Biomechanical studies on type B aortic dissection

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Wall Shear Stress Assessment of the False Lumen in Acute Type B Aortic Dissection Visualized by Four-Dimensional Flow Magnetic Resonance Imaging (4D flow MRI) An ex-vivo study.

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ABSTRACT

Background

Four-dimensional flow magnetic resonance imaging (4D flow MRI) can visualize and quantify flow and provide hemodynamic information such as wall shear stress (WSS). More insight in the hemodynamic changes during cardiac cycle in the true and false lumen of uncomplicated acute type B aortic dissection (ABAD) might result in prediction of adverse outcomes.

Methods

A porcine aorta dissection model with an artificial dissection was positioned in a validated ex-vivo circulatory system with physiological pulsatile flow. 4D flow MR images with three set heartrates (HR; 60, 80 and 100 bpm) were acquired. False lumen volume per cycle (FLV), mean and peak systolic WSS were determined from 4D flow MRI data. For validation, the experiment was repeated with a second porcine aorta dissection model.

Results

During both experiments an increase in FLV (initial experiment: ΔFLV = 2.05 ml, $p<0.001$, repeated experiment: ΔFLV = 1.08 ml, $p=0.005$) and peak WSS (initial experiment: ΔWSS = 1.2 Pa, $p=0.004$, repeated experiment: ΔWSS = 1.79 Pa, $p=0.016$) was observed when HR increased from 60 to 80 bpm. Raising the HR from 80 to 100 bpm, no significant increase in FLV ($p=0.073$, $p=0.139$) was seen during both experiments. The false lumen mean peak WSS increased significant during initial (2.71 to 3.85 Pa; $p=0.013$) and non-significant during repeated experiment (3.22 to 4.00 Pa; $p=0.320$)

Conclusion

Our experiments showed that an increase in HR from 60 to 80 bpm resulted in a significant increase of FLV and WSS of the false lumen. We suggest that strict heart rate control is of major importance to reduce the mean and peak WSS in uncomplicated ABAD. Because of limitations of an ex-vivo study, 4D flow MRI will have to be performed in clinical setting to determine whether this imaging model would be of value to predict the course of uncomplicated ABAD.

INTRODUCTION

An uncomplicated Acute Type B Aortic Dissection (ABAD) will worsen into a complicated ABAD in approximately 20-30% of cases.[1-3] Once complications occur the prognosis of ABAD dramatically declines to 30 days hospital mortality of over 10%. [1,2,4] Guidelines are well established regarding complicated ABAD and there are no controversies regarding the need to treat them with TEVAR.[5] On the contrary, the uncomplicated acute type B aortic dissections are prone to discussion.[3] Uncomplicated ABAD has a relatively poor prognosis. The reason for this is due to the heterogeneity of the disease and unpredictable course.[6] Identification of clinical and imaging predictors of adverse outcomes in uncomplicated ABAD seems mandatory in order to identify those patients who will benefit from early intervention by TEVAR.[7]

The gold standard for imaging ABAD is Computed Tomography Angiography (CTA).[8] However, because of the static aspect of CTA images, interpretation of the volume and flow changes in the true and false lumen during cardiac cycle is not possible. To get more insight in these hemodynamic changes Four-dimensional flow magnetic resonance imaging **(**4D flow MRI) might be helpful.[9] This imaging technique can accurately visualize and quantify flow and provide hemodynamic information such as wall shear stress (WSS).[10-12] In arterial blood flow, the WSS expresses the viscous force per unit area applied by the fluid on the wall in a direction at the local interface.[13] Gaining more insight of these forces in the true but especially the false lumen in uncomplicated ABAD during optimal medical treatment, might result in prediction of adverse outcomes. Several ex-vivo and in-vivo studies simulating chronic type B aortic dissection (CBAD) showed an increase in false lumen pressure during the longer diastolic phase resulting in increased wall tension over a longer period of the cardiac cycle.[14,15] These studies clearly showed how changes in heart rate can affect lumen pressure in CBAD. However, it can be argued that these ex- and in-vitro results in a CBAD model cannot be translated to dissection in the acute setting due to difference in dissection flap stiffness between ABAD and CBAD. The dissection flap changes during the transition from the acute to the chronic stage with an observed increase of dissection flap thickness over time.[16 17] In ABAD there might be more expansion of the false lumen resulting in higher wall shear stress (WSS) compared to CBAD. However, this has not been examined before in a validated ABAD model. Therefore, the purpose of this study was to examine the influence of heart rate (HR) on the volume, mean and peak WSS by 4D flow MRI in the false lumen in a validated ex-vivo porcine aorta dissection model inserted in a pulsatile flow-model simulating uncomplicated ABAD.

