Concepts and Designs of a Percutaneous Temporary Aortic Valve

Concepts and Designs of a Percutaneous Temporary Aortic Valve:

An Anthology

By

Paul C. Ho

Cambridge Scholars Publishing

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This textbook is written with admiration, respect, and love for my mentor,
Dr. Julius Melbin, Professor Emeritus in the Department
of Bioengineering at the University of Pennsylvania.

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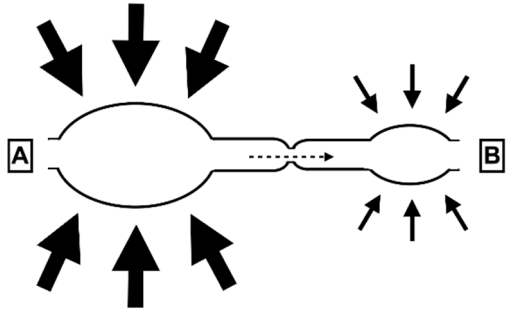
PREFACE

This anthology contains previously published manuscripts on the subject of a catheter-based temporary aortic valve. Each chapter represents a manuscript, and all the chapters together demonstrate the gradual development of this innovative device.

The concept of a temporary aortic valve stemmed from two ideas: a fixed orifice can serve the functions of an aortic valve, and the need for hemodynamic support when the native aortic valve is acutely nonfunctional. During medical school, studying the natural history of aortic stenosis instilled a fascinating realization. As aortic stenosis progresses, the leaflet mobility is gradually restricted due to a variety of pathological factors, including calcific deposits, fibrosis, tissue thickening, inflammation, scarring, and fusion. The end result may be a fixed orifice with virtually no leaflet mobility, resulting in a fixed degree of aortic stenosis and regurgitation.

In any artificial flow environment, such as the plumbing system of a building, a fixed hole could never work as a valve. A standard valve, in the engineering sense, requires complete closure and full opening at their respective flow cycles. Yet, in the mammalian circulatory system, a fixed aortic orifice can function well enough to keep the patient alive. This ability of the natural system to correct for the valvular "flaw" has to do with the presence of pulsatile flow and arterial afterload.

Imagine two hand-squeeze rubber bulb water pumps, connected by a conduit with a narrowing, being squeezed alternately, one at a time (see illustration). If both sides were equal in every way, e.g., the bulb size, strength of the hand squeeze, etc., there would be no net flow. However, if A is consistently more forceful than B, more flow would travel from A to B than from B to A. Hence, there would be net flow going toward B. In the compensated state of aortic stenosis, the cardiac output is always greater than the regurgitant flow generated by the arterial afterload. As such, the fixed aortic orifice can function as a valve parceling out a net positive forward flow. The static orifice also reduces diastolic regurgitation (flow from B to A), and thus, helps to sustain arterial pressure for survival.



A fixed orifice design was the obvious choice for the first-generation catheter-based temporary aortic valve. Can we deliver a device (such as a balloon on a catheter) that creates a fixed orifice while deployed in the ascending aorta to replace the function of the native valve when it is acutely nonfunctional (with severe regurgitation)? After the overview summary of chapter 1, chapters 2 and 3 introduce the mathematical concepts of the fixed orifice temporary aortic valve. The theoretical models include a system for transcatheter aortic valve replacement because the marriage of these ideas is logical when the temporary valve could allow for transcatheter removal of the diseased valve prior to replacement with the prosthesis. However, this concept has not yet been tested experimentally. Chapters 5, 7, and 8 are the bench and animal validations of the fixed orifice temporary aortic valve design.

A significant disadvantage of the fixed orifice design is the inherent forward flow resistance, which could limit its use, especially in those with existing left ventricular compromise. Could this device be made to disappear (or reduce in size) during systole and re-expand during diastole? Chapter 4 and 6 present two different approaches to reduce the forward flow resistance of the temporary valve; the first model requires an “active” system of balloon deflation mechanism and an extracorporeal console, similar to the intra-aortic balloon pump. The latter model utilizes a passive mechanism leveraging the natural forces of the pulsatile flow. Chapter 6 further tests the passive design in a bench flow chamber study.

Chapter 9, while not from a published study, is a collection of final design challenges that are deemed necessary to be overcome in order to achieve design freeze of the preclinical temporary aortic valve prototype. Through our design, modeling, and testing processes, I hope that this book will inspire discussions and stimulate bioengineering innovations in all aspects of cardiovascular device therapeutics and interventions.

