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Current Clinical Evidence on Rapid Deployment Aortic Valve Replacement

Sutureless Aortic Bioprostheses

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Abstract: Aortic stenosis is the most common valvular heart disease in the Western world. It is caused primarily by age-related degeneration and progressive calcification typically detected in patients 65 years and older. In patients presenting with symptoms of heart failure, the average survival rate is only 2 years without appropriate treatment. Approximately one half of all patients die within the first 2 to 3 years of symptom onset. In addition, the age of the patients presenting for aortic valve replacement (AVR) is increased along with the demographic changes. The Society of Thoracic Surgeons (STS) database shows that the number of patients older than 80 years has increased from 12% to 24% during the past 20 years. At the same time, the percentage of candidates requiring AVR as well as concomitant coronary bypass surgery has increased from 5% to 25%. Surgical AVR continues to be the criterion standard for treatment of aortic stenosis, improving survival and quality of life. Recent advances in prosthetic valve technology, such as transcatheter AVR, have expanded the indication for AVR to the extreme high-risk population, and the most recent surgical innovation, rapid deployment AVR, provides an additional tool to the surgeons' armamentarium.

Key Words: Sutureless aortic valve, Aortic bioprostheses, Aortic stenosis, Rapid deployment aortic valve replacement.

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Aortic stenosis (AS) is the most common valvular heart disease in the Western world. It is caused primarily by age-related degeneration and progressive calcification typically detected in patients 65 years and older.[1] In patients presenting with symptoms of heart failure, the average survival rate is only 2 years without appropriate treatment. Approximately one half of all patients die within the first 2 to 3 years of symptom onset.[2] In addition, age of the patients presenting for aortic valve replacement (AVR) is increased along with the demographic changes. The Society of Thoracic Surgeons (STS) database shows that the number of patients older than 80 years has increased from 12% to 24% during the past 20 years. At the same time, the percentage of candidates requiring AVR as well as concomitant coronary bypass surgery has increased from 5% to 25%. Surgical AVR continues to be the criterion standard for treatment of AS, improving survival and quality of life. Recent advances in prosthetic valve technology, such as transcatheter AVR (TAVR), have expanded the indication for AVR to the extreme high-risk population, and the most recent surgical innovation, rapid deployment AVR (RDAVR), provides an additional tool to the surgeons' armamentarium. The term RDAVR as used in this review will refer to surgically implanted AVRs using novel fixation techniques with minimal or no use of traditional annular sutures.

The concept of RDAVR is not a new one. Soon after the first reported AVR in 1960, Dr George Magovern, professor of surgery at the University of Pittsburgh, and Harry Cromie, an engineer, in 1962 developed a prosthetic valve that would enable surgeons to perform a more rapid valve replacement.[3–5] The Magovern-Cromie caged ball valve featured a double-barbed anchoring ring with a snap-on mechanism that sandwiched the native annulus to facilitate sutureless valve anchoring. According to Dr Magovern, his motivation was to "simplify the method of fixation, lessen (cardiopulmonary) bypass time, and reduce thrombus formation." Modern rapid deployment valves have undergone considerable modifications with the advent of bovine pericardial surgical heart valves and balloon- and self-expandable transcatheter heart valves. Although percutaneous aortic valve implantation has been proposed as an alternative to surgical aortic valve implantation, this approach does not allow the treatment of combined pathologies of the aortic valve and

the coronary arteries. New rapid deployment valve prostheses have been introduced, keeping the advantages of the classical surgical valves while trying to reduce their disadvantage, namely, the necessity to anchor them with sutures. The advantages of RDAVR are as follows: (1) absence or reduction for the necessity of anchoring sutures, thereby reducing the cross-clamp times (XCTs) and consequently extracorporeal circulation times; (2) decalcification of the annulus as well as valve implantation under direct vision to minimize paravalvular leaks by proper fitting of the prosthesis into the annulus; and (3) the possibility of performing necessary concomitant procedures, such as coronary artery bypass grafting (CABG).[6] Regarding the first advantage, Ranucci et al[7] reported that the aortic XCT is an independent predictor of severe cardiovascular morbidity, with an increased risk of 1.4% per 1-minute increase. Therefore, RDAVR may be especially advantageous in combined cases because the total XCTs are potentially shorter because of the absence of sutures.

Currently, there are three different rapid deployment aortic valves commercially available in Europe: the EDWARDS INTUITY from Edwards Lifesciences Corp, Irvine, CA USA; 3F ENABLE* from Medtronic, Inc, Minneapolis, MN USA; and, Perceval S from Sorin, Milan, Italy. This review will focus on technical design and procedural considerations for each valve as well as summarize its early clinical experience. See Table 1 and Supplementary Table 2, http://links.lww.com/INNOV/A72, for reference.

