

STATE-OF-THE-ART PAPER

# Current Status of Transcatheter Aortic Valve Replacement

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Surgical aortic valve replacement (SAVR) has long been the mainstay of therapy for severe aortic stenosis. However, transcatheter aortic valve replacement (TAVR) is now generally accepted as the new standard of care for patients with symptomatic aortic stenosis who are not candidates for open surgery. Arguably TAVR may also be a preferred alternative to SAVR in carefully selected high-risk, but still operable, patients in whom morbidity and mortality may be reduced. Although TAVR outcomes continue to improve, concerns remain with respect to vascular injury, stroke, paravalvular regurgitation, and valve durability. However, it seems likely that with ongoing refinement of transcatheter valve systems, techniques, and patient selection TAVR is becoming an increasingly appealing option for a much broader range of patients. Randomized trials and ongoing surveillance will play an important role as we enter a new era of rigorous clinical evaluation for minimally invasive therapies for structural heart disease. (J Am Coll Cardiol 2012;60:483-92) © 2012 by the American College of Cardiology Foundation

When patients develop symptoms due to aortic stenosis, functional limitation is inevitably followed by physical deterioration, heart failure, and mortality. Aortic valve replacement (AVR), specifically surgical AVR (SAVR), improves symptoms and is generally accepted to prolong survival on the basis of historical comparisons and long experience (1). However, many symptomatic patients do not undergo surgery, because they are not referred, are refused, or are declined as candidates (1).

Since transcatheter AVR (TAVR) was first accomplished just over a decade ago, clinical outcomes have steadily improved (2). Recently TAVR became the only intervention for aortic stenosis shown to prolong life in a randomized trial (3). Arguably TAVR is now the standard of care for extremely high-risk or “inoperable” patients and is a valid alternative to surgery for many high-risk but “operable” patients (4). As we pass 10 years of clinical experience with TAVR and over 50,000 implants in over 40 countries, a review of contemporary TAVR seems appropriate.

## Transcatheter Valves

**The SAPIEN valve.** The current state-of-the-art Edwards SAPIEN XT transcatheter heart valve (THV) (Edwards Lifesciences Inc., Irvine, California) utilizes a balloon-

expandable cobalt chromium alloy tubular frame within which are sewn leaflets constructed from bovine pericardium. The inflow of the frame is covered with fabric to provide an annular seal (Fig. 1).

For transarterial implantation the THV is compressed onto a low-profile NovaFlex (Edwards Lifesciences) delivery catheter and introduced through a sheath placed in the femoral artery. Alternatively a sheath can be placed surgically in the left ventricular apex or ascending aorta. In either case the THV is balloon-expanded within the diseased native valve displacing the diseased native leaflets (Fig. 2). The low-profile (16-F to 19-F) SAPIEN XT/NovaFlex transfemoral system is in widespread clinical use around the world. However, availability in the United States remains limited to patients enrolled in the randomized PARTNER-2 (Placement of AoRTic TraNscathetER Valve-2) trial. At this time only the earlier generation RetroFlex transfemoral system (Edwards Lifesciences) is clinically available in the United States (Figs. 1 and 2). These systems utilize the earlier SAPIEN THV, which requires the use of larger diameter 22-F to 24-F sheaths.

**CoreValve.** The CoreValve ReValving System (Medtronic Inc., Minneapolis, Minnesota) utilizes a self-expanding nitinol (a nickel-titanium alloy that is malleable at low temperature, but relatively rigid at body temperature) frame. The leaflets and annular seal are constructed of porcine pericardium (Fig. 3). This THV is compressed within its Accutrak delivery catheter (Medtronic) and introduced through an 18-F sheath into the common femoral or subclavian artery. Once positioned within the diseased native valve the delivery catheter is withdrawn, releasing the

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**Abbreviations and acronyms**

- AVR** = aortic valve replacement
- MDCT** = multidetector computed tomography
- SAVR** = surgical aortic valve replacement
- STS** = Society of Thoracic Surgeons
- TAVR** = transcatheter aortic valve replacement
- THV** = transcatheter heart valve

THV. The long multistaged frame is anchored within the aortic annulus, but also extends superiorly to anchor in the supracoronary aorta.

**Comparisons.** These 2 valve systems share more similarities than differences (Table 1). Both devices utilize similar low-profile delivery systems, are compatible with fully percutaneous access, and can be implanted in a conventional cardiac catheterization laboratory with fluoroscopic guidance alone under local anesthesia.

Only limited nonrandomized comparisons are available (5,6). Deployment of the CoreValve device may be more intuitive, and does not require rapid pacing, while deployment of the SAPIEN device may be more targeted. The CoreValve device can, up to a point, be repositioned or removed. However this process may not be benign (7). Coronary obstruction may rarely occur with both THVs, but may be more frequent with the SAPIEN type valves. Atrioventricular block requiring pacemaker implantation is more common with CoreValve. Currently, the SAPIEN THV is supported by the randomized PARTNER (Placement of AoRTic traNscathetER valve) studies (4). However there is extensive experience with the CoreValve device and similar rigorous evaluation is underway. Regardless of current differences, both THV systems continue to evolve and iterative improvements can be anticipated.

