Percutaneous aortic valve replacement: gross anatomy and histological findings after transapical and endoluminal resection of human aortic valves in situ

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Abstract

Objective: Transluminal resection of the aortic valve was already successfully carried out by our group. The aim of this study was the analysis of the gross anatomy and the histology of the surrounding tissue after resection.

Methods: Aortic valve resection was performed in postmortem human hearts (endoluminal (EL) n = 9, transapical (TA) n = 4). After deployment of the aortic valve isolation chamber, the leaflets were resected with a Thullium:YAG laser scalpel (cw, 20 W). After resection, the hearts were analyzed to check for lesions caused by resecting the associated tools. Therefore, gross anatomy and histological analysis were performed (H&E staining).

Results: Lesions of the aortic annulus were seen in 3/9 (EL) (depth: 583 ± 186 μm) and 2/4 (TA) (120 μm and one complete perforation), lesions of the aorta (ascending-arch-descending) in 4-9-0/9 (EL) and 0-0-0/4 (TA), lesions of the mitral valve in 0/9 (EL) and 0/4 (TA), lesions of the papillary muscle in 0/9 (EL) and 2/4 (TA) (depth: 400 μm and 450 μm), lesions of the endomyocardium in 0/9 (EL) and 4/4 (TA) (depth: 258 ± 102 μm). The coronary ostia remained unaffected.

Conclusions: This study shows fewer severe lesions in the aorta after transapical antegrade access compared to the transluminal retrograde approach. Especially noteworthy is that the aortic arch remains unaffected by the transapical procedure. These data demonstrate the transapical approach as less hazardous.

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Keywords: Resection; Histology; Percutaneous; Endovascular; Transapical; Human; Aortic valve; In situ

1. Introduction

Less invasive strategies for cardiosurgical procedures have become more important in the last years since pioneer work in this field began [1,2]; especially catheter based valve interventions are upcoming.

Nonetheless, catheter-induced complications are seen too often. Tissue injuries, aneurysms, even vascular ruptures still occur. ‘… A rupture of the iliac artery is a serious, potentially life-threatening complication …’ [3].

The above complications with atherosclerotic peripheral arteries and aortas also occurred in conjunction with percutaneous valve interventions [4]. These catheter systems have significant larger outer diameters than catheters for coronary interventions [5].

The novel alternative via a transapical access might be less traumatic, especially since it avoids crossing of the aortic arch [6–8].

In this study we analyze the gross anatomy and the histological findings after retrograde versus transapical aortic valve isolation and resection in a human cadaver model.

2. Materials and methods

2.1. The aortic valve isolation chamber (AVIC)

In the following setup, two different kinds of AVICs were used: an AVIC system for a retrograde approach (Fig. 1A) and an AVIC system for transapical use (Fig. 2A).

The pressure of AVIC balloons was monitored on-line to prevent unnoticed pressure decrease caused by leakage with a subsequent unstable chamber function.
0.3 l/min was established by rotary pump (Stoeckert Instruments GmbH, Munich, Germany) to ensure a clear view.

### 2.2. Aortic valve resection tool

The aortic valves were resected by means of a continuous wave Thulium:YAG laser (ITL 2000, LISA laser products OHG, Kaltenburg/Lindau, Germany) emitting at a wavelength of 2.01 μm with a maximum power of 60 W. The radiation was transmitted by an optical low-OH quartz fibre with a core diameter of 365 μm (HCL-MO 365 Laser Components GmbH, Olching, Germany). A laser power of 20 W was used for tissue resection.

The fibre was controlled by a flexible endoscope (Richard Wolf® GmbH, Knittlingen, Germany) with an outer diameter of 7.5 F and a length of 600 mm.

### 2.3. Human preparations

Before death, these people gave a written consent to the Institute of Anatomy of the Christian-Albrechts-University of Kiel (n = 13, age: 71 ± 10 years; gender: 6 female, 7 male; weight: 67.2 ± 10.6 kg; height: 169.9 ± 8.0 cm). The study has been approved by the ethics committee of the University of Kiel from the 24th of November 2004 (D 434/04).

### 2.4. AVIC deployment

For endoluminal resection from retrograde, the AVIC system was deployed via the descending aorta (Fig. 1B). The resection endoscope was inserted via the right carotid artery (Fig. 1C).

The transapical AVIC was deployed via an intercostal approach of the left thorax (intercostal space IV–V) (Fig. 2B). The apex of the left ventricle was secured with two 3.0 monofil purse string sutures. For transapical resection, the endoscope was inserted via the main AVIC system.

