics	
No. of patients	35
No. of aneurysms	37 (2 patients with 2 IAs)
Men	10 (29%)
Age (years, mean $\pm$ SD)	66 $\pm$ 9
Mean aneurysm size (mm, mean $\pm$ SD)	7.0 $\pm$ 1.7
Hypertension	19 (54%)
Systolic/diastolic blood pressure before MRI (mmHg, mean $\pm$ SD)	142 $\pm$ 19 / 85 $\pm$ 10
Intracranial aneurysm location (number, proportion)	
Anterior communicating artery	10 (27%)
Basilar artery	2 (5%)
Internal carotid artery	8 (22%)
Middle cerebral artery	17 (46%)
Intracranial aneurysm morphology (mean $\pm$ SD)	
Major Axis Length (mm)	7.0 $\pm$ 1.7
Area (mm ²)	153 $\pm$ 70

Volume (mm ³)	132 ± 91
Flatness	0.81 ± 0.05
Shape index	0.30 ± 0.11
Curvedness	2.39 ± 0.18
Intracranial aneurysm hemodynamics (mean +/- SD)	
WSS _{MAX} (Pa)	3.9 ± 1.5
WSS _{MEAN} (Pa)	0.94 ± 0.27
Oscillatory shear index	0.27 ± 0.06
Mean velocity (cm/s)	23 ± 7
vPI	0.73 ± 0.11
IA, intracranial aneurysm; WSS, wall shear stress; WSS _{MAX} , WSS calculated at peak systole; WSS _{MEAN} , time averaged WSS; OSI, oscillatory shear index; vPI, velocity pulsatility index.	

Table 2. Correlation between hemodynamic parameters and morphological 3D proxy parameters of aneurysm instability.

		Major Axis length	Volume	Area	Flatness	Shape index	Curvedness
WSS _{MAX}	Pearson' ρ	-0.67	-0.67	-0.69	0.03	0.61	0.04
	CI 95%	-0.82 to -0.44	-0.82 to -0.44	-0.83 to -0.47	-0.3 to 0.35	0.36 to 0.78	-0.29 to 0.36
WSS _{MEAN}	Pearson' ρ	-0.64	-0.70	-0.67	-0.35	0.49	0.08
	CI 95%	-0.80 to -0.40	-0.83 to -0.49	-0.82 to -0.44	-0.61 to -0.029	0.2 to 0.7	-0.25 to 0.39
OSI	Pearson' ρ	0.87	0.77	0.76	0.54	-0.82	-0.12
	CI 95%	0.76 to 0.93	0.59 to 0.88	0.58 to 0.87	0.26 to 0.74	-0.9 to -0.68	-0.43 to 0.21
Mean velocity	Pearson' ρ	-0.05	0.04	0.01	-0.33	-0.08	-0.13
	CI 95%	-0.37 to 0.28	-0.29 to 0.36	-0.32 to 0.33	-0.59 to -0.007	-0.39 to 0.25	-0.44 to 0.2
vPI	Pearson' ρ	-0.09	-0.06	-0.03	0.19	0.03	0.12
	CI 95%	-0.4 to 0.24	-0.38 to 0.27	-0.35 to 0.3	-0.14 to 0.48	-0.3 to 0.35	-0.21 to 0.43

WSS, wall shear stress; WSS_{MAX}, WSS calculated at peak systole; WSS_{MEAN}, time averaged WSS; OSI, oscillatory shear index; vPI, velocity pulsatility

Figure 1. An included subject with an anterior communicating artery aneurysm with a major axis length of 8.5mm. A) Maximum intensity projection of the TOF MRA image showing the aneurysm (red arrow). B) Representation of the blood flow analysis using the CAAS software for the reconstructed 4D PC-MRI images. C) Wall shear stress map.