ACKNOWLEDGMENTS

Giving credit to everyone who has positively influenced me in creating this book is an impossible task. Most notably, I want to thank my bioengineering professors at the University of Pennsylvania, Abraham Noordergraaf, PhD, and Julius Melbin, DVM, PhD, who were the first to inspire me to study cardiovascular hemodynamics. I also owe a shout-out to my study co-authors, Marie Nguyen, MD, and Patrick Golden, MD. Most importantly, I will always remember the unforgettable lessons learned from the handful of patients who presented with cardiogenic shock due to acute aortic valve regurgitation. Although we could not save them at the time, their unique conditions inspired my desire for a clinically viable temporary aortic valve catheter.

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CHAPTER 1

AN OVERVIEW OF A HEMODYNAMIC SUPPORT SYSTEM FOR ACUTE AORTIC INSUFFICIENCY

Overview

A percutaneous temporary aortic valve hemodynamic support catheter is a device that can conceptually maintain stable hemodynamics when significant structural damage occurs to the native aortic valve ensuing acute severe aortic insufficiency. Applications may include a bridge to surgery in active aortic valve endocarditis and an option to allow for diseased valve resection prior to transcatheter aortic valve replacement. An early prototype has undergone successful fundamental mathematical, bench and animal proof-of-concept studies. Design, concept and early data are presented and discussed. [Originally published: Ho PC. Percutaneous temporary aortic valve: a hemodynamic support system for acute aortic insufficiency. *Cardiovasc Revasc Med* 2013;14(3):149-153.]

Introduction

Isolated structural damage to the aortic valve can occur from endocarditis or deliberate removal prior to valve replacement. In transcatheter aortic valve replacement (TAVR), resection of the diseased valve prior to valve replacement has perceived advantages and has been proposed as a strategy (1–3). Contemporary hemodynamic support devices, including the intra-aortic balloon pump, TandemHeart device (Cardiac Assist Inc, Pittsburgh, PA) and Impella (Abiomed Inc, Danvers, MA) all require a competent aortic valve to operate (4). The need for a hemodynamic support system to manage acute aortic insufficiency (AI) is apparent.

Search for the "temporary aortic valve" design began several decades ago; few models have been studied (5–8) but none reached clinical application. The reasons are likely multifactorial mirroring the difficulties for the device to satisfy several essential design criteria: ability of the device to approximate native aortic valve hemodynamics, to maintain adequate

cardiac output, to afford acceptable coronary perfusion, to allow for aortic valve intervention (resection, replacement), ease of insertion and retrievability percutaneously as needed based on hemodynamic stability.

A prototype of a new percutaneous temporary aortic valve (TAV) catheter (HOCOR) is designed with all of the above criteria in mind. Early mathematical, bench and animal proof-of-concept models (3,9–12) are presented and discussed.

Brief summary of the temporary aortic valve prototype

The balloon-based TAV is designed with the intention of a hemodynamic support device capable of insertion and retrieval like a catheter on demand based on the severity of the acute AI. A series of parallel balloons are built at the tip of a guiding catheter; the balloons serve as the temporary aortic valve when inflated in the ascending aorta, while the guiding catheter can function as a conduit for aortic valve resection and replacement.

Theoretical concept and mathematical model

During TAV balloon inflation in the ascending aorta, the gaps between the balloons and the aortic wall will determine the effective aortic stenosis (eAS) and insufficiency (eAI) at the site of the TAV deployment (Figure 1). The degree of eAS and eAI can be controlled based on the balloon configurations (balloon number, size and shape) and counter-pulsations in synchrony with the cardiac cycle (3,10). Insignificant ranges of eAS and eAI can readily be established in the ascending aorta by the TAV to support significant acute AI that can result from native aortic valve damage. Hemodynamic stability can be restored. The gaps between the balloons and the aorta will also allow for coronary perfusion avoiding myocardial ischemia during TAV deployment. A simple 3-balloon TAV design was initially used for mathematical modeling (3) (Figure 1); the calculated eAS and eAI fell within mild-to-moderate ranges and should be well tolerated by a subject with normal left ventricle when the native aortic valve is rendered nonfunctional. Subsequent mathematical models of various balloon configurations and counter-pulsations were also provided (10).

