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The Influence of Aortic Wall Elasticity on the False Lumen in Aortic Dissection: An In Vitro Study

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Abstract

Background: Hemodynamics, dissection morphology, and aortic wall elasticity have a major influence on the pressure in the false lumen. In contrast to aortic wall elasticity, the influence of hemodynamics and dissection morphology have been investigated often in multiple in vitro and ex vivo studies. The purpose of this study was to evaluate the influence of aortic wall elasticity on the diameter and pressure of the false lumen in aortic dissection. **Methods:** An artificial dissection was created in 3 ex vivo porcine aortas. The aorta models were consecutively positioned in a validated in vitro circulatory system with physiological pulsatile flow. Each model was imaged with ultrasound on 4 positions along the aorta and the dissection. At these 4 locations, pressure measurement was also performed in the true and false lumen with an arterial catheter. After baseline experiments, the aortic wall elasticity was adjusted with silicon and the experiments were repeated. **Results:** The aortic wall elasticity was decreased in all 3 models after siliconizing. In all 3 siliconized models, the diameters of the true and false lumen increased at proximal, mid, and distal location, while the mean arterial pressure did not significantly change. **Conclusions:** In this in vitro study, we showed that aortic wall elasticity is an important parameter altering the false lumen. An aortic wall with reduced elasticity results in an increased false lumen diameter in the mid and distal part of the false lumen. These results can only be transferred to corresponding clinical situations to a limited extent.

Keywords

dissection, false lumen, wall elasticity, wall stiffness, in vitro model

Introduction

Consensus has been established to manage uncomplicated acute type B aortic dissection (ABAD) in the acute phase (0-2 weeks) with surveillance and optimal medical treatment (OMT) with control of hypertension and heart rate.[1] The reported 30-day in-hospital mortality of an uncomplicated ABAD is 2.4%, but when an uncomplicated ABAD converts to a complicated ABAD, the 30 days in hospital mortality quadruples.[2] In the subacute phase of an uncomplicated ABAD with suitable anatomy, there is increasing evidence of improved survival and less progression of disease at 5 years after elective thoracic endovascular aortic repair (TEVAR).[3,4] Gaining more insight in the false lumen behavior of the acute uncomplicated ABAD may result in identifying those patients who are at high risk of developing complications and may benefit from elective TEVAR in the acute phase.

Aortic dissection is defined as a pathological condition characterized by the presence of an aortic intimal tear and medial dissection, in which blood flows from the entry site into the false lumen.[5] Hemodynamics, dissection morphology, and aortic wall elasticity have a major influence on the pressure in the false lumen.[6] In contrast to the aortic wall elasticity, the influence of hemodynamics and dissection morphology have been investigated often in multiple in vitro and ex vivo studies.[7,8] Aortic wall elasticity is variable and often altered in aortic dissections.[9,10] The aortic wall elasticity can be influenced by aging and atherosclerosis.[11]

Today's literature on the influence of aortic wall elasticity on the pressure of the false lumen consists of only 1 in vitro study using a lumped parameter model.[12] This study described the role of wall elasticity as a determinant of intraluminal pressures and flow patterns.[12] Additional research is needed to