We hypothesized that HR, volume and WSS have a linear correlation within the false lumen of patients with uncomplicated ABAD.

MATERIALS AND METHODS

Aortic dissection model

Frozen unmodified porcine aortas were obtained from the abattoir. They were thawed and prepared as follows: from the aortic arch to the iliac bifurcation all side branches were ligated with 5.0 Prolene. The aorta was inverted inside out and the wall was punctured by a needle. Injection of water resulted in a dissection and the dissection flap was cut in a proximal location to create a primary entry. This technique was previously described by Qing et al.[18]

The created false lumen in the media depicts an anatomic situation comparable to an acute human aortic dissection.[7] In order to study reproducibility, the experiment was repeated with another porcine aorta with a similar morphology. Institutional Review Board (IRB) approval was not needed because no animals were sacrificed specifically for this study.

In-vitro circulatory system

A validated in-vitro circulatory system with physiological flow and pressure characteristics was used to mimic the human circulatory system.[7,19,20] The main components of this circulatory system are a pneumatically-driven pulsatile pump, a compliance chamber and the watertight synthetic box with the aortic dissection model (Figure 1).[7] All components are connected by a silicone tubing

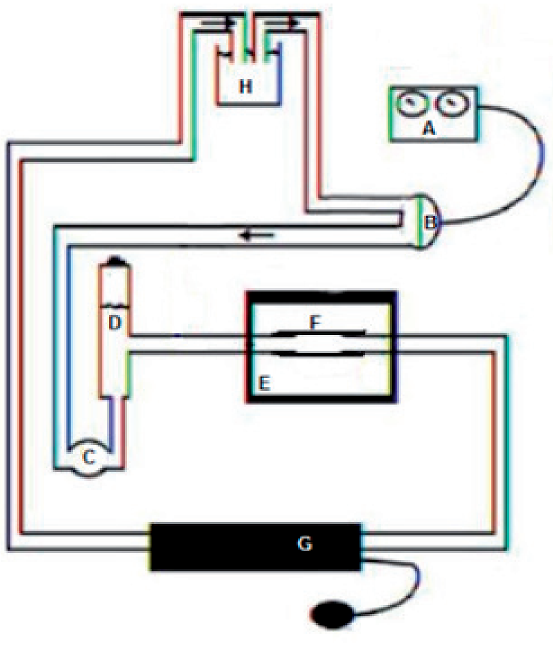

Figure 1. Circulation set-up. A schematic representation of the circulation set-up, which consisted of an artificial heart driver (A), left ventricle (B), a ball valve (C), an air chamber (D), a watertight synthetic box (E), the aortic dissection model (F), a blood pressure cuff (G) an open reservoir (H).

system and water was used for circulating fluid.[7] The synthetic box with the aortic dissection model was placed inside the MRI gantry. Before MRI-scanning started, blood pressure was set to 120/80 mmHg. Both models were imaged at a HR of 60 bpm, 80 bpm and 100 bpm. An arterial catheter (Patient Draeger Infinity Delta Monitor (Drager, Inc. Telford, Pennsylvania, USA)) was used to keep the blood pressure at 120/80 mmHg during the experiments.

Imaging

3D Time resolved MRI imaging with velocity encoding in three directions was performed to obtain 4D Flow MRI data. Imaging was performed on a *1.5T* MRI system (Ingenia; Philips Healthcare, Best, the Netherlands).

For each 4D Flow MRI acquisition, 35 phases were retrospectively reconstructed. The acquired spatial resolution in the MRI protocol was $1 \times 2 \times 2$ mm^3. Specific imaging parameters were as follows: echo time 4.2 ms, repetition time 7.9 ms, flip angle 10°, slice thickness 2 mm, field-of-view 133×300 mm^2, matrix size 133×152 and velocity encoding with sensitivity of 100 or 120 cm/s. Acceleration was achieved by Echo Planar Imaging to factor of 5.

Image analysis was performed using in-house developed and validated MASS software using manual contour segmentation.[21] In order to obtain the false lumen volume (FLV), the dissection segment was divided into three equal parts, the proximal, mid and distal part. Subsequently, the lumen region of both true and false lumen was manually segmented for all three parts separately and at each phase of the cardiac cycle for a total of 40 phases. True and false lumen area (in mm^2) versus time graphs were defined. After segmentation, an average false lumen was obtained.