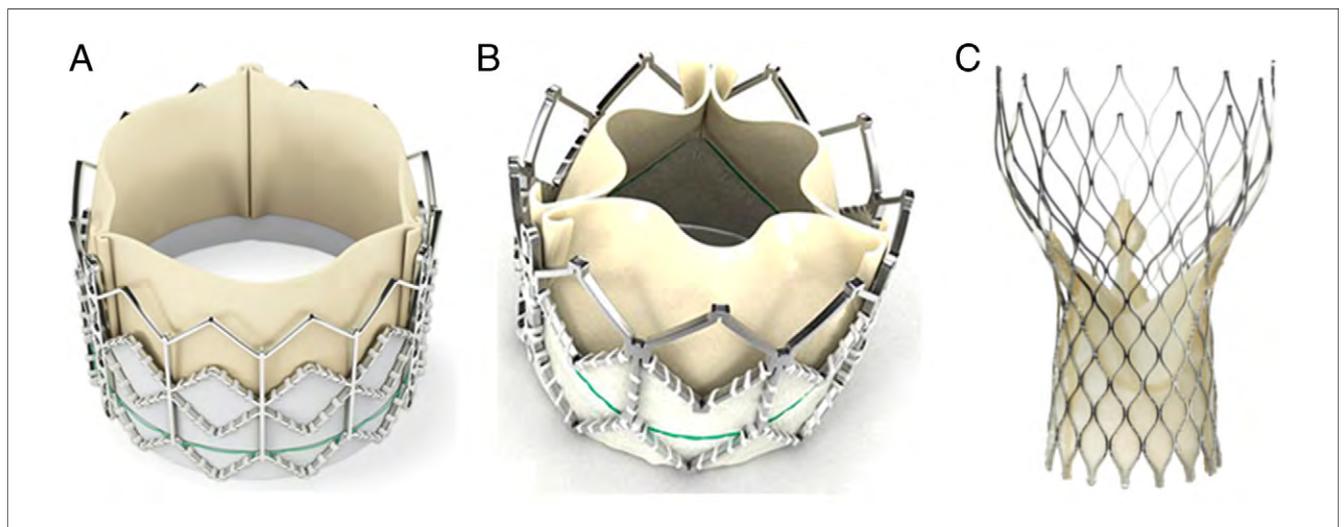
**Newer valves.** A number of newer transcatheter valves are in early clinical evaluation. In general these incorporate features, which reduce delivery catheter diameter, improve

ease of positioning and sealing, or facilitate repositioning or removal (Fig. 4). For the most part these next generation valves are constructed of self-expanding nitinol. Some valves have unique expansion mechanisms: the Lotus valve (Boston Scientific Inc., Natick, Massachusetts) is designed to expand laterally as longitudinal nitinol wires are retracted and the Direct Flow valve (Direct Flow Medical Inc., Santa Rosa, California) has a tubular fabric frame, which is inflated with a rapid setting polymerizing agent. Self-expandable systems offer the potential for recapture, repositioning, and removal if desired.

The Acurate (Symetis Inc., Ecublens, Switzerland) and Portico (St. Jude Medical Inc., St. Paul, Minnesota) devices extend from the annulus to the supracoronary aorta to assist in coaxial alignment and fixation, as does CoreValve. The Engager (Medtronic), JenaClip (JenaValve Inc., Munich, Germany), and Acurate valves incorporate features that facilitate positioning and anatomical orientation in relation to the native valve commissures and coronaries. Other valves incorporate new sealing mechanisms to reduce paravalvular leaks.

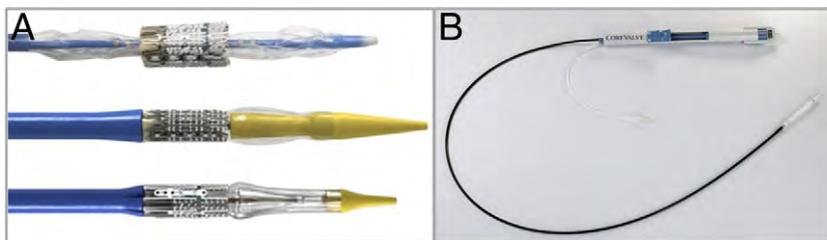
Although these newer valves offer many desirable features, there are concerns with respect to radial strength, symmetric expansion, and late fracture with nitinol. Experience with newer leaflet technology is limited. Repositionable valves may be associated with aortic injury, atheroembolism, or reduced durability. Whether clinical outcomes will be equivalent or superior to currently available THVs will need to be evaluated.

**Patient evaluation.** TAVR is technically feasible in most patients with aortic stenosis. There are, however, several necessary anatomic evaluations specific to TAVR. The dimensions of the aortic annulus dimensions must be evaluated noninvasively in order to select an appropriately



**Figure 1** Current Widely Available Transcatheter Valves

- (A) The Edwards SAPIEN THV balloon-expandable valve (Edwards Lifesciences, Irvine, California) incorporates a stainless steel frame, bovine pericardial leaflets, and a fabric sealing cuff.
- (B) The SAPIEN XT THV (Edwards Lifesciences) utilizes a cobalt chromium alloy frame and is compatible with lower profile delivery catheters.
- (C) The Medtronic CoreValve (Medtronic, Minneapolis, Minnesota) incorporates a self-expandable frame, porcine pericardial leaflets, and a pericardial seal.



**Figure 2** Valve Delivery Catheters

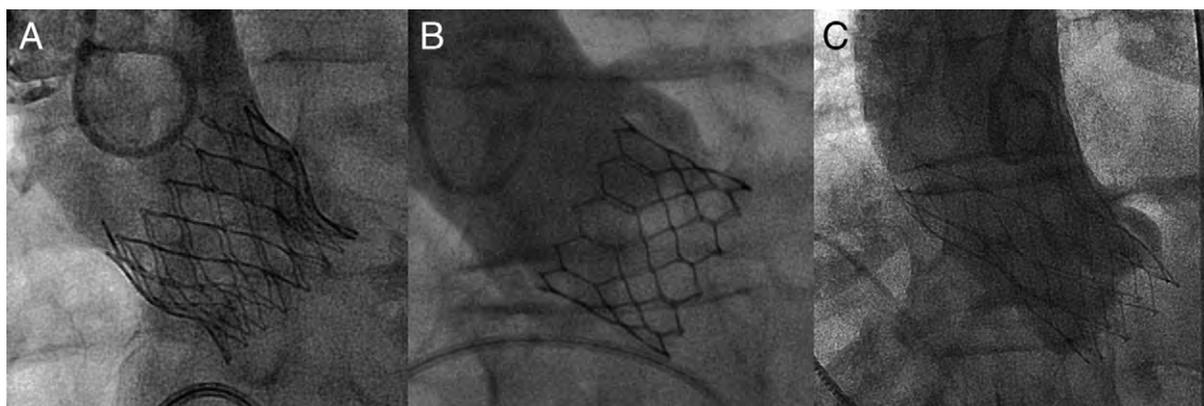
(A, top) The RetroFlex 1 delivery system for the Edwards SAPIEN THV (Edwards Lifesciences, Irvine, California) as used in the PARTNER 1 (Placement of AoRTic TraNscathetER Valve 1) trials (8 mm diameter). (A, Middle) The RetroFlex 3 system (Edwards Lifesciences). (A, Bottom) The NovaFlex/SAPIEN XT system (6 mm diameter; Edwards Lifesciences). (B) The Accutrak delivery system with the Medtronic CoreValve (6 mm diameter, also with a tapered nosecone; Medtronic, Minneapolis, Minnesota). The prosthesis is enclosed within an outer sheath.

sized valve. Transesophageal echocardiographic (8,9), multidetector computed tomography (MDCT), and magnetic resonance imaging measurements are widely utilized (10-12). Arterial access is generally assessed with invasive angiography or contrast MDCT. Most arteries are somewhat compliant and can accommodate sheaths slightly (~1 to 2 mm) larger than their internal diameter, although this may not be the case when the artery is diffusely diseased, tortuous, or calcified. The aorta should be evaluated with invasive angiography or contrast MDCT to assess technical issues related to the delivery and implantation of the specific valve type, aortic root and valvular calcification, and the risk of coronary obstruction.