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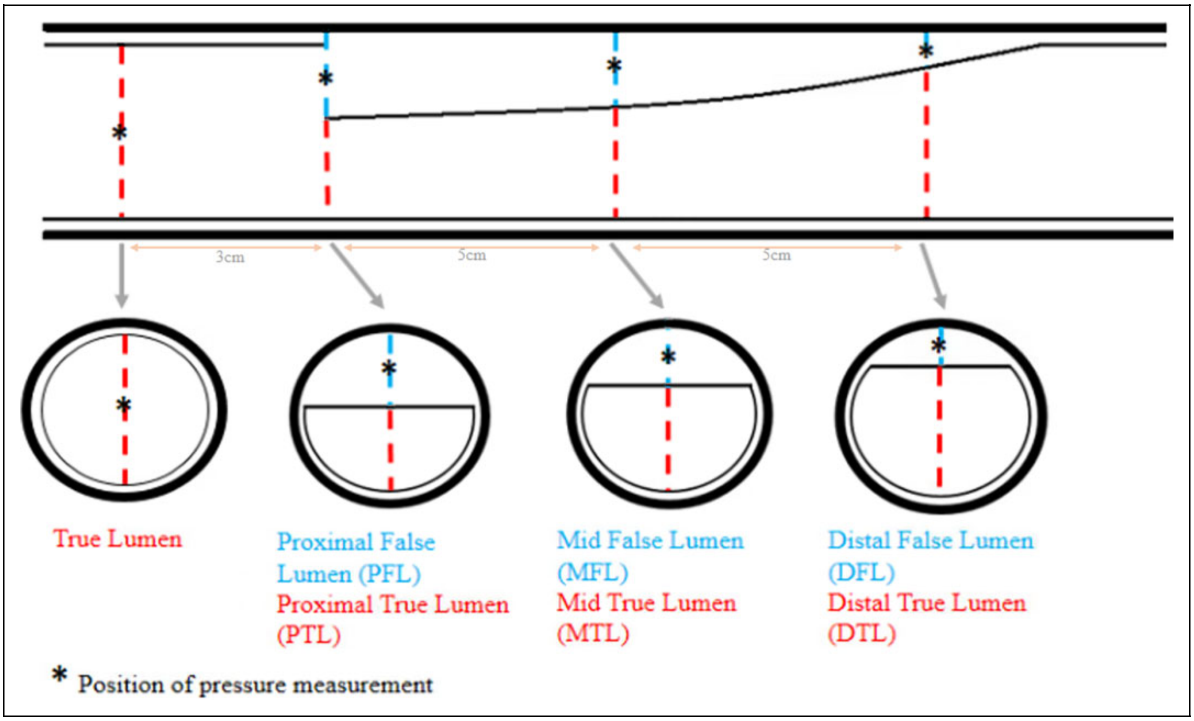

Figure 1. Schematic overview of the aortic dissection model. The 4 imaging planes and pressure measurement positions are presented. *Position of pressure measurement.

better understand the role of aortic wall elasticity and its relation to false lumen diameter and false lumen pressure characteristics in uncomplicated ABAD. We hypothesize that a less elastic aortic wall will result in an increase in false lumen pressure and diameter. We studied this hypothesis by adjusting the aortic wall elasticity in a validated in vitro porcine aorta dissection model in a pulsatile flow model.

Materials and Methods

Aortic Dissection Model

To create a porcine type B aortic dissection model with patent false lumen, we used a technique that was previously described by Qing et al.[12] Fresh porcine aortas were obtained frozen from the abattoir. The porcine aortas were defrosted and prepared as following: from the aortic arch to the iliac bifurcation, all side branches were ligated with 5.0 Prolene. The porcine aorta was everted with the help of a clamp. Before starting, orifices of small branches on the intimal surface were observed, and the route of creating the dissection flap was carefully planned.[13] A 24-GA intravenous catheter was used to puncture the intima till mid-portion of media, and approximately 10 mL of saline was injected, creating an intramural haematoma.[13] The dissection was extended by both injecting saline and pressing the bleb without rupturing the dissection flap resulting in a dissection with a length of 11 cm. Subsequently, the dissection flap was cut in a proximal location to create a primary entry. Finally, the aorta was everted back to finish the procedure. The dissection area was longitudinally divided in proximal, mid, and distal (Figure 1). A total of 3 aortic dissection models with all similar morphology, a primary entry tear, and a dissection length of 11 cm were made (Figure 1). After baseline experiments (see below), the aortic wall elasticity of each aortic model was adjusted by applying a synthetic polymer made up of silicon to the outer layer of the aortic model (Silicone; Bison), and the experiment was repeated. The basis to choose for this method of siliconizing was to achieve a more rigid aortic wall as can be seen by aging and atherosclerosis.[11] The effect of siliconizing the outer wall was evaluated by measuring the lumen diameter under flow conditions prior to the dissection. Approval of the institutional review board was not needed because no animals were killed 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.[14-16] 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 2). All components are connected by a silicone tubing system and water was used for circulating fluid. During the experiments, the pneumatically driven pulsatile pump was set on normotensive (pressure 130/70 mm Hg; mean arterial pressure [MAP] 90 mm Hg) and normocardia (60 beats per minute), parameters to simulate optimal hemodynamic parameters. The synthetic box was filled with water resulting in a submerged aortic dissection for optimal ultrasound visualization.