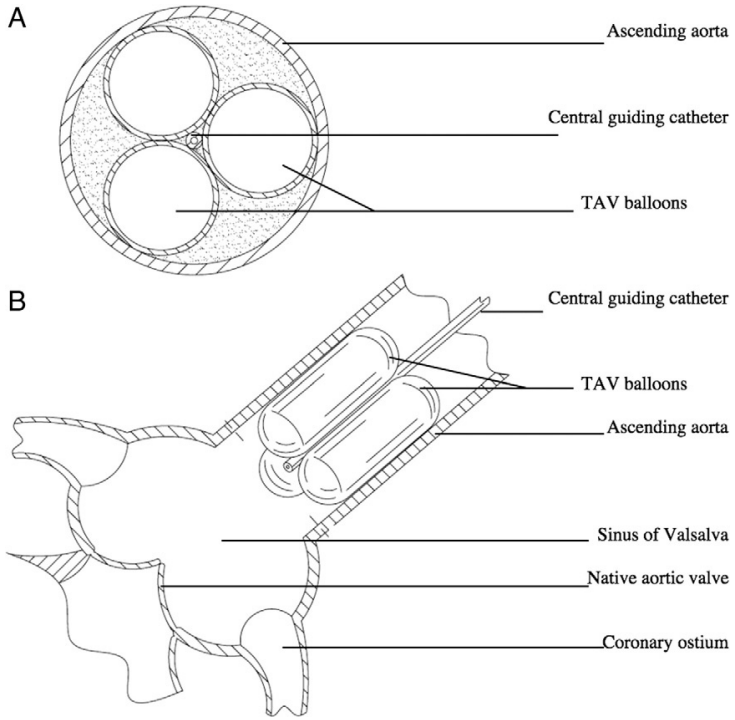

Figure 1. (A) Cross-sectional illustration for the 3-balloon percutaneous temporary aortic valve (TAV) in the inflated, deployed position against the wall of the ascending aorta. (B) Longitudinal view of the TAV system in the deployed position above the Sinus of Valsalva and downstream from the coronary ostia.

In vitro flow model

A flow apparatus, using a system of water tanks, clear polyvinyl chloride (PVC) tubings and electrically controlled valves, was constructed to model the pulsatile conditions of the ascending aorta with and without simulated AI as shown in Figure 2. The 3-balloon TAV prototype was created with standard peripheral angioplasty balloons and indeflator for inflation–deflation of the device (Figure 3). The TAV was sized, when inflated, to fit the inner dimensions of the PVC tubing such that the gap space between the balloons and the tubing would fall within a calculated range in accordance to the mathematical model (3,11). While the gaps could add a small amount of forward flow resistance (eAS) at the site of the TAV during systole, it would prevent massive regurgitation of fluid volume retrograde into the left

ventricle during diastole (eAI). The gaps could theoretically allow for diastolic coronary perfusion in an animal subject.

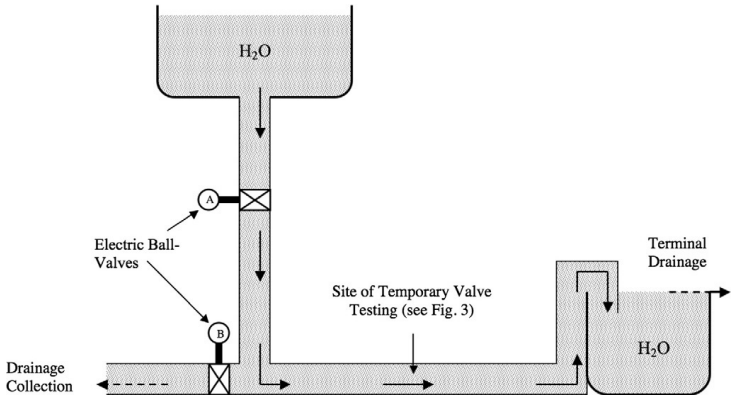

Figure 2. Schematic diagram of the in vitro flow model for TAV testing. Fluid flow is driven by pressure-head of a water column set to provide a systolic pressure of 100–120 mmHg; the arrows in the tubing represent the direction of flow. The ball-valves are electronically linked to a timer and to each other. During normal conditions, ball-valve (A) opens during systole and closes during diastole at the speed set by the timer representing the cardiac cycle. To simulate significant aortic insufficiency (AI), ball-valve (B) opens when ball-valve (A) is closed during diastole, creating wide-open AI and a reversal of aortic flow. During systole when ball-valve (A) is open, ball-valve (B) will be closed, representing the lack of influence of AI to the antegrade systolic flow. The shorter column of water at the terminal drainage site represents arterial afterload and creates the potential for retrograde flow during AI.