Whether TAVR is advisable depends not only on various technical considerations, but also on the likelihood of functional and survival benefit. Increasingly evaluation is directed on identifying patients in whom a significant improvement in quality and duration of life is likely and avoiding unnecessary intervention in patients where the

procedure can be performed, but benefit is unlikely due to advanced age and comorbidities. For this reason evaluation of neurocognitive functioning, frailty, functional status, mobility, and supports is increasingly being recognized as important in patient selection.

**Centers of expertise.** Evaluation and management of TAVR candidates is a complex process requiring the special skills of interventional cardiologists with expertise in structural heart disease, cardiac and vascular surgeons, anesthesiologists, imaging specialists, and specialized nursing. This cooperative, noncompetitive approach to dealing with this high-risk and intensive procedure has been popularized as the multidisciplinary heart team. Ideally TAVR is best performed in a specialized procedural suite able to utilize whatever percutaneous or open access techniques are necessary and to deal appropriately with complications. The concept of a hybrid room has been advocated; large enough to accommodate sophisticated x-ray imaging, anesthesia, echocardiography, and cardiopulmonary support (1).



**Figure 3** Fluoroscopic Images of Some Newer Valves Undergoing Early Evaluation in Patients

The CENTERA valve (A) is self-expandable and utilizes an electronic motorized release and retrieval system, while the S3 valve (B) incorporates an improved sealing system and utilizes a 14-F expandable sheath (Edwards Lifesciences, Irvine, California). (C) The Portico valve (St. Jude Medical Inc., St. Paul, Minnesota) is self-expandable, retrievable, and repositionable.

**Table 1** Comparison of the Edwards SAPIEN XT and Medtronic CoreValve Prostheses

Characteristics	Edwards SAPIEN XT	Medtronic CoreValve
Frame	Cobalt chromium	Nitinol
Leaflets	Bovine pericardial	Porcine pericardial
Seal	Synthetic	Porcine pericardial
Expansion	Balloon expandable	Self-expanding
Repositionable	No	Yes
Retrievable	No	Yes
Annular/valvular fixation	Yes	Yes
Ascending aorta fixation	No	Yes
Manufacturers diameter*	23, 26 mm	26, 29 mm
Treatable annulus diameter*	18–25 mm	20–27 mm
Length	15–17 mm	53–55 mm
Sheath internal diameter	18-F, 19-F	18-F
Sheath external diameter	~7 mm	~7 mm
Minimal arterial diameter	6 mm	6 mm
Suitable for		
Aortic stenosis	Yes	Yes
Aortic regurgitation	If calcific stenosis present	If size appropriate
Dilated ascending aorta	Yes	No
Pulmonary position	Yes	No
Valve-in-valve	All 4 valve positions	Aortic only
Transapical access	Yes	No
Transaxillary access	Yes, limited experience	Yes
Transaortic access	Yes	Yes
Longest published follow-up	>6 yrs	>4 yrs
Pacemaker requirement	3%–8%	14%–40%
CE mark approval	Yes (2007)	Yes (2007)
FDA approval	SAPIEN transfemoral only	No
Randomized trial results	PARTNER A and B	Results anticipated 2013

\*SAPIEN XT 20, 29 mm (Edwards Lifesciences, Irvine, California); and CoreValve 31 mm (Medtronic, Minneapolis, Minnesota) devices are available in some countries.  
CE = Conformance Européenne; FDA = Food and Drug Administration; PARTNER = Placement of Aortic Transcatheter Valve Trial.

Recently the American College of Cardiology and the Society of Thoracic Surgeons (STS) noted that procedural risks are high, valve interventions are rarely emergent, and that extensive support infrastructure and procedural volumes are necessary for optimal outcomes and efficiencies. Restricting this new therapy to regional centers of excellence was recommended (1). With well over 1,000 cardiac surgical programs in the United States with an average volume of 60 aortic cases per year, this will undoubtedly be controversial.

**Endovascular access.** The femoral artery has been the most popular access site. Although originally requiring a surgical cutdown most experienced groups now utilize a percutaneous puncture and suture pre-closure technique avoiding the need for open surgical access (Fig. 5). Current consensus, with some exceptions, strongly favors transfemoral arterial access as the preferred, default approach for TAVR.

Current transcatheter valve systems utilize vascular access sheaths, which are typically described in terms of their inner

diameter in French size (3 × internal diameter in millimeters). Sheath external diameters are slightly larger. The only approved device in the United States (SAPIEN valve) requires a 22-F or 24-F sheath with outer diameters of just over 8 or 9 mm, respectively. However, current generation systems generally utilized outside the United States utilize smaller sheaths (≤18-F with outer diameters of ~7 mm). A relatively compliant nondiseased artery can generally accommodate a sheath slightly larger than its internal diameter. In the absence of severe calcification, tortuosity, or atheroma an arterial diameter >6 mm might be adequate for an 18-F system, while an arterial diameter of >8 mm might be required for a 24-F system. Assessing this minimal arterial diameter is fundamental to patient selection.