**The 3F Enable is no longer commercially available but discussion of the valve's engineering and clinical outcomes remains key to the overall understanding of sutureless valve technology and is therefore included in this manuscript.*

EDWARDS INTUITY

Design and Implantation Technique

The EDWARDS INTUITY Elite is a trileaflet valve composed of bovine pericardium built on a balloon expandable stainless steel cloth-covered frame incorporated into the inflow aspect of the valve. It is built on the design platform of the Carpentier-Edwards PERIMOUNT Magna Ease aortic bioprosthesis and uses the same anticalcification technology (THERMAFIX), which has demonstrated long-term durability for up to 20 years.[8,9] INTUITY Elite received Conformite Européenne (CE) Mark in 2012 and is currently available in the European market. Available sizes are 19, 21, 23, 25, and 27 mm.

Conventional implantation starts with a hockey-stick aortotomy crossing the sinotubular junction, complete excision of the diseased leaflets, and standard debridement of calcified tissue. The valve is then positioned and secured with three equidistant simple sutures placed at the nadir of each coronary cusp. These sutures guide the placement of the INTUITY Elite valve frame into the native annulus. The scalloped sewing ring is designed to conform to the natural aortic annulus. The valve is deployed using a specialized delivery system, which facilitates balloon expansion of the cobalt chromium frame within the left ventricular outflow tract immediately subjacent to the native annulus. Thus, the sewing ring above the annulus and the cuffed frame below it function to sandwich the annulus, thereby stabilizing the INTUITY Elite valve. After the delivery system and valve are secured into the position, the three sutures are secured using Rumel tourniquets, and the balloon catheter is inflated to a pressure appropriate for the corresponding valve size (3.0–5.0 atm). The cloth skirt covering around the ventricular inlet of the frame

TABLE 1. Design Characteristics



	Edwards INTUITY	Sorin Perceval S	Medtronic 3F Enable
CE mark	2012	2011	2012
Available patient follow-up	3 y	5 y	5 y
Design platform	Bovine pericardium, trileaflet, balloon expandable, stainless steel cloth-covered frame	Bovine pericardium, trileaflet, self-expandable nitinol frame with additional proximal and distal rings for annulus fixation	Three equal sections of equine pericardial tissue forming tubular structure, self-expandable nitinol frame covered in polyester fabric, equally spaced commissural tabs reinforced with polyester material
Available sizes	19, 21, 23, 25, 27 mm	21, 23, 25 mm	19, 21, 23, 25, 27, 29 mm
Rinsing	2 times, 60 s each	Not required	3 times 120 s each
Sutures	3 actual sutures	None/only guiding sutures	0/1 actual suture
Collapsible	Crimped	Yes, with collapsing tool	Yes, manual folding

CE, Conformité Européenne.

promotes sealing between the aortic annulus and the frame preventing paravalvular leak, while promoting host tissue ingrowth. After frame is deployed, the delivery system and valve holder are removed as a single unit. Finally, the suture snares are removed, the three guiding sutures are tied, and the aortotomy is closed in the usual fashion. The system may be used in both traditional and less invasive surgical approaches for AVR.

Clinical Outcomes

The TRITON trial, a prospective, multicenter (six European), single-arm study investigated the safety and performance of the INTUITY and INTUITY Elite valve system in patients with severe AS who required elective AVR with or without concomitant CABG. One-year results of this study were reported in 2013 by Kocher et al.[10] The cohort included 146 patients who were operated on using a full sternotomy (70%) or a minimally invasive approach (30%). Baseline characteristics included a mean (SD) age of 75 (6.7) years; 52.7% female sex; logistic EuroSCORE of 7.9 (6.5); and 46.6% New York Heart Association (NYHA) class III or IV. Device technical success, defined as the successful delivery and deployment of the INTUITY valve within two attempts, was achieved in 96% of the patients.