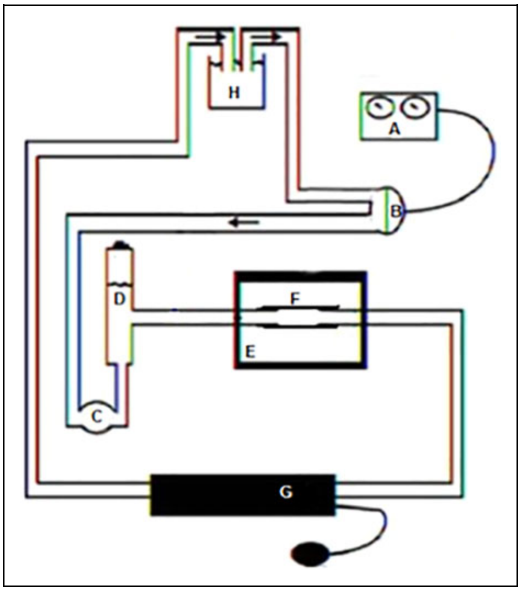

Figure 2. Circulation setup. A schematic representation of the circulation setup, which consisted of an artificial heart driver (A), left ventricle (B), a ball valve (C), an air chamber (D), a watertight synthetic box (E), the aortic dissection model (F), a blood pressure cuff (G), and an open reservoir (H).

Imaging

Ultrasound (Zonare) was used for imaging. The linear transducer (14 mHz) was used to visualize the transverse plane at 4 different locations in the model: the true lumen (TL), the proximal false lumen (PFL), the mid false lumen (MFL), and the distal false lumen (DFL; Figure 1).

Five cardiac cycles were recorded in the transverse plane at the 4 different locations in each model (Figure 1). Anterior–posterior (AP) lumen diameter measurements were performed at baseline and after siliconizing. The maximal and minimal AP lumen diameter (AP_{max}, AP_{min}) were identified as the ultrasound image with the largest and smallest lumen diameter during cardiac cycle. In order to prevent interobserver variability, AP_{max} and AP_{min} measurements were performed by 2 different observers (H.T.C.V. and E.H.P.) blinded to the first outcome.

Pressure Measurements

Pressure measurements were performed in the center of the 4 different locations in the model: the TL, the PFL, the MFL, and the DFL (Figure 1). An arterial catheter (Patient Draeger Infinity Delta Monitor; Draeger, Inc) was used for pressure measurements. Pressure measurements in the TL were maintained stable at MAP 90 mm Hg by arterial catheter monitoring. The arterial catheter was visualized by ultrasound and positioned in the center of each location (Figure 3). After 10 seconds, the pressure was recorded.

Statistics

Lumen diameters AP_{max}, AP_{min} and pressure measurements of the true and false lumen at all 4 locations in the aortic dissection planes were determined at baseline and after siliconizing. Mean values and SDs are reported. Paired *t* tests were used to determine statistical significance in diameter and pressure change at each location in the aortic dissection model. Statistical significance was assumed at $P < .05$. To calculate the significance, IBM SPSS Statistics version 24.0 was used.

Results

At baseline, each model had the same morphology and dissection length, though the diameters and dissection width differed (Table 1).

True lumen: The aortic wall elasticity was decreased in all 3 models after siliconizing. Model 1 showed a mean TL reduction of 3.2%, 18.8 to 18.2 mm (median 18.5 ± 0.40 mm, $P = .01$); model 2 a reduction of 4.1%, 18.5 to 17.7 mm (median 18.1 ± 0.50 mm, $P = .01$); and model 3 showed a reduction of 14.0%, 17.9 to 15.4 mm (median 16.7 ± 1.77 mm, $P = .05$). The MAP in the TL was maintained stable at 90 mm Hg.