To calculate the WSS CAAS MR Solutions software v5.0 (Pie Medical Imaging, Maastricht, The Netherlands) was used. Both models were manually segmented at each HR for five phases (two before and two after peak systole) separately. The segmented WSS was then determined for each phase. For each phase a mean and peak segmented WSS was calculated. Thereafter the mean of the five phases was used to measure the difference between two HR's for each model.

Statistics

To calculate the data IBM SPSS Statistics version 24.0 (Armonk, NY) was used. Mean values and standard deviations are reported. A paired t-test was used to compare the mean between two separate HR's within the same model. A p-value <0.05 was considered significant.

RESULTS

Heart rate increase from 60 to 80 bpm

The FLV increased significant during the initial (13.3 to 15.3 ml; $p<0.001$) and repeated experiment (12.8 to 13.9 ml; $p=0.005$). The TLV decreased during the initial experiment but slightly increased in the repeated experiment (19.7 to 17.0ml; $p<0.001$). The false lumen mean WSS increased significant during initial (0.44 to 0.63 Pa; *p=0.007*) and repeated experiment (0.31 to 0.56 Pa; *p=0.009*) (Table 1.; Figures 3 and 4.). The false lumen mean peak WSS increased significant during initial (1.51 to 2.71 Pa; *p=0.004*) and repeated experiment (1.43 to 3.22 Pa; *p=0.016*) (Table 1.; Figures 3 and 4.).

Table 1. Results FLV and WSS

	Initial experiment			**Repeated experiment**		
Heart rate (bpm)	60	80*	100	60	80	100
RR (mmHg)	120/80	120/80	120/80	120/80	120/80	120/80
True lumen volume (ml)	19.7±0.05	17.0±0.01	16.9±0.03	18.5±0.07	18.8±0.02	18.8±0.03
p-value		<0.001	0.250		0.010	0.742
False lumen volume (ml)	13.3±0.02	15.3±0.02	15.3±0.04	12.83±0.11	13.9±0.02	13.7±0.11
p-value		<0.001	0.073		0.005	0.139
False lumen WSS (Pa)	0.462	0.728	0.383	0.306	0.565	0.601
	0.431	0.608	0.493	0.317	0.448	0.645
	0.430	0.660	0.474	0.327	0.625	0.734
	0.438	0.492	0.463	0.353	#	0.572
	0.447	0.666	0.393	0.302	0.617	0.612
False lumen mean WSS (Pa)	0.44 ± 0.01	0.63 ± 0.09	0.44 ± 0.05	0.31 ± 0.01	0.56 ± 0.08	0.65 ± 0.06
p-value		0.007	0.027		0.009	0.154
False lumen Peak WSS (Pa)	1.487	2.548	3.312	1.288	3.673	3.132
	1.650	2.510	3.858	1.374	2.117	3.462
	1.553	2.559	4.648	1.496	3.407	5.763
	1.463	3.460	4.100	1.656	#	2.744
	1.390	2.488	3.326	1.565	3.684	3.653
False lumen Mean Peak WSS (Pa)	1.51 ± 0.10	2.71 ± 0.42	3.85 ± 0.56	1.43 ± 0.12	3.22 ± 0.75	4.00 ± 1.19
p-value		0.004	0.013		0.016	0.320

* See Figure 2. for illustration.
# CAAS did not allow to access five phases for model 2 with HR 80 bpm, therefore in this case, only 4 phases were available.

Heart rate increase from 80 to 100 bpm

There was no significant change neither in FLV during the initial (15.3 to 15.3 ml; *p=0.07*) and repeated experiment (13.9 to 13.7 ml; *p=0.139*) nor in TLV during the initial (17.0 to 16.9 ml; *p=0.25*) and repeated experiment (18.8 to 18.8 ml; *p=0.74*). The false lumen mean WSS decreased significant during initial experiment (0.63 to 0.44 Pa; *p=0.027*) but increased significant during repeated experiment (0.56 to 0.65 Pa; *p=0.154*) (Table 1.; Figures 3 and 4.). The false lumen mean