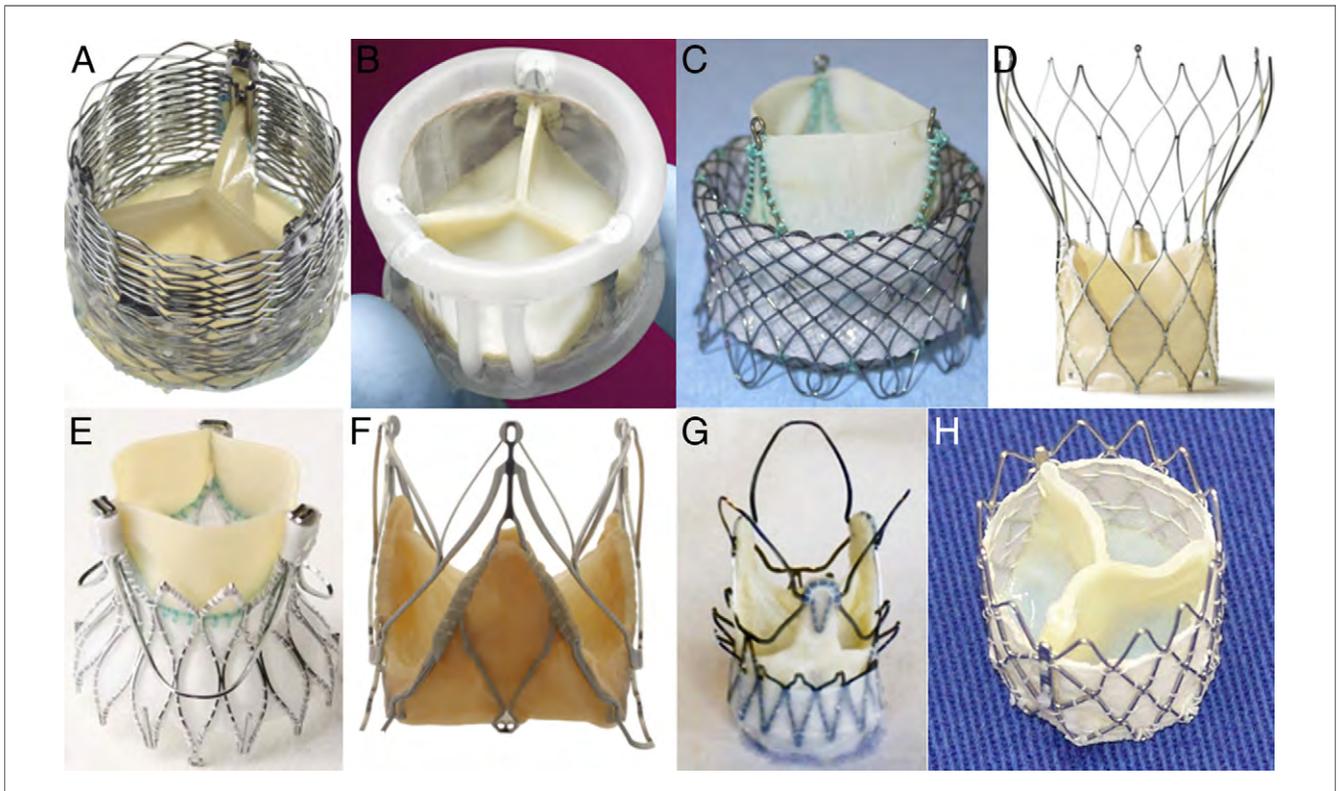
However, many patients have small or diseased femoral arteries. On occasion an open surgical retroperitoneal approach is utilized to gain access to the larger iliac artery in patients with femoral disease. Recently, transaxillary (sometimes referred to as subclavian) access has gained popularity as an alternative to femoral access, although a surgical cutdown is generally utilized (6,13,14).

A transapical approach, with direct access to the left ventricle through an intercostal thoracotomy, has several potential advantages: a low risk of peripheral vascular injury, a direct pathway to the aortic valve, and easier antegrade crossing of the diseased aortic valve. Concerns relate to direct myocardial injury, bleeding, mitral injury, hemodynamic instability, and post-operative respiratory compromise and thoracotomy pain. The transapical procedure is generally associated with the Edwards SAPIEN valve, although a number of newer valves (e.g., JenaClip, Engager, Portico, Acurate) have been developed for this application.

Most recently, a transaortic approach with direct access to the ascending aorta has been advocated. Although requiring a mini-thoracotomy and aortotomy, potential advantages over the transapical approach include a reduced risk of myocardial injury and bleeding and an access route more familiar to cardiac surgeons.

### Valve Function

In vitro testing generally suggests performance equivalent or superior to surgically implanted valves, in part due to the absence of a bulky sewing ring. Large clinical registries routinely report mean transaortic systolic gradients of around ≤10 mm Hg and an orifice area ranging between 1.2 and 1.9 cm<sup>2</sup>, depending on prosthesis size and type (2). The only randomized comparison of TAVR and SAVR (the 699-patient PARTNER 1A trial) documented superior hemodynamic function with the SAPIEN valve (mean gradient 10.2 ± 4.3 mm Hg vs. 11.5 ± 5.4 mm Hg, p = 0.008; mean orifice area 1.59 ± 0.48 cm<sup>2</sup> vs. 1.44 ± 0.47 cm<sup>2</sup>, p = 0.002 at 1 year) (3). As with SAVR, relief of aortic stenosis with TAVR is associated with favorable effects on left ventricular mass, volumes, and function. Left ventricular