### 2.4.1. AVIC deployment force

Additionally, the deployment force of AVIC from retrograde to pass the aortic arch was analyzed. For analyzing the deployment force, the aortic arches were explanted and fixed onto a rectangular metal mesh. This mesh was four-point-fixed with four metal strings, hanging from the ceiling of the lab. A Newton-measuring device was placed on the short side of the mesh. There, the femoral arteries were placed. Then, the investigated catheter was inserted into the aorta and the deployment force was measured.

### 2.5. Endovascular aortic valve resection

The endoscope was controlled by a cardiac surgeon. Three assistants handled the forceps catheter, endoscopic visualization, chamber perfusion, and pressures of AVIC (balloons and chamber) (Figs. 1D and 2C).

The resection process was similar in both setups. The aortic leaflets were stabilized with the forceps catheter (Ø 1.3 mm, Richard Wolf® GmbH, Knittlingen, Germany), and the resection
was performed. The process was video controlled (using a 30 in. TV) and digitally recorded. The leaflets were excised 2–3 mm from the insertion point of the annulus. Fragments of the resected leaflets were removed through AVIC. After resection, the AVIC, resection endoscope, and port were removed.

2.6. Analyzed parameters

The lesions observed in the surrounding tissue were protocolled. Gross anatomy and micropathology of the following structures were analyzed: aorta, including the descending aorta, the aortic arch, and the ascending aorta, the aortic annulus, the endomyocardium, the mitral valve, and the papillary muscles.

For gross anatomy, the structures were closely inspected and digitally photo documented (Exilim, Casio, 10.1 megapixels). The lesions were excised and subsequently fixed in 4% neutral buffered formalin. These specimens were embedded in paraffin and processed for routine microscopy procedures. The character of the general architectural features was evaluated using Hematoxylin–Eosin stain.

3. Results

3.1. Gross anatomy findings after AVIC use with consecutive resection

The results were shown in Table 1.

3.2. Retrograde approach

Three lesions in the aortic annulus were observed after resection of the aortic valve (Fig. 3A). Gross anatomy of the ascending aorta showed abrasions of the intima (Fig. 3B). All aortas (71 ± 10 years) showed moderate to severe atherosclerosis, as already known especially in regions of significant blood stream turbulence. Therefore, after passing the arch with the AVIC system, superficial damage up to complete

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TL; transluminal, TA; transapical, X; lesion.

Fig. 3. (A) View from the ascending aorta to the resected aortic valve. One lesion is located right coronary annulus and the second one in the annulus near the commissure coronary to left coronary leaflet (red rings). (B) Abrasion of the intima in the ascending aorta (red ring). (I–VI) Different lesions of the aortic arches were shown by red rings. The symbol ‘star’ indicated the brachiocephalic trunk. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

Fig. 4. (A) Lesion of the annulus after resection from transapical (red ring). The mitral valve remains unaffected. (B) The analysis of papillary muscles demonstrated minor lesions in the trabecular area (red rings). (C) The endomyocardium was slightly affected by the insertion of the AVIC (red ring).
separations of calcified plaques were demonstrated (Fig. 3I—VI). No lesions were observed in the region of the mitral valve, the papillary muscles, and the endomyocardium.

3.2.1. AVIC deployment force

The force to pass the arch for the customized catheter was 12 N (range 10—14 N) and 9.5 N (range 3—15 N) for the AVIC system (Fig. 4).

3.3. Transapical approach

Gross anatomy showed no lesions in the aorta during AVIC deployment and aortic valve resection. After resection, the annulus was affected twice (Fig. 5A). The inspection of the endomyocardium demonstrated superficial abrasions in all cases (Fig. 5B). The mitral valve was unaffected and only minor slight lesions were found on the papillary muscles after AVIC deployment (Fig. 5C). The other structures appeared unaffected by the resection process.

3.4. Micropathology findings after AVIC use with consecutive resection

3.4.1. Retrograde approach

The presence of lesions in selected tissue samples was proven by light microscopy. The aortic structure was disrupted by calcified plaques, especially in the aortic arch close to the brachiocephalic trunk (Fig. 6A,B).

The lesions in the ascending aorta were located in the intima layer of the aorta with a depth of $488 \pm 103 \mu m$ (Fig. 6C).

After resection, three lesions were observed in the annulus with a depth of $583 \pm 186 \mu m$ (Fig. 6D—F).

3.4.2. Transapical approach

The histopathology of the annular lesions indicated one lesion with a depth of $120 \mu m$ (Fig. 7A) and one complete perforation (Fig. 7B). On average the superficial abrasions of the endomyocardium were $258 \pm 102 \mu m$ (Fig. 7C). The abrasions of the papillary muscle showed a depth of $425 \pm 35 \mu m$.