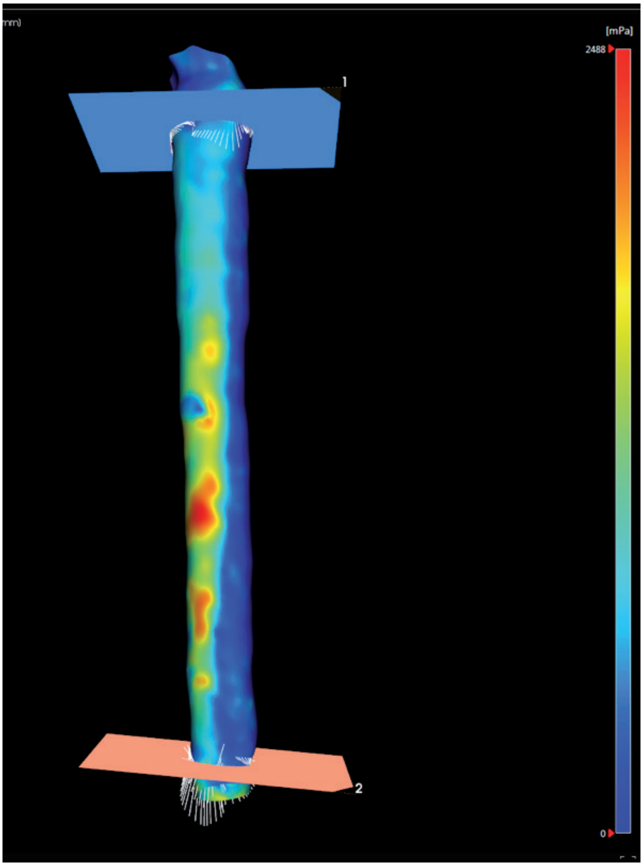

Figure 2. 4D MRI image of initial experiment at a HR of 80 bpm. A map of WSS based on 4D MR images (blue = low WSS, red = high WSS).

peak WSS increased significant during initial (2.71 to 3.85 Pa; $p=0.013$) and non-significant during repeated experiment (3.22 to 4.00 Pa; $p=0.320$) (Table 1.; Figures 3 and 4.).

DISCUSSION

Still today it is difficult to predict the clinical course of uncomplicated ABAD. The optimum management of patients with uncomplicated ABAD is unclear.[3] The principal management of ABAD remains aggressive medical therapy for all patients, with TEVAR primarily reserved for those who develop complications.[3] In order to gain more understanding in uncomplicated ABAD it might be helpful to clarify the hemodynamic changes during the cardiac cycle with 4D flow MRI.[9]

4D flow MRI can accurately visualize and quantify the functional flow and access hemodynamic information such as WSS.[10,11] During a recent in-vivo scan-rescan study by van der Palen et al, the

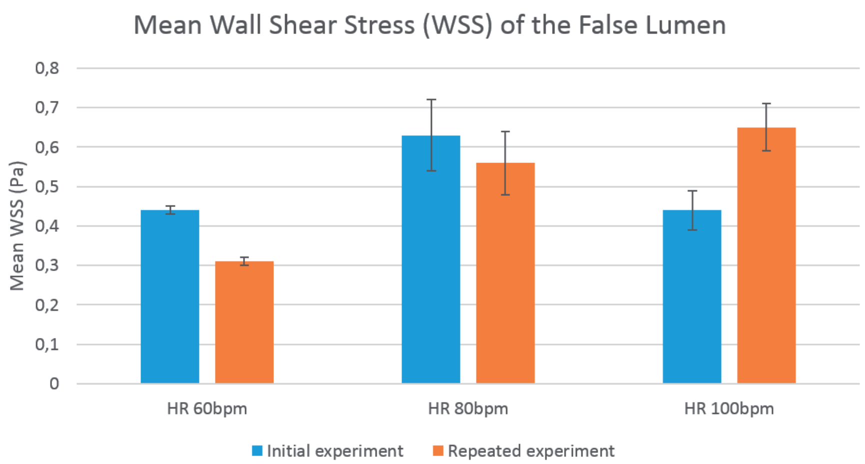

Figure 3. Mean Wall Shear Stress (WSS) of the False Lumen during both experiments