**Figure 4** Valves Undergoing Early Evaluation

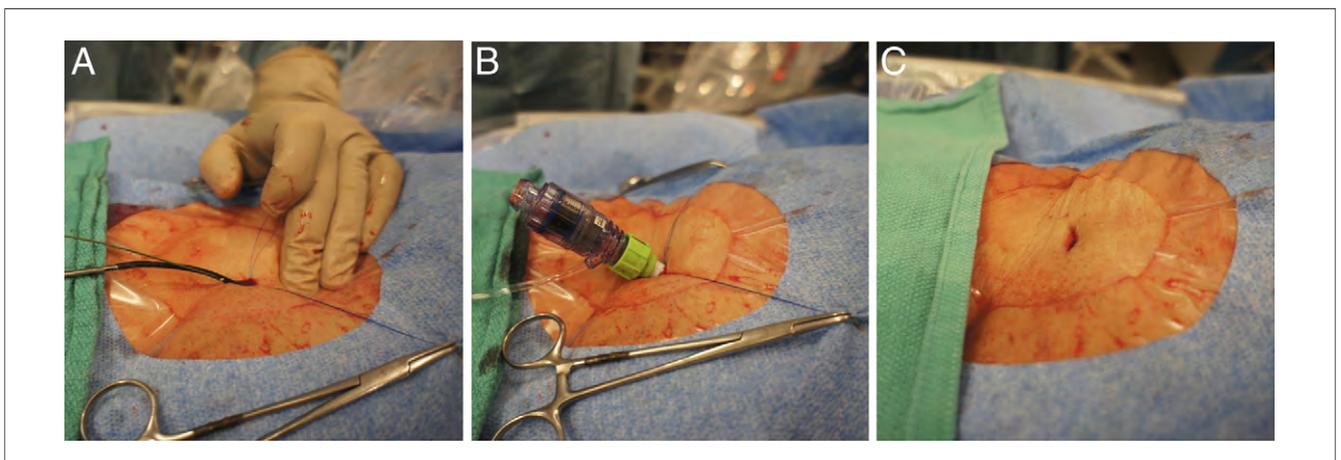
(A) Lotus (Boston Scientific Inc., Natick, Massachusetts), (B) Direct Flow (Direct Flow Medical Inc., Santa Rosa, California), (C) HLT (Bracco Inc., Princeton, New Jersey), (D) Portico (St. Jude Medical Inc., St. Paul, Minnesota), (E) Engager (Medtronic Inc., Minneapolis Minnesota), (F) JenaClip (JenaValve Inc., Munich, Germany), (G) Acurate valve (Symetis Inc., Ecublens, Switzerland), and (H) Inovare (Braille Biomedica Inc., São José do Rio Preto, Brazil) valves.

function typically improves to a small degree immediately and may continue to improve with time, particularly in the absence of infarction (15).

**Aortic regurgitation.** Significant transvalvular regurgitation is rare after transcatheter AVR (3). However, paravalvular regurgitation, due to incomplete annular sealing, is

common. Paravalvular leaks may occur due to prosthesis undersizing or incomplete expansion, or due to implantation of a prosthesis too high or too low such that the sealing cuff is not apposed to annular tissue.

Core lab echocardiographic evaluation in the PARTNER trials documented greater than or equal to moderate para-



**Figure 5** Percutaneous Access and Closure

(A) The femoral artery is punctured and a guidewire placed within the artery. Percutaneous sutures are placed using a “pre-closure” device. (B) The large vascular access sheath is inserted. (C) Following sheath removal the sutures are tightened.

valvular aortic regurgitation after TAVR in 11.8% of the inoperable patients and 12.2% of operable patients (3,4). However, net aortic regurgitation (both valvular and paravalvular combined) was actually reduced after TAVR (3,4,9,13).

Severe paravalvular regurgitation may result in severe hemodynamic consequences, although improved implantation techniques and more accurate annulus sizing have made such severe leaks increasingly less common. Most leaks are, in fact, mild to moderate, well tolerated, not associated with hemolysis, and do not worsen with time (13,14). Nevertheless, it is clear that moderate and even mild leaks are associated with a less favorable late survival than no leak (16,17). Whether this association represents cause and effect is unknown. When paravalvular regurgitation is excessive redilation, repositioning, or implantation of a second, overlapping transcatheter valve can often reduce or correct the problem (13,18). However, these interventions may be associated with a poorly understood increased risk of embolic stroke and should not be taken too lightly (7,19).

**Valve durability.** Clinical and echocardiographic follow-up of both the SAPIEN and CoreValve prostheses beyond 3 and up to 5 years has been well documented (15–17,20). To date, late leaflet failure has been exceedingly rare and in vitro accelerated wear testing is consistent with durability comparable to surgical bioprostheses. Mid term durability of the SAPIEN and CoreValve frames has been documented and frame fracture has not been observed. However, only time will tell if durability matches that of surgical bioprostheses.

## Clinical Outcomes

**Survival.** Contemporary registry series routinely document procedural success (defined loosely here as implantation of a functional valve with the patient surviving the procedure) in over 95% and procedural survival (30 days) in over 90% of high-risk patients (2,5,18,21). More rigorous assessments are now available from the randomized PARTNER trials.

As the first of 2 parallel trials completed, PARTNER 1B randomized 358 “inoperable” patients (in whom surgical risk was prohibitive as judged by experienced surgeons) to either transarterial (femoral artery access) TAVR or best medical management (Fig. 6) (4). Despite early generation large-diameter systems and minimal operator experience with TAVR, the 30-day mortality of 6.4% among patients assigned to TAVR compared very favorably with the STS mortality estimate of 11.6% with surgery. By way of comparison, the STS National Cardiac Database reports that among patients (low- and high-risk combined) actually undergoing SAVR in the United States, mortality was similarly 6.4%. Patients managed medically had a mortality exceeding 50% at 1 year. The PARTNER 1B trial documented a dramatic 20% absolute reduction in mortality at 1 year with transarterial TAVR, meeting statistical tests for superiority. At 2 years the survival curves continue to

diverge with an additional 16.9% difference in mortality accruing between 1 and 2 years (16).

The parallel trial, PARTNER 1A, was completed a year later (Fig. 7) (3). In this trial 699 high-risk patients were randomized to either TAVR (either a transfemoral or transapical as determined by access considerations) or SAVR. The mean STS score was just under 12%, representing the top 5% of patients in terms of operative risk. Mortality at 30 days was actually lower with TAVR than SAVR (3.4% vs. 6.5%,  $p = 0.07$ ) and at 1 year (24.2% vs. 26.8%,  $p = 0.44$ ); not statistically significant, but still meeting tests for noninferiority.

