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Percutaneous aortic valve replacement: valvuloplasty studies *in vitro*

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Abstract

Objective: Valvuloplasty of the aortic valve is currently used in selected patients for severe calcified aortic valve disease, but clinical effectiveness is low and complication rate remains high. In this study, the total particle load after valvuloplasty and the embolization risk of calcific debris into the coronary arteries was analyzed in an *in vitro* model. **Methods:** Three highly calcified human aortic leaflets have been sutured into a porcine annulus ($N = 9$). Both coronary arteries were separated and each was anastomized to a silicon line, which was drained off into a measuring beaker. Then valvuloplasty was performed (Thyshak II, 20 mm, 1.5 atm). After removal of the balloon, 100 ml of sodium chloride solution irrigated the ascending aorta. After passing through the separated coronary arteries, the solution was filtered (filter size 0.45 μm), dried, and the total amount of particles was analyzed microscopically. **Results:** Nine experiments were analyzed. After valvuloplasty, all hearts showed a median of 18 particles larger than 1 mm in the coronary arteries (range 0–307). The amount of particles smaller than 1 mm was 6574 (median, range 2207–14200). In five cases, coronary arteries were completely occluded by bulky particles. **Conclusion:** This study demonstrated a large amount of calcific particles after valvuloplasty with a consequently high risk for coronary embolic events in case of highly calcified aortic valves. In times of valvuloplasty rediscovering as part of transcatheter valve implantation, the risk of embolization should be taken into consideration and filtering techniques have to be developed.

Keywords: Percutaneous; Aortic valve; Valvuloplasty; In vitro

1. Introduction

Calcified aortic valve stenosis is a common disease in the elderly. The gold standard to treat a symptomatic aortic valve stenosis is surgical valve replacement. In the past, valvuloplasty of the aortic valve was used as a bridge to operation or as a palliative attempt. The outcome after valvuloplasty was poor when compared with the complication rate. Common complications are stroke, myocardial infarction, and aortic dissections. Therefore, the use for valvuloplasty in clinical routine remains limited [1]. Transcatheter technology for aortic valve implantation led to a renaissance of valvuloplasty. Different types of valved stents can be implanted using an antegrade or a retrograde approach [2]. The results of the antegrade approach from the left-ventricular apex are promising [3]. Valvuloplasty is obligatory to dilate the native, commonly calcified annulus before the valved stent can be implanted [4]. Despite the results of a sole valvuloplasty, there are no data regarding the amount of particles resulting from the dilation of the valve.

In this study, the amount of particles that embolized into the coronary arteries after valvuloplasty was analyzed in an *in vitro* model.

2. Material and methods

2.1. Human calcified aortic leaflets

Highly calcified human aortic leaflets were taken from the operation room. The procedure was approved by the Ethics Committee of the Christian–Albrechts–University of Kiel from the 24th of November 2004 (D 434/04).

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2.2. Valvuloplasty device

For all valvuloplasties, a commercially available valvuloplasty balloon Thyshak II® (NuMED, Inc., New York, USA) with an outer diameter of 20 mm and a maximum pressure of 1.5 atm was used.

2.3. Experimental setup

To obtain an aortic annulus to analyze the debris rate in the coronaries after valvuloplasty, nine isolated porcine hearts (approximately 300 g) were taken from the slaughterhouse. All hearts were prepared as follows: the ascending aorta was dissected 4 cm distal to the aortic valve. The aortic diameter was 2.0 $\pm$ 0.1 cm (mean $\pm$ SD). Thereafter, left and the right stem of the coronary arteries were dissected approximately 2 cm distal to the coronary ostia (Fig. 1(A)). Coronary arteries were dissected and subsequently anastomized to a silicon tube with an outer diameter of 2.5 mm, using a monofil suture (Prolene® 6.0). These 15 cm-long 'neo-coronaries' were drained into a measuring beaker (Fig. 1(B)).

All three calcified leaflets of one aortic valve were prepared. Each leaflet was sutured into each coronary sinus of the native porcine annulus using a running monofil suture (Prolene® 5.0) (Fig. 1(C)–(E)).

2.4. Valvuloplasty procedure

The heart was fixed in a box (Fig. 2(A)). Then, the valvuloplasty was performed with a fully inflated Thyshak II balloon under fluoroscopy and computed tomography (CT) scan control (Fig. 2(B) and (C)). After removal of the balloon, irrigation water (saline solution, 0.9%) was administered into the ascending aorta. This irrigation water could only pass through the coronaries or the aortic valve into the left ventricle. However, the water had no possibility to leave the aorta. The distal aorta was functionally closed. Once 100 ml saline solution passed the neo-coronaries, the irrigation water was filtered on a plane filter paper 10 cm in diameter and a porosity size of 0.45 μm. Thereafter, the filter was dried, and the quantity and quality of calcific particles were microscopically analyzed. The amount of particles was ordered to 100 ml saline solution.