Hemodynamic outcomes at 1 year compared favorably with those of the Carpentier-Edwards PERIMOUNT surgical heart valve, and both XCT and cardiopulmonary bypass time (CPBT) were significantly shortened.[11] Mean (SD) effective orifice area (EOA) and mean (SD) pressure gradient were 1.7 (0.2) cm^2 and 8.8 (3.0) mm Hg at 3 months, respectively, and, 1.7 (0.2) cm^2 and 8.4 (3.4) mm Hg at 1 year, respectively. Mean (SD) aortic XCTs were 41 (11) and 60 (19) minutes for isolated AVR and combined AVR + CABG, respectively. Cardiopulmonary bypass times were 66 (19) and 96 (30) minutes for isolated AVR and AVR + CABG, respectively. Compared with standard surgical heart valves, this represented a 45% reduction in XCT for isolated AVR and a 39% reduction for AVR + CABG.[12] Moreover, mean CPBT was reduced by 38% for isolated AVR and 29% for AVR + CABG.[12] Of note, new permanent pacemaker implantation (PPM) was required in 5.0% at 30 days and 0.8% at late follow-up. Most of these patients had preexisting conduction abnormalities.

Three-year hemodynamic and outcomes data from the TRITON trial were published by Haverich et al,[13] expanding on the original cohort of Kocher et al with 287 patients treated with the INTUITY valve. A minimally invasive approach was used in 55% of the patients in this study, compared with 30% in initial study. Device technical success was slightly improved at 97%. The next-generation device, INTUITY Elite, was used in 48% (138 of 287). The INTUITY Elite incorporates three small modifications designed to improve sizing, positioning, and deployment of the valve. The number of cloth layers on the balloon-expandable frame was reduced, and the cloth was moved closer to the ventricular inflow edge of the frame, reducing the tissue annulus diameter by 1.0 mm. Moreover, to reduce the implant profile, the single crimped cloth covering the expandable frame was modified to a double crimped frame. Finally, to promote visibility of the nadir suture markers, the valve holder was mounted to the cusp portion of the sewing ring instead of to the commissural posts.

Mean (SD) patient age was 75.7 (6.7) years, mean (SD) logistic EuroSCORE was 8.4 (6.7), NYHA class of 3 or higher was 53%, and 49.34 were female. Clinical outcomes showed low mean transvalvular gradients, significant left ventricular (LV) regression, and excellent safety outcomes. At 3 months, 1 year, and 3 years, the mean (SD) transvalvular gradient was 9.0 (3.4), 9.0 (3.6), and 8.7 (4.1) mm Hg, respectively, significantly lower than at discharge ($P < 0.0001$ for discharge vs 3 months and 1 year, $P = 0.0031$ for discharge vs 3 years). Significant LV mass regression was observed compared with discharge versus 3 months, 1 year, and 3 years at 196.6 (49.8), 184.3 (47.7), and 178.5 (42.8) g, respectively. The LV mass index at 3 years decreased by 16% compared with that at discharge ($P < 0.001$). All-cause mortality at 30 days was 1.7%, and no cases of valve-related mortality were reported. Late all-cause mortality was 3.7%, with two deaths adjudicated as valve related.

Schlömicher et al[14] studied RDAVR using the EDWARDS INTUITY valve exclusively with the minimally invasive approach. Sixty patients underwent minimally invasive AVR through an upper hemisternotomy. Baseline characteristics included a mean (SD) age of 75.5 (6.2) years, mean (SD) logistic EuroSCORE of 8.4% (4.2%), NYHA class III or IV in 75%, and female sex in 39%. Mean (SD) XCT was 26 (7) minutes, which compared favorably to the surgical literature.[14] The rate of new PPM was low in this series, with only one patient (1.7%) requiring pacing in the early period and none at late follow-up. Overall, device technical success was 98%, with only one patient requiring conversion to a standard surgical valve secondary to a significant paravalvular leak. At discharge, the mean (SD) EOA was 1.8 (0.3) cm^2, which remained unchanged at 12 months. The mean (SD) transvalvular gradient was 11.7 (4.3) mm Hg at discharge and 10.3 (3.8) mm Hg at 12 months, both comparable with conventional surgical valve outcomes.[11,15] All-cause and valve-related 30-day mortality were 1.7% (1 of 60) and 1.7% (1 of 60), respectively, and all-cause and valve-related late mortality were 5.1% (3 of 59) and 3.4% (2 of 59), respectively.

The CADENCE MIS clinical trial was a multicenter (five sites), randomized controlled trial comparing minimally invasive RDAVR (MIS-RDAVR) through an upper hemisternotomy, using the Edwards INTUITY valve, to a full sternotomy with a conventional surgical valve (FS-AVR).[16] The study included 94 patients, MIS-RDAVR in 46 and FS-AVR in 48. Mean age was similar in both groups at 73 to 74 years. Female patients comprised 41% of the MIS-RDAVR group and 56% of the FS-AVR group; NYHA class III or IV was present in 67% of the MIS-RDAVR group and 60% of the FS-AVR group. Device technical success was achieved in 94% of the MIS-RDAVR group, with three operative conversions to a conventional valve because of sizing issues in two patients and one experiencing an aortic annular tear.