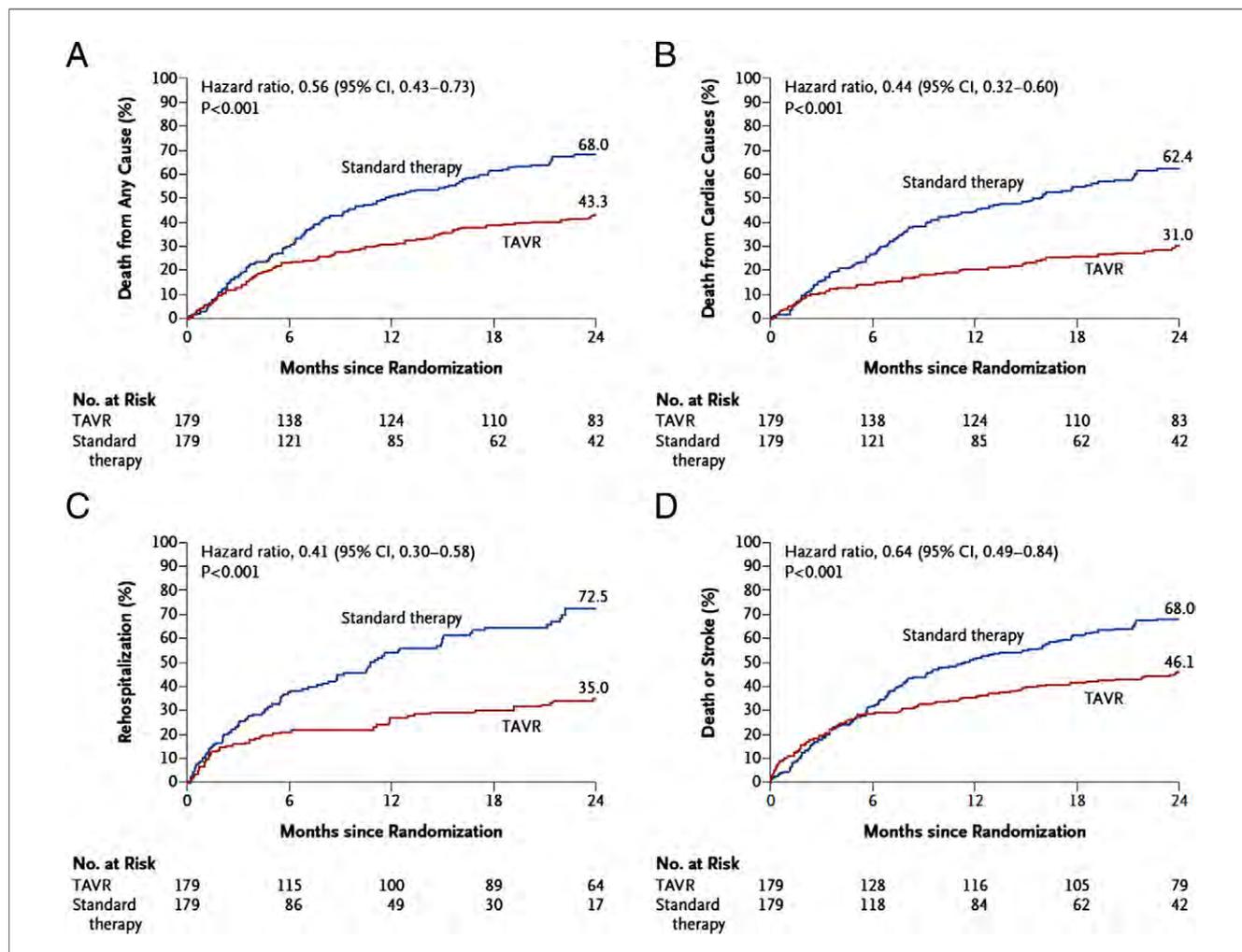
In addition to the previous intention-to-treat analysis (treatment assigned, 30 days from randomization), the as-treated analysis (treatment received, 30 days from the procedure) has assumed relevance as surgical patients were less likely to undergo their assigned procedure within 30 days, thereby reducing procedural deaths within 30 days of randomization. In the as-treated analysis femoral transarterial TAVR 30-day mortality was less than one half that with SAVR (3.7% vs. 8.2%,  $p = 0.05$ ). As in previous observational studies of TAVR, mortality was higher among patients that underwent a transapical procedure. The transapical procedure did not, on its own, meet the test of noninferiority. To what degree this difference is attributable to selection of higher-risk patients and a learning curve in the transapical group is controversial.

**Functional benefit.** For many elderly patients morbidity may be a greater concern than mortality. A marked and durable improvement in functional class and quality of life after TAVR has been well documented (15,22,23). The randomized PARTNER trials documented a marked reduction in rehospitalization with transfemoral TAVR as compared with medical management and, in comparison with surgery, a significantly shorter length of stay as well as earlier improvement in functional status (3,4,22).

**Late survival.** Registries report survival 1 year following TAVR ranging from 69% to 85% (3–5,15,18,21). Similarly, 1-year survival in the PARTNER trials following TAVR was 69% in inoperable patients and 76% in high-risk operable patients. Late mortality was primarily the result of advanced age and debilitating comorbidities such as severe pulmonary and renal disease (3,4,15). Given the invasive nature of the procedure and limited resources it may be as important to decide who will *not* benefit, as who will.

## Specific Risks of TAVR

**Neurological concerns.** Stroke is a known potential complication with both SAVR and TAVR (24). For perspective, the recent European SOURCE (SAPIEN Aortic Bioprosthesis Multi-Region Outcome Registry) and United Kingdom high-risk TAVR registries reported stroke rates of 2.4% and 4.0%, respectively. The rigorously monitored



**Figure 6** The PARTNER 1B Trial Compared Transarterial TAVR to Medical Management in Extremely High-Risk (Inoperable) Patients

Time to event analyses of death (A), death due to cardiac causes (B), rehospitalization (C), and the combined endpoint of death or stroke (D). Redrawn from Leon MR, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597–607, with information from Makkor RR, Fontana GP, Jilaihawi H, et al. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. *N Engl J Med* 2012;366:1696–704, with permission from the Massachusetts Medical Society. PARTNER = Placement of AoRTic TraNscathetER Valve; TAVR = transcatheter aortic valve replacement.