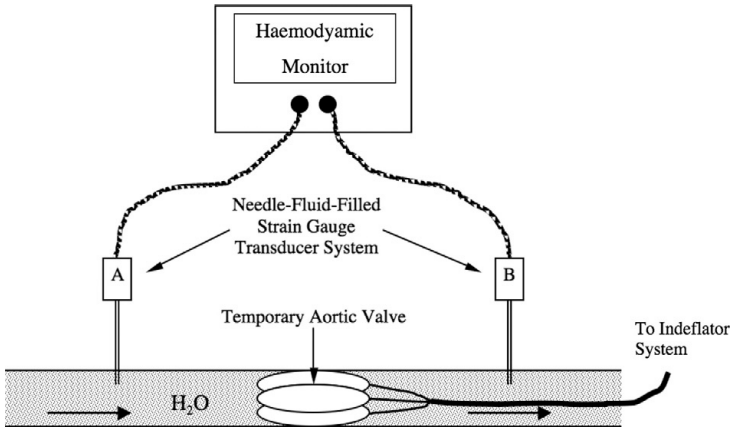

Figure 3. The temporary aortic valve (TAV) prototype is inserted retrograde through the tubing from the terminal drainage site. The delivery mimics the percutaneous retrograde arterial delivery approach often used in the clinical setting. Pressure waveform measurements were recorded without the TAV with and without AI. After deployment of the TAV prototype, pressure waveform measurements were recorded at the proximal port (A) and the distal port (B) to the TAV device as shown.

Table 1
Summary of hemodynamic results from a one-minute run cycle.

Mean (standard deviation)	No AI (Baseline)	With induced AI			p-Value*
		(Baseline)	(Proximal TAV)	(Distal TAV)	
Systolic pressure (mmHg)	90.7 (1.2)	91.0 (1.7)	90.3 (2.1)	87.7 (1.2)	0.11
Diastolic pressure (mmHg)	22.3 (1.0)	8.7 (1.5)	7.3 (0.6)	11.0 (1.0)	0.01** 0.27***
Regurgitant volume (l)	0	5.5 (0.2)	5.0 (0.2)	5.0 (0.2)	0.05
Cardiac output (l min^{-1})	9.6 (0.1)	8.2 (0.2)	8.1 (0.2)	8.1 (0.2)	0.56
Cycles (RPM)	12	12	12	12	

* p-values are calculated for the parameters with induced AI only.
** p-value of 0.01 is between proximal and distal TAV.
*** p-value of 0.27 is between the baseline with AI and proximal TAV.

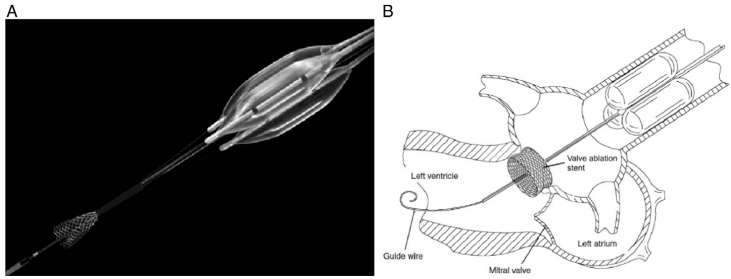

Figure 4. (A) Black-and-white photograph of the original 3-balloon temporary aortic valve prototype system. The 3-balloons are shown in the inflated position. The self-expanding valve ablation stent is shown to be emerging from the central guide catheter. (B) Schematic illustration of the aortic valve ablation stent as delivered and deployed via the TAV's guiding catheter.

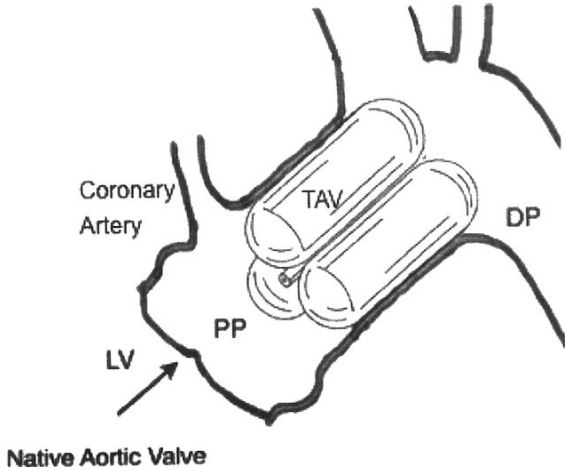

Figure 5. Schematic illustration of the porcine proximal aorta and the experimental temporary aortic valve (TAV) prototype indicating the locations of pressure measurements: LV = left ventricle, PP = proximal to TAV, DP = distal to TAV.

