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Biomechanical studies on type B aortic dissection

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General Discussion

The studies presented in this thesis provide novel insight in mechanistic aspects of the dissection process. Although it is clear that treatment of cTBAD with TEVAR has resulted in improved outcomes optimal management of uTBAD at presentation remains an issue of much debate. First, the in hospital mortality of this group patients treated medically is around 12 % and secondly without early intervention there is a 20% long term risk of significant aortic aneurysm formation.[1] The current treatment paradigm of TEVAR in uTBAD when complications develop is based on the unfavorable risk-to-benefit ratio previously associated with TEVAR. As the discussion continues whether to treat acute uTBAD by early TEVAR it is of great importance to identify patients at risk of developing cTBAD and at the same assesment of risk factors leading to complications due to TEVAR should be defined and reduced.

uTBAD CONVERTING TO cTBAD

Most previous studies have looked at clinical parameters or CTA based anatomic characteristics that may predict an adverse outcome. Some of these predictors can be used in the clinical setting to advocate early intervention in uTBAD. However there is little knowledge on basic mechanistic pathofysiologic processes that define the dissection process and in particular false lumen behaviour. Therefore we created a porcine model to experimentally examine some anatomic and haemodynamic elements and used clinical imaging studies to delineate the dissection process.

Incomplete thrombosis or patent false lumen portends a poor outcome.[2 3 4] The occurrence of thrombosis in the false lumen depends on coagulability, endothelial injury/dysfunction and blood flow. The blood flow in the false lumen is highly variable due to morphological differences between various types of dissections. [5]

It is conceivable that patent branch vessels originating from the false lumen in TBAD may contribute to persistent blood flow and patent false lumen, and thus to prognosis. Our in-vitro study showed that outflow through a branch vessel originating from the false lumen in TBAD results in expansion of cross-sectional false lumen area. False lumen expansion might result in higher stress in the aortic wall, increasing the risk of dilatation which contributes to the conversion of uTBAD into cTBAD. Besides the limitations inherent to replicating in vivo conditions as discussed later in this section the model represents an TBAD with an intact dissection flap with no distal tear or partial thrombosis occluding distal tears, impending outflow resulting in a blind sac from where a single branch vessel originates.

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 haemodynamic parameters studied. Although it is known that aortic wall elasticity is variable and often altered in aortic dissections. [6]

We showed in a porcine aortic dissection model 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 support the evidence that wall elasticity is clearly altering intraluminal haemodynamics compared to a rigid-wall simulation and should be taken into account when assessing and studying aortic dissections. This highlights the potential of new non-invasive imaging techniques that can give us the hemodynamic information compared to conventional imaging modalities.

The gold standard for imaging TBAD is Computed Tomography Angiography (CTA). [7]

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. There are no clinical hemodynamic studies that help to predict the clinical behavior of acute TBAD. Hemodynamic parameters such as flow pattern, volume and velocity have a role in false lumen expansion. [8 9] 4D flow MRI can accurately visualize and quantify the functional flow and access hemodynamic information such as Wall Shear Stress. 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. [10]

Earlier research on aortic dissection by 4D flow MRI was performed using silicon models mimicking chronic TBAD and resulted in hemodynamic insights. We focused on studying hemodynamics of the false lumen in acute TBAD simulated by a porcine aorta model. A significant increase in FLV, mean WSS and peak WSS was observed when heart rate raised from 60 to 80 baets per minute (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. [11]

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. 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. In uTBAD 4D flow MRI could be implemented as additional imaging to understand the WSS at presentation but also during OMT. It might be of relevance in the future as this knowledge can suggest more aggressive blood pressure lowering therapy and better heart rate control as well as to select those who will benefit from early intervention.