Mean (SD) aortic XCT for MIS-RDAVR was similar to that reported in TRITON[10] at 41.3 (20.3) minutes. The mortality and stroke rate was slightly higher and the device technical success rate was lower than those reported in TRITON. However, in comparison with the full-sternotomy group, the MIS-RDAVR group had a significantly shorter mean XCT and better valve hemodynamic performance. Indeed, the mean reduction in XCT was 12.7 minutes. Patients undergoing RDAVR had a significantly lower mean transvalvular gradient (8.5 vs 10.3 mm Hg,

$P < 0.044$) and a lower prevalence of patient-prosthesis mismatch (0% vs 15.0%, $P < 0.013$) 3 months postoperatively compared with the FS-AVR patients.

Functional improvement in NYHA class was observed as early as 30 days and continued through the 3-month follow-up for both groups. By 3 months, 83% of the MIS-RDAVR group experienced improvement by at least one NYHA class, compared with 73% of the FS-AVR group. Quality of life measures, using EQ-5D, remained constant and were similar for both groups from discharge to 3 months postoperatively. In summary, RDAVR by the MIS approach was associated with significantly reduced myocardial ischemic time and better valvular hemodynamic function than FS-AVR with a conventional stented bioprosthesis. The authors concluded that rapid deployment valves may facilitate the performance of minimally invasive AVR.

PERCEVAL S

Design and Implantation Technique

The Perceval S bioprosthesis is a trileaflet bovine pericardial valve mounted on a self-expandable nitinol frame. Two ring segments, on the proximal and distal ends of the valve, are held together by connecting elements that support the valve and allow the prosthesis to anchor within the sinuses of Valsalva. The proximal (ventricular) ring has three loops through which temporary guiding sutures are passed. Perceval S currently is available in four sizes—21, 23, 25, and 27 mm—for aortic annuli ranging between 19 and 24 mm. A transverse aortotomy is performed in a site distal to the sinotubular junction, thereby preserving an intact segment of ascending aorta cephalad to the device. Complete decalcification of the aortic annulus is not necessary, although a smooth annular profile is recommended to reduce the risk of paravalvular leak. The three guide sutures are used to accurately align the ventricular aspect of the Perceval S within the surgical annulus. These sutures are placed 2 mm below the nadir of the aortic annulus within the left ventricular outflow tract and then passed through the corresponding loops on the inflow ring.

The design of the delivery system allows the Perceval S to be compressed by means of a proprietary collapsing process before implantation. After the valve is loaded onto the delivery device, it is parachuted along the three guiding sutures to a subannular position. Once positioned, the Perceval S is released from the holder, and balloon dilatation is performed at 4 atm of pressure for 30 seconds. The guide sutures are then removed. The valve is bathed continuously with sterile water at 37°C to achieve full expansion and fixation of the nitinol stent against the intra-aortic wall.

Clinical Outcomes

Premarket assessment for the Perceval S was initiated in a pilot study, which assessed safety in 30 patients with symptomatic severe AS, 75 years or older. The feasibility study then was followed by a pivotal trial in 150 high-risk patients, evaluating the hemodynamic performance of the Perceval S at 3 to 6 months after implantation. Finally, the CAVALIER Trial was conducted, which was designed to evaluate the safety and effectiveness of Perceval S at 12 months in patients 65 years or older. Based on these favorable early clinical experiences, the Perceval S received CE mark in 2011.

Rubino et al[17] reported early- and intermediate-term clinical results on 314 patients at five European centers, who underwent AVR using the Perceval S rapid deployment valve with or without concomitant CABG. The patients underwent operation using either a full sternotomy (55.4%) or minimal access (44.5%) approaches. Mean (SD) age was 77.9 (5.0) years, 60.2% of the patients were female, mean (SD) log EuroSCORE II was 9.0% (7.6%), and the prevalence of NYHA functional class III or IV was 16%. Of note, device technical success was achieved in nearly all patients (99.7%).