The findings of the in vitro flow model of the TAV showed encouraging results of the device's ability to improve the hemodynamics from flow conditions of simulated severe AI. Specifically in simulated AI, the TAV was shown to increase the distal diastolic pressure, to reduce the widened pulse pressure, to protect the left ventricle by lowering its diastolic pressure and to reduce the aortic regurgitant volume. The TAV's systolic pressure

gradient did not cause significant reduction in the forward flow (cardiac output). Table 1 summarizes the results of in vitro flow testing of the TAV (11).

Animal model

Porcine models of approximately 90 kg were used for the studies. A prototype was constructed using 3 standard peripheral angioplasty balloons, indeflator and a guiding catheter capable of delivering a self-expanding stent to ablate the native aortic valve to create acute severe AI (Figure 4). The procedure was performed entirely percutaneously, closed-chest. Hemodynamic parameters including concomitant ECG were recorded at baseline conditions, at acute severe AI after the aortic valve was ablated and at acute AI with TAV protection. Pressure measurements were obtained in the left ventricle, proximal and distal to the TAV as indicated in Figure 5.

The results of the animal studies were also encouraging. First, the guiding catheter was able to deliver a self-expanding stent to the aortic annulus and successfully ablate the valve. As a result of the stent ablation, acute severe AI ensued. There was a significant drop in the aortic diastolic pressure, an equalization of the left ventricular and aortic diastolic pressures, an acute elevation of the left ventricular diastolic pressure, and a widened aortic pulse pressure.

Furthermore, in the presence of induced acute AI, deployment of the TAV in the proximal aorta was able to significantly lower the left ventricular diastolic pressure, increase the distal aortic diastolic pressure and narrow the widened pulse pressure. There was a mild systolic pressure gradient across the TAV, which did not significantly affect the cardiac output.

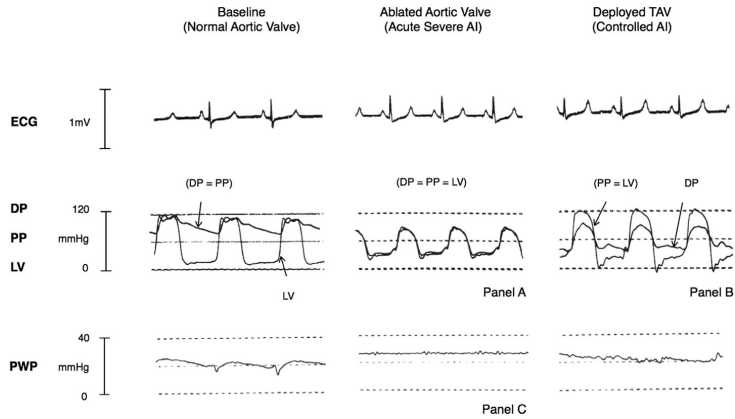

Figure 6. Representative waveform tracings at baseline condition, after native aortic valve ablation and with TAV deployment in acute severe aortic insufficiency (AI). Electrocardiogram (ECG) tracings showed no significant changes across aortic valve conditions. With ablated aortic valve, the pressure tracings in the proximal aorta signified massive severe AI with equalization of the left ventricular (LV) and proximal aortic pressures (Panel A). With TAV deployment to control the AI, diastolic pressure separation was observed proximal vs. distal to the TAV pressures (PP vs. DP), as well as a mild to moderate systolic pressure gradient (Panel B). As a result, distal pulse pressure (at DP) narrowed, while the proximal to TAV (PP) diastolic pressure lowered to protect the LV from acute volume overload. The PP waveform resembled the LV prior to stent ablation. The pulmonary wedge pressure (PWP) was slightly altered with the induced AI (Panel C) and with the TAV support though not statistically significant.

No ischemic changes on the ECG was noted during the TAV deployment. Figure 6 and Table 2 summarize the results of the animal studies (12).

Table 2
Hemodynamic Data from a 10-Cycle (Pulses) Run at Baseline, with Induced AI and with TAV Support.

	Baseline (Normal Aortic Valve)		Ablated Aortic Valve	Deployed TAV (Controlled AI)		P value
	Ao	LV	(Acute Severe AI)	PP	DP	
Systolic (mmHg)	113.3 ± 3.2	112.9 ± 4.2	87.5 ± 1.1	116.3 ± 3.5	85.1 ± 2.3	<0.001
Diastolic (mmHg)	76.2 ± 2.5	12.6 ± 1.1	32.4 ± 2.0	21.5 ± 1.5	45.0 ± 1.3	<0.001
CO (l/min)	5.5		5.2	5.6		*
PWP (mmHg)	22.1 ± 2.5		25.7 ± 4.1	23.4 ± 3.5		NS

TAV = temporary aortic valve; CO = cardiac output; PWP = pulmonary wedge pressure; AI = aortic insufficiency; Ao = proximal aortic pressure; LV = left ventricular pressure; PP = aortic pressure measured proximal to the TAV; DP = aortic pressure measured distal to the TAV; pressure data is expressed as continuous variables; * = no statistical calculation due to single value representing the 10-cycle run; NS = non-significant.