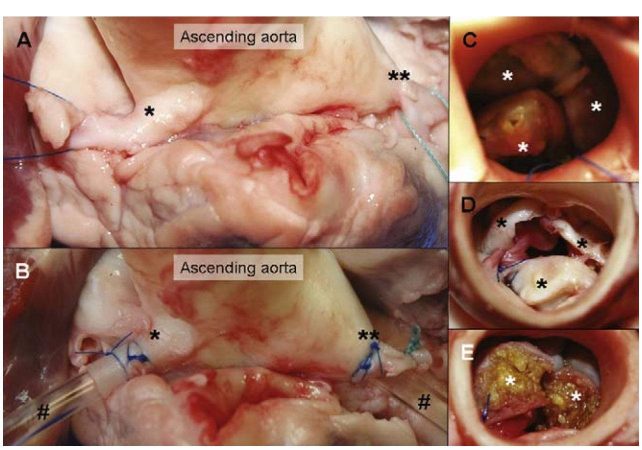

Fig. 1. (A) Dissection and isolation of both coronary arteries (*: right coronary artery; **: left coronary artery) in an isolated porcine heart. (B) After isolation both coronary arteries (*, **) were cut and each anastomized with silicon tubes (#). (C–E) Then, highly calcified human aortic leaflets (*) were sutured into the aortic annulus.

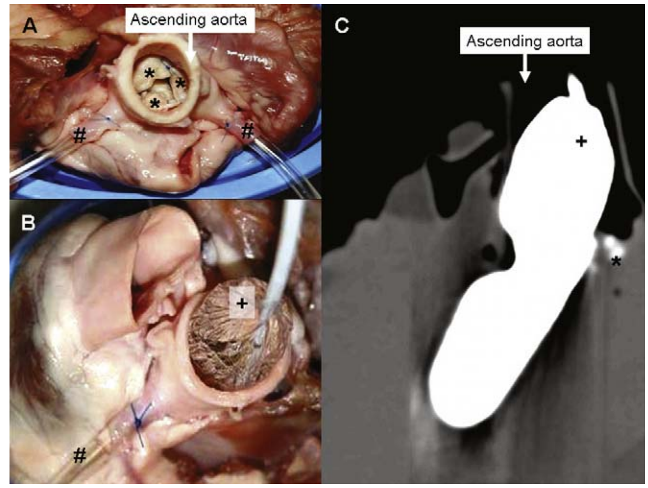

Fig. 2. (A) Prepared experimental setup. (B) Insertion of the valvuloplasty balloon (Thyshak II, +). (C) CT scan of the valvuloplasty balloon (+) during procedure (* highly calcified human-aortic leaflets).

2.5. Analyzed data

The filter paper was dried and fixed into a Petri dish (diameter 10 cm). Then, the filter paper was divided into representative equal pieces. The particles of one piece were counted using a binocular microscope. Subsequently, the amount of particles was multiplied with the number of pieces. The graduation was differentiated in particles smaller and larger than 1 mm. There was no previous determination of the debris coming from the left or the right coronary artery. The data were presented as minimum, maximum, and median values.

3. Results

All experiments were analyzed. The results of the particles counted after valvuloplasty are displayed in Fig. 3. In five cases, a median of 18 particles larger than 1 mm with a range from 0 to 307 were observed. In all these cases, the coronary

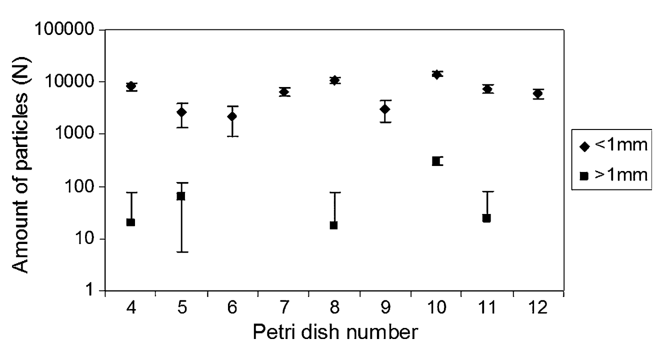

Fig. 3. The amount of particles in each Petri dish is displayed. In all nine cases, there were particles smaller than 1 mm observed. Only five experiments showed particles lager than 1 mm. The scale is logarithmic.

arteries were completely obstructed. In four experiments, no particles larger than 1 mm were observed. The median of particles smaller than 1 mm was 6574 with a range from 2207 to 14 200. No major events, such as disruption of the aortic annulus or dissection of the coronary ostia, were observed after valvuloplasty.