Proximal false lumen: The PFL diameter only decreased significantly in model 2 after siliconizing. In model 1 and 3, there were no significant diameter changes. The MAP did not change significantly after siliconizing in all 3 models (Table 1).

Mid and distal false lumen: In all 3 siliconized models, a significant increase in the MFL diameter was observed after siliconizing (Figure 4), although the MAP did not show statistically significant difference (Table 1).

Discussion

In this study, the influence of aortic wall elasticity on the diameter and pressure of the false lumen in porcine aortic dissection models was evaluated. The main findings of this study are that an aortic wall with reduced elasticity results in an increased false lumen diameter in the mid and distal part of the false lumen.

Uncomplicated ABAD in the acute phase (0-2 weeks) are managed with surveillance and OMT with control of hypertension and heart rate.[1] When the uncomplicated ABAD converts to a complicated ABAD, the mortality quadruples.[2] Gaining more insight in the false lumen behavior of the uncomplicated ABAD might result in identifying those who are at high risk of developing complications in the acute phase.

The majority of experimental flow studies in the field of aortic diseases are based on rigid wall models, under the assumption that the effect of wall elasticity on the quantitative results is rather limited for the hemodynamic parameters studied. These studies using mainly silicon tubing showed that lack of a distal tear results in a significant increase in diastolic pressure presumably due to an impairment of outflow from the false lumen to the TL.[7] Increased pressure of the false lumen results in increased wall stress of the false lumen.[8] This may contribute to a progression of the dissection and convert an uncomplicated into a complicated dissection. However, besides hemodynamic changes and dissection morphology, aortic wall

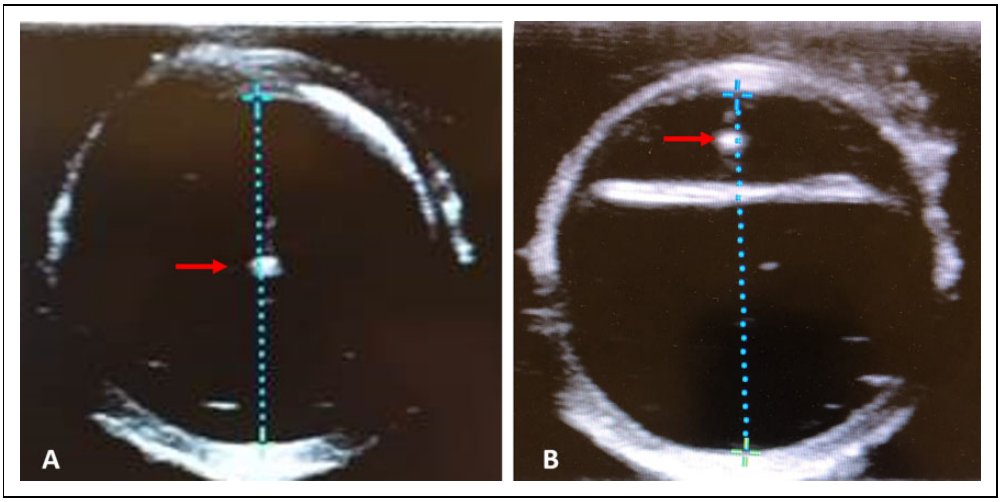

Figure 3. Ultrasound image of diameter and pressure measurement in the true (A) and false (B) lumen. Arrow: the tip of the arterial catheter. Line: anterior–posterior (AP) lumen diameter.

Table 1. Characteristics of Baseline and Siliconized Models.