Conclusions

The HOCOR TAV is at early stages of development as shown by the qualitative bench tests and few animal models. Further extensive preclinical work will continue to include comprehensive understanding of the TAV's effects on coronary flow and survival. Counterpulsation features of the TAV will also be studied. Nonetheless, these initial results showed promise for a percutaneous device to manage acutely occurring AI and the added potential for the same device to perform percutaneous aortic valve intervention simultaneously.

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CHAPTER 2

PERCUTANEOUS AORTIC VALVE REPLACEMENT: A NOVEL DESIGN OF THE DELIVERY AND DEPLOYMENT SYSTEM

Overview

The frontier of percutaneous aortic valve replacement is challenged by hemodynamic and anatomic obstacles in the precise positioning of the device. With vital structures such as the mitral valve apparatus and the coronary ostia on either side, the margin of error is only within a few millimeters in the placement of the percutaneous aortic valve. An optimal system of delivery and deployment of this device has yet to be made commercially available. A novel design of a system of delivery and deployment of currently investigational aortic valved-stent is presented. In the proposed procedural and equipment strategy, the local hemodynamic and anatomic conditions are controlled to allow for precise placement of the device, and overall improvement of the patient stability and safety can be made possible. Continued efforts in innovative designs in this area are encouraged such that the percutaneous valvular intervention can become mainstay as it has in the arena of percutaneous coronary intervention. [Originally published: Ho PC. Percutaneous aortic valve replacement: a novel design of the delivery and deployment system. *Minim Invasive Ther Allied Technol* 2008;17(3):190-194.]

Introduction

The current standard of care for patients with significant aortic valve disease is still surgical aortic valve replacement. As the treatment of many cardiovascular diseases has become minimally invasive and catheter-based, endovascular techniques and equipment have led to the development of

percutaneous aortic valve (PAV) replacement as a potential clinical reality. PAV replacement is currently an investigational procedure.

The notion of PAV replacement was first introduced in 1992 by Andersen et al. in a swine model (1). The first human implantation of a percutaneous valved-stent was performed in the pulmonic position reported by Bonhoeffer et al. in 2000 (2). The first human implantation of a PAV was described in 2002 using a valved-stent design by Cribier et al. via the antegrade/ inter-atrial septal puncture approach (3). Other techniques such as retrograde and transapical approaches of delivery and deployment of the PAV were introduced later (4,5).

In the PAV replacement procedure, most of the cardiac complications occur at the required precise placement of the PAV during implantation. Because the aortic valve's close proximity to the coronary ostia on one side and the mitral valve on the other, misalignment of the PAV can cause serious compromise of coronary or mitral valve function (6,7). Misplacement of the PAV has been shown to be a significant problem observed in clinical investigations with available devices (8). Significant hemodynamic forces encountered at the left ventricular outflow tract to the ascending aorta and the obstructive nature of the native diseased aortic valve can add to the difficulty of precise placement of the PAV and the risk of device embolization. A novel design of a PAV delivery and deployment system is presented with specific features to optimize precise PAV placement and deployment while maintaining patient stability during the procedure.

Material and methods

Salient features of the delivery and deployment system of the PAV should possess the following: The capability to achieve an adequately stable physiologic and anatomic environment for device positioning and deployment, and to maintain a sustainable hemodynamic condition to allow for completion of the procedure without undue patient instability. To achieve a stable environment for both PAV implantation and patient safety, a temporary ''aortic valve ''is proposed for the ascending aorta. To simplify the local anatomy allowing for a relatively unobstructed PAV placement, ablation of the native aortic valve is also proposed. Specific equipment design and step-by-step procedural recommendations are considered as follows.

Temporary aortic valve

The temporary aortic valve (TAV) system comprises of a 3-supporting-balloon and a central guiding catheter mechanism as shown in Figures 1a and 1b. The 3-balloon TAV system is intended to be placed in the ascending aorta. The gaps between the three balloons and the wall of the aorta create temporary effective aortic insufficiency (AI) and aortic stenosis (AS) during diastole and systole, respectively (Figure 1a). The temporary AI and AS have been deliberately designed to serve important functions during the PAV implant procedure.