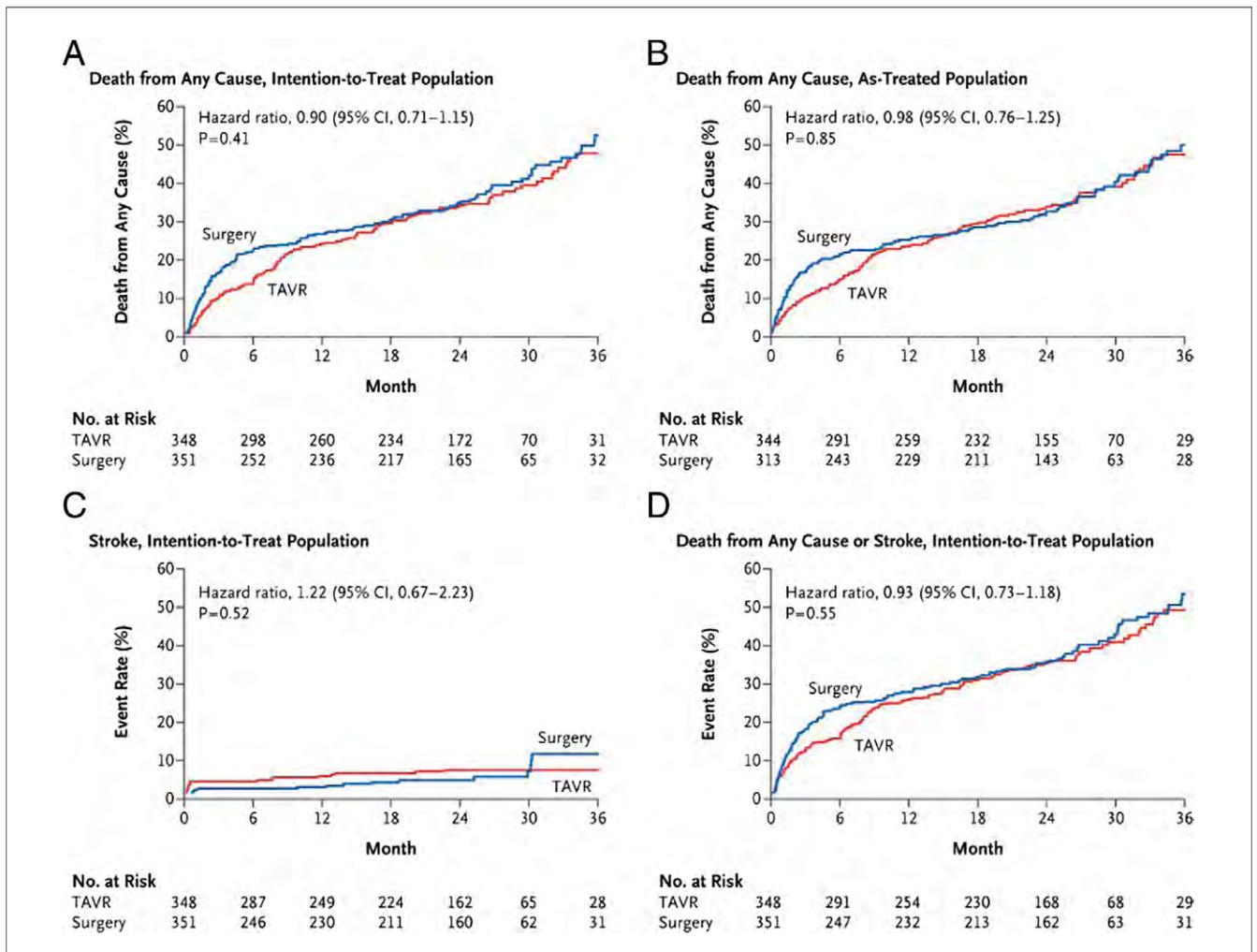
PARTNER 1B “inoperable” trial reported an increase in major stroke rate of 4%, arguably justified given the overall 21.9% reduction in death and/or stroke at 2 years (number needed to treat = 4.6) (16).

The PARTNER 1A trial allows direct comparison of stroke rates between TAVR and SAVR. Major strokes (strokes with permanent deficit) were similar: 3.8% versus 2.1% at 30 days ( $p = 0.20$ ) (25). As there were relatively few strokes, an analysis of all neurological events (including transient ischemic attacks and minor strokes without permanent deficit) was performed. Neurological events (with and without clinical deficit) were increased with TAVR (5.5% vs. 2.4% at 30 days,  $p = 0.04$ ). Predictors of neurological events with TAVR included a prior neurological event, more severe atherosclerotic burden, worse functional disability, smaller valve area, and transapical access. The temporal pattern of neurological events was similar for

the 2 groups, with an increased risk over the first week, but no subsequent increased hazard over SAVR out beyond 2 years. At 2-year follow up there was no significant difference in the overall numbers of strokes with TAVR and SAVR (17). The composite of death and/or stroke with disability was actually lower (although nonsignificantly) with TAVR (femoral and apical combined) as compared to SAVR (26.5% vs. 28.0% at 1 year,  $p = 0.68$ ) (Fig. 7).

Although data are preliminary, the risk of stroke seems to be falling with smaller, less traumatic catheters (Fig. 3), improved technique, and lower-risk patients (13,24). A potential role for devices designed to capture or deflect embolic material is currently being evaluated (2,21).

**Access concerns.** Vascular events have been the most common major complication associated with TAVR and are often implicated in procedural mortality. Using the large-diameter 22-F and 24-F RetroFlex delivery system, the



**Figure 7** The PARTNER 1A 2-Year Outcomes After Transcatheter or Surgical Aortic Valve Replacement

Kaplan-Meier time-to-event curves are shown for death by intention to treat (A) and as-treated (B), stroke (C), and the composite of death or stroke (D). Mortality and stroke rates were similar. Reprinted from Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187–98, with the permission of the Massachusetts Medical Society. PARTNER = Placement of Aortic Transcatheter Valve.

European SOURCE registry, the PARTNER 1B and 1A studies reported vascular complication rates of 17.9%, 16.2%, and 11.0%, respectively (3,4,18,21). More recent experience suggests a marked reduction in vascular complications with lower profile delivery systems, increased experience, and better vascular screening. As major vascular injury has been associated with a doubling of procedural mortality, a favorable impact on survival appears likely. Surgical access to the femoral artery is giving way to routine percutaneous access and closure. Moreover, when vascular complications do occur they are better managed and are less likely to be associated with mortality. In our own experience the risk of major vascular complications and major bleeds has fallen dramatically, into the low single digits (26). Newer, ultra low-profile systems (down to 14-F) are currently under evaluation and will likely make transfemoral technically feasible in the majority of patients.

