

Chapter 6: History of Transcatheter Aortic Valve Replacement (TAVR)

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Severe, symptomatic aortic stenosis is the most commonly diagnosed valvular heart disease in the elderly and is associated with poor clinical outcomes if left untreated [1]. During the past 50 years, the standard of care for severe, symptomatic aortic stenosis has been surgical aortic valve replacement (SAVR), which significantly improves survival, symptoms, and quality of life. [2] However, it has been estimated that 30-40% of patients are deemed unsuitable for SAVR due to increased periprocedural risk from multiple comorbidities. [3] In addition, there are anatomic factors, such as a porcelain aorta or a patent left internal mammary artery that crosses the midline from previous coronary bypass surgery, that may increase the risk of conventional SAVR. [4] For these reasons, it is estimated that at least one third of patients with severe, symptomatic aortic stenosis are not referred for or denied surgical therapy. [3] For decades, clinical investigators sought an alternate, less invasive approach to treat aortic stenosis in patients deemed inoperable surgical candidates.

The first attempts to treat aortic valvular disease percutaneously were aimed at managing aortic regurgitation. In 1965, Davies was the first to describe a catheter-mounted cone-shaped valve that had a parachute configuration which prevented aortic regurgitation and allowed forward flow, demonstrating feasibility in several animal models using the carotid artery as the primary access point. [5] Mouloupoulos et al. then introduced several prototype devices aimed at preventing aortic regurgitation; these involved balloons that were placed percutaneously, inflated at diastole and deflated during systole, the timing of which was managed by an external system. [6] The final iteration of these valves involved an umbrella-shaped valve that would close passively during systole and open during diastole, allowing for forward systolic flow without regurgitation. [7] In 1976, Phillips et al designed a single cusp valve with an umbrella shape that was mounted on a catheter and advanced into the ascending aorta from the carotid artery, using the same principles of closing during systole and opening during diastole. [8] In the early 1990s, Matsubara et al. published another prototype of a balloon catheter with two latex check valves, which prevented backwards flow during diastole. [9] All of these designs were able to provide a reduction in aortic regurgitation and left ventricular diastolic pressures both *in vitro* and in animal models; however, these designs were not applicable to the clinical setting as they could not be safely implanted and fixed in the aortic position *in vivo*. [7]

In the mid-1980s, there was initial optimism that balloon aortic valvuloplasty (BAV) would become the standard of care for percutaneously treating severe aortic stenosis in inoperable patients. However, growing evidence of procedural complications, prohibitive early restenosis, and lack of mortality benefit relegated the use of BAV to either palliative therapy or as a bridge to definite valve replacement with surgery [4, 10, 11]. Thus, the search for a percutaneous aortic valve intervention continued.

In 1992, Anderson et al. published the first report of an artificial valve design that could be implanted percutaneously *in vivo*. [12] The device consisted of a porcine aortic valve mounted on a steel

frame constructed with 2 wires with a diameter of 0.55 mm; 50 prolene sutures fixed the aortic annulus and valve to the frame. [7] The frame was compressed and mounted onto a deflated balloon dilation catheter, with a final diameter of 41F. The group successfully implanted the valve in 9 pig models, using a midline laparotomy, to access the abdominal aorta. Angiographic and hemodynamic evaluation after implantation revealed no significant stenosis in any of the nine valves and trivial regurgitation in two. Complications were associated with restriction of the coronary blood flow in three animals. While this revolutionary study demonstrated the feasibility of catheter-mounted valves, the device was still too large to safely implant in humans.

The first report of a successful percutaneously implanted valve in humans was published in 2000 by Bonhoeffer et al. [13] The valve design consisted of a bovine jugular vein valve sutured onto a platinum/iridium stent. Following several experimental implants in sheep, the valve was successfully deployed into the pulmonic position of a 12-year-old boy with pulmonic stenosis and insufficiency. There was optimism that a similar concept valve could succeed in the aortic position.