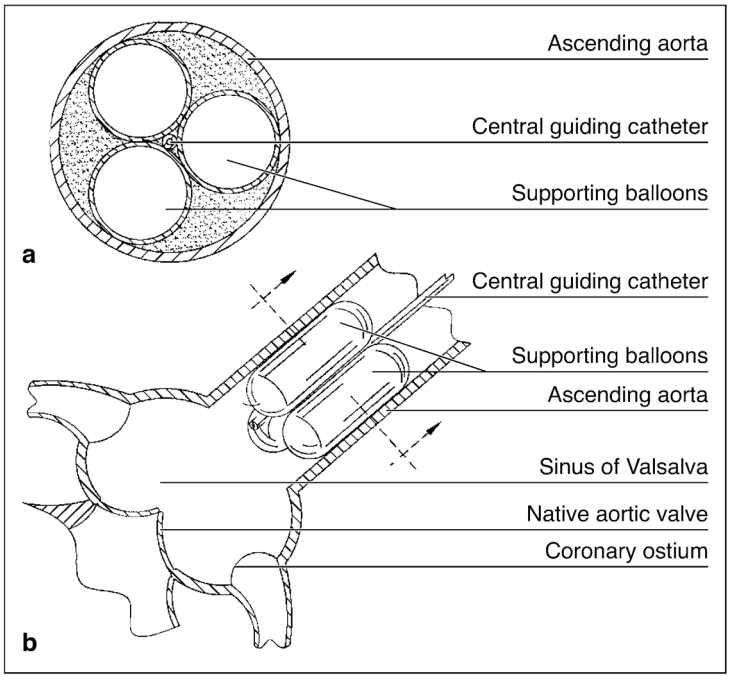

Figure 1. (a) Cross-sectional illustration of the 3-balloon temporary aortic valve system (TAV) in the inflated, deployed position against the wall of the ascending aorta. (b) Longitudinal view of the TAV system in the deployed position above the Sinus of Valsalva and downstream from the coronary ostia.

The AI at the TAV allows for continued diastolic filling of the coronary arteries. After the native aortic valve has been ablated (see below) and acute wide open AI occurs at the level of the aortic annulus, the TAV also serves as a control valve for the amount of AI rushing back to the left ventricle. Massive acute AI will be prevented, thus maintaining patient stability (see mathematical considerations below) (Figure 2).

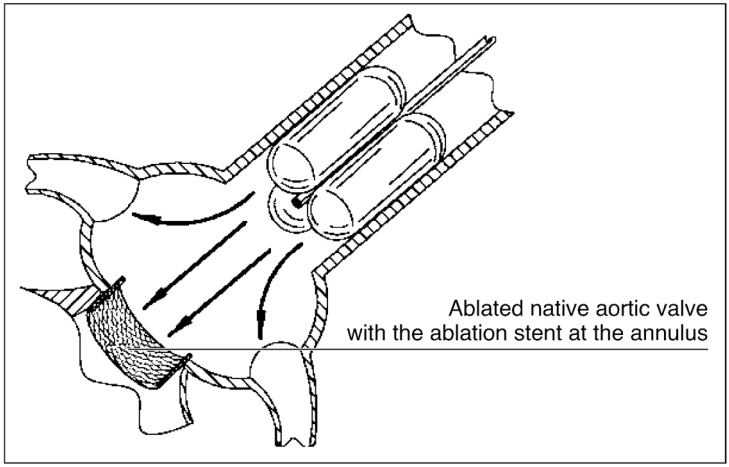

Figure 2. Schematic illustration of the deployed TAV system during diastole. The arrows represent retrograde blood flow in diastole; the TAV limits the amount of aortic insufficiency into the left ventricle while allowing for coronary perfusion.

The AS at the TAV will be less than the critical value at the native aortic valve stenosis (see mathematical considerations below). Because the TAV is located above the level of the coronary ostia, it can serve two major purposes. First, it can partially enhance the systolic filling of the coronary arteries. Second, after the native aortic valve is ablated, thus eliminating the native aortic stenosis, the lower degree of AS offered by the TAV will immediately relieve the effective transvalvular pressure gradient (Figure 3) and enhances patient stability. Lastly, because wide-open blood flow is prevented between the left ventricle and the TAV, relative quiescent hemodynamic conditions may allow for fine positioning, placement and deployment of the PAV within this region.