![Fig. 6.](image)  
Fig. 6. (A) Annular lesion after resection of the aortic valve. (B) Complete perforation (arrow) of the aortic annulus after resection. (C) Superficial abrasion of the endomyocardium after transapical deployment of the AVIC system. (H&E staining.)

![Fig. 7.](image)  
Fig. 7. The deployment force in Newton (N) of the customized catheter and the AVIC system been displayed.
3.4.3. Resection process
In case of anatomical differences of the aortic root and the ascending aorta, the resection procedure cannot be performed in an accurate way. Therefore complete removal of the valve was not possible. Optimizing the exact tractability of the resection devices used is one of the important milestones for the future.

4. Discussion
This study shows that the transapical access to the aortic valve is less traumatic than the retrograde access via the aorta.

In both groups, lesions were found on different cardiac structures, but the lesions have varying hazards. The cadaver group in this study was not previously selected based on clinical parameters. Calcified femoral vessels occurred in all cadavers.

The vulnerable structures in the transapical group were indicated as the apex, the endomyocardium, and the papillary muscles. The apex was not analyzed in this study, but experimental and clinical experiences demonstrated rare complications due to the transmyocardial access [9,10]. Superficial lesions of the endomyocardium may not result in severe complications, as well as slight abrasions of the papillary muscles. In the worst case, the papillary muscle damage may lead to mitral dysfunction. The transapical way as an access to the aortic valve seems to be less risky.

In comparison to the transapical access, the main vulnerable structure in the retrograde group was indicated as the 'road' to the valve: the aorta, especially the aortic arch and the iliac and femoral vessels. Moderate to severe atherosclerosis was observed in nine of nine aortas. As shown in the results, six of nine aortic arches were injured after AVIC installation. The deployment force to cross the aortic arch was high, not only by using the self-constructed AVIC system, but also by using a customary application catheter. As observed in the experiments, calcified plaques peeled off during AVIC and customary catheter deployment. In a living organism, the injury of the aortic intima may result in intrusion of blood between the intima and media. A type A or B dissection of the aorta may occur.

Webb et al. already invented a catheter with a steerable distal tip that alleviates the arch cross and helps to pass the diseased aortic valve [11]. One main intent in percutaneous valve procedures should be to secure the aorta. The incidence of stroke in clinical trials is fortunately low. The pre-interventional screening of patients is important to detect calcifications of the aorta. Then, interventional procedures may be performed more safely and this will prevent aortic injuries and atheroembolisms [10,12].

The analyzed iliac and femoral arteries in this study were mostly diseased and calcified. During the experiments, it was neither possible to insert the standard catheter nor the AVIC system. In clinical routine, this problem is well known, also in cardiac surgery, if a femoral—femoral bypass is necessary and the vessels were not suitable for cannulation [13–15]. The above-mentioned screening has to include the peripheral vessels before starting percutaneous valve interventions [10].

The amount of analyzed lesions in the gross anatomy and the histology is not significantly different. But here the nature and the region of the lesions are most important. The complication risk of a superficial lesion of the endomyocardium is not comparable to a dissection of a calcified plaque in the aortic arch. Therefore, a statistical analysis has not been performed. A risk stratification score might be more helpful and will be designed.

In consideration of the gross anatomy and the histopathological results of this study, the transapical access to the aortic valve might less traumatic. The comparison of clinical trials should be a further step to underline these results.

The presented study group might not be comparable to the clinical situation due the pre-interventional selection. In the presented cadavers all femoral vessels showed calcifications. Therefore, a more proximal approach has been chosen. But on the other hand, this shows that a relatively high number of patients may be rejected for the percutaneous approach due to the calcifications.

In this study, the main topic deals with the lesions of the surrounding structures, such as the peripheral and central vessels, and the heart tissue, such as the endomyocardium, the valves, and the coronary ostia. The resection procedure used in this analysis has been already described elsewhere in detail [16], and is not the subject of this analysis.

Up to now, an optical system provides best imaging for the aortic valve resection. It is more difficult to implement an optical system due to the transparency of the AVIC medium. But in the future, other visualization methods, such as 3D echo, MRI or CT will be more helpful for a precise surgical manipulation in the heart. The resection of the aortic valve with the actual procedure cannot be used clinically. The perforation of the annulus is a serious injury that has to be avoided. The invention of a safe tractability of all resection instruments and an optimal visualization is ongoing.

The future goal of catheter-based aortic valve replacement will be use of the percutaneous approach. The transapical method has a good chance to become relevant in clinical routine, but preparations of the annulus even to complete removal of the native diseased valve will be key, especially in younger patients. If a safe surgical percutaneous technology with an equal outcome to current open aortic valve replacement is available in 10 or 20 years, every patient would choose this technique. Therefore, the tractability and the preciseness of the resection tools have to improve to perform a safe, fast and complete pre-treatment of the valve.