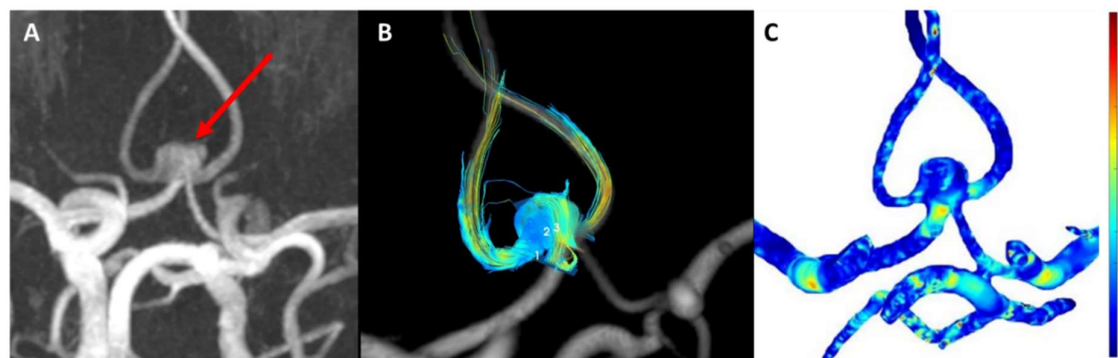


Figure 2: Visualization of correlations for hemodynamic versus morphological parameters. The correlations are scaled between -1 and +1, whereby a positive correlation is shown in blue, and negative correlation in red. The larger the circle, the higher the correlation between the hemodynamic and morphological parameter. The shaded circles represent correlations falling below the minimum value of 0.5, which the sample size of this study was designed to achieve statistical power for. The parameters volume and area had similar correlations and are therefore presented as one size parameter. A blank space means no significant correlation found between the parameters.

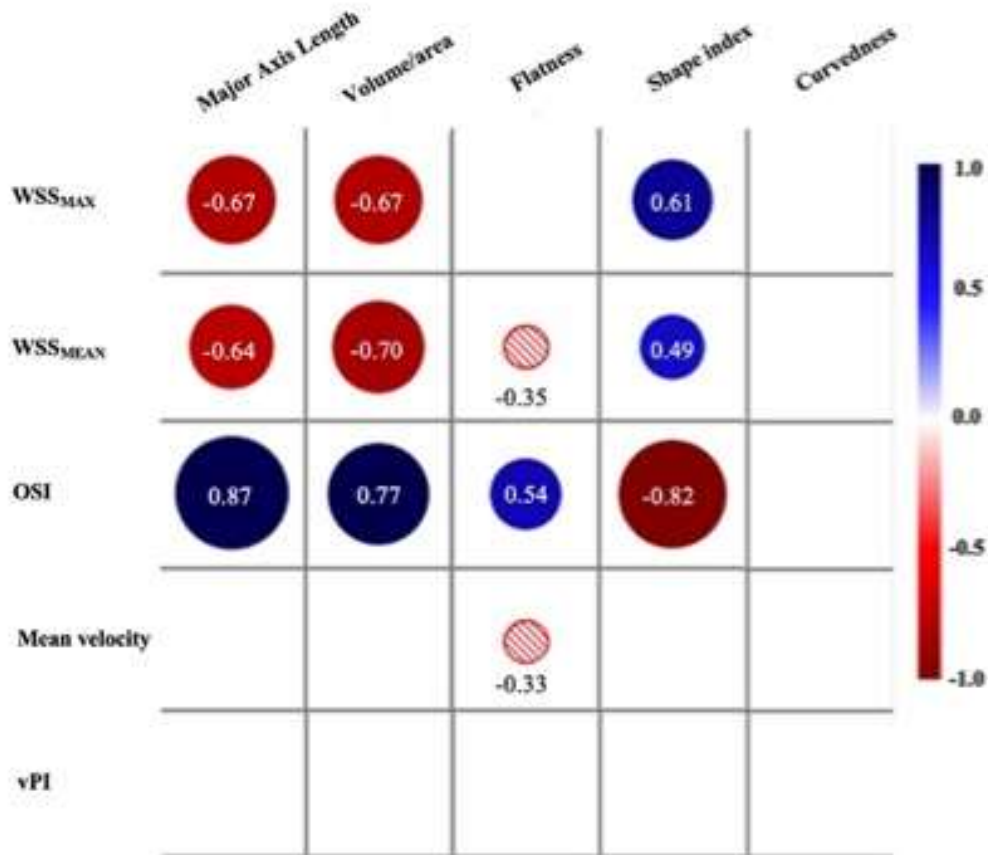


Figure 3: Scatterplots for peak-systolic wall shear stress (WSS_{MAX}), time-averaged wall shear stress (WSS_{MEAN}) (Pascal) and oscillatory shear index (OSI) on the Y-axis, related to major axis length on the X-axis of the unruptured intracranial aneurysm (IA) (mm) for all 37 IAs. A) WSS_{MAX} is negatively correlated with major axis length of the IA ($Y=7.73-0.54X$) ($R^2=0.45$, $p<0.001$). B) WSS_{MEAN} is also negatively correlated with the major axis length of IA ($Y=1.64-0.1X$) ($R^2=0.41$, $p<0.001$). C) the OSI is positively correlated with the major axis length of IA ($Y=0.04+0.03X$) ($R^2=0.75$, $p<0.001$).