	Model 1		Model 2		Model 3	
	Baseline	Siliconized	Baseline	Siliconized	Baseline	Siliconized
True lumen—prior to the dissection (mm)	18.8 ± 0.3	18.2 ± 2.1	18.5 ± 0.5	17.7 ± 0.3	17.9 ± 0.6	15.4 ± 0.4
P value	.01		.01		.02	
True lumen reduction (%)	3.2		4.1		14.0	
Mean arterial pressure (MAP; mm Hg)	90		90		90	
Total proximal lumen (mm)	19.5 ± 1.3	18.1 ± 0.8	18.9 ± 1.5	17.8 ± 1.6	17.1 ± 0.5	15.1 ± 1.5
Total mid lumen (mm)	18.5 ± 0.6	17.4 ± 2.2	18.6 ± 2.4	17.2 ± 2.8	16.1 ± 1.0	14.8 ± 0.8
Total distal lumen (mm)	17.8 ± 1.0	17.0 ± 0.3	17.7 ± 0.6	16.3 ± 1.1	15.7 ± 0.6	14.1 ± 1.4
Proximal true lumen (PTL) (mm)	13.2 ± 1.1	13.0 ± 0.3	11.9 ± 1.2	11.5 ± 0.5	10.6 ± 0.2	9.5 ± 0.2
Mid true lumen (MTL) (mm)	11.9 ± 0.3	10.6 ± 1.4	10.5 ± 2.2	7.1 ± 0.7	9.6 ± 0.4	7.7 ± 0.4
Distal true lumen (DTL) (mm)	10.9 ± 0.2	9.3 ± 0.2	9.1 ± 0.2	3.8 ± 0.6	9.0 ± 0.4	6.3 ± 0.3
Proximal false lumen (PFL) (mm)	6.3 ± 0.2	5.1 ± 0.5	7.0 ± 0.3	6.1 ± 1.1	6.5 ± 0.3	5.6 ± 1.3
P value	.07		.04		.08	
PFL MAP (mm Hg)	90 ± 2.3	92 ± 2.8	90 ± 2.3	91 ± 2.0	90 ± 1.9	94 ± 2.3
P value	.08		.36		.25	
MFL (mm)	6.6 ± 0.3	6.8 ± 0.8	8.1 ± 0.2	10.1 ± 2.1	6.5 ± 0.6	7.1 ± 0.4
P value	.01		.01		.03	
MFL MAP (mm Hg)	90 ± 1.4	92 ± 1.8	90 ± 0.6	91 ± 2.1	91 ± 2.6	95 ± 3.2
P value	*0.9*		*0.8*		*0.6*	
DFL (mm)	6.9 ± 0.8	7.7 ± 0.1	8.6 ± 0.4	12.5 ± 0.5	6.7 ± 0.2	7.8 ± 1.1
P value	.04		<.01		.03	
DFL MAP (mm Hg)	91 ± 2.2	92 ± 1.3	90 ± 1.5	92 ± 1.3	91 ± 0.6	95 ± 3.2
P value	.9		.8		.8	

elasticity may have a major influence on the course of the false lumen.

Currently, there is one published article that compares pressure in the false lumen with a changing elasticity of the aorta wall.[12] However, synthetic polymer of silicon tubing was used in their in vitro study. No further studies have examined the unique effect of wall elasticity on the false lumen, independent of other parameters. An in vitro study in the previously