4.1. Limitations
The human cadavers were preserved with formalin and the experiments have not been performed under pulsation or pressure. The results may be different in an in vivo model. The customized catheter used was not deflectable. The deployment force may be reduced in using a steerable catheter.

Acknowledgements
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their great work and support. Special thanks to Professor Sievers, Professor Wedel, and Marion Krüger.

Sincere thanks to Gerburg Lutter and Lasse Bombien.

References


[12] Schachner T, Vertacnik K, Laufer G, Bonatti J. Axillary artery cannulation with the transapical device or will you also work with the intravascular device? And also maybe you can elaborate a little bit more on the reason for the aortic annulus rupture that you have shown us. Now, the results that you have shown mimic a little bit the results with the transcatheter valve implantation in that so far we do not see cerebrovascular accidents with the transapical approach, so I think this is pertinent.

[13] Maybe you can elaborate also a little bit more on what you said about having to decalcify the annulus. The prostheses we implant now show about in 10–15% more than grade 2 paravalvular leaks but not more, and they show excellent hemodynamics. So I am not quite sure whether you really have in the future to decalcify the annulus. But if you do it, what kind of valves do you want to implant in the decalcified annulus, because the valves you implant right now all need the calcified support of the annulus.

and then my last question would just be what is your perspective for the future, because you don’t elaborate in your paper very much on this. Is this planned to be on-pump, off-pump, and how can you imagine this kind of procedure in a living human being?

Dr Bombien: In the past we started with the intravascular approach for the resection, but the transapical approach offers a better way to the valve: it is direct and the aortic arch remains untouched. Nevertheless, the development of the intravascular approach is also ongoing because this will be a future aim, to reduce the outer diameter of the system and to improve the tractability of the instruments with access through the groin.

Regarding the annulus perforation, this was a technical problem: the resection device was pressed into the annulus before we could stop the laser, so there was a complete perforation of the annulus. We must avoid this in the future.

The next point that we fortunately did not see many cerebrovascular insults in the actual trials is right. Results depend on the structure of the aortic arch. If the aortic arch is also very calcified, more problems with cerebrovascular insults will occur.

The third question was about the anchoring of the valve and decalcifying the annulus. As each cardiac surgeon in the operating room dealing with bulky calcified aortic leaflets observed, they cannot be pushed well into the aortic annulus. The aim of the resection is to prepare the annulus for an implantation that means to remove these bulky calcifications, not to decalcify the whole annulus. The calcium is necessary to anchor the valve, as you mentioned.

Regarding future prospects, we are now working on a beating-heart, pump-supported approach, and I believe we will be able to successfully accomplish it off-pump on a beating heart.

Dr F. Casselman (Aalst, Belgium): I totally agree with the idea of their group that if we want to move forward with this technology that it is important to respect the native aortic valve. What specific tools did you use or do you look at in the future to precisely measure the depth or the distance at which you have to resect the valve?

Dr Bombien: That is a very good point.

Dr Casselman: TEE, any other tools? What is the value of three-dimensional TEE vs two-dimensional TEE or any other tools that you may look at?

Dr Bombien: I think it is very important to have good imaging for the entire procedure. Now we are using a direct vision, so we can see endoscopically. But we are just working on computer-assisted visualization and micro-system tools, to improve the accuracy of the resection.

Dr C. Huber (London, United Kingdom): If you were to focus more on the transapical approach rather than the transfemoral percutaneous approach, would this allow you to have a less flexible system, and therefore shorten resection time as you then might be able to have a more automatic end bloc continuous laser removal of the valve instead of having this quite challenging point-by-point laser burning?

Dr Bombien: I think we have started to reach this goal in the last experiments, by reducing the resection time accessing transcatheterically because you do not have to cross the aortic arch.

Dr Lutter: As you have already explained, the key is to proceed further with this project despite these small microscopic and macroscopic lesions caused by the ablation of the aortic valve. That means we must make the jump to transapically ablate the aortic valve on a beating heart. We are very confident that this procedure will be possible, and, as you have demonstrated to us, from year to year we are making much progress in improving this technology.

Appendix A. Conference discussion

Dr R. Lange (Munich, Germany): What you have shown is that decalcification of the annulus is possible by the laser and that there are lesions by the laser. Now, reading your paper, there are some things I am missing, but I am sure you can clarify this.

First, in terms of the results, will you continue your study in the future now exclusively with the transapical device or will you also work with the