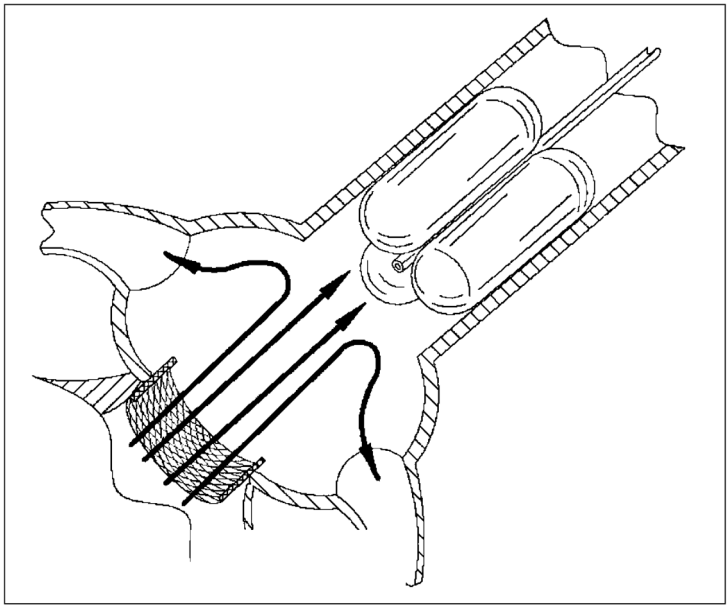

Figure 3. Schematic illustration of the deployed TAV system during systole. The TAV allows for temporary pressure build-up in the region of the Sinus of Valsalva, and can enhance partial systolic coronary perfusion. After the native aortic valve is ablated, the pressure gradient along the flow path is relocated from the native aortic valve to the TAV.

Mathematical considerations of AI / AS at the TAV

As shown in the cross-sectional illustration in Figures 1a and 4, the shaded area represents the effective AI (during diastole) and AS (during systole) as created by the 3-balloon system against the aortic wall. The calculation of the effective AI and AS is as follows (Figure 4):

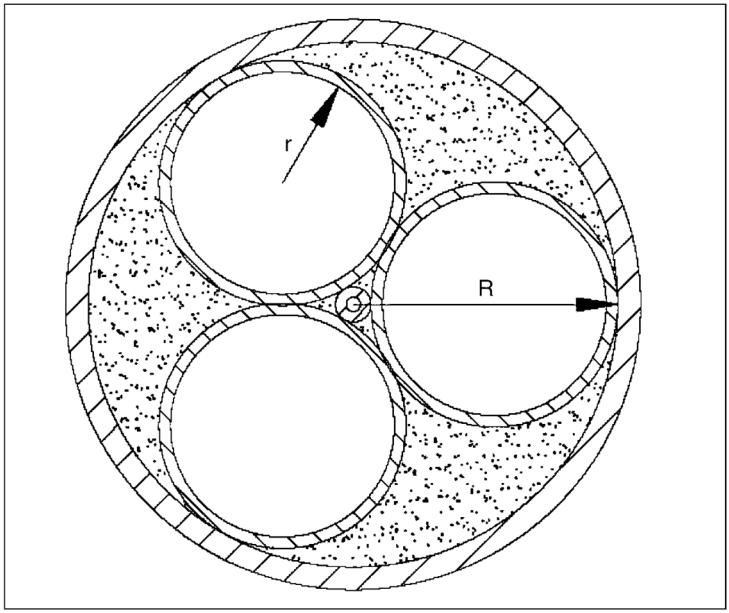

Figure 4. Cross-sectional representation of the relative dimensions of the TAV balloons and the ascending aorta. R=radius of the ascending aorta; r=radius of the TAV balloon, assuming all three balloons have the same dimensions. The shaded area represents the gaps for blood flow between the wall of the aorta and the TAV.

R = radius of the ascending aorta
r = radius of a supporting balloon; all three balloons are equal in size
R ~ 2.15r, assuming adequate apposition of the balloons to the aortic wall
Area (shaded) ~ **35%** Area of the ascending aorta; cross-sectional view

Well documented physiologic significant AI begins at >60% of the cross-sectional area of the aortic annulus, as measurable by Doppler echocardiography in the parasternal short-axis view (9). In comparison with the TAV in the ascending aorta position, the calculated effective AI of 35% is categorized as moderate range in severity and should be well tolerated by the patient even if it occurs acutely (eg., after complete ablation of the native aortic valve).

Clinically significant AS is considered when the aortic valve area (AVA) is reduced to <25% of its original cross-sectional area (10). For example, a normal adult aortic orifice area is approximately 3 cm^2, a calculated AVA of <0.75 cm^2 is considered significant. The calculated effective AS of the