Coronary flow obstruction in percutaneous aortic valve replacement. An in vitro study[☆]

Erwan M. Flecher, John W. Curry, Thomas M. Joudinaud, Corrine L. Kegel, Patricia A. Weber, Carlos M.G. Duran[*]

The International Heart Institute of Montana Foundation at Saint Patrick Hospital and Health Sciences Center and The University of Montana, Missoula, Montana, USA

Abstract

Objective: Coronary flow obstruction is a serious complication reported in percutaneous aortic valve replacement. In an in vitro study of porcine hearts, the effects of valved stent implantation on coronary artery flow were studied with the native valve's leaflets intact and excised. **Methods:** The right and left main coronary arteries of porcine hearts were dissected 20 mm distal to the aortic root and directed into lengths of latex tubing leading to collection flasks. The ascending aorta was cut proximal to the brachiocephalic trunk, cannulated, and attached to a constant-head water supply. After steady flow was achieved, the flow rate from each coronary artery was measured. In Group A ($n = 10$), a tubular pericardial valve sutured into a cylindrical, cobalt—nickel stent was deployed orthotopically using a valvuloplasty balloon catheter. In Group B ($n = 10$), the native leaflets were removed before similar valve deployment. Coronary flow measurements were repeated post-implantation. **Results:** In Group A, valve implantation resulted in a significant decrease in both left and right coronary flows. In Group B, no significant change in either right or left coronary flow was found after valve placement. **Conclusion:** Implantation of a percutaneous valved stent in the orthotopic position with the native valve in place causes coronary ostial obstruction. This problem highlights the need for modified stents that are designed for implantation in patients with non-retracted, fibrotic, or calcified leaflets.
© 2007 European Association for Cardio-horacic Surgery. Published by Elsevier B.V. All rights reserved.

Keywords: Aortic valve; Replacement; Percutaneous; Coronary artery flow

1. Introduction

Orthotopic percutaneous aortic valve replacement (PAVR) in pigs was first reported by Andersen in 1992 [1]. He described obstruction of the coronary ostia as one of the major issues associated with this procedure. This problem, frequently reported in experimental animal studies [2,3,4], has also been encountered in humans, albeit less frequently [5,6]. This discrepancy might be due to the presence of normal valve leaflets in the animal versus fibrotic and calcified leaflets in human patients. This fact would exclude PAVR in cases of pure regurgitation. To elucidate this issue and explore possible technical alternatives, we undertook an in vitro study of the diastolic coronary flow after deployment of a valved stent in an isolated pig heart with intact and excised valve leaflets.

2. Materials and methods

Twenty explanted pig hearts were divided into two equal groups of 10. In each specimen, the left and right coronary arteries were isolated and transversely cut 2 cm distal to their origin. The cut ends of the coronaries were directed into lengths of five-eighths-inch standard laboratory latex tubing leading to two graduated plastic collection flasks. The aorta was cut just proximal to the brachiocephalic branch and attached with zip ties to a 1.125-in. diameter cannula. The cannula was fixed with a ring stand and attached to a constant head pressure source set to provide 60 mmHg of pressure. A valve was placed between the cannula and the pressure tank to start and stop flow.

Baseline coronary flow with the native aortic valve was measured and recorded for each specimen. Flow rate was determined for each coronary artery by measuring flow volume over a timed 30-s interval. In Group A ($n = 10$), a valved stent was placed under direct vision in the native position and fully expanded without the removal of the native leaflets. In Group B ($n = 10$), the same procedure was performed after the native leaflets were removed. After the
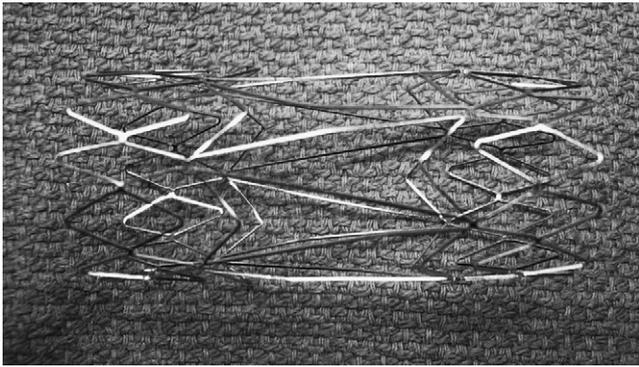
Fig. 1. The percutaneous aortic valve stent used in this study.

valved stent was expanded, coronary flow was again measured for each specimen.