In 2000, Cribier et al., in affiliation with Percutaneous Valve Technologies, Inc., introduced a percutaneous heart valve consisting of 3 bovine pericardial leaflets mounted on a balloon-expandable stent. The valve was successfully implanted in several sheep via a 24 F sheath. [14] One year later in 2001, Paniagua et al. described the Paniagua Heart Valve, consisting of bovine pericardial leaflets with smaller crossing profiles of 11F – 16F. [15] The device was implanted successfully in 15 out of 17 animal models, with no evidence of inflammation and adequate endothelization at 13 month histological follow up examination. [16]

These successful implants set the stage for the first transcatheter aortic valve replacement, performed on April 16, 2002 by Cribier et al. [17] The patient was a 57-year-old man with severe calcific aortic stenosis and peripheral vascular disease with a previous aorto-bifemoral bypass. He presented in cardiogenic shock in the setting of subacute ischemia of the right leg due to occlusion of the aorto-femoral bypass. An aortic balloon valvuloplasty was performed with an initial improvement but subsequent decline over the next seven days. As a last resort, Cribier and his colleagues crimped their percutaneous heart valve onto a 30 mm balloon and advanced a 24 F sheath into the right femoral vein, obtaining access to the aortic valve antegrade via transseptal techniques (Figure 1 and 2). The valve was then positioned and deployed with rapid inflation and deflation of the balloon. TEE showed gradients across the aortic valve immediately normalize and the patient's clinical status continued to improve over the next seven days. The implanted valve continued to maintain adequate hemodynamic performance on echocardiograms 9 weeks post-procedure. The patient eventually died 17 weeks following valve implantation due to several non-cardiac complications. However, the procedure was heralded as a revolutionary success for percutaneous treatment of aortic valve disease.

The first retrograde transcatheter valve implant was reported by Paniagua et al in 2005. [16] The patient was a 62-year-old man with inoperable severe aortic stenosis, cardiogenic shock, and an LVEF of 15%. Transfemoral access was obtained with a 16 F Cook Catheter and the valve was successfully crimped and deployed using a 20 mm balloon (Figure 2). The patient had immediate clinical improvement in cardiac output and was able to be extubated; however, he ultimately deteriorated and died 5 days following implant due to refractory cardiogenic shock.

Following these two initial case reports, data emerged revealing early success with transcatheter aortic valve implantation. Cribier et al. reported in JACC successful implant in 27 out of 36 patients (75%) that were formerly declined by surgery and recruited on a compassionate use basis, with a 26% rate of major complications within 30 days. [18, 19]. 23 of 27 successful procedures were performed via the antegrade approach. All patients who had received a successful valve implant reported significant improvement in their symptoms. At 9-month follow-up, 11 patients were still alive, with echocardiograms showing unchanged valve function; notably, no deaths were related to the device.

In 2006, Webb et al. published a series of 15 successful valve implants in 18 patients via the retrograde approach using 22 and 24 F sheaths inserted via the femoral artery. [20] Injury to the iliac artery occurred in two patients; however, there were no intraprocedural deaths. At an average follow-up of 75 days, 16 of the patients (89%) were alive with echocardiography showing the valves to be fully functional. These investigators also reported the use of rapid ventricular pacing during valve deployment to minimize pulsatile transaortic flow, which would otherwise act to eject the inflated device-deployment balloon. This experience suggested that retrograde percutaneous aortic valve implantation was feasible in selected patients with adequate short-term outcomes. Several years later, Walther et al. published a 50-patient case series of balloon-expandable aortic valve implants via the transapical approach, achieving procedural success in 94% (n = 47) of patients, demonstrating the feasibility of alternative access in high risk patients. [21]

TAVR has gradually matured since its first clinical use in 2002, and new designs continue to improve the efficacy and feasibility of the procedure while limiting complications, allowing the use of this technology in an expanding patient population. This revolutionary procedure is a disruptive technology that transformed the modern management of aortic stenosis. The early valve designs and clinical investigations laid the foundation for the now robust clinical data from both randomized trials and registries that support the use of TAVR currently in intermediate risk, high risk, and inoperable patients.