4. Discussion

There is little known about the occurrence of debris embolizing into coronary arteries during valvuloplasty of calcified aortic valves. Literature reported a stroke rate of 1.3—4% [5,6]. In this study, the debris rate in an *in vitro* model with severely calcified aortic valves has been analyzed. The data show a high number of particles smaller than 1 mm in all cases. A high number of small particles make sense during valvuloplasty. However, what happens with these particles in the clinical setup?

Valvuloplasty is generally carried out during a period of rapid pacing. With the first heartbeat after this pacing, approximately, 50—60% of its volume will be flushed in to the aorta. Suspecting a physical model, low-density particles will be carried faster into the circulatory system, especially into the brain. This model matches with the findings of stroke after valvuloplasty. In most cases, only mild transient cerebral malfunctions are observed. A current publication analyses high-intensity transient signals (HITS) in the carotid arteries during implantation of valved stents [8]. Such particles were observed in all patients. The highest amount of microembolic events was detected during valvuloplasty and positioning of the valved stent in the aortic annulus. After the procedure, there were no clinical signs of cerebral ischemia. By contrast, particles with high density will be more inert with a higher risk of embolization into the coronary ostia during the first heartbeats. After passing the aortic arch, embolization into the mesenteric arteries, the kidneys, and the lower extremities would also be possible. Our experimental results demonstrated occlusion of the coronary ostia in five cases. In a clinical setup, myocardial ischemia up to myocardial infarction may occur [7]. Nevertheless, in the current guidelines of transcatheter valve implantation, there are no data concerning stroke risk caused by the valvuloplasty procedure or the subsequent implantation of the valved stent [4]. In addition, there are no strategies to avoid the debris problems.

The particles in this study demonstrated the total amount of particles that will be distributed to the whole body. This seems to be high, but because there are no other comparable experimental data, we can only hypothesize about their impact in the patient. We predict that a large number of calcified particles will be released during the actual transcatheter valve stent implantation in highly calcified aortic valves without post-procedural clinical signs of stroke or myocardial ischemia. However, ignoring the occurrence of these particles will not solve the problem, especially in young patients. To secure the circulatory system from these emboli, different options have been assessed in the past [9—11]. Unfortunately, currently, there are no valuable filtering systems for clinical routine used in the actual transapical or transfemoral procedures. In addition, debris also occurs during the placement of the whole delivery system. In a recent *in vitro* study, it could be shown that there are more plaque ruptures and aortic lesions using a transfemoral approach [12].

The particles in the *in vitro* experiments were not allocated to their origin coronary ostium. It will be important if the patients' dorsal position forward the left-main stem occlusion by particles with higher density [13]. Furthermore, the results may lead to the assumption that this experimental model overestimates the number of embolic events in contrast to the clinical setting. There are two possible explanations: firstly, the human calcified aortic leaflets were reinserted into the porcine annulus — a predetermined breaking point can occur at the suture line and can release more particles during valvuloplasty. On the other hand, the annular line is the part of the aortic valve which may be mostly affected by radial stress during valvuloplasty. If the surface layer of the valve has been lacerated, calcified debris can be released, too. Secondly, a 100% realistic circulatory situation could not be displayed in the current model. Therefore, an *in vivo* model is planned to evaluate the results of this study in detail.

The identification of calcific debris in the coronary arteries before and after valvuloplasty and consecutive valved stent implantation will be advantageous.

Another important point is the rapid-pacing sequence during valvuloplasty and valve implantation. The necessity of rapid pacing generates a volumetric overload of the left ventricle. In case of a severe aortic valve calcification and stenosis, the left-ventricular myocardium is hypertrophic. An overexpansion of the myofibrils can result in ventricular fibrillation and in a significant decrease of the global ventricular function [14]. Therefore, it will be superior to avoid any volumetric overload.

The avoidance of extensive valvuloplasty and the occurrence of obstructive calcified debris might be very important, if the transcatheter valve-implantation technology is to be used in young patients. Therefore, removal of highly calcified aortic valves will be necessary and has to be done under safe conditions. The aortic valve isolation chamber is a preliminary experimental technique to isolate the aortic valve during resection and implantation of the new valved stent [15—17].

5. Conclusion

It will be important to develop a system for aortic valve replacement without an unsecured valvuloplasty under rapid pacing of the diseased heart muscle to come closer to the surgical gold standard of aortic valve replacement.

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