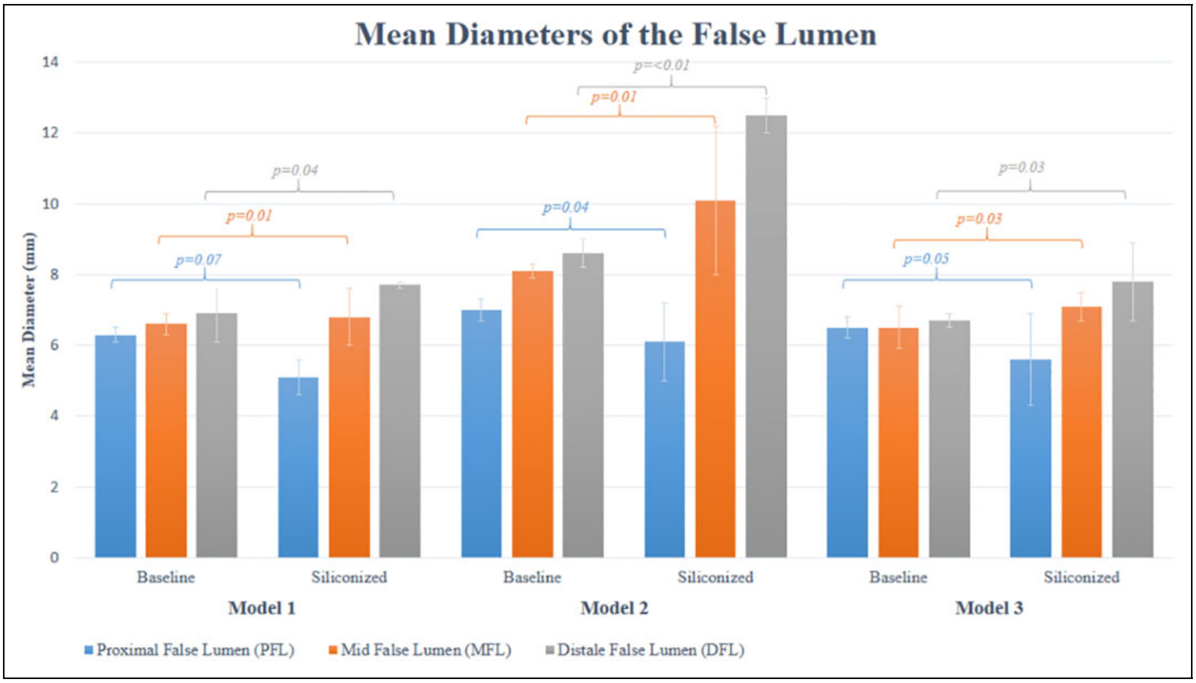

Figure 4. Mean diameters of the false lumen.

validated aortic dissection model has the potential to study a specific parameter in a controlled setting.[14,17] In this study, a porcine aorta—instead of synthetic polymer or silicon tubing—was used as a “modeled” aorta.[7,18] Research showed that elasticity and morphology of a young porcine aorta corresponds to the human thoracic aorta under 65 years.[19] In addition, the morphology of a surgically created false lumen in a porcine aorta dissection is comparable to a human aortic dissection.[13] In this study, the baseline models mimic the thoracic aorta under 65 years, where the siliconized model mimics the more rigid (atherosclerotic) thoracic aorta. This study and our previous studies showed that this ex vivo porcine model is a representative model to study different aspects of ABAD.[14,17] In all 3 models, the aortic wall elasticity (expressed in AP diameter change) was significantly decreased after siliconizing. The diameter of the MFL and DFL expanded significantly in all models when the aortic wall elasticity decreased. The MAP did not significantly change in the MFL and DFL in all 3 models. The observed increase in false lumen diameter of the MFL and DFL can be explained by the fact that the dissection flap is thinner than the (partial thickness media with adventitia) outer aortic wall. When the outer aortic wall stiffness disproportionately increases compared to the dissection flap stiffness, the dissection flap will be pushed further away from the outer aortic wall, resulting in an increase in the false lumen diameter.

The presented in vitro model has limitations. First, we used water instead of blood as a circulating fluid, which has a much lower viscosity than blood. However, in our experimental setup, blood cannot be used because of the thrombotic effect which will affect the tubing system or pulsatile pump.[13] Secondly, the aortas were defrosted, prepared, and thawed within 1 day, which could have affected the elasticity of the aortic wall at baseline. Furthermore, the diameter of a porcine aorta is smaller than that of humans. Still, this study demonstrates that wall elasticity is clearly altering the false lumen and should be taken into account when assessing and studying aortic dissections. With the rapid development of new magnetic resonance imaging technology for vessel wall imaging, wall elasticity can be determined although translation of the results of this study to a physiological situation is limited and evaluation of patients should be performed to confirm our findings.

In conclusion, this in vitro study showed that an aortic wall with reduced elasticity of the outer aortic layers results in an increased false lumen diameter in the mid and distal part of the false lumen. False lumen expansion might result in higher stress of the aortic wall and at the ending of the dissection. The present model provides information on the role of the elasticity of the outer aortic layers in the context of experimental aortic dissection, but the results can certainly only be transferred to corresponding clinical situations to a limited extent.

Declaration of Conflicting Interests

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