With the Perceval S, the mean (SD) XCT for isolated AVR was 39 (15) minutes, and the mean (SD) CPBT was 66 (23) minutes, irrespective of surgical approach. Twenty-nine percent of the operations saw XCTs less than 30 minutes, whereas 42% had CPBTs less than 1 hour. Full sternotomy was associated with a shorter mean XCT compared with upper hemisternotomy [35 (16.3) vs 41 (14.3) minutes], with a comparable risk-adjusted mortality rate ($P = 0.92$; odds ratio, 0.89; 95% confidence interval, 0.06–12.34). These early outcomes were similar to those reported for INTUITY and compared favorably to procedure times for surgical AVR for Mitroflow, Epic, and Magna.[12,18,19] However, the rate of new PPM was high at 8% (25 of 313). Stroke was observed in 1.9% (6 of 313), and 1.6% required new postoperative hemodialysis (5 of 313). Reoperation for bleeding was performed in 2.5% of the patients (8 of 313). Paravalvular leak was detected in 12.7% (40 of 313); two were classified as severe (0.6%), and the remainder was mild (12.1%). Mean (SD) hospital length of stay was 13.4 (6.5) days, and in-hospital mortality was 3.2% (10 of 313), which is favorable to conventional AVR, as was shown in a recent meta-analysis where operative mortality was reported at 3.3% for isolated AVR and 5.5% for concomitant CABG.[20]

A clinical series with longer-term follow-up was published by Folliguet et al,[21] with 4-year clinical outcomes of their prospective multicenter, single-arm cohort of 208 high-risk patients undergoing AVR with the Perceval S, with or without concomitant procedures. At baseline, the mean (SD) age was 79 (5.3) years, 67.7% were female, and all patients were in NYHA functional class III/IV. Mean (SD) log EuroSCORE was 8.7% (5.3%). Significant hemodynamic and functional status improvement was observed from the early postoperative period through up to 4 years of follow-up. Full sternotomy and minimal access approaches were used in 80% and 20%, respectively. Device technical success was achieved in 95.6% of the patients.

Preoperative and postoperative mean (SD) transvalvular gradients were 48.6 (18.6) and 8.7 (3.7) mm Hg, respectively, and mean (SD) EOAs were 0.7 (0.2) and 1.4 (0.4) cm^2, respectively. A significant improvement in the functional capacity of most patients undergoing AVR was observed, with 82% of the patients in NYHA functional class I or II at 1 and 2 years of follow-up. New PPM was required in 8% of the patients (16 of 208), which was comparable with the findings of Rubino et al.[17] Mean (SD) XCT was relatively short at 30.1 (12.2) minutes, and mean (SD) CPBT was 50.3 (22.8) minutes, for both full sternotomy and minimal access isolated AVR procedures. Twenty-two patients (10.5%) required reoperation,

11 for bleeding, 9 because of paravalvular leak (PVL), and 1 each for prosthetic valve endocarditis and nonstructural valve dysfunction (pannus in-growth with leaflet restriction). Ten thromboembolic events were reported, including two strokes (1%), one transient ischemic attack, and six systemic embolic events. Hospital mortality rate was 2.4% (5 of 208), consistent with that in Rubino et al.[17]

In a multicenter study from Canada, Mazine et al[22] reported on 215 patients across six hospitals, who received Perceval S with or without concomitant operations. Full sternotomy was used in 80%, and a minimal access incision in 20%. Fifty-six percent of the subjects were in NYHA function class III or IV, and the mean (SD) logistic EuroSCORE was 7.2% (8.4%). Mean (SD) age was 78.9 (5.9), and 54% were female. Of note, technical success was achieved in 100% of the patients.

Mean (SD) aortic XCT for isolated AVR was 40.5 (11.6) minutes, with a mean (SD) CPBT of 56.6 (16.6) minutes. Baseline mean (SD) transvalvular pressure gradient was 47.3 (18.9) mm Hg, which improved significantly to 13.3 (6.4) mm Hg at hospital discharge. Mean (SD) EOA improved from 0.78 (0.25) cm^2 at baseline to 1.56 (0.37) cm^2 postoperatively. New PPM was required in 17% of the patients (37 of 215), with 18 reporting a history of preoperative conduction disturbances. The need for pacemaker implantation was associated with prosthetic valve size, with 9%, 12%, 24% and 50% implants occurring with the small, medium, large, and extra large prosthesis, respectively ($P = 0.02$). Stroke was reported in 3.3% (7 of 215), with full recovery in three and residual hemiparesis in four. Acute kidney injury was reported in 19.5% of the patients (42 of 215); all were reported to have chronic kidney disease at baseline. Reoperation for bleeding occurred in 4.6% of the patients (10 of 215). Significantly, there were no reported cases of postoperative paravalvular leak.