INTERVENTION RISK

Retrograde dissection, spinal cord ischemia and paraplegia are known complications after TEVAR. Retrograde dissection is the most feared complication of TEVAR and it is of great importance to prevent retrograde dissection. The stress yielded by the endograft seems to play a predominant role in its occurrence. The currently available stentgrafts have been designed for thoracic atherosclerotic aneurysms, a different disease where strong radial force for adequat sealing is needed. Gently transferred forces (radial and "spring-back" force) of the stentgraft on the fragile inner

wall at the proximal landing zone in aorta dissection are crucial to prevent intimal damage and thereby the occurance of a new tear. As the spring-back force is an important factor in the stent graft-induced injury as the more the endograft is bent, the higher the stress might be. Also is there increased stress at the end closer to the curving point of the endograft than at the other end. A dissection-specific stentgraft calls for lower radial force and higher flexibility (reduced "spring-back" force). The diameter of the distal true lumen would be added into the preoperative sizing, and a tapered device might be conducive if the distal true lumen is far smaller than the proximal landing zone. Research on the currently available stentgrafts and the radial and "spring-back" force will show the stentgraft with the best characteristics. Another aspect of TEVAR is the layer of fabric that covers the intercostal arteries and can result in postprocedural new-onset paraplegia due to ischemic spinal cord injury. The dissection-specific stentgraft could be a hybrid design of proximal covered and distale bare stents.

In cTBAD malperfusion is caused by dynamic or static obstruction. Endovascular aortic fenestration quickly reduces the high pressure in the false lumen by communicating the false with the true lumen directly relieving organ or limb ischemia in a faster way than by aortic graft replacement. [12 13] It is useful in malperfusion syndromes and in cases not suitable for proximal aortic tear coverage. [12 13] A recent study shows that cTBAD complicated by malperfusion treated with endovascular fenestration/bare metal stenting has excellent short- and longterm outcomes.[14] It remains unclear where the optimal location of these fenestrations should be chosen. Two different fenestrations strategies in a validated ex-vivo porcine aorta dissection model in a pulsatile flow-model were studied. The observations were that performing a distal fenestration in the dissection flap resulted in significant false lumen volume decrease compared to performing a proximal fenestration. A more distal location of the fenestration in the false lumen lead to better equilibration of pressures and false lumen reduction. Endovascular fenestration/stenting is an effective tool to treat malperfusion (dynamic and static) in acute TBAD and is a valuable adjunct to both medical and surgical therapy (TEVAR and open repair).[14]

Due to limitations inherent to replicating in vivo conditions preclinical testing has a limited ability in reproducing clinical settings. Therefore, the limitations of the pulsatile flow model need to be addressed and suggestions for improvement are made. Water was used as a circulatory medium instead of blood, which has a different viscosity and is not a thrombotic medium. Spontaneous thrombosis could either block the tubing system or disturb the function of the pulsatile pump. The use of anticoagulation in the circulatory system might prevent this. The option of adjusting the viscosity of the circulatory fluid in the flow model would result in a more realistic simulation of the human circulatory system. Secondly the applied pulsatile flow was not equal to human aortic flow. Adding the aortic valve and arch to the porcine dissection model would have made it more representative. Thirdly the aortic model was submerged in water without support, which is not representative for the connective tissue normally surrounding the aorta. Beside the previously mentioned adjustments one could replace water for silicon with the same properties as human peri aortic connective tissue in future experiments to represent reality.

In conclusion, the studies described in this thesis used a created porcine TBAD model under pulsatile conditions to sort out the effects of biomechanical parameters on the false lumen in TBAD. For many decades fenestration of the false lumen is performed to achieve a quickly decrease of the pressure gradient of the false lumen. Untill our research it remained unclear where the optimal location of these fenestrations should be chosen. We showed in our model that distal fenestration of the false lumen in aortic dissection will result in the largest false lumen reduction.

We proved in our model that outflow through branch vessels of the false lumen, aortic wall compliance and hemodynamics have a major impact on the false lumen in uTBAD. The static aspect of CTA images makes it unpossible to be well informed on these biomechanical parameters. Advancement of non-invasive diagnostic imaging as 4D MRI should be further studied in the clinical setting as an alternative to the static imaging technique in current practice. This may help to better delineate risk factors that propagate a more complicated dissection course and determine which patients should undergo TEVAR in the early stages of uTBAD.

For our research group, the studies presented in this thesis form a foundation to formulate novel clinically driven questions related to TBAD. Continued research by our group will focus on the additional value of 4D MRI in acute uTBAD in clinical setting.

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