Customized, cylindrical cobalt—nickel stents with lengths of 32 mm (Medtronic Inc., Minneapolis, MN, USA) were used in this study (Fig. 1). The pericardial valve sutured inside the stent was manufactured in our laboratory as reported by Goetz et al. [7] from a flat piece of fresh sheep pericardium. The fat and fibrous strands of the mediastinal surface of the pericardium were cleaned. The tissue was treated with 0.6% buffered glutaraldehyde for 10 min and rinsed with 0.9% sodium chloride. A flat template with a trapezoidal shape of the appropriate size was placed on the treated pericardium (Fig. 2). The pericardium was then cut into a flat, trapezoidal shape. The locations of three equidistant commissures were marked with three 5—0 polypropylene sutures placed on the longer, or outflow, length of the pericardium.

The pericardium was wrapped over a plastic holding cylinder with an appropriate diameter, and its lateral sides were sutured together with a running 5—0 polypropylene suture to convert the flat pericardium into a truncated cone with smaller inflow and larger outflow diameters (Fig. 3). The inflow end of the valve was then sutured with interrupted stitches of 6—0 polypropylene at each intersection of the metal stent loops. To avoid paravalvular leaks between these stitches, a 2—0 polyester suture was placed and tied around the inflow orifice of the stent. The spaces between the above stitches were then closed with further stitches between the valve rim and the 2—0 suture. The outflow orifice of the pericardial tube was anchored to the stent at only the
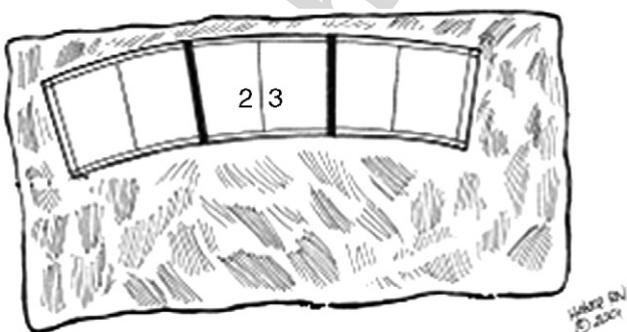

Fig. 2. Construction of the pericardial tubular aortic valve. Trapezoidal shaped flat template of the appropriate size is used to trim a flat rectangle of glutaraldehyde-treated pericardium. From [7], with permission.
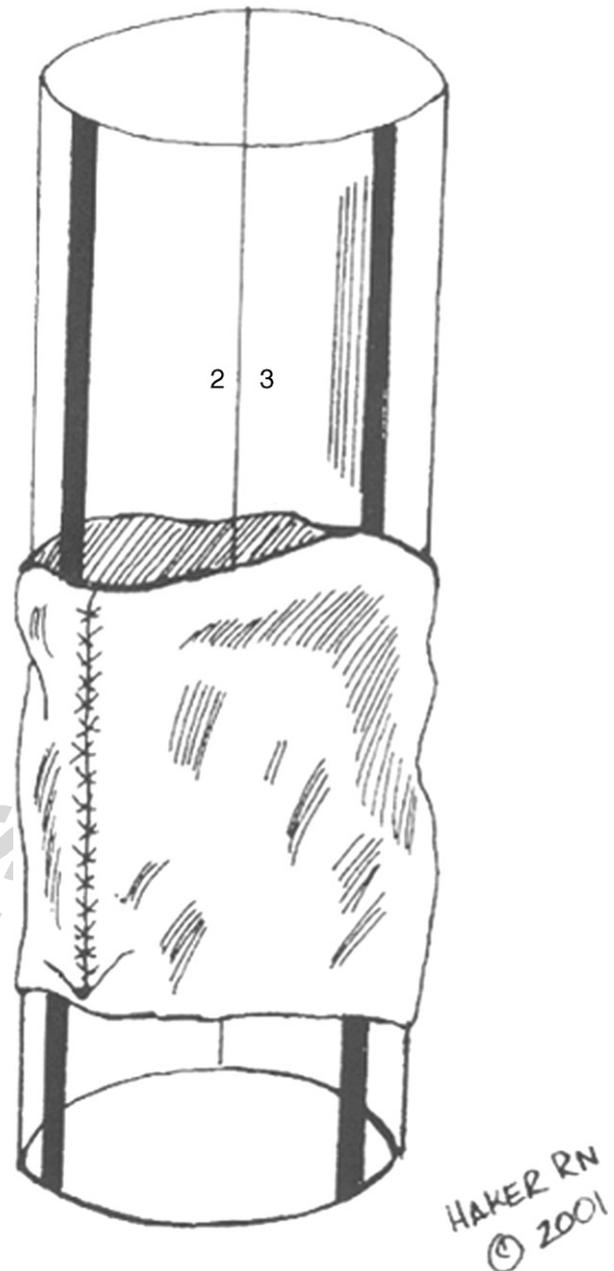
Fig. 3. Construction of the pericardial tubular valve. The trimmed pericardium is wrapped over a plastic holding cylinder with an appropriate diameter. The lateral sides of the pericardium are sutured together with a running 5—0 polypropylene suture to form a truncated cone with a smaller inflow and larger outflow diameters. From [7], with permission.