To date, the largest series of patients receiving the Perceval S valve was reported by Shrestha et al.[23] Seven hundred thirty-one patients underwent AVR with or without concomitant procedures through full sternotomy (74%) or minimal access (26%) approaches. Baseline characteristics included a mean (SD) age of 78.5 (5.3) years, 32% were female, with NYHA functional class was III or IV in 75%, and a mean (SD) logistic EuroSCORE of 10.9% (8.2%). Device technical success was achieved in 95.6% of the patients. Mean (SD) XCT and CPBT for isolated AVR were 33.3 (11.7) minutes and 55.8 (20.5) minutes, respectively. For minimal access operations, the mean (SD) XCT was 37.6 (12) minutes. Valve hemodynamics improved in most patients, with a mean transvalvular gradient of 10.3 mm Hg at discharge, which remained stable at 2-, 3-, and 4-year follow-up. Mean EOA was 1.5 cm^2 at 3- to 6-month follow-up and remained unchanged at 12 months. New PPM was required in 6% of the subjects. Stroke was observed in 1.6% of the patients (12 of 731). Paravalvular leak was reported as moderate or severe in 1.4% (10 of 731). The early all-cause mortality rate was 3.4%, and the cardiac mortality rate was 1.9%. At 5 years, nonstructural valve dysfunction was reported in 3.6% of the patients (26 of 731), and no case of structural valve deterioration was observed. The 5-year mortality rate was 10.4% (76 of 731). In summary, this intermediate-term study demonstrated a reduction in mean XCT for both full sternotomy and minimal access approaches, with clinical outcomes similar to those observed in conventional AVR, thus confirming the safety and efficacy of Perceval S.[24,25]

In a large single-center report on minimal access AVR (exclusively right anterior thoracotomy) comparing Perceval S and conventional aortic valves, Gilmanov et al[26] reported their series of 515 patients. Propensity matching was used, and 133 pairs of patients were analyzed. Baseline characteristics demonstrated comparability between groups, with mean age of 74 years (control) and 75 years (Perceval S); female sex at 43% (control) and 44% (Perceval S); logistic EuroSCORE I of 5.5% (control) and 5.8% (Perceval S); and NYHA functional class III or IV of 30% (control) and 29% (Perceval S).

Mean XCT and CPBT were significantly shorter with Perceval S [XCT, 88 (control) vs 56 minutes (Perceval S); CPBT, 120 (control) vs 90 minutes (Perceval S)]. However, this did not translate into differences in clinical outcomes with regard to mortality, stroke, and new PPM. This may be ascribed to the small number of reported adverse events. Finally, no significant difference was observed in hemodynamic performance between the Perceval S rapid deployment valve and conventional valves. The authors concluded that rapid deployment valve technology facilitates minimal access AVR and might offer better midterm survival in elderly patients.

Although TAVR has offered new therapeutic possibilities in patients who are at prohibitive or extreme high risk for conventional AVR, it is associated with significant complications, including paravalvular leak and severe conduction disturbances. To address a rather provocative question, Biancari et al[27] compared the early outcomes of TAVR with those of RDAVR, using the Perceval S, in a propensity-matched series of patients. In this retrospective multicenter analysis of 773 patients, of whom 394 underwent TAVR and 379 underwent surgical AVR with Perceval S, propensity matching generated 144 pairs with similar baseline characteristics and risk profiles. Mean age was similar for both groups at 79 years. Perceval S was implanted using minimal access techniques in 54%, whereas the transfemoral approach was used in all TAVR subjects. Rates of PVL and new PPM favored Perceval S over TAVR (0.3% vs 14.1% and 9.8% vs 17.3%, respectively). Furthermore, hospital mortality favored Perceval S over TAVR (2.6% vs 5.3%, respectively). The authors concluded that Perceval S was a reasonable alternative to TAVR in patients at intermediate risk for surgical AVR.

3F ENABLE

Design and Implantation Technique

The 3F Enable is composed of three symmetric, independent equine pericardial leaflets attached to a self-expanding nitinol frame, which is covered at its ventricular inflow aspect by polyester fabric. The leaflets interlock at three equally spaced commissural tabs, which are reinforced with polyester material, to form a tubular structure. The original 3F Enable valve received CE mark in 2010, but it has since been redesigned to enhance visualization, facilitate radial crimping, and improve positionability by enlarging the inflow skirt. Currently, it is available in sizes 19, 21, 23, 25, 27, and 29 mm.