**Renal concerns.** Registry data suggests that a rise in creatinine following TAVR occurs in 5% to 28% of cases, albeit generally mild, reversible, and to a lesser degree than with SAVR (27). Clinical experience suggests that renal function often improves in response to increased cardiac output. When renal function does deteriorate this is often a consequence of hypoperfusion, contrast, and transfusion. Similarly the randomized PARTNER trials suggested a reduced need for renal replacement therapy after TAVR as compared with medical management (1.2% vs. 1.7%) or SAVR (3.8% vs. 4.6%), although these differences were not statistically significant.

**Coronary concerns.** Nonrevascularized coronary artery disease is common and, when severe, can increase procedural risk. If there is a large ischemic burden percutaneous revascularization may be desirable. However, clinical experience suggests that the majority of coronary disease in elderly patients can be managed conservatively with suffi-

cient reduction in angina accrued from relief of aortic stenosis alone. TAVR facilitates a strategy of staged revascularization as required.

Acute coronary obstruction may rarely occur, generally due to displacement of a bulky native valve leaflet over a coronary ostium (usually the left). Large series suggest a risk of <0.5% with the SAPIEN valve and a somewhat lower risk with CoreValve (2,21). When coronary obstruction does occur successful management may require temporary cardiopulmonary support and revascularization (28). Factors that increase the risk of coronary obstruction include an unusually bulky native leaflet (adjacent to a coronary ostium), a low origin of the coronary ostium (often defined as <12 mm from the basal leaflet insertion as assessed by MDCT), a shallow sinus of Valsalva (offering less room for the native leaflet), an oversized prosthesis, and high implantation.

**Concomitant mitral regurgitation.** Mitral regurgitation is common in patients with aortic stenosis, increasing both TAVR and SAVR procedural risk. However, mitral regurgitation may be better tolerated following successful AVR by either modality (29,30). Furthermore mitral regurgitation may sometimes improve following AVR, particularly when regurgitation is functional. In the PARTNER 1B trial, 22% of patients had moderate or severe mitral regurgitation. Mitral regurgitation was a marker of higher TAVR procedural mortality, but also of greater procedural benefit in comparison to medical management. Similarly, in the PARTNER 1A study, 20% of patients had moderate or severe mitral regurgitation. Mitral regurgitation was a predictor of increased procedural mortality; however, this risk was less with TAVR than SAVR (24.2% vs. 35%) (3). A therapeutic strategy of replacing the aortic valve alone may be reasonable in some patients in whom the risk of double valve surgery might be prohibitive.

**The conduction system.** The atrioventricular conduction system passes superficially through the interventricular septum immediately below the aortic valve. Injury during valve implantation may result in partial or complete heart block. Risk factors include advanced age, right bundle branch block, atrioventricular delay, along with prosthesis oversizing and ventricular positioning.

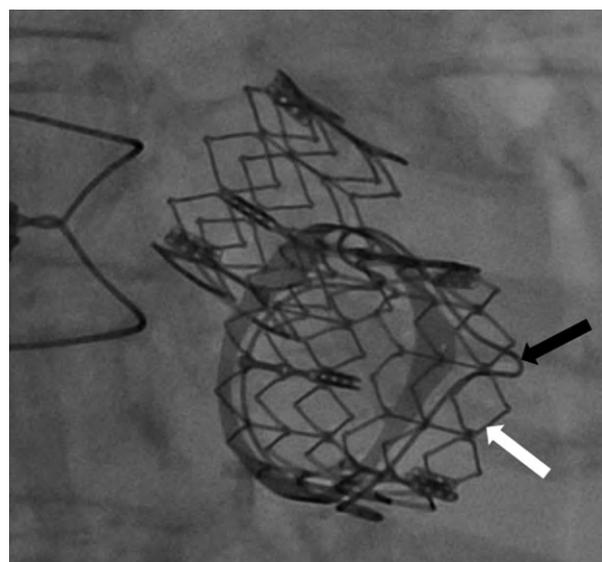
In the PARTNER randomized studies new pacemakers were no more frequent 1 year following SAPIEN valve implantation than with medical management (4.5% vs. 7.8%,  $p = 0.27$ ) or with SAVR (5.7% vs. 5.0%,  $p = 0.68$ ) (3,4). However, CoreValve implantation is more frequently associated early and late atrioventricular block, presumably due to greater extension into the left ventricular outflow tract with compression of the septal conduction tissues. The requirement for new pacemakers was 3-fold higher following CoreValve, as compared with SAPIEN, implantation in both the United Kingdom and French national registries (5,6). For this reason routine prophylactic temporary pacing leads are routinely used, with more prolonged electrocardiographic monitoring (31).

## Failed Surgical Prostheses

**Valve-in-valve.** Reoperation to replace failed surgical bioprostheses may be associated with significant risk. Experience with implantation of transcatheter valves within failed bioprostheses has been encouraging (Fig. 8). The rigid frame of most bioprostheses facilitates THV positioning and paravalvular sealing, while reducing the risk of atrioventricular block, annular rupture, and coronary obstruction. However, some surgical bioprostheses are radiolucent, stentless, or have externally mounted leaflets with the potential for coronary ostial obstruction if diseased bioprosthetic leaflets are in close proximity to the coronary ostia (32). Small-diameter surgical bioprostheses (particularly  $\leq 19$  mm) may not allow for optimal expansion of current transcatheter implants (32–35). Evidence that valve-in-valve implants are durable remains limited. However, early experience confirms that TAVR may be a repeatable therapeutic strategy with important implications (32,34).

## Future Directions

Currently, SAVR remains the standard of care for most patients with symptomatic severe aortic stenosis. However, transarterial AVR has arguably become the standard of care for patients for whom surgical risk is prohibitive and an increasingly reasonable alternative for selected operable patients in whom the high-risk of either mortality or morbidity is “high.” Broader application will require further



**Figure 8** Double Valve Replacement

A SAPIEN XT THV (Edwards Lifesciences, Irvine, California) was implanted inside a stenotic native aortic valve (top left). As a single stage procedure a second SAPIEN XT (Edwards Lifesciences) (open arrow) was implanted inside a severely regurgitant surgical mitral bioprostheses (valve-in-valve) (solid arrow). The patient remains well at 3-year follow up.

refinement as well as more rigorous and longer follow-up. It is possible that, with time, TAVR will become a preferred option for a much broader group of patients. A major concern may well be the following: When are patients too ill, frail, or old to gain significant benefit in terms of duration or quality of life?

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