three (previously marked) equidistant 'commissural' points (Fig. 4).

The valved stents were expanded using a percutaneous valvuloplasty catheter (Z-MED II, NuMED Inc., Denton, TX, USA) inflated to a pressure of 2 atm for 20 s. The native aortic annulus was measured using Duran spherical sizers (Medtronic Inc., Minneapolis, MN, USA). The stent was over-expanded in each case, then the next available balloon size larger than the native diameter was used to deploy the valved stent. In each experiment, the valved stent was positioned so that the annulus and commissures of the

Fig. 4. Final aspect of the pericardial tubular valve sutured within the endovascular stent.

prosthesis were aligned with the native annulus and commissures.

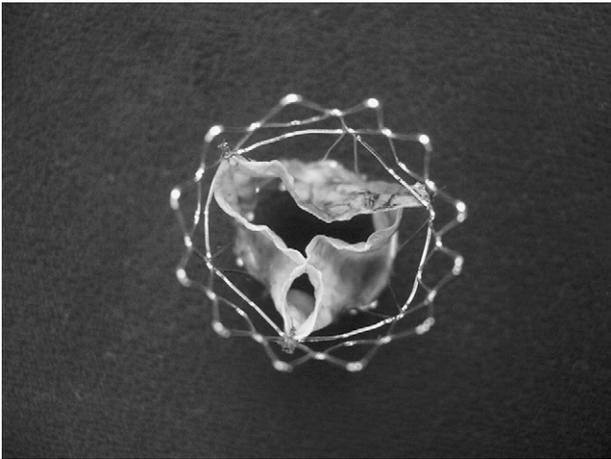After each experiment, the ascending aorta was longitudinally opened, and the exact position of the stent was checked. The distances from coronary ostia to stent, coronary ostia to native leaflets free edge ('intact' group), and coronary ostia to leaflet remnants ('excised' group) were measured.

Student's *t*-test was used to compare measurements between the two groups, and a *p* value less than 0.05 was considered significant.

3. Results

Implantation of the valved stent caused a significant decrease in both left and right coronary flows for the group with the native valve intact (Group A). No significant change in coronary flow was observed when the native leaflets had been excised (Group B). The results are shown in Table 1.

In Group A, the decrease in left coronary artery flow was significantly greater than in Group B. A partial obstruction or total occlusion of the left ostia was found in 9 of 10 specimens. In each of these cases, the obstruction was due to native leaflet sandwiched between the stent and the aortic wall. The right ostium was obstructed in 2 out of 10 specimens: in one case due to the native leaflet acting as a flap on the ostium and in the other because of ostial

Table 1
Pre- and post-valve implant coronary flow measurements for Group A (native leaflets intact) and Group B (native leaflets removed)

	Flow baseline (ml/s)	Flow post-implant (ml/s)	Percent change
Group A			
Left (*n* = 10)	24.25 ± 7.24	18.61 ± 10.24	−42.8[*]
Right (*n* = 10)	20.26 ± 3.99	16.32 ± 4.76	−18.2[*]
Group B			
Left (*n* = 10)	30.38 ± 4.77	30.64 ± 4.78	+1.0
Right (*n* = 10)	19.80 ± 5.34	19.26 ± 5.09	−1.8

All readings were taken at a constant aortic pressure of 60 mmHg.
[*] $p < 0.05$.

obstruction by malrotation of a commissure of the valved stent. At the end of the procedure, the stent's proximal inflow orifice was found correctly placed at the level of the native annulus in each case.