Because of the considerable height of the 3F Enable device, it is recommended that a transverse aortotomy be placed at least 3.5 cm above the ostium of the right coronary artery. Before implantation, the diseased native leaflets are excised, and the annulus is debrided of calcified tissue. Proper sizing is important because the prosthesis is fixed by radial forces at the level of the annulus only and leaflet mobility is determined by the dimension of the deployed nitinol frame. After rinsing the valve is submerged in ice cold water three times for 30 seconds each. A double-armed 4-0 polypropylene suture is placed into the nadir of the noncoronary sinus and the corresponding site on the upper flange of the sewing ring. With the use of this suture, the valve is guided down into the annulus. Rinsing the valve in situ expands the nitinol stent and brings the commissural tabs into close proximity with the aortic wall.

Early experience was reported by Martens et al[28] based on a prospective, multicenter, single-arm trial designed to evaluate 3F Enable's safety and efficacy. In a cohort of 140 patients, the mean (SD) age was 76 (6) years, 62% were female, and 63% were in NYHA functional class III or IV. The surgical approach was through a full sternotomy in 80% and minimal access in 20%. Isolated AVR was performed in 70% of cases and concomitant procedures in 30%. Device technical success was achieved in 85.6% of the patients, a rate ostensibly lower than either INTUITY or Perceval S.

The mean (SD) XCT and CPBT were 57.9 (25.1) and 84.6 (34.2) minutes, respectively, which compared unfavorably to the early experience reported for EDWARDS INTUITY and Perceval S.[10,17] However, two of the centers reported mean (SD) XCT and CPBT of only 36.8 (7.7) and 54.8 (11.5) minutes, respectively, for isolated AVR. The authors attributed this to learning curve. Mean (SD) pressure gradient and EOA were 10.2 (4.2) mm Hg and 1.7 (0.5) cm^2, respectively, at 12 months. Major PVL was detected in 2.1% (3 of 140), and the early mortality rate was 3.6% (5 of 140).

Long-term clinical outcomes of the 3F Enable were published by Englberger et al.[29] From a technical perspective, 85% of 3F Enable valves required only one suture, and 12% required none. At 5 years, the mean (SD) pressure gradient and EOA was 7.4 (3.4) mm Hg and 1.6 (0.2) cm^2, respectively. Freedom from all-cause and valve-related mortality at 1 year and 5 years were 88% (3%) and 97% (2%) (n = 113) at 1 year, respectively, and 77 (8%) and 94 (5%) at 5 years (n = 24), respectively. This compared favorably to Perceval S at 4 years.[21] Structural valve deterioration was not observed in this series. However, the rate of paravalvular leak for 3F Enable was high at 10%, particularly in comparison with Perceval S (1.4%).[22] However, both of these studies had relatively few patients followed up for 5 years (Perceval, 30 patients; 3F Enable, 24 patients), and longer follow-up is needed to substantiate any claims of durability or freedom from adverse events.[23,29]

DISCUSSION

Aortic valve replacement has been widely accepted as the criterion standard for the treatment of patients with aortic valve stenosis. Since 1960, the basic surgical technique has not changed. The diseased aortic valve is replaced with a prosthetic valve (either mechanical or biological) under direct surgical vision via extracorporeal circulation and cardioplegic cardiac arrest. Although various valve prostheses designs have been proposed and introduced into the market, in all cases, the valve prosthesis is anchored within the aortic annulus by multiple sutures. Until recently, options for AVR were limited to conventionally sewn mechanical and tissue prostheses. During the last two decades, important refinements have been made for both types. Mechanical valve design has been modified to reduce turbulence, which may ameliorate the inherent risk of thrombogenicity.[30] Newer bioprosthetic valve designs achieve a larger EOA, thereby reducing the risk of severe prosthesis-patient mismatch.[15] Moreover, our understanding of the fundamental mechanisms of structural valve deterioration has continued to advance, and next-generation anticalcification treatments have been developed, which may further extend the durability of tissue valves.[31] Progress in this area may promote the feasibility of tissue valves in younger patients and in other subgroups at high risk for valve failure (eg, end-stage renal disease).