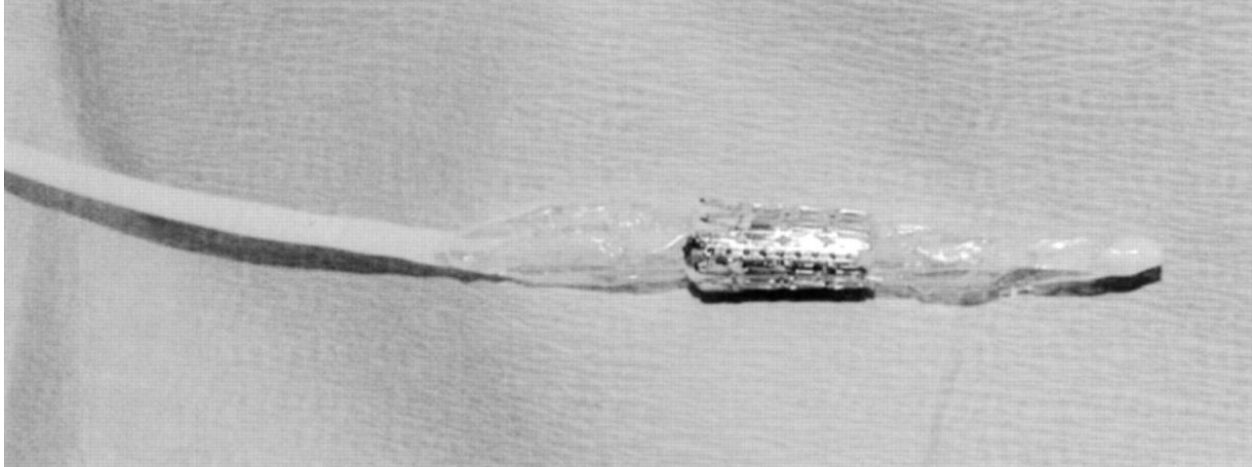


Figure 1. The percutaneous valve crimped on 30 mm balloon. (4)

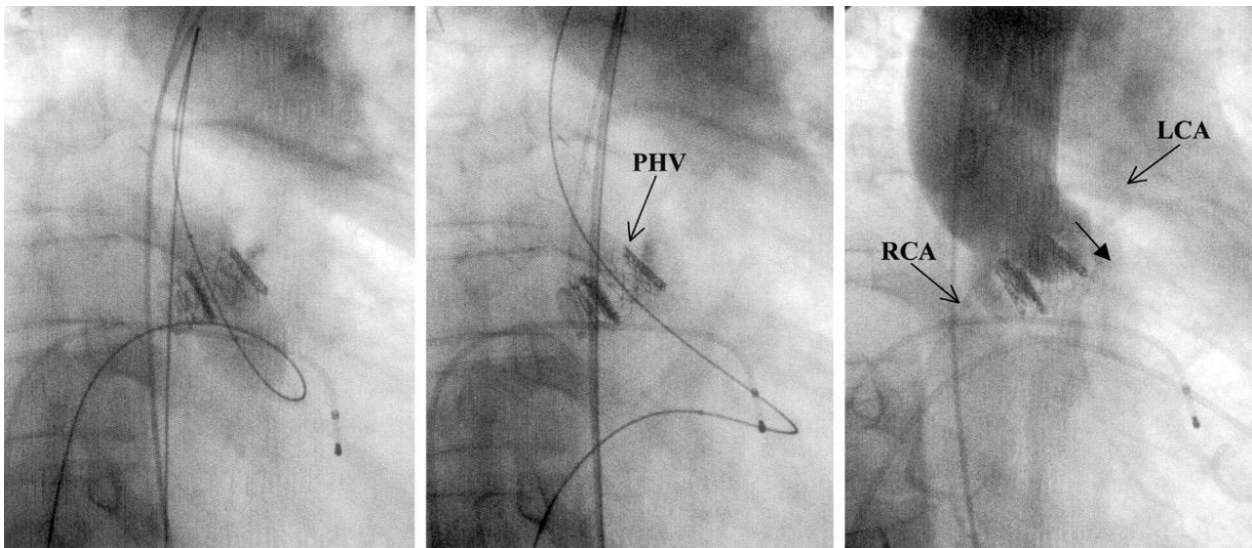


Figure 2. PHV delivery within the native calcific valve via antegrade approach. Left, Maximal balloon inflation (23 mm) for valve delivery. Middle, The PHV in position at mid part of the native aortic valve, pushing aside the calcific leaflets. Right, Supraaortic angiogram after PHV implantation showing no aortic regurgitation across the PHV and a mild paravalvular regurgitation (arrow). Both coronary ostia are patent and removed from the valve prosthesis [17]



Figure 3. Delivery of the percutaneous heart valve via retrograde access. [16]

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