In Group B, no significant modification of coronary flow was found. With one exception, each stent's proximal inflow orifice was found well placed at the end of the procedure. The excepted stent had migrated 1 cm below the aortic annulus into the outflow tract of the left ventricle.

4. Discussion

Our results confirm that coronary ostia obstruction may occur after PAVR. We identified the native leaflets as the main cause of right or left coronary obstruction. To our knowledge, this is the first in vitro study to investigate the mechanism of coronary obstruction in PAVR. In this animal model, the left leaflet was the most frequent offender. Although it is currently accepted that the sizes of the three sinuses of Valsalva are different, the fact that the order of magnitude changes according to species is less recognized. The left cusp was the largest in our model because the left cusp is largest in pigs, followed by the right, then the non-coronary sinus [8]. Further, a tilt angle between the plane of the aortic annulus and the plane of the sinotubular junction that is directed posteriorly and to the left [9] makes the left sinus the lowest. In humans, the non-coronary sinus is the largest, followed by the right, then the left [10]. These geometric relationships have been ignored in the design of modern aortic valve stents.

To avoid coronary obstruction by the patient's aortic leaflets, two options could be considered by the surgeon or interventional cardiologist. The first option would be removal of the native valve. The use of a high-pressure stream scalpel as a method for endovascular resection of human calcified aortic valves has recently been evaluated [11]. However, these experimental techniques require the capture of all debris to prevent embolization.

The second option would be the development of a stent designed to address the native leaflets. Specially designed stents could be developed that allow safe implantation without coronary obstruction and without removal of the native leaflets. A shorter stent placed as low as possible in the aortic annulus has obvious theoretical advantages, but its potential protrusion into the left ventricular outflow tract could damage the anterior leaflet of the mitral valve. The height of the Cribier—Edwards aortic prosthesis (Edwards Lifesciences, CA, USA) is only 14 mm, theoretically allowing implantation in the sub-coronary position without interference with the ostia. However, coronary obstruction of the left main trunk has recently been reported with this device leading to the death of the patient [6]. Alternately, the device reported by Boudjemline and Bonhoeffer [3] has a higher profile but an orientation mechanism that permits successful sandwiching of the native leaflets to immobilize them. Coronary obstruction by the native leaflets is probably less relevant in stenotic cases with very fibrotic and/or calcified leaflets; however, the search for methods to address the native leaflets should continue to expand the indications of PAVR to predominant regurgitant lesions.

With regard to the risk of coronary obstruction, another approach might be to use an original delivery catheter that allows repositioning of the valved stent after implantation in case of obvious acute coronary event. It has recently been described [12], and we may anticipate that the safety improvement offered by this new technology might favor the development of percutaneous valve replacement in clinical practice.

5. Limitations of the study

The main limitation of the study is that it is an in vitro study in an animal model with normal aortic valves. However, in vitro studies should be undertaken prior to expensive in vivo studies; they should serve as a filter to test and eliminate early designs and techniques. The long, cylindrical stent used in this study was a convenient model to analyze this problem because it enhanced the conditions for coronary obstruction by the valve leaflets. The superior in vivo approach would also be limited by the lack of an experimental animal model with calcific aortic stenosis. Recognition of the multiple limitations of present day models does not invalidate attempts at dissecting the multiple problems of PAVR.

6. Conclusions

This in vitro study shows that the deployment of a cylindrical, stented aortic valve can severely affect coronary flow by obstructing the coronary ostia with the native leaflets. Despite the model's limitations, these results suggest the design of novel stents for development and testing before animal or human implants are considered.

References

[1] Andersen HR, Knudsen LL, Hasenkam JM. Transluminal implantation of artificial heart valves. Description of a new expandable aortic valve and initial results with implantation by catheter technique in closed chest pigs. Eur Heart J 1992;13:704–8.

[2] Lutter G, Kuklinski D, Berg G, Von Samson P, Martin J, Handke M, Uhrmeister P, Beyersdorf F. Percutaneous aortic valve replacement: an experimental study. I. Studies on implantation. J Thorac Cardiovasc Surg 2002;123:768–76.