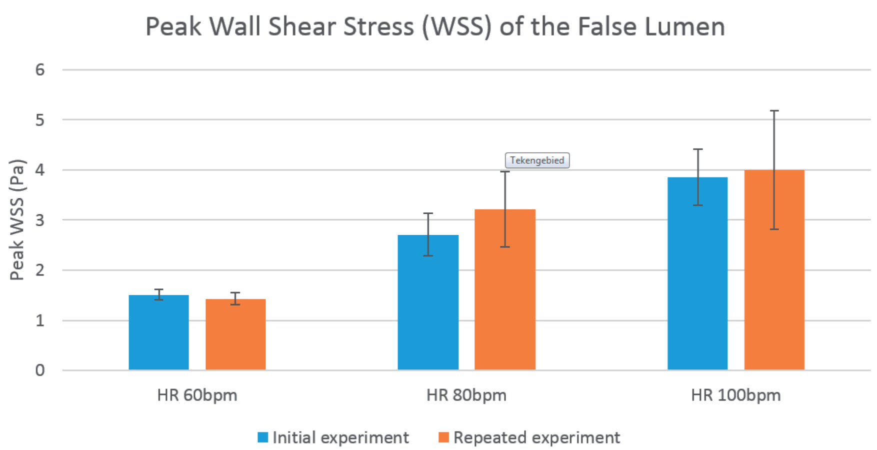

Figure 4. Peak Wall Shear Stress (WSS) of the False Lumen during both experiments

reproducibility of segmental aortic 3D systolic WSS by phase-specific segmentation with 4D flow MRI was evaluated and showed a very accurate reproducibility of the WSS assesments. During our study the same tools, with respect to 4D flow MRI acquisition and analysis were used.[12]

The presented porcine aortic dissection models simulate ABAD, as the morphology of a surgically created false lumen in a porcine aorta dissection is comparable to a human aortic dissection and the dissection flaps are soft.[16] Furthermore, de Beaufort et al. showed that morphology and elasticity of young porcine aortas corresponds to the human thoracic aortic under 65 years.[22] This implies together with our previously published studies that our ex-vivo porcine aorta model is a representative model to study uncomplicated ABAD.[7,23] Earlier research on aortic dissection by 4D flow MRI was only performed using silicon models and resulted in hemodynamic insights into aortic dissection.[4] Other in-vitro study on hemodynamics in aorta dissection showed that if a distal tear in the false lumen was absent the diastolic pressure in the false lumen increased compared to the true lumen diastolic pressure.[14] However, it should be noted that these last two mentioned studies did not use biological tissue but were based on experiments with synthetic polymer or silicon tubing.[4,14,24] Data from these studies were intended to mimic a chronic dissection model. The set-up of our study by using an ex-vivo porcine aorta model is more representative to simulate ABAD.

This study showed a significant increase in FLV, mean WSS and peak WSS during the initial and repeated experiment when HR raised from 60 to 80 bpm. These results support the recommendations of goal-directed therapy to establish and control a heart rate of less than 60 bpm in the 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease.[25] Interestingly, when the HR raised from 80 to 100 bpm, no significant increase in FLV was observed but increase of mean and peak WSS were measured (Table 1, Figures 3 and 4). This finding indicates that a stable FLV does not exclude an increase in mean and peak WSS. It illustrates the added value of 4D MRI, in gaining additional hemodynamic information compared to conventional imaging modalities. Our hypothesis that HR and WSS have a linear correlation within the false lumen of uncomplicated ABAD could only be proved statistically in our ex-vivo porcine aorta dissection model when HR raised from 60 to 80 bpm.

Our study has several limitations being an experimental ex-vivo model. Firstly the porcine aorta models during the initial and repeated experiment have the same morphology but there are mild differences (Table 1.). These might be responsible for the observed differences between the initial and repeated experiment. Secondly, the diameter of a porcine aortic is smaller than that of humans. Thirdly, the viscosity of water is much lower than that of blood which might have its influence on the wall shear stress. However, blood could not be used in our set-up because of a risk of thrombosis, which can block the tubing system or the pulsatile pump.[16] Lastly, the porcine aorta in our model was no longer surrounded by connective tissue that also affects aorta compliance.

In conclusion, 4D flow MRI compared to CTA provides insight into hemodynamic dimensions such as WSS. This information might result in better understanding of the false and true lumen behavior in uncomplicated ABAD at presentation and might provide the opportunity to better predict the clinical course of this disease. Our ex-vivo research illustrated that an increase in HR from 60 to 80 bpm resulted in a significantly increase of the FLV and WSS of the false lumen. We suggest that strict heart rate control is of major importance to reduce the mean and peak WSS in uncomplicated ABAD. Because of the limitations of an ex-vivo study, 4D flow MRI will have to be performed in clinical setting to determine whether this imaging model would be of value to predict the course of uncomplicated ABAD.

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