Although important refinements in valve design have been made, the basic technique of surgical valve implantation, with suture fixation to the aortic annulus, has not significantly changed since its inception in the early 1960s. The early 2000s saw several new options for patients needing AVR. Transcatheter AVR has permanently altered the landscape for patients with symptomatic, severe AS at prohibitive or extreme high risk for surgery. Recently presented outcomes of the Sapien 3 TAVR system in high-risk patients (mean STS PROM, 8.6%; mean age, 82.6 years) demonstrated a 30-day mortality rate of 2.2%; stroke, 1.5%; major vascular complications, 5.0%; and major bleeding, 6.3%. Furthermore, the median hospital length of stay was only 5 days (range, 1–33 days).[32] The clinical success of percutaneous AVR has impelled surgeons and their partners in industry to rethink implantation and deployment techniques, particularly with the goal of facilitating minimal access approaches. Such creative dialectic eventually led to appropriate scrutiny of the need for 12 to 14 sutures to achieve a secure valve implant. Indeed, benefits that might accrue from simplifying the suture technique or eliminating sutures altogether may include (1) shortening the time to implant, thereby reducing the duration of myocardial ischemia; (2) optimizing the EOA by either eliminating the purse-string effect invariably associated with circumferential sutures or reshaping the left ventricular outflow tract to optimize flow characteristics through the bioprosthesis; and (3) facilitating minimal access approaches to achieve putative benefits of less blood loss, shorter hospital stay, faster recovery, and enhanced cosmesis.[33] Appropriate concerns for widespread adoption of RDAVR are the possible increase in paravalvular leak and need for pacemaker insertion due to the fixation technique used; this would negatively impact long-term survival in this patient population. Kodali et al[34] have demonstrated this as a concern in the Partner trial data with only a mild paravalvular leak resulting in an increased mortality early on after TAVR.

All three rapid deployment valves currently available for clinical use in Europe have distinct advantages and disadvantages. The 3F Enable and Perceval S valves essentially require no permanent sutures and, therefore, are truly "sutureless" as opposed to the INTUITY valve, which uses three guiding

sutures to ensure accurate and stable valve positioning. The 3F Enable and Perceval S valves both have novel nitinol self-expanding frames, whereas the INTUITY valve is composed of a standard Carpentier-Edwards PERIMOUNT (CEP) Magna Ease aortic bioprosthetic valve mounted on a balloon-expandable stent. In the latter case, the pericardial valve tissue is neither compressed nor traumatized. The manufacturing considerations for these valves are unique to each model and deserve comment. The INTUITY valve is made of bovine pericardium and undergoes the same tissue fixation and anticalcification treatment as the PERIMOUNT Magna Ease valve that currently is in widespread clinical use. Excellent long-term durability of PERIMOUNT valves have been reported in three recently published studies.[8,9,35] In contrast, long-term durability is uncertain for either equine (3F Enable) or bovine (Perceval S) pericardial tissue mounted on a nitinol frame. Because a central tenet when choosing the appropriate bioprosthetic valve for a patient is the freedom from valve explantation for structural valve deterioration, the long-term performance of equine and bovine pericardial valves mounted on a nitinol frame must be carefully scrutinized and proven to have equivalent or superior clinical outcomes compared with conventional stented surgical bovine pericardial valves. Obviously, this may require many years of long-term clinical follow-up; however, unlike the current target population for TAVR—prohibitive and extreme high-risk patients with few treatment options—most patients undergoing RDAVR are, in fact, suitable candidates for AVR using a standard commercially available bioprosthesis. Accordingly, long-term valve durability should not be compromised in these patients for the putative advantage of lessening the aortic XCT. This point cannot be overemphasized as better clinical outcomes are reported with percutaneous AVR and its use becomes expanded into lower risk and younger patient populations, where long-term valve durability eventually may be the only remaining advantage for conventional isolated AVR.

The growing adoption of percutaneous AVR likely will compel more surgeons to explore minimal access approaches for isolated AVR, if it is not currently part of their surgical toolbox. However, before rapid deployment heart valves can be widely endorsed, specific safety concerns that have been reported more frequently in this category of valves, such as paravalvular leak and severe electrical conduction abnormalities, must be addressed through refined patient selection, enhanced procedural management, and technological improvements in valve design. Importantly, the learning curve for rapid deployment heart valves cannot be discounted, which highlights the importance of device-specific training, whether sponsored by industry or by the professional societies. The need for systematic education and training is particularly urgent for the large cadre of surgeons who are naive to both minimal access incisions and rapid deployment heart valves yet wish to learn how to incorporate both into their practice. Finally, although the early clinical outcomes seem satisfactory and comparable with conventional heart valves, the important issue of long-term valve durability remains unanswered. Accordingly, patients who have received rapid deployment heart valves should be assiduously followed up, with a low threshold for obtaining a transthoracic echocardiogram whenever clinical suspicion is raised. In expert hands, conventional and minimal access AVR is associated with low risk and outstanding long-term results that were unheard of even a decade ago. The transition from conventional surgical AVR to rapid deployment AVR by our specialty must be performed in a deliberate and methodical fashion so that the benefits accrued during the last 55 years will not be squandered.

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