[3] Boudjemline Y, Bonhoeffer P. Steps toward percutaneous aortic valve replacement. Circulation 2002;105:775–8.

[4] Huber CH, Cohn LH, von Segesser LK. Direct-access valve replacement: a novel approach for off-pump valve implantation using valved stents. J Am Coll Cardiol 2005;46:366–70.

[5] Webb JG, Chandavimol M, Thompson CR, Ricci DR, Carere RG, Munt BI, Buller CE, Pasupati S, Lichtenstein S. Percutaneous aortic valve implantation retrograde from the femoral artery. Circulation 2006;113:842–50.

[6] Lichtenstein SV, Cheung A, Ye J, Thompson CR, Carere RG, Pasupati S, Webb JG. Transapical transcatheter aortic valve implantation in humans: initial clinical experience. Circulation 2006;114(6):591–6.

[7] Goetz WA, Lim HS, Lansac E, Weber PA, Duran CMG. A temporarily stented, autologous pericardial aortic valve prosthesis. J Heart Valve Dis 2002;11:696–702.

[8] Grande KJ, Kunzelman KS, Cochran RP, David TE, Verrier ED. Porcine aortic leaflet arrangement may contribute to clinical xenograft failure. ASAIO J 1993;39:918–22.

[9] Lansac E, Lim HS, Shomura Y, Lim KH, Rice NT, Goetz WA, Acar C, Duran CMG. A four-dimensional study of the aortic root dynamics. Eur J Cardiothorac Surg 2002;22:497–503.

[10] Choo SJ, McRae G, Olomon JP, St George G, Davis W, Burleson-Bowles CL, Pang D, Luo HH, Vavra D, Cheung DT, Oury JH, Duran CM. Aortic root geometry: pattern of differences between leaflets and sinuses of Valsalva. J Heart Valve Dis 1999;8:407–15.

[11] Quaden R, Attmann T, Boening A, Cremer J, Lutter G. Percutaneous aortic valve replacement: resection before implantation. Eur J Cardiothorac Surg 2005;27:836–40.

[12] Zegdi R, Khabbaz Z, Borenstein N, Fabiani J-N. A repositionable valved stent for endovascular treatment of deteriorated bioprostheses. J Am Coll Cardiol 2006;48:1365–8.

Appendix A. Conference discussion

Dr P. Kappetein (*Rotterdam, The Netherlands*): How sure are you that you can extrapolate your findings to the devices that are currently investigated in feasibility studies like the Cribier–-Edwards valve and the CoreValve? You said that it depends on the stent design and this design may vary among the different types.

Dr Flecher: Yes, the stent design I think is the main problem, and in the Cribier stent, the stent, as I said, is very, very short, and in the CoreValve there is a curve just in front of the coronary ostium to try to avoid obstructions. This is only an in vitro study and it was performed with normal leaflets, which I think also is important, because there is no calcium, it is not a calcified model, and the leaflets are very soft, very thin, and you can easily push them against the aortic wall. We were working on animals and that was the problem we had, and we don't have, as far as I know, a calcified model to do that.

Dr Kappetein: And so you use pig hearts?

Dr Flecher: Yes.

Dr Kappetein: Is the positioning of the stent of these valves more difficult in pig hearts than in human beings?

Dr Flecher: I think the most difficult ones are in sheep, because in sheep the distance is really, really very short between the coronary ostium and the native annulus. In pig hearts this distance is longer, and in human it is, again, longer too.

Dr Kappetein: But especially in human beings, the distance between the aortic annulus and the mitral valve is different from that in pigs.

Dr Flecher: It was interesting, but also we had much more decrease in the left coronary artery, because in the pig, the left coronary sinus is the most developed, it is the most important.

Dr A. Poostizadeh (*Vancouver, British Columbia*): I commend you for your study, but your study is talking about the pliable normal leaflet of the pig as opposed to a hard calcified leaflet of an aortic stenosis. Certainly we haven't seen it, or our cardiologists in over 70 percutaneous valves haven't really seen coronary flow obstruction. So I think it is a little different. It is a beautiful study, but I think it is just different anatomics.

Dr Flecher: You are right. In fact, human hearts were not easily available in